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Assessment of the health risks for professionals exposed to atypical working hours, especially night work

ANSES opinion
Collective expert report

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Request No 2011-SA-0088

The Deputy Director General

Maisons-Alfort, 18 May 2016

OPINION
of the French Agency for Food, Environmental and Occupational Health & Safety

on the "Assessment of the health risks associated with night work"

ANSES undertakes independent and pluralistic scientific expert assessments.
ANSES's public health mission involves ensuring environmental, occupational and food safety as well as assessing the potential health risks they may entail.
It also contributes to the protection of the health and welfare of animals, the protection of plant health and the evaluation of the nutritional characteristics of food.

It provides the competent authorities with the necessary information concerning these risks as well as the requisite expertise and technical support for drafting legislative and statutory provisions and implementing risk management strategies (Article L.1313-1 of the French Public Health Code).

Its opinions are made public.
This opinion is a translation of the original French version. In the event of any discrepancy or ambiguity the French language text dated..... shall prevail.

On 22 March 2011, ANSES received a formal request from the French Confederation of Christian Workers (CFTC) to undertake the following expert appraisal: "Assessment of the health risks for professionals exposed to atypical working hours, especially at night".

1. BACKGROUND AND PURPOSE OF THE REQUEST

The request for an assessment of the risks for professionals exposed to atypical working hours comes within a specific socio-economic and scientific context: the way in which work is organised is changing, leading today to an enormous number of workers being concerned by so-called "atypical" working hours and rhythms.

The expression "atypical hours" applies to all working time arrangements situated outside the framework of the "standard" week[1]. The best known forms of atypical hours are shift work[2], night work and weekend work. Atypical hours also include non-contiguous working hours, compressed work schedules and working hours that can change from day to day.

The adoption of the proposed law on professional equality of men and women in 2001 removed the legal ban on women working at night, mainly to bring French law into compliance with European law and transpose European Directive 93/104/EC concerning certain aspects of the organisation of working time.

[1] Working hours between 5am and 11pm, 5 days a week, at a rate of 8 hours daily.

[2] Shift work (i.e. work in successive teams) concerns employees forming different teams that take over from each other on a given workstation without ever overlapping. This way of organising working time is intended to ensure continuity on a given workstation.

The number of night workers has almost doubled in twenty years, as can be seen in the latest study by the Directorate for Research, Studies and Statistics (DARES) of the French Ministry of Labour, published in August 2014.

Night work is accompanied by a desynchronisation of biological, social and family rhythms, which can then have an impact on the state of health.

The International Agency for Research on Cancer (IARC) studied the impact of this organisation of work on the risk of cancer, leading it to add shift work that disrupts circadian rhythms to the list of agents that are "probably carcinogenic" (Group 2A) in 2007.

In France in 2012, the French National Authority for Health (HAS) published recommendations on good practices for monitoring shift and/or night workers.

The health effects associated with atypical working hours constitute a complex field of study that requires the application of a wide variety of scientific disciplines. Many effects are mentioned in the literature and mainly concern:

- sleep disorders and reduced alertness;
- gastro-intestinal diseases;
- the occurrence of accidents;
- fertility, reproduction and pregnancy;
- cancer (especially breast cancer in women);
- metabolic disorders and cardiovascular diseases.

In this context, on 22 March 2011, ANSES received a formal request from the French Confederation of Christian Workers (CFTC) to conduct an assessment of the health risks for professionals exposed to atypical working hours, especially those subject to night work, whether or not this is regular. In its request, the CFTC asked whether the conclusions issued by the IARC in 2007 could be broadened to all workers subjected to atypical hours.
Taking into account, on the one hand, the magnitude and complexity of the issue, but also, on the other hand, the existence of new scientific data published since the IARC monograph was issued in 2010, in particular concerning the effects of light on circadian rhythms, ANSES then proposed answering the question in two steps:

- initially, by carrying out an update of the expert appraisal relative to the health risks to which professionals are exposed when working night hours[3];
- subsequently, by studying specifically, according to the data available, the health effects potentially associated with other forms of atypical working hours.

2. ORGANISATION OF THE EXPERT APPRAISAL

ANSES entrusted the expert appraisal to the working group on "Assessment of the health risks for professionals exposed to atypical working hours, especially night work", under the auspices of the Expert Committee (CES) on "Physical agents, new technologies and development areas".

The working group was set up on 8 August 2012. It met 27 times in plenary sessions between 14 November 2012 and 26 January 2016.

The collective expert appraisal was mainly based on a critical analysis and summary of the data published in the literature (scientific articles, reports, etc.). The working group studied the health effects, as well as the socio-economic aspects associated with night work. The risk assessment method applied by the Working Group was based on the following main steps:

- a literature search;

[3] Night work is defined by Article L.3122-29 of the French Labour Code as "any work performed between 9pm and 6am".

- prioritisation of health effects;
- analysis of the publications identified;
- assessment of the evidence for each effect studied.

The Working Group also interviewed external experts (a total of nine hearings including three with stakeholders) likely to provide useful information and additional data for the expert appraisal.

An international consultation was organised with national agencies and authorities in the areas of health and/or occupational safety, in Europe and in North America, in order to identify studies conducted abroad on the theme of night work and find out which particular health effects were studied.

Lastly, a Research and Development Agreement (CRD) was established between ANSES and the French National Institute for Health and Medical Research (INSERM), with the aim of exploiting field data from the national survey on "Medical surveillance of exposure to occupational hazards" (Sumer, 2010).

The methodological and scientific aspects of this group's work were regularly submitted to the CES. The report produced by the working group takes account of the observations and additional information provided by the CES members. This expert appraisal was therefore conducted by a group of experts with complementary skills. It was carried out in accordance with the French Standard NF X 50-110 "Quality in Expertise Activities".

ANSES analyses the links of interest declared by the experts prior to their appointment and throughout the work, in order to avoid potential conflicts of interest with regard to the matters dealt with as part of the expert appraisal.

The experts' declarations of interests are made public via the ANSES website (www.anses.fr).

The Expert Committee on "Physical agents, new technologies and development areas" adopted the collective expert appraisal work along with its conclusions and recommendations as described in this collective expert appraisal summary, at its meeting of 15 March 2016. One of its members abstained from the vote on the validation of the collective expert appraisal summary, referring, apart from their substantive agreement, to reservations on the editorial form.

3. ANALYSIS AND CONCLUSIONS OF THE CES

The reality of night and/or shift work in France

An analysis conducted by the DARES[4] based on data from the "Working conditions" survey of 2012 revealed that 15.4% of employees (21.5% of men and 9.3% of women), or 3.5 million people, worked at night, regularly or occasionally. These figures are on an upward trend, with the increase being particularly sharp for women. Night work is most widespread in the tertiary sector, and concerns 30% of public-sector employees and 42% in private services companies. Drivers of vehicles, police and military personnel, nurses, care assistants and skilled workers in processing and/or assembly industries are the professional categories most concerned by night work. Temporary workers, men in their thirties and women under 30 years of age are the groups most frequently working at night.
Again according to the "Working conditions" survey of 2012, employees who work at night have higher remuneration but markedly more difficult working conditions than other employees: they are subjected to more numerous physical hardship factors, greater time pressure (hours, rhythm constraints, deadlines, *etc.*), and more frequent tensions with their colleagues or the public.

A clear regulatory framework for night work

[4] Source DARES, Analyses, Le travail de nuit en 2012 [Analyses, Night Work in 2012] No. 062, August 2014

French legislation (Article L. 3122-29 of the Labour Code) defines *night work* as *"any work performed between 9pm and 6am".* It also defines a *night worker* as any worker who performs a fraction of their working time between 9pm and 6am: at least 3 hours twice a week, or at least 270 hours over twelve consecutive months[5]. These definitions may be modified within certain limits by collective agreement or extended agreement. This strict regulatory framework is modulated by numerous waivers, depending on the sectors and professions concerned.

According to Article L. 3122-32 of the French Labour Code, the use of night work must remain exceptional and take into account the requirements to protect the health and safety of workers. It must also be justified by the need to ensure the continuity of economic activity or services of social value.

The status of night worker includes compensatory measures (for example in terms of rest and salary), as well as provisions designed to protect employee health, mainly by limiting the maximum duration of the work, although these provisions are modulated by numerous waivers. In addition, a series of specific measures have been adopted, aimed at preventing health risks for pregnant women when they perform night work.

Shift work is not defined in the French Labour Code; it is therefore far less regulated. The provisions specific to shift work are, for the most part, laid down in collective professional agreements and collective branch agreements.

Socio-economic aspects of night work

Night work may be introduced to ensure the continuity of services of social value, such as health services and on-call police officers or other surveillance services, or it may be a work organisation method, for example for a company that wishes to maximise the profitability of its equipment by getting machines and people to work around the clock.

The social cost of night and/or shift work is not limited to the health care provided to employees but should also take into account the cost of the impact on family life, costs induced by transport, and absenteeism. This social cost of night and/or shift work is however very difficult to assess, because there are very few statistics associating the medical and social consequences with the working hours.

While the health effects of atypical hours, and in particular night work and shift work, have been documented in the scientific literature, the same is not true for the record of the employees' life outside work. Indeed, although since the 1980s some researchers have been warning of the need to begin examining this field of research, few scientific studies have focused on the impact of these hours on family and social life. Life outside work is undeniably linked to health as defined by the WHO, i.e. physical, mental, psychological and social[6].

[5] Art. R. 3122-8 of the French Labour Code

[6] According to the World Health Organisation (WHO), "Health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity".

Concerning the effect of night and shift work on social life

Shift or night work creates a limitation on social life because of the time mismatch between the shift worker's rhythm of life and that of society as a whole. It is therefore not so much a lack of free time that causes difficulty but its position on the nychthemeron[7]. This is manifested by: difficulties in organising social encounters resulting in a tendency to spend more time with colleagues with a similar rhythm of life, difficulty accessing social activities in a structured framework (cultural, sports, associations) due to their strong rooting in a rigid and socially predetermined time period, and a tendency to opt for more individual and flexible leisure activities requiring no synchronisation with others. The diversity of shift work situations, organisational specifics, the variety of social contexts, the weight of individual characteristics, all constitute key factors that determine how people go about their lives outside the workplace.

Concerning the effect of night and shift work on family life

Depending on how it is organised, shift work may, for couples, result in limited time for meeting and sharing, changes to marital relations and sex life, and the emergence of imbalances in the functioning of the family that are felt more acutely by their spouses than by the employees themselves. In the long term, these difficulties can also be manifested by psychological disorders associated with guilt and frustration, the recurrence of inter-marital tensions and changes in the state of health. Some research relating to the impact of shift work on relations between shift workers and their children shows a decrease in the frequency and duration of family interactions and in the perceived quality of parenthood, as well as a deterioration in the nature and quality of parental functions. However, the effects of night work on the socio-familial environment are not universal and their assessment therefore requires the employment conditions of the households and the economic and cultural context of the country to be taken into consideration.

Health effects of night work

1. <u>Effect on the quantity and quality of sleep</u>

The difficulties experienced by night workers in falling asleep after a period of work at irregular hours are easily understandable and often recognised by all the parties in the world of work. Night work is accompanied by a need for the reorganisation of biological rhythms, of which sleep is the most sensitive to these environmental conditions of irregular hours.

On the physiological level, during night work, a desynchronisation occurs between the circadian rhythms that are aligned with daytime hours, and the new activity-rest/awake-asleep cycle imposed by the night work. This desynchronisation is also promoted by environmental conditions that are not conducive to sleep: daylight during rest, temperature usually higher than at night, higher noise levels during the day, social and family obligations. All these physical and sociological environmental factors contribute to disrupting the biological rhythms and sleep. The sleep difficulties reported by night workers concern both the quality and quantity of sleep.
Experimental studies in humans using actigraphy[8] and polysomnography[9] show a reduction in sleep time among night workers.
The evidence from epidemiological studies is sufficient to conclude that there is an effect on the health of workers.
Accordingly, the effect of night work on sleep quality and the reduction of sleep time is proven.

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[7] Physiological unit of time lasting 24 hours, comprising one night and one day, a period of sleep and a period of wakefulness.

[8] This test involves measurement and recording using an actigraph attached to the wrist. It is used to determine the patient's activity/rest rhythm over several weeks (evaluation of their phase shifts, or the quantity and especially quality of sleep).

[9] Polysomnography is the complete recording of sleep. This examination involves capturing the electric rhythms coming from a patient's body in order to deduce the stages of sleep.

2. Sleepiness and cognitive disorders

The studies carried out in the laboratory have shown that circadian desynchronisation is accompanied by cognitive impairment. The sleepiness associated with these symptoms is explained by both the desynchronisation of the working day compared to the circadian clock, and the "sleep debt" developed by shift and night workers.

- *Sleepiness*

The evidence provided by epidemiological studies is sufficient to conclude that there is an effect.

In addition, many fundamental studies in humans (mechanistic studies in the laboratory) have also observed this proven sleepiness whose intensity depends on the rhythm of shift work (including at night) but also chronobiological and homeostatic factors related to sleep debt, depending on the reduction in sleep time and the time interval between the last sleep episode and the beginning of the work period.

Accordingly, the effect of night work on sleepiness is proven.

- *Cognitive performance*

While most studies use the objective measurement known as the PVT (Psychomotor Vigilance Test), which measures reaction time, a few offer other interesting assessment methods. Of the eleven studies analysed, six show that shift work, including night work, may be associated with a decline in cognitive performance. However, some studies show that the decrease in psychomotor performance in the PVT may be more affected by sleep deprivation prior to starting the shift than by the actual time of the shift. There is limited evidence from epidemiological studies to conclude as to whether or not there is an effect.

The fundamental studies conducted in humans with shift work simulated in the laboratory confirm the effects of these irregular hours on cognitive performance, in particular, but not exclusively, assessed by the PVT.

Accordingly, the effect of night work on cognitive performance is probable.

3. Effect on psychological health

Night workers collectively report problems with their psychological health: mood disorders, depression, irritability, anxiety and personality disorders. Long regarded as a consequence of mental disorders, changes to the circadian system could actually be involved in causing these disorders. Indeed, the direct involvement of changes to the circadian system – and therefore potentially night work – in the development of mental illnesses is currently being proposed in some studies.

Night work may influence psychosocial risk factors and sleep disorders, which in turn could increase the risk of mental disorders. The consequence of this result is that controlling for confounding factors is essential to determine the nature of the effect of the night work itself. As there are so many of these confounding factors, they are never all controlled in any one study.

The data show an association in the majority of studies, with the exception of the only longitudinal study available, for which it is not possible to exclude all the biases and confounding factors. Thus, the evidence supporting the existence of an effect of night work on mental health is limited.

A recent experimental study (Boudreau *et al*., 2013) conducted with shift workers in the laboratory reported better mood quality when there was an increase in circadian synchronisation (between the internal biological clock and the wakefulness-sleep schedule imposed by night work). This laboratory study also provides limited evidence supporting the existence of an effect of night work on mental health.

Accordingly, the effect of night work on psychological health is probable.

4. **Metabolic disorders and cardiovascular diseases**

Many studies have been conducted to assess the association between shift work and the risk of metabolic disorders: obesity or overweight, diabetes, high blood pressure, dyslipidaemias or metabolic syndrome.

- *Obesity and overweight*

Several of the studies analysed, in particular the case-control studies, showed a significant association between shift work, including night work, and weight gain. There is limited evidence provided by the epidemiological studies to conclude as to whether or not there is an effect.

Studies suggest that the increase in food intake (generally sweet) may be a compensatory homeostatic response to sleep deprivation, which is observed in shift work with night hours.

Taking into account the evidence provided by the epidemiological studies and the plausible mechanisms from experimental studies, *the effect of night work on obesity and overweight is probable.*

- *Type 2 diabetes*

A significant dose-response relationship between the duration of shift work, including night work, and the risk of type 2 diabetes was shown in two cohort studies analysed. In the different studies selected, it was shown that shift work is associated with a significantly increased risk of type 2 diabetes, particularly among shift workers on rotating hours. The evidence in the epidemiological studies is limited.

On the mechanistic level, the effects of circadian disruption and/or sleep restriction on insulin-resistance are plausible. In the majority of studies testing the effect of circadian disruption in humans or animals, impaired glucose metabolism, as well as sensitivity to insulin, were observed.

Thus, taking into account the evidence provided by the epidemiological studies and the plausible mechanisms from experimental studies, *the effect of night work on diabetes is probable.*

- *Dyslipidaemias*

Epidemiological studies on this subject mainly focused on minimum and mean values in years of rotating shift work, resulting in an increase in cholesterol. However, most of these studies do not take into account the sub-fractions of cholesterol (HDL-C, LDL-C), or triglycerides. Given the methodological limitations and the few available studies taking these parameters into account, the evidence provided by the epidemiological studies cannot be used to draw any conclusions about the existence or not of any effect.
Taking into account the evidence provided by the epidemiological studies and the plausible mechanisms studied in experimental studies, *the effect of night work on dyslipidaemia is possible*.

- *Metabolic syndrome*

There are several definitions of metabolic syndrome. One of the most recent (2005) defines this syndrome as the simultaneous presence of at least three out of five criteria on biological and clinical parameters related to waist size, blood pressure, blood triglyceride, blood cholesterol and blood sugar levels.

While most of the studies are cross-sectional, several cohort studies are available, including one proposing a higher rate of incidence of metabolic syndrome for shift workers, including night workers, compared to day workers.

Concerning the epidemiological studies, there is sufficient evidence to conclude that there is an effect. On the mechanistic level, the effects of circadian disruption and/or sleep restriction on the components of metabolic syndrome are plausible.

The presence of a dose-effect relationship with the duration of the shift work, including night work, has been highlighted in several studies.

Accordingly, the effect of night work on the occurrence of metabolic syndrome is proven.

It should be noted that metabolic syndrome is defined as a combination of several biological or clinical parameters that are not necessarily all disrupted. This explains why the effect on this syndrome is regarded as proven whereas the effects for the diseases taken individually are probable.

- *Cardiovascular diseases*

The association between night/shift work and cardiovascular disorders is plausible on the basis of the risk factors examined. Nevertheless, it should be noted that most of the studies are affected by selection and information bias. These are related to the imprecise definition and quantification of exposure, the incorrect classification of cases and controls, the type of study (cross-sectional, longitudinal), the groups/sectors examined, the diagnostic criteria, the reporting methods, the confounding and risk factors considered, and the "healthy worker effect" (ageing, recruitment, periodic medical surveillance).
Taking into account the evidence provided by the epidemiological studies and experimental studies in humans examined:

- *the effect of night work on coronary heart diseases (coronary ischaemia and myocardial infarction) is probable;*
- *the effect of night work on high blood pressure and its relationship with ischaemic stroke are possible.*

5. Cancer

The assessment by the IARC of the carcinogenicity of night work causing disruptions to circadian rhythm concluded in 2010 that there was a limited level of evidence in humans, on the basis of eight epidemiological studies on breast cancer in women and a small number of studies on cancers of the prostate, colon and endometrium. Since this assessment, new epidemiological studies have been published.
The evidence provided by the epidemiological studies to assess the cancer risk associated with shift work, including night work, are presented below by cancer site.
This is followed by a global presentation of the assessment of the level of evidence of the risk of cancer associated with shift work, including night work.

- *Breast cancer in women*

The assessment of the evidence provided by the epidemiological studies focused on 24 studies on breast cancer conducted in North America, Europe and Asia, including the eight studies evaluated in the IARC monograph. Eight cohort studies and seven case-control studies nested in the cohorts focused on nurses (six studies), radio operators, military personnel, textile workers and groups of employees identified in population or employer registers. Nine case-control studies carried out in the general population were also taken into account, covering a wide range of occupations and sectors of activity.

Of all the studies analysed, some had major methodological limitations and did not play a predominant role in the final assessment, due to the inadequate measurement of exposure, the possibility of selection bias of subjects, the small sample size, or the fact that confounding factors were not taken into account. Conversely, some case-control studies in the population or nested in cohorts were given precedence due to their higher methodological quality. These studies generally provided new elements compared to the assessment by the IARC, because they focused on diversified professional groups, the night and/or shift hours were defined more precisely than in the earlier studies, the exposure to night work was measured over the entire professional career, and the main risk factors for breast cancer likely to play a confounding role were taken into account. Lastly, some studies also collected information on the duration of sleep and on the chronotype of individuals as intermediary factors or modifiers of the relationship between night work and risk of breast cancer.

The main studies showed that there were statistical associations, generally low, between breast cancer and night or shift work. However, the definitions used to characterise the exposure to night work vary widely from one study to another and make it difficult, if not impossible, to compare results. Depending on the different studies, the observed associations concerned the duration in years of night work, its intensity (number of nights per week or per month), the number of consecutive nights worked, the total number of nights worked throughout the whole career, fixed or rotating night work, or night work measured on a scale enabling the degree of circadian disruption to be assessed, with long durations of exposure of more than 20 years being associated with breast cancer in some studies, but not in all.

In conclusion, the expert group recognises that the recent epidemiological studies provide new evidence on the possible links between night work and breast cancer. However it underlines the lack of standardisation in the characterisation of exposure. Unless the results can be replicated reliably from one study to another, it is not possible at this stage to draw a coherent picture of the increase in the risk of breast cancer among women working at night or working shifts according to the duration, frequency or intensity of exposure. It also considers that it is not possible to rule out, with certainty, the existence of residual confounding factors, in relation with, for example, concomitant occupational exposure, which could explain some of the observed associations.

The epidemiological studies supporting an effect of shift work, including night work, provide more evidence on the increase in the risk of breast cancer than was available in 2010. This evidence is, however, limited.

- *Prostate cancer*

The literature review focused on eight epidemiological studies with an individual assessment of exposure to night work or shift work (five cohort studies and three case-control studies), two of which had been taken into account in the IARC monograph. The cohort studies do not report any increase in the risk of prostate cancer associated with night work or shift work, with the exception of the first publication relating to a small Japanese cohort. In these studies, the measurement of exposure to night work is generally not very precise, is based on a short period in the career of the subjects, or is evaluated from a jobs-exposure matrix responsible for ranking errors. Among the three case-control studies, the results show associations with the durations of exposure or indices of cumulative exposure to night work. The most recent study reporting links between night work and the advanced stages of prostate cancer, and studying the modifier effect of the chronotype, provides more convincing evidence, but these elements must be underpinned by new studies.

On the basis of the available epidemiological studies, the results suggest the possibility of an increased risk, but the evidence is insufficient, and must be confirmed by further studies.

- *Other cancers*

A small number of epidemiological studies have analysed the links between night work and cancers of the ovary, lung and pancreas, and colorectal cancers, as well as several other cancer sites, in particular in the cohort studies. In these studies, the exposure to night/shift work is usually assessed in an imprecise way, and the covariables that can play a confounding role are not systematically taken into account. The results of studies on the same cancer sites reporting

associations with night work are contradictory for a given cancer site.
On the basis of the available epidemiological studies, it is not possible to conclude as to the effects of night work on the other cancer sites.

- *Overall conclusion on the risk of cancer*

The expert group conducted a critical analysis of the epidemiological studies on the risk of cancer related to shift work, including night work. On this basis, it considers that there are elements supporting an excess risk of breast cancer associated with night work, with limited evidence. It is not possible to conclude as to an effect for the other cancer sites on the basis of the available studies.
The expert group also considered the results of experimental studies in animals examining the links between disruptions caused to the circadian rhythm and the onset of cancer. In addition, it stresses the existence of physiopathological mechanisms that may explain the carcinogenic effects of disruptions to the circadian rhythm.
Based on the results of the epidemiological studies analysed and the results of experimental and biological studies, the CES finds a probable effect of night work on the risk of cancer.

Accidentology and traumatic pathology

The studies examined show that the frequency and severity of accidents occurring during shift work, including night work, are generally higher. This situation is explained both by the physiological mechanisms involved (sleepiness, sleep debt, chronobiology), and by organisational, environmental (working conditions) and managerial factors.

Modulators

The effects of night and shift work on the health of employees subjected to it are not unambiguous and systematic. They depend on a combination of factors based on the employees' individual, social and family characteristics and the characteristics of the work and work situation. These multiple factors will modulate, i.e. reduce or amplify, the effects of night work and shift work on the health of the employees. National surveys also show that night workers accumulate time constraints (work at the weekend, reduced freedom in the organisation of working time, *etc*.) and hardship factors (alertness constraints, physical hardship). Adaptation strategies put in place by the workers on rotating and night hours in work and "outside work" contribute to the control of risks in terms of work, personal life and health. But they are not always sufficient. The readjustments observed in actual work to anticipate variations in sleepiness, transfers of tasks, mutual assistance and rest are only possible when there is room for manoeuvre in the work situation.

Table 1: Classification of the health effects studied

Effect studied		Is there evidence of the existence of the effect in experimental studies in humans or animals?	Evidence of the existence of the studied effect in clinical and epidemiological studies	Classification of the level of evidence in humans
Sleep	Sleep quality	**yes**	**Sufficient**	**Proven effect**
	Sleep time	**yes**	**Sufficient**	
Cognitive performance	Sleepiness and alertness	**yes**	**Sufficient**	**Proven effect**
	Cognitive performance	**yes**	**Limited** Six studies out of 11 show an association.	**Probable effect**
Psychological health		**yes**	**Limited** Eighteen studies out of 20 show an association between night work (fixed or rotating) and diminished mental health. A more indirect link in the other eight studies is mediated by psychosocial risk factors associated with the content and organisation of night work.	**Probable effect**
Cancer	Breast cancer	**yes**	**Limited** There is more evidence supporting an effect of work, including night work, than in 2010; however, it is limited.	**Probable effect**
	Prostate cancer	**yes**	**No conclusion can be drawn**	
	Other cancers (ovary, pancreas, colorectal)	**yes**	**No conclusion can be drawn**	
Cardiovascular diseases and metabolic disorders	Metabolic syndrome	**yes**	**Sufficient**	**Proven effect**

	Obesity or overweight	**yes**	**Limited** Several case-control studies show a significant association with night-shift work One cohort study, despite its methodological limitations, suggests deleterious effects.	**Probable effect**
	Type 2 diabetes	**yes**	**Limited** A significant dose-response relationship between the duration of shift work with night hours and the risk of type 2 diabetes was shown in two cohorts.	**Probable effect**
	Dyslipidaemias	**yes**	**No conclusion can be drawn**	**Possible effect**
	Coronary heart diseases	**yes**	**Limited** Selection and information bias affect most of the studies.	**Probable effect**
	High blood pressure	**yes**	**No conclusion can be drawn**	**Possible effect**
	Ischaemic stroke	**yes**	**No conclusion can be drawn**	**Possible effect**

4. AGENCY CONCLUSIONS AND RECOMMENDATIONS

The population concerned by night work, whether regular or occasional, has almost doubled in 20 years. In 2012, it represented 15.4% of employees, or 3.5 million people, and continues to increase. According to Article L. 3122-32 of the French Labour Code, the use of night work must remain exceptional.

The working conditions of employees working at night are more difficult than for others: they are for example subjected to more numerous physical hardship factors, greater time pressure and more frequent tensions with their colleagues or the public.

The Agency emphasises the important work carried out by the expert groups entrusted with the expert appraisal, covering aspects relating to definitions and regulations, and a description of the situation in France. Using a specific method, the assessment of the health risks associated with night work led to the level of evidence for the studied effects being ranked. In a ground-breaking context, this work focused on an expanded description of the health effects associated with this type of activity. The description of the societal and economic contexts of night work supplements this complex expert appraisal and thus shows the importance of taking the social and family aspects into account to understand the issue of the health effects of night work in its entirety. This first part of the Agency's study is devoted to the issue of night work. This study will continue, in accordance with the original formal request, on the more general issue of the other forms of atypical working hours.

ANSES endorses all the conclusions, reiterated in Section 3 of this opinion, and the recommendations of its Expert Committee on "Physical agents, new technologies and development areas".

The results of the expert appraisal highlight the health effects of shift work including night work:

- proven effects on sleepiness, sleep quality and the reduction of total sleep time, and metabolic syndrome;
- probable effects on cancer, psychological health, cognitive performance, obesity and weight gain, type 2 diabetes and coronary heart diseases (coronary ischaemia and myocardial infarction);
- and possible effects on dyslipidaemias, high blood pressure and ischemic stroke.

The Agency reiterates the first principle of removing the hazards to which workers are exposed, in the framework of the general principles of risk prevention laid down by the French Labour Code.

Accordingly, the Agency recommends limiting the use of night work solely to situations where there is a need to ensure the provision of services of social value or the continuity of economic activity. In this context, the Agency notes that that there is currently no regulatory definition covering the “continuity of economic activity”, used in some cases to justify the use of night work.

Furthermore, the Agency recommends assessing the adaptation of the regulatory framework in force to protect the health of night workers, and modifying it, if appropriate, while taking the European dimension into account.

In addition to ensuring correct application of the regulatory provisions relating to night work, the Agency recommends conducting a review of practices in the field designed to protect the health of night workers (maximum duration of daily work, break times, minimum daily rest, compensatory rest, medical supervision, etc.). This could be achieved, for example, by means of a survey of the main sectors concerned.

In addition, the Agency advocates:

- initially, assessing the health impact of the effects of night work (number of cases for each potential disease in the worker population);
- subsequently, assessing the social costs associated with the use of night work (work stoppages, occupational disease, absenteeism, etc.) that could be set against the potential benefits.

In the meantime, it appears necessary to immediately:

- adjust the medical surveillance of night workers, especially after the cessation of their night work;
- present the conclusions of this expert appraisal to the bodies in charge of assessing the relevance of listing certain pathologies in the occupational diseases table.

The Agency advocates optimising the ways in which night work is organised, in order to minimise the impact on workers' personal and professional lives. The organisational recommendations identified by the Agency's expert groups must therefore be emphasised. In particular, anything that reduces desynchronisation and sleep debt is favourable in principle, but specific organisational recommendations, on which there is currently no scientific consensus, should be examined collectively in the appropriate social dialogue bodies.

Lastly, concerning research on the health effects of night work, the Agency recommends:

- continuing the studies, especially on effects for which the evidence is limited;
- continuing the implementation of epidemiological studies, ensuring that exposure is better characterised (with standardised questionnaires, for example), and better taking into account possible confounding factors;
- conducting experimental studies in humans in the laboratory and in actual conditions, including subjective and quantitative assessments of the impact of night work on the amplitude and phase of the circadian system, sleep, sleepiness, cognition, metabolism, cardiovascular diseases, the immune system, etc.;
- acquiring data on companies (internal reports/grey literature) in order to increase knowledge on the effects of this type of time organisation in an actual work context.

The Deputy Director General

Caroline GARDETTE

KEYWORDS

Health effects:

- changes to the circadian system
- sleep disturbances
- metabolic and hormonal syndromes/disorders (fertility, diabetes)
- cancers
- gastrointestinal effects
- cardiovascular effects
- effects on the immune system
- psychological effects
- cognitive effects

Effects on work:

- cognitive effects
- accidentology (occupational accidents and commuting accidents)
- reliability
- performance
- work activity

Effects on life outside work:

- family life (marital life, relationship with children)
- social life

Assessment of the health risks for professionals exposed to atypical working hours, especially night work

Request No 2011-SA-0088 "Atypical working hours"

Collective Expert Appraisal
REPORT

Expert Committee on "Physical agents, new technologies and development areas"
Working Group on "Assessment of the health risks for professionals exposed to atypical working hours, especially night work"

March 2016

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- family life (marital life, relationship with children)
- social life

Presentation of participants

PREAMBLE: Outside experts, Expert Committee and Working Group members, or designated rapporteurs are all appointed in their personal capacity, *intuitu personae*, and do not represent their parent organisation.

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HEARINGS WITH EXTERNAL EXPERTS

French Confederation of Christian Workers (CFTC)

Pierre Yves MONTÉLÉON and Christophe KETELS, 15 February 2013

French Employers' Confederation (MEDEF)

François PELLET, 15 February 2013

General Employers' Confederation for Small and Medium Enterprises (CGPME)

Philippe CHOGNARD, 15 February 2013

Prof Eva SCHERNHAMMER – **Harvard School of Public Health**, Boston, United States, 15 January 2014

Prof Eero PUKKALA – **Institute for Statistical and Epidemiological Cancer Research**, Finland, 15 January 2014

Prof Kurt STRAIF – **International Agency for Research on Cancer**, Lyon, France, 28 November 2013

Prof Till RONNEBERG – **Institute of Medical Psychology at Ludwig-Maximilian University**, Munich, Germany, 19 February 2014

Prof Philippe ASKENAZY – Research Director at CNRS, Researcher at the **Paris School of Economics**, 12 January 2015

Prof Philippe CABON – Lecturer – Authorised to supervise research**, Laboratory for Work – Individual Adaptations**, Paris Descartes University, 12 January 2015

CONTRIBUTIONS FROM OUTSIDE THE GROUP(S)

Purpose of the contribution: "Legal study relating to night work and shift work"; Verdier Le Prat Legal Firm.

Research and Development Agreement (RDA) drawn up between ANSES and the French National Institute for Health and Medical Research (INSERM), with the aim of exploiting field data from the national survey on "Medical surveillance of exposure to occupational hazards" (Sumer, 2010) conducted by DARES and the Directorate General for Labour (DGT) - Occupational Health Inspectorate.

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Collective expert appraisal: summary of justification and conclusions

COLLECTIVE EXPERT APPRAISAL: SUMMARY AND CONCLUSIONS

on the "Assessment of the health risks associated with night work"

This document summarises the work of the Expert Committee on "Physical agents, new technologies and development areas" and the Working Group on "Atypical working hours".

Presentation of the issue

In March 2011, ANSES received a formal request from the French Confederation of Christian Workers (CFTC) to conduct an assessment of the health risks to which professionals working atypical hours are exposed, especially with regard to night work, whether or not this is regular.

Following the classification, in 2007, by the International Agency for Research on Cancer (IARC), of shift work involving night work in Group 2A[1] as "probably carcinogenic", mainly on the basis of epidemiological studies conducted on nurses and flight attendants, the CFTC asked in its request about the possibility of extending this assessment to all workers subjected to atypical working hours.

Faced with the magnitude and complexity of the issue, and also taking into account the availability of new scientific data since the IARC's monograph was published, ANSES then proposed to begin by updating the expert appraisal of the health risks to which professionals working at night are exposed. The health effects potentially associated with other forms of atypical working hours could be assessed as part of a second phase of the expert appraisal.

Scientific, social and regulatory context

The request for an assessment of the risks for professionals exposed to atypical working hours, in particular those working at night, comes within a specific socio-economic and scientific context: the way in which work is organised is changing, leading today to an enormous number of workers being concerned by working hours and rhythms deemed "atypical".

The expression "atypical hours" applies to all working time arrangements situated outside the framework of the "standard" week[2]. The best known forms of atypical hours are shift work[3], night

[1] The IARC classified shift work that disrupts circadian rhythms as probably carcinogenic (2A).

[2] Working hours between 5am and 11pm, 5 days a week, at a rate of 8 hours daily.

[3] Shift work (i.e. work in successive teams) concerns employees forming different teams that take over from each other on a given workstation without ever overlapping. This way of organising working time is intended to ensure continuity on a given workstation.

work and weekend work. Atypical hours also include non-contiguous working hours, compressed work schedules and working hours that can change from day to day.

The adoption of the proposed law on professional equality of men and women in 2001 removed the legal ban on women working at night, mainly to bring French law into compliance with European law and transpose European Directive 93/104/EC. The number of night workers has almost doubled in twenty years, as can be seen in the latest study by the Directorate for Research, Studies and Statistics (DARES) of the French Ministry of Labour, published in August 2014 (DARES, 2014).

The International Agency for Research on Cancer added shift work that disrupts circadian rhythms to the list of agents that are "probably carcinogenic" (Group 2A) in 2007. In France in 2012, the French National Authority for Health (HAS) published recommendations on good practices for monitoring shift and/or night workers.

Since the IARC publication, new scientific data have become available, in particular concerning the effects of light on circadian rhythms.

The health effects associated with atypical working hours constitute a complex field of study that requires the application of a wide variety of scientific disciplines. The effects mentioned in the literature mainly concern:

- sleep disorders and reduced vigilance;
- gastro-intestinal diseases;
- the occurrence of accidents;
- fertility, reproduction and pregnancy;
- cancer (especially breast cancer in women);
- metabolic disorders and cardiovascular diseases.

Organisation of the expert appraisal

ANSES entrusted the expert appraisal to the Working Group on "Assessment of the health risks for professionals exposed to atypical working hours, especially night work", under the auspices of the Expert Committee (CES) on "Physical agents, new technologies and development areas".

The Working Group was set up on 8 August 2012. It met 27 times in plenary sessions between 14 November 2012 and 26 January 2016. The collective expert appraisal was mainly based on a critical analysis and summary of the data published in the literature (scientific articles, reports, *etc.*).

The Working Group also interviewed external experts (a total of nine hearings including three with stakeholders) likely to provide useful information and additional data for the expert appraisal.

An international consultation was organised with national agencies and authorities in the areas of health and/or occupational safety (Europe and North America), in order to identify studies conducted abroad and find out which particular health effects were studied.

Lastly, a Research and Development Agreement (RDA) was drawn up between ANSES and the French National Institute for Health and Medical Research (INSERM), with the aim of exploiting field data from the national survey on "Medical surveillance of exposure to occupational hazards" (Sumer, 2010).

The methodological and scientific aspects of this group’s work were regularly submitted to the CES. The report produced by the Working Group takes account of the observations and additional information provided by the CES members. This expert appraisal was therefore conducted by a group of experts with complementary skills. It was carried out in accordance with the French Standard NF X 50-110 "Quality in Expertise Activities".

Description of the expert appraisal method

The concept of atypical working hours, which is very broad, was defined precisely in the framework of the Agency's work. The effects studied by the Working Group in this first phase of the expert appraisal relate to shift work including night work.

For the study of the socio-economic aspects, the Working Group adopted an expert appraisal method adapted to publications in the human and social sciences, while drawing on the knowledge and skills of the expert members of the group. Among the many publications identified, the experts gave priority to those of key importance, of good quality, or those that posed interesting and new questions. In particular, these studies were able to provide background information to the epidemiological results and factual data that better reflected the reality of the work.

For the part on the health effects of shift work including night work, the Working Group adopted the expert appraisal method described below.

Literature search

A literature search was conducted, as exhaustively as possible, from January 2010 to December 2014, considering all the health effects reported in the literature and related to shift work including night work.

The scientific publications (original articles written in English or French) were identified using a set of key words from a list drawn up by the Working Group.

Once identified, the documents were classified on the basis of the described health effects. Within each group of articles corresponding to a given health effect, the studies were also classified by type:

- epidemiological studies (cross-sectional, case-control, cohort) on humans;
- experimental studies on humans or *in vitro* on cellular models of human origin.

The Group also considered experimental studies in animals (*in vivo* or *in vitro*), when they were available, in order to provide information on the biological mechanisms, physiological functions or alterations to living systems.

Some key studies, published from January to June 2015, were also included in the expert appraisal when they were deemed especially relevant and of satisfactory quality. Furthermore, a review of studies published before 2010 was conducted for each health effect studied.

Certain expert appraisal reports were also analysed in detail, such as the report by the French National Authority for Health (HAS), published in 2012.

Prioritisation of health effects

Given the large number of publications identified by the literature search, the diversity of health effects identified and the time constraints associated with conducting the scientific expert appraisal, the Working Group decided to prioritise the work to be carried out.

The following health effects were selected and underwent detailed analysis:

- sleep disturbance;
- cognitive and psychomotor effects, and effects on vigilance;
- effects on mental and physical health, addiction;
- metabolic disorders and cardiovascular diseases;
- cancer.

Other health effects not selected for the detailed analysis are, however, described in the expert appraisal report in a dedicated chapter, based on recent summaries and reports.

Reproduction and pregnancy, as well as the link between gastrointestinal diseases and night work, have been widely studied, including by the French National Authority for Health (see HAS, 2012). A considerable number of articles are indeed available on this subject, but few publications have appeared since 2010.

Lastly, few data are available on the effects associated with the immune system or the effects relating to the interaction between pharmacology and night work.

Analysis of publications

In practice, each article was selected on the basis of its title and abstract in order to determine its relevance with regard to the issue being addressed. The articles selected were then analysed in detail by two experts, this analysis being recorded in a matrix. These analyses were discussed in sub-group meetings, in order to collectively define the publication's quality level.

The main quality criteria for the studies were based on a sound definition of the study population, a clear characterisation of exposure, the taking into account of potential confounding factors, and satisfactory statistical methods.

Assessment of the evidence for each effect studied

In this expert appraisal, the method for assessing the level of evidence for each health effect studied was mainly based on the available data in humans, in particular from human experimental and epidemiological studies.

Indeed, because animal studies are generally conducted in nocturnal rodents that are sensitive to light, it is very difficult, if not impossible, to reproduce the equivalent of night or shift work in animals, even if *in vivo* studies on animal models are available for health effects such as cancer, metabolic system disorders and/or cardiovascular diseases. For the health effects associated with mental or psychological health, there is no validated animal model currently available.

Thus, the procedure for assessing the evidence gives priority to human epidemiological and experimental studies. The comparison of these two types of evidence enabled the group to classify the studied effects according to five levels of evidence: proven effect, probable effect, possible effect, it is not possible to draw any conclusions from the available data, and probably no effect (see table below).

Classification table of health effects according to the level of evidence

<table>
<tr><td colspan="2" rowspan="2"></td><td colspan="2">Evidence of the existence of the effect in experimental studies in humans or animals</td></tr>
<tr><td>Evidence supporting the existence of an effect</td><td>No evidence supporting the existence of an effect</td></tr>
<tr><td rowspan="5">Evidence of the existence of the studied effect in epidemiological studies</td><td>Sufficient evidence to conclude as to the existence of an effect</td><td colspan="2">Proven effect</td></tr>
<tr><td>Limited evidence supporting the existence of an effect</td><td>Probable effect</td><td>Possible effect</td></tr>
<tr><td>It is not possible to conclude from the evidence as to whether or not there is an effect</td><td rowspan="2">Possible effect</td><td rowspan="2">It is not possible to conclude from the available data as to whether or not the studied effect exists</td></tr>
<tr><td>Lack of quality data</td></tr>
<tr><td>The available data do not show any effect</td><td>It is not possible to conclude from the available data as to whether or not the studied effect exists</td><td>Probably no effect</td></tr>
</table>

In addition, the Group considered experimental studies in animals (*in vivo* or *in vitro*), when they were available, in order to provide information on the biological mechanisms, physiological functions or alterations to living systems.

The information was examined as a whole in order to make an overall assessment for humans of the impact of shift work including night work (fixed or rotating shifts) for each effect studied.

Results and conclusions of the expert appraisal

The Expert Committee on "Physical agents, new technologies and development areas" adopted the collective expert appraisal work along with its conclusions and recommendations as described in this collective expert appraisal summary, at its meeting on 14 March 2016.

The reality of night and/or shift work in France

An analysis conducted by DARES[4] based on data from the "Working conditions" survey of 2012 revealed that 15.4% of employees (21.5% of men and 9.3% of women), or 3.5 million people, worked at night, regularly or occasionally. These figures are on an upward trend, with the increase being particularly sharp for women. Night work is most widespread in the tertiary sector: it concerns 30% of public-sector employees and 42% of those in private service companies. Drivers, police and military personnel, nurses, caregivers and skilled workers in processing and/or assembly industries are the professional categories most concerned by night work. Temporary workers, men in their thirties and women under 30 years of age are the groups most frequently working at night.

Again according to the "Working conditions" survey of 2012, employees who work at night have higher remuneration but markedly more difficult working conditions than other employees: they are subjected to more numerous physical hardship factors, greater time pressure (hours, rhythm constraints, deadlines, *etc.*), and more frequent tensions with their colleagues or the public.

A clear regulatory framework for night work

French legislation (Article L. 3122-29 of the Labour Code) defines *night work* as *"any work performed between 9pm and 6am".* It also defines a *night worker* as any worker who performs a fraction of their working time between 9pm and 6am: at least 3 hours twice a week, or at least 270 hours over twelve consecutive months[5]. These definitions may be modified within certain limits by collective agreement or extended agreement. This strict regulatory framework is modulated by numerous waivers, depending on the sectors and professions concerned.

The status of night worker includes compensatory measures, mainly a limit on the maximum duration of the work, salary and rest, but these are also modulated by numerous waivers. In addition, a series of specific measures have been adopted, aimed at preventing health risks for pregnant women when they perform night work.

According to Article L. 3122-32 of the French Labour Code, the use of night work must remain exceptional and take into account the requirements to protect the health and safety of workers. It must also be justified by the need to ensure the continuity of economic activity or services of social value.

Shift work is not defined in the French Labour Code; it is therefore far less regulated. The provisions specific to shift work are, for the most part, laid down in collective professional agreements and collective branch agreements.

Socio-economic aspects of night work

Night work may be introduced to ensure the continuity of services of social value, such as health services and on-call police officers or other surveillance services, or it may be a work organisation method, for example for a company that wishes to maximise the profitability of its equipment by getting machines and people to work around the clock.

The social cost of night and/or shift work is not limited to the health care provided to employees but should also take into account the cost of its impact on family life, costs induced by transport, and absenteeism. This social cost of night and/or shift work is however very difficult to assess, given that the statistics linking the medical and social consequences with the work schedule are scarce.

[4] Source DARES, Analyses, Le travail de nuit en 2012 [Analyses, Night Work in 2012] No. 062, August 2014

[5] Article R. 3122-8 of the French Labour Code

While the health effects of atypical hours, particularly night work and shift work, have been documented in the scientific literature, the same is not true for the record of the employees' life outside work. Indeed, although some researchers have been warning of the need to begin researching this field since the 1980s, few scientific studies have focused on the impact of these hours on family and social life. Life outside work is undeniably linked to physical, mental, psychological and social[6] health, as defined by the WHO.

Concerning the effect of night and shift work on social life

Shift or night work creates a limitation on social life because of the temporal mismatch between the shift worker's rhythm of life and that of society as a whole. It is therefore not so much a lack of free time that causes difficulty but its position on the nychthemeron[7]. This is manifested by: difficulties in organising social encounters resulting in a tendency to spend more time with colleagues with a similar rhythm of life, difficulty accessing social activities in a structured framework (cultural, sports, associations) due to their strong rooting in a rigid and socially predetermined time period, and a tendency to opt for more individual and flexible leisure activities requiring no synchronisation with others. The diversity of shift work situations and organisational specificities, the variety of social contexts, and the weight of individual characteristics all constitute key factors that determine how people go about their lives outside the workplace.

Concerning the effect of night and shift work on family life

Depending on how it is organised, shift work may, for couples, result in limited time for meeting and sharing, changes to marital relations and sex life, and the emergence of imbalances in the functioning of the family that are felt more acutely by spouses than by the employees themselves. In the long term, these difficulties can also be manifested by psychological disorders associated with guilt and frustration, the recurrence of inter-marital tensions and changes in health. Some research on the impact of shift work on relations between shift workers and their children shows a decrease in the frequency and duration of family interactions and in the perceived quality of parenthood, as well as a deterioration in the nature and quality of parental functions. However, the effects of night work on the socio-familial environment are not universal and their assessment therefore requires the employment conditions of the households and the economic and cultural context of the country to be taken into consideration.

Health effects of night work

1. <u>Effect on the quantity and quality of sleep</u>

The difficulties experienced by night workers in falling asleep after a period of work at irregular hours are easily understandable and often recognised by all the parties in the professional world. Night work is accompanied by a need for the reorganisation of biological rhythms, of which sleep is the most sensitive to the environmental conditions imposed by irregular hours.

On the physiological level, during night work, a desynchronisation occurs between the circadian rhythms that are aligned with daytime hours, and the new rest-activity/sleep-wake cycle imposed by the night work. This desynchronisation is also promoted by environmental conditions that are not conducive to sleep: daylight during rest, temperature usually higher than at night, higher noise levels during the day, social rhythm and family obligations. All these factors of the physical and sociological environment contribute to disrupting biological rhythms and sleep. The sleep difficulties reported by night workers concern both the quality and quantity of sleep.

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[6] According to the World Health Organisation (WHO), "Health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity".

[7] Physiological unit of time lasting 24 hours, comprising one night and one day, a period of sleep and a period of wakefulness.

Experimental studies in humans using actigraphy[8] and polysomnography[9] show a reduction in sleep time among night workers.

The evidence from epidemiological studies is sufficient to conclude that there is an effect on the health of workers.

Accordingly, the effect of night work on sleep quality and the reduction of sleep time is proven.

2. Sleepiness and cognitive disorders

Laboratory studies have shown that circadian desynchronisation is accompanied by cognitive impairment. The sleepiness associated with these symptoms is explained by both the desynchronisation of the working day in relation to the circadian clock, and the "sleep debt" developed by shift and night workers.

- *Sleepiness*

The evidence provided by epidemiological studies is sufficient to conclude that there is an effect.

In addition, many fundamental studies in humans (mechanistic laboratory studies) have also confirmed that sleepiness is present, and that its intensity depends on the rhythm of shift work (including night work) and also on chronobiological and homeostatic factors related to sleep debt, depending on the reduction in sleep time and the time interval between the last sleep episode and the beginning of the work period.

Accordingly, the effect of night work on sleepiness is proven.

- *Cognitive performance*

While most studies use the objective measurement known as the PVT (Psychomotor Vigilance Test), which measures reaction time, a few offer other interesting assessment methods. Of the eleven studies analysed, six show that shift work, including night work, may be associated with a decline in cognitive performance. However, some studies show that the decrease in psychomotor performance in the PVT may be more affected by sleep deprivation prior to starting the shift than by the actual timing of the shift. There is limited evidence from epidemiological studies to conclude as to whether or not there is an effect.

The fundamental studies conducted in humans with simulated shift work in the laboratory confirm the effects of these irregular hours on cognitive performance, assessed primarily by the PVT, but not exclusively,.

Accordingly, the effect of night work on cognitive performance is probable.

3. Effect on psychological health

Night workers collectively report problems with their psychological health: mood disorders, depression, irritability, anxiety and personality disorders. Long regarded as a consequence of mental disorders, changes to the circadian system could actually be involved in causing these disorders. Indeed, the direct involvement of changes to the circadian system – and therefore

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[8] This test involves measurement and recording using an actigraph attached to the wrist. It is used to determine the patient's activity/rest rhythm over several weeks (evaluation of their phase shifts, or the quantity and especially quality of sleep).

[9] Polysomnography is the complete recording of sleep. This examination involves capturing the electric rhythms coming from a subject's body in order to deduce the stages of sleep.

potentially of night work – in the development of mental illnesses is currently being proposed in some studies.

Night work may influence psychosocial risk factors and sleep disorders, which in turn could increase the risk of mental disorders. Consequently, controlling for confounding factors is essential to determine the nature of the effect of the night work itself. Given the multitude of confounding factors, they are never all controlled in a single study.

The data show an association in the majority of studies, with the exception of the only longitudinal study available, for which it is not possible to exclude all biases and confounding factors. Thus, the evidence supporting the existence of an effect of night work on mental health is limited.

A recent experimental study (Boudreau *et al*., 2013) conducted with shift workers in the laboratory reported better mood quality when there was an increase in circadian synchronisation (between the internal biological clock and the sleep-wake schedule imposed by night work). This laboratory study also provides limited evidence supporting the existence of an effect of night work on mental health.

Accordingly, the effect of night work on psychological health is probable.

4. Metabolic disorders and cardiovascular diseases

Many studies have been conducted to assess the association between shift work and the risk of metabolic disorders: obesity or excess weight, diabetes, high blood pressure, dyslipidaemias or metabolic syndrome.

- *Obesity and excess weight*

Several of the studies analysed, especially case-control studies, showed a significant association between shift work, including night work, and weight gain. There is limited evidence provided by epidemiological studies to conclude as to whether or not there is an effect.

Results show that the forced desynchrony protocol (associated with desynchronisation of the circadian clock and sleep restriction) leads to hyperglycaemia consecutive to inadequate pancreatic compensation, in men and women regardless of age.

Taking into account the evidence provided by the epidemiological studies and the plausible mechanisms examined in experimental studies, *the effect of night work on obesity and excess weight is probable.*

- *Type 2 diabetes*

A significant dose-response relationship between the duration of shift work, including night work, and the risk of type 2 diabetes was shown in two cohort studies analysed. In the different studies selected, it was shown that shift work is associated with a significantly increased risk of type 2 diabetes, particularly among shift workers on rotating shifts. The evidence in the epidemiological studies is limited.

On the mechanistic level, the effects of circadian disruption and/or sleep restriction on insulin-resistance are plausible. In the majority of studies testing the effect of circadian disruption in humans or animals, impaired glucose metabolism, as well as sensitivity to insulin, were observed.

Thus, taking into account the evidence provided by the epidemiological studies and the plausible mechanisms from experimental studies, *the effect of night work on diabetes is probable.*

- *Dyslipidaemias*

Epidemiological studies on this subject mainly focused on minimum and mean values in years of rotating shift work, resulting in an increase in cholesterol. However, most of these studies do not take into account the sub-fractions of cholesterol (HDL-C, LDL-C), or triglycerides. Given the methodological limitations and the few available studies taking these parameters into account, the evidence provided by the epidemiological studies cannot be used to draw any conclusions about the existence of an effect.

Taking into account the evidence provided by the epidemiological studies and the plausible mechanisms from experimental studies, *the effect of night work on dyslipidaemia is possible*.

- *Cardiovascular diseases*

The association between night/shift work and cardiovascular disorders is plausible on the basis of the risk factors examined. Nevertheless, it should be noted that most of the studies suffer from selection and information bias. These are related to the imprecise definition and quantification of exposure, the incorrect classification of cases and controls, the type of study (cross-sectional, longitudinal), the groups/sectors examined, the diagnostic criteria, the reporting methods, the confounding and risk factors considered, and the "healthy worker effect" (ageing, recruitment, periodic medical surveillance).

Taking into account the evidence provided by the epidemiological studies and the human experimental studies examined:

- *the effect of night work on coronary heart diseases (coronary ischaemia and myocardial infarction) is probable;*
- *the effect of night work on high blood pressure and its relationship with ischaemic stroke are possible.*

- *Metabolic syndrome*

There are several definitions of metabolic syndrome. One of the most recent (2005) defines this syndrome as the simultaneous presence of at least three out of five criteria on biological and clinical parameters related to waist size, blood pressure, blood triglyceride, blood cholesterol and blood sugar levels.

While most of the studies are cross-sectional, several cohort studies are available, including one proposing a higher rate of incidence of metabolic syndrome for shift workers, including night workers, compared to day workers.

Concerning the epidemiological studies, there is sufficient evidence to conclude that there is an effect. On the mechanistic level, the effects of circadian disruption and/or sleep restriction on the components of metabolic syndrome are plausible.

The presence of a dose-effect relationship with the duration of the shift work, including night work, has been highlighted in several studies.

Accordingly, the effect of night work on the occurrence of metabolic syndrome is proven.

It should be noted that metabolic syndrome is defined as a combination of several biological or clinical parameters that are not necessarily all disrupted. This explains why the effect on this syndrome is regarded as proven whereas the effects for the diseases taken individually are probable.

5. Cancer

The assessment by the IARC of the carcinogenicity of night work causing disruptions to circadian rhythm concluded in 2010 that there was limited evidence in humans, on the basis of eight epidemiological studies on breast cancer in women and a small number of studies on cancers of the prostate, colon and endometrium. Since this assessment, new epidemiological studies have been published.

The evidence provided by the epidemiological studies to assess the cancer risk associated with shift work, including night work, is presented below by cancer site.

This is followed by a global presentation of the assessment of the level of evidence of the risk of cancer associated with night work.

- *Breast cancer in women*

The assessment of the evidence provided by epidemiological studies focused on 24 studies on breast cancer conducted in North America, Europe, and Asia, including the eight studies evaluated in the IARC monograph. Eight cohort studies and seven case-control studies nested in the cohorts focused on nurses (six studies), radio operators, military personnel, textile workers and groups of employees identified in population or employer registers. Nine case-control studies carried out in the general population were also taken into account, covering a wide range of occupations and sectors of activity.

Of all the studies analysed, some had major methodological limitations and did not play a predominant role in the final assessment, due to the inadequate measurement of exposure, the possibility of subject selection bias, the small sample size, or the fact that confounding factors were not taken into account. Conversely, some case-control studies in the population or nested in cohorts were given precedence due to their higher methodological quality. These studies generally provided new elements compared to the assessment by the IARC, because they focused on diversified professional groups, the night and/or shift hours were defined more precisely than in the earlier studies, the exposure to night work was measured over the entire professional career, and the main risk factors for breast cancer likely to play a confounding role were taken into account. Lastly, some studies also collected information on the duration of sleep and on the chronotype of individuals as intermediary factors or modifiers of the relationship between night work and risk of breast cancer.

The main studies showed that there were statistical associations, generally low, between breast cancer and night or shift work. However, the definitions used to characterise the exposure to night work vary widely from one study to another and make it difficult, if not impossible, to compare results. Depending on the different studies, the observed associations concerned the duration in years of night work, its intensity (number of nights per week or per month), the number of consecutive nights worked, the total number of nights worked throughout the whole career, fixed or rotating night work, or night work measured on a scale enabling the degree of circadian disruption to be assessed, with long durations of exposure of more than 20 years being associated with breast cancer in some studies, but not in all.

In conclusion, the expert group recognises that the recent epidemiological studies provide new evidence on the possible links between night work and breast cancer. However it underlines the lack of standardisation in the characterisation of exposure. Unless the results can be replicated reliably from one study to another, it is not possible at this stage to draw a coherent picture of the increase in the risk of breast cancer among women working at night or working shifts according to the duration, frequency or intensity of exposure. It also considers that it is not possible to rule out, with certainty, the existence of residual confounding factors, in relation with, for example, concomitant occupational exposure, which could explain some of the observed associations.

The epidemiological studies supporting an effect of night work provide more evidence on the increase in the risk of breast cancer than was available in 2010. This evidence is, however, limited.

- *Prostate cancer*

The literature review focused on eight epidemiological studies with an individual assessment of exposure to night work or shift work (five cohort studies and three case-control studies), two of which had been taken into account in the IARC monograph. The cohort studies do not report any increase in the risk of prostate cancer associated with night work or shift work, with the exception of the first publication relating to a small Japanese cohort. In these studies, the measurement of exposure to night work is generally not very precise, is based on a short period in the career of the subjects, or is evaluated from a jobs-exposure matrix leading to classification errors. Among the three case-control studies, results show associations with the durations of exposure or indices of cumulative exposure to night work. The most recent study reporting links between night work and the advanced stages of prostate cancer, and studying the modifying effect of chronotype, provides more convincing evidence, but these elements should be underpinned by new studies.

On the basis of the available epidemiological studies, the results suggest the possibility of an increased risk, but the evidence is insufficient, and must be confirmed by further studies.

- *Other cancers*

A small number of epidemiological studies have analysed the links between night work and ovarian, lung, pancreatic, and colorectal cancers, as well as several other cancer sites, particularly in the cohort studies. In these studies, the exposure to night/shift work is usually assessed in an imprecise way, and the covariables that can play a confounding role are not systematically taken into account. The results of studies on the same cancer sites reporting associations with night work are contradictory for a given cancer site.

On the basis of the available epidemiological studies, it is not possible to conclude as to the effects of night work on the other cancer sites.

- *Overall conclusion on the risk of cancer*

The expert group conducted a critical analysis of epidemiological studies on the risk of cancer related to shift work, including night work. On this basis, it considers that there are elements supporting an excess risk of breast cancer associated with night work, with limited evidence. It is not possible to conclude as to an effect for the other cancer sites on the basis of the available studies.

The expert group also considered the results of experimental studies in animals examining the links between disruptions caused to circadian rhythm and the onset of cancer. In addition, it stresses the existence of physiopathological mechanisms that may explain the carcinogenic effects of disruptions to circadian rhythm.

Based on the results of the epidemiological studies analysed and the results of experimental and biological studies, the CES finds a probable effect of night work on the risk of cancer.

Accidentology and traumatic pathology

The examined studies show that the frequency and severity of accidents occurring during shift work, including night work, are generally higher. This situation is explained both by the physiological mechanisms involved (sleepiness, sleep debt, chronobiology), and by organisational, environmental (working conditions), and managerial factors.

Modulators

The effects of night and shift work on the health of employees subjected to it are not unambiguous or systematic. They depend on a combination of factors based on the employees' individual, social and family characteristics, and the characteristics of the work and work situation. These multiple factors will modulate, i.e. reduce or amplify, the effects of night work and shift work on the health of the employees. National surveys also show that night workers accumulate time constraints (work during the weekend, reduced freedom in the organisation of working time, *etc.*) and hardship factors (vigilance constraints, physical hardship). Adaptation strategies adopted by workers on rotating and night shifts, both in the workplace and outside of work, help control the risks in terms of work, personal life and health. However, they are not always sufficient. The readjustments observed in actual work to anticipate variations in sleepiness, transfer of tasks, peer support and rest are only possible when there is room for manoeuvre in the work situation.

Summary table of the classification of the health effects studied

Studied effect		Is there evidence of the existence of the effect in experimental studies in humans or animals?	Evidence of the existence of the studied effect in clinical and epidemiological studies	Classification of the level of evidence in humans
Sleep	Sleep quality	**yes**	**Sufficient**	**Proven effect**
	Sleep time	**yes**	**Sufficient**	
Cognitive performance	Sleepiness and vigilance	**yes**	**Sufficient**	**Proven effect**
	Cognitive performance	**yes**	**Limited** Six studies out of 11 show an association.	**Probable effect**
Psychological health		**yes**	**Limited** Eighteen studies out of 20 show an association between night work (fixed or rotating) and diminished mental health. A more indirect link in the other eight studies is mediated by psychosocial risk factors associated with the content and organisation of night work. It is not possible to exclude all bias and confounding factors.	**Probable effect**
Cancer	Breast cancer	**yes**	**Limited** There is more evidence supporting an effect of work, including night work, than in 2010; however, it is limited, because it is not possible to rule out the existence of bias with a sufficient degree of certainty.	**Probable effect**
	Prostate cancer	**yes**	**No conclusion can be drawn**	
	Other cancers (ovarian, pancreatic, colorectal)	**yes**	**No conclusion can be drawn**	
Cardiovascular diseases	Metabolic syndrome	**yes**	**Sufficient**	**Proven effect**

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and metabolic disorders	Obesity or excess weight	**yes**	**Limited** Several case-control studies show a significant association with night shift work. One cohort study, despite its methodological limitations, suggests deleterious effects	**Probable effect**
	Type 2 diabetes	**yes**	**Limited** A significant dose-response relationship between the duration of shift work with night hours and the risk of type 2 diabetes was shown in two cohorts.	**Probable effect**
	Dyslipidaemias	**yes**	**No conclusion can be drawn**	**Possible effect**
	Coronary heart diseases	**yes**	**Limited** Selection and information bias affect most of the studies.	**Probable effect**
	High blood pressure	**yes**	**No conclusion can be drawn**	**Possible effect**
	Ischaemic stroke	**yes**	**No conclusion can be drawn**	**Possible effect**

Recommendations of the collective expert appraisal

According to Article L. 3122-32 of the French Labour Code, the use of night work must remain exceptional and take into account the requirements to protect the health and safety of workers. It must also be justified by the need to ensure the continuity of economic activity or services of social value. It cannot be implemented without collective bargaining.

Night work concerns a considerably large population. In 2012, 15.4% of employees, or 3.5 million people, worked at night, regularly or occasionally. This corresponds to a million employees more than in 1991, and this increase concerns women in particular. The working conditions of these employees are more difficult than for others: they are subjected to more numerous physical hardship factors, greater time pressure, and more frequent tensions with their colleagues or the public.

Recommendations for preventing the risks associated with exposure to night work

The health risk assessment conducted by the Working Group on "Atypical working hours" concluded as to the existence of a number of possible, probable and proven human health effects of shift work including night work.

The CES therefore recommends, by application of the principles of primary prevention used in the occupational health field, eliminating night work if possible or, failing this, reducing the number of people working these types of hours.

In the event that it is impossible to eliminate this way of organising working time, the CES recommends that various means of prevention be implemented to reduce the impact of night work on the health of the employees concerned.
In terms of recommendations at work:

- adjust the length of the night shift according to the arduous nature of the tasks (physical or mental load, *etc.*) and their conditions of execution (physical or environmental atmosphere of the work);
- adjust the nature of the night worker's tasks in particular by taking care to reduce constraints relating to rate, physical effort, attention, memory, *etc.*;
- shorten rather than lengthen the duration of night shifts, in order to avoid combining the negative effects of circadian desynchronisation with those of sleep pressure and sleep debt;
- favour a maximum number of weekends of rest;
- increase the number of days of rest and preferably arrange them after the night shift, to enable a faster recovery from fatigue and lack of sleep;
- insert appropriate rest breaks during the shift, leaving sufficient time to encourage short naps, and improve rest conditions;
- organise sufficient overlap time between the shifts, and therefore between teams, to enable the transmission of oral information that enhances the quality of the work, safety, and reliability;
- promote the collective aspect of the work to limit worker isolation, enable quality social support, increase the reliability of the system, and enable error recovery;
- when designing shift and night work schedules, take into account the balance between the different spheres of life (life at work and life outside work) on which the employees' state of health also depends;
- get personnel involved in drawing up shift work systems;
- give employees the option of organising their tasks and leave them room to manoeuvre when deciding on their chronological order, according to the fluctuation of their cognitive and physical capabilities;

- encourage suitable lighting that helps maintain vigilance during the shift and improve the quality of sleep at home (increase light during the night shift, and then sleep in the dark).

In terms of the recommendations for prevention stakeholders (occupational physicians, committees on health, safety and working conditions, general practitioners, safety engineers, staff representatives, *etc.*):

- insist on the importance of fostering quality sleep at home.

Moreover, information campaigns on the risks associated with night work should be conducted among physicians.

Lastly, the CES reiterates the conclusions of the Working Group, which stated that anything that reduces desynchronisation and sleep debt is favourable in principle, but that care should be exercised in the general recommendations, firstly due to inter-individual variability (in chronotype, sex, age, *etc.*), and secondly because of work organisation elements that may be favourable for one shift but may prove unfavourable for a team on another shift. Some other means of prevention, listed in the report, currently suffer from a lack of consensus in the scientific community, either because of a lack of studies or contradictory results. These are listed below:

- limiting the number of consecutive night shifts: there is no consensus on an acceptable number of nights;
- adopting rapid rotation regimes in order to limit the number of consecutive night shifts could be favourable to sleep, but unfavourable to circadian rhythmicity: there is no consensus on the best frequency to adopt;
- generally preferring to rotate shifts in a clockwise direction (morning/afternoon/night), because it follows the natural periodicity of most individuals' biological circadian rhythms (except for morning chronotypes for which an anticlockwise rotation may be less detrimental), and in order to benefit from longer rest periods between shifts;
- not starting the morning shift too early, in order to limit sleep debt and avoid excessive daytime sleepiness;
- not finishing too late in the evening, in order to limit family desynchronisation.

Recommendations concerning possible directions for scientific research

For experimental studies

The CES reiterates:

- that there are too few experimental studies in humans;
- that the nocturnal models (in particular rats and mice) are unsuitable for assessing the health effects of night shift work: animal studies are usually conducted in nocturnal rodents that are sensitive to light, very different from diurnal animals and human beings. It is not possible to reproduce the equivalent of night or shift work in nocturnal animals;
- that the majority of animal studies are carried out on males (to avoid interference from hormonal cycles);
- the failure to systematically take modulators (such as age, sex and chronotype) and environmental influences into account.

The CES therefore recommends:

- prioritising experimental studies in diurnal animal models and humans;
- promoting experimental studies on animal models, in males and females in equal measure;
- studying the effects of co-exposures and environmental influences in the experimental studies;
- for the experimental studies in humans, clearly defining the model of shift/night work and the types of tasks performed;
- assessing the effect of key modulators such as age, sex and chronotype.

For epidemiological studies

The CES reiterates:

- the many methodological limitations identified during the analysis of the epidemiological studies, in particular with regard to characterisation and duration of exposure, or accounting for confounding factors and the "healthy worker" effect;
- the fact that modulating effects and differences in work content and organisation between day and night shifts are not adequately taken into account;
- the uncertainties that persist concerning the effects of shift/night work on some cancers and other poorly documented diseases.

Accordingly, the CES recommends:

- implementing studies to gain a better understanding of the effect of co-exposures and interactions between night shift work and other risk factors;
- ensuring a better characterisation of exposure in epidemiological studies, using standardised questionnaires (IARC workshop 2009; Stevens, 2011), incorporating the following parameters when possible:
    - the type of shift work (continuous or semi-continuous);
    - the time at which the shift begins and ends;
    - the duration of the shifts considered;
    - the type of system (rotating or fixed);
    - the speed and direction of rotation;
    - the regularity or irregularity of the rotation cycle;
    - the cumulative duration of the shift work;
    - the number and position of rest periods between shifts.
- implementing studies to assess prevention policies

It is also important, in these studies, to assess the personal and behavioural aspects of the workers, such as sleep quantity and quality, diet, commute duration between home and the workplace, exposure to light during the night, chronotype, and the duration of exposure to these working hours. The CES recommends:

- better characterising the study populations: age at the time of the study, age when starting shift work including partial nights or number of years of exposure, sex, family situation (number and age of children), chronotype, sleep duration during and outside the work period, light exposure profiles, *etc.*;
- ensuring that confounding factors and factors specific to the considered effect are better taken into account. This entails more effectively assessing certain personal and behavioural aspects of the workers, such as sleep quantity and quality, diet, light

exposure during the night, chronotype, alcohol and tobacco consumption, type of housing, *etc.*;

- favouring longitudinal (cohort or case-control) studies in order to better appraise the causal relationship, the healthy worker effect and the dose/response relationship (thresholds);
- in the large general cohort studies under way, integrating information on the characterisation of exposure and of populations, and taking confounding factors into account.

It also recommends, with regard to the studies on cancer:

- that the associations between night work and breast cancer should, when possible, be studied separately in women working in varied industry sectors, in order to assess the possible effects of different systems of working hours;
- precisely characterising the sub-groups of individuals (menopausal status, breast cancer tumour receptors) that could be differently associated to night work. In the immediate future, the Expert Committee recommends that initiatives be taken to analyse existing studies in groups, by characterising exposure uniformly from available data. Such an analysis would enable the stratification of individuals by sub-group (menopausal status, main sectors of activity, hormonal receptors) while maintaining a satisfactory statistical power.

<u>For studies on the secondary means of prevention</u>[10]

Considering the lack of consensus on:

- the preferable direction of rotation (clockwise/anticlockwise);
- the acceptable number of consecutive night shifts;
- the frequency of rotations (fast/slow) that is least detrimental to the physiology;
- the best chronobiological approaches for fostering circadian synchronisation and the quality of wakefulness and sleep;
- the use of melatonin supplements;
- the effectiveness of pharmacological approaches;

the CES recommends conducting experimental studies in the laboratory and in real conditions, in which subjective and quantitative assessments of the impact of night work are carried out (on the amplitude and phase of the circadian system, sleep, sleepiness, cognition, metabolism, cardiovascular diseases, immunity, light exposure), making it possible to;

- assess the effect of the direction of rotation (clockwise/anticlockwise), and the association between the effect and the chronotype of individuals;
- seek the existence of a threshold for the number of consecutive night shifts without an effect;
- determine the frequency of rotations (fast/slow) that is least detrimental to the body and to the well-being of individuals;
- assess the chronobiological approaches confirmed as effective in the laboratory for fostering circadian synchronisation and improving the quality of vigilance and sleep:
    - o napping before and during the night shift;

[10] In secondary prevention, the measures involve identifying the health problem at its earliest stage and applying a fast and efficient treatment to limit the adverse consequences.

  - increasing light intensity during the shift;
  - reducing exposure to light in the morning and during the day;
  - determining the optimal hours for phototherapy.
- determine rapidly (the same day) and precisely the phase of the circadian system (internal clock), in order to be able to optimise the effectiveness of the abovementioned chronobiological approaches (and determine the ideal time to increase and decrease exposure to light in order to favour synchronisation of the circadian system);
- determine optimal times for administering melatonin for its sleep-inducing effect and its synchronising effect on the circadian clock. As these times are dependent on the internal clock of individuals, it will be necessary to precisely determine the phase of their circadian system (see above point);
- assess the relevance and effectiveness of pharmacological approaches to promote synchronisation of the circadian system (melatonin supplements) and increase vigilance during the shift (caffeine, *etc.*).

In addition, considering:

- the difficulty of quantifying the change in sleep time;
- the lack of consensus on the definition of fatigue;
- the difficulties encountered by the Working Group in accessing data, in particular on occupational accidents and commuting accidents;

the CES recommends:

- quantifying the change in the time and number of sleep episodes using actigraphy;
- developing studies on fatigue, in order to obtain a better metrological assessment, as well as scales suited to the different types of fatigue: physical, cognitive, psychological;
- conducting studies on accidentology at work, with a methodology that would make it possible to jointly analyse the content of the work and the "time" aspects of accidents: time of occurrence, shift concerned, its place in the rotation, *etc.*;
- proposing a reflection process on the under-reporting of accidents during or after night/rotating shifts;
- conducting studies to understand the determinants of the under-reporting of occupational accidents at night or following the night shift, from the perspective of both employers and employees;
- examining in greater detail the link between night work and the severity of occupational accidents;
- promoting the availability of data from studies conducted in companies (internal reports/grey literature) to researchers, in order to enhance knowledge on the effects of this type of time organisation in an actual work context – consider a process for anonymising companies if there are concerns about the organisation's structure being revealed. The data collection methods should be available to judge their quality and limitations.

For studies on the socio-economic impact of night shift work

Considering:

- the absence of data on the social and economic cost of night work and shift work;
- the results of studies on family and social life;

the CES recommends:

- implementing sociological and economics studies on the social and economic cost of night shift work, in order to put into perspective the economic benefits gained and the social costs incurred (occupational accidents, occupational diseases, absenteeism, staff turnover, *etc.*) both on a company and society level (indirect negative consequences of shift and/or night work);
- expanding the framework of analysis to the entire family unit and not being limited to exclusively studying the effects on the workers themselves: accentuating research on the impact of shift work including night work on family life (relationships with partners and children, schooling of children, *etc.*);
- developing studies on women working shifts including at night, as well as single-parent families;
- continuing scientific work on the social life of night shift workers in order to shed light on the social impact created by these hours.

For ergonomic and qualitative studies

Considering:

- the need to distinguish the effects of the work schedule from that of the specific requirements of the profession itself, in order to understand their respective impacts on health and personal life;
- the need to take into account the reality of turnover and the reality of the actual work performed, rather than focusing solely on what is planned and authorised;
- the need to understand the adjustments made by employees in order to manage the impacts of shift work, including at night, on their health and personal life;
- the lack of studies in ergonomics, sociology and, more generally, the human and social sciences on the subject;

the CES recommends:

- continuing work to precisely characterise the work situations, working conditions, the content and requirements of the shift and night workers' tasks;
- carrying out qualitative studies in work situations based on real work, with various shift systems (2x12h, *etc.*);
- conducting studies or research-actions to assess the organisational means of prevention for shift and night work (collective work, naps, tools promoting work/family reconciliation, *etc.*).

The Expert Committee on "Physical agents, new technologies and development areas" adopted the collective expert appraisal work along with its conclusions and recommendations as described in this collective expert appraisal summary, at its meeting of 15 March 2016. One of its members, Pierre Ducimetière, abstained from the vote on the validation of the collective expert appraisal summary, invoking a disagreement on the editorial form, but not on the substance.

Date of validation of the report by the Expert Committee: 15 March 2016

Acronyms and abbreviations

OA: Occupational accidents
CES: Expert Committee *(« Comité d'experts scientifiques »)*
CFTC: French Confederation of Christian Workers
CGPME: General Employers' Confederation for Small and Medium Enterprises
CHSCT: Committee on health, safety and working conditions
IARC: International Agency for Research on Cancer
CNAMTS: National Health Insurance Fund for Salaried Workers
DARES: Directorate for research, studies and statistics
WG: Working Group
HAS: French National Authority for Health
MEDEF: French Employers' Confederation
Sumer: A periodic survey reporting on medical surveillance of exposure to occupational risks

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Glossary

Incidence: the incidence is the number of new cases of disease, in relation to the size of the population, occurring during a given time period, usually a year.

Confidence Interval (CI): the rough estimate of the statistical analysis aims to quantify the studied effect and the degree of certainty of this estimate through a confidence interval (CI), which generally identifies a range of values on both sides of the estimate. A 95% CI represents the range within which there is 95% certainty of finding the actual value.

If the confidence interval includes 1, it is considered that there is no significant difference between the two groups studied.

Prevalence: the prevalence is the ratio between the number of people affected by a disease at a given time and the size of the population.

Relative risk (RR): the relative risk corresponds to the proportion of sick individuals among those exposed to the studied risk factor in relation to the proportion of sick individuals among those not exposed.

The relative risk is used to express the association between an exposure (to a treatment or a risk factor) and a disease: it is the factor by which the risk of disease is multiplied in the presence of the exposure.

Odds ratio (OR): The odds ratio (abbreviated to "OR") is one of the ways of quantifying the association between a property A (for example: existence or not of a disease) and a property B (for example: existence or not of an exposure), determined for all individuals in a population. The odds ratio corresponds to the ratio between the odds "presence of A/absence of A" among the individuals exposed to B, and the odds "presence of A/absence of A" among individuals not exposed to B. In some circumstances, it is interpreted in the same way as a relative risk.

Main types of epidemiological studies:

- ecological studies examine the association between exposure and disease on data aggregated by geographical or time-related unit;
- cross-sectional studies examine, for each individual in the study, their exposure and the presence of disease at a given time point;
- case-control studies are used to compare the frequency of past exposure of a sample of cases (sick individuals) to that of a control sample of individuals not suffering from this disease, which must be representative of the population from which the cases are drawn;
- cohort studies are used to compare the occurrence of diseases between non-exposed individuals and individuals subjected to the exposure of interest, monitoring the incidence of diseases over time.

1 Background, purpose and procedure for handling the request

1.1 Background

The request for a risk assessment for professionals exposed to atypical working hours, in particular those working at night, comes within a specific socio-economic and scientific context: the way in which work is organised is changing, with an enormous number of workers today being concerned by atypical work rhythms.

The "standard" work week is defined by four criteria: hours worked between 7 am and 9 pm, five days of full-time work (at least 5 hours of work per day), weekly duration between 35 and 44 hours, and two consecutive rest days. The expression "atypical hours" applies to all working time arrangements situated outside the framework of the "standard" week. The best-known forms of atypical hours are shift work, night or evening work, and weekend work. Atypical hours also include disjointed working hours, compressed work schedules and work hours that can change from day to day. The concept of atypical work hours is very broad, and was therefore defined precisely for the purpose of the Agency's work.

The adoption of the proposed law on professional equality of men and women in 2001 removed the legal ban on women working at night, mainly to bring French law into compliance with European law. The number of night workers has almost doubled in twenty years, as can be seen in the latest study by the Directorate for Research, Studies and Statistics (DARES), published in August 2014 (DARES, 2014).

The health effects on workers of atypical hours constitute a complex field of study that requires the application of a wide variety of scientific disciplines. The most frequently cited effects are: sleep and disorders of vigilance, an increase in the risk of accidents, an increase in the risk of certain cancers (especially breast cancer in women), and endocrine disruption (in particular increasing the risk of obesity). New scientific studies in the past few years have supplemented the available data, which led the International Agency for Research on Cancer (IARC) in 2007 to add night shift work to the list of agents that are "probably carcinogenic to humans" (Group 2A). In turn, the French National Authority for Health (HAS) published a report in 2012 issuing recommendations for medical-professional monitoring of shift and/or night workers.

1.2 Purpose of the request

In this context, in March 2011, ANSES received a formal request from the French Confederation of Christian Workers (CFTC) to conduct an assessment of the health risks for professionals exposed to atypical working hours, especially those subject to night work, whether or not this is regular (see Annex 1).

Following the IARC's evaluation work in 2007 and the classification of night work in Group 2A as "probably carcinogenic", on the basis of epidemiological studies mainly conducted on nurses and flight attendants, the CFTC asked about extending this finding to all workers subjected to atypical working hours.

In response to this request, ANSES proposed initially carrying out an expert appraisal of the health risks to which professionals are exposed when working night hours and, more specifically, those exposed to night work and shift work including night hours. The health effects potentially associated with other forms of atypical working hours could be assessed as part of a second phase of the expert appraisal.

The different elements examined in the context of this request are as follows:

- a reminder of the regulatory definitions of shift work and night work;
- a current overview of night work and shift work in France;
- a review of knowledge on biological rhythms, their regulation by a system of biological circadian clocks, and a presentation of the impacts of the disruption of this circadian system induced mainly by atypical working hours;
- an international review of expert appraisals on shift work;
- a review of the socio-economic aspects surrounding shift work including night work;
- an assessment of the health effects associated with night work and shift work including night work;
- a review of the qualitative studies on the realities of situations involving shift work with night hours;
- a review of the means of prevention reported by the literature.

1.2.1 Types of atypical working hours studied

Mainly following exchanges between ANSES and representatives of the CFTC, and with MEDEF and the CGPME (hearings of 15 February 2013), and considering the diversity of situations of exposure to atypical working hours, the Agency decided to conduct the expert appraisal in two phases:

- an initial phase addressing the question of shift work and night work, for which data on the health risks are already available;
- a second phase, which will consist in assessing the health risks associated with other forms of atypical working hours, and will require an adapted expert appraisal approach.

1.2.2 The health effects studied

Given the large number of health effects identified, the effects to be studied were ranked in order of priority (see Section 6).

1.3 Procedure: means implemented and organisation

ANSES entrusted the Working Group (WG) on "Assessment of the health risks for professionals exposed to atypical working hours, especially night work" with responding to this formal request, reporting to the Expert Committee (CES) on "Physical agents, new technologies and development areas". The first meeting of the WG was held in November 2012.

The work was mainly based on a summary and critical analysis of data published in the literature (scientific articles, reports, *etc.*).

The Working Group also interviewed external experts likely to contribute useful information and additional data for the expert appraisal (context, health effects, *etc.*).

An international consultation was held with national agencies and authorities in the areas of health and/or occupational safety (Europe and North America), in order to find out about studies conducted abroad and the particular health effects studied.

Lastly, a Research and Development Agreement (RDA) was drawn up between ANSES and the French National Institute for Health and Medical Research (INSERM), with the aim of exploiting field data from the national survey on "Medical surveillance of exposure to occupational hazards" (Sumer) conducted by DARES and the Directorate General for Labour (DGT) - Occupational Health Inspectorate.

The methodological and scientific aspects of the WG's expert appraisal work were regularly submitted to the CES. The report issued by the WG takes into account the comments and additional information provided by the members of the CES. This work was therefore conducted by a group of experts with complementary skills.

The Group's work was adopted by the CES at its meeting on 9 February 2016.

The expert appraisal was carried out in compliance with French standard NF X 50-110 "Quality in Expert Appraisal Activities – General Requirements of Competence for Expert Appraisals" (May 2003) with the aim of respecting the following points: competence, independence and transparency.

1.4 Prevention of risks of conflicts of interest

ANSES analyses the relationships of interest declared by the experts prior to their appointment and throughout the work, in order to avoid potential conflicts of interest with regard to the matters dealt with as part of the expert appraisal.

The experts' declarations of interests are made public *via* the ANSES website (www.anses.fr).

2 Regulations, definitions and reality of atypical working hours in France

2.1 Definitions and regulations

Warning: A legal review was carried out in April 2015. All the information contained below was applicable on the date this review took place. This section is not indicative of any possible changes to the regulations between April 2015 and the date of publication of this collective expert appraisal report.

2.1.1 Regulations applicable to night work

2.1.1.1 The history of night work regulations in France

Until 2001, French domestic law contained very few provisions relating to night work (examples: the ban since 1892 on night work for women in industry and Article 24 of Act No. 91-1 of 3 January 1991).

It was in fact Act No. 2001-397 of 9 May 2001 *on professional equality between men and women* that provided a precise legal framework for night work. This Act was also an opportunity, for French legislators, to bring national law into line with European Union law. This text, removing the ban on night work for women, in fact arose in response to rulings made by the Court of Justice of the European Communities (CJEC), which later became the Court of Justice of the European Union (CJEU).

French law applicable to night work is therefore the result of Act No. 2001-397 of 9 May 2001, Decree No. 2002-792 of 3 May 2002 and DRT Circular No. 2002-09 *on night work,* which comments on the entire system. Act No. 2001-397 of 9 May 2001 therefore transposed, with some delay, Council Directive 93/104/EC of 23 November 1993 into French law.

Directive 93/104/EC concerning certain aspects of the organisation of working time was then amended for the first time by Directive 2000/34/EC of 22 June 2000 (OJEU L. 195 of 1 August 2000, p. 41). This Directive was once again amended and consolidated by Directive 2003/88/EC of 4 November 2003 (OJEU L. 299 of 18 November 2003, p. 9). In its Article 27, this new Directive provides for the repeal of Directive 93/104/EC, as amended by Directive 2000/34/EC. Only Directive 2003/88/EC therefore remains applicable. As such, it should be clarified that even though Directive 93/104/EC was substantially amended, only marginal changes have been made to the provisions specific to night work and shift work (Articles 8 to 13), mainly concerning cases of derogation from the maximum daily duration of 8 hours for night workers (Article 17).

Changes to European Union regulations on night work are soon likely to emerge, insofar as the European Commission has begun a complete review of Directive 2003/88/EC *on working time* in order to take into account the "*fundamental changes that have occurred in the world of work and the economy*". A public consultation on this review was organised, which ended on 18 March 2015 (http://ec.europa.eu/). This review is therefore ongoing.

2.1.1.2 Definitions of night work and the night worker

2.1.1.2.1 Definitions in European Union law

Article 2 of Directive 2003/88/EC defines "*night time*" as:

"any period of at least seven hours, as defined by national law, and which must include, in any case, the period between midnight and 5:00."

The same provision defines "night worker" as:

"a) on the one hand, any worker who, during night time, works at least three hours of his habitual daily working time; and
b) on the other hand, any worker who is likely to, during night time, work a certain proportion of his annual working time, defined according to the choice of the Member State concerned:
i) by national legislation, following consultation with the two sides of industry; or
ii) by collective agreements or agreements concluded between the two sides of industry at national or regional level; […]."

Concerning the definition of "night worker", differences emerge between Member States. In Ireland, for example, a night worker is one who normally works three hours of his daily working time between midnight and 7am and who works at night for at least half of his working time over the course of a year (*Organisation of Working Time Act*, 1997 and http://www.citizensinformation.ie). In the United Kingdom, a night worker is, in principle, defined as one who typically works three hours of his daily working time at night, which, by default, is set between 11pm and 6am. Different definitions can, however, be laid down by collective agreement or workforce agreement (*The Working Time Regulations*, 1998 and https://www.gov.uk/night-working-hours/).

2.1.1.2.2 Definitions used in French domestic law

Definitions of night work

There is not one but several definitions of night work in French law.

2.1.1.2.2.1 The legal definition

In compliance with the minimum requirements laid down by European Union law, French legislators defined night work in Article L. 3122-29 of the French Labour Code as "*any work* [performed] *between 9pm and 6am*" (Article L. 3122-29, Subparagraph 1, of the Labour Code), subject to specific provisions laid down for young workers.

This legal definition is the result of choices made by French legislators on the basis of the options offered to them by European Union law. Other Member States have thus been able to retain a different legal definition of night time. This is particularly the case in Germany, where "night work" is defined as any work of a duration greater than two hours during the period of time between 11pm and 6am[11]; in Italy, where night time includes at least seven consecutive hours including the interval between midnight and 5am[12]; or in Belgium, where night work is understood to mean work carried out between 8pm and 6am[13].

2.1.1.2.2.2 The convention-based definition

Besides this legal definition, the French Labour Code allows for the possibility of establishing by extended collective labour convention or agreement, or company or establishment agreement, another period of nine consecutive hours, between 9pm and 7am. The period thus defined must then include the interval between midnight and 5am (Article L. 3122-29, Subparagraph 2 of the Labour Code). This is a requirement laid down by European Union law (Article 2 of Directive 2003/88/EC).

2.1.1.2.2.3 The definition after authorisation by the labour inspector

[11] Article 2 of the Act *on working time*, Arbeitszeitgesetz; ArbZG.

[12] Article 1 d) of Legislative Decree No. 66 of 8 April 2003 *transposing Directives 93/104/EC and 2000/34/EC and relating to certain aspects of the organisation of working time*.

[13] Article 35 of the Act of 16 March 1971 *on work*.

In the absence of an agreement and when warranted by the specific characteristics of the company's activity, the change to the adopted period may also be authorised by the labour inspector, following consultation of the trade union delegates and an opinion by the works council or employee delegates where they exist (Article L. 3122-29, Subparagraph 3 of the Labour Code).

2.1.1.2.2.4 The case of specific activities

Besides these principles, French legislators have provided for derogations for activities relating to editorial and industrial production of press, radio and television, cinema production and exhibition, live performances and discotheques. For these activities, night time is fixed between midnight and 7am. Here too, it is possible to establish another period by extended collective branch convention or agreement, or collective company or establishment agreement. In accordance with Directive 2003/88/EC, this period of substitution must include the interval between midnight and 5am (Article L. 3122-30 of the Labour Code).

<u>The night worker</u>

It is not enough to work occasionally at night to be considered a "night worker" and to benefit from the guarantees inherent to this status. Indeed, in application of the provisions of Article L. 3122-31 of the Labour Code, a night worker is a worker:

- whose usual working hours lead them, at least twice a week, to perform at least three hours of their daily working time in the period considered as night work in their company, or;
- who, during a reference period, performs a minimum number of hours of night work in the period defined as such in the company. The minimum number of hours of night work and the reference period are, in principle, determined by an extended collective labour convention or agreement. In the absence of such convention provisions, a night worker is considered to be an employee who performs, over a period of 12 consecutive months, 270 hours of night work (Article R. 3122-8 of the Labour Code).

2.1.1.3 <u>The scope of night work</u>

2.1.1.3.1 The companies and employees concerned by night work

<u>The companies concerned</u>

All industry sectors are concerned by the regulations on night work (Article L. 3111-1 of the Labour Code), it being understood that specific provisions are laid down for the travelling and flying personnel of transport companies mentioned in Article L. 1321-1 of the French Transport Code (Articles L. 1321-6 to L. 1321-8 of the Transport Code). In particular, Articles L. 3122-34 and L. 3122-35 of the Labour Code relating to the maximum daily and weekly working times for night workers are not applicable to them (Article L. 1321-6 of the Labour Code). A specific definition of night work is also laid down for the travelling and flying employees of transport companies (Article L. 1321-7 of the Labour Code).

<u>The employees concerned</u>

Directive 2003/88/EC expressly stipulates in its Recital 12 that its provisions are not applicable to seafarers due to the fact that "*a European Agreement in respect of the working time of seafarers has been put into effect by means of Council Directive 1999/63/EC of 21 June 1999 concerning the Agreement on the organisation of working time of seafarers, concluded by the European Community Shipowners' Association (ECSA) and the Federation of Transport Workers' Unions in the European Union (FST), based on Article 139(2) of the Treaty*".

In France, the regulations relating to night work apply to all employees, men and women, over the age of 18, including company trainees (Article L. 124-14 of the Education Code).

In principle, night work is prohibited for young employees under the age of 18 (Articles L. 3163-2 and L. 6222-26 of the French Labour Code, Article 10 of Directive 2003/88/EC, Article 9 of Council Directive 94/33/EC of 22 June 1994 *on the protection of young people at work* and Article 7.8 of the European Social Charter).

As such, Article L. 3163-1 of the Labour Code provides different definitions of night work for employed minors. In application of this text, night work is considered to be:

- for young people over 16 and under 18 years of age, any work between 10pm and 6am.
- for young people under 16 years of age, any work between 8pm and 6am[14].

Derogations may, however, be granted by the labour inspector, in particular for a few sectors (hotels, catering, bakery, horse shows and racing), listed exhaustively by the Labour Code and under certain conditions (Article L. 3163-2 and R. 3163-1 to R. 3163-5 of the Labour Code). In any case, no derogation is possible between midnight and 4am, except in cases of extreme urgency (Articles L. 3163-2, Subparagraph 4, and L. 3163-3 of the Labour Code).

2.1.1.3.2 The exceptional nature of the use of night work

The conditions for the use of night work are strictly regulated. According to Article L. 3122-32 of the French Labour Code, the use of night work must remain exceptional and take into account the requirements to protect the health and safety of workers. It must also be justified by the need to ensure the continuity of economic activity or services of social value. This last condition is not fulfilled, for example, in the food trade (Court of Cassation, Criminal Division, 2 September 2014, No. 13-83.304) or the perfumery trade (Court of Cassation, Social Division, 24 September 2014, No. 13-24.851).

Article L. 3122-32 of the French Labour Code thus confirms the general principle according to which the use of night work must remain exceptional. The provisions of this text have been declared in keeping with the Constitution (Constitutional Council, 4 April 2014, QPC No. 2014-373).

In "reaction" to the *Sephora* ruling, the Macron Bill[15] endeavoured to find a balance between firstly, the necessarily exceptional nature of night work due to its proven harmfulness to employee health, and secondly, the need to take into account criteria of the commercial attractiveness of tourist areas as well as the particular profitability of opening shops at night. In substance, the Bill intends to authorise mainly retail outlets located in international tourist zones (ZTI) to employ staff until midnight. However, this possibility would be subject to the following terms and conditions:

- a collective agreement should stipulate this option as well as a number of measures in favour of the employees, including a means of transport provided and paid for by the employer to allow them to return home;
- each of the hours of work performed during the period established between 9pm and the beginning of the period of night work (which may be deferred until midnight) must

[14] Note that Article 9 of Directive 94/33/EC retains the age of 15 years as a criterion for applying one or other of the night time periods.

[15] Article 81 of the Bill for *growth, activity and equality of economic opportunities*, Adopted Text No. 473, "Minor Bill", 19 February 2015. On 19 February 2015, following the rejection of the motion of no confidence tabled by the opposition following the Prime Minister's decision to hold the government responsible for this text under Article 49.3 of the Constitution, the Bill was in fact adopted at its first reading in the National Assembly and sent to the Senate. It was to be discussed by the Senate in a public meeting on 7 April 2015.

be paid at a rate at least double that normally due and give rise to compensatory rest of equivalent duration.

Only volunteering employees who have given their agreement in writing to their employer will be able to work between 9pm and midnight.

2.1.1.4 Implementation of night work

2.1.1.4.1 The prior formalities

Under French domestic law, employers wishing to establish or expand night work within their company must first submit their plan to a number of bodies. First of all, they must consult the works council, or in its absence, the employee delegates. Indeed, in the framework of its economic powers, the works council must be informed and consulted on general issues relating to working conditions resulting from the organisation of work (Article L. 2323-27 of the Labour Code).

The employer must then consult the CHSCT (Committee on health, safety and working conditions). While the provisions relating to night work contained in the Labour Code do not require the intervention of the CHSCT, this committee does however seem legitimate in that (i) the CHSCT must be consulted prior to any major organisation decision amending the health and safety conditions or working conditions (Article L. 4612-8 of the Labour Code) and (ii) the works council can call on it for an opinion or commission it to conduct a study on any matter within its competence (Articles L. 2323-27, Subparagraph 2 and L. 2323-28 of the Labour Code).

2.1.1.4.2 The principle: mandatory use of collective bargaining

The implementation of night work, as well as its extension to new categories of employees, is subject to the prior conclusion of an extended collective branch convention or agreement, or company or establishment agreement (Article L. 3122-33, Subparagraph 1 of the Labour Code). The collective convention or agreement must include the justifications for the use of night work (Article L. 3122-33, Subparagraph 2 of the Labour Code).

The agreement must, in addition, stipulate[16]:

- the types of jobs potentially concerned by night work;
- compensatory measures in the form of rest and, where appropriate, salary;
- measures to improve the employees' working conditions (example: designated break or dining rooms);
- measures to facilitate coordination of the employees' night work activity with their family and social responsibilities, in particular concerning means of transport (example: provision of a vehicle and a secure car park, employee buses, *etc.*);
- measures to ensure professional equality between men and women, in particular through access to training;
- organisation of break times.

Lastly, where convenient, measures to ensure employee safety could be stipulated in the agreement (example: emergency telephones, provision of alarm devices, security guards, ban on working alone, *etc.*).

[16] DRT Circular No. 2002-09 of 5 May 2002 *on night work*, NOR: MEST0210106C.

2.1.1.4.3 The exception: assignment to night work after authorisation by the labour inspector

In the absence of any collective labour convention or agreement, the employer can assign employees to night shifts when authorised by the labour inspector (Article L. 3122-36 of the Labour Code). To be authorised by the labour inspector to resort to night work, employers must be able to justify having entered into fair and serious negotiations, in the 12 months preceding the application, in view of implementing night work in the company. This implies that they have (i) convened the representative trade union organisations in the company, (ii) established the venue and schedule for meetings, (iii) communicated to the parties all information necessary for the negotiation and (iv) responded to any proposals from the trade union organisations.

Employers must also (Article R. 3122-16 of the French Labour Code):

- justify the constraints specific to the nature of the activity or the company's operation that make the night work necessary, in view of the requirements relating to continuity of economic activity or services of social value;
- ensure a number of points, mainly the existence of compensatory measures and break times;
- demonstrate that they have taken into account the employees' health and safety imperatives;
- attach to their application the opinion issued by the works council, or in its absence, the employee delegates. In the absence of any staff representative body, employers should send the labour inspector any document certifying that employees have been given prior notification.

2.1.1.5 <u>The protective status of the night worker</u>

2.1.1.5.1 Duration of the night work

<u>Maximum daily working time</u>

Under French domestic law, the daily period of work performed by a night worker may not exceed eight hours (Article L. 3122-34, Subparagraph 1, of the Labour Code). The distinction made in the European Directive was not therefore adopted by French legislators.

DRT Circular No. 2002-09 specifies that the maximum daily working time "is defined as eight consecutive hours over the period worked by the night worker, which can include all or part of the night work reference period." It therefore matters little that not all the working hours are actually at night.

2.1.1.5.1.1 Derogations

French legislators have only partly adopted the derogations to the maximum daily duration of eight hours provided for by Directive 2003/88/EC and specify, for each of the derogations adopted, the procedures that employers must follow to be authorised to use them. As such, Article L. 3122-34 of the Labour Code accepts a derogation from the maximum daily eight hours by collective agreement or when authorised by the labour inspector. Article R. 3122-14 of the same Code also accepts that employers may derogate from it, under their own responsibility, in certain circumstances.

Article 3.2 of DRT Circular No. 2002-09 of 5 May 2002 considers that the derogation from the maximum daily duration of eight hours, laid down by collective agreement or when authorised by the labour inspector, can increase this to 12 hours.

<u>Maximum weekly working time of night workers</u>

Article L. 3121-35, Subparagraph 1 of the Labour Code also sets the maximum weekly working time in principle for all employees at 48 hours. Derogations are however provided for.

Thus, for night workers, under French domestic law, the maximum weekly working time is lowered to 40 hours over 12 consecutive weeks (Article L. 3122-35 of the Labour Code). There are, however, two types of derogation to this maximum duration:

- convention-based derogations: when warranted by the characteristics specific to the activity of a sector, the maximum weekly working time may be extended to 44 hours over 12 consecutive weeks, by extended branch convention or agreement, or company or establishment convention or agreement. According to DRT Circular No. 2002-09, "A parallel can be drawn with the sectors that structurally fall within the scope of the derogations to the maximum daily working time".
- regulatory derogations: Article L. 3122-35, Subparagraph 3 of the Labour Code has also laid down the possibility of establishing by decree the list of sectors for which the weekly working time is set between 40 and 44 hours over 12 consecutive weeks.

<u>Break times</u>

The collective agreement establishing the night work must stipulate break times, which may include the minimum break of 20 minutes that must be granted to employees as soon as the daily working time reaches 6 hours (Article 6 of Directive 2003/88/EC, Article L. 3121-33 of the Labour Code and DRT Circular No. 2002-09 of 5 May 2002 *on night work*).

The employer has the same obligation when the night work has been implemented after authorisation by the labour inspector.

<u>Minimum daily rest</u>

Night workers must be allowed a daily rest period of at least 11 consecutive hours, which must be taken immediately at the end of the work period (Article 3 of Directive 2003/88/EC, Article L. 3131-1 of the Labour Code and Court of Cassation, Social Division, 27 June 2012, No. 10-21.306). Thus, an employee working from 6pm to 2 in the morning may not resume their shift before 1pm (Article 2.2 of DRT Circular No. 2002-09).

2.1.1.5.2 Compensatory measures for night work

Alongside the compensatory measures laid down in the event of derogation from the maximum daily working time of 8 hours, night workers must be allowed compensatory rest. This mandatory rest period may, if appropriate, be supplemented by salary compensation.

<u>Implementation of compensatory measures</u>

The compensatory measures for night work are stipulated by the collective agreement that implemented it. When the night work is implemented after authorisation by the labour inspector, employers must include, with their application, evidence of the existence of compensatory measures.

<u>Mandatory compensatory rest</u>

Night workers must be allowed a period of compensatory rest under Article L. 3122-39 of the Labour Code. This compensatory rest must exist in every case and may not be substituted by a salary increase. In addition it must be specific to night workers and paid in full (DRT Circular No. 2002-09 of 5 May 2002). In the absence of a collective agreement, the compensatory rest is the only mandatory compensatory measure for night work.

<u>Optional salary compensation</u>

The collective agreement implementing the night work may stipulate salary compensation for the hours of work carried out at night (Article L. 3122-39 of the Labour Code). This salary compensation may be added to the compensatory rest, but in no case may it be a substitute for it.

The derogation provided for the benefit of the activities mentioned in Article L. 3122-30 of the Labour Code (media and entertainment)

Some activities benefit from a specific regime. This concerns activities relating to editorial and industrial production of press, radio and television, cinema production and exhibition, live performances and discotheques (Article L. 3122-30 of the Labour Code). For these activities, when the effective duration of night work is less than the legal duration, the compensatory measures granted to night workers are not necessarily given in the form of compensatory rest (Article L. 3122-41 of the Labour Code).

2.1.1.6 The guarantees and rights granted to night workers

2.1.1.6.1 Increased medical surveillance

Taking European Union requirements into account, French legislators have implemented a system designed to ensure increased medical surveillance for employees assigned to a night shift. The aim of this surveillance is to enable the occupational physician to assess the potential consequences of night work on the health and safety of night workers, especially due to changes in chronobiological rhythms, and to determine the potential impact on their social life (Article R. 3122-18 of the Labour Code).

"Technical Instruction (IT) RT No. 2 of 8 August 1977 on the medical surveillance of shift workers" by the Ministry of Labour - Labour Relations Directorate, Sub-Directorate against Occupational Risks (not published in the *Official Journal*) makes reference to the *Official Journal* of 24 July 1977, which states that "work in rotating teams including a night shift has been included in the list of work giving rise to special medical surveillance". This IT No. 2 contains a brief summary of the health problems associated with shift work and presents four short sections:

- Examination prior to assignment;
- Medical surveillance of shift workers;
- Surveillance of transferred workers;
- General considerations.

Under Article L. 3122-42 of the Labour Code, all night workers benefit from special medical surveillance before their assignment to a night shift as well as, subsequently, at regular intervals that may not exceed 6 months. Workers can therefore only be assigned to a night shift if they have previously been examined by the occupational physician and if the fitness report certifies that their state of health is compatible with such a posting (Article R. 3122-19 of the Labour Code).

The increased medical surveillance provided for the night worker also includes other provisions (Article R. 3122-19 of the Labour Code):

- the occupational physician must be informed by the employer of any absence of night workers due to illness;
- any night worker can request a medical examination, besides the periodic visits;
- occupational physicians may, if deemed useful, prescribe additional specialised examinations at the employer's expense.

The Labour Code also stipulates that occupational physicians should inform night workers, and more particularly pregnant women and ageing workers, of the potential health consequences of night work. This information takes into account the specificity of the hours (fixed or rotating shifts). The occupational physician advises them on any precautions to be taken (Article R. 3122-21 of the Labour Code).

In addition, Article R. 3122-20 of the Labour Code stipulates that the occupational physician should analyse the possible impact of the night working conditions on the health of workers.

They must, more specifically, examine the consequences of shift rotation and its frequency in the case of work in rotating teams including a night shift. For this purpose, it is stipulated that the occupational physician should, "*during the time periods during which night workers are employed*", study the working conditions and the work station. They should then analyse the content of the job and its constraints for each employee. On the basis of the evidence thus collected, the occupational physician advises the employer on the method of organising the night work that is best suited to the workers according to the type of activity (Article R. 3122-20 of the Labour Code). Indeed, one of the tasks of the occupational physician is to advise the employer (Article R. 4623-1 of the Labour Code).

Lastly, the Labour Code stipulates that the issue of night work should be addressed in the framework of the occupational physician's annual activity report (Articles L. 4612-6 and R. 3122-22 of the Labour Code).

2.1.1.6.2 Taking the night worker's family obligations into account

Taking the night worker's vital family obligations into account

The legislators have adopted protective provisions in favour of night workers to enable them to reconcile their professional lives with their family obligations.

Thus, it is stipulated that, when the night work is incompatible with vital family obligations, including the care of a child or the support of a dependent person, the employee may refuse to accept this change of hours without this refusal constituting misconduct or a reason for dismissal (Article L. 3122-37 of the Labour Code).

Furthermore, Article L. 3122-44 of the Labour Code stipulates that, when the night work is incompatible with vital family obligations, including the care of a child or the support of a dependent person, the employee may request assignment to a day shift.

The specific provisions applicable to pregnant women

A series of specific measures have been adopted to prevent the health risks to female employees medically certified as pregnant or who have recently given birth, when they perform night work.

Under French labour law, female employees thus benefit from the right to be assigned to a day shift for the duration of their pregnancy and their statutory postnatal leave, on condition that they submit a request. A similar right is available, but only for the duration of the pregnancy, if the occupational physician states in writing that the night shift is incompatible with their status. The occupational physician may also, for the postnatal leave and after the employee's return from this leave for a period not exceeding one month, authorise the extension of this employee's assignment to a day shift if they state in writing that the night shift remains incompatible with the employee's state of health (Article L. 1225-9 of the Labour Code).

The change of assignment must not lead to any reduction in remuneration, and any assignment to another establishment shall be subject to the employee's agreement (Article L. 1225-9 of the Labour Code).

If the employer is unable to propose another job to the female night worker, the reasons making this assignment impossible must be explained to her and to the occupational physician, in writing. The employee's employment contract is then suspended until the start date of the statutory maternity leave and possibly during the additional period that follows the end of this leave. In this case, the employee benefits from a guarantee of remuneration during the suspension of the employment contract (Article L. 1225-10 of the Labour Code).

2.1.1.6.3 Priority access to day work

Under Article L. 3122-43 of the Labour Code, night workers wishing to occupy or resume a day shift, or day workers wishing to occupy or resume a night shift, are given priority for the assignment of a job within their occupational category. The employer must inform them of the list of corresponding available jobs.

2.1.2 Regulations applicable to shift work

2.1.2.1 Definitions of shift work and the shift worker

2.1.2.1.1 Definitions in European Union law

Directive 2003/88/EC of 4 November 2003 concerning certain aspects of the organisation of working time has given a definition of "shift work". According to this text, "shift work" means: "Any method of organising work in shifts, whereby workers succeed each other at the same work stations according to a certain pattern, including a rotating pattern, and which may be continuous or discontinuous, entailing the need for workers to work at different times over a given period of days or weeks; […]".

Within the meaning of this Directive, a "shift worker" means: "any worker whose work schedule is part of shift work; […]".

2.1.2.1.2 Shift work considered in France

There is no definition of shift work in the French Labour Code.

According to legal theory, supported by certain collective agreements (see in particular: Framework Agreement of 17 March 1975 *on the improvement of working conditions*), shift work (i.e. work in successive teams) refers to where employees, forming different teams, take over from each other on a given work station without ever overlapping. This way of organising working time is intended to ensure continuity on a given workstation.

In practice, three ways of organising shift work can be distinguished:

- Discontinuous shift work

According to this system, the work is organised into two teams that follow one another on the same work stations: a "morning" team and an "evening" team. The work is interrupted at the end of the day and at the end of the week, at least on Sundays.

- Semi-continuous shift work

According to this system, the work is organised into three teams that follow one another on the same work stations: a "morning" team, an "evening" team and a "night" team. The work is interrupted at the end of the week, at least on Sundays.

- Continuous shift work

According to this system, the work is organised into four or five teams working uninterruptedly around the clock, including during the period of paid leave. The shift work then makes it possible to operate the company continuously, seven days a week, day and night, around the clock.

In the context of shift work, regardless of the type, the teams can be fixed, i.e. the same employees always work in the "morning" team, or the "evening" team, or the "night" team. They are most often rotating or alternating: employees switch from the morning shift to the evening shift and then to the night shift, during clockwise rotations.

2.1.2.2 Implementation of shift work

Due to the adverse impact that shift work can have on employee health, the use of such work organisation is regulated.

2.1.2.2.1 Common rules

<u>The type of shift work</u>

Regardless of which system is being considered for organising shift work, the employer must first consult the staff representatives, the works council or, in its absence, the employee delegates (Articles L. 2323-27 *et seq.* of the Labour Code), and the CHSCT (Articles L. 4612-8 *et seq.* of the Labour Code). It must then inform these bodies of the decisions taken (Article 12 of the National Interprofessional Agreement of 17 March 1975). In addition, since the implementation of shift work is likely to result in a significant change to the working conditions, the Court of Cassation considered that the CHSCT should be able to call on external experts.

<u>The different options for resorting to shift work</u>

It is possible to resort to shift work on the basis of a number of regulatory texts, concerning certain industrial branches. This is the case, for example, with the Decree of 17 November 1936 for the construction and public works and construction material manufacturing industries, and the Decree of 27 October 1936 for the metallurgy and metalwork industries.

Shift work may also be established by extended collective labour convention or agreement, or company or establishment convention or agreement pursuant to Article L. 3122-47 of the Labour Code.

2.1.2.2.2 The implementation of semi-continuous and continuous shift work for technical reasons

Continuous shift work can be implemented in companies permitted to derogate from the Sunday rest period. Accordingly, the Labour Code authorises some companies to legally derogate from the rule regarding the Sunday rest period for technical reasons, i.e. when the facilities cannot be shut down due to the nature of the work carried out.

However, even assuming that the company is allowed to legally derogate from the rule regarding the Sunday rest period for technical reasons, the implementation of continuous shift work implies the concluding of an extended collective branch agreement, or collective company or establishment agreement due to the regulation of night work. This is also the case with semi-continuous shift work.

Because these two systems for organising shift work (semi-continuous and continuous) assume the existence of a night team and the employees who are assigned to it are qualified as "night workers", their assignment or extension to new activities is subject, in principle, to the existence of an extended collective branch convention or agreement, or collective company or establishment agreement (Articles L. 3122-33 *et seq.* of the Labour Code).

2.1.2.2.3 The implementation of continuous shift work for economic reasons

Continuous shift work may also be used in sectors or industrial companies for economic reasons.

In this case, regardless of the activity, it can only be implemented or extended in application of an extended collective branch, company or establishment agreement (Article L. 3132-14 of the Labour Code).

In the absence of such an agreement, continuous shift work for economic reasons may be authorised by the labour inspector, after consulting the trade union delegates and obtaining an opinion from the works council or employee delegates, if they exist, under the conditions laid down in Articles R. 3132-9, R. 3132-13 and R. 3132-14 of the Labour Code, i.e. if it aims to make better use of the production equipment and maintains or increases the number of existing jobs.

2.1.2.3 The protective status of the shift worker

2.1.2.3.1 Regulations based on law but more particularly on conventions

Shift work is not covered by a specific section of the Labour Code. Because of its implications, shift work is subject to disparate provisions of the Labour Code.

It is however addressed specifically in a few regulatory texts with a very precise scope or purpose[17].

Given the constraints generated by this form of work organisation, especially when it includes night work, work on a Sunday or a rotation of working hours, specific regulations based on conventions, whose purpose is to regulate the shift work and grant special benefits to the workers concerned, have been introduced.

The provisions specific to shift work are therefore, for the most part, laid down in collective professional agreements and collective branch agreements.

2.1.2.3.2 Duration, break times and compensatory measures

Maximum average working time of shift workers

Under Article L. 3132-15 of the French Labour Code:

"The working time of employees working permanently in successive teams according to a continuous cycle must not be greater on average, over one year, than thirty-five hours per week worked."

This text applies to the form of shift work deemed the most constraining, namely the organisation in successive teams according to a continuous cycle. It therefore concerns employees working in establishments operating continuously, i.e. which meet the three conditions mentioned by DRT Circular No. 94/4 of 21 April 1994 *on the organisation of work*.

DRT Circular No. 94/4 of 21 April 1994 defines the "cycle" as "*a brief period, a multiple of the week in which the period of work is distributed in a fixed and repetitive way*".

It is sufficient for the company to operate permanently and continuously with successive teams for this text to apply to employees assigned to one of these teams, including if these employees are intermittently subject to normal working hours.

The maximum daily and weekly working times

The maximum duration of the working day may not exceed 10 hours, unless a derogation is granted, as with other employees (Article L. 3121-34 of the Labour Code). However, the working time of shift employees, qualified as night workers, may not in principle exceed 8 hours (Article L. 3122-34 of the Labour Code and Article 8 of Directive 2003/88/EC).

For shift workers, as with other employees, the maximum duration of the working week is fixed at 48 hours, unless a derogation is granted (Article L. 3121-35 of the Labour Code and Article 6 of Directive 2003/88/EC). The maximum duration over a period of 12 consecutive weeks is 44 hours, unless a derogation is granted (Article L. 3121-36 of the Labour Code).

In addition, for shift workers, qualified as night workers, the maximum weekly working time, calculated over any period of 12 consecutive weeks, is reduced to 40 hours, unless a derogation is granted (Article L. 3122-35 of the Labour Code).

[17] Examples: the **Ministerial Order of 10 June 2009** ***defining the information contained by the company record provided for in Article R. 717-31 of the Rural Code and repealing the Ministerial Order of 12 July 1994***, Article 8 of Decree No. 2004-1290 of 26 November 2004 *laying down the allowance scheme applicable to staff recruited by certain public establishments involved in the field of public health or health and safety*, Articles 18 and 21 of Decree No. 2003-849 of 4 September 2003 *on the procedures for implementing the Labour Code concerning the working time of staff of companies providing catering services or operating sleeping compartments in trains*, or Article 4 of the **Ministerial Order of 16 April 2002** ***on implementation by the Ministry of Culture and Communication of Decree No. 2000-815 of 25 August 2000 on the organisation and reduction of working time in public service for the State***.

Break times

Shift workers must, like other employees, be allowed a break period, equal to at least 20 minutes, during any shift equal to or longer than 6 hours (Article L. 3121-33 of the Labour Code and Article 4 of Directive 2003/88/EC).

If during this time employees are required to remain at the employer's disposal and cannot therefore attend to their personal affairs, this time is then regarded as actual working time (Court of Cassation, Social Division, 10 March 1998, No. 95-43.003) but is qualified as break time once work has actually stopped.

Daily rest period

Shift workers must, like other employees, be allowed a daily rest period of 11 consecutive hours between two shifts (Article L. 3131-1 of the Labour Code and Article 3 of Directive 2003/88/EC).

However, an extended collective branch agreement, or collective company or establishment agreement may reduce this minimum duration of daily rest to 9 hours in certain cases (Articles D. 3131-1 and D. 3131-2 of the Labour Code).

In addition, Article D. 3132-2 of the Labour Code stipulates that in the event of increased activity, an extended collective labour convention or agreement, or company or establishment agreement may provide for a reduction in the duration of the daily rest period.

Furthermore, Articles D. 3131-4 and D. 3131-5 of the Labour Code stipulate, in the absence of a collective labour agreement, other possibilities for derogation from the daily rest period, either after authorisation by the labour inspector in the case of increased activity, or at the employer's initiative acting "*under its sole responsibility*" in the event of "*urgent work*". In this latter case, the employer shall inform the labour inspector.

Weekly rest period

Shift workers must, like other employees, be allowed a weekly rest period of 35 consecutive hours (Article L. 3132-2 of the Labour Code and Article 5 of Directive 2003/88/EC).

In addition, the same shift worker may not work more than 6 days per calendar week (Article L. 3132-1 of the Labour Code). However, when the shift work is organised on a continuous cycle, this weekly rest period does not necessarily have to be on Sunday, given that in the framework of this work organisation, under certain conditions, a derogation from the rule regarding the Sunday rest period may be provided for.

The establishment of "substitute" teams, whose purpose is to replace the teams of employees working in the week during their weekly rest day(s) (Article L. 3132-16 of the Labour Code), offers employers the opportunity to limit some of the adverse consequences of classic shift work by authorising regular weekly rest for shift workers. The employees making up the substitute teams then often work the weekend or the last three days of the week while not being regarded as shift workers themselves. The Labour Code sets out the conditions authorising the establishment of this substitute team authorised to work on Sundays (Articles L. 3132-16 *et seq.* and R. 3132-10 of the Labour Code).

The ban on assigning an employee to two successive teams

Article R. 3122-1 of the Labour Code prohibits the same employee from being assigned to two successive teams, except in exceptional circumstances and for vital operational reasons. When such an assignment has extended the employee's working time by more than two hours, the employer shall communicate the reasons to the labour inspector within 48 hours.

Organisation of working hours in the framework of a period longer than one week

The working hours of shift workers are most often organised in the framework of a distribution of the working time over a period longer than one week, in order to allow weekly rest periods to be taken by rotation (Sunday rest in particular).

The distribution of the working time over a period longer than one week can be established, by a collective company, establishment or, failing this, branch agreement (Article L. 3122-2 of the Labour Code). This collective agreement must then stipulate a number of points (in particular, the conditions and prior notice of changes to the duration or hours of work). By way of derogation, it is accepted that in companies that operate continuously, the organisation of working time can be arranged over several weeks by a unilateral decision of the employer (Article L. 3122-3 of the Labour Code).

Compensatory measures for shift work

Article 12 of the National Interprofessional Agreement of 17 March 1975 *on the improvement of working conditions* stipulates that collective agreements must contain financial benefits and compensation for employees working continuously. These benefits or compensation may in particular consist of breaks, priority assignment to non-continuous jobs or compensatory rest.

2.1.2.4 The guarantees and rights granted to shift workers

2.1.2.4.1 The duty to display and communicate the hours of shift workers

Shift workers are, by definition, most often subject to a collective schedule insofar as they work in teams. This collective schedule must be submitted to the staff representatives (works council or, in its absence, employee delegates)[18].

In addition, the names of each team member, including employees provided by a temporary employment agency, must be displayed at the entrance of the work place or recorded in a register kept constantly up to date and made available to the labour inspector, as well as to employee delegates (Article D. 3171-7 of the Labour Code).

Furthermore, the collective schedule must be displayed at the entrance of the work place. This notice must state the number of weeks in the period over which the working hours are distributed, and the distribution of the working time over each of the weeks in this period if the hours of the employee teams are organised according to a period longer than one week (Articles D. 3171-1 and D. 3171-5 of the Labour Code).

Lastly, when employees working as a team have individual working hours, an individual document showing the daily and weekly hours worked by each employee must be kept by the employer (Article D. 3171-8 of the Labour Code).

2.1.2.4.2 Preferential hiring for another vacant position in the company

In application of Article 12 of the National Interprofessional Agreement of 17 March 1975 *on the improvement of working conditions*, employees working a continuous shift for 5 years and having, during their professional life, worked continually for 20 years, whether or not consecutive, benefit from priority assignment to another vacant non-continuous position in the company.

A number of agreements have been signed in this respect and provide more protective schemes (example: in the chemical industry).

[18] Article L. 2323-29 of the French Labour Code.

2.1.2.4.3 Medical surveillance of shift workers

We are unaware of any text introducing increased medical surveillance for shift workers comparable to what exists for night workers (Article L. 3122-42 of the Labour Code).

However, the occupational physician is responsible for the procedures for implementing increased medical surveillance for certain employees for whom this surveillance may not be imposed by the Labour Code (Article R. 4624-19 of the Labour Code).

2.1.2.4.4 Early cessation of work by shift workers

Several collective agreements enable employees who have completed a number of years of work in successive teams to benefit from early retirement schemes, under certain conditions. These convention-based schemes now join the measures put in place by French legislators in support of employees who, in the framework of their jobs, are faced with factors of physical hardship and occupational risks.

2.1.3 Night work and shift work: factors of physical hardship and occupational risks

2.1.3.1 The specific risks to night workers and shift workers

Various reports have led to a number of risks being identified[19]. This is why night work and shift work are taken into account in the framework of occupational risk assessment and prevention, and were recently considered in the framework of laws on arduous working conditions through various devices.

2.1.3.2 Taking night work and shift work into account in the framework of arduous working conditions and the prevention of occupational risks

Arduous working conditions and occupational risks faced by night workers and shift workers are mainly taken into account in the framework of the "single document" and the "exposure prevention record".

The single document on risk assessment (DUER)

A single document on assessment of the health and safety risks of workers has been created under French law.

Employers have a general duty to ensure the safety and health of workers (Article 5.1 of Directive 89/391/EEC) and must conduct an assessment of the risks, including those generated by night work and shift work. The results of this assessment are recorded in the single document (Articles L. 4121-1 *et seq.* and R. 4121-1 to R. 4121-4 of the Labour Code).

The single document must be updated at least once a year (Article R. 4121-2 of the Labour Code). It takes shift work and/or night work into account in a much broader way, and not just the arduous nature of this exposure as defined for the exposure prevention record, which takes account of thresholds.

[19] For example: Report of the French Economic, Social and Environmental Council, "*Le travail de nuit : impact sur les conditions de travail et de vie des salariés*" ["*Night work: impact on working conditions and the life of employees*"], report written by François Edouard, August 2010 and DARES, Analysis No. 062, August 2014.

The exposure prevention record

Alongside the single document and in keeping with the assessment of risks for which the employer is responsible (Articles L. 4161-1 and L. 4121-3 of the Labour Code), an individual exposure record should be completed by the employer for each employee exposed, above certain thresholds and after the application of collective (sound insulation, air suction system, lifting gear, *etc.*) and personal (hard hats, breathing apparatus, *etc.*) protective measures, to one or more occupational risk factors related to specific constraints, in particular certain working rhythms liable to have lasting identifiable and irreversible consequences on health (Articles L. 4161-1, D. 4161-1 and D. 4161-4 of the Labour Code).

The employer must therefore note in this record the physical hardship conditions to which the worker is exposed, the period during which this exposure takes place and the preventive measures applied to eliminate or reduce the exposure to such factors during this period (Article D. 4121-6 of the Labour Code). The ten risk factors set out exhaustively by Article D. 4161-2 of the Labour Code include "*under certain working rhythms*" night work under the conditions laid down in Articles L. 3122-29 to L. 3122-31, working in successive rotating teams (or shift work), as well as repetitive work.

Of the ten physical hardship factors, four have been in force since 1 January 2015 (activities carried out in a hyperbaric environment, night work, work in successive rotating teams, and repetitive work). The date of application for the other six (manual handling of loads, painful physical positions, mechanical vibrations, hazardous chemical agents, extreme temperatures, and noise) was deferred to 1 January 2016 (Decree No. 2014-1159 of 9 October 2014).

This exposure record must be communicated to the occupational health department, which sends it to the occupational physician. It is added to each worker's occupational health medical record.

2.1.3.2.1 Compensation for arduous working conditions

Lowering of the retirement age

Act No. 2010-1330 of 9 November 2010 *on pension reform* offers employees suffering from significant sequelae of occupational origin the possibility of early retirement, under certain conditions. Since night workers and shift workers are exposed to occupational risks and physical hardship factors, they may be subject to this Act if they fulfil its conditions.

Creation by Act No. 2014-40 of 20 January 2014 of the personal account for prevention of physical hardship

The factors of physical hardship and occupational risks laid down in Articles L. 4161-1 and D. 4161-2 of the Labour Code, which include night work and work in successive rotating teams (or shift work), are taken into account not only for the exposure prevention record but also in the framework of the personal account for prevention of physical hardship (CPPP).

The CPPP was created by Act No. 2014-40 of 20 January 2014. The provisions of this Act relating to the personal account for prevention of physical hardship came into force on 1 January 2015 (Articles L. 4162-1 *et seq.* of the Labour Code). Six decrees published on 9 October 2014[20] provided clarification regarding the CPPP. In addition, an interministerial instruction of 13 March 2015 details the operation of the CPPP for the year 2015[21]. This instruction contains nine technical data sheets explaining the mode of operation of the physical hardship account.

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[20] Decrees No. 2014-1155 to 2014-1160, 9 October 2014, OJ 10 October 2014, p. 16468 to 16479.

[21] DGT-DSS Instruction No. 1, 13 March 2015, NOR: ETST1504534J.

The CPPP entitles the holder to points, in particular, for covering the cost of hours of continuing vocational training with a view to gaining access to employment with no exposure or lower exposure, funding an allowance in the event of a transition to part-time work, or funding an increase in the duration of pension provision and retirement before the legal age (Article L. 4162-4 of the Labour Code).

2.1.3.2.2 The requirement for certain employers to negotiate agreements or action plans supporting prevention of physical hardship

The factors of physical hardship and occupational risks laid down in Articles L. 4161-1 and D. 4161-2 of the Labour Code, which include night work and work in successive rotating teams (or shift work), can also be used to determine the cases in which agreements or action plans supporting prevention of physical hardship should be negotiated or reached.

2.2 Comparison of regulations and types of working hours in Europe

Given the considerable work involved in analysing and comparing regulations on night work in French domestic law and European Union law, it is difficult to comprehensively discuss internal legislation, which differs from one country to the next.

However, the research conducted revealed a number of points on the regulations concerning night work in the European states. These are as follows:

Definition of night worker

Regarding the definitions of night work and night worker, differences exist between the various EU Member States (see Table 1, the comparison for all the countries of Europe is given in Annex 2).

Table 1: Time period regarded as night time, by country

	18	19	20	21	22	23	24	1	2	3	4	5	6	7	8
Austria						■	■	■	■	■	■	■			
Belgium				■	■	■	■	■	■	■	■	■	■		
Bulgaria															
Cyprus							■	■	■	■	■	■	■		
Croatia						■	■	■	■	■	■	■	■		
Czech Rep						■	■	■	■	■	■	■	■		
Denmark								■	■	■	■	■			
Estonia						■	■	■	■	■	■	■	■		
Finland							■	■	■	■	■	■	■		
France					■	■	■	■	■	■	■	■	■		
Germany						■	■	■	■	■	■	■	■		
Greece						■	■	■	■	■	■	■	■		
Hungary						■	■	■	■	■	■	■	■		
Ireland								■	■	■	■	■	■	■	
Italy								■	■	■	■	■	■		
Latvia						■	■	■	■	■	■	■	■		
Lithuania						■	■	■	■	■	■	■	■		
Luxembourg						■	■	■	■	■	■	■	■		
Malta						■	■	■	■	■	■	■	■		
Netherlands															
Poland						■	■	■	■	■	■	■	■		
Portugal								■	■	■	■	■			
Romania						■	■	■	■	■	■	■	■		
Slovakia						■	■	■	■	■	■	■			
Slovenia							■	■	■	■	■	■	■		
Spain						■	■	■	■	■	■	■	■		
Sweden						■	■	■	■	■	■	■	■		
United Kingdom							■	■	■	■	■	■	■		

Maximum working time of night workers

To ensure compliance with the maximum daily and weekly working times, English law requires employers to keep a register on the working time of their night workers so that they can justify compliance with these maximum durations. These records must be kept by employers for two years (*The Working Time Regulations*, 1998 and https://www.gov.uk/night-working-hours/).

Compensation provided for night workers

In comparison, in Germany, in the absence of a collective agreement, the employer has the choice between firstly, the granting of compensatory rest and secondly, salary increases (Article 6(5) *of the Act on working time*, *Arbeitszeitgesetz*; ArbZG).

Medical surveillance of night workers

In Germany, night workers benefit from a medical examination before their assignment to a night shift. Medical examinations of night workers must then take place at least every three years. For employees over the age of 50, the medical visits are held every year.

Irish law stipulates that the employer must ensure the health and safety of night workers. As such, before hiring a candidate for night work and at regular intervals thereafter, the employer must ensure that the employee is examined to assess the possible effects of the job on their health.

English law also stipulates that, before their assignment to a night shift and then at regular intervals, night workers should benefit from a free medical assessment, which may take the form of a simple questionnaire developed with the assistance of a health professional.

The specific provisions applicable to pregnant women working at night

With regard to the specific provisions for pregnant women, regulations offering more protection than in France can be found in some European countries. Thus, German law has enacted a ban in principle on night work between 8pm and 6am for pregnant or breastfeeding women. Some exceptions to this ban have however been provided for in the hotel, cafe, restaurant, agriculture and entertainment sectors.

In Italy, it is also prohibited to require women to work between midnight and 6am from the time their pregnancy is "recognised" until the child reaches one year of age (Article 11 of Legislative Decree No. 66 of 8 April 2003 *transposing Directives 93/104/EC and 2000/34/EC and relating to certain aspects of the organisation of working time*).

In Ireland, if an employee is pregnant and usually performs at least a quarter of her working time at night, she may be exempted from night work if a doctor certifies that she could jeopardise her health or safety or that of her baby. In the event that no alternative day job is available, the employee may be granted "*health and safety leave*". This system applies until the 14th week following the birth of the child.

2.3 The characteristics of shift systems including night work

Shift work and night work cover a multitude of realities: various shift systems, known as 2x9, 3x8, 4x8, 5x8, 2x12 hours, fixed nights, *etc.*, and great variability for the "same shift system" (3x8 for example). This is because a shift system is defined from a combination of multiple characteristics, resulting from choices made at a given time in the company or establishment. As a reminder, working hours are the result of collective bargaining (see preceding sections). These characteristics are the criteria, forming the basis for the "benchmarks" listed and analysed by Quéinnec, Teiger and de Terssac (2008) in their book "*Repères pour négocier le travail posté"* [*"Benchmarks for negotiating shift work"*]. These characteristics relate to the shift system and to the individuals, i.e. the teams, that work these shifts.

The work shifts

- *Number:* this is the number of work periods, corresponding to the breakdown of the work process: 2 shifts (2x9h, 2x12h), 3 shifts (3x8h), 4 shifts (4x6h), 5 shifts, *etc.* The shifts can follow each other and/or overlap. There may, in addition, be day shifts.
- *Duration*: the duration of the shifts is generally related to the number of shifts needed to cover 24h. For example, if two shifts cover 24h, in general they each last 12h. This being said, the shifts may be of variable duration: 6h, 8h, 10h, or 7½h, 9h10m, they may also be of unequal duration: for example, a night shift may be longer than a morning shift.
- *Structure of shifts:* the shift is continuous (e.g. 8 consecutive hours) or disconnected/fragmented (with a break of more than 2 hours) such as in large retail outlets or in certain social work professions.
- *Shift start and end time*: the time at which shifts begin varies depending on the number of workers, the duration of the shift and the structure. They can therefore be early in the morning (4am or 6.30am), or late (8pm or 11pm), or flexible, as is the case with flexitime.

- *Overlap time between shifts* (handover): where this handover time exists, it corresponds to the duration of the overlap between two shifts for transferring instructions between the two teams. Otherwise, information is transmitted between the shifts via oral reports, a transmission notebook, *etc.*

The teams

- *Number of teams:* number of groups of people who follow one another to staff the different work stations. There may be three shifts (3x8h) with 4, 5 or 6 different teams rotating on these three shifts. The fewer the teams, the more the rotation is constrained.
- *Size of the teams:* number of people in each team. The size of the teams may vary from one shift to another; in some work situations, staff is reduced during the night shifts.
- *Fixed or rotating nature of the teams*
  - Fixed teams: The teams are assigned, more or less permanently, to the same time period (e.g. fixed night teams).
  - Rotating teams: different teams alternately work the different shifts (morning, afternoon, night, for example).

Cycle of rotation

- Regular or irregular rotation: regular rotation (e.g. 1 week mornings / 1 week afternoons / 1 week nights) or irregular rotation (e.g. 1 week mornings / 2 weeks afternoons / 2 weeks mornings / 3 weeks afternoons / 2 weeks rest / 3 weeks mornings / 1 week rest / 2 weeks afternoons, *etc.*)
- Speed of rotation: quick rotations (1-3 days on the same shift) and slow rotations (5 days or more on the same shift).
- Direction of rotation: forward (clockwise) day-evening-night or backward (anti-clockwise) night-evening-day.
- Predictability or unpredictability of the cycle: the schedule is not always known in advance. If it is, the number of days prior to its implementation may vary.
- *Rotation cycle - arrangement of work/rest*: number of successive shifts and number of successive rest days.

  Understanding this arrangement helps, for example, to determine the effective duration of the working week, and the position of the rest days over the weekend or during the week, in order to identify any "lengthy rest periods", *etc.*

The combination of these characteristics defines the shift system in place at the local level. All of these characteristics, and not merely the fact of being a shift or night worker, can influence the degree of physiological disruption (including circadian desynchronisation) and destabilisation of social and family life rhythms experienced by the worker.

2.4 The reality of shift work and night work in France: exposure according to the professional sectors

2.4.1 Introduction

2.4.1.1 Background

Following an initial analysis of studies published on the health effects of atypical working hours on professionals, the Working Group concluded that it was necessary to update knowledge on the exposure of professionals to shift work including night work, in particular from existing surveys.

With this aim, an epidemiology research laboratory was commissioned to conduct a study considering two of the most recent surveys describing exposure to occupational risks and constraints: the "Medical surveillance of exposure to occupational risks (Sumer)" survey published in 2010 and the "Working conditions" survey published in 2013, both carried out by the Directorate for Research, Studies and Statistics (DARES) of the Ministry of Labour.

- the "Sumer" survey provides a better definition of exposure, as well as a decision issued by the occupational physician, but there are no data on "non-work" aspects or on compensation;
- the "Working conditions" survey presents a better definition of the work constraints, and gives access to personal information on the employees (remuneration, composition of the household, reconciliation of private-professional life); the "employer" questionnaire provides links between night work, the company's situation and the ways in which work is organised.

Due to the time constraints associated with conducting this study, priority was given to exploiting the data from the *Sumer* survey, which has a sound definition of occupational exposure to night work.

The analysis was entrusted to the "Cancer-Environment" team at INSERM's Centre for Research in Epidemiology and Population Health (CESP, U1018), in the framework of a research and development agreement drawn up with ANSES. The detailed objectives of the analysis, described in a specification, were proposed by the Monitoring Group for this agreement.

2.4.1.2 General study objectives

The main objective of this study was to produce a typology of employees working shifts including at night, according to their working conditions (exposure to physical constraints, different working rhythms, psychosocial constraints). More specifically, the requested analysis aimed to examine the links between shift work including night work and different variables of interest available in the *Sumer* survey concerning:

1. the population: distribution by age, sex, employment status of the population concerned;
2. the job: trades concerned (industry sectors, occupations);
3. the work: working constraints (time-related, organisational, relational, *etc.*);
4. short-term health: observation of the physical and mental health of workers.

The information obtained was to be used to supplement that from DARES publications based on the exploitation of data from job surveys[22].

2.4.1.3 The main steps of the work

Defining atypical working hours is complex because it depends on various parameters that are often closely interlinked (night work, evening work, shift work, number of nights per year, predictability of hours, *etc.*). It seemed appropriate to begin by identifying the specific profiles of organisation of working hours in such a way as to define the main categories of workers subject to atypical hours. Subsequently, the distribution of the variables of interest was compared between these groups of workers.

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22 http://travail-emploi.gouv.fr/IMG/pdf/2014-062.pdf; http://travail-emploi.gouv.fr/IMG/pdf/2011-009v2.pdf.

2.4.2 Method

2.4.2.1 Presentation of the source survey: *Sumer*

The *Sumer* 2010 survey is a joint investigation by DARES and the General Directorate for Labour (DGT). It aimed to determine the hazards to which employees are exposed, and followed on from the *Sumer* 1994 and *Sumer* 2003 surveys. The 2010 survey focused on all employees followed by occupational physicians under the general scheme and the Agricultural Mutual Insurance Scheme (MSA), as well as employees of public hospitals, EDF, SNCF, the French postal service (La Poste) and Air France. A total of 45,725 employees were involved in the survey, 43% of whom were women. The survey is representative of 22 million employees in France (or 92% of the employed population).

A questionnaire was completed by the occupational physician during the periodic visit and was accompanied by a self-administered questionnaire (completed by the employee) on psychosocial risks.

2.4.2.2 Characterisation of types of workers subject to atypical working hours

The first step was to establish a typology of employees according to their responses to the questions below ("characteristics of the working time" from the survey questionnaire):

- Q103: Do you work in a shift? If so, 2x8; 3x8; 4x8; 2x12; others?

- Q106: Do you work at night (between midnight and 5am)? If so, how many times a year?

- Q107: Do you work in the evening (between 8pm and midnight)? If so, how many times a year?

- Q110: Do you know the hours you will have to work:

a- tomorrow?

b- next week?

2.4.2.3 Method of classification

The method used to define homogeneous groups of subjects was codified[23], and contained several steps: a multiple correspondence analysis (MCA), the definition of *cluster* and the consolidation of *clusters* by the CART (Classification and Regression Tree) method. The latter was used to obtain a precise description of the groups of workers subject to atypical hours defined according to a decision tree.

2.4.2.4 Analysis of the relationships between night work/shift work and the variables of interest

The variables describing the job, the work constraints, occupational exposure and perceived health were compared between groups of workers defined according to this typology.

The sets of variables studied corresponded to the major sections of the survey questionnaire:

- characteristics of the employer establishment;
- characteristics of the employee;
- categories of professions (PSC: occupations and socio-professional categories);
- characteristics of the working time;
- time pressure;
- varieties of tasks and room for manoeuvre;

[23] "*Approche pragmatique de la classification*" [Pragmatic classification approach] - JP. Nakache, J. Confais, Editions Technip, Paris, 2005.

- work errors;
- mutual assistance and support;
- abuse;
- physical constraints;
- exposure to carcinogens during the last week worked;
- physical hardship and exposure to risks;
- perceived health;
- absences;
- right to withdraw.

The *odds ratios* (OR) for exposure and their 95% confidence intervals were calculated using unconditional logistic models in order to measure the association between a modality of the variable studied and the group of workers subject to atypical hours considered, using the group of workers subject to standard hours as a reference. The variables for the 14 sets defined above were introduced into the model, either alone (raw OR), or simultaneously with other variables (adjusted OR). A systematic adjustment for age (in groups), occupation and socio-professional category (PCS) (level 1: 4 groups) was performed. These analyses were conducted separately for women and men.

2.4.3 Results

An analysis conducted in 2014 by DARES[24] on the basis of data from the 2012 job survey revealed that 30% of night workers are public-sector employees and 42% work in service companies. The five occupational categories most concerned are: drivers, police and military personnel, nurses, care assistants, and skilled workers in processing industries (paper, chemical, agro-food, pharmaceuticals, *etc.*). Certain age groups were also highlighted: men in their thirties and women under 30 years of age. This study also highlighted markedly more difficult working conditions than those encountered by other employees (working standard hours), with more numerous physical hardship factors, greater time pressure, and more frequent tensions with colleagues and the public.

The results of the present analysis, carried out on the basis of data from the *Sumer* 2010 survey[25], lead to the same conclusion. The analysis that distinguished between men and women did not reveal any major difference in terms of working conditions. While the number of subjects and their distribution in the different groups were not the same, there were differences in the age group and socio-professional category, which enabled the categories of occupation concerned to be identified. Some differences to the detriment of women were, however, identified (consequences of errors, on exposure to carcinogens, number of accidents, *etc.*).

The service sector is also more strongly represented in the fixed night work group among men, and accounts for a large majority of women in each of the groups. Public companies are more strongly represented in the atypical working hours groups than in the reference groups.

Employees working shifts including night work are generally more frequently faced with work on Saturdays and Sundays than employees working standard hours. With regard to working conditions, there is a more frequent association with physical hardship factors, certain work constraints and psychosocial risk factors with night and shift workers than with employees working standard hours, irrespective of sex. As was found by DARES, this is mainly reflected by greater time pressure, increased versatility, risks and consequences of errors regarded as

[24] http://travail-emploi.gouv.fr/IMG/pdf/2014-062.pdf

[25] http://travail-emploi.gouv.fr/etudes-recherches-statistiques-de,76/statistiques,78/conditions-de-travail-et-sante,80/les-enquetes-surveillance-medicale,1999/l-enquete-Sumer-2010,15981.html

more serious for safety, and more frequent physical or sexual abuse than for employees working standard hours.

2.4.3.1 Typology of workers subject to atypical working hours

2.4.3.1.1 Definition of groups of workers according to the working hours

The classification method was used to characterise nine types of working hours for men (see Table 2) and women (see Table 3). The group of employees working standard hours were used as a reference group in the analyses.

In men:

Group 1: "standard" working hours

15,162 men.

Group 2: "fixed night work"

1,115 men: people working more than 90 nights a year, most (75%) of whom also work more than 90 evenings a year, and only a small minority work 3x8 or "other" shift types.

Group 3: "frequent night shift work - Type A"

1,267 men: people working between 50 and 89 nights a year, most (80%) of whom also work between 50 and 89 evenings a year, 60% work 3x8, and 20% work "other" shift types.

Group 4: "occasional night shift work - Type B"

1,434 men: 50% work between 1 and 49 nights a year, 40% work 3x8 and 60% work "other" shift types, 45% work between 1 and 49 evenings a year.

The distinction between the "Type A shift work" (G3) and "Type B shift work" (G4) groups lies in a greater number of nights/evenings per year in G3 compared to G4, and in the greater frequency of the 3x8 shift in G3 and "other" shift types in G4. The *Sumer* questionnaire offered the answer "other" to the question about the shift work, but no additional details were provided.

Group 5: **"evening work"**

1,597 men: no/few people work nights; 70% work more than 90 evenings a year, 30% work between 50 and 89 evenings a year, the people subject to this type of shift work do 2x8 shifts only.

Group 6: **"hours the following day unknown"**

1,438 men: little/no night work, little/no evening work, nearly 100% do not work shifts, 100% do not know their hours the following day.

Group 7: "hours for the week unknown"

1,067 men: group identical to G6 but the hours the following day are known, 100% of people do not know their hours a week in advance.

Group 8: "occasional night work"

2,076 men. 100% work between 1 and 49 nights a year, almost 90% work between 1 and 49 evenings a year, no one works shifts (or they work a 2x8 shift).

Group 9: "2x8 shift work"

927 men. 100% do not work nights, no/few people work evenings, 100% work a 2x8 shift.

Table 2: Number of workers reporting that they work nights or evenings according to the working hours groups in men

		All	Night work		Nights/year		Evening work		Evenings/year	
		N	N	%	mean	sd	N	%	mean	sd
G1	standard	15,162	0	0%	0.0	-	2,124	14%	1.6	5.7
G2	fixed night	1,115	1,115	100%	144.0	18.3	897	80%	108.0	61.9
G3	type A shift	1,267	1,267	100%	64.0	10.6	1,229	97%	74.0	34.6
G4	type B shift	1,434	752	52%	22.4	14.1	977	68%	34.0	44.8
G5	evening	1,597	352	22%	15.7	12.9	1,597	100%	119.0	40.7
G6	hours tomorrow unknown	1,438	331	23%	11.2	10.3	660	46%	6.4	10.5
G7	hours for the week unknown	1,067	253	24%	11.5	11.1	456	43%	6.3	10.6
G8	occasional night	2,076	2,076	100%	9.6	10.3	1,804	87%	10.5	11.1
G9	shift 2x8	927	0	0%	0.0	-	227	24%	4.6	9.6
All		26,083	6,146	24%	47.3		9,971	38%	44.3	

In women:

Group 1: "standard" working hours

13,520 women.

Group 2: "fixed night work"

379 women: people working more than 90 nights a year, most (85%) of whom work more than 90 evenings a year, only a small minority work 3x8 or "other" shift types.

Group 3: "frequent night shift work - Type A"

183 women: people working between 50 and 89 nights per year, most (80%) of whom work between 50 and 89 evenings a year, 50% work 3x8, and 20% work "other" shift types.

Group 4: "occasional night shift work - Type B"

340 women: 100% work 3x8 shift types, half (50%) work between 1 and 49 nights a year, 35% work between 1 and 49 evenings a year.

The main distinction between the type A shift work (G3) and type B shift work (G4) groups lies in a greater number of nights/evenings a year in G3 than in G4.

Group 5: **"evening work"**

1,043 women: little or no night work, most (70%) work more than 90 evenings a year, 30% work between 50 and 89 evenings a year, 2x8 shifts only.

Group 6: **"hours the following day unknown"**

570 women: little/no night work, little evening work, nearly 100% do not work shifts, 100% do not know their hours the following day.

Group 7: "hours for the week unknown"

771 women: similar to G6 but the hours the following day are known, 100% do not know their hours a week in advance.

Group 8: "occasional evening work"

2,131 women: no/little night work, 100% work between 1 and 49 evenings a year, no-one works shifts (or they work a 2x8 shift).

Group 9: "other shift work"

705 women: little/no night work, little/no evening work, 100% work "other" shift types.

Table 3: Number of workers reporting that they work nights or evenings according to the working hours groups in women

		All	Night work		Nights/year		Evening work		Evenings/year	
		N	N	%	mean	sd	N	%	mean	sd
G1	standard	13,520	60	0%	9.4	11.1	0	0%	-	-
G2	fixed night	379	379	100%	144	17.3	335	88%	141	27.2
G3	type A shift	183	183	100%	63	10.4	178	97%	77	33.3
G4	type B shift	340	169	50%	25	14	213	63%	63	48.4
G5	evening	1,043	160	15%	13.2	11.9	1,043	100%	115	40
G6	hours tomorrow unknown	570	91	16%	12.3	11.5	251	44%	37	45.8
G7	hours for the week unknown	771	80	10%	14.1	13.1	337	44%	47	51.8
G8	occasional evening	2,131	405	19%	10.8	11.6	2,131	100%	13.6	13
G9	other shift	705	133	19%	17	12.9	305	43%	59	49.6
All		19,642	1,660	8%	49.4	55.6	4,793	24%	56	56.4

2.4.3.1.2 Sector, age and socio-professional category

Compared to the groups working standard hours, the service sector is more strongly represented in the fixed night work group among men, and accounts for a large majority of women in each of the groups (>70%). Public companies are more strongly represented in the fixed night work, shift work including night work, and shift work groups than in the groups working standard hours.

While the proportion of men over the age of 50 in the atypical hours groups is lower than in the other groups, there is no clear trend among women. It can be seen that after the age of 40, they are found in greater proportion in the fixed night work group but also in the group working standard hours. It seems that a greater proportion of women under the age of 30 years than men are faced with working atypical hours.

The occupational categories concerned by the fixed night work and shift work differ in men and women (see Table 4). For men, these are skilled and unskilled workers from the industrial sector, police and military personnel, as well as drivers in the fixed night work group. Skilled and unskilled workers from the industrial sector and materials-handling workers predominate in the shift work groups. For women, civilian employees and civil servants, intermediate health and social work professions, and personal services employees predominate in the fixed night work and shift work groups.

Table 4: Table of the most represented occupations and socio-professional categories by group

Types of hours	Standard hours		Fixed Night		Shift type A		Shift type B		Evening work	
Occupations	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women
Intermediary administrative and commercial professions		15%								
Civilian employees and civil servants		13%		**37%**		**14%**		**30%**		
Intermediary health and social work professions				**16%**		**27%**		**28%**		15%
Direct personal services employees				**12%**						
Skilled industrial workers			**13%**		**34%**	8%	**15%**		16%	
Unskilled industrial workers			**10%**		**9%**	16%	**10%**			
Commercial employees										10%
Company administrative employees		22%								
Company engineers and technical managers	12%									
Skilled artisanal workers	11%									
Police and military personnel			**14%**							
Drivers			**14%**							
Foremen and inspecting officers					11%					
Skilled handling, warehouse and transport workers					12%					
Administrative and commercial managers									10%	

2.4.3.2 Working conditions and constraints of exposure

Warning: It is important to emphasise here that the following points of analysis concern a relationship of association, rather than causality. Indeed, the link with the variable of interest may depend on the content of the work and not just the fact of working atypical hours.

2.4.3.2.1 Characteristics of the working time

The observed trend is the same for men and women: work on Saturdays and Sundays is strongly associated with night work and/or shift work.

2.4.3.2.2 Pressure, variety of tasks, room for manoeuvre

Overall, the time constraints are more frequent and more numerous in the atypical hours groups than in the groups working standard hours. Thus, the "time pressure" appears greater in the groups of workers subject to fixed night work or shifts with or without night work.

The men in the fixed night work groups more often report being obliged to rush their work than those in the group working standard hours. This is not the case for the shift work groups. For women, the opposite applies.

The questionnaire proposed selecting from among the following nine constraints as potentially enforcing the pace of work:

- automatic movement of a product or part;
- automatic rate of a machine;
- other technical constraints;
- immediate dependence with regard to one or more colleagues;
- production standards or deadlines to be met in one hour or more;
- production standards or deadlines to be met in one day or more;
- an external request requiring an immediate response;
- permanent controls or monitoring exercised by line management;
- computerised control or tracking.

In the groups working standard hours, it was observed that around 80% of people reported having at least one of the nine proposed constraints and almost 20% reported having four or more constraints.

In the atypical hours groups (fixed night, shift, evening), these figures were even higher with 85 to 92% of men and 84% to 91% of women reporting that they had at least one of the nine proposed constraints.

Versatility (ability to carry out several types of tasks) is a concept that is often reported in studies on atypical working hours. The analysis of the data shows that the most versatile groups are the shift work groups. Abnormal situations tend to be managed individually in specific cases for the fixed night work groups as well as in the shift work groups.

The scope of work in the fixed night work or shift groups is often rigid, with identical, strict procedures. These workers appear to have less freedom and less varied tasks than the group working standard hours.

2.4.3.2.3 Tension and aggression

Experiencing situations of tension with the public is also clearly apparent, with more frequent situations of regular or permanent tension in all the atypical hours groups.

Regarding verbal abuse from the public in the past 12 months, this was more frequent in the atypical hours groups than in the group working standard hours. This trend was also observed for physical or sexual abuse from the public in the past 12 months and verbal abuse from colleagues or superiors.

2.4.3.2.4 Consequences on health, risk of errors and accidents

In all groups working atypical hours, between 53 and 83% of men considered that an error at work could have dangerous consequences for health, compared with only 43% in the group working standard hours (significant association).

This trend was also observed in women, with between 30 and 70% of women in the atypical hours groups considering that an error at work could have dangerous consequences for health, compared with 22% in the group working standard hours.

While an increased number of occupational accidents in the past 12 months was not identified in men working atypical hours, in women, the atypical hours groups were associated, to various degrees, with an increased number of occupational accidents in the past 12 months.

2.4.3.2.5 Decision of the occupational physician

The verdict of the occupational physician on the quality of the work shift according to the working hours was as follows:

- on the organisation of work: for women, it is more often seen as bad or very bad in the groups working atypical hours compared to standard hours; for men, it is considered worse for the fixed night work and evening work groups;
- on the prevention of exposure to physical constraints: no significant difference from the group working standard hours;
- on the prevention of exposure to chemical agents: it is seen as good, or better for the fixed night work and shift work groups than for the groups working standard hours.

2.4.3.2.6 Physical constraints and exposure to carcinogens

Among men, there is no association between physical constraints and the atypical working hours groups. Among women, physical constraints are more frequent in the groups of women working atypical hours compared to the reference group.

Despite the low numbers exposed to each of the carcinogens in the atypical hours groups, some associations are especially evident.

When the groups are compared to one another, the shift work groups are associated with a greater number of exposures to carcinogens (≥9) than the occasional evening work group (8 exposures), the group exposed to "other" shift types (5 exposures), the evening work group (3 exposures) and the fixed night work group (2 exposures). When looking at multiple exposures (the same individual being subject to several types of exposure), exposure to three or more carcinogens is more frequent in "occasional shift work" men, while exposure to two or more carcinogens is more frequent in "frequent shift work" men and "occasional evening work" men.

2.4.3.2.7 Perceived health, absences and right to withdraw

The questions on perceived health come from a self-administered questionnaire.

It should be noted that in all the groups working atypical hours, a higher percentage of workers think that their work is fairly bad for their health compared with the group working standard hours.

Lastly, the employees in the atypical hours groups report having interrupted a task more often than the employees in the group working standard hours, in order to safeguard their health or safety during the past 12 months.

3 The circadian system and the impact of circadian disruption

3.1 The circadian system

3.1.1 Mechanisms of circadian rhythmicity

3.1.1.1 The circadian biological clock

The body has to fulfil many biological functions during a 24-hour day: regulation of wakefulness and sleep, hormone secretion, control of body temperature, cell division, DNA repair, behaviour adjustment, *etc*. For these functions to take place smoothly and effectively, it is essential that they occur at the right time of day or night. This temporal organisation is so important that all living things, from bacteria to humans, have a complex time measurement system whose role is to coordinate these functions and enable their activation at the appropriate time. This system relies on a network of circadian (*circa:* around - *dies:* day) biological clocks, comprising a main (or central) clock located in the suprachiasmatic nuclei of the hypothalamus (Moore and Eichler, 1972), and a multitude of secondary (or peripheral) clocks located in almost every tissue of the body, such as the retina, liver, heart, lung, skin, *etc*. (Mohawk *et al., 2012*). This entire network of circadian clocks harmonises the physiological, psychological and behavioural functioning of the body according to a rhythm of approximately 24 hours, called the circadian rhythm.

The first fundamental characteristic of this circadian system is that its rhythmic activity is endogenous, i.e. specific to it and not imposed. Circadian rhythms therefore continue being expressed with a cycle of approximately 24 hours, even when the body is placed in a constant environment where nothing distinguishes day from night. This phenomenon was observed in humans at the beginning of the 1960s (see Figure 1) with the "time-isolation" experiments of Michel Siffre (1962) and Nathaniel Kleitman (1959). These circadian rhythms result from the activity of endogenous clocks whose circadian operation depends on approximately ten "*clock*" genes*.* The clock genes/proteins control the rhythms of cell electrical and biochemical activity with a period close to 24 hours (Reppert and Weaver, 2002).

The second fundamental characteristic of the circadian biological system is that its activity has to be synchronised with the astronomical cycle of the Earth, i.e. that of the Earth's rotation around its axis, which has a period of 24 hours. Thus, since the endogenous rhythm of the biological clock is slightly different from 24 hours (an average of 24.2 hours in humans (Czeisler *et al.,* 1999; Duffy *et al.*, 2011)), the clock must be reset on a daily basis so that its activity remains in phase with the day/night cycle (i.e. so that the internal circadian time is synchronised with the external daily time). In mammals, the light perceived by the retina is the most powerful synchroniser of the main circadian clock, so the 24-hour period of light-dark alternation ensures the main clock's daily synchronisation.

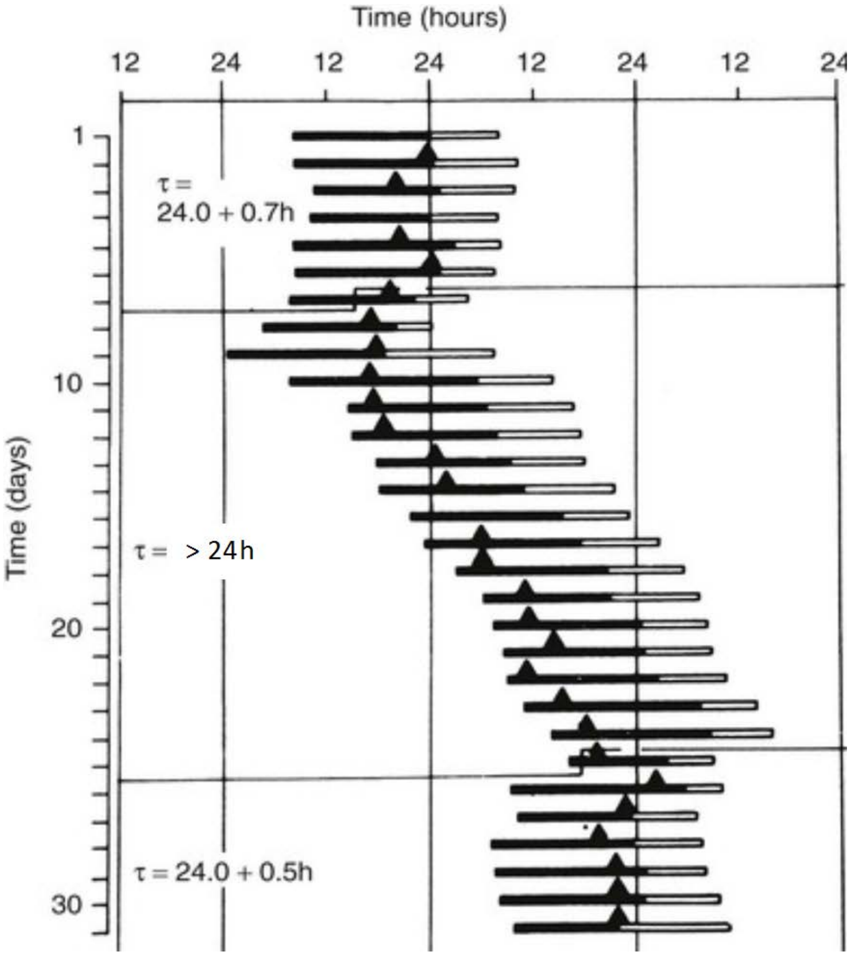

Figure 1: Synchronised and free-running circadian rhythms of a human subject

Circadian rhythms of wakefulness (black bars), sleep (white bars), and maximum rectal temperature (triangles) in a human subject who was synchronised over 24 hours during the first and last 7 days, and otherwise free-running (not synchronised) between days 8 and 24 (study by Jurgen Aschoff, in Georges Copinschi, Fred W. Turek and Eve Van Cauter, Endocrine Rhythms, the Sleep-Wake Cycle, and Biological Clocks, in Jameson LJ, DeGroot LJ (Eds), Endocrinology, 6th Edition, Philadelphia: Elsevier-Saunders, 2010).

Figure 1 shows the sleep-wake cycle (sleep is represented by white bars, while wakefulness is represented by black bars), and maximum rectal temperature (triangles) in a human subject who was synchronised over 24 hours during the first and last 7 days, and otherwise given free-running (not synchronised) between days 8 and 24. In "natural conditions", the sleep-wake cycle is stable and sleep is nocturnal (the system is said to be synchronised over 24 hours). On the other hand, temporal isolation enables a free-running sleep-wake cycle to develop, with the hours of sleep being later each day than the previous day (the sleep-wake cycle is said to be endogenous or not synchronised). This rhythm represents the expression of the circadian clock's endogenous rhythm because it occurs in conditions where the light conditions prevent synchronisation of the circadian clock (as was tested by Michel Siffre in his "beyond time" experiment, as has been seen in the laboratory [Gronfier *et al* 2007], or as is observed in many blind people).

3.1.1.2 Functions controlled by the circadian clock

Many different biological functions are controlled by the main circadian clock. Their synchronisation with the 24-hour rhythm and with each other enables them to optimise their physiological roles with respect to time so that each function is expressed at the right time, and allows, for instance, consolidated (stable) sleep at night and quality wakefulness during the day. Figure 2 illustrates some of the human functions that have a daily rhythmicity with maximums/minimums that take place at different times over the day/night cycle. Thus, in humans, vigilance, performance, memory and physiological activation are at their highest during the day, and associated with a higher core body temperature. In contrast, secretion of the hormone melatonin, relaxation of the muscles and sleep propensity are highest during the night, associated to a lower core body temperature. Consequently, the main biological clock can be regarded as an orchestra conductor, harmonising the internal physiology, and synchronising it optimally with external time. In addition, in each organ and each cell of our body, some functions present a circadian rhythmicity. Depending on the organs, between 8 and 20% of the genome is expressed rhythmically. This rhythmicity depends on the central clock and also on the peripheral clocks found in all the body's cells and organs. These peripheral clocks generate a local endogenous circadian rhythm but also receive the signal from the central clock to remain synchronised with one another and with the 24-hour cycle. These peripheral circadian clocks are particularly involved in cellular metabolism, control of cell division, apoptosis, proliferation of cancer cells (Granda *et al.,* 2005), and DNA repair (Collis and Boulton, 2007).

The integrity of the circadian clocks and their proper synchronisation with the day/night cycle are crucial for human health. All these regulations give an indication of how disruption of the circadian system could be responsible for certain pathologies and the increased risk of cancer.

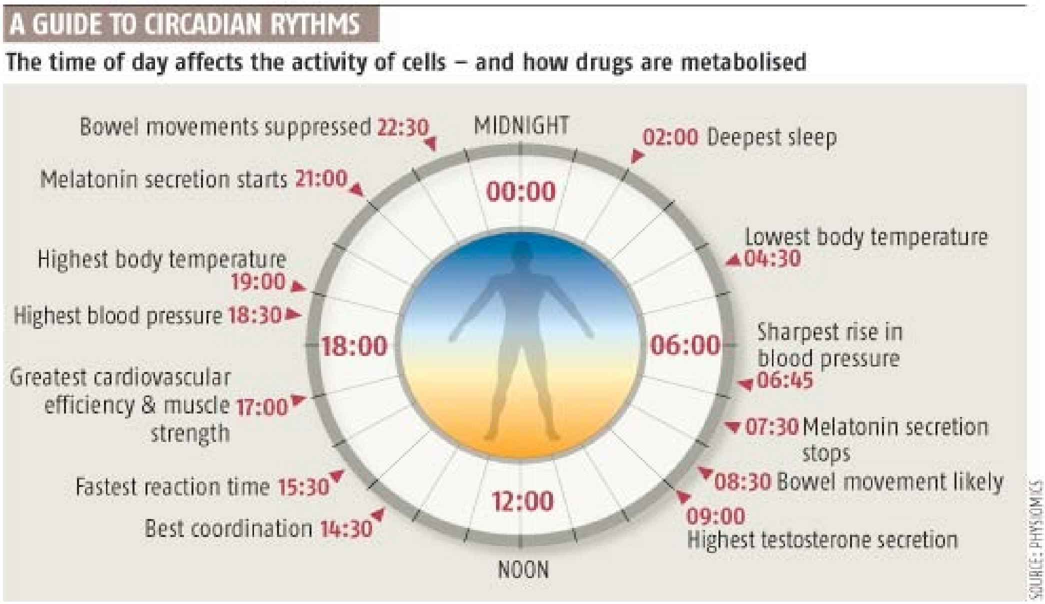

Figure 2: **Temporal distribution of several biological functions in humans**

Temporal distribution of several biological functions in humans over a 24 h day, where external night starts at 6pm and ends at 6am. It is a schematic representation, where the times are only indicated as an example (they vary from one individual to another, particularly according to chronotype).

The times given, which may vary slightly according to individual differences, indicate the peak of a biological function. For example, the time when blood pressure is highest is around 6.30pm.

3.1.1.3 Synchronisation of the circadian clock by light

Because its endogenous rhythm is close to but not exactly 24 hours, the central circadian clock must constantly be synchronised with the day/night cycle of the environment. In mammals, light, or more specifically exposure to the light-dark cycle, is the most powerful synchroniser of the internal clock.

The effects of light depend on five main parameters:

- time of light exposure (Khalsa *et al.,* 2003);
- light intensity (Zeitzer *et al.*, 2000);
- duration of light exposure (Chang *et al.,* 2012);
- the light spectrum (Brainard *et al.*, 2001, Thapan *et al.,* 2001, Najjar *et al.,* 2014);
- prior photic history (Smith *et al.,* 2004, Mure *et al.,* 2009).

The moment when the circadian clock is stimulated by light exposure determines whether the clock will be advanced or delayed. This time-dependent effect of light is represented by what is known as the phase response curve (see Figure 3; Khalsa *et al*., 2003). Exposure to light at the end of the day and beginning of the night has the effect of delaying the clock, so that the different biological functions controlled by the circadian clock will occur later. In contrast, exposure to light at the end of the night and beginning of the day has the effect of advancing the clock. For individuals whose clock has a period of more than 24 hours (around 75% of the population according to Duffy *et al.,* 2011), morning exposure to light is very important for the synchronisation of their clock. In contrast, for people with an internal cycle of less than 24 hours, light received in the evening will delay the time of their internal clock and tend to synchronise it.

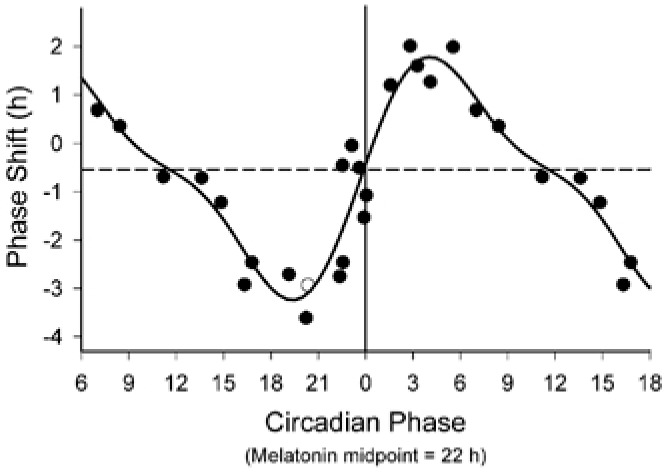

Figure 3: Phase response curve (in diurnal individuals) to a light stimulus applied at different times in the circadian cycle to individuals placed in constant darkness, who are therefore free-running

The circadian phase 0 corresponds to the minimum point of the temperature rhythm, at around 5 in the morning on average. By convention, negative phase shifts correspond to phase delays and the positive ones correspond to phase advances.

On average in humans, a light stimulus applied between 5pm and 5am induces a phase delay with a maximum effect (a 3-hour delay for a 10,000 lux white fluorescent light stimulus for 6.7 hours) at around the normal bedtime. On the contrary, when the light stimulus is applied between 5am and 5pm, it leads to a phase advance with a maximum effect (2-hour advance for this stimulus) observed around the usual waking up time (Khalsa *et al*., 2003).

Thus, synchronisation of the circadian clock takes place through exposure to the light perceived over the 24 hours. Under normal conditions, light during the day and darkness at night enable the clock to be appropriately synchronised to ensure quality sleep at night and optimal vigilance during the day. A lack of exposure to light (in the blind or in people not working in daylight) may be responsible for a desynchronisation of circadian rhythms. In addition, night-time or irregular exposure to light will disrupt the activity of the circadian clock, which will affect how biological functions are synchronised with the environment.

The ability of light to synchronise the clock facilitates adaptation to the time change following a move to a different time zone, for example, ensuring that physiological activation continues to occur during the day, and sleep at night. Unfortunately, this same characteristic hampers the adjustment of the worker who wishes to be active at night (for their job) and sleep during the day (when returning from their shift). Indeed, the worker's biological clock persists in adjusting to the light-dark cycle of the environment and not the sleep-wake cycle they are trying to adopt; the clock therefore continues to promote sleep at night (when the worker is at work) and wakefulness during the day (when they are trying to sleep).

To influence the circadian biological clock, light must be perceived by the retina. However, sensitivity to light for circadian adjustment is different from that of vision. Indeed, in addition to the cones and rods involved in image formation, the circadian system preferentially uses a second system of photosensitive cells: melanopsin-containing retinal ganglion cells (Berson *et al.,* 2002). Their sensitivity to light depends on different wavelengths than those of the cones and rods of the visual system. Vision is particularly sensitive in the yellow/green region of the light spectrum (~550 nm), whereas melanopsin shows maximum sensitivity in the region corresponding to blue (~480 nm) and is relatively insensitive to red (Brainard *et al.,* 2001; Thapan *et al.,* 2001, Najjar *et al.,* 2014). Apart from their role in synchronising the biological clock, melanopsin cells are involved in other non-visual effects of light, in particular concerning mood, vigilance, memory and cognition (Najjar *et al.*, 2014). Consequently, light is now regarded as an essential regulator of physiology, and many on-going studies are aiming to develop light-based therapy methods specific to circadian disorders, including those observed in night and shift workers.

In addition to light, it has been proposed that the central circadian clock may be sensitive to other "non-photic" factors, such as the sleep schedule, regular social activities, physical activity, psychophysiological activation, and meal times (hour and composition of meals) (Mistlberger and Skene, 2005; Barger *et al.*, 2004; Danilenko *et al.*, 2003). However, the vast majority of these potential synchronisers have a very minor effect in humans compared to that of light. Melatonin is the only powerful non-photic synchroniser currently used to treat certain disorders of the circadian system (Lewy *et al.*, 2006).

3.1.2 The hormone melatonin

3.1.2.1 The rhythm of melatonin secretion

Melatonin is a hormone secreted by the pineal gland, which is located roughly in the middle of the brain. The moment of melatonin secretion is determined by the biological clock, and secretion follows a very pronounced circadian rhythm. In a person who is active during the day and whose clock is synchronised normally, secretion begins in the evening, around two hours before bedtime, then reaches a peak towards the middle of the night (between 2 and 5 in the morning) before returning to very low, sometimes undetectable levels in the morning and for the rest of the day. The interval between the beginning and end of the melatonin secretion episode represents the biological night. In diurnal species such as humans, it corresponds to the rest phase, conducive to sleep and recovery.

The melatonin secretion profile can be established by measuring the concentration of melatonin either in plasma, which implies blood samples at regular intervals that can be taken while the subject is asleep, or in saliva, a less invasive method that nevertheless requires that the person remains awake at night in order to obtain a 24-hour profile. An alternative technique is to measure a metabolite of melatonin, 6-sulphatoxymelatonin (aMT6s), in urine samples. With a sufficient number of samples over the 24 hours and in suitable measurement conditions, these approaches make it possible to establish an individual melatonin secretion profile and estimate the time of each subject's biological night.

Melatonin secretion is only possible in the dark or in very subdued light, because its synthesis is sensitive to light. The light signal perceived by the melanopsin-containing retinal ganglion cells is transmitted to the clock, which immediately inhibits the secretion of melatonin by the pineal gland (Najjar *et al.,* 2014; Rahman *et al.,* 2015). Depending on the light spectrum (with blue being the most active colour), and the intensity and duration of exposure to light, melatonin secretion will be inhibited or may even completely cease during the entire period of exposure. Light sensitivity varies according to individuals, sex and age, and the same light intensity may completely block secretion in one person and produce a small decrease in another.

In any one person, the characteristics of the rhythm of melatonin secretion are generally very stable (the amplitude of the rhythm and its position in the 24 hours, its phase, are highly reproducible from one day to the next). In contrast, the amount of melatonin secreted and the shape and amplitude of the secretion profile vary greatly from one person to another. Because highly variable amounts of melatonin are found in individuals in excellent health, it is currently impossible to establish the extent to which the quantity of secreted melatonin contributes to an individual's health, or to establish thresholds of normality. In addition, as it is measured indirectly, it is difficult to determine whether the individual variations reflect differences of secretion by the pineal gland or differences in the metabolism of melatonin.

3.1.2.2 The effects of melatonin

Melatonin influences the functioning of the main circadian clock through MT1 and MT2 melatonin receptors located in the suprachiasmatic nuclei. Melatonin, in endogenous form or ingested in the form of a supplement (tablets, capsule, *etc*.), has a different effect on these two types of receptors (Dubocovitch *et al*., 2007). Activation of the MT1 receptors inhibits the neuronal activity of the suprachiasmatic nuclei. Among diurnal species such as humans, this inhibition reduces the biological clock's activating effects on vigilance, which increases drowsiness and the sleep propensity. Activation of the MT1 receptors is therefore responsible for the "*hypnotic*" effects of melatonin and explains its use to facilitate sleep. Activation of the MT2 receptors produces a different effect, since it modifies the circadian moment of neuronal activity of the suprachiasmatic nuclei and can therefore change the internal time of the biological clock. Thus, not only does the biological clock control the secretion of melatonin by the pineal gland, but its own functioning is also modulated by the retroactive effect of melatonin. This hormone is therefore said to play a "chronobiotic" role as a non-photic synchroniser of the clock, a property that is used in sleep medicine or to help synchronisation following jet lag (Arendt *et al.*, 2008).

The effect of melatonin administration is the opposite of that caused by exposure to light: the clock is advanced following administration in early evening and can be delayed slightly following administration in the morning (with this effect not always being observed in scientific studies). Nowadays, several melatonin formulations are available to treat different sleep rhythm disorders (see Table 5).

Table 5: Formulations of the melatonin agonists currently available

Agomelatine is a melatonin agonist (MT1/MT2) and weak 5-HT2C antagonist approved in Europe for the treatment of depression. It also has sleep-inducing effects.
Ramelteon is a melatonin agonist (MT1/MT2 and low affinity for MT3) approved in the United States and Japan for the treatment of insomnia. Its effects on sleep are modest.
Tasimelteon is a selective MT1/MT2 receptor agonist recently approved in the United States for the treatment of free-running disorder in the blind.
Circadin is a sustained-release melatonin formulation, approved in Europe, with an agonist effect like melatonin on the MT1/MT2 and MT3 receptors.
Melatonin, in a magistral (compounded) formulation (in pharmacies) may be prescribed for primary insomnia in the elderly.

As well as its effects on the circadian biological clock, melatonin has other physiological properties that can potentially have health repercussions (see Table 6). These effects are based firstly on a broad distribution of MT1 and MT2 receptors, in addition to the suprachiasmatic nuclei, and secondly on the pharmacological effects of melatonin, in particular antioxidant effects, independent from the MT1 and MT2 receptors and involving another binding site called MT3.

Table 6: Reported effects of melatonin in humans and animals

(Simonneaux and Ribelayga, 2003; Pandi-Perumal *et al*., 2005; Pandi-Perumal *et al*., 2006; Ritzenthaler *et al*., 2009)

Effects of melatonin	
Humans	**Animals (*in vivo* or *in vitro*)**
Chronobiotic (synchroniser) effect with a phase advance of the clock if melatonin is administered in the evening, or at the beginning of the night; generally no effect if administered in the morning	Chronobiotic effect with a different phase response depending on whether the species is nocturnal or diurnal.
Sedative/hypnotic effect on sleep (latency) if melatonin is administered during the day (if administered at night, there is no systematic effect on sleep).	Synchronising effect on certain biological functions (reproduction, metabolism, coat) in seasonal species.
Positive effect in chronic treatment (6 months) of primary insomnia in elderly subjects: decrease in sleep onset latency, increase in slow-wave sleep, and reduction in sleep fragmentation.	Local role in retinal physiology.
Hypothermic effect (temperature decrease) on core temperature and hyperthermic effect on peripheral temperature, *via* a peripheral vasodilator effect linked to the presence of melatonin receptors in the vasculature.	Regulation of blood pressure (anti-hypertensive effect).
Positive effects in some cases on the treatment of sleep disorders in Alzheimer's patients, with a possible effect on the cognitive sphere in these patients.	Inhibition of the progressive increase in beta-amyloid protein in the brain on the rodent model of Alzheimer's disease.
No indisputable anti-cancer effect of melatonin in humans.	Anti-oxidising effect at a high dose.
	Oncostatic effect.
	Regulation of the immune system.
	Regulation of neurotransmission.

3.1.3 Circadian regulation of biological and psychological functions

3.1.3.1 Circadian regulation of sleep and wakefulness

Sleep is regulated by two processes: the *circadian process*, which represents the influence of the biological clock, and the *homeostatic process*, which represents the increase in sleep need the longer a person has been awake (Dijk and Czeisler 1994, Wyatt *et al.,* 1999 – see Figure 4 below). The circadian clock has a particularly marked influence on the stimulation of wakefulness. In a person who is active during the day and whose clock is synchronised with the environmental day-night cycle, the circadian propensity for wakefulness gradually increases throughout the day to reach a peak around two hours before normal bedtime. It is so difficult to fall asleep at the circadian signal's peak of wakefulness that this circadian time-point has been named the "forbidden zone for sleep" (Lavie *et al.,* 1986). After this moment of strong stimulation of wakefulness, the electrical activity of the suprachiasmatic nuclei decreases, melatonin secretion begins and body temperature falls. These physiological events, which are all under the control of the circadian clock, contribute to reducing the propensity for wakefulness and prepare the body for sleep. The circadian propensity for wakefulness continues to decrease during the night to reach a minimum around two hours before the normal waking time, before starting its gradual increase again.

The influence of the circadian clock is not independent, but operates in interaction with the influence of the homeostatic process. The homeostatic process works in such a way that the longer a person is awake, the more they feel the need for sleep. Conversely, the longer an episode of sleep, the more sleep need decreases and the greater the likelihood of waking up. Thus, sleep need is normally very low after a good night's sleep. The homeostatic sleep process should therefore be seen as a mechanism involved in increasing sleep pressure during daytime wakefulness, and dissipating it during night-time sleep.

Thus, the homeostatic need for sleep increases progressively throughout the day, but is offset by the increase in the circadian stimulation of wakefulness. It is therefore the combined action of the circadian and homeostatic processes that makes it possible to maintain a relatively constant level of vigilance and performance during the day. Similarly, the decrease in sleep need during night-time sleep is offset by the decrease in the circadian signal of wakefulness, which enables consolidated sleep (not fragmented by wakefulness) throughout the night.

The combined action of the circadian and homeostatic processes is remarkably effective in people who adopt a regular sleep schedule that respects the internal time of their biological clock. In contrast, this same mechanism is a major source of insomnia and sleepiness when the hours of sleep and wakefulness are no longer in phase with the signals of the circadian clock, as is the case for jet-lagged travellers or night workers. Indeed, in a night worker, the daytime increase in the circadian signal of wakefulness can result in short, fragmented sleep during the day, while the absence of a signal of wakefulness at night will make it more difficult to stay awake and alert at work, especially after several hours of wakefulness.

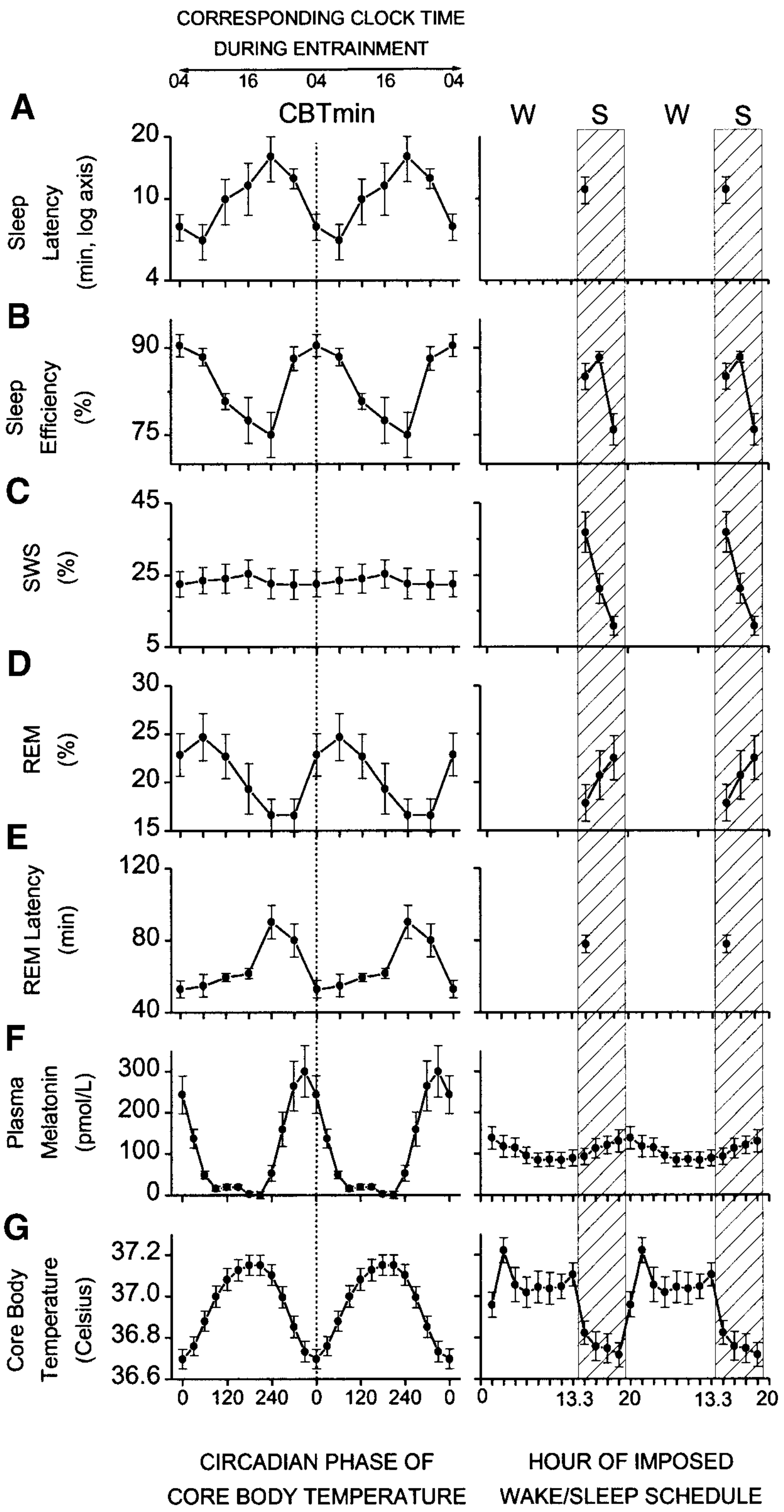

Figure 4: Circadian and homeostatic regulation of sleep

Sleep latency, sleep efficiency and REM sleep are mainly controlled by the circadian system (they have a circadian rhythm – left-hand column), and their intensity will mainly depend on the time at which sleep takes place. Slow-wave sleep (SWS) will mainly be controlled by sleep pressure, being greater at the beginning of the sleep period and decreasing in intensity during the night (figure from Wyatt et al., 1999).

3.1.3.2 Circadian regulation of other biological functions

The biological clock regulates not only the sleep-wake rhythm, but also a large number of other biological functions such as metabolism, the cardiovascular system, hormonal secretion, internal temperature, the cell cycle, and even vigilance and mood (see Figure 2). For this reason, the disruption of an individual's daily organisation (during night work or jet lag) can, in addition to sleep disorders, disrupt these biological functions.

3.1.3.2.1 Cell functions

Each neuron of the suprachiasmatic nuclei has a circadian oscillator, and the robust coupling of all of these neurons forms the main circadian clock. However, it has now been established that many other cells of the human body (skin, liver, lungs, digestive tract, *etc*.) also have a "cellular" circadian clock. For example, in fibroblasts isolated in culture, the clock genes oscillate independently for several consecutive days with a period of around 24 hours (see Figure 5) (Nagoshi *et al.*, 2004).

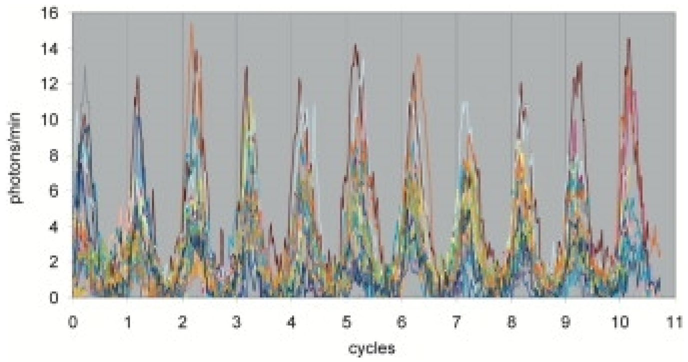

Figure 5: Recording of circadian oscillations of the bioluminescence of 25 fibroblasts in primary culture for 11 days

Even though each of these cells has a sustained circadian oscillation, there is little coupling between these cellular oscillators within a tissue or organ, and frequent resynchronisation is necessary for them to work together as a secondary clock. The cellular clocks control the circadian rhythm of many other genes of cellular metabolism and are also closely involved in gene expression during the cell cycle. There is therefore a robust coupling between the circadian clock and the cell cycle (Feillet *et al.*, 2015). The cellular circadian clock controls the duration of cell cycles and may thus be involved in the renewal of certain cells such as those of the skin (one sixth of the epidermal cells are renewed each day in humans), and the immune and haematopoietic systems. It has been suggested that disruption of the skin's cellular clocks leads to premature ageing of the epidermis (Janich *et al.*, 2011). Experiments in mice have also shown that, after partial hepatectomy, liver regeneration (which depends on liver cell-division cycles) is slower in individuals lacking a clock gene (Matsuo *et al.*, 2003). Several studies have shown that a malfunction between the circadian clock and the cell cycle can lead to cancer. Moreover, cancer cells have an impaired circadian clock, which can cause abnormal cell proliferation.

3.1.3.2.2 Metabolic functions

The circadian clocks rhythmically regulate numerous metabolic processes in response to the fluctuating needs regarding energy intake and expenditure throughout the day. Indeed, energy intake and consumption vary according to the sleep-wake and feeding-fasting cycles, with the times of these different periods depending on the species' diurnal or nocturnal nature. In each case, the period of wakefulness and feeding coincides with a high level of metabolism, anabolism and thermogenesis, while sleep and fasting correspond to a state of low metabolism and catabolism (Jha *et al.*, 2015). Food intake during the active period ensures the absorption and storage of energy substrates such as carbohydrates, fats and amino acids, which are needed to maintain a high metabolic rate. During the rest period, stored substrates such as glycogen and fats are metabolised to sustain basic energy expenditure. The circadian system plays a key role in the orchestration of these metabolic functions (Kumar Jha *et al.*, 2015).

The central clock of the suprachiasmatic nuclei orchestrates circadian rhythmicity in other brain areas and in the peripheral tissues by sending neurological and hormonal signals. The peripheral "metabolic" clocks located in the liver, adipose tissue, muscle, pancreas, adrenal glands, stomach and intestine are involved in the circadian rhythmicity of plasma glucose, free fatty acids, and the different hormones regulating appetite and metabolism (cortisol, adiponectin, leptin, ghrelin, *etc*.). In return, hormonal signals from the periphery exert their effects on energy balance by transmitting circadian messages to the brain, particularly to the hypothalamus, on peripheral energy reserves or requirements.

Cortisol secretion, which follows a daily rhythm with a peak at the end of the rest period/beginning of the active period, enables the induction of gluconeogenesis (manufacture of glucose from non-carbohydrate precursors such as amino acids) to supply the brain with glucose at the beginning of the period of activity, even in the event of insufficient food intake. In turn, high blood sugar levels inhibit production of this hormone, whose rates are reduced during and after the three main meals.

Leptin, an adipokine mainly secreted by the white adipose tissue and transported to the arcuate nucleus, whose action leads to a reduction in food intake (Kalra *et al.*, 2003; Sobrino Crespo *et al.*, 2014), also follows a daily rhythm. In humans, peak leptin secretion occurs at night (during the fasting period) in order to decrease appetite. Its concentration is also high after meals, which is a signal to the hypothalamus that peripheral energy demand has been or will be met. The rhythm of leptin is important for achieving a weight balance: its presence in large amounts increases energy expenditure by boosting thermogenesis, induces lipolysis, inhibits lipogenesis and increases insulin sensitivity; a reduction in leptin leads to an increase in the storage of body fat and in appetite for food.

Ghrelin, unlike leptin, is an orexigenic hormone that is mainly secreted by the parietal cells of the stomach. Its rate increases before meals and decreases afterwards; it increases food intake and body fat. It also provides feedback regulation of the central clock.

Plasma glucose concentration results from the coordinated regulation of glucose intake (dietary intake, glucose production) and use (uptake by skeletal and cardiac muscles, and adipose tissue). The central clock rhythmically regulates the production and use of glucose, most likely through efferent signals from the autonomous nervous system towards the peripheral organs (liver, muscle, pancreas). In humans, blood glucose levels exhibit a daily rhythm, with a peak before the period of wakefulness (Arslanian *et al.*, 1990; Bolli *et al.*, 1984). Glucose tolerance and insulin sensitivity also vary during the course of the day with greater efficiency in the morning.

While the central clock plays a fundamental role as synchroniser and integrator, enabling metabolic functions to be coordinated with the diet and rest-activity cycles, the peripheral clocks also play a specific role in glucose and lipid homeostasis and the circadian variation of the different substrates. The liver plays a pivotal role in metabolic regulation, particularly by maintaining an optimum level of circulating glucose through the balance between hepatic glucose production and output. Even though the influence of the autonomous nervous system and circulating hormones such as glucocorticoids is essential, disruption of the molecular mechanisms of the hepatic clock may alter glucose tolerance (Kalsbeek *et al.*, 2014).

In the pancreas, secretions of insulin and glucagon by the islets of Langerhans cells constitute vital signals for glucose homeostasis. Autonomous circadian rhythms have been observed in human pancreatic islets (Allaman-Pillet *et al.*, 2004).

Circadian rhythms have also been demonstrated in striated skeletal muscle, with more than 200 genes expressing rhythmicity (McCarthy *et al.*, 2007). Nevertheless, the effects of muscle clock disruption on the circadian desynchronisation of carbohydrate metabolism have not yet been clearly defined (Kalsbeek *et al.*, 2014).

Lastly, adipose tissue, now recognised as an essential endocrine organ in the control of energy, glucose and lipid metabolism, also has a functional clock that exerts circadian control over many genes. At cell level, the genes involved in lipid synthesis and fatty acid oxidation are rhythmically activated and suppressed by basic clock proteins (Shostak *et al.,* 2013; Otway *et al.*, 2011; Gomez-Santos *et al.*, 2009).

Thus, the central biological clock influences many aspects of the metabolic process by playing an integrative role in coordinating metabolic functions with the feeding and rest-activity cycles. In addition, peripheral clocks are also involved in the regulation of specific carbohydrate and lipid metabolic pathways.

3.1.3.2.3 Cardiovascular functions

The functional organisation of the cardiovascular system has a circadian rhythmicity that is clearly orchestrated by the central biological clock: arterial blood pressure, heart rate, peripheral resistance and the activity of the vasodilator and vasoconstrictor hormones show pronounced circadian variations. In humans, blood pressure is lower during the night (10 to 20% lower compared to the day), reaching a minimum around 3am, and then peaking after waking up (9am); a second peak is often seen in the early evening (7pm). In healthy young adults, the morning increase in systolic blood pressure is 20-25 mm Hg, but in the elderly, who have less compliant and elastic arteries, it can be as high as 40-60 mm Hg. The fall in pressure during sleep is more marked in women than in men. The circadian rhythm of heart rate closely matches that of blood pressure in normal conditions and shows a strong genetic dependence regarding daily average, amplitude of variations, and peak time during the 24 hours. Although blood pressure and heart rate are normally in parallel, several studies suggest that the circadian rhythms of these two cardiovascular parameters may be differentially regulated. Cardiac rhythms seem to be more intrinsic, driven largely by the daily variations in the activity of the autonomous, sympathetic and parasympathetic nervous systems. Studies have shown that the central clock may modulate cardiac function by direct nerve stimulation. There is a strong correlation between the daily variations in cardiovascular parameters and plasma levels of noradrenaline and adrenaline *(*Young *et al.,* 2006*)*.

Although the circadian rhythms of heart rate, blood pressure and cardiac output are classically attributed to the rhythms of the neuroendocrine constituents, rhythms at the cellular level also play an important role. There are cellular clocks in at least two main types of cells of the cardiovascular system: cardiomyocytes and vascular smooth muscles cells. Genetic manipulation of the components of the circadian clock, such as CLOCK and BMAL1, variations in the human clock gene PER3, and genetic ablation of the circadian clock in endothelial or vascular smooth muscle cells, significantly alter or eliminate the circadian rhythms of heart rate and blood pressure (Portaluppi *et al.,* 2012). The clocks of the cardiovascular system potentially influence cardiovascular function by enabling anticipation of the action of neuro-hormonal factors, thereby ensuring a rapid, appropriate response.

A complex interaction between environmental factors and the endogenous circadian system (central and peripheral clocks) therefore contributes to changes in cardiovascular function throughout the day. In addition to heart rate and blood pressure, other cardiovascular system parameters also present circadian variations, for example systolic volume, cardiac output, blood flow, peripheral resistance, electrocardiographic parameters, plasma concentrations of hormones (noradrenaline, renin, angiotensin, aldosterone, atrial natriuretic hormone), blood viscosity and fibrinolytic activity (Lemmer *et al.*, 2006). It should be noted that myocardial infarction is two to three times more common in the morning, between 6am and noon, than at night and that circadian variations have also been established in the presentation of both supraventricular and ventricular arrhythmias. Lastly, circadian rhythms also affect the pharmacokinetics and pharmacodynamics of cardiovascular drugs. The daily rhythms of the risks of heart rhythm disorders, morbidity and mortality from cardiovascular diseases, as well as the underlying pathophysiological mechanisms, are therefore different. This suggests that preventive and therapeutic interventions should be adapted accordingly to improve health and working conditions.

3.1.3.2.4 Cognition

It has been clearly demonstrated that cognitive abilities vary over 24 hours depending on the state of wakefulness and sleep (see Figure 8 below). Cognitive performance is regulated both by the circadian system (higher level during the biological day and lower during the biological night), and by sleep pressure (reduced levels of performance the longer a person is awake), independently or otherwise. Depending on the moment of the day-night cycle at which a cognitive performance is required, reaction time and sustained attention capacity will differ. This contributes to a daily rhythm of the relevance of the motor or cognitive response. Reaction time and the possibility of inappropriate responses (lapses), which are often assessed by the psychomotor performance test, evolve in the same way as perceived sleepiness throughout the day-night cycle (which can be assessed by scales such as the Karolinska Sleepiness Scale (KSS)).

This circadian regulation of cognition helps maintain a stable level of performance over the course of the day, in conditions where the biological clock is synchronised and sleep is nocturnal. However, in conditions where the clock is desynchronised, as occurs during night work for example, the combination of an inappropriate biological time and long-duration wakefulness (the duration of wakefulness is greater before beginning a night shift than a day shift) drastically lowers cognitive performance and the level of vigilance.

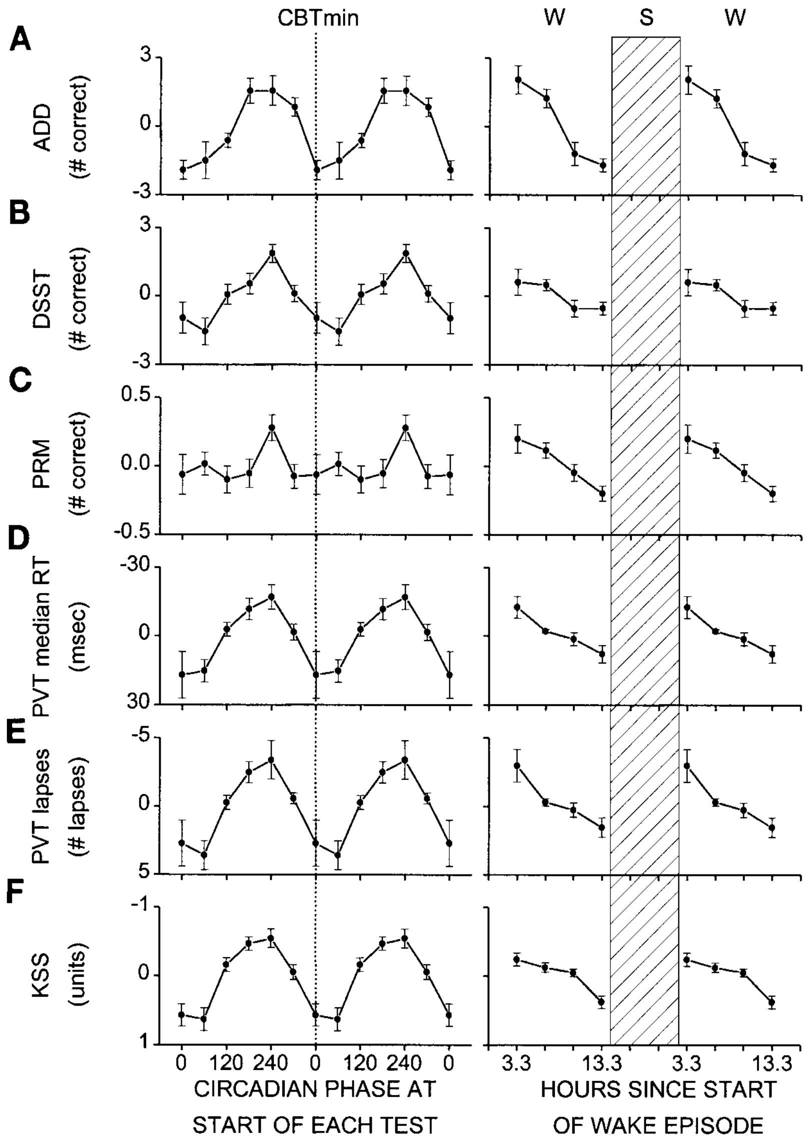

Figure 6: Circadian and homeostatic regulation of cognitive, memory and psychomotor performance

Performance in the addition/calculation test (ADD), digital symbol substitution test (DSST), probed recall memory test (PRM), and the test to measure reaction time (PVT) are controlled by the circadian system (left-hand column, their level depends on the time at which the task is performed) and by the homeostatic process (performance decreases during the day in parallel with the increase in sleep pressure). Figure from Wyatt et al., 1999.

3.1.3.2.5 Mood

Laboratory studies in humans show that mood is influenced by a complex, non-additive interaction between the internal biological time (the circadian phase) and the duration of prior wakefulness (see Figure 7).

The nature of this interaction is such that modest changes in the synchronisation of the sleep-wake cycle (the position of sleep in the 24 hours) can have major effects on subsequent mood (Boivin *et al.*, 1997). In other words, mood is regulated by the circadian system in such a way as to be more positive during the day than at night. In addition, mood deteriorates progressively with the sleep pressure that accumulates during wakefulness.

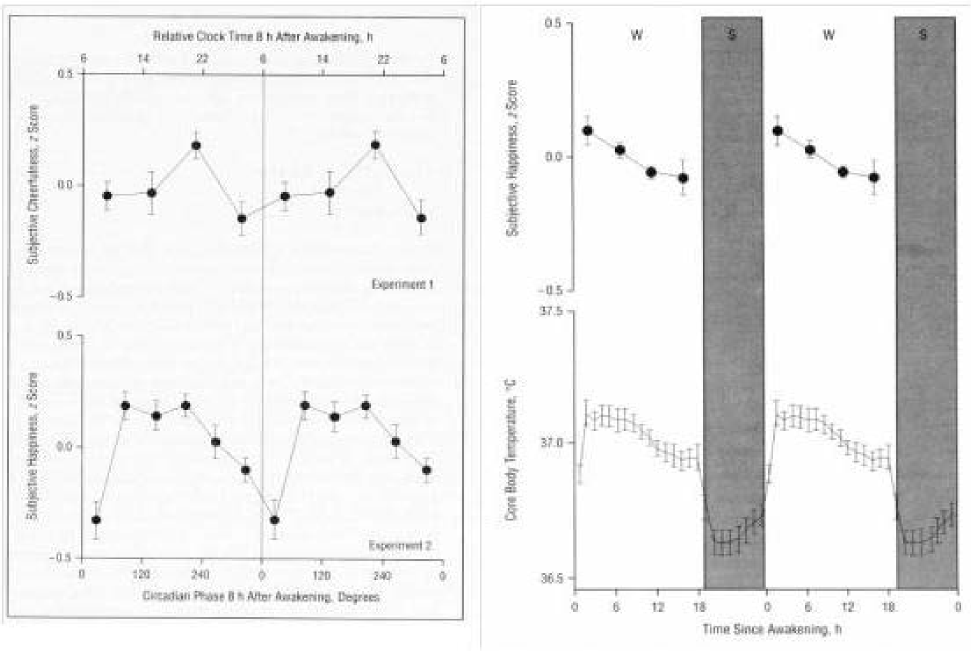

Figure 7: Circadian regulation of mood

The figure on the left shows the circadian regulation of mood, which is highest during the day and lowest at night. On the right, at the top, mood can be seen as gradually deteriorating during wakefulness; from Boivin et al. (1997).

As with cognitive performance, in conditions where the biological clock is synchronised and sleep is nocturnal, this dual regulation of mood helps maintain a stable level of mood over the course of the day. In conditions where the clock is desynchronised, in particular during night work, mood is lowest during night-time wakefulness. This phenomenon could contribute to the anxious and depressive mood observed in some shift workers.

3.1.4 Individual differences

3.1.4.1 Chronotypes

The moments of high or low vigilance do not occur at the same time of day in all individuals, meaning that the daily sleep episode can be shifted to varying degrees in relation to the day-night cycle. This individual characteristic defines the *chronotype*. Thus, some people will tend to wake up later and go to bed later when they have no obligation: these are the "night owls" who are defined by an evening chronotype. Conversely, people who naturally tend to go to bed and wake up early have a morning chronotype: these are the "early birds". The morning and evening chronotypes each form around 20% of the population; most people are of the intermediate chronotype.

An individual's chronobiological phenotype is multifactorial in origin (genetic, environmental, behavioural). In most cases, it reflects the internal time of the biological clock: earlier in morning chronotypes and later in evening chronotypes. These differences are partly based on the existence of a faster endogenous circadian rhythm (with a period of less than 24 hours) in morning chronotypes and a slower one (with a period greater than 24 hours) in evening chronotypes (Duffy *et al.,* 2001). The earlier or later time of the circadian clock can also result from the action of synchronisers, in particular light, which can produce a phase advance or delay. In both cases, when the internal time of the circadian clock is advanced or delayed, not only the sleep episode but also all other circadian rhythms occur earlier or later, including melatonin secretion.

Individuals with an evening chronotype are more alert and efficient in the evening, whereas those with a morning chronotype are more vigilant and efficient in the morning. The latter are generally less flexible in their sleep schedules: they have trouble staying awake in the evening and at night, they find it difficult to sleep during the day and, in general, cannot tolerate sleep deprivation (Review: Adan *et al*., 2012; Selvi *et al.,* 2007).

3.1.4.2 Age

Adjustment of the internal clock changes with age. There is usually a gradual delay in the clock during adolescence, which reaches a peak at the age of around 20. Adolescents and young adults therefore more often tend to have an evening chronotype. The biological clock then gradually becomes progressively earlier with age, which leads to an increasingly pronounced tendency to go to bed and wake up early. This trend is clearly manifested as early as middle age and is even more evident after the age of 60. The characteristics of the biological clock also show other changes with advancing age. It adjusts far more slowly following a time change, which is particularly evident in situations of jet lag. It generates a less robust circadian rhythm, yielding rhythms of lower amplitude, which are therefore more subject to desynchronisation. Lastly, the quality and duration of sleep also diminish with age, which makes recovery more difficult after sleep deprivation.

3.1.4.3 Sex

On average, women are more likely than men to have a morning chronotype. This may be linked to the fact that women have a significantly faster clock than that of men (Duffy *et al.*, 2011). The difference between the sexes is probably also related to sex hormones, because it becomes apparent at puberty and disappears after menopause. In addition, studies on female rodents have clearly shown that the endogenous circadian period varies depending on the reproductive cycle (Labyak and Lee, 1995).

3.1.4.4 Genetic differences

The quality and structure of sleep, as well as the quality of wakefulness, may also depend on genetically-determined factors.

Studies show that several genetic polymorphisms or mutations may be involved in sleep disorders (Tafti *et al*., 2007). The mutation of the Per2 clock gene has been observed in advanced sleep phase syndrome (a circadian rhythm disorder of the sleep-wake cycle in which the phase is advanced) (Toh *et al.,* 2001; Xu *et al.,* 2005). The mutation of the Per1 gene has been described in extreme morning chronotypes (Carpen *et al.,* 2006). In contrast, delayed sleep phase syndrome (a circadian rhythm disorder of the sleep-wake cycle in which the phase is delayed) and individuals of an extremely late chronotype have been associated with a polymorphism of the Per3 gene (Robillard *et al.,* 2002; Archer *et al.,* 2002). In animals, a mutation of the NPAS2 gene, a paralogue of the CLOCK gene, results in impaired sleep. Lastly, deletion of the BMAL1 clock gene and the melanopsin gene (the retinal photopigment responsible for transmission of light information from the retina to the internal clock) disrupts the structure of sleep, as well as the response to sleep deprivation (Laposky *et al.*, 2005). In healthy subjects, it has been observed that the polymorphism of the Per3 gene was involved in the internal structure of sleep (Per3 5/5 individuals had a particularly dense deep slow-wave sleep (Viola *et al.,* 2007)).

There is also great interindividual variability in the ability to resist sleep debt. The negative effects of sleep debt (Viola *et al*., 2007) and sleep pressure (Maire *et al.*, 2014) on vigilance and psychomotor performance are in fact particularly pronounced in individuals with the type 5/5 Per3 clock gene polymorphism. Thus, these individuals will have difficulty maintaining long-duration wakefulness, whereas this will be easier or more bearable for others.

The effects of caffeine consumption on wakefulness vary depending on the individuals and are also based on genetic factors. Studies have shown that the disruption of sleep by caffeine was linked to the blocking of the adenosine type 2A receptors, and that a common variation of this receptor in humans (ADORA2A) was involved in individual responses to caffeine (Retey *et al.*, 2007).

In conclusion, wakefulness, sleep, sleep pressure and the effects of caffeine on sleep are not the same in all individuals, partly because of genetic factors.

3.2 Impact of circadian disruption

3.2.1 Impacts of circadian disruption on physiology: animal models

The specific effects of circadian disruption on physiology are difficult to assess from epidemiological studies in humans, because of the lack of objective measurement tools, the great variability of exposure, the types of rhythms and hours practised and the potential contribution of other factors (diet, social stress, sleep disruption, use of psychostimulants). Moreover, even if laboratory studies in humans can help assess the impact of circadian disruption by controlling for confounding factors, they cannot be used to analyse the cellular and molecular mechanistic aspects. For this reason, it is necessary to model circadian disruption using animal models, under well-controlled experimental conditions, and while measuring the impacts up to gene level.

While animal studies are essential for understanding the cellular and molecular mechanisms underlying circadian disruption, it is important to mention some major limitations of animal models in chronobiology when extrapolating results directly to humans. Most studies have been, and still are, carried out with nocturnal animals (rats, mice, hamsters), whereas humans are diurnal. Indeed, with the notable exception of melatonin, which is always produced at night regardless of the species, production of many hormones (cortisol/corticosterone, glucose, leptin, testosterone) and a large number of biological functions (food intake, activity, sleep, cardiac function, vigilance) have their rhythms reversed between diurnal and nocturnal species. In addition, the two categories do not live in the same light environment and are not equally sensitive to the synchronising effects of light. Nocturnal animals limit their exposure to light during the day because they are for the most part photophobic, while humans are exposed to an average of 16 hours of light, whether solar or artificial. Rats, or any other nocturnal species, only need a few minutes of light per day to synchronise their biological clocks to 24 hours, while humans, under the same light conditions, would be completely desynchronised. The circadian system in rodents is virtually insensitive to light during the day, while that of humans is sensitive throughout the entire 24 hours (see Figure 3). Lastly, diurnal and nocturnal animals do not react in the same way to light and melatonin. While light has an awakening and pro-cognitive effect in humans, it has a hypnotic effect in nocturnal animals; a few minutes of moderate intensity light are enough to plunge a mouse into the deepest sleep (LeGates *et al.,* 2012 and Tsai *et al.*, 2012), whereas humans would be rendered temporarily insomniac by the same stimulus in the middle of the night (Cajochen *et al.*, 2005). Conversely, melatonin produces a hypnotic effect in humans, but not in nocturnal species.

From an experimental point of view*,* the models of shift work applied to animals are phase-shift models, which consist in forcing an advance or a delay in the time of the internal clock, with different amplitudes and speeds of rotation, in such a way as to reproduce the conditions of shift work in humans. Generally the times at which lights are switched on and off are shifted, but the times for feeding or locomotor activity can also be modified. This helps get as close as possible to the conditions experienced in humans in whom the light shift is usually associated with a shift in physical activity and mealtimes. However, the protocol cannot fully reproduce the workload of night shift work, because there is nothing to prevent the rodent from sleeping during the new period of darkness following the time shift (its new "period of night work"), nor anything obliging it to be active.

One last point to note is also that the majority of animal studies use male rodents, to avoid the interaction of circadian disruption with the typical reproductive cycles of females.

However, many women are also subject to irregular working hours, which could potentially alter their rhythm of reproduction.

Taking into account all of the physiological and experimental aspects described above, there is not at the present time any appropriate animal protocol or model for night work. Animal models are essential for investigating biological mechanisms, but care must be taken not to directly extrapolate the results to humans. As a result, the Working Group considered that the results obtained from studies carried out in animals could not be used as evidence of a health effect of night work. Nevertheless, the high degree of convergence between the observations in humans and the results in animals have contributed to the understanding of the mechanisms involved in the physiological consequences of circadian disturbances, such as those that can be caused by night work.

Studies in animals show that the central circadian clock in the suprachiasmatic nuclei resynchronises more quickly with new schedules than the peripheral clocks (located in the liver, heart, *etc*.). This is because the central circadian clock receives the light signals directly from the environment and can therefore rapidly resynchronise following a change in the light-dark cycle. In contrast, the peripheral clocks resynchronise more slowly, because they depend on signals from the central clock and are also sensitive to other synchronisers, such as hormonal (e.g. cortisol) and dietary factors. This difference in synchronisation speed leads to an internal desynchronisation between the different organs of the same body for several days, which disrupts their optimal functioning and the coordination of their functions.

The main consequences observed during circadian disruption imposed on laboratory rodents are:

1) a decrease in longevity, for example in mice subjected to weekly inversions of the light-dark cycle;

2) an acceleration of tumour growth, for example with lung tumours in rats subjected to chronic time shifts;

3) the onset of metabolic syndrome and a reduction in glucose tolerance, probably related to food consumption at inappropriate times;

4) considerable disruption of blood pressure and heart rate rhythms; in hypertensive and obese rodent models, the chronic shift in the light-dark cycle increases blood pressure and cardiovascular risk factors, ultimately leading to a decrease in survival time;

5) disruption of the occurrence of the peak of preovulatory LH[26] and oestrous cycles in female rats, and compromised gestation in mice subjected to 6-hour phase advances every 5 days;

6) the onset of depressive type symptoms with nevertheless great variability depending on the species and the type of circadian disruption practised but, as a general rule, light applied at night to nocturnal mice leads to anxious behaviour;

7) a decrease in cognitive performance and a reduction in hippocampal neurogenesis in rats subjected to simulated jet lag;

8) a deterioration in the immune system, or an increased inflammatory response, for example in rats or mice subjected to chronic inversions of the light-dark cycle, phenomena which tend to aggravate cardiovascular and metabolic disorders as well as the occurrence of cancer.

Although it is likely that some of the mechanisms involved are shared in mammals, caution should still be exercised when extrapolating animal data to humans.

[26] Luteinising hormone.

3.2.2 Impacts of circadian disruption on physiology: experimental studies in humans

3.2.2.1 Impacts of circadian disruption on sleep and wakefulness

The first manifestation of circadian disruption is a sleep or wakefulness disorder. As the propensity for sleep and wakefulness is largely under the control of the circadian clock (see Section 3), a misalignment between the sleep schedule and the internal cycle of the circadian clock is manifested by sleepiness (during wakefulness) or sleep disorders that can go as far as insomnia. The role of environmental factors (such as noise, high temperatures or light) has often been blamed in the disruption of daytime sleep. These factors certainly play an important role in causing sleep disorders in night workers, but laboratory studies demonstrate that they are not solely responsible. Indeed, the systematic displacement of the sleep schedule under controlled laboratory conditions has shown that the later the episode of sleep is shifted in the night, the shorter its duration (Akerstedt and Gillberg, 1981 and 1982). The circadian influence, which increases the propensity for wakefulness during the day, proves to be strong enough to wake the sleeper prematurely, which could explain why the later the night worker goes to bed, the shorter the duration of their sleep (Foret and Benoit, 1974). In addition, the inversion of the sleep-wake cycle in the laboratory reveals that the quality of sleep is also diminished and that this disruption may persist more than three weeks after the inversion (Weitzman and Kripke, 1981). An increase is observed in the stages of light sleep and the number of awakenings, as well as frequent changes in the stages of sleep. These changes to the internal structure of sleep are indicators of sleep that is unstable and of poorer quality. The decrease in sleep quality following an inversion in the daily cycle can occur at any age, but it is even more pronounced in people over the age of 40 (Gaudreau *et al.*, 2001).

Sleep that is too short and of poorer quality is accompanied by a decrease in vigilance levels during the period of wakefulness, which is also observed in night workers (Akerstedt and Wright, 2009). This decrease in vigilance is felt subjectively but can also be measured objectively by recording an electroencephalogram (EEG) during wakefulness. A greater proportion of slower EEG waves is associated with greater sleepiness, which has been measured both in the laboratory and in the field among night workers (Akerstedt and Gillberg, 1982).

3.2.2.2 Impacts of circadian disruption on other biological functions

As explained in the previous section, the main circadian clock helps synchronise a great many biological functions with the day-night cycles of the environment (see Figure 2). A modified daily cycle or exposure to light during the night will therefore modify the functioning of the circadian clock, the nocturnal production of melatonin and all the biological functions synchronised by this clock. Even when the main clock is resynchronised, following a trip to another time zone, for example, there is a lag between the resynchronisation speed of the main clock and that of the peripheral clocks, leading to a temporary state of internal desynchronisation of the body's clocks (in animals: Yamazaki *et al.* in 2000, in humans: James *et al.* in 2007). While working irregular hours or at night, the main clock is generally unable to resynchronise completely because of conflicting signals from the light-dark and sleep-wake cycles. In addition, sleep impairment caused by sleep that is too short and of poor quality also has an indirect impact on many physiological functions.

3.2.2.2.1 Impact on cell functions

To date, very few studies have been performed in humans to analyse the effect of phase shift or working irregular hours on cell functions and the peripheral clocks. A recent study showed that in humans subject to a 10-hour phase delay in their sleep-wake activity, the central clock resynchronised to the new schedule more quickly than that of the peripheral blood mononuclear cells (PBMCs) (James *et al.*, 2007). Interestingly, the ingestion of glucocorticoids in the late afternoon can specifically resynchronise the circadian rhythm of the PBMCs, independently from that of the main clock (Cuesta *et al.*, 2015). In humans, the production of cortisol, which has a circadian rhythm with a peak that takes place upon waking, could thus help resynchronise the peripheral clocks. In workers subject to irregular hours, the combined action of light acting on the main clock and glucocorticoids acting on the peripheral cellular clocks could serve as a basis for the development of a treatment to promote the resynchronisation of all the clocks of the human body.

3.2.2.2.2 Impact on metabolic functions

The circadian system is closely involved in the regulation of a series of processes related to metabolism: food intake, liver and intestinal activities, synthesis of neuropeptides (neuropeptide Y, orexins) and secretion of hormones (leptin, glucose, ghrelin, insulin, glucagon) involved in metabolism. In recent years, many epidemiological studies have suggested that work at irregular hours, including night work, has a negative impact on the metabolic parameters, in particular on body weight. It has been proposed that the time lag between the moment of food intake and the circadian rhythms of metabolism (intestinal and liver activity, *etc.*) may be responsible for metabolic disorders such as diabetes and excess weight or obesity. In addition, other epidemiological studies have shown an association between reduced sleep duration and metabolic disorders. Indeed, laboratory studies suggest that sleep deprivation impairs the metabolism of glucose, and could induce diabetes and obesity. Restriction of sleep decreases the secretion of leptin, a hormone signalling the state of satiety to the brain, and increases orexin, a hormone involved in appetite. The result is an increase in appetite and the consumption of high-calorie foods (sweet or fatty foods) (Balbo *et al*., 2010; Meerlo *et al.,* 2008; Spiegel *et al.,* 2009). Given that the circadian clocks are involved in metabolic rhythms and sleep regulation, disruption of the circadian system could lead directly and indirectly to metabolic disorders as a result of impaired sleep.

3.2.2.2.3 Impact on cardiovascular functions

The daily rhythm of cardiovascular functions depends on endogenous circadian rhythmicity, the sleep-wake cycle, environmental factors such as posture, and physical and mental activities.

There is a circadian rhythm in the function of the autonomous nervous system, with sympathetic tone dominating during the day and vagal tone dominating for much of night-time sleep (van der Pin *et al.,* 1994). In people who are active during the day, plasma levels of noradrenaline and adrenaline are higher in the morning and in the first few hours of activity, and are lower during night-time sleep. The nocturnal decrease in noradrenaline was observed even in healthy volunteers who were prevented from sleeping for 24 hours by forced activity and hourly food consumption, confirming its circadian control (Candito *et al.,* 1992).

Circadian desynchronisation disrupts the rhythms of the cardiovascular system. For example, the cells of the heart use fatty acids inefficiently, which leads to an accumulation of intracellular long-chain acids. This causes a malfunction of the heart's contractile properties *via* effects on the ionic channels, protein kinase C activity, the production of reactive oxygen species, and apoptosis regulation. The accumulation of harmful derivatives is associated with insulin resistance, glucose intolerance, dyslipidaemia, insulin deficiency, and an increase in vascular resistance. It is therefore easy to imagine how disruption of the central and peripheral circadian clocks may contribute to various alterations of the cardiovascular system (Young and Bray, 2007).

3.2.2.2.4 Impact on cognitive functions

The impact of circadian disruption on cognition is very clear. It can be explained by the significant control exercised by the circadian system on the brain structures involved in vigilance, attention and cognition. Laboratory studies, especially those making use of forced desynchrony, show a very clear decrease in cognitive and memory performance during the biological night, and a fall in psychomotor reaction time (Wyatt *et al.*, 1999). The studies also show that memory and cognitive functions are impaired not only in individuals not synchronised with the light-dark cycle (for instance free-running individuals, such as the blind), but also in those synchronised inappropriately (Wright *et al.*, 2006).

Since sleep and sleep pressure also play a role in cognitive performance, the impact of circadian desynchronisation also depends on the extent of sleep debt. Typically, the greater the sleep debt, the greater the sleepiness, the more the capacity for sustained attention is diminished and the greater the likelihood of making mistakes.

The varying influence of sleep-wake rhythms on a cognitive task depends on the nature of the task and its duration, complexity, interest or monotony. While taking this possibility of independent modulation into account, it is however accepted that circadian disruption may be accompanied by cognitive disorders. It is first worth mentioning the recent International Classification of Sleep Disorders, ICSD-3, which addresses in a specific section all the circadian rhythm disorders of sleep, including disorders related to working irregular hours and at night. It expressly mentions impaired mental abilities as one of the consequences of shift or night work, because of a decrease in vigilance, reduced performance with consequences on safety, and a greater risk of errors and accidents, especially in the early hours of the morning. Similarly, the ICSD-3 insists on the fact that "the level of vigilance demanded by the type of work, in addition to the intensity of the symptoms, must be taken into account during the medical assessment".

Aside from these disturbances related to wakefulness, there are others related to poor sleep. The role of sleep, especially slow-wave sleep and REM sleep, in learning, attention, encoding and memory consolidation has been demonstrated by many studies in both humans and animals (Walker and Robertson, 2016; Lavilléon *et al.*, 2015; Dudai *et al.,* 2015). Disruption or reduction of sleep time, independently of their consequences on vigilance, play a part in cognitive impairment *via* their impact on the circadian clock.

The cognitive process involved in a work task is difficult to analyse in real conditions. However, studies carried out in shift and night workers have focused on assessing cognition with batteries of standard tests falling more within the scope of fundamental research (see the recommendations of the French National Authority for Health). The first night resuming shift or night work has a particularly deleterious impact on cognitive performance. Other studies have reported that the decrease in performance over the night shifts could be explained by the anti-clockwise direction of the rotations, by accumulated sleep debt (loss of one hour of sleep every 24 hours) and also by the duration of the cycle or the working time (very long cycles or work for 10 and 12 hours). These attention disorders can cause accidents. In the summary produced for the recommendations of the French National Authority for Health (HAS) on occupational health monitoring of shift and/or night workers, it was reported that:

- night work, shift work and the duration of the shift are associated with an increased risk of road traffic accidents and near-accidents (occupational event during which personal injury or damage to health could have occurred) according to an OR ranging from 1.14 to 5.9 depending on the studies;
- the risks of road traffic accidents and near-accidents are greater during the commute home after a night shift;
- the risk of accident is significantly associated with sleepiness, as has been shown for example in studies of healthcare personnel
- night work, shift work and the duration of the shift appear to be associated with a higher risk of errors at work.

3.2.2.2.5 Impact on mood

The relationship between the biological clock and mood seems to be bidirectional. Circadian rhythm anomalies and daily variations in mood are often some of the symptoms of major depression. Indeed, although daily mood variations are observed in both healthy people and those suffering from depression, they are much more pronounced during episodes of depression (Morris *et al.,* 2007). In addition, other circadian rhythms are often disrupted in depressed subjects, in particular those of cortisol secretion and body temperature, which suggests disruption of the biological clock. Conversely, a disruption of circadian rhythms is frequently accompanied by depressive symptoms. As with vigilance, the combination of the circadian effect and the effect of the duration of wakefulness helps maintain a relatively stable mood during the period of wakefulness. Therefore, a time misalignment between the endogenous circadian rhythm and the sleep-wake cycle can cause mood to deteriorate during the period of wakefulness. Even though it is difficult to separate the effects of lack of sleep caused by circadian disruption from the direct circadian effect on mood, it is important to stress the frequent presence of depressive disorders in people suffering from a shift in their sleep-wake cycle (Lee *et al.,* 2011; Abe *et al.,* 2011).

3.2.3 Impacts on family and social life and links with health

Atypical working hours, whether at night or in the form of shifts, have effects on health that have been described and analysed in the literature. The related studies are of direct interest to companies that wish to preserve the health of their employees and are concerned about the associated costs (work or commuting accidents, occupational diseases, absenteeism, staff turnover rates). Studies examining the area of private life are less well known and attract only minimal interest from companies. However, what happens in the area of personal life will also have an impact on employee health: this is where many trade-offs occur and controls are established regarding the effects of shift work.

Working shifts and at night, and therefore against the predominant social rhythm, does indeed have consequences on personal life. Being occupied by a work activity at the times when most family and social activities are socially planned condemns the employee to exclusion. It thus becomes difficult to participate in meetings of associations, sporting events and social get-togethers, and the time devoted to children, to their care and following their progress in school, can be affected. There are few studies on the subject but they all show that the family environment can be adversely affected by the practice of atypical working hours, parental relationships can be impacted, and the understanding between couples can deteriorate. There are, however, major differences according to the characteristics of the employee's shift system, the number and age of the children, and whether or not the spouse also has a job (Prunier-Poulmaire and Gadbois, 2004).

But besides the intrinsic value of understanding these major disruptions to personal life related to difficulties reconciling time, it is important to examine the extent to which they may have an effect on the health of employees. While it is easy to conceive how the deterioration of social life and destabilisation of family life are accompanied by effects on the psychological and mental health of individuals, it is less obvious to imagine the extent to which this affects their physical health. However, doing without a short nap before a night shift – while the physiological need is actually felt – in order to share a family dinner constitutes a trade-off in favour of family life to the detriment of sleep, and therefore health. Similarly, not going to bed immediately after a night shift in order to care for one's children and take them to school is a trade-off that places the requirements of family life before those of a biological nature.

Thus, employees do not passively submit to the destructuring effects of their atypical working hours, they actively seek to reconcile and harmonise the time requirements of their professional activity with those of the other areas of their lives. But in this framework, finding a balance requires endless compromises and the establishment of control strategies designed to minimise health effects. Measuring the health effects of working hours therefore requires the consideration of the employees' extra-professional situation, where control strategies are adopted that may strengthen or reduce the adverse effects of the hours practised.

It is therefore to this effect and in this systemic conception of the effects of atypical working hours that it seems essential to consider the controls at play in life inside and outside of work (see Figure 8). This approach then requires a systemic and multifactorial approach to be developed in order to understand and act on the effects of shift work, whether or not it includes night work.

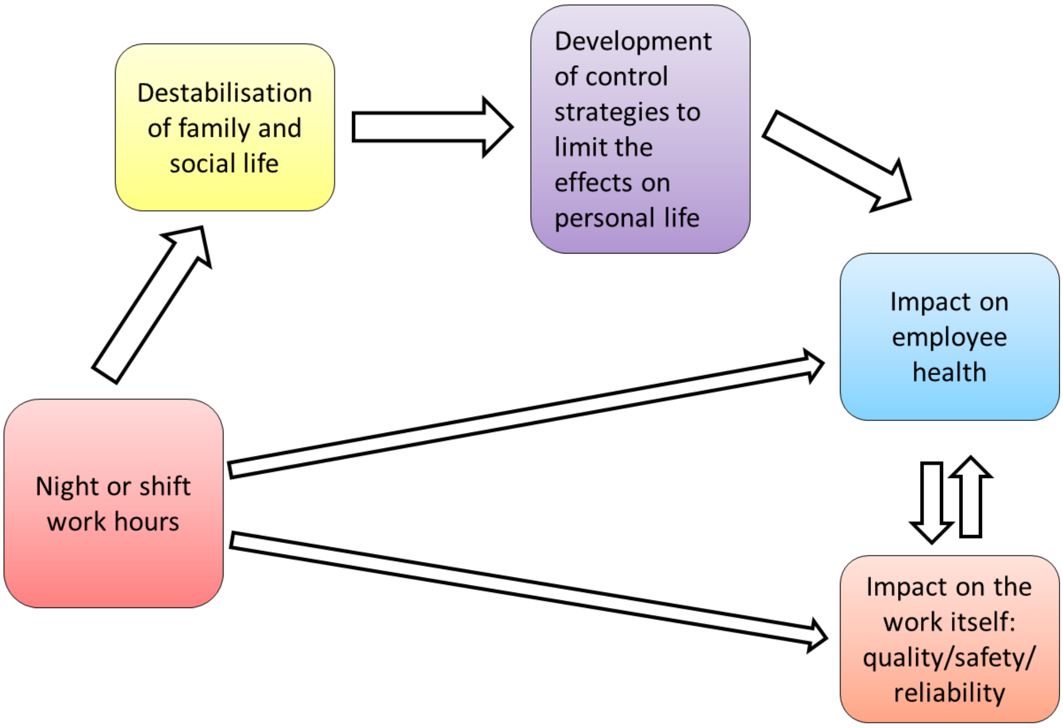

Figure 8: Multifactorial approach to the impacts of night or shift work hours on employee health and work quality

3.2.4 Impacts of the disruption of circadian rhythms induced by atypical working hours: systemic and multifactorial approach

Shift work including night work upsets the mechanisms of circadian rhythmicity both at the biological level (rhythms regarding sleep and wake, meals, hormonal secretions, vigilance and mood) and in the time organisation of social and family life.

In view of these multiple deregulations and because employees actively seek to manage them, the links between rotating hours including night work and the health effects are not direct or unequivocal. To understand them, it is necessary to account for the complexity of the situation in which night and shift workers are placed.

For example, a salary increase linked to shift work could enable an employee to take a loan to purchase a private home, which would then oblige them, even if their health were to deteriorate, to continue working these hours for the entire duration of the loan. In the same way, nurses for example, who work at night and whose shift ends at 6am, will not all go to bed immediately after their shift; some will choose (for family or financial reasons) to take care of their children during the day, to the detriment of the recovery of their sleep debt and their health. Another example: when prison guards on 2 x 12 hour shift systems work successive day and night shifts in order to accumulate days off and go home to their families living hundreds of kilometres away, it is to the detriment of their sleep and sometimes the quality and reliability of their work.

Thus, the dimensions that are affected by the issue of shift and night work and that will collectively affect employee health relate to characteristics of both the individual and the work (see Figure 9).

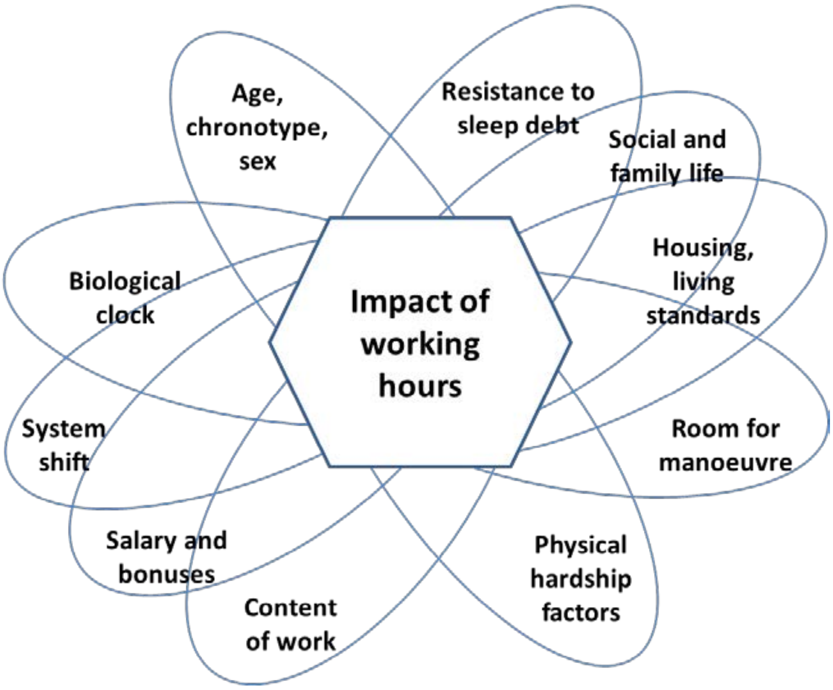

Figure 9: Multifactorial and systemic approach to the effects of working hours (adapted from Quéinnec, Teiger and Terssac, 2008)

The employees' individual characteristics, such as age, sex and gender-related social roles, resistance to sleep deprivation, and chronotype (morning, evening), will determine a higher or lower tolerance to the circadian desynchronisation imposed by shift work including night hours.

The individuals' family and social characteristics will also play a part in this tolerance to the desynchronisation induced by irregular hours. Indeed, the family situation, whether or not the worker has children (especially young ones), whether or not they have a spouse in their family, their degree of participation in domestic life and parenthood, the spouse's working hours, as well as the distance from home to work, the quality of the housing (for example in terms of noise, lighting, comfortable temperature), level of income, *etc*., are just some of the sociological elements that will make it easier or more difficult for individuals to reconcile their working lives with their lives outside work, and to recover their sleep debt.

Lastly, these individual characteristics, whether physiological or sociological, evolve during the working life and as the person ages. Thus, the duration of exposure to shift and night work will have an impact on health, and changes to the worker's personal life (marital life, arrival of a child, growing-up of children, but also separation, shared custody, departure of children from the home, *etc*.) will affect the reconciliation strategies adopted at a given time in the working life.

Other dimensions relating to work and the work situation should be taken into consideration. The specificity of the shift system in place, i.e. the time at which the shift begins (4am or 7am for example for the morning shift), the shift duration (8 or 12 hours), the direction of rotation (clockwise or anti-clockwise), the number of consecutive nights, the predictability of the schedule, *etc*. have differentiated effects on mood, fatigue, vigilance and health. But the time envelope of the shift or night work is not the only factor responsible. The amount of the salary and associated bonuses affect the standard of living, and therefore the quality of the housing, the childcare options and the possibility of recovering sleep debt. The content of the work itself and any combination with other hardship factors (exposure to noise, toxins, high work rates, *etc*.) will impact health. The specific context of night work (little or no line management, closure of other departments, *etc*.) can enable the employee to work in quieter conditions, to learn, to take on responsibilities, but conversely, can be a source of stress. These points should be taken into account in addition to the shift system itself.

Lastly, individuals do not passively submit to the effects of the hours, they actively seek to harmonise their working hours with the constraints and resources of the other dimensions. To manage this balance between these identified dimensions, when there is room for manoeuvre, employees actively adopt control strategies designed to minimise the health effects, at work and outside work. This adds complexity to any analysis of the impacts of disrupted physiological and sociological rhythms induced by shift and night work.

The impacts of the physiological and sociological destabilisation due to working hours can only be measured through the prism of the interactions between the different dimensions with which the working hours either align or clash.

4 International review of expert appraisal work

4.1 Objective of the review

ANSES launched a consultation among several foreign occupational health organisations, through its European and International Affairs Department (DAEI), with the aim of gathering information on studies under way concerning shift work including night work, to support the health risk assessment conducted by the Working Group.

4.2 Method used and results obtained

A literature review was conducted to identify studies on shift work including night work already carried out or currently in progress in Europe and elsewhere in the world. This helped target more effectively the main actors involved in this topic (a summary table of the studies identified is provided in **Annex 3.**).

Once these actors had been targeted, along with other ANSES partners, these organisations were emailed directly with a questionnaire. This questionnaire, drawn up by ANSES and validated by the Working Group, was based on three major themes:

- health impact and assessment of health risks;
- existing available data;
- public policy, importance placed on the topic and regulatory context.

This questionnaire can be seen in Annex 4.

This consultation was launched on 15 February 2015 and was aimed at twelve organisations located in nine countries.

After approximately two months, seven organisations had replied with a detailed response to ANSES (see Table 7 below).

Table 7: List of organisations responding to the Agency's consultation

Organisation	Country
Federal Institute for Occupational Safety and Health (BAuA)	Germany
Occupational Cancer Research Centre (OCRC)	Canada
The National Institute for Occupational Safety and Health (NIOSH)	United States
Health and Safety Authority	Ireland
National Institute for Public Health and the Environment (RIVM)	The Netherlands
Health and Safety Executive (HSE)	United Kingdom
Finnish Institute for Occupational Health (FIOH)	Finland

The main elements that emerged from this consultation are as follows (the full overview is available in **Annex 5.**):

- Health effects

The Working Group noted the main effects examined by the studies and was thus able to assess the relevance of the choices made in the framework of this expert appraisal.

The health effects reported most frequently in the studies were cancer, metabolic disorders and cardiovascular diseases, in particular because of their high incidence and growing health impact. In addition, this consultation highlighted the fact that some organisations are also working on other less documented aspects, such as immune functions, infections, and effects on the reproductive system (menstrual cycles, pregnancy complications, miscarriage, premature births, *etc*.).

- Other studies in progress

Work is being carried out in the Netherlands in the laboratories of the RIVM (National Institute for Public Health and the Environment) to characterise the physiological effects of human night-time exposure to light. In particular, some of the work is aiming to determine the biomarkers involved in circadian disruption.

- Longer-term research needs

As regards research needs in the longer term, this consultation revealed the following points:

- the need to better define shift and night work, in order to better quantify exposure;
- the need to determine whether there are causal links between shift and night work, and the health effects;
- the identification of occupational groups who are more at risk, and the development of preventive measures to mitigate the risk;
- the establishment of new cohort studies to assess the link between breast cancer and shift work.

This international consultation led to a closer working relationship being initiated with the RIVM. Discussions took place and provided the opportunity to communicate more specifically on the work in progress on this topic. In more practical terms, the literature references identified by the Working Group for all the studied health effects were made available to the RIVM.

Moreover, the reporting of other health effects being examined in studies by different organisations reinforced the need, in the framework of this expert appraisal report, to supplement the documentation on the other identified effects that were not selected for in-depth analysis.

5 Assessment of the non-health risks associated with shift work including night work

5.1 Expert appraisal method

5.1.1 A specific working method for aspects concerning the human and social sciences

As with the study of the health effects, keyword searches were initially performed on the *Scopus* search engine (www.scopus.com) for the period from 2010 to 2014, leading to a large number of publications being identified (more than 1000 articles).

Because of the numerous publications identified and the inadequacy of some of these in relation to the subject in question, as became clear following a brief review of the abstracts, the Working Group decided to adopt a specific, more suitable method. In order to support their findings, the experts used all the publications they deemed useful, "giving priority to those of key importance, of good quality, or those that posed interesting and new questions". The criteria for the inclusion of articles were therefore mainly based on the experts' specific knowledge and skills.

5.1.1.1 The effects of atypical working hours: a complex subject of study

The subject of this expert appraisal report relates to "the health effects of atypical working hours, especially night work". However, the effects of atypical working hours are only meaningful because individuals are subject to these particular hours and because these individuals work during these hours.

These individuals can be women or men, young or old, needing a lot of sleep or only a little, from couples without children or with one or more children, or the heads of single-parent families, living in a noisy urban dwelling or a quiet countryside setting, *etc*.; the tasks that these atypical individuals have to accomplish during these particular hours may be mediocre and repetitive, enriching and varied, cognitive or physical, at high or low work rates, carried out alone or as part of a team, with limited or very broad autonomy, *etc.* (see Section 2.4 on the reality of shift work and night work in France). It is therefore necessary to include in this subject of study the diversity of the individuals and working situations, and the multiplicity of health, psychological and social repercussions likely to result. This systemic and holistic approach to the health effects of atypical working hours is discussed and developed in this section.

Accordingly, some of the studies consulted in the analysis for the sections on the socio-economic consequences and the modulators of the effects of shift work including night work relate to actual situations of atypical working hours, in all their variability and complexity. These studies mainly focus on issues of ergonomics. Taking the specific characteristics of the situations into account is of major importance for the prevention of these effects and for the action to be taken. It is not the effect that is measured directly in these studies but the relationships between the different components of the studied system that can modulate the effect. This essential analysis cannot be done using epidemiological or experimental studies. It involves a supplementary analysis to which the same methodological rules do not apply.

5.1.1.2 Validity of the studies on this subject of study

A valid study is one that provides an answer to the research question asked. With a research subject such as the one we have just defined, it is therefore an interdisciplinary study that takes into account all (or as many as possible) of the factors and sources of variability that could provide insight into the link between atypical working hours and health, also incorporating the physiological, cognitive and social dimensions of the individuals and an analysis of the work performed during these hours. It is a study that is part of a transformation process, and therefore, a study that enables action.

Thus, concerning the method used, the clinical method is most often preferred, being the most appropriate, and the case study. In the words of Falzon (Falzon, 1998): "The case study is one way of addressing the complexity of natural situations".

5.1.1.3 Level of evidence of the studies on this subject

These studies provide insights into individual and collective work situations, and sometimes levers of action that better take into account the reality of the work. They can also help with the analysis and discussion of the results of epidemiological studies, which are unable to address this complexity of work situations quite so comprehensively.

Many of the studies exploited are qualitative, seeking to illustrate the complexity and multiplicity of work situations as well as the diversity of the populations working atypical hours, rather than aiming for statistical representativeness. As the resulting observations and analyses cannot necessarily be generalised, there can be no question here of level of evidence.

According to Falzon, it may be possible to generalise, and therefore increase the level of evidence for the investigated links, using case studies. This generalisation is subject to different conditions: prospective reuse, retrospective reuse, and the repetition of cases (Falzon, 1998).

5.2 Socio-economic aspects of night work and shift work

According to the World Health Organisation (WHO), "Health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity". It is therefore important to consider the workers in their entirety, in order to identify the indirect effects of night work and shift work on their well-being, social life and family life. It was for this reason that the Working Group decided to address the socio-economic aspects of night work and shift work in this section. The aim of this approach is to gain a systemic and holistic view of the issue addressed.

5.2.1 Justification of atypical working hours (night and shift work)

According to Article L. 3122-32 of the French Labour Code, *the use of night work [must be] exceptional*. *It must take into account the requirements to protect the health and safety of workers and be justified by the need to ensure the continuity of economic activity or services of social value".* Employers must therefore justify in what way resorting to night work is necessary to ensure the continuity of their economic activity or is "socially" useful.

In this framework, and as an example, some sectors have put forward the following arguments to justify shift and night work:

- maintaining security, health issues: hospitals, police, armed forces;
- consumption and service activities: hotel and catering sector, breakdown services, transport, radio station personnel and, nowadays, museums, shops, *etc*.;
- economic arguments: amortising investments by extending the use of assets, energy cheaper at night, *etc*.;
- work abroad (different time zone): transport, corporate lawyers, *etc*.;
- use or manufacture of rapidly perishable materials (industry);
- climatic variations and production imperatives in agriculture.

Besides the most recent developments in the legislative context (presented in Section 2), it should be mentioned here that many negotiations on working time now take place at professional branch level, in particular for small and very small companies. Collective bargaining is used to define ways of organising working time that best suit the situation of the companies; this is reflected in the emergence and spread of increasingly atypical working hours.

5.2.2 Economic dimension

5.2.2.1 Continuous, round-the-clock work: different rationales according to the sectors

Night work may be unavoidable by nature, imposed by public service constraints, such as with health services, on-call police officers or other surveillance services, or it may simply be a work organisation method, for example with a company that wishes to maximise the profitability of its equipment by getting machines and people to work around the clock.

In the first case, for example in hospitals, the obligation to provide the service partly does away with the need for any profitability calculation, even though with "activity-based pricing" in hospitals, the situation has changed considerably. The different work organisation methods[27] invite comparison: the 2x12h shift system is popular among managers, because this type of rotation can reduce the number of employees needed over the 24h by reducing shift handovers (2 instead of 3 over the 24h). However, this type of public interest service is still primarily underpinned by a need for continuity of the public service, even if this has to be at the expense of a purely managerial optimisation of the financial and human resources.

In the case of industry or service sectors, the logic is different: here the cost-benefit ratio is the result of a financial optimisation calculation by management[28], which takes amortisation of production equipment into account and relates it to the additional costs incurred by the night and/or shift work: heating and lighting of the premises, higher salary costs, *etc*. Therefore, the more an industry is "capital-intensive" (i.e. a sector that mobilises a large volume of tangible assets per employee), the more night work will potentially be profitable in accounting terms.

This is illustrated by the example of a tyre production plant operating a 3x8h system (3 rotating shifts over 24h) which, to avoid closure, has suggested to employees the establishment of a 4x8 system, i.e. still organised as 3x8h, but with four teams rotating on these shifts instead of the five teams in place previously. This decrease in the number of teams imposes a more rapid pace of work, with more weekends in the rotation and less rest between the shifts.

5.2.2.2 The concept of negative externalities and compensatory mechanisms

An analysis of the economic impact of night and/or shift work cannot be limited solely to the scope of the company or institution. The consequences on employee health largely extend beyond this framework, as has been seen with other occupational risks, such as those related to psychosocial factors at work. The socio-economic consequences primarily concern the social welfare system, which is required to bear the costs associated with this deterioration of employee health, mainly because night and/or shift work have not been included in the occupational diseases table.

To better understand this mechanism, it is necessary to refer to the concept of "negative externalities" developed by economists. They define "externality" or "external effect" as the

[27] See the report by Boulin and Taddei on the organisation of working time, still relevant (Journal "Travail et Emploi" No. 40 - 02/1989).

[28] Aykin, T. (1996) Optimal Shift Scheduling with Multiple Break Windows, *Management Science, 42, 591-602.*

fact that "*the production or consumption activity of an agent affects the well-being of another without either party receiving or paying compensation for this effect. An externality thus has two characteristic features. On the one hand, it concerns a secondary effect, an external impact of a main production or consumption activity. On the other hand, the interaction between the issuer and the receiver of this effect does not give rise to any market compensation*[29]". Thus, all forms of pollution are a typical example of a negative externality: when a factory discharges waste into the environment, it can cause a nuisance to the inhabitants of the region, without paying any compensation.

If one of the characteristics of night work is that it can contribute to a deterioration in the health of the employees concerned, it should be considered that the monetary compensation offered to the employees does not cover the full cost to society, even if from the employee's point of view, the recovery time or the bonus paid directly can "compensate" for the constraints and hardship induced by the atypical working hours[30]. In addition, this cost is borne by the social security healthcare scheme and not the work accidents and occupational diseases scheme. There is therefore clearly a case of "negative externalities" here, which deserves to be quantified. However, quantification can still be difficult because of the "time lag" between exposure and any associated disorders. Any assessment of a willingness to pay to avoid the risk of a possible long-term health problem occurring (resulting from the night/shift work) compared with an immediate "profit" (from the job) would most likely favour the short term: the employee working atypical hours therefore minimises the risk and the monetarisation of any health consequences.

The only example of compensation obtained by employees for the deterioration – related to night work – of their state of health comes from Denmark, which in 2008 awarded indemnities to 37 women with breast cancer that was linked to night work. The indemnities were paid by the employers' insurance companies. This Scandinavian country was even considering adding the effects of night work to the list of occupational diseases – provided that it took place at least once a week over 20 to 30 years of employment.

Since then, Denmark's Occupational Diseases Committee[31] has examined the link between night work and breast cancer. Based on the scientific studies analysed, it considered that there was insufficient medical knowledge to confirm the existence of a link between night work and the risk of developing breast cancer, for women exposed to night work once a week over 25 years. On the other hand, in cases of several nights worked per week, over a period of less than 25 years, the dossiers are examined by the Committee on a case-by-case basis, and can give rise to compensation[32].

In France, it is possible to declare and have recognised as an occupational disease a condition causing a level of permanent partial disability ≥ 25% (which is usually the case with cancer), by the regional committees for the recognition of occupational diseases (CRRMP). Theoretically, it is now possible to get a disease related to night/shift work recognised in this framework (it nevertheless requires the victim to prove a direct and essential link between the work and the disease in question, which in practice is very difficult).

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[29] Dominique HENRIET, "EXTERNALITÉ, *économie*" [Externality, economics], *Encyclopædia Universalis* - http://www.universalis.fr/encyclopedie/externalite-economie/, Guerrien B., (2005). *Dictionnaire d'analyse économique;* Repères-La découverte 568p.

[30] Michel Gollac, Christian Baudelot, *"Economie et statistique"* [Economics and Statistics] 1993 Issue 265, pp. 65-84.

[31] Denmark: Revision of the criteria for recognition of breast cancer related to night work www.eurogip.fr/en/eurogip-infos-news?id=3733.

[32] Wise J. *Danish night shift workers with breast cancer awarded compensation*. BMJ 2009; 338.

5.2.2.3 The social cost of night and/or shift work extends beyond the purely health-related costs

The social cost to the community of shift work including night work is not limited to the healthcare provided to employees: it should also include the cost of social consequences such as the impact on family life (cost of child care, divorces, *etc*.) and the costs induced by transport (setting up public transport night services, commuting accidents, *etc*.).

The generalisation of shift work including night work over the last few years has led to a transfer of value from civil society towards companies using atypical working hours, a transfer that obviously does not give rise to any compensation (with the exception of the salary supplement, which can be estimated at 8.1%[33]).

This social cost of shift work including night work is very difficult to assess, because there are almost no statistics associating the medical and social consequences with the working hours. For example, it seems as though work accident reports in France generally do not mention the type of working hours practised. This means that a work accident occurring at noon to an employee working normal hours, who therefore started the day at 8 or 9am, is viewed in the same way as a work accident occurring at the same time, but to an employee who started their working day at 4 in the morning.

Quantifying such externalities is very complex, given the multidimensional nature of the consequences of shift work including night work. It is obviously possible, but requires specific studies[34], needing significant resources, which no doubt explains why such studies are currently unavailable in France.

As an illustration, Philippe Askenazy[35], an economics researcher interviewed by the Working Group, informed us of a few studies [(Kostiuk, 1990), (Lanfranchi *et al.,* 2002), (Schumacher and Hirsch, 1997), (DeBeaumonte and Nsiah, 2010)], but these most often address very specific points, such as the most cost-effective way for the company to organise shift work, the impacts of atypical working hours on staff turnover and absenteeism, or the role of the salary bonus in the decision to work at night. This is a long way from estimating the costs of the deterioration in employee health following night and/or shift work.

5.2.3 Repercussions of night and shift work on social and family life

While the effects of night and shift work on health have been relatively well documented in the scientific literature, the same is not true for their effects on the employees' life outside work.

Indeed, few scientific studies have focused on the impact of these hours on family and social life, although there has been renewed interest in recent years. This lack of studies can certainly be explained by the difficulties faced by researchers when embarking on this specific field of study, but also by the minimal interest it attracts from companies, which are

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[33] According to DARES (DARES Analyses, No. 062), in 2012, the salary supplement associated with regular night work was estimated at 8.1% and that associated with occasional night work was 3.6%, compared to employees who never work at night. This salary supplement is established from the net hourly rate: it is calculated by dividing the net monthly salary (including monthly bonuses) by the number of hours worked on a monthly basis, both of which were reported to the 2012 job survey (after adjustment for non-responses). Apprentices and trainees are excluded from the count.

[34] A Swiss study examined the effects of unfavourable working conditions on the health of workers, and their economic consequences [Elisabeth Conne-Perréard, Marie-José Glardon, Jean Parrat, Massimo Usel: *Effets des conditions de travail défavorables sur la santé des travailleurs et leurs conséquences économiques*. Swiss Romande & Ticino Conference of the Offices for Worker Protection, December 2001].

[35] Philippe Askenazy, Research Director at CNRS, Researcher at the Paris School of Economics, and Doctor at the School for Advanced Studies in Social Sciences (EHESS).

more interested in assessing the health effects of working hours in order to counter and combat their potential economic consequences: absenteeism, accidents at work, commuting accidents, *etc*.

What happens in the area of a worker's personal life because of the working hours they perform may also give rise to health effects. Social and family disruptions can, in and by themselves, be a cause of health problems. And yet knowledge in this area remains partial and highly inadequate, even though since the 1980s certain researchers have been warning about the need to explore this field of research (Rutenfranz *et al.* 1981; Loudoun and Bohle, 1997; Prunier-Poulmaire, 1997; Gadbois, 2004; Camerino *et al.*, 2010).

In addition, it is in the area of a worker's private life that methods to control the effects of shift work are established, and where many trade-offs occur, most often favouring family life over health. In this respect, life outside work is then undeniably linked to health, as defined by the WHO, i.e. physical, mental, psychological and social.

The effects observed on employee health are not exclusively the result of biological desynchronisation, but are a combination of the biological consequences of performing these types of hours and the consequences resulting from the complex trade-offs and costly attempts at reconciliation between the private and professional spheres (Ramaciotti *et al.*, 1990; Prunier-Poulmaire, 1997, Wight, Raley and Bianchi, 2008, Handy, 2010). Ramaciotti *et al.* thus argue that the shift workers with the most health disorders are those who assess their work as arduous and feel that it adversely affects their lives outside work (Ramaciotti *et al.*, 1990; Ramaciotti *et al.*, 2005). This was also reported by the authors of the BEST Bulletin (Eurofound, 2000) when they stressed that social and family requirements can pressurise workers to stay awake in the evening, or interrupt their sleep to eat a meal with their family or take care of domestic tasks; which leads the shift workers to shorten their sleep time.

We should stress, before developing our point, the difficulty summarising the results from the literature on this specific topic. Finding an agreement at the international level on the specific effects of working hours on family and social life is complex because of social rhythms and lifestyles that are unique to each country (differences in daily and weekly school rhythms, varying degree of community involvement according to cultural tradition, opening and closing times of shops and public services, mealtimes, *etc*.). Accordingly, ending a shift at 7pm may seem inconvenient for employees in a northern European country where dinner is generally eaten early, but has no particular effect on those in southern Europe, where cultural habits are very different in this regard. However, the studies tend to show that the more atypical the hours, the more employees feel it is difficult to reconcile family and professional life and organise themselves (Fagnani and Letablier, 2003; Campéon, Martin *et al.*, 2005; Le Bihan and Martin, 2007; Meurs and Charpentier, 1987).

5.2.3.1 Impact on family life

Among the research carried out on the consequences of night and shift work, some scientific studies have focused on effects due to the fact that the shift work is out of phase with the employees' family lives. The periods of availability provided by these hours do not coincide with the most widely accepted social calendar, and this mismatch disrupts the shift workers' lives outside work (Quéinnec, Maury and Miquel, 1992). A deterioration in exchanges within the family unit and disruptions to everyday life also constitute the theme of the complaints most frequently reported by shift workers (Bunnage, 1984; Smith and Folkard, 1993; Pierce *et al.*, 1989; Meurs and Charpentier, 1987). Gadbois drew on the results of several American and European surveys to describe the consequences of these working hours on the lives of shift workers and their families: *"...they are often only available at times of the day (or week) when many activities cannot be performed or can only be performed in unsuitable conditions... the shift workers often attach more importance to these family and social disruptions than to the physiological consequences: fatigue, sleep and health disorders."* (Gadbois, 2004). The first studies on this theme date back to the mid-1960s and they have continued, on a fairly regular basis, up to the present. In the remainder of this document, reference will sometimes be made to earlier studies that are still widely cited today in the literature because of the advances they represent and the methods used.

5.2.3.1.1 Constraints of shift work faced by couples

- *Limited time for meeting and sharing*

Studies (Gadbois, 2004; Prunier-Poulmaire and Gadbois, 2004) relating to family life report a change in the relationship between shift workers and their spouses. The hours result in the workers in question being less available at times that are extremely important for family life (meals, evenings, *etc*.): either they are at work, or they are at home but have a physiological need to rest and overcome the fatigue generated by their work rhythm. It may therefore be necessary to consider the physical and psychological status of shift workers during their free time: in addition to the "effective mobilisation" experienced at their place of work, there is a "consecutive mobilisation" during their non-work time while they recover from the completed shift, and also an "anticipatory mobilisation" in which they prepare themselves for the shift to come (nap, daytime sleep before a night shift) (Prunier-Poulmaire, 1997). A survey of nurses working fixed night shifts supports this hypothesis: a large proportion of them admitted seeing as a constraint the fact that they had to deal with their children's school work on their return home (Zerr-Perardel, 1988). Yet, as shown by the study of Lowson *et al.* (2014), which included interviews and questionnaires with English nurses and midwives, these employees tried to minimise the effects on their families of the nights worked by resuming household chores and the family rhythm as soon as possible after the night shift: by cutting short their sleep to pick up their children from school and prepare meals. But this has physical and psychological consequences.

The time available for their families also decreases in quantity and quality. Shift workers say they feel unable to devote enough time to their families and keep their commitments in the marital and domestic sphere (Nachreiner and Rutenfranz, 1975). Changes in conjugal relations may be partly related to this lack of time for sharing with each other (Meurs and Charpentier, 1987). Thus, a survey by Wedderburn (1981) revealed that 39% of steel industry workers performing shift work were unhappy about the scarcity of shared time with their spouses. The same year, a study by Gadbois (1981) on 800 nurses provided similar results: 85% of nurses on rotating shifts felt that the time spent with their spouse was insufficient, compared with 60% of those on fixed day and fixed night shifts. This feeling was shared by the spouses of the nurses on rotating shifts: only 13% reported that they were satisfied with their spouses' hours compared with 29% of those whose wives worked fixed night shifts and 54% of those whose spouses were on fixed day shifts.

- *A change in conjugal relations and sex life, the emergence of role conflicts*

The change in couples' relationships has not only been addressed from the perspective of how much time is spent together, but also with regard to the quality of inter-conjugal relations (Maume and Sebastian, 2012). The reduction in shared time can lead to a feeling of frustration, which alters the very nature of the relationship between a couple gradually deprived of common references. The earlier work by Mott *et al.* conducted in 1965 remains a reference in this area. This study of around a thousand shift workers in five American factories sought to compare three types of shifts (3x8 continuous, fixed afternoon shifts, permanent night shifts) as to their effects on couples' relationships. Regardless of which aspect of conjugal relations was considered, it was the workers on rotating shifts that faced the greatest difficulties in their marital lives. They primarily regretted being unable to ensure the protection of their spouses, being unable to spend time with them to carry out activities together, having unsatisfactory sexual relations, and being unable to demonstrate better mutual understanding or decide the major family priorities together. Although carried out a long time ago and in a North American context, the particular importance of this research is that it identifies the actual nature of the difficulties encountered by shift workers with their spouses, depending on the shift systems practised: with regard to ensuring the protection of their spouses and having unsatisfactory sexual relations, permanent night workers faced the same difficulties as those on rotating shifts. This same study revealed that workers on a 3x8 system, or working fixed nights or afternoons, felt less fulfilled in their marital lives than their colleagues working regular daytime hours. It is also interesting from a methodological point of view: assessing the constraints imposed by shift work on family life requires a thorough analysis of partner relations in all its constituent dimensions, differing according to the specificities of the shift being practised. The work of Koller *et al.* (1990) led to similar results: shift workers at an oil refinery questioned about the quality of their marital relations five years apart reported experiencing a deterioration in the quality of these relationships. It should further be noted that a deterioration in marital understanding and difficulties in couples' relationships may also, in the longer term, be manifested as psychological disorders related to guilt, frustration, the recurrence of inter-marital tensions, and disruptions to the state of health (Mott *et al.*, 1965).

Only a few rare studies of the impacts of shift work have been conducted by questioning the partners of those who perform it. However, they show that the social life of families is diminished (especially the opportunity to participate in recreational activities at the weekend), the hours disrupt the lives of the shift workers' partners, and the work leads to dissatisfaction among a majority of partners, who are therefore not in favour of it (Smith and Folkard, 1993). This study by Smith and Folkard showed that 75% of the partners of nuclear power plant workers complained of strong disagreements with their spouses, 55% felt that their sex lives were affected, 58% reported that their personal social lives were hampered, while 60% considered that their shared social lives were reduced due to their spouses' working hours.

With a methodology that was also based on collecting spouses' opinions, Lee *et al.* (1982) showed that the inconveniences of shift work performed by Korean workers (rubber and steel industries) were considered greater by their partners than by the shift workers themselves: 48% compared with 24% complained of the restricted time spent with their children, 51% compared with 27% complained of a limit to the amount of family leisure time, 33% compared with 25% complained about intimacy as a couple. This same survey revealed that 57% of the partners of shift workers said they argued with their partner on topics related to the shift work.

The hypothesis that performing shift work may increase the frequency of divorce has been put forward. This is suggested by a longitudinal survey (over 5 years) performed on a national sample of American families, which revealed that among men with children, the probability of a divorce or separation was six times higher for those working fixed night hours than for those working regular daytime hours; among women with children, the probability of a break-up associated with performing fixed night work was tripled (Presser, 2000). The work of Kalil *et al.* (2010) used data from the *National Longitudinal Survey of Youth* on a sample of 2893 young married Americans. This study confirmed Presser's results: the practice of night work among women increases the risk of separation and divorce. However, the scarcity of studies and data available means that caution should be exercised on this specific point. Nevertheless, it should be stressed that the constraints associated with shift or night work are such that the partners of the employees concerned would prefer that they worked different hours: this was the case for more than half of the partners of the operators at a Canadian refinery, who would prefer that their spouses had a regular day job (Bourdhouxe *et al.,* 1997), and one third of the partners of the operators at an English nuclear power station, who tried to convince their spouses to give up the shift work (Smith and Folkard, 1993).

5.2.3.1.2 Children affected by the time constraints of their parents

- *Parental relationships under pressure from atypical rhythms*

The few studies conducted to date that have sought to analyse the impact of shift work on the relationships between employees and their children have shown a decrease in family interactions due to the constraints inherent to these types of hours. They show that two factors modulate these effects: the age of the children and the specific characteristics of the shift system.

A study by Nachreiner *et al.* (1984) sought to perform a comparison of shift workers' involvement in their children's lives for three different types of hours and for children of three distinct ages. The father's degree of involvement varied according to the shift system, and the same shift system had contrasting effects depending on the age of the children. Lenzing and Nachreiner (2000) compared two groups of children whose fathers worked in the German police force, either on shift work or daytime hours. They showed that the children's social lives were not identical: those whose fathers' jobs required shift work had a more limited social life before the age of 12. They had fewer friends, engaged in more solitary activities and rarely participated in programmed activities. They spent more time and shared more activities with their fathers, with the exception of those activities that had to be carried out at fixed and specific times. For children over 12 years of age, the time shared with the shift-worker fathers was restricted and essentially took place in the evenings. But besides the time spent together, the quality of the relationships seemed to be different: before the age of 12, the children of police officers on shifts confided in their fathers more often than their mothers, while after this age it was to their mothers that they turned.

Gordon *et al.*, (1981) also showed a decrease in socially-planned activities among shift workers from different professional sectors and their children, compared to those working regular hours: 11% of workers doing fixed night work and 28% of those on rotating shifts participated in *"meetings, scouting activities, ball games and following their children's progress in school"* compared with 64% of workers doing regular daytime hours. However, engaging in activities that do not require prior planning (such as simply spending time and relaxing with children, watching television or making plans for the future) was equally common in both groups.

The study by Sizane *et al.* (2011) also showed that performing night work affects the parent/child links: the relationships between mothers and their adolescent children were analysed according to whether the mothers worked during the day or at night. Two groups of 35 mothers and their adolescents completed a questionnaire. The results showed that the adolescents of mothers who worked during the day saw communication and problem resolution as being more effective than the adolescents of those who worked at night. The authors believe that night work diminishes the perceived quality of parenthood.

- *Long-term effects*

A decrease in the frequency and duration of interactions between shift workers and their children could ultimately damage the nature and quality of parental functions (Meurs and Charpentier, 1987; Hervet and Vallery, 2005). This was suggested in any case in a study (Koller *et al.*, 1990) on oil refinery workers in Austria, which revealed a deterioration, over a period of five years, in the sense of authority of the shift workers over their children, while this phenomenon was not manifested in the control group of daytime workers. Also, in shift workers at two Dutch plants, almost 70% believed that their wife took on a greater share of their children's education (Thierry and Jansen, 1982). But the real impact of these repercussions remains particularly difficult to grasp, which may also explain the limited number of studies devoted to substantiating knowledge of the long-term effects of shift work on the parent-child relationship. One study (Han *et al.,* 2010) examined the effects of the parents' working hours on the risk behaviour of adolescents aged 13 or 14 years. It was based on exploitation of the *National Longitudinal Survey of Youth: Child Supplement*. It showed that mothers who often worked at night spent far less time with their children and experienced less favourable domestic environments, with these two factors being significantly linked to risk behaviours in adolescents.

Some studies have attempted to measure these impacts from the perspective of school performance, psychological well-being, emotional balance and personality development.

- *School performance*

Diekmann *et al.* (1981) found, in the children of German public service shift workers, a lower chance of academic success and continuation of long-term studies, regardless of the level of qualifications of the father and mother. This was also suggested by another German study (Jugel *et al.*, 1978), which showed lower school performance in the children of shift workers compared to those whose fathers only worked regular daytime hours. This study also showed that parents doing shift work were less present at parent-teacher meetings and school council meetings because of their schedules. Similar results were obtained by Maasen (1979) in Belgium: children of shift workers were less likely to continue their studies beyond the mandatory age, leading to them entering employment earlier and with fewer qualifications. However, these last two studies, unlike the one by Diekmann (1981), did not control for an important factor likely to impact the results: the level of the parents' education in the two groups of workers (shift and non-shift). These last two studies should therefore be considered with caution, because the possibility cannot be excluded that the school results of these children are related more to their parents' level of education than to their night or shift work.

A more recent study from the data provided by the *National Longitudinal Survey of Youth* on the basis of interviews with women, examined the relationship between the parents' atypical working hours and the cognitive trajectories of children aged 5 to 14 years. Scores in mathematics tests were lower when the father or mother worked evenings or nights. Reading scores were poor when the mother worked at night (Han and Fox, 2011).

Unlike the previous studies, a British longitudinal survey conducted in 1976 on 16,000 children found no effects on children's school performance, or on emotional balance (Lambert and Hart, 1976).

- *A new baby… an obstacle to practising shift work?*

The arrival of children within a family creates an upheaval that requires a rethink of how daily life is organised. This seems to be even more of an issue when one of the two parents works shifts. Organisation of daily life is confronted with the time constraints imposed by the job: the resulting complexity can then be a reason for giving up shift work.

A study conducted in 2005 found that working hours and rhythms were a decisive factor in the perception of the difficulties of reconciling life at work/life outside work, and showed that night work was often identified as the most problematic issue with respect to organising life: 62% of employees (72% of women with children and 68% of men with children) working nights at least once a week said that they found the reconciliation of professional life/personal life very difficult or a little difficult, compared with 56% of those working nights less than once a week (Garner *et al.*, 2005). Even in the absence of young children, these time constraints were perceived, for more than half of the men and women, as incompatible with their family lives. However, the presence of young children (under 11 years of age) in the home makes it more difficult to reconcile family life and work.

Seibt *et al. (*1990) thus found that out of 4000 textile workers in the former GDR, only 7.5% of those working 3x8 shifts had children under 11 years of age, and that problems related to the children's education were among the main reasons reported for giving up shift work. Similarly, a survey conducted on 10 hospitals revealed that in women working rotating shifts with more than four nights a month, only 20% had children and for 11% of them, these children were under three years of age (Logeay, 1986).

Such results, although they cannot be generalised to all shift work situations, help identify the possibility of serious long-term repercussions, concerning not only the employees themselves but also the members of their families.

The arrival of children within a family and their growing up, which comes with new time constraints (school rhythms, issue of child care, etc.), can cause the employees to give up rotating shifts.

These findings call for the repercussions to be examined in studies over the long term, because they are neither immediate nor easily detectable. Moreover, these studies should not be limited to exclusively examining the effects on the workers themselves, but should expand the framework of analysis to the entire family unit.

5.2.3.1.3 Different effects depending on the characteristics of the hours worked

The available shared time between a shift worker and their child can be assessed by superimposing the work schedule on the school timetable. The results of this analysis reveal that the volume of shared free time differs greatly according to the shift system and the school timetable, and therefore the age of the child (Nachreiner *et al.*, 1984; Hook and Wolfe, 2013). Thus, on a twenty-four week cycle, for workers on both slow rotation and rapid rotation shifts, the shared free time with a child aged eleven in primary education is 22% lower than their colleagues working regular daytime hours.

- *Effects of the fixed or rotating nature of shift work*

The question of parental relationships arises differently according to the specificities of the hours worked: a non-rotating shift system means predictability in the timetable, which enables a stable organisation of family life to be established. This stability is seen as precious, particularly with regard to child care (Robson and Wedderburn, 1990). In this sense, employees working rotating shifts including at night are faced with a more complex and disadvantageous situation. This was shown by the study of Vallery and Hervet (2005), which measured the effect of three different time arrangements (fixed night shift, 3x8, and 3x8 with a 10-hour night shift) on the family and social lives of 30 nurses. All the employees working rotating shifts considered that the evening shift restricted their family role, including that relating to their children's education. Indeed, the night shift implies sleep during the day, and often restorative naps. Employees working rotating shifts believe that they benefit from less time than their permanent night work colleagues (Mott *et al.*, 1965). The study by Vallery and Hervet (2005) confirmed that fixed night work was far more beneficial than the rotating mode with regard to relationships with children: all the employees working fixed night shifts were satisfied (n = 8/8) compared with only 2 out of 6 nurses working 3x8 (with an 8-hour night) and 2 out of 4 working 3x8 (with a 10-hour night). The work by Simunic and Gregoc (2012) supports this finding: 129 nurses at three Croatian hospitals were divided into four groups according to their working hours (study by questionnaire). Those working a fixed morning shift were less aware of the difficulty of reconciling professional life/family life than the nurses that rotated morning, afternoon, and night.

Hewitt *et al.* (2012) showed, from a telephone survey of 300 fathers practising different working hours, that night workers spent significantly more time doing household chores and caring for their children. In the case of a fixed shift, the afternoon shifts seemed to be the most restrictive from the point of view of the relations between parents and children. Workers doing fixed afternoon shifts felt that they were able to spend less time with their children than workers on rotating shifts, who regularly had afternoons free (Mott *et al.*, 1965). However, the work by Hook and Wolfe (2013) calls for caution in generalising the results: using "timetable" surveys conducted in the United States (2003), Germany (2001), Norway (2000), and the United Kingdom (2000) (n=6835), they examined, in two-parent families, the opportunities to spend time with children according to the working hours performed. Thus, the American fathers working in the evenings spent more time alone with their children, regardless of the professional situation of the mothers, whereas this was not true for Norwegian fathers. Here, like Mills and Taht (2010), these authors confirm an essential idea: the effects of night work on the socio-familial environment are not universal and the employment conditions of the households and the economic and cultural context of the country therefore need to be taken into consideration.

- *The effects of the time at which the shift begins and ends, and of weekend work*

The time at which the shift begins and ends also has an impact on the duration, quality and nature of the contact between shift workers and their children: the encroachment of the afternoon shift on the evening (a time that is conducive to family relationships) has a different effect according to whether it ends at 6pm or 9pm. The same is true for the end of the night shift, which determines the presence, or absence, of the employee when children are getting up and leaving for school. The degree of concordance between the shift hours and the children's daily or weekly rhythm plays a decisive role. From this perspective, it is easy to imagine the difference induced by a semi-continuous or continuous shift system: the latter imposes an absence from the home at the weekend during periods that are most favourable to the development of family relationships (Garhammer, 1994; Meurs and Charpentier, 1987). The study by Meurs and Charpentier, performed on 300 employees, showed that almost half of the employees working at the weekend reported having less contact with members of their family (in the broad sense of the term), and focusing where possible on their spouse and children.

5.2.3.1.4 Mitigation strategies

As in the area of health, employees do not remain passive when faced with the direct and immediate effects of shift work on their family lives; they develop control strategies to cope with the difficulties encountered. These aim to align the rhythms of family life with the shift worker's hours as closely as possible. They are particularly important here, because they often involve the family unit in its entirety. Postponing an activity from the preferred time, reducing the time allocated to one activity for the benefit of another that is more urgent, delegating the activity to someone else (Curie, Hajjar, 1981; Gadbois, 1984) are common strategies implemented by night and shift workers. They can also in turn have "knock-on" effects on family life (Prunier-Poulmaire, 1997) and health.

- *Families living at the rhythm of shift work*

These strategies can particularly be observed with the hours at which the spouse gets up and goes to bed, as they are trying to synchronise with their partner's time constraints. Similarly, mealtimes are also often conditioned by the hours at which the shift worker returns home (Van Uchelien *et al.*, 1991). The same observation was made in a study by Rutenfranz, Knaut and Angersbach (1981) regarding the partners of service sector employees working very irregular hours, who interrupted their sleep at night to share breakfast with their spouses, whose shifts started at four in the morning. Many studies on male shift worker populations emphasise the vital back-up role fulfilled by the partner, who strives to maintain the quality of family life. They try and compensate for the constraints of shift work by limiting their effects. A study by Handy (2010) underlined the active and essential role of the partner in reducing constraints. Conducted in a petrochemical plant in New Zealand by interview with 74 shift workers and their partners, it showed that while the shift workers were concerned about the difficulties encountered when dealing with family life at the end of a night shift, their spouses were primarily concerned with how they could best harmonise and coordinate the family rhythm with that of the shift worker (adapting mealtimes, keeping children away/occupied outdoors during naps, *etc*.).

The studies on this subject show that this "back-up" role is more effective if the spouses do not themselves have a job: the partner's professional activity may considerably modulate the influence of shift work on family life. This was confirmed by the study of Grzech-Sukalo and Nachreiner (1997) on German police officers with different types of shift work: those whose partners worked full-time encountered more difficulties than those whose partners worked only part-time or not at all.

It should also be noted that women exercising a professional activity have more difficulty coping with the constraints of their spouses' shift work (Bourdhouxe *et al.*, 1997). The professional activity of the shift workers' partners may also be subject to the weight of the constraints of the shift system practised. Léonard and Claisse (1991) thus showed that the rate of women in employment decreased according to the constraints of their spouses' shift systems: 58% of the partners of workers on 2x8 shifts, 40% of those on fixed night shifts, 36% for semi-continuous 3x8 and 21% for continuous 3x8 shifts.

Due to the fact that they are relatively old, most of the studies were conducted in a context of low female participation in the labour market. A study by Presser (1986) showed that at the beginning of the 1980s, 51% of American shift workers had a partner who was not working and for those who were in employment, 57% worked full-time, 20% part-time and 20% did shift work. However, the continually increasing rate of female participation in the labour market in the world has been accompanied by profound changes, since the function of compensation or substitution regarding the negative effects of shift work can no longer be fulfilled. The family lives of workers practising these types of hours are therefore complicated, and the presence of children in the couple increases this difficulty (Garner *et al.*, 2005). Presser (1986) and Oginska *et al.* (1990) provide a few illustrations of this phenomenon. When women are mobilised by a professional activity, they then have to resort to new control strategies to mitigate the complex effects of shift work on the family sphere (paying for external child care, crèche *etc*.). Men have more difficulties when their spouses work full-time rather than part-time, or when they work on fixed-term or temporary contracts (Garner *et al.*, 2005).

The considerable growth in the rate of female employment is, from this perspective, an element that fundamentally alters the effects of shift work on marital and family life. The professional activity of shift workers' wives is an important factor that affects the shared free time of both the couple and the entire family. These same studies also show that these strategies are difficult to develop, relatively short term, and often only partially effective. Their choice and implementation appear to be dependent on the household's financial resources. They can also generate frustration: finding a method of child care for the evenings and at night is very complex and cannot in any case replace the time spent in the company of one's children.

While there is agreement about the vital role played by the spouse in the regulation, minimisation and compensation of the effects of shift or night work on children, it is important to underline the difficulties that can be experienced by single parents working night or shift hours. Moreover, according to the National Institute for Statistics and Economic Studies (INSEE, 2015) single-parent families are on the increase. Whereas fifteen years ago they accounted for only 17% of households with children, this rate had risen to 22% in 2014. It should also be noted that 85% of parents in single-parent families are women. Again according to INSEE, in 2011, 1.5 million people were living without a spouse and with at least one minor child.

5.2.3.2 Impact on social life: social desynchronisation

All human activities are subject to social rhythms whose organisation is essentially determined with reference to regular daytime working hours. Most everyday activities are thus socially programmed to the point where they can only be carried out at particular times that are specific and limited in time. Accordingly, certain activities cannot easily be practised by employees whose jobs involve shift or night work, who are regularly mobilised by work in the evening or at night, and thus obliged to sleep during the day. This creates an out-of-phase situation that is detrimental to the expansion of the individual's social life. A few rare scientific studies have aimed to shed light on the incidence of the effects of this out-of-phase nature of shift and night work in light of the predominant social rhythms. Some studies suggest that many shift workers attribute more importance to the effects of their working hours on their social life than to the sleep problems they experience, the physical hardship generated by the night work or even the deleterious effects of dietary dysrhythmia (Rutenfranz *et al.*, 1981; Wedderburn, 1981).

5.2.3.2.1 A constraint on social life

The fact remains that shift workers agree primarily on the idea of a constraint on social life. Shift or night workers may be free at times when certain social activities cannot take place or only under unsatisfactory conditions (Bunnage, 1979; Thierry & Jansen, 1982). In a context of such strongly determined social rhythms, shift workers constantly find themselves out of phase. It is therefore not so much a lack of free time that causes difficulty but its position on the nychthemeron.

Although it is accepted that shift hours play a restrictive and penalising role from the point of view of social life, the scientific studies do not always agree on the magnitude or nature of these restrictions. Apart from the difficulty of making international comparisons, which has already been mentioned, this is due to the fact that the strength of the impact on social life varies according to the specific characteristics of the working hours (start and end time, frequency of rotations, *etc*.) (Bunnage, 1979; Costa, 1996), the employees' individual characteristics (age, gender, family situation, *etc*.) (Gadbois, 1990), and also the nature of the tasks entrusted to them (Guérin and Durrmeyer, 1974; Prunier-Poulmaire, 1997; Pavageau, 2006).

Researchers interested in measuring the impact of atypical working hours on the personal lives of employees often start from the assumption that each hour of the day and night has a certain social utility value (Knauth, 1978). This value is conferred by the dominant social rhythms and corresponds to the opportunity to perform different social and family activities, without any constraints. In this model, the hours at the end of the day or at the weekend are especially valued. From this point of view, this can put shift workers at a disadvantage, as they do not necessarily have access to these hours, which are the most favourable for performing certain socio-family activities regarded as essential. Obviously, in this system, not all shift hours offer the same advantages or the same constraints, depending on how they are organised and in particular how the free time they provide is distributed across the different hours of the day and week. It is therefore possible to compare the limitations suffered by shift workers in their lives outside work according to the organisational conditions of a shift (start and end times, rate of rotation, etc.) (Prunier-Poulmaire, 1997; Pavageau, 2006) and according to the distribution in hours of the free time that it provides over the day and week (Knauth, 1978).

The impact of the effects depends on the characteristics and specificities of the working hours practised. Thus, Tasto and Colligan (1978) showed that the satisfaction of shift workers with regard to social activities was closely linked to the fixed or rotating nature of the work shifts and their position on the nychthemeron: in this study, employees working fixed night shifts reported a greater level of satisfaction than those working fixed afternoon shifts or rotating shifts.

The social utility value of an hour in the day or week is also specific to a given population, which itself is part of a living environment with social rhythms having their own local particularity (opening hours of shops, administrations and services, cultural offers, *etc*.). Regarding the individual characteristics, the employees' family situation determines this social utility value: whether or not they are part of a couple, with or without children, the age of any dependent children, whether or not the spouse has a job, whether this job is full-time or involves atypical working hours, all these issues will alter the value attributed by each individual to a specific time of the day.

For example, Homberger and Knauth (1993) showed, among workers in a chemical factory, that morning hours were rated more highly by older workers and those with dependent children, while younger workers and those without children attributed more value to the hours of the evening and the weekend.

The fundamental role of the employees' socio-demographic characteristics in the valuation of free time was also illustrated by a study by Gadbois (1981) on nurses and care assistants. The complementary nature of everyone's tasks led hospital management to establish one single shift system. While the nurses embraced this new rotating day/night system, the care assistants strongly rejected it, by far preferring the stability of a fixed night shift. An analysis of the population's characteristics then provided valuable insight: while the nurses were mainly young and single, the care assistants were older and had children. The stability of the fixed night shift was essential to enable them to cope as well as possible with the constraints of their situation as mothers with families.

It is also important to stress that the socio-geographical context has an effect: the results on social and family life can vary according to whether the studied populations live in rural or urban areas. This parameter determines the type and commute duration, which will in turn influence the free time available for sharing (Costa *et al.*, 1986; Prunier-Poulmaire and Gadbois, 2000).

The earlier scientific studies that focused on the social dynamism of shift workers concluded that working these types of hours made the organisation of social encounters particularly difficult (Mauritius and Monteuil, 1965) and significantly impeded the extension of the workers' network of contacts (Mott *et al.,* 1965). In the first place, rotating shift work introduces uncertainty when carrying out extra-professional activities, for the employees themselves but also for their circle of friends. This may gradually lead to a change in the relationships they have, or hope to have, with their circle. This complexity of coordinating social encounters may then lead to a tendency to spend more time with colleagues with a similar rhythm of life to their own, who understand the constraints that weigh on them (Meurs, Charpentier, 1987).

5.2.3.2.2 The difficulty of accessing social activities in a formalised framework

The studies that sought to reveal the harmful effects of night or shift work on social life essentially demonstrated the difficulty of taking part in formal social activities such as cultural, sporting, or community events, mainly due to their strong rooting in a rigid and socially predetermined time period (Blakelock, 1960; Maurice, 1971; Prunier-Poulmaire, 1997).

This same work then revealed that the employees turned towards more informal activities that can be performed on an individual basis regardless of the time of day (Meurs and Charpentier, 1987).

The temporal mismatch between the pace of life of the whole of society and that of shift workers could gradually and insidiously lead to them being marginalised. The change to the terms of their lives outside work, as a result of the working hours, could constitute one of the steps in the operation of this "social breakdown" process. Some particularly strong terms have been found over time in the scientific literature: as early as 1965, Mauritius and Monteuil spoke of "social isolation", in the same year Andlauer and Fourré choose the term "social segregation", in 1979 Bunnage stressed the "social marginalisation," while Quéinnec *et al.* (2008) spoke of "social death".

5.2.3.2.3 Recreation

Shift work may therefore rule out the regular practice of socially shared activities at fixed and previously programmed times. This may concern the shift workers themselves but also possibly the other members of their families. Difficulties reconciling their timetables with those of their friends may lead shift workers to adopt individual pastimes instead (DIY, gardening, reading, walking, etc.), which by nature require no synchronisation and do not impose any time constraints apart from the workers' own. In addition, they may favour flexible activities that can be carried out at any time of the day or night, rejecting rigid activities that have to be performed at a specific time of the day (Vroom, 1964; Bunnage, 1979).

A study carried out among customs officers (Prunier-Poulmaire, 1997) showed that working 4x6 and 3x8 shift systems had an extremely limiting effect on leisure activities. Individual activities were preferred for the reasons mentioned above. Thus, the officers working 4x6 and 3x8 shifts practised a solitary sport activity: 60% compared with 40% for those working during the day. As for the customs officers working 2x12 shifts, they were able to engage in collective activities more often. This study concluded that the 4x6 shift severely limited the opening of the social domain, the 3x8 shift offered more favourable social openness, and the 2x12 shift fostered an increase in the relational field. In general, this type of organisation based on 12h is preferred by employees because of the possibility of concentrating their free time, and the scientific studies show that these hours are more conducive to the expansion of social and family life (Pavageau, 2006). Conversely, some shift systems, such as 4x6, break the free time up over the day, fragment it over the week and are seen as particularly detrimental to life outside work (Prunier-Poulmaire, 1997; Pavageau, 2006).

5.2.3.2.4 Community activities

Participation in community activities figured prominently among the indicators most frequently studied by the authors to confirm the effects of shift work on life outside work. Indeed, it provides information on the shift workers' social integration and degree of social investment, and can account for the actual interaction between shift workers and society. It also shows the opportunities to take part in collective, social and formal activities imposing meetings at times when most members are available, namely the end of the day or the weekend. Community activities are thus often considered as the archetype of very inflexible activities. While the results of scientific studies are not unanimous on this point, they do, nonetheless, reveal a trend of lower community participation among shift workers and a limitation of the time devoted to it (Vallery and Hervet, 2005). For example, Wedderburn (1981) reported that one of the negative effects most often cited by the English steelworkers that were the subject of his study, was the adverse impact of their working hours on their social lives (61%) and, in this specific area, the difficulty they encountered when wishing to participate in community activities (61%).

Jamal and Jamal (1982) also found, in two distinct shift populations – nurses and agri-food industry employees – a limitation of community life that was manifested as a reduction in the monthly participation in meetings and fewer hours devoted to these activities. While they also observed a reduction in the number of monthly hours devoted to community life, Frost and Jamal (1979) found no statistically significant difference between shift and non-shift work regarding the taking on of specific responsibilities or total number of memberships. These results contradict those of Mott *et al.* (1965), whose work revealed an effect of shift work on the number of memberships (1.7 for day workers, 1.27 for fixed-afternoon shift workers and 1.37 for permanent night and rotating shift workers) and the taking on of responsibility (37% of day workers compared with between 20% to 24% of shift workers took on an official role in their associations), but not on the hours actually devoted to community life. It can be seen here that the magnitude of the effect depends on the types of hours practised, fixed or rotating, and the type of shift. In a study on French customs brigades, Prunier-Poulmaire (1997) reported similar results. Regardless of the type of shift system (2x12, 3x8, 4x6), a reduction in community life and participation was noted: one third of shift workers said they were members of an association compared with half working regular daytime hours; 30% of customs officers working office hours said they attended meetings of associations at least once or twice a month compared with 20% of those working 4x6 and 3x8 shifts.

Night work can be also very penalising when it comes to involvement in trade union or professional associations. A Danish survey (Bunnage, 1979) thus revealed a difference between 2x8 and 3x8 shift workers regarding membership of a professional association, trade union or political party. Participation in professional associations, for example, for employees working 2x8, was half the rate of those working 3x8 shifts. Nachreiner (1975) obtained similar results, since 28% of employees working 2x8 shifts considered that they did not have enough time to devote to community activities compared with 64% of those on 3x8 shifts.

It is not possible to determine unambiguously and definitively from a comparison of these different studies whether or not the opportunities to participate in community activities are reduced when practising shift or night work. However, it does suggest an exclusion from community life, which seems to be a problem for the employees.

5.2.3.2.5 Different effects depending on the types of hours

It can thus be seen that the type of shift work is an essential parameter and is accompanied by widely varying effects on social life. The same is true for the rate of rotation (slow or fast) of the shifts.

Wedderburn (1967) was one of the first to question the specific role of the shift rotation rate on life outside work. He carried out a study on steel industry workers who were trade union members and who worked a rapid-rotation shift system. A third of them believed that their hours had a negative effect on their participation in union activities (on this point, the results agreed with those of Thierry *et al.,* 1983). However, 90% had a favourable opinion of their working hours due to the rapid nature of the sequencing of the shifts, which offered the possibility of access, over a week, to periods of free time situated at different times of the day. Therefore, according to these two studies, it seems more unfavourable to have identical long fixed periods of time over one week in the framework of a slow rotation than over two or three days in the framework of a rapid rotation (Gadbois and Prunier-Poulmaire, 1996).

5.2.4 Conclusion

This literature review showed how few studies have been devoted to the effects of shift work and night work on life outside work, and the heterogeneity of the results obtained. This is probably due to the multiplicity of factors that determine the adoption of a leisure behaviour or lifestyle. The diversity of shift work situations, the organisational specifics, the variety of social contexts and the weight of individual characteristics, all constitute key factors that determine how people go about their lives outside the workplace. It should also be remembered that the content of the tasks performed can influence the social acceptability: repetitive and monotonous work may, for example, be accompanied by a kind of social inertia. Thus, the structuring of the shift workers' social lives reflects the degree of the constraints related to the atypical structuring of the working hours, which can "keep them at a distance" from a social life. Moreover, the problem is not exclusively quantitative: the state of health (physical and psychological) and the fatigue experienced by shift workers in their free time will also determine their possibilities for action and social interaction.

This means that besides the "effective mobilisation" of the employees by their working hours, it is also necessary to consider what happens to them before and afterwards, namely the need for an "anticipatory mobilisation", which involves preparing themselves for the shift to come with a nap or rest, and a "consecutive mobilisation", which involves resting and trying to recover from the shift they have just completed (Prunier-Poulmaire, 1997). These mobilisations "through work", which continue "outside work" in terms of recovery from or preparation for it, therefore also keep the shift worker apart from the social and family sphere. It is also conceivable that the reduction in leisure activities and deterioration of social life can, besides the effect of the shift itself, lead to fatigue or to a deterioration in the state of health associated with the practice of shift work (Ramaciotti *et al.*, 1990). Having time available means being able to take ownership of it and use it as one wishes. The study by Kundi *et al.* (1995) with nurses working 3x8h and 2x12h shifts showed that these shift systems made the reconciliation of life at work and outside work more complicated, and also that the need for recovery from the 12-hour shifts reduced the time that could be devoted to their personal lives, to the same level as that of nurses working 3x8h shifts. The fact remains that these elements could combine and potentiate over time.

Overall, the small number of studies investigating the effects of night or shift work on social life and the gradual desertion of this research theme may seem surprising. It is all the more astonishing since these time arrangements are proliferating and questions about work-life balance are among the most central and in-demand topics. The change in the general rhythms of society can no doubt partly explain this phenomenon: the increase in the extent of the opening of shops and services, sports halls open late in the evenings, banks open on Saturdays and sometimes even on Sunday mornings, shops open on the weekend, crèches opening early in the morning until very late in the evening, the possibility of watching numerous TV programmes or films on demand, *etc*. This easy access to services, regardless of the time of day, seems to be a consequence of the increase in the number of employees working atypical hours but also, necessarily, contributes to this increase. It is therefore possible to imagine that these conditions gradually reduce the inequalities between shift workers and day workers regarding their social lives, and lessen the impact of the difficulties associated with this type of organisation.

However, the question remains of the balance of family life. At a time when the forms of atypical working hours are proliferating and the number of single parent families is simultaneously increasing, and when French employees say that they attach the utmost and ever greater importance to the balance of their lives and the boundaries marking the spheres of their personal and professional lives, research to further investigate this scientific field can only be encouraged.

Many recent studies attest to the health effects of the imbalance of life *in and outside* work. Geurts *et al. (1999)* showed that a conflict between the personal and professional spheres was a predictor of psychosomatic disorders and sleep disorders, as well as two of the three dimensions of burn-out: emotional exhaustion and depersonalisation. They showed that the perception of the interface between work and home life acted as a mediating variable in the relationship between work load and perceived health. The meta-analysis by Allen *et al. (2000)* confirmed that conflicts between personal life and work life greatly affect the individual, causing anxiety, depression, perceived stress, and psychosomatic disorders. Quick *et al.* (1997), *like* Lourel and Guéguen (2007), found that "private life/work life" conflict increased the stress level perceived by employees. The emergence of an awareness of psychosocial risks in companies in recent years led us to broaden our approach by considering people through their different spheres of life and action.

By doing so, the prospects for action are expanded: this state of well-being and quality of life at work, the stated objective of the third occupational health plan, has its source inside the office or factory, but not exclusively. It can be seen to what extent the professional rhythm affects the worker's entire life down to its most intimate components. It is therefore urgent to do away with the boundaries between scientific disciplines (this report is an illustration) as well as those that compartmentalise life at work and life outside work. This is the most likely route to long-term solutions to the issues relating to work, including night and/or shift work.

6 Assessment of the health risks associated with shift-work, including night work

6.1 Expert appraisal method: from monitoring the literature to assessing levels of evidence

6.1.1 Identification of articles studying the health effects of night work (fixed or rotating shifts)

The coordinating team for the Working Group on "Assessment of the health risks for professionals exposed to atypical working hours, especially night work", ANSES's monitoring unit, and the Working Group's experts conducted a search, as exhaustive as possible, of the international scientific literature on the potential human health effects of night work (fixed or rotating shifts) through, in particular, the identification of primarily *in vivo* effects and clinical and epidemiological data.

6.1.1.1 Reference period

The expert appraisal was undertaken for the period from January 2010 to December 2014. Some key studies, published from January to June 2015, were also included when they were deemed relevant and of satisfactory quality. In addition, the experts included studies published before 2010 when this seemed necessary, in particular to present state-of-the-art reviews in the introductions to the sections on health effects.

6.1.1.2 Search engines

The search engine used for this expert appraisal was the *Scopus* search engine (*http://www.scopus.com/home.url)* which is a multidisciplinary database of scientific literature particularly indexing biological and medical publications as well as publications in the areas of human and social sciences.

6.1.1.3 Types of analysed documents

Various types of documents were taken into account in the expert appraisal:

- scientific articles published in peer-reviewed journals, without prejudice to their impact factor;
- expert appraisal reports of national and international organisations (IARC[36], HAS[37] etc.);

Only original articles written in English or French were systematically analysed by the Working Group.

Descriptive and narrative reviews, which consist in summarising all published studies on a given topic, were not analysed. Meta-analyses, which are systematic reviews combining the results of several independent studies to produce risk assessments, were included.

[36] International Agency for Research on Cancer, http://monographs.iarc.fr/ENG/Monographs/vol98/mono98-8.pdf

[37] French National Authority for Health, http://www.chu-rouen.fr/sfmt/autres/Reco_HAS_Travai_%20poste-Argumentaire_30-05-2012.pdf.

6.1.1.4 Keywords used

6.1.1.4.1 Forms of work taken into account

This report is a first stage in the investigation of the health effects of atypical working hours in the broad sense. It is limited to health effects related to shift work, including night work (fixed or rotating shifts, see Table 8).

Table 8: forms of night work taken into account

English term	Equivalent French term
Night work, Night-work, Nightwork	Travail de nuit
Shift work, Shiftwork, Shift-work	Travail posté
Rotating work	Travail rotatif
12-hour shift	Poste de 12 heures
Evening shift	Poste en soirée
Night shift	Poste de nuit
Morning shift	Poste du matin

6.1.1.4.2 Health effects studied

The Working Group first sought to identify, as exhaustively as possible, publications dealing with all of the health effects related to shift work, including night work, reported in the literature.

6.1.1.5 Classification of articles

6.1.1.5.1 Sorting by type of effect

Once identified, the documents were sorted on the basis of the health effects studied. This classification was established by collecting publications from the search equation cross-referencing keywords by health effect with keywords associated with night work and shift work.

6.1.1.5.2 Sorting by type of study

Within each of the examined health effects, studies were also classified by type:

- epidemiological studies (cross-sectional, case-control, cohort) on humans;
- *in vivo* or *in vitro* (cellular models) experimental studies on humans.

Studies with animal models were not systematically identified, due to limitations in transposing the results of these studies to human health effects.

6.1.1.6 Prioritisation of the health effects studied

Given the very large number of health effects identified and publications targeted by the literature search, as well as time constraints associated with conducting the scientific expert appraisal, the Working Group, in agreement with the Agency's Scientific Affairs Department, decided to prioritise the work to be carried out in the framework of this expert appraisal. For example, after drawing up an exhaustive list of all of the health effects explored by the scientific literature, the Working Group prioritised some of them.

This prioritisation in no way calls into question the scientific relevance or the significance of the health effects previously listed that were not studied in detail. The aim of this prioritisation exercise, organised by the Working Group, was to allow for further investigation of the few effects chosen by the group instead of briefly reviewing a larger quantity.

A total of 12 main classes of health effects were identified in the scientific literature:

1. sleep disturbance;
2. disruption of circadian rhythms;
3. cognitive effects, psychomotor effects, and effects on vigilance;
4. traumatic injuries, accidentology;
5. effects on psychological and mental health, addiction;
6. obesity and metabolic disorders;
7. cardiovascular diseases;
8. gastro-intestinal diseases;
9. cancers;
10. effects on fertility, reproduction and pregnancy;
11. effects on the immune system;
12. interaction between pharmacology, toxicology and shift and/or night work.

The six selected health effects, which underwent a detailed analysis, were as follows:

- sleep disturbance;
- cognitive and psychomotor effects, and effects on vigilance;
- effects on psychological and mental health, addiction;
- metabolic disorders;
- cardiovascular diseases;
- cancers.

The connection between night work and traumatic injuries and accidentology was studied in detail using a dual approach, firstly by studying the publications from the literature search in *Scopus*, and secondly by adding references selected by the experts, taken in particular from the French scientific literature.

Other health effects not selected for the detailed analysis have, however, been described in the expert appraisal report. The main results observed for these topics are reviewed in a separate section.

- The connection between night work and the disruption of circadian rhythms was not analysed in detail. Circadian rhythms have been assessed in many experimental studies but in very few epidemiological studies;
- The connection between gastro-intestinal diseases and night work has not been addressed in detail. A considerable number of articles are indeed available on this subject, but few publications have appeared since 2010;
- Reproduction and pregnancy have been widely studied, including by the French National Authority for Health (see HAS, 2012);
- Lastly, not enough data are available on the effects associated with fertility or the immune system or the effects relating to the interaction between pharmacology and night work.

6.1.2 Analysis of publications

The Working Group systematically read all of the original articles identified using the search criteria defined above, according to the procedure set out below.

6.1.2.1 A collective analysis

The Working Group's experts pooled their complementary skills to collectively analyse studies on the health effects of shift work including night work (fixed or rotating shifts).

Five sub-groups were formed within the Working Group, in order to analyse articles studying the following health effects:

- sleep disturbance;
- cognitive effects, psychomotor effects, and effects on vigilance;
- effects on psychological and mental health, addiction;
- obesity, metabolic disorders and cardiovascular diseases;
- cancers.

Each article was selected based on its title and abstract to determine its relevance to the topic at hand. The articles selected were then analysed in detail by two experts, with this critical assessment being recorded in an analysis matrix. These analyses were then discussed in sub-group meetings, in order to collectively define the methodological quality of the publication and add justifications and comments.

6.1.2.2 Quality criteria used to analyse the studies

During the first work sessions, the Working Group established a list of objective criteria for assessing the quality of the analysed studies irrespective of the results stated in the publication. Each expert reviewer thus completed an analysis grid with the support of the ANSES scientific coordinators.

6.1.2.2.1 Quality criteria in epidemiological studies

Epidemiology is the study of relationships between diseases and various personal (family history, lifestyle, etc.), social (way of life, living space, etc.) and environmental (type of work, pollution, etc.) factors likely to influence their frequency, distribution and progression. Aetiological epidemiology compares populations with or without an attribute of interest ("exposure") to determine the causes of diseases. This search for factors likely to cause health effects involves highlighting statistical associations between the factor in question and the risk of a health effect.

Various types of epidemiological studies can be undertaken to assess the risks associated with the exposure of interest.

Main types of epidemiological studies

- Ecological studies examine the association between exposure and disease from data aggregated by geographical or time-related unit (descriptive epidemiological study);
- Cross-sectional studies examine, for each individual in the study, their exposure and the presence of disease at a given point in time;
- Case-control studies are used to compare the frequency of past exposure of a sample of cases (sick people) to that of a control sample of people not suffering from this disease, which must be representative of the population from which the cases are drawn;
- Cohort studies are used to compare the occurrence of diseases between non-exposed individuals and individuals exposed to the exposure of interest, monitoring the incidence of diseases over time.

Cross-sectional studies generate many biases. The most vulnerable subjects, or those who have developed the disease, may have been exempt from the exposure of interest (night work) at the time of the study, as they may have been reassigned to other unexposed shifts or left the workplace; in this case, they are not included in the studied population of workers. This phenomenon can give rise to a bias called the healthy worker effect, causing the association between exposure and disease to be underestimated. Another limitation of cross-sectional studies is that they deal with prevalent cases of the disease (i.e. cases occurring at the time of the study, not taking into account the incidence date), which does not provide assurance that the studied exposure preceded the development of the disease (criterion of temporality). For these reasons, cross-sectional studies do not enable causal relationships to be established.

Case-control studies and cohort studies are aetiological studies whose objective is to study the association between exposure and the occurrence of disease. No aetiological studies are in themselves sufficient to infer a causal relationship. Depending on their methodological quality, not all studies have been given the same weight in the expert appraisal. To conclude as to the level of evidence intended to assess the existence of a causal relationship, the expert group relied on the quality criteria defined below.

6.1.2.2.1.1 Have the subjects in the studied sample been properly selected?

In cohort studies, the participants must be free of the disease upon inclusion. Health events occurring during the follow-up period (i.e. incident cases of the disease) must be recorded in the same way for exposed and unexposed individuals. If some participants are lost-to-follow-up, this must not depend on the presence or absence of exposure.

In case-control studies, the recruitment of cases and controls must satisfy certain rules:

For cases, the absence of selection biases can be ensured through the exhaustive recruitment of new disease cases (incident cases) occurring in the source population during the study period;

Ideally, controls should be randomly selected from exhaustive lists of the population from which cases are drawn (telephone lists, lists of residents, etc.);

Lastly, the recruitment of cases and controls must be independent of the studied exposure. If eligible subjects refuse to participate in a study, this must not depend on the exposure of interest.

When these conditions are not met, the study is subject to selection biases that may increase or lower the measured association between exposure and disease.

6.1.2.2.1.2 Have exposure and the health effect been properly characterised?

The data sources on exposure to night work or shift work (questionnaire, employer files, job-exposure matrices, etc.) must be clearly presented by the authors, and exposure must be measured in the same way for people with and without the studied disease. Factual data used to assess exposure (administrative documents indicating the job title (nurse for example), from which exposure can be evaluated) are generally reliable and do not cause memory biases, which can affect data collected using questionnaires (e.g. questions on jobs held with working hours). However, administrative data are less precise than data collected by questionnaire.

The same characteristics apply to the collection of information about the studied health effect: the identification of the disease must be the same for exposed and unexposed individuals; information about the disease is more reliable when collected from medical records than by questionnaire.

6.1.2.2.1.3 Have confounding factors been taken into account?

There is a confounding effect when a statistical association between exposure and disease is related to another factor (typically age, gender, tobacco use, etc.) associated with both the studied exposure and the disease. For example, in the framework of studies on night work and breast cancer, excess weight could have a confounding effect, since it is a recognised risk factor in breast cancer after menopause and is often associated with night work due to bad eating habits.

Confounding factors can be taken into account during analysis by statistical adjustment, provided of course that the required information was collected in the study.

6.1.2.2.1.4 Is there sufficient statistical power?

The number of subjects included in epidemiological studies must be sufficient to achieve the statistical power required to demonstrate a statistically significant association between exposure and disease. Statistical power also depends on the proportion of subjects exposed to the risk factor of interest in the study population.

While calculations of statistical power are seldom presented in publications, it is clear that, all other things being equal and in the absence of biases, the results of a study including several hundred cases of a disease carry more weight than those of a study with only a few dozen cases.

6.1.2.2.1.5 Are the statistical methods used relevant?

The statistical methods used to produce risk assessments, absolute rates of cancer or other diseases, confidence intervals, and significance tests, and to take into account potential confounders, must have been clearly stated by the authors and be suited to the nature of the analysed data.

6.1.2.3 Definition of three quality levels for studies

According to the quality criteria defined above, the Working Group classified studies into three quality levels:

- Good-quality study: the quality criteria described above are met;
- Study with minor methodological limitations: the above criteria are largely met or the identified limitations do not call into question the results;
- Study with major methodological limitations: the above criteria are not adequately met and the limitations call the results into question.

6.1.3 Presentation of the results from the literature review

The results of the studies considered by the Working Group's experts as useful for assessing the health effects of shift work including night work in humans are briefly presented for each studied effect. These are studies fulfilling the minimum quality criteria defined above, i.e. having no major methodological limitations or problems. The sections on health effects for which there were numerous studies do not describe all these studies in detail.

The aim of this report is not to summarise all of the published studies that were analysed. Those that were considered as having major methodological limitations (exposure not characterised, no comparison group, calculation errors, not undertaken with enough animals, etc.) according to the quality criteria set out above are listed in tables in the Annexes.

6.1.4 Assessment of the evidence for each effect studied

In order to include all of the available data in the assessment process, summaries were prepared for each studied effect, taking into account publications considered of good quality or with minor methodological limitations, published since January 2010. These summaries were written, reviewed and shared by the members of the sub-groups and then by the entire Working Group. They were then used to establish levels of evidence related to the potential effects of shift work including night work.

The quality of a study was the criterion for its inclusion in the assessment of the studied effect, not its results. Thus, if the Working Group identified major methodological limitations in an article, it was not taken into account to assess the level of evidence for the studied effect.

6.1.4.1 Role of animal studies in the assessment of an effect

The issue of taking animal studies into account for risk assessment is delicate when dealing with the health effects of night work and shift work. The limitations of animal models to study the effects of night work on humans have been described above; animal studies are generally undertaken with rodents, which are photophobic nocturnal animals, very different from human beings (see Section 3). It is also impossible to model, in animals, all of the constraints, in addition to the simple time difference, associated with shift work including night work. It is therefore very difficult to reproduce the equivalent of night or shift work in animals, even though there are *in vivo* studies using animal models for health effects such as cancer, or metabolic and cardiovascular risks. In addition, for other health effects, for example those associated with mental or psychological health, there is no suitable animal model.

The Working Group reiterates that the results obtained in studies undertaken in animals cannot be used as evidence of a health effect of night work in humans. Nonetheless, the high degree of convergence between observations in humans and certain results in animals helps to clarify the physiological mechanisms involved in the consequences of night work and the resulting circadian disruptions.

The expert appraisal methodology thus relied primarily on data obtained for humans, especially in epidemiological and experimental studies, for all of the studied health effects. Considering that there are many such studies, the Working Group decided to undertake its analysis based on their results. *In vivo* and *in vitro* studies modelling time differences in animals to clarify the biological mechanisms potentially involved in the disruption of physiological functions were considered by the experts and used to support the results already available for humans. Thus, for these studies, the systematic analysis of the publications, as described in Section 6.1.2, was not applied. However, recent good-quality literature reviews were taken into account.

In short, given the absence of suitable/validated animal models for night work, the approach adopted by the Working Group to establish the level of evidence was to use:

- epidemiological studies in humans;
- mechanistic (laboratory) studies in humans when available;
- mechanistic data on animals, taken into account particularly thanks to recent reviews (with no systematic analysis of the original articles), in order to support the existence of plausible physiological mechanisms in humans.

Note: Different methodological approaches were chosen by two sub-groups:

For the sub-group studying cancer:

Several major epidemiological studies providing relevant information relating to cancer have been published since the IARC's monograph in 2007. The sub-group of experts focused mainly on the analysis of all of the epidemiological data. To assess the level of evidence, it also relied on the results of experimental studies in animals and on assumptions regarding possible carcinogenesis mechanisms based on literature reviews, without examining each publication in detail.

For the sub-group studying metabolic disorders and cardiovascular diseases:

Similarly, the sub-group firstly considered the available epidemiological studies for the examination of this health effect. Mechanistic studies with animal models were documented using literature reviews in order to report on the state of knowledge. Here they also support the available epidemiological data.

6.1.4.2 Study of the effects of night work (fixed or rotating shifts) on humans

Evidence relating to the studied effect has been classified, based on the available information from epidemiological studies in humans, according to the following flow chart (Figure 10):

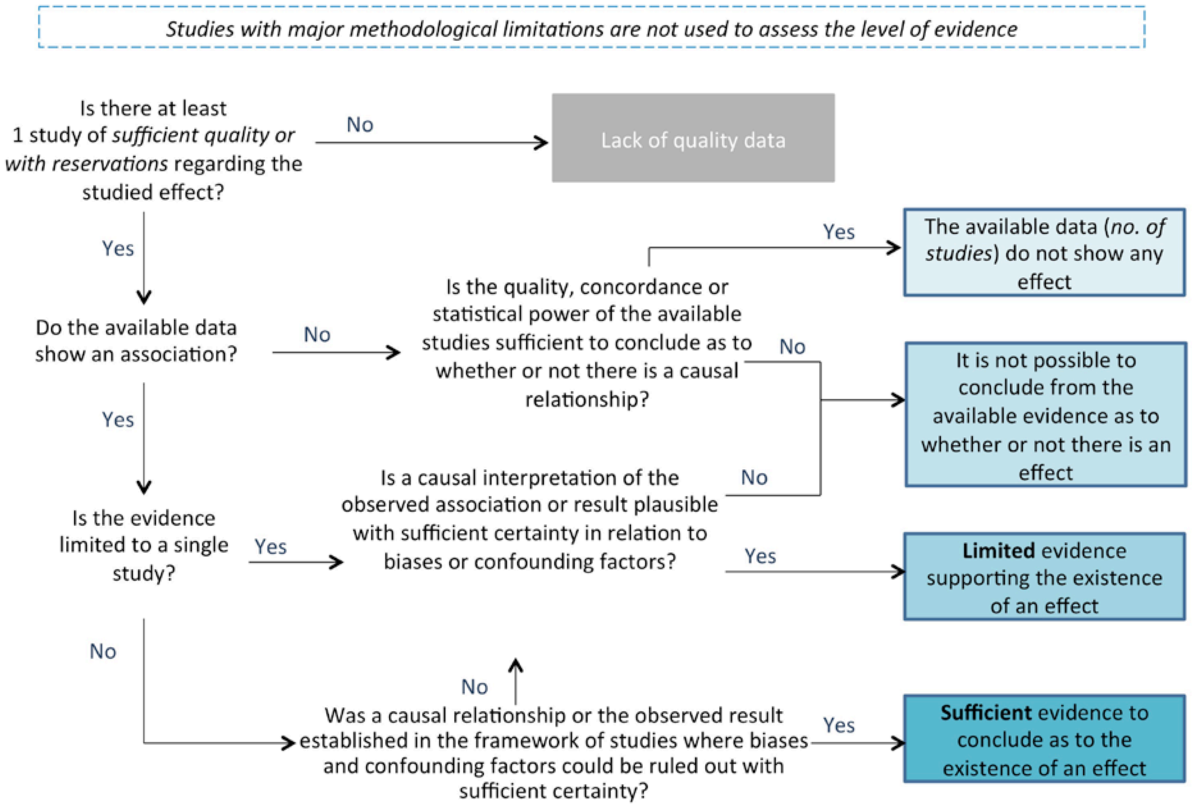

Figure 10: flow chart for the assessment of evidence relating to a given effect in human studies

Sufficient evidence to conclude as to the existence of an effect: there is a likely causal relationship between exposure to night work (fixed or rotating shifts) and the studied effect in humans. In other words, a positive relationship has been established between exposure and the occurrence of the effect, in the framework of studies where biases and confounding factors could be ruled out with sufficient certainty.

Limited evidence supporting the existence of an effect: an association has been established between exposure to night work (fixed or rotating shifts) and the occurrence of the studied effect. The experts consider that a causal interpretation of this association is plausible but that the existence of biases or confounding factors in the analysed studies cannot be completely ruled out.

It is not possible to conclude from the available evidence as to whether or not there is an effect: the quality, concordance or statistical power of the available studies is not sufficient to conclude as to whether or not there is a relationship between exposure to night work (fixed or rotating shifts) and the studied effect.

The available data do not show any effect: several adequate studies, covering all of the exposure levels known to be encountered in humans, with converging results, show no positive association between exposure to night work (fixed or rotating shifts) and the studied effect, regardless of the examined exposure level. The results of these studies, whether alone or combined, should have narrow confidence intervals, whose upper limit should be close to the null value (e.g. a relative risk of 1.0). Biases and confounding factors must be ruled out with reasonable certainty, and the studies should have a long enough follow-up period. When the available information suggests "no effect", this conclusion can apply only to the studied effect, to night work (fixed or rotating shifts), to the conditions and levels of exposure, and to the observation period taken into consideration in the available studies. Even so, the potential existence of a very low risk at the exposure levels studied can never be completely ruled out.

6.1.4.3 Overall assessment

In the end, all the information was examined as a whole in order to make an overall assessment for humans of the impact of night work (fixed or rotating shifts) for each effect studied (see Figure 11).

Each effect studied was classified in one of the following categories (inspired by those used by ANSES to study the health effects of radiofrequencies for example, or the carcinogenicity of an agent in the IARC monographs). The classification of an effect was a matter of scientific judgement and relied on the more or less conclusive nature of the information taken from studies in humans as well as other relevant information such as studies on biological mechanisms, physiological functions, or alterations to living systems. The overall assessment was discussed by the Working Group, which issued a collective opinion.

<table>
<tr><td></td><td></td><td colspan="2">Evidence of the existence of the effect in experimental studies in humans or animals</td></tr>
<tr><td></td><td></td><td>Evidence supporting the existence of an effect</td><td>No evidence supporting the existence of an effect</td></tr>
<tr><td rowspan="5">Evidence of the existence of the studied effect in epidemiological studies</td><td>Sufficient evidence to conclude as to the existence of an effect</td><td colspan="2">Proven effect</td></tr>
<tr><td>Limited evidence supporting the existence of an effect</td><td>Probable effect</td><td>Possible effect</td></tr>
<tr><td>It is not possible to conclude from the evidence as to whether or not there is an effect</td><td rowspan="2">Possible effect</td><td rowspan="2">It is not possible to conclude from the available data as to whether or not the studied effect exists</td></tr>
<tr><td>Lack of quality data</td></tr>
<tr><td>The available data do not show any effect</td><td>It is not possible to conclude from the available data as to whether or not the studied effect exists</td><td>Probably no effect</td></tr>
</table>

Figure 11: diagram for the classification of health effects

The studied effect is proven for humans

This category is used only when there is *sufficient evidence* of the existence of the studied effect for humans.

The studied effect is probable or possible for humans

If the studied effect is not proven for humans, experimental studies in humans or animals (*in vivo* or *in vitro*) are taken into account, together with epidemiological studies, to make an overall assessment for humans of the impact of night work (fixed or rotating shifts).

This category includes effects for which, at the most, there is *limited* evidence supporting the existence of the studied effect in epidemiological studies and, at the least, there are no epidemiological studies but there is *sufficient* evidence supporting the existence of the studied effect in *in vitro* or *in vivo* studies. The said effects are classified either in the *probable effect for humans* category or in the *possible effect for humans* category, based on evidence from epidemiological and experimental studies, mechanistic data, and other relevant information.

Probable effect indicates a higher level of evidence than *possible effect.*

a- Probable effect for humans

This category is used when there is *limited* evidence supporting the existence of the studied effect in epidemiological studies, and evidence *supporting the existence of an effect* in *in vitro* or *in vivo* studies.

b- Possible effect for humans

This category includes effects for which there is *limited* evidence supporting the existence of the studied effect in epidemiological studies, and for which there is no evidence in *in vivo* and *in vitro* studies. It can also be used when there is *inconclusive* evidence in epidemiological studies but there is evidence supporting the effect in *in vivo* and *in vitro* studies, corroborated by mechanistic and other relevant data.

It is not possible to conclude from the available data as to whether or not the effect exists

This category includes effects for which the evidence supporting the existence of the studied effect is *inconclusive* or *non-existent* in epidemiological studies and *non-existent* in *in vivo* and *in vitro* studies.

Effects that do not correspond to any other category are also classified in this category.

Classification in this category does not indicate overall safety or the absence of an effect. It often means that further research is required, especially when data on the studied effect can be interpreted differently.

Probably no effect for humans

This category includes studied effects for which there is evidence suggesting there is *no effect* in clinical and epidemiological studies and in *in vivo* and *in vitro* studies for a large number of exposure conditions or scenarios. It is very difficult to demonstrate the absence of an effect.

6.2 Considerations relating to the analysed studies

This section aims to address all of the weaknesses identified in the studies taken into account by the Working Group in the framework of this expert appraisal. There are two major aspects that limit the validity of several of these studies: a very rough estimation of exposure to shift work and night work, and a partial and heterogeneous assessment of other confounding factors that can act as "competitors" or "mediators" or "confounders" of the effect. These problems are described in each of the sections on the analysed health effects. These common considerations have therefore been highlighted in this section.

6.2.1 Problems related to the characterisation of exposure to shift work and night work

6.2.1.1 Identification of workers as night workers

This information is extremely limited and sometimes relies on only one question whose expected answer is yes or no:

- "Have you been involved in shift work including night work?"
- "In total, how many years have you worked in rotating shifts with at least three night shifts per month, in addition to day and evening shift work?" (Schernhammer *et al.,* 2001 and 2006; Viswanathan *et al.*, 2007; Poole *et al.*, 2011).

In some studies, exposure to night work is sometimes based on work in sectors in which there are varying proportions of shift workers, with or without night work. For example, the study by Hansen *et al.* (2001) considered "exposed" workers to be those who had worked for at least six months in the five years preceding the diagnosis in one or more job sectors in which at least 60% of employees work night shifts; "unexposed" workers were those who had worked in sectors with less than 40% of people involved in night shifts.

In short, there is often a considerable lack of precision in the identification and classification of exposure.

6.2.1.2 Duration of exposure to shift work including night work

The decisive criterion for minimum exposure to night work also differs considerably between studies, ranging from a simple job title ("employed as a hospital nurse") (Lie *et al.,* 2006) to a precise definition of the number of years and the number of nights per week or per month (Davis *et al.,* 2001; Schernhammer *et al.,* 2001 and 2006; O'Leary *et al.*, 2006), or a minimum number of months in a job considered as having a high proportion of night workers (Hansen *et al.*, 2001; Schwartzbaum *et al.,* 2007).

Several studies use arbitrarily defined categories, with narrow (five-year thresholds) or very broad (> 15 years) groupings, or based on the distribution of the collected data (medians, quartiles, etc.): all this makes it difficult to compare the results of different studies.

6.2.1.3 Taking into account the current schedule but not past exposure

When past exposure is taken into account, it is generally estimated from a questionnaire and based on an *a posteriori* reconstruction. It does not always take into consideration possible exposure in a previous job.

For example, in the case-control study by Davis *et al.* (2001), involving various employment sectors, exposure was estimated through an interview dealing with average weekly hours worked in night shifts during the ten years preceding the diagnosis. In the retrospective study by O'Leary *et al.* (2006), exposure was estimated based on an *a posteriori* reconstruction of the time worked in night teams in the previous 15 years.

6.2.1.4 Healthy worker effect

In some studies, there is a possible selection and observation bias due to the "healthy worker effect". This bias occurs because workers who develop the most health problems tend to leave their jobs. Only the most resistant ("healthy workers") keep the same job for a long time, i.e. shift and night work in this case. This bias causes the health problems associated with night work to be underestimated. It can occur when there is no background information about the schedules of workers participating in a study. This bias is also observed when the health status of workers is compared to that of the entire general population, which is made up of workers as well as disabled people and people whose health status is less optimal than that usually found in active workers.

6.2.1.5 Arbitrary and heterogeneous determination of the time period defining night work

The definition of night working hours (and therefore the identification of night workers) is slightly different for each study. The time period considered can run from 5pm to 9am depending on the study. These heterogeneous definitions generate confusion between night work, evening work and early-morning work, whereas these different types of schedules have different health and psychosocial consequences.

6.2.2 Taking into account confounding factors

A confounding factor is a variable (typically age, gender, tobacco use, occupational co-exposure, etc.) associated both with the studied exposure and the disease. This factor, when not taken into account, can bias the statistical association between exposure and disease; this association is then influenced by the presence of the confounding factor and not only the exposure of interest. It is important to emphasise the high level of variability between studies for the numbers and types of confounding factors considered and the way in which they are taken into account in the analyses. Confounding factors change depending on the health effect in question and should be adjusted accordingly.

6.2.3 Consideration regarding the studies examined for the risk assessment

In light of the above, the Working Group gave more consideration to studies showing superior quality, in terms of the definition of night work (more details when characterising the type of shift work including night work), control for confounding factors, the characterisation of exposure, and the study design (in particular the number of workers taken into consideration and the length of the risk exposure period).

6.3 Results of the assessment of health effects

6.3.1 Effects on sleep

6.3.1.1 Introduction

The difficulties experienced by shift workers including night workers in falling asleep after a period of work at irregular hours are easily understandable and often recognised by all the parties in the workplace. Shift work including night work is accompanied by a need for the reorganisation of personal physiological rhythms at home, of which sleep is the most sensitive to these environmental conditions at irregular hours.

On the physiological level, as was described in Section 3, during night work, desynchronisation occurs between the circadian rhythms that are aligned with daytime hours, and the new rest-activity/sleep-wake cycle imposed by the night work. The result is the disruption and desynchronisation of the physiological and biological rhythms described above, including: the sleep-wake rhythm, eating habits, internal body temperature, cardiac and respiratory function, hormones (cortisol, melatonin), etc.

This desynchronisation is also promoted by environmental conditions that are not conducive to sleep during the rest period: daylight, temperature usually higher than at night, higher noise levels during the day, social life and family obligations. All these physical and sociological environmental factors contribute to disrupting physiological rhythms and the quality and quantity of sleep.

The sleep difficulties reported by shift workers including night workers concern both the quality and quantity of sleep:

- sleep quality: difficulty falling asleep, nocturnal awakenings with problems falling back asleep, waking up earlier than planned, feeling of non-restorative sleep. When one or more of these symptoms have been present at least three times a week for at least one month, it is considered as "insomnia" (as defined in the following classifications: International Classification of Sleep Disorders, 3rd edition, ICSD-3, and Diagnostic and Statistical Manual of Mental Disorders, 5th edition, DSM-V). When the complaint of insomnia is combined with a complaint of sleepiness in workers with atypical hours, it is described as "shift work sleep disorder" (SWSD), according to the International Classification of Sleep Disorders (ICSD-3, ref. 2014).

- sleep quantity: a reduction in sleep time per 24 hours is also typically reported by these workers, due to difficulty prolonging their main sleep episode in unfavourable environmental conditions. This is combined with difficulty supplementing the main episode with a brief or longer nap to keep from being sleep deprived. Some atypical work rhythms give operators the opportunity to sleep more on rest days and thus offset, in the short term, the sleep debt generated by previous rhythms. It has been shown that other rhythms do not enable short-term recovery from this debt. Furthermore, the physical and socio-family environment sometimes makes recovery difficult, whether voluntarily or involuntarily. For example, reconciling a career involving night shift work with life as a parent with small children at home, whose hours are not easily adaptable, contributes to this chronic sleep deprivation.

In recent years, several studies have demonstrated an association between too little sleep per 24 hours (less than six hours) and metabolic (obesity, type-2 diabetes) (Singh *et al.*, 2005; Gangwisch *et al.*, 2007; Cappuccio *et al.*, 2010) and cardiovascular (Altman *et al.*, 2012; Faraut *et al.*, 2012) comorbidities, as well as an increased risk of accidents. This association is found in conditions of chronic sleep restriction, irrespective of atypical hours.

The purpose of this Working Group was not to re-analyse the health effects of too little sleep. However, the risks related to lack of sleep are continuously reaffirmed in the literature and should be considered as possible explanations for the link between shift work including night work and the metabolic and cardiovascular comorbidity observed.

6.3.1.2 Review of the conclusions of the pre-existing literature (original publications dating before 2010 and literature reviews)

The recommendations of the French National Authority for Health (HAS) on the monitoring of shift and/or night workers concluded that the analysis and summary of the literature demonstrate that shift work and night work:

- are associated with a significant decrease in total sleep time per 24 hours (of around one to two hours per 24 hours, ultimately leading to chronic sleep deprivation) (level of evidence NP2[38] according to the HAS);
- are associated with a significant increase in the prevalence of insomnia (level of evidence NP3 according to the HAS).

In this section, the link between shift work including night work (fixed or rotating shifts) and sleep disorders is explored through a detailed analysis of 115 publications selected after preliminary sorting, based on their titles and abstracts.

After an in-depth reading of the 115 publications, ten were excluded for the assessment of the level of evidence:

- five studies were not deemed relevant to the assessed topic or were literature reviews;

[38] The HAS has defined four levels of evidence (NP1: established scientific evidence, NP2: scientific presumption, NP3: low level of evidence, NP4: low level of evidence, based on studies with major biases).

- five other studies were excluded due to major methodological limitations.

In the end, the effect explored in this section was based on an analysis of 105 relevant publications of sufficient methodological quality, published between 2010 and 2014.

Of these 105 publications:

- 43 publications were considered of good quality;
- 62 publications were considered as having minor methodological limitations.

6.3.1.3 Impaired sleep quality

Several recent studies confirmed the effects of shift work including night work on sleep quality in the working population or in targeted groups of workers.

6.3.1.3.1 In the working population

In the working population, Wilsmore *et al.* (2013) compared the prevalence of insomnia in shift and/or night workers to that of day workers, within a cohort of 22,389 Australian blood donors. They found that fixed-shift night workers had a higher proportion of primary insomnia (26%) than day workers (19%).

Similarly, in a group of 18,794 subjects representative of the Taiwanese population, Chiu *et al.* (2010) found a higher prevalence of insomnia in evening and night shift workers than in day workers.

6.3.1.3.2 In professional groups

Exposure - non-exposure

Akerstedt *et al.* (2010), in a five-year prospective study of 3077 exposed employees, showed that difficulties in falling asleep increased when entering shift work and decreased when leaving it. Working at night made it more difficult to wake up, and this problem did not disappear with the cessation of exposure.

The effects of exposure and cessation of exposure to shift work including night work on sleep quality were also studied by Bjorvatn *et al.,* 2012. Seventy percent of the nurses (136 women and 14 men) in an intensive care unit in Norway had poor-quality sleep according to the Pittsburgh Sleep Quality Index (PSQI) with shift work including night work. But these sleep problems tended to decrease with lack of exposure and recur with re-exposure. Moreover, 68.3% of the 60 Brazilian nurses interviewed by Mendes and De Martino (2012) had a PSQI score suggesting poor sleep and a significantly altered sleep quality score (VAS) for sleep around night shifts.

Influence of personal rhythm of life

Interestingly, De Almondes *et al.* (2011) studied subjective sleep problems in 141 Brazilian day (42) and shift (99) workers, taking into account lifestyle irregularity. They showed that in the entire group of workers, lifestyle was irregular and sleep quality was poor (average PSQI of 6.22 +/- 3.3), regardless of their working hours. However, the sleep quality on the PSQI scale[39] of day workers was significantly better than that of shift workers, whereas there was no difference between the two groups in terms of lifestyle regularity. This study concluded that lifestyle regularity is not decisive for the sleep quality of shift workers. Similarly, Courtney *et al.* (2013) showed, in a group of 150 Australian paramedic shift and night workers compared to a control group, that the increase in complaints of poor sleep in the shift and night worker group was independent of gender and age, and therefore of these paramedics' personal characteristics.

Morning shift - evening shift - night shift

According to Korompeli *et al.* (2013), interviewing 311 male and female Greek nurses working night shifts about their sleep (questionnaire not listed), "morning shift" work has a negative influence on sleep quality (shift workers had more sleep difficulties when they worked rotating morning shifts than when they worked fixed morning shifts). The influence of family structure on sleep is also explored in this study. For example, sleep disturbances are more severe in females, where they are more frequently associated with chronic fatigue. Sleep problems also increase with the number of people in the family (there are more sleep problems when there are more than three people in the family). Work experience is also significantly associated with sleep disturbances (more sleep problems with more than 18 years of work experience).

According to Flo *et al.* (2013), insomnia evaluated with a specific questionnaire among 1586 Norwegian nurses working 2x8 and 3x8 rotation schedules is significantly more frequent for the evening shift in 2x8 workers than in 3x8 workers (29.8% *vs* 19.8%). It is more frequent with the night shift in 3x8 workers than in permanent night workers (67.7% *vs* 41.7%). Rest-day insomnia is more frequent for permanent night workers than for 2x8 and 3x8 rotation workers (11.4% *vs* 4.2% and 3.6%). Surani *et al.* (2014) showed, in varied groups of nurses, that intensive care unit (ICU) nurses have the most reports of abnormal sleep quality (PSQI). All problems, i.e. sleep disturbance, sleepiness and fatigue, are more pronounced in night shift nurses.

Sleep disorders and professional consequences

Rajaratnam *et al.* (2011) report sleep disorders for 4957 North American police officers, most of whom have atypical shift and/or night hours, but whose rhythms are not precisely known. Of the 4957 participants, 40.4% screened positive for at least one sleep disorder; most of them had not been diagnosed previously. 1666 (33.6%) participants had obstructive sleep apnoea; 281 (6.5%) had moderate or severe insomnia; and 269 (5.4%) had SWSD (14.5% of those working the night shift).

The analysis (monthly follow-up for a two-year period) showed that the participants with a sleep disorder reported a higher rate of serious administrative error (17.9% *vs* 12.7%; adjusted odds ratio (OR) = 1.43 [95% CI, 1.23-1.67]), falling asleep while driving (14.4% *vs* 9.2%; OR = 1.51 [95% CI, 1.20-1.90]), making an error or safety violation attributed to fatigue (23.7% *vs* 15.5%; OR = 1.63 [95% CI, 1.43-1.85]), and exhibiting other adverse work-related outcomes: uncontrolled anger toward suspects (34.1% *vs* 28.5%; OR = 1.25 [95% CI, 1.09-1.43]), absenteeism (26.0% *vs* 20.9%; OR = 1.23 [95% CI, 1.08-1.40]), and falling asleep during meetings (14.1% *vs* 7.0%; OR = 1.95 [95% CI, 1.52-2.52]). There may be a possible

[39] Pittsburgh Sleep Quality Index, a questionnaire used to better understand the origin and extent of sleep disorders.

recruiting bias in this study, illustrated by the high prevalence (33.6%) of sleep apnoea syndrome reported during screening. This possible bias does not call into question the results but may have increased the apparent impact of night work.

<u>Sleep disorders following retirement</u>

Guo *et al.* (2013) focused on the effects on sleep of past night and shift work in 26,463 retired Chinese industrial employees (average age 63.6 years) by investigating, using questionnaires, sleep quality by PSQI and other comorbidities including type-2 diabetes and arterial hypertension. They found that shift work had a significant effect on sleep quality [OR = 1.18, 95% CI (1.09-1.27)], fairly similar to that found for diabetes [OR = 1.10, 95% CI (1.03-1.17)] and hypertension [OR = 1.05, 95% CI (1.01-1.09)]. They showed a gradual decrease in the harmful effects of night work on sleep quality as time elapsed from the last shift-work period, from [OR = 1.34, 95% CI (1.08-1.60)] one to four years after leaving shift work to [OR = 1.05, 95% CI (1.01–1.09)] at least 20 years after leaving shift work.

Monk *et al.* (2012) also investigated the sleep quality of 1133 retired American shift and/or night workers, with an average age of 74.7 +/- 6.3 years, and found that night shift work was associated with a worse (higher by one unit) PSQI score; this score was 0.6 units higher after 15 years of exposure.

In the shorter term, a study of 62 Taiwanese nurses (Cheng *et al.*, 2014) sought to determine how many days of rest it would take for nurses working atypical shift and night hours to regain sleep quality comparable to that of day nurses. Their sleep time and quality declined throughout the five successive nights of their work shift. The authors concluded they needed four days to recover nights of good-quality rest after this shift.

<u>Effects of shift length (12 hours of work)</u>

Hansen and Holmen, in 2011, submitted a questionnaire (not validated) to 496 male and 18 female night workers in a Norwegian shipping company working either 2x12 shifts or 4x6 shifts. They concluded that six-hour shift work was significantly associated with more sleep disorders than 12-hour shift work ($p < 0.01$). They did not find any differences in terms of work capacities or safety between the two schedules. Six-hour workers were more affected by noise than 12-hour workers ($p < 0.01$). No difference was found between the two groups regarding sleep disturbances at home. *[Note: not all the questionnaires used in this study were validated].*

This type of study is undertaken with highly specific professional groups who have come to work on offshore sites or construction sites. Employees come to work on the site for several weeks and then go home. In this context, it is understandable that 12-hour rhythms are considered less cumbersome than six-hour rhythms. But the conclusions of this type of study cannot be applied to all activities with atypical night and/or shift rhythms.

<u>Shift work including night work in sleep clinics</u>

A completely different objective was pursued by Walia *et al.* (2012), whose study involved a group of 1275 workers with atypical shift and night hours, out of 2298 people consulting in a North American clinic for a sleep disorder. This study found that patients with shift and night hours had more severe insomnia than those working day shifts and those not working, since after adjustment for confounding factors, shift and/or night workers reported more symptoms of insomnia (difficulties falling asleep, night waking, non-restorative sleep), with a relative risk of 4.8 for sleep onset difficulties. *[Note: This study did not deal with the general population of night workers but with a sample of night workers consulting in a sleep clinic, which may have overestimated the relative risk of insomnia].*

6.3.1.3.3 Assessment of the level of evidence

The epidemiological studies analysed enabled the Working Group to conclude that there was sufficient evidence showing that night work is responsible for impaired sleep quality (Figure 12).

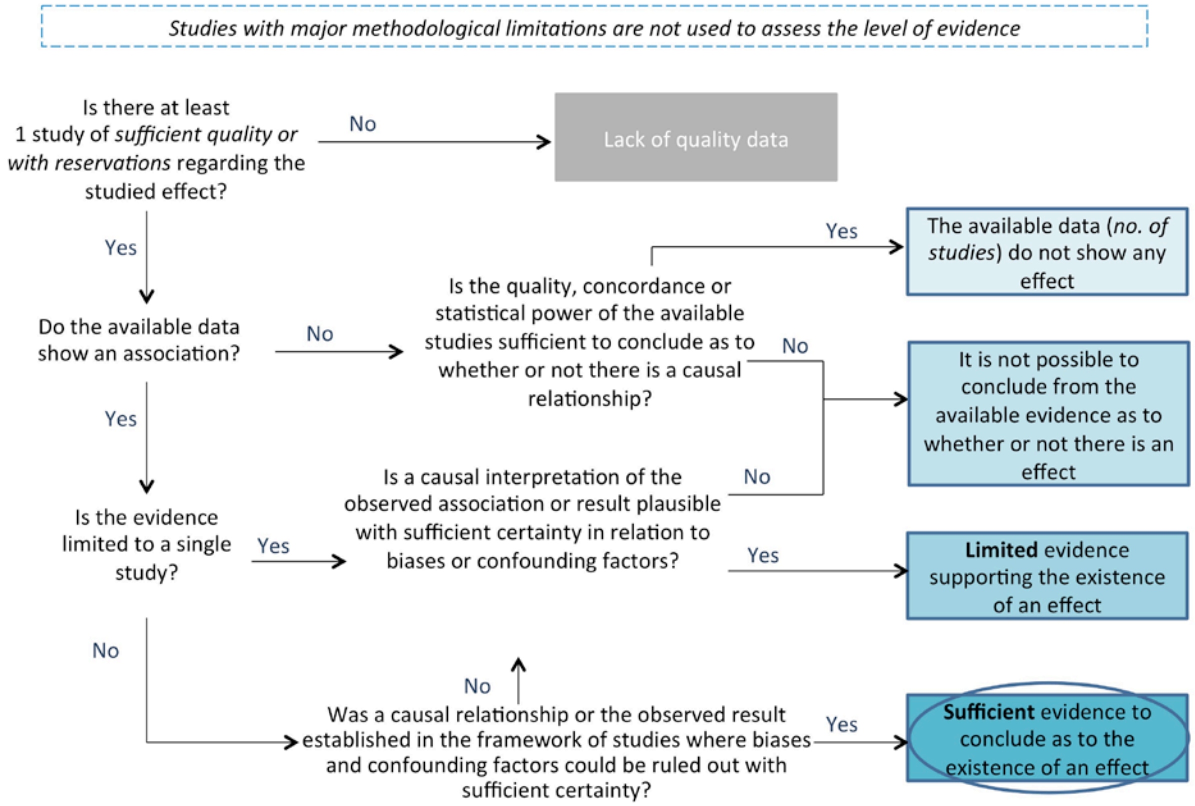

Figure 12: diagram for assessing the level of evidence for sleep disorders

In addition, most experimental studies in humans showed that shift or night work had negative effects on sleep quality and symptoms of insomnia (Rajaratnam *et al*., 2001; Akerstedt, 2003; Czeisler *et al*., 2007; Kantermann *et al.,* 2010; Vetter *et al.,* 2015).

This led the group to classify the effect of night work on sleep disorders as a proven effect (Figure 13).

<table>
<tr><td colspan="2" rowspan="2"></td><td colspan="2">Evidence of the existence of the effect in experimental studies in humans or animals</td></tr>
<tr><td>Evidence supporting the existence of an effect</td><td>No evidence supporting the existence of an effect</td></tr>
<tr><td rowspan="5">Evidence of the existence of the studied effect in epidemiological studies</td><td>Sufficient evidence to conclude as to the existence of an effect</td><td colspan="2">Proven effect</td></tr>
<tr><td>Limited evidence supporting the existence of an effect</td><td>Probable effect</td><td>Possible effect</td></tr>
<tr><td>It is not possible to conclude from the evidence as to whether or not there is an effect</td><td rowspan="2">Possible effect</td><td rowspan="2">It is not possible to conclude from the available data as to whether or not the studied effect exists</td></tr>
<tr><td>Lack of quality data</td></tr>
<tr><td>The available data do not show any effect</td><td>It is not possible to conclude from the available data as to whether or not the studied effect exists</td><td>Probably no effect</td></tr>
</table>

Figure 13: classification of the effect of night work on sleep quality

6.3.1.4 Reduction of total sleep time (TST)

Several studies confirm the effects of shift work including night work on the reduction of total sleep time, evaluated subjectively or objectively.

6.3.1.4.1 Subjective assessment

Ohayon *et al.* (2010) studied the effects of work schedule on sleep duration in 3345 participants (out of 4113 contacted, 81% response rate) in the state of New York in the United States, representing the general population. Sixty-five percent of the people surveyed were employed at the time of the interview: day workers represented 38%, rotating day-evening workers 14%, rotating day-evening-night workers 8%, fixed night workers 2%, and fixed evening workers 3%. Workers slept 6.7 ± 1.5 hours on average, but 40% slept less than 6.5 hours per sleep episode. Short sleep duration (< 6 hours) was strongly associated with night work (OR = 1.7) and rotating day-evening-night work (OR = 1.3). This author concluded that, compared to the other types of schedules, night work and rotating day-evening-night work were associated with short sleep duration, a risk of sleepiness and sleep attacks (falling asleep), and increased driving accident risk.

The same type of study undertaken in the general population (Ryu *et al.*, 2011), not focusing on atypical shift and night hours, examined 4411 Korean subjects, of whom 15% had atypical shift or night hours. The authors also found a significant association between a usual total sleep time (TST) of < 6 hours and atypical shift and night hours.

In a cross-sectional study of 264,422 American employees, undertaken using an online survey, Bushnell *et al.* (2010) observed that sleep time was shorter for 8-hour night shifts (relative risk (RR) = 1.22 [95% CI 1.05-1.43]) but not for 10-hour or 12-hour night shifts, for all rotating shifts (8 hours: RR = 1.15 [95% CI 1.02-1.30], 10 hours: RR = 1.60 [95% CI 1.29-1.99], 12 hours: RR = 1.29 [95% CI 1.12-1.49]), and for 10-hour (RR = 1.12, [95% CI 1.00-1.26] and 12-hour (RR = 1.31, [95% CI 1.09-1.58] day shifts compared to 8-hour day shifts. This study showed that, compared to the other types of schedules, night work and rotating day-evening-night work were associated with short sleep duration and a risk of sleepiness or sleep attacks.

Di Milia *et al.* (2013) also specified sleep time reported in the previous 24 and 48 hours by 1006 professional drivers (including 609 working at night) stopped for a control by the Australian police force. Of them, 20.9% of night workers *vs* 5.8% of non-night workers reported getting less than five hours of sleep in the previous 24 hours and 17.6% *vs* 4.2% getting less than 10 hours of sleep in the previous 48 hours.

<u>Reduction of sleep time and cortisol levels</u>

Cortisol levels are important for understanding the effects of atypical shift and night hours on sleep quality:

- firstly, because cortisol secretion by the adrenals is closely related to sleep. Its acrophase generally occurs at the end of the sleep period;
- secondly, because a high level of cortisol (stress hormone) can negatively impact sleep quality and has been associated with insomnia. As affirmed by Niu *et al.* (2011) in a summary of 28 studies including 27 non-randomised trials (review): the acrophase of cortisol is observed after six hours for day workers, seven hours for evening workers and 11 hours for night workers. Daytime cortisol concentrations remain high for night workers, lowering sleep quality during these periods. Niu *et al.* also specify, based on the same studies and trials, that night workers sleep one to four hours less than day workers on average (with a median of two hours).

Bostock and Steptoe (2013) also showed that for airline pilots working atypical shift and night hours, the morning shift (starting before 6am) was associated with a significant decrease in sleep time and a significant increase in cortisol levels.

<u>Morning shift-Evening shift-Night shift</u>

Tucker *et al.* (2010) focused on the effects of atypical shift and night hours on the total sleep time (TST) of 336 junior doctors in the UK with an average age of 28.7 +/- 4.8 years. TST was significantly reduced for cycles of several nights (up to seven consecutive nights) compared to day cycles, especially on the seventh night of a long cycle ($F = 43.39$, $P < 0.001$). Related to this reduction in sleep, fatigue significantly increased with:

- the cycle's duration;
- one day or less of rest between two cycles;
- weekly working time > 48 hours.

[Note: not all the questionnaires used in this study were validated]

It was in a group of 85 North American police officers that Ramey *et al.* (2012) studied the association between atypical shift and night hours and TST. According to their conclusions, night and evening workers slept significantly less than day workers (TST < 6 hours per night = 37% *vs* 3%, OR = 14.3 [95% CI 2-103]). Reduction in sleep time (TST < 6 hours per night) was significantly associated with more frequent reports of poor sleep quality (OR = 2.4 [95%

CI 1.1-5.2]). In other words, PSQI scores were significantly higher for short sleepers < 6 hours (total PSQI score = 7.6 +/- 3.0 *vs* 5.4 +/- 2.7). Taking into account other parameters such as stress and fatigue, the authors concluded that TST was a predictive variable for health in their group of police officers working at night or in shifts and recommended promoting sleep times of seven to eight hours per 24 hours for night and/or shift workers.

In a study undertaken among 289 nurses working a three-shift schedule (day, evening, night shifts), Flo *et al.* (2012) tested the validity of an assessment scale (the Bergen Shift Work Sleep Questionnaire, BSWSQ) compared to standard scales for the assessment of sleep, sleepiness and fatigue. The results suggest that this scale is valid for evaluating sleep disorders with shift work; they show that all the scales used have higher scores for night shift work and that symptoms of insomnia are also more common for night shifts than for other shifts. *[Note: the main objective of this study was not to assess the health consequences of night work, but the results are relevant].*

<u>Changes over a lifetime</u>

Tucker *et al.* (2010) examined the effects of atypical shift and night hours on the lifelong sleep of 3237 current or retired employees monitored by the VISAT study in France. Sleep problems related to shift and/or night work appeared significantly more severe in the fourth decade of life. There was a significant decrease in sleep problems associated with atypical shift and/or night work after the age of 50. This decrease was above all related to a decrease in the proportion of workers still working atypical shift or night hours. But people with atypical shift or night hours throughout their career still had significantly impaired sleep compared to others after the age of 50. Between the ages of 32 and 42 however, sleep problems were already significantly more severe for those who were or had been shift and/or night workers, revealing the triggering and initiating effects of sleep problems on the work experience of these subjects. *[Note: good-quality study but scales not validated].*

Of particular note, considering the other possible consequences mentioned in this review, is that TST was found to be significantly reduced in pregnant women in New Zealand working at night compared to those working during the day, in a study of 358 Maori and 717 non-Maori women (Signal *et al.,* 2014).

6.3.1.4.2 Objective assessment by actigraphy

Actigraphy is a **test that involves measurement and recording** using an actigraph attached to the wrist. It is used to determine the patient's rest-activity rhythm over several weeks (evaluation of their phase shifts, or the quantity and especially quality of sleep).

<u>Usefulness of actigraphy in assessing TST</u>

Dorrian *et al.* (2011) showed the usefulness of actigraphy for measuring sleep time in workers with atypical shift and night hours by studying 90 employees in an Australian rail company. Results were reported for 723 analysed shifts and showed that on average, operators slept for 7.2 hours, with 12 hours of wakefulness prior to work and eight hours of work. But for the studied shifts, 13% of the subjects slept less than five hours, 16% were awake for more than 16 hours before working, and 7% worked for more than 10 hours. Based on this study, it is not possible to conclude as to the effect of this type of work shift on sleep time, due to the small and heterogeneous sample. However, it had the advantage of comparing sleep duration to wakefulness duration prior to work, as well as theoretical and practical working time. It showed the usefulness of actigraphy for objectively measuring the TST of workers with atypical hours and for measuring duration of wakefulness prior to sleep. The study showed that night work and the total number of working hours per week were major predictors of sleep time.

The usefulness of actigraphy for assessing sleep time was also confirmed by Ertel *et al.* (2011) in a group of 271 women and 61 men working in a long-term care facility in the United States.

Morning shift-Evening shift-Night shift

Ferguson *et al.* (2012) also used actigraphy to compare 29 Australian miners to themselves for two types of schedules: at night from 5:30pm to 6am and during the day from 5:45am to 6pm. The latter schedule with early rising was accompanied by a significantly reduced TST (6.1 hours +/- 1.2) compared to sleep time on rest days (7.3 hours +/- 1.2). Night hours were also associated with a significantly reduced TST (5.7 hours +/- 1.5).

Actigraphy was also used by Paech *et al.* (2010) to observe the total sleep time of Australian miners working 12-hour shifts, either during the day from 6am to 6pm or at night from 6pm to 6am. TST was significantly reduced during working periods (day TST = 6.0 hours +/- 1.0; night TST = 6.2 hours +/- 1.6) compared to TST during rest periods (7.0 hours +/- 1.9). TST did not significantly vary during day cycles. However, regardless of the type of rotation, sleep time varied significantly during a night cycle. In a 4 x 4 rotation: TST N1 (first night shift) was significantly longer compared to N2 (second night shift) ($p < 0.05$); for the 7 x 4 rotation: N1 was significantly longer compared to N3 (third night shift), N5, N6 and N7 ($p<0.05$). For the 10 x 5 and 7 x 14 rotations: TST N1 was significantly longer compared to the following nights and to sleep during the day cycle ($p<0.001$). Therefore, regardless of the type of rotation, there was cumulative sleep debt, indicating insufficient recovery that should be improved by increasing the rest periods between two cycles.

Haire *et al.* (2012) also used actigraphy to measure the sleep time of 11 administrative employees in an Australian emergency department during 120 day (8am to 5:30pm) or night (10:30pm to 8am) shifts, with 7.1 years of average exposure (5-13). This study, limited to a small group, did not show a significant difference in cumulative sleep time between day periods and night periods, following adaptation. Time spent awake before sleeping with the night shift was significantly longer than before a day shift. *[Note: this study had moderate statistical power since it was undertaken with a limited number of participants].*

Polysomnography (PSG)

Polysomnography (PSG) is a technique for the complete recording of sleep using electroencephalogram, electromyogram and electrooculogram to precisely define stages of sleep. It is considered the gold standard for assessing sleep quality. However, PSG is technically difficult, even though its outpatient use is possible, requiring multiple electrodes to be attached to the subject's scalp and skin. PSG is therefore difficult to perform under normal working conditions. Chung *et al.* (2012) used PSG to confirm the reduction in sleep time in regular morning-shift nurses, matched with nurses working "during the day". Sleep time after the morning shift was significantly shorter than for all other shifts.

6.3.1.4.3 Assessment of the level of evidence

Considering all of the analysed epidemiological studies, there is sufficient evidence showing a reduction in sleep time related to night work (see Figure 14).

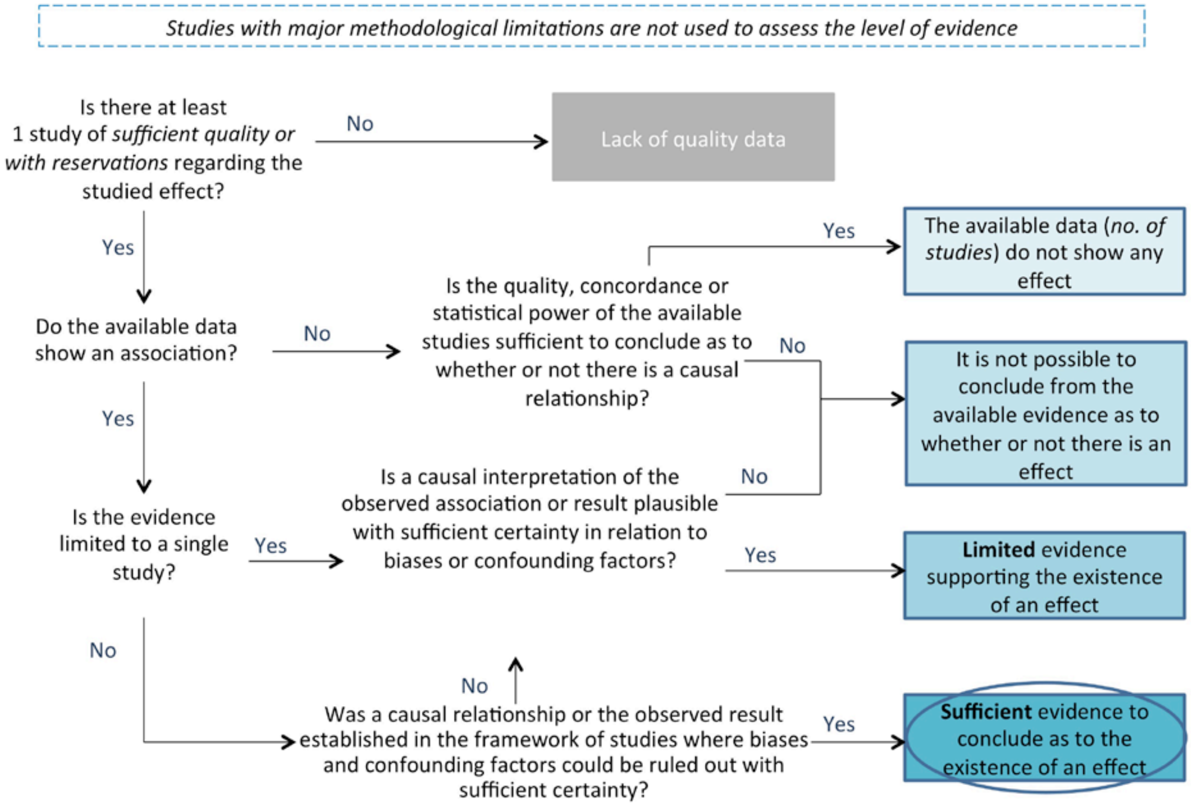

Figure 14: assessment of the level of evidence for the effect of night work on the reduction in total sleep time

From an experimental standpoint, the cited studies, especially those using actigraphy, confirm this reduction in sleep time.

Therefore, and given the large number of experimental studies in humans supporting this finding, the Working Group concludes that the effect of night work on the reduction in sleep time is proven (see Figure 15).

		Evidence of the existence of the effect in experimental studies in humans or animals	
		Evidence supporting the existence of an effect	No evidence supporting the existence of an effect
Evidence of the existence of the studied effect in epidemiological studies	**Sufficient** evidence to conclude as to the existence of an effect	***Proven effect***	
	Limited evidence supporting the existence of an effect	***Probable effect***	***Possible effect***
	It is not possible to conclude from the evidence as to whether or not there is an effect	***Possible effect***	***It is not possible to conclude from the available data as to whether or not the studied effect exists***
	Lack of quality data		
	The available data do not show any effect	***It is not possible to conclude from the available data as to whether or not the studied effect exists***	***Probably no effect***

Figure 15: assessment of the effect of night work on the reduction in total sleep time

6.3.1.5 Shift work sleep disorder

As described above, when a complaint of insomnia is combined with a complaint of sleepiness in workers with atypical hours, this is referred to as "shift work sleep disorder" (SWSD), according to the International Classification of Sleep Disorders (ICSD-3, ref. 2014): "the most common symptoms are difficulty initiating or maintaining sleep, as well as excessive daytime sleepiness .../... and adverse effects on cognitive performance...".

In a questionnaire-based study undertaken among 1156 female and 42 male nurses, Asaoka *et al.* (2013) showed that shift work disorder (SWD) affected 24.4% of these professionals. A logistic regression analysis showed that time spent working at night (compared to other shifts), missing opportunities to nap, having an evening chronotype, and rapid-rotation schedules were associated with a high prevalence of SWD.

Flo *et al.* (2012) found an even higher prevalence of SWD (37.6%) in 1968 male and female Norwegian nurses working three eight-hour night shifts (majority) or with other schedules. After logistic regression, the prevalence of SWD increased with the number of nights per year (dose-effect relationship).

Gumenyuk *et al.* (2010) used polysomnography (PSG) to better specify the severity of the sleep disorders of workers with SWD (compared to night workers without sleep disorders and day workers). This study involved 26 North American subjects including nine night workers without sleep disorders, eight night workers with SWD, and nine day workers. The night workers and those with SWD slept significantly less than the day workers. Sleep efficiency (ratio of TST/time spent in bed) was significantly reduced only for subjects with SWD (85% sleep efficiency, *vs* 95% for night workers and 96% for day workers). There was no significant difference between the groups for sleep onset latency or for the distribution of sleep stages.

Di Milia *et al.* (2013), in a questionnaire-based study undertaken among 1194 Australian workers, found that SWD was present in 32% of night workers (*vs* 10.1% of day workers, $p < 0.001$). Severe SWD was also found in 1.3% of day workers *vs* 9.1% of night workers. The logistic regression analysis found a significant association between SWD and short sleep of less than six hours (OR = 2.93 [95% CI 1.94-4.41]). People complaining of severe SWD slept an average of 0.8 hours less per 24 hours than the others ($p < 0.001$).

There are research opportunities to attempt to better characterise the phenotypes of subjects with SWD, depending in particular on whether their problems are mainly due to circadian misalignment with predominant sleepiness (showing, according to Gumenyuk *et al.* (2015), a long tandem repeat on the Per3 gene) or without circadian misalignment, marked with "alert insomnia", with a long allele of the Per3 gene.

A prospective study (Waage *et al.,* 2014) undertaken with 1533 nurses included in a national cohort of night and shift workers (SUrvey of Shift Work, Sleep and Health, SUSSH), initiated in 2008, concluded five years post-follow-up that the risk of triggering SWD was statistically significantly related to:

- the number of nights worked per year;
- having already worked night shifts in the year prior to follow-up;
- and having at least one symptom of SWD when hired.

6.3.1.6 Light therapy and sleep disorders of night shift workers

The effect of exposing shift workers with insomnia to bright light (1000 lux) at the start of the work shift was investigated by Huang *et al.* (2013) in 92 Chinese nurses with insomnia (randomised exposed *versus* unexposed trial). Exposure to high-intensity light in the first weeks of a night or evening shift led to a decrease in the severity of insomnia (according to the Insomnia Severity Index (ISI)), and in depression and anxiety.

Boivin *et al.* (2012) also showed the effectiveness of exposure to bright light in the first six hours of night work combined with dark goggles worn after work in nine night nurses compared to six without light therapy. TST after the night shift was 30 minutes longer per night in the "light" group than in the no-light group (TST = 706 +/- 0:08 *vs* 6:36 +/- 0:11, $p = 0.04$). The authors did not find a significant difference with light exposure in terms of sleep efficiency or sleep onset latency.

Thorne *et al.* (2010) also showed the benefits of using light therapy combining exposure to light and darkness during the first five 24 hours of returning to a day schedule after a prolonged period of night work in 10 men working on an oil platform in the North Sea, the criterion being TST measured by actigraphy over 15-day periods. There was a significant improvement in sleep efficiency in treatment phases combining darkness and light therapy for the first five days of treatment (86.7% +/- 5.8% (with treatment) *versus* 79.4% +/- 10.3% (without treatment)). For the next nine days (days 6 to 14), TST was significantly increased by light therapy in the light treatment leg (6.75 +/- 0.50 hours *versus* 5.76 +/- 0.73 hours).

These aspects are addressed in the section on countermeasures aiming to limit the effects of night work.

6.3.2 Sleepiness, cognitive effects and vigilance

6.3.2.1 Introduction

The desynchronisation between circadian rhythms and the rest-activity/sleep-wake cycle that results from night work leads to the disruption and desynchronisation of the physiological and biological rhythms described above, including: sleep rhythm, internal temperature, cardiac and respiratory function, hormonal secretions (cortisol, melatonin), etc. Laboratory studies have additionally shown that circadian desynchronisation is also accompanied by cognitive impairment. Memory, attentional processes, response time and executive functions are related to the state of vigilance, as well as the state of fatigue, anxiety or depression, and are therefore also sensitive to the restriction of sleep time. Since night work is accompanied by circadian desynchronisation and restriction of sleep time, vigilance and cognitive performance can be negatively affected in shift workers including night workers.

On a mechanistic level (see Section 3), it is the attentional phase, in which memory and cognitive quality are set, that is altered by sleepiness and poor sleep. But poor sleep quality can also negatively affect the cognitive processes of perception and memory consolidation that occur during sleep, especially during slow-wave sleep and paradoxical sleep (REM sleep).

Sleepiness is characteristically associated with shift and night work. This sleepiness is explained by both the desynchronisation of the working day compared to the circadian clock, and the "sleep debt" developed by shift and night workers.

6.3.2.2 Review of the conclusions of the pre-existing literature (original publications dating to before 2010 and literature reviews)

The recommendations of the HAS on the monitoring of shift and/or night workers concluded in particular that "the analysis and summary of the literature demonstrate that shift and night work are associated with a significant increase in the risk of sleepiness during the waking period (NP3), itself associated with a decline in cognitive performance in relation to day work (NP3)" (HAS, 2012).

Regarding the risk of errors at work, the HAS recommendations specified that "the data in the literature were limited". Since most of the analysed studies deal with specific populations (interns and nurses), it is not possible to extrapolate their results to other populations or give general conclusions. However, no analyses of other cognitive impairments such as attention problems, memory impairment or decreased performance were mentioned in the HAS's recommendations.

A recent study (Marquié *et al.*, 2015), comparing employed and retired shift workers to non-shift workers, suggested there were increased cognitive and memory impairments in the employed and retired shift workers (1484 subjects in a cohort compared to 1635 controls). The study reported that these impairments were also associated with the length of exposure, since those who had worked for more than 10 years had significantly impaired cognition compared to those who had worked for less than 10 years. Interestingly, the study also reported that these impairments were related to shift work and were in part reversible, since those who had left shift work more than five years earlier were less impaired than those who had left it within the last five years.

6.3.2.3 Analysis of the literature for the various effects

In this section, publications have been classified according to the main effects described by each article:

- sleepiness and vigilance in general;
- sleepiness outside of work;
- performance and cognition;

- fatigue.

In this section, the link between night work (fixed or rotating shifts) and sleepiness and cognitive parameters is explored through a detailed analysis of 75 publications selected after preliminary sorting based on their titles and abstracts (out of a total of 393 identified publications).

After an in-depth reading of the 75 publications, 40 studies were not taken into account in the group's deliberations and the classification of effects:

- twenty-eight studies were not deemed relevant to the assessed topic or were literature reviews and were thus excluded from the analysis;
- ten other studies were excluded due to major methodological limitations;
- two publications could not be obtained and therefore analysed. These were the studies by Hemamalini (2014) and Mawdsley (Mawdsley *et al.*, 2014).

In the end, the effect explored in this section is based on an analysis of 35 relevant publications of sufficient methodological quality published between 2010 and 2014. Of these 35 publications:

- eleven were considered of good quality;
- twenty-four had minor methodological limitations.

6.3.2.3.1 Effects of atypical shift and night hours on sleepiness and vigilance

Sleepiness is characterised by the occurrence of unintended sleep episodes during wakefulness. This sleepiness can be assessed using subjective scales (Epworth Sleepiness Scale (ESS), Karolinska Sleepiness Scale (KSS) or Stanford Sleepiness Scale (SSS)) and objectively using a Multiple Sleep Latency Test (MSLT) or a Maintenance of Wakefulness Test (MWT). This sleepiness varies depending on the time of day (circadian rhythm) and also depending on the duration of the previous sleep and prior waking period, and therefore the potential accumulated sleep debt (homeostatic factor).

A score above 10 on the Epworth Sleepiness Scale indicates abnormal sleepiness. A score above seven on the Karolinska Sleepiness Scale indicates severe sleepiness.

Ten epidemiological studies of adequate methodological quality dealing with the issue of sleepiness were subject to a detailed analysis, presented below. They include cohort studies and cross-sectional studies involving populations of shift workers.

- Seven epidemiological studies (one prospective cohort study: Akerstedt *et al.,* 2010, and six cross-sectional studies: Chang *et al.,* 2013; Geiger - Brown *et al.*, 2012; Geiger - Brown *et al*., 2014; Ohayon *et al.*, 2010; Di Milia *et al.*, 2013; Surani *et al.,* 2014) confirmed an association between night/shift work and sleepiness:

Akerstedt *et al.* (2010) conducted a longitudinal study of 3077 shift and/or night workers with two waves for the assessment of sleep and sleepiness separated by five years (77% response rate for the second assessment). During the second assessment, the authors found an increase in sleepiness and the risk of falling asleep at work for shift workers (OR = 1.63; [95% CI 1.30-2.05]) and night workers (OR = 1.56; [95% CI 1.01-2.41]). This risk was also very high for workers entering shift and/or night work (OR = 2.91; [95% CI 1.26-6.72]). The risk did not significantly decrease for those leaving shift and/or night work for retirement or day work (OR = 1.85 [95% CI 0.99-3.44]).

Chang *et al.* (2013) objectively (MWT and MSLT) and subjectively (SSS) assessed vigilance and sleepiness during the day in 20 nurses who had worked two consecutive nights compared to 23 nurses who had been off-duty for at least three days. The off-duty nurses were more able to maintain wakefulness (MWT) but were not significantly different from the nurses leaving the night shift for MSLT sleep latency or for subjective sleepiness. The authors concluded that nurses can underestimate their ability to maintain wakefulness after two consecutive night shifts. *[Note: This study had some minor methodological limitations].*

Geiger Brown *et al.* (2012) also compared, in a cross-sectional study, the sleepiness of 80 nurses working 12-hour shifts when they worked at night *versus* during the day, using the KSS scale. Sleepiness was high (KSS > 7) for 45% of the nurses. The study showed that sleepiness significantly increased with the number of successive 12-hour shifts, both for day shifts and for night shifts, that it was higher at the end of the shift than at the start of the shift, and that it increased significantly faster during the night shift than in the morning. The authors reported that increased sleepiness was associated with high caffeine consumption. The assumption was that the increase in sleepiness during shifts was related to cumulative sleep debt with successive shifts and that the night shift amplified this effect.

In another study, with a sample of 40 nurses working 12-hour shifts (night shifts, day shifts or rotating shifts), Geiger Brown *et al.* (2014) reported that severe sleepiness (KSS > 7) was higher for night shifts (OR = 3.5 [95% CI 1.9-6.5]) than for day shifts, that it was higher in the third consecutive shift than in the first (OR = 5.4 [95% CI 1.3-22.5]), and that the existence of a sleep disorder increased the risk of high sleepiness (OR = 2.8 [95% CI 1.0-7.4]). In this study, sleepiness was reduced for nurses with a morning chronotype. *[Note: This study had some minor methodological limitations].*

Ohayon (2010) reported a cross-sectional epidemiological study including 3345 participants (out of 4113 contacted, 81% response rate). Sixty-five percent of the people surveyed were employed at the time of the interview: day workers represented 38%, rotating day-evening workers 14%, rotating day-evening-night workers 8%, fixed night workers 2% and fixed evening workers 3%. Twenty percent of the workers showed excessive sleepiness in situations requiring high attention. This sleepiness was associated with night work (OR = 3.3) and rotating day-evening-night work (OR = 1.5). Five percent of the workers reported sleep attacks, but these were three times more frequent for night work (OR = 3.2). Driving accidents, reported by 3.6% of the workers, were associated with night work (OR = 3.3) and rotating day-evening-night work (OR = 2.1).

Di Milia *et al.* (2013) presented a cross-sectional questionnaire-based study on the chronic sleepiness of 649 night drivers compared to day drivers; 18% of the surveyed drivers reported chronic sleepiness. Night workers showed higher average sleepiness (% of subjects with KSS > 7), which may have been related to shorter sleep for these workers (three times more individuals receiving less than five hours of sleep per 24 hours [20.9% *versus* 5.8%], and four times more receiving less than 10 hours of sleep per 48 hours [17.6% *versus* 4.2%]) and longer working hours (78% *vs* 39.2%).

Surani *et al.* (2014) studied 70 nurses working 12-hour shifts and compared the night shift to the day shift, and work in the intensive care unit to work on the general floor. The average ESS score was not significantly higher for the night shift, but there were significantly more night nurses with an abnormal ESS score (42%) than day nurses (12%). However, this study had minor methodological limitations, especially low statistical power.

- Two cross-sectional studies showed no association between night work and sleepiness. However, these studies focused on very specific populations:

Forberg *et al.* (2010a) studied the sleepiness of tunnel workers subject to 21 consecutive days of night work followed by 21 days of rest. Sleepiness was assessed at the end of the shift using a non-validated scale for cumulative sleepiness and was not different at the end of the night shift (6pm to 4am) than at the end of the day shift (6am to 4pm). *[Note: This study had some minor methodological limitations, due especially to the selection of subjects representing a very particular population (in an extreme environment) and the absence of a validated scale for assessing sleepiness].*

Walia *et al.* (2012) studied complaints of sleepiness by ESS and the consumption of more than six cups of coffee per day in 1275 workers consulting in a sleep clinic between 2007 and 2009: 23% worked rotating shifts and 8% worked fixed evening or night shifts. They were compared to day workers. Night and evening workers had higher odds (RR = 3.3) of having higher coffee consumption than day workers, but it was not significantly different from that of rotating-shift workers. Reports of sleepiness were not significantly different between the three groups. *[Note: This study had a minor methodological limitation since it dealt with a group of patients in a sleep clinic, not representative of the population of shift workers]*.

- Lastly, one study focused on the factors that influence sleepiness:

Waage *et al.* (2012) examined a group of oil rig workers. The aim was to assess the effects of three different work schedules (two weeks of day work, two weeks of night work and two weeks of swing shift work [one week of night work and one week of day work]) on sleepiness (KSS) and reaction time. Sleepiness appeared higher on the first few days after night work and in the middle of the two-week work period, but it gradually decreased with the number of nights worked. Sleepiness at home was higher after night work. *[Note: given the highly selected population, studied in a very particular environment, with a very unusual schedule, this study's results cannot be generalised. The WG also notes that this study had a low number of subjects and a large volume of missing data].*

6.3.2.3.2 Effects of atypical shift and night hours on cognition and psychomotor performance

The effects of shift and night work on cognition and performance are often studied using a tool called the psychomotor vigilance task (PVT). This psychomotor performance test, which has been validated in numerous experimental conditions, measures the speed at which a subject responds to a visual or auditory stimulus during a test that usually takes 10 minutes, but can last anywhere from three to 20 minutes.

The results of this test reflect the cognitive and attention processes associated with vigilance and are highly sensitive to sleep deprivation. Since it is so simple, this test cannot be used to predict an individual's ability to perform complex tasks found in the workplace. However, the PVT is a point of reference for sleep research and medicine and most studies show a slower response time in shift and night workers, as in the five following studies (one experimental study by Boudreau *et al.*, 2013, three cross-sectional studies, by Ferguson *et al.,* 2012, Surani *et al.*, 2014 and Vetter *et al.,* 2012, and one repeated-measures study by Wagonner *et al*., 2012).

Boudreau *et al.* (2013), in an experimental study, compared the performance of two groups of police officers (seven men and eight women on patrol): a group with circadian adaptation to night work (thanks to light, tinted goggles, etc.) *versus* a non-adapted group. They found that after seven nights of work, the daytime sleep of the police officers adapted to night work was of the same quality as their nighttime sleep before the change of shifts. This was not the case for the police officers not adapted to night work: there was a decrease in total sleep time and proportions of non-REM and REM sleep and an increase in wake after sleep onset. PVT reaction speeds were faster at the end of the waking period for the police officers adapted to night work than for the non-adapted officers, indicating better performance in this test and thus a higher level of attention and vigilance.

Ferguson *et al.* (2011) undertook a cross-sectional study with portable PVTs in 35 miners working three types of rotating shifts over a 12-hour period, during the day or at night. The workers were compared to themselves (repeated measurements) at the beginning and end of each day and night shift for a full rotation sequence (16 to 22 days depending on the type of rotation). Performance was significantly ($p < 0.001$) more impaired at the end of the night shift than at the end of the day shift. It was not different at the start of the day, end of the day and start of the night. There was also a positive relationship between the quantity of accumulated sleep in the 24 hours before the start of the shift ($p < 0.05$) and performance. In this study, getting less than six hours of sleep was associated with lower performance than getting more than seven hours of sleep. The decline in performance at the end of the night shift confirmed several prior studies, but this study highlighted the significance of sleep as a mediator of field performance.

Surani *et al.* (2014) conducted a cross-sectional study of 67 nurses working permanent 12-hour day (n=43) or night (n=24) shifts, in intensive care or on the general floor. The average PVT response time was significantly slower before the night shift than the day shift (reflecting the impact of time spent awake before work, which was longer for night workers), whereas there was no difference between the end of the night shift and the end of the day shift. No difference was found for omissions (errors) between the two shifts. This study had minor methodological limitations due to the small number of night workers (low statistical power) and a probable selection bias since the participants were recruited on a voluntary basis through signs and word of mouth.

Vetter *et al.* (2012) analysed the influence of chronotype and time awake on PVT response time and error risk in a repeated-measures study, where the same workers were evaluated during a day, morning and night shift. The lowest performance was measured during the morning shift (average rising time of 4:30am) and the highest during the evening shift. Here again, the decline in performance during the night and morning shifts was related to the time spent awake before the shift for the night shift (longer than for the day shift) and the prior duration of sleep for the morning shift (shorter than for the day shift). In this population of young workers (20-36 years of age) with a late chronotype, chronotype had an impact on performance, especially *via* its effect on sleep duration and time. The results of this study thus also underline the major role played by sleep duration before the start of the shift, in terms of vigilance at work, whether at night or early in the morning.

Waggoner *et al.* (2012) undertook a methodological study that proposed and tested the validity of a combined method for assessing the consequences of shift work for police officers: this method combined the measurement of performance with the PVT, the assessment of sleepiness with the KSS scale, and simulated driving with the measurement of deviations from the centre line. Repeated measurements were taken in the morning after five consecutive nights of work and in the morning after three consecutive days off duty. The authors observed a decline in performance, attention and subjective vigilance in the morning after five nights of work compared to in the morning after three days off duty, indicating a negative effect of night work. *[Note: this study had some minor methodological limitations since it was unable to isolate the effect of night work, as the control condition was the morning after a night of sleep. However, its results are consistent with those of other studies showing the significance of sleep before the start of the shift for the subsequent vigilance level].*

A sixth cross-sectional study also used the PVT to assess vigilance but did not find any significant effect of night work:

Geiger-Brown *et al.* (2012) reported PVT results for 80 nurses working 12-hour shifts. PVT scores were not significantly different, whether for the response time or the number of errors (slow response time), between day and night shifts, between successive shifts, or between the start and end of the shift. However, error frequency was associated with the severe reduction in sleep time observed over successive shifts. This study also suggested that the individuals did not have the same vulnerability to sleepiness. KSS sleepiness increased faster during the night shift.

Other cognitive assessment methods, which are not standardised like the PVT, were also used in five studies (four cross-sectional studies by Cheeseman *et al.,* 2011; Höelzle *et al.*, 2014; Johnson *et al.*, 2010; Shwetha and Sudhakar*,* 2012; and one repeated-measures study by MacHi, 2012). The five studies concluded there was an association between cognitive performance and night/shift work.

In the study by Cheeseman *et al.* (2011), the authors investigated the computer recognition of drug labels by anaesthesia trainees. Mean confirmation reaction times were slower during night shifts than during day shifts (mean difference 60 msec [95% CI 1-120], $p = 0.048$).

There was no difference in error rates. *[Note: the small sample and absence of test times were (minor) methodological limitations of this study]*.

Hölzle *et al.* (2014) studied the effects of shift work on the handwriting of 34 employees (32 men and two women) of an electrical equipment factory. The subjects were compared to themselves (repeated measurements) and the criteria were writing speed, vertical script size, and the frequency of high and low modifications per second, measured by micro-computers. The authors showed that writing speed and size were affected by shift work. Contrary to expectations, it was not during the night shift that performance was the lowest, but during the morning shift, especially at the start of the shift. Since the shift in this study started very early (6am), the results suggest a decisive influence of short sleep duration before the start of the shift.

Johnson *et al.* (2010) observed, in a correlational cross-sectional study, the effects of sleep deprivation on the psychomotor performance of 289 night-shift nurses. The authors used the "d2" Test of Attention, which is a validated paper and pencil test of approximately eight minute that asks participants to identify targets surrounded by distractors. The total number of errors (by omission and commission) provides the test result. The authors found a significant association between the number of hours of sleep and test performance ($p = 0.018$). There was no group of day workers, but the participants' results showed performance below the normative values. *[Note: this study had some minor methodological limitations since a single test was used just once during the night, and not at the same time for all the subjects. In addition, sleep duration was very approximate since it was obtained by retrospective estimation]*.

MacHi *et al.* (2012) studied the effects of night work on the short-term memory of 13 emergency physicians with a decline during the day shift and night shift but with significantly more cognitive parameters affected (Stroop test, cognitive processing) during the night shift. These results show that the night shift had more of an impact than the day shift on memory and certain cognitive and learning processes, which may have consequences for decision-making at the end of the night shift. *[Note: the small sample and failure to take into account circadian factors and sleep latency were minor methodological limitations]*.

Shwetha *et al.* (Shwetha and Sudhakar, 2012) conducted a cross-sectional study in which they used standard neuropsychological tests to assess a set of cognitive parameters (mental speed, sustained attention-vigilance, verbal learning and memory, executive functions (inhibition and working memory)) in 50 workers on rotating night shifts compared to 50 workers on permanent day shifts. The tests were administered at the end of the work period. The authors concluded that rotating night shifts affect certain cognitive functions (mental speed, learning and memory, response inhibition) but not others (attention-vigilance, working memory). *[Note: the study had some minor methodological limitations: there were several possible confounders, which were not controlled or described, such as the times and duration of the shifts, the type of rotation, schedule regularity, and differences in the nature of the tasks performed by shift workers and day workers]*.

6.3.2.3.3 Effects of atypical shift and night hours on fatigue

Fatigue and sleepiness are often confused with one another other. They are two phenomena that are sometimes mixed up but are actually very different:

Sleepiness is defined as "an intermediate state between wakefulness and sleep characterised by an irresistible tendency to nod off if the person is not stimulated"[40]. In practice, it occurs when there is a strong need to sleep. It then becomes increasingly difficult to stay awake and only sleep can effectively respond to this sensation by durably restoring vigilance (which is thus the exact opposite of sleepiness).

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[40] Louise BÉRUBÉ, Terminologie de neuropsychologie et de neurologie du comportement, Montréal, Les Éditions de la Chenelière Inc., 1991, 176 p., p. 87.

Fatigue is a sensation of physical or mental exhaustion occurring after sustained effort. Only rest can effectively meet this need by restoring a good level of energy and performance (which is thus the opposite of fatigue). Fatigue can be associated in particular with reduced attention and concentration. Psychological fatigue or psychasthenia is a component of depression. Fatigue is often described as a consequence of atypical shift and night hours, without being objectively assessed.

We selected three cross-sectional studies for this analysis (Dorrian *et al.,* 2011; Ferguson *et al.,* 2010; Geiger-Brown *et al.,* 2012).

Dorrian *et al.* (2011) studied 90 employees with a variety of jobs (drivers, maintenance, etc.) in a large railway company; observations were made for a total of 713 shifts. Fatigue was estimated using the validated Samn-Perelli Fatigue Scale with seven levels, where levels 6 and 7 indicate extreme fatigue. The authors reported that night workers were twice as likely to experience fatigue than morning workers and noted that sleep duration, shift duration and workload were all predictive factors for extreme fatigue. They specified that every hour of sleep reduced the risk of fatigue by 12% and that every hour of work increased it by 19%. *[Note: the generalisation of this study's results is nonetheless limited by the heterogeneity of the study population and the rather unusual shift start and end times: 3 to 11am for "morning" work and 7pm to 3am for night work]*.

Ferguson *et al.* (2010) studied 29 miners working 12-hour shifts, with seven night shifts (5:15pm to 5:45am) and seven day shifts (5:15am to 5:45pm) followed by 14 days of rest. They showed that fatigue (estimated using the Samn-Perelli scale) was greater during day shifts than during night shifts and on days off. Note that the workers, housed in camps near the mine, had to get up at 3:45am to be at work at 5:15am and that sleep duration (approximately six hours) was similar for the day and night shifts. Fatigue was significantly associated with a sensation of non-restorative sleep. This study showed that even in the absence of family constraints, short sleep and high fatigue were associated with 12-hour shifts. *[Note: this study had a minor methodological limitation given the particular study population, limiting the generalisation of the results]*.

Geiger-Brown *et al.* (2012) explored fatigue as well as sleepiness in a cross-sectional study of nurses working 12-hour shifts. Severe fatigue affected one-third of the nurses, where not recovering from the previous shift at the start of the next shift was the selection criterion. However, there was no specific information enabling the effects of 12-hour night work to be clearly distinguished.

6.3.2.3.4 Effects of atypical shift and night hours on shift work sleep disorder (SWSD)

Two articles by the same team attempted to objectively describe cognitive and vigilance impairments related to shift work sleep disorder (SWSD). It should be noted that excessive sleepiness at work is one of the main diagnostic criteria for this disorder and therefore the studied patients were not representative of all shift and night workers.

Gumenyuk *et al.* (2010) studied neurophysiological changes in the attention and memory functions of 26 night workers with SWSD, using event-related brain potentials. They compared eight night workers with SWSD to nine healthy night workers and nine healthy day workers. They identified a decline in memory and excessive reaction to novelty in the night workers with SWSD, similar to that of insomniacs. The results also showed that sleep duration and quality were reduced in night workers, with and without SWSD, in relation to day workers. These results were compatible with the polysomnographic measurements taken in a laboratory that showed that the patients with SWSD had lower sleep efficiency than the healthy night workers and day workers, with the latter two groups having similar sleep. The study indicated sensory memory reduction and attentional hyper-reaction (quantified by the study of event-related potentials) in the night workers with SWSD, but it is not possible to conclude with certainty that this was a functional neurobiological impact of night work, given the small number of subjects and the experimental conditions of this study.

Moreover, the study provided no information regarding the characteristics of the night work (tasks, schedule, duration of the experiment, etc.) or the circadian influence which may have affected these parameters.

Gumenyuk *et al.* (2012), in another study by the same team, focused on the dim light melatonin onset (DLMO) profile of two groups of five night workers, with or without a diagnosis of SWSD. The results showed that the DLMO of asymptomatic night workers occurred much later (4:42) than that of night workers with SWSD (20:42), which indicated circadian adjustment for the healthy night workers and circadian misalignment for the workers with SWSD. Compared to the healthy workers, the patients showed greater physiological sleepiness during the night (measured by MSLT) but no significant difference for sleep parameters. However, a significant correlation was found between DLMO and the severity of insomnia. Workers with SWSD received more light in the morning, which may have contributed to their lack of circadian adjustment. The higher propensity for sleep at night combined with the lack of sleep differences for workers with SWSD suggest that the decline in vigilance at night was mainly related to the lack of circadian adjustment. *[Note: the very small number of participants and the non-characterisation of night work were methodological limitations of this study]*.

6.3.2.4 Assessment of the level of evidence

6.3.2.4.1 Sleepiness

6.3.2.4.1.1 Epidemiological studies

Of the 10 studies dealing with sleepiness, seven showed a positive association between sleepiness and night/shift work. In particular, two independent studies of very good quality (one longitudinal (Åkerstedt *et al.,* 2010) and one cross-sectional (Ohayon *et al.*, 2010)) undertaken among a large number of night workers showed an increase in sleepiness for night workers; in addition, sleepiness increased with the duration of exposure (dose-response effect). Two studies showed no association, but in both cases, the results were obtained with very specific populations: respectively highly selected workers working 21 days in a row in an extreme environment (Forberg *et al.,* 2010), and patients (shift and day workers) in a sleep clinic (Walia *et al.,* 2012). It is therefore difficult to generalise the results of these two studies to all shift and night workers. A last study (Waage *et al.,* 2012) made no direct comparison between day work and night work, but showed that sleepiness was higher during the first few days of night work and then gradually decreased, and that sleepiness was also very high the first few days of returning home after two weeks of night work. This study thus indirectly supported the occurrence of an effect of night work on sleepiness, which decreases depending on the workers' degree of circadian adaptation to their schedule.

The experts therefore considered that the evidence from the epidemiological studies is sufficient to conclude there is an effect on sleepiness (see Figure 16).

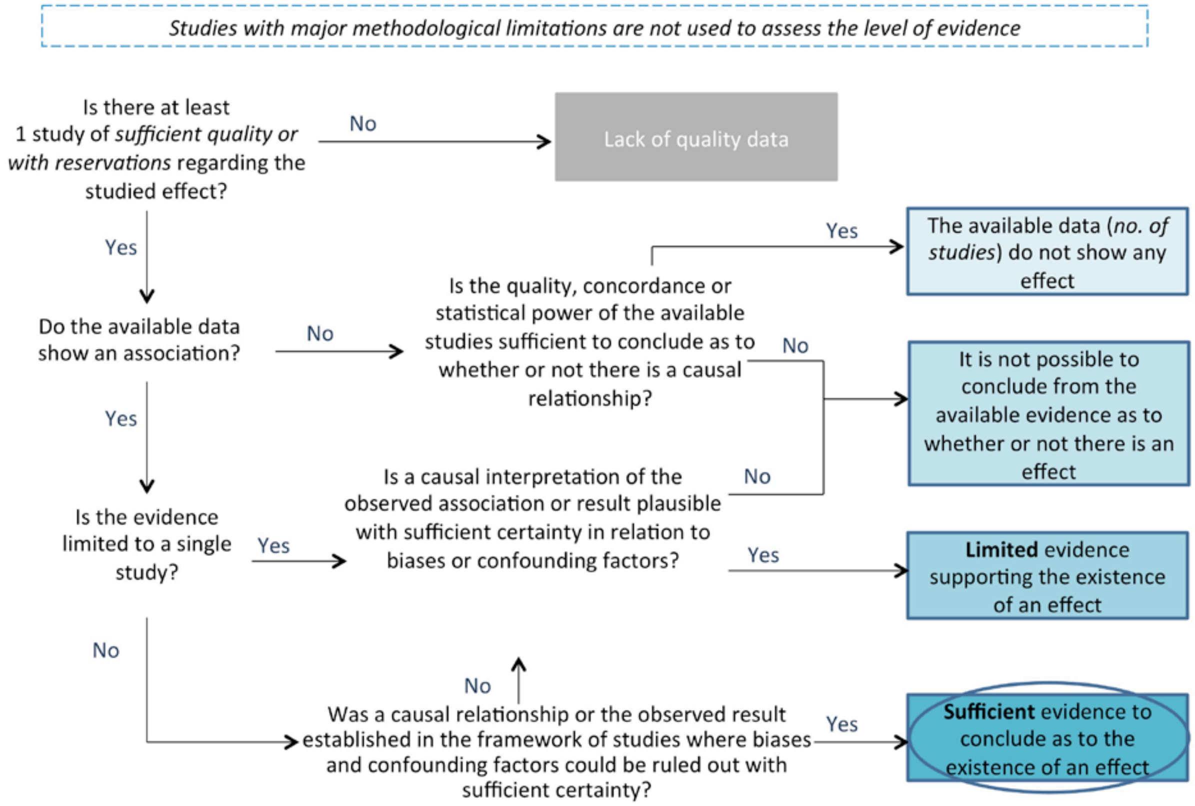

Figure 16: Assessment of epidemiological studies dealing with sleepiness

6.3.2.4.1.2 Experimental studies

The results of these epidemiological studies are completely in line with the observations that have been made for over 30 years among night workers (Akerstedt and Gillberg, 1982) and in experimental studies (Akerstedt and Gillberg, 1982). The most recent experimental studies have also shown that sleepiness increases at night, in relation to the lack of circadian adjustment and due to the long waking period preceding the start of the shift (Santhi *et al.,* 2005), (Smith *et al.*, 2004), (Chapdelaine *et al.*, 2012). The experimental studies undertaken in humans with laboratory-simulated shift work confirm the proven effects of these atypical hours on sleepiness, which is always present but varies depending on the imposed shift work schedule, age, and related chronobiological and homeostatic factors.

6.3.2.4.1.3 Conclusion

In accordance with the method adopted by the Working Group and considering the evidence provided by the epidemiological studies and experimental studies, the experts conclude that night work has a proven effect on sleepiness in humans (see Figure 17).

<table>
<tr><td colspan="2" rowspan="2"></td><td colspan="2">Evidence of the existence of the effect in experimental studies in humans or animals</td></tr>
<tr><td>Evidence supporting the existence of an effect</td><td>No evidence supporting the existence of an effect</td></tr>
<tr><td rowspan="5">Evidence of the existence of the studied effect in epidemiological studies</td><td>Sufficient evidence to conclude as to the existence of an effect</td><td colspan="2">Proven effect</td></tr>
<tr><td>Limited evidence supporting the existence of an effect</td><td>Probable effect</td><td>Possible effect</td></tr>
<tr><td>It is not possible to conclude from the evidence as to whether or not there is an effect</td><td rowspan="2">Possible effect</td><td rowspan="2">It is not possible to conclude from the available data as to whether or not the studied effect exists</td></tr>
<tr><td>Lack of quality data</td></tr>
<tr><td>The available data do not show any effect</td><td>It is not possible to conclude from the available data as to whether or not the studied effect exists</td><td>Probably no effect</td></tr>
</table>

Figure 17: classification of the effect of night work on sleepiness

6.3.2.4.1 Cognitive performance

6.3.2.4.1.1 Epidemiological studies

Of the 11 studies analysing the impact of night/shift work on cognitive performance, six showed a positive association, two did not compare night work and day work (Boudreau *et al.*, 2013; Johnson *et al.*, 2010), two reported lower performance during the morning shift than during the night shift (Vetter *et al.*, 2012; Hölzle *et al.*, 2014), and one showed no association (Geiger-Brown, 2012). While most studies use the objective measurement known as the PVT, a few offer other interesting assessment methods. Several conflicting results show that the decline in psychomotor performance in the PVT may be more affected by sleep deprivation prior to starting the shift than by the actual time of the shift, whether it is a night or day shift. An experimental study (Boudreau *et al.*, 2013) showed that circadian adjustment to night work simultaneously improved daytime sleep quality and psychomotor performance. Two studies that used standard neurophysiological tests to assess cognitive functions (MacHi *et al.,* 2012; Shwetha and Sudhakar, 2012) suggested that certain cognitive functions are more affected by night work than others, but these results need to be corroborated with a larger number of workers.

It is important to note that many studies have investigated sustained attention and reaction time; studies on long-term cognitive disorders have not been analysed in detail in this report.

The experts therefore considered that the evidence from the epidemiological studies is limited to conclude there is an effect on cognitive performance (see Figure 18).

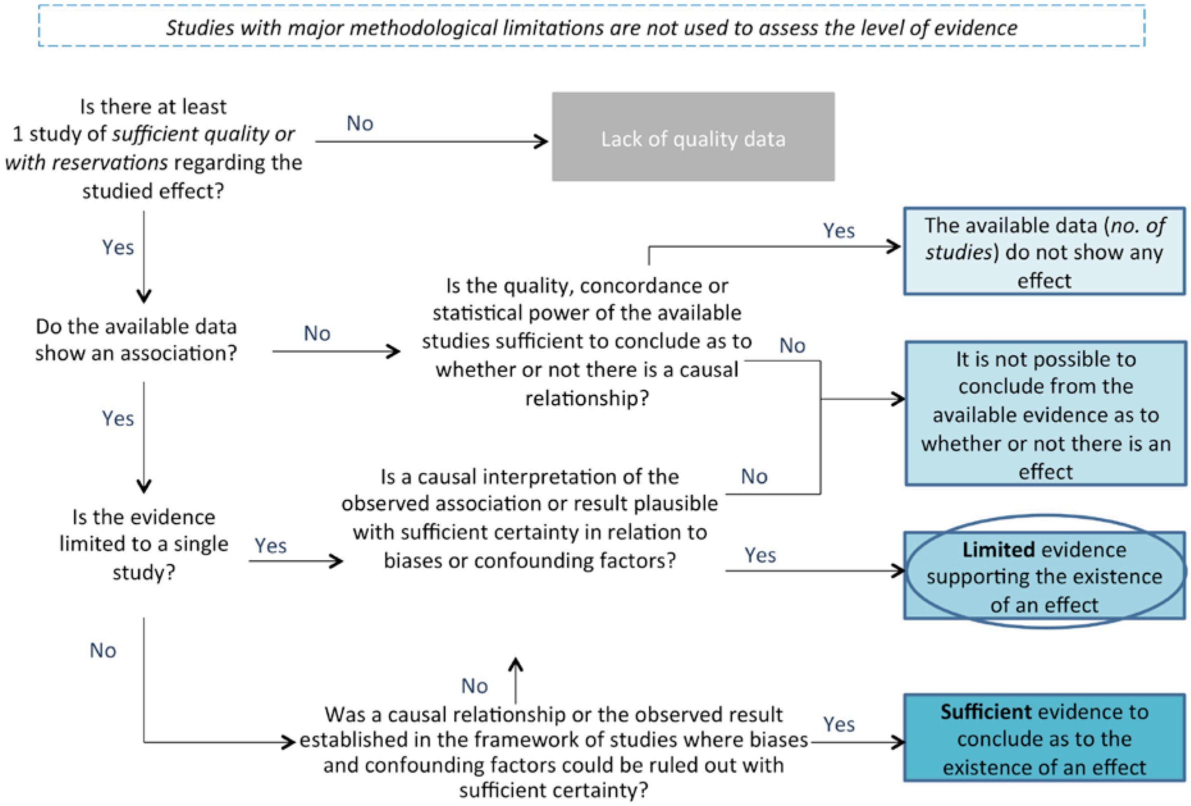

Figure 18: assessment of epidemiological studies dealing with cognitive performance

6.3.2.4.1.1 Experimental studies

The studies conducted in humans with laboratory-simulated shift work confirm the effects of these irregular hours on cognitive performance, in particular, but not exclusively, assessed by the PVT.

The experimental studies in humans show that cognitive performance is reduced at night (Akerstedt *et al.*, 2007; Wyatt *et al.,* 1999); (Dijk and Czeisler, 1994); (Schmidt *et al.,* 2007). However, as with the epidemiological studies described above, very few studies have used cognitive performance tests that can reflect the actual tasks performed by night workers on the job. Most studies have used the PVT response time test, a short and monotonous task that is particularly sensitive to sleep deprivation. However, all these studies show that sleep deprivation has a major effect on psychomotor performance. The studies also show a decline in performance when tests are taken at circadian times of low propensity to wakefulness. This circadian effect is also demonstrated by studies showing the recovery of normal response time following circadian realignment in conditions of actual or simulated night work (Czeisler *et al.,* 1990), (Boudreau *et al.*, 2013). Other aspects limit the ability to generalise laboratory data to field workers. On the one hand, laboratory studies cannot be used to assess the long-term effects of night work on performance or determine whether performance improves or continues to decline with the duration of the experiment. On the other hand, it is difficult for laboratory studies to take into account motivational effects occurring in the field. For example, there is reason to believe that the motivation to perform a medical procedure on a patient differs from the motivation to take a response time test in a laboratory, and some studies suggest that tasks that require the greatest cognitive load (such as logical reasoning) are less affected by sleep deprivation (Akerstedt *et al.*, 2007). However, there are physiological mechanisms suggesting that the repeated circadian disruption experienced by night and shift workers may cause cognitive damage. Indeed, it has been shown in animals that experimental jet lag reduces hippocampal neurogenesis and produces pronounced deficits in learning and memory, and that these deficits persist even after a return to a regular cycle (Gibson *et al.,* 2010). There is therefore experimental evidence showing that sleep deprivation and circadian disruption can produce cognitive deficits, but the degree to which these observations can be transposed to night workers over the long term is still uncertain and remains to be demonstrated. However, there was one study that, while it needs to be reproduced, showed cognitive deficits and reduced temporal lobe volume in flight attendants subject to chronic jet lag (Cho *et al.,* 2001). The effects of sleep deprivation and circadian disruption on the impairment of short-term cognitive function have already been proven.

6.3.2.4.1.2 Conclusion

In accordance with the method adopted by the Working Group and considering the evidence provided by the epidemiological studies and the data suggesting the existence of an effect in experimental studies, the experts conclude that night work has a probable effect on cognitive performance in humans (see Figure 19).

<table>
<tr><td colspan="2" rowspan="2"></td><td colspan="2">Evidence of the existence of the effect in experimental studies in humans or animals</td></tr>
<tr><td>Evidence supporting the existence of an effect</td><td>No evidence supporting the existence of an effect</td></tr>
<tr><td rowspan="5">Evidence of the existence of the studied effect in epidemiological studies</td><td>Sufficient evidence to conclude as to the existence of an effect</td><td colspan="2">Proven effect</td></tr>
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<tr><td>It is not possible to conclude from the evidence as to whether or not there is an effect</td><td rowspan="2">Possible effect</td><td rowspan="2">It is not possible to conclude from the available data as to whether or not the studied effect exists</td></tr>
<tr><td>Lack of quality data</td></tr>
<tr><td>The available data do not show any effect</td><td>It is not possible to conclude from the available data as to whether or not the studied effect exists</td><td>Probably no effect</td></tr>
</table>

Figure 19: classification of the effect of night work on cognitive performance

6.3.2.4.2 Fatigue

As specified at the beginning of this section, there are currently multiple definitions of fatigue, but there is no consensus on any one. Even though night workers often complain of fatigue, it remains extremely difficult to systematically assess and there are no objective measurements of fatigue.

Two of the studies analysed here used the Samn-Perelli scale, which is a validated seven-point scale for estimating fatigue, but the results were inconclusive. The first (Dorrian *et al.*, 2011) showed that sleep duration, shift duration and workload were just as significant as night work in predicting subjective fatigue. The second (Ferguson *et al.,* 2011) found more fatigue in day workers than in night workers, but since the day workers had to get up at 3:45am, it was likely that the results here demonstrated the effects of sleep deprivation, irrespective of the shift.

As fatigue is the effect of some wear, it cannot be experimentally assessed since night-work simulations are necessarily short-lived. In addition to the lack of a clear definition of fatigue and a valid objective measurement, there are also no studies supporting a mechanistic basis for the effects of night work on fatigue.

The experts conclude that it makes more sense to underline the proven risk of sleepiness than to vaguely describe, in unscientific terms, the effects on fatigue. Thus, considering the state of the available definitions and knowledge, this effect has not been classified.

6.3.3 Effects on psychological health

6.3.3.1 Introduction

The link between shift work including night work (fixed or rotating shifts) and mental health and addiction is explored in this section through a detailed analysis of 21 relevant publications of sufficient methodological quality (published between 2010 and 2014). All of the analysed studies except two – i.e. 19 studies – showed a positive association. In five of the 18 epidemiological studies, this association was directly related to schedule characteristics (shift duration, number of nights and night work experience); in eight others, it was related to sleep impairment further to night work, although the link seemed more indirect since it may have been mediated by factors related to work content. The only available experimental study showed an improvement in mood when there was better circadian synchronisation in shift workers studied in a laboratory.

6.3.3.2 Review of the conclusions of the pre-existing literature (original publications dating to before 2010 and literature reviews)

Shift workers including night workers collectively report problems with their psychological health: mood disorders, depression, irritability, anxiety and personality disorders (Rohr *et al.,* 2003; Ruggiero, 2003; Bara and Arber, 2009; Vogel *et al.,* 2012). Changes to the circadian system, long regarded as a consequence of mental disorders, could actually be involved in causing these disorders. Indeed, the direct involvement of changes to the circadian system – and therefore potentially night work – in the development of mental illnesses is currently suspected. Night work, whether fixed or rotating, is thought to affect mental health *via* disruptions to temporal organisation: impairment of sleep quantity and quality, desynchronisation of biological, social and family rhythms, changes in the perception of photic synchronisers, among other things (Wirz-Justice, 2007; Wirz-Justice, 2012). Sleep disorders are suspected of being involved in causing depressive disorders in shift workers (Scott *et al.*, 1997) and in the decision to leave shift work (Lai *et al.*, 2008). Recent data derived from advances in molecular biology even suggest that the circadian system is more directly involved in the aetiology of mental illnesses *via* "clock gene" alterations in cerebral regions involved in neuropsychiatric disorders (Menet and Rosbash, 2011). The emerging notion that well-synchronised internal biological rhythms reduce the incidence and severity of the symptoms associated with mental illnesses also supports this assumption (Menet and Rosbash, 2011). However, since the majority of studies have been cross-sectional, precautions are required when drawing conclusions: this notion is also discussed for mental health in a recent review (Vogel *et al.*, 2012).

In a now-dated study relying on telephone interviews, depression score was positively associated with shift-work experience (Scott *et al.*, 1997). On this same topic, a "dose-response" effect was recently established by Bara and Arber (2009), showing an increased effect on depression and anxiety according to night-work experience, which varied according to gender. However, no association between the shift-work system and depressive disorders or anxiety symptoms was found in the study by Geiger-Brown *et al.* (2004) or in the older study by Skipper *et al.* (1990) in nurses.

Regarding the schedule arrangements of shifts and the organisation of rotations, some studies have explored the link with mental health, especially through the recovery time available between two shifts. These studies show that very short rest times between two shifts (less than 11 hours of rest between the end of a shift and the resumption of work, very common for transitions between the afternoon shift and morning shift) affect the well-being of night workers (Hakola *et al.*, 2010; Barton and Folkard, 1993), whereas no effects have been found on anxiety or depression (Eldevik *et al.*, 2013). The results remain fairly inconsistent, leaving this aspect of the issue of the effects on mental health open for now.

Other studies suggest that night work has an indirect effect on mental health, mediated by work content. Work (its content, conditions and organisation) is a potential source of mental health impairment (Chouanière *et al.*, 2011) *via* commonly recognised psychosocial risk factors (Gollac and Bodier, 2011). These factors can be divided into six categories: they can be related to the intensity of work and working time, emotional requirements, insufficient autonomy, the poor quality of social relations at work, value conflicts or job insecurity.

The link between psychosocial risks at work and mental health problems has now been established (Bonde, 2008; Chouanière *et al.*, 2011; Cohidon *et al.*, 2012).

Working the night shift (fixed or rotating shifts) is identified in the report by Gollac and by the French National Research and Safety Institute (INRS) as a psychosocial risk factor (Gollac and Bodier, 2011; INRS – Horaires atypiques de travail, 2013). Workers subject to night hours are doubly exposed to psychosocial risks: firstly, night work itself is a stress factor and secondly, working the night shift more significantly exposes them, by the work itself being different, to other psychosocial risk factors. This notion of dual constraint has been clearly illustrated in major national surveys undertaken by the French Ministry of Labour ("Working conditions" survey of 2013; "Sumer" survey of 2010). The "Working conditions" survey of 2013 (DARES, 2014, no. 49) (34,000 workers) showed that on average, employees working at night described markedly more difficult working conditions than other employees. With other similar characteristics, night workers are subject to more physical hardship factors, greater time pressure, and more frequent tensions with their colleagues or the public (contact with people in distress and verbal abuse, especially). These differences are partly due to the types of jobs held (police officers, caregivers, etc.), although they persist with "equivalent jobs" (DARES, 2014, no. 62). Similarly, the Sumer 2010 survey of a large population (DARES, 2014, no. 44) demonstrated that hostile behaviour is more common when the organisation of work is marked by atypical hours (2x8 and 3x8 work).

This notion of more difficult working conditions is clearly illustrated in a recent literature review on police officers (Chae *et al.*, 2013). This summary highlights the importance of the interactions between several factors for the mental health of police officers, including shift work, combined with others such as work-related stress, overtime during night shifts, dissatisfaction at work, and the risk of suicidal thoughts, which are correlated with the regularity of night shifts. This accumulation of work-related stress factors is also pointed out in the study by Nabe-Nielsen *et al.* (2009), one of the few dealing with permanent night and/or evening work in the sector of elderly care. This study showed an accumulation of psychosocial risk factors in the fixed evening and night teams (lack of decision-making latitude, low level of social support from managers, more exposure to physical and psychological violence, and a greater physical load) compared to the fixed day teams. However, the evening and night teams were less exposed to high quantitative and emotional demands. This study showed that exposure to psychosocial risk factors varied depending on the type of schedule and implied that work was not the same in a night/evening shift and in a day shift.

In any event, all of these studies and surveys, which support an effect of night work mediated by work content, underline certain recommendations for future research, in particular the need, in order to understand a health effect – *per se* – of shift/night work, for studies to adequately adjust work-related factors.

Night work also interacts with another component of mental health, which is addictive behaviour. A literature review (Puttonen *et al.*, 2010) suggests that shift work increases tobacco consumption *via* stress related to the lack of control over work hours. Bushnell *et al.* (2010) cited a review by Boggild and Knutsson (1999) that examined 13 cross-sectional studies on the association between shift work and tobacco use: six found a positive association, one showed a negative association and six found no association. A more recent review by Zhao and Turner (2008) including five studies showed that four of them found a positive association between night work and tobacco use. A link between shift/night work and drug abuse – alcohol and medications in particular – has also been suggested by now-dated studies (Niedhammer *et al.*, 1995; Trinkoff *et al.*, 1998). It is clear that for addictions as well, although a majority of older studies show an association between night work and addictive behaviour, the results are not consensual.

The latest HAS report on the "Medico-professional monitoring of shift and/or night workers" in 2012 identified four studies, published between 2004 and 2011, investigating the relationship between shift and/or night work and mental health; it concluded that the analysis of the data in the literature suggested that shift and/or night workers are more likely to experience depression and/or anxiety, but with a low level of evidence. In this same report, four studies on addictions published between 2006 and 2010 were analysed. Two supported an association between tobacco use and shift work while the other two showed no association, leading the report's authors to conclude that based on the analysis of the literature, it was not possible to draw a conclusion as to an association between shift work and increased tobacco use (HAS, 2012).

6.3.3.3 Analysis of publications since 2010 (2010-2014)

6.3.3.3.1 Analytical methodology

This section presents studies that have assessed the effects of shift and/or night work on various parameters associated with mental health, including mood disorders (depression and anxiety), burn-out, and addiction (alcohol, tobacco, caffeine). One study explored emotional eating disorders in male and female nurses. Two publications indirectly analysed psychosocial risk factors such as internal violence.

Following the preliminary sorting undertaken when reviewing the study abstracts (165 abstracts in total), 46 publications were selected for analysis. These publications consist of research articles published between 2010 and 2014.

After an in-depth reading by two experts, 15 studies were excluded, as they were not considered relevant to the assessed topic. Ten other studies were excluded from the assessment of effects due to major methodological limitations.

In the end, 21 studies were thus identified by the experts as relevant and of sufficient methodological quality to contribute to the assessment of the effects of shift work including night work on psychological health. They were all cross-sectional epidemiological studies except for two: the recent longitudinal epidemiological study by Thun *et al.* (2014) and the laboratory experimental study carried out by Boudreau *et al.* (2013).

Nine of these studies were considered as being of good quality and 12 as having minor methodological limitations. These 21 studies, which are broken down and discussed below, were taken into account to establish the level of evidence.

A summary of the selected studies, and the reasons for excluding the non-selected studies, are given in the tables found in Annex 8 and Annex 9.

6.3.3.3.2 Analysis of the effects of night work (fixed or rotating shifts) on mental health

Two studies – the cross-sectional study by Oyane *et al.* (2013) and the longitudinal study by Thun *et al.* (2014) – showed no association between shift work including night work and deteriorated mental health, but they could not rule out an effect, due to a possible response bias.

The objective of the study by Oyane *et al.* (2013) was to assess the relationship between night work and anxiety, depression, insomnia, sleepiness and fatigue in Norwegian nurses between the ages of 21 and 63. The data from this cross-sectional study were obtained through questionnaires mailed by post. Although the number of participants (90% women) was high (2059), the response rate was fairly low (38%). The respondents were divided into three categories: those who had never worked at night (n=229), those who worked at night at the time of the study (n=1315), and those who had worked at night in the past (n=491). One of this study's strengths was that it considered the number of nights worked in the past year. No differences were observed between the groups for symptoms of depression or anxiety and no significant association was found between these symptoms and the number of nights worked in the past year. These results were consistent with those of some prior studies (Skipper *et al.,* 1991; Parkes, 1999) but not others (Bara and Arber, 2009; Scott *et al.,* 1997). *[Note: it is difficult to conclude as to the absence of a relationship between night work and depression and anxiety with this study's results due to the strong possibility of a response bias (recognised by the authors themselves), since more depressed or anxious people were less likely to complete this type of questionnaire, and the effect of this bias was probably amplified by the low response rate. Another limitation of the study stemmed from the fact that most of the nurses not working at night still worked rotating shifts, and shift start and end times were not taken into account, which may have diluted the results].*

The study by Thun *et al.* (2014) was the only longitudinal study published on the topic between 2010 and 2014. It investigated the relationship between the type of shift work (permanent night shift or 3x8 work) and levels of anxiety and depression in 633 nurses. With two years of follow-up and three data collection times, this study wanted to determine whether the type of shift work predicted levels of anxiety and depression at T_0. However, the population sample analysed was relatively small in certain sub-groups: day or 2x8 work = 188; night or 3x8 work = 325; day or 2x8 work at T_1 and permanent night or 3x8 work at T_3 = 33; permanent night or 3x8 work at T_1 and day or 2x8 work at T_3 = 87. The study was original in that it took into account, in addition to the standard age factor, certain personality traits and the circadian type. "Languidity" (feeling of sleepiness, lethargy) was related to higher anxiety and depression; the opposite was noted for "hardiness" (resilience, resistance to difficulties). It is interesting to note that the change in depression and anxiety scores over time was significantly associated with non-standard personality factors. It would be useful to verify the independence of the variables in relation to one another; this statistical aspect is not mentioned in the publication. The study did not show effects of night work *per se* on anxiety and depression: the type of shift work did not explain the initial level of depression or anxiety or the change in these conditions - except in the group that switched from "night work" to "day work": depression scores improved for state-certified nurses leaving night work (selection process? healthy worker effect?). The results showed that the mental health of employees leaving night work was not as good as that of those remaining and thus suggested the possibility of a healthy worker effect (see definition, p. 124-125). *[Note: it would have been interesting to know the reasons for the shift change requests, but these are not provided in the article. In any event, the study's results should be put into perspective, since a healthy worker effect could not be ruled out and may have caused the effects of night work on the health effect in question to be underestimated].*

The 18 studies analysed in the rest of this section showed a more or less direct association between night work and impaired mental health.

- Five cross-sectional studies directly linked schedule characteristics (12-hour shift duration) and/or the organisation of the shift-work system (number of nights, shift work experience) to the mediation of the effects of shift work on mental health.

The study by Kaneita *et al.* (2010) examined the addictive behaviour (tobacco and alcohol) of Japanese physicians. The researchers had monitored a cohort since 2000 and reported the follow-up results from 2008 for 3486 participants. This was a cross-sectional study in which the researchers assessed factors that could distinguish current smokers from former smokers and people who had never smoked. Shift work was one of the assessed factors, defined by the number of days per month on call or working the night shift. All the information was obtained through self-administered questionnaires. The results showed that smoking was significantly associated with working eight days or more per month on call or at night and was much more common in men than in women. The researchers also reported a strong association between smoking and daily alcohol consumption, suggesting a connection between these two forms of addiction. *[Note: in addition to a high response rate, one of this study's strengths was that it assessed the frequency of days on call or working the night shift, which led to the conclusion that it was not night work or on-call work itself but rather their high frequency that was associated with smoking. Note however that the use of self-administered questionnaires and the failure to distinguish between on-call work and actual night work may have caused the effects of night work on addiction problems to be under-estimated].*

Bushnell *et al.* (2010) focused on behaviours that have an impact on the health of workers, including smoking, lack of exercise, alcohol use, body mass index and short sleep duration. They assessed the prevalence of these risk factors by work schedule type (day, night or rotating) and shift duration (8, 10 or 12 hours), controlling for age, gender, marital status and type of work shift. It was a very broad study, including 26,442 participants working for a multinational company primarily in the United States, in a variety of positions including production, maintenance, administration and sales. Data were collected using an anonymous online survey on a voluntary basis. Risks were assessed in comparison to the group of eight-hour day shift workers. All the work shifts except the 10-hour day shift showed a higher rate of smoking than the eight-hour day shift. The highest rates were found with the 12-hour day and rotating shifts. Only the 12-hour rotating shift workers showed heavy alcohol consumption. This study therefore showed an increase in smoking with night and shift work, but long shift duration (12 hours) seemed to be the determining variable. No relationship was found between night work and moderate or heavy alcohol consumption. *[Note: despite the large number of participants, it is difficult to assess the representativeness of respondents for a voluntary online survey. The number of participants in the various sub-groups also varied considerably (it was much lower for the sub-groups of 10-hour and 12-hour night shift workers) and the number of hours worked per week was not taken into account. In spite of its limitations, this study demonstrated the importance of considering work shift duration when assessing the health effects of night and shift work].*

It nonetheless seems essential to determine whether or not there is a link between smoking and night work, since several studies dealing with cardiovascular disorders in shift workers consider smoking as a confounder in their analyses. The results of adjusted analyses are necessarily skewed if shift work itself leads to an increase in tobacco use. However, it is very difficult to determine whether there is a causal relationship between shift work and smoking. For example, another study (Nabe-Nielsen *et al.*, 2008) showed that a larger number of evening and night workers had already been smokers before they started working, raising the possibility that these work shifts attract more evening chronotypes, known to be heavier smokers than other chronotypes (Wittmann *et al.*, 2010).

Wong *et al.*, 2010 investigated the relationship between shift work and eating behaviour in nurses in three hospitals in Hong Kong. The study, undertaken with 378 mainly female (91.5% women) individuals, found that the number of nights worked per month was positively associated with abnormal eating behaviour among nurses. The results showed that nurses working more than four nights per month were 2.91 times more likely to have an emotional eating disorder and 3.35 times more likely to have restrained eating (a desire to limit dietary intake to lose weight) than those not working at night. *[Note: even though the study had a modest response rate (57.1%) and mainly involved female nurses, its results suggested a connection between night work and eating behaviour. Given the link between eating behaviour and metabolism, it seems appropriate to inform night workers of food hygiene principles]*.

Khajehnasiri *et al.,* 2013 studied antioxidant capacity and levels of malondialdehyde (a biomarker of oxidative stress) in 139 shift workers showing depressive symptoms (the inclusion criterion was a depression score on the Beck scale ≥ 10). *[Note: this study was not designed to assess the relationship between night work and psychiatric symptoms. Even so,* *the results indicate a significant correlation between the depression score (quantified by questionnaires) and shift work experience].*

In a study in the same population, but with broader inclusion criteria – 189 shift workers with depression scores ranging from zero (not depressed = score from 0 to 9: 53 employees) to 29 – the same authors, Khajehnasiri *et al.,* 2014, determined levels of depression. They found a linear relationship between the depression score and shift work experience. A significant difference was found for depression based on the level of education (higher depression score for the highest educational level), but this result disappeared when adjusted for shift work experience.

- Five studies explored the impact on mental health of sleep disturbance (changes in sleep quantity and quality) further to night work.

Lin *et al.,* 2012 focused on the effects of shift work on the sleep and mental health of registered nurses*.* In their study, the authors attempted to compare various types of shift work (with varying numbers of days off and cumulative nights) in terms of effects on sleep and mental health. The aim was to determine the amount of rest needed after a night of work and find the adequate number of nights to limit the harmful effects of shift work. The results showed that sleep quality and mental health were not as good for registered nurses working the rotating shift (3x8 schedule) as for those working the day shift. But nurses with two or more days off after the last night of work had improved sleep quality and mental health compared to those with only one day off. Furthermore, the higher the frequency of night shifts in the past two months, the poorer the sleep quality. The link between shift work and mental health may have been mediated by poor sleep quality. *[Note: changing the number of days off following night shifts and limiting the frequency of nights worked thus appear to be relevant organisational measures for preventionists]*.

The contribution of the study by Flo *et al.,* 2012 to the assessment of the effects of night and shift work on psychological health was indirect. The objective of the study was to assess the prevalence of shift work disorder (SWD) symptoms and their link to various individual, health and work variables in Norwegian nurses. SWD was defined in the study as a sleep or sleepiness problem associated with the work schedule occurring for at least one month. Data were obtained through a questionnaire administered by mail to 1968 nurses (90% women, 38% response rate) of whom 37.6% had SWD. Note that of these, 146 did not work at night and so their sleep or sleepiness problem was caused by another unspecified factor. For those involved in night work, the occurrence of SWD was significantly associated with night work, the number of nights worked over the last 12 months, and the number of shifts separated by less than 11 hours. Symptoms of anxiety and depression were assessed solely in relation to SWD. The authors reported an association between anxiety and SWD that disappeared when other sleep disorders were included in the analysis, and an association between depression and SWD that was significant only when insomnia severity criteria were included in the analysis. No link was found between SWD and alcohol or caffeine consumption. *[Note: based on this article, it is not possible to conclude that night work is associated with psychological health impairment; nor can this possibility be ruled out, since there was no comparison between day work and night work in the study. However, the results suggest that depression and anxiety symptoms may be mediated by sleep and sleepiness problems associated with difficulties adapting to shift work]*.

The study by Walia *et al.,* 2012 investigated the relationship between shift work experience and the severity of a set of symptoms in 1275 patients monitored in a sleep clinic. The results showed more insomnia and sleepiness symptoms in patients working in the evening or at night. After adjusting for confounding factors, patients working a fixed evening or night shift were 4.8 times more likely to report difficulty falling asleep, 3.3 times more likely to report excessive caffeine consumption, and 1.8 times more likely to report driving while sleepy than permanent day workers. *[Note: even though this study did not deal with the general population but with a population of patients in a sleep clinic, the increase in caffeine* *consumption for these evening and night workers should be taken into account. Indeed, while caffeine consumption is not recommended for night work due to its effects on subsequent sleep (SFMT-HAS 2012 report), it is commonly used to combat loss of vigilance by night workers. It may therefore be an aggravating factor for patients with sleep disorders].*

Morikawa *et al.*, 2013 studied the relationship between sleep problems related to shift work and alcohol consumption. The authors investigated sleep quality and alcohol consumption by administering subjective questionnaires to 530 day workers, 72 shift workers who did not work at night, and 290 shift workers involved in night work. The results showed no difference in alcohol consumption (volume and frequency of drinking) between night workers and day workers. However, night workers complaining of poor-quality sleep were twice as likely to consume large quantities of alcohol (60 g/day) than workers not working at night. Day workers with poor-quality sleep had no increased odds of heavy alcohol consumption. The results suggested that night workers, saying they had a sleep problem, consumed significantly more alcohol than the others, and raised the possibility that alcohol was used by night workers to cope with their sleep problem, which was not the case for day workers. The study also reported that smoking was significantly correlated with heavy alcohol consumption (current and former smokers).

Vallières *et al.* (2014) studied the negative impact of insomnia on the perceived (physical and mental) health of night shift workers compared to day workers. A second objective of the study was to investigate the impact of insomnia on the quality of life, work, and behaviour of night shift workers. Night workers and shift workers had poorer sleep quality than day workers (irrespective of insomnia). Night work contributed to substance use for sleeping. Insomnia was associated with an increase in sleepiness for shift workers only. This study showed an interaction between work schedule and sleep status: shift workers with insomnia had lower quality of life (social dimension and "pain" dimension). Regarding addictive behaviours, it appeared that day workers consumed more alcohol, while among night workers there were more regular smokers, a behaviour that was exacerbated in the event of insomnia. However, the study showed no differences for levels of anxiety and depression.

- Lastly, eight cross-sectional studies explored the link between shift work and several indicators of mental health (depressed mood, psychological distress, burn-out, etc.) and highlighted some indirect work-related factors that may modulate these effects.

The content of night work is not the same as the content of the same work during the day and this bias is seldom controlled (or controllable) in studies. The role of psychosocial risk factors at work in this mediation of effects cannot be ruled out in light of the analysed studies. Moreover, the role of stress factors in non-work life, which are greater with shift work, is also suspected.

Driesen *et al.* (2010), in a cross-sectional study exploring the relationship between depressed mood and shift work in 8000 employees with all types of jobs, showed some associations between shift work and an increased prevalence of depressed mood. However, this link did not seem to be direct. The study specified the type of shift work (3x8, 5x8 or irregular work) as well as the number of weekly hours worked and also explored the gender effect. It is interesting to note that this study did not explore depression but depressed mood (earlier detection), which seems relevant since people with depression seldom go to work. The prevalence of depressed mood seemed higher in 3x8 workers, especially men, but this difference was not significant after controlling for certain factors related to work content. Due to the possibility that the content of 3x8 work was different from that of 5x8 work, no conclusions could be drawn as to the direct effects of shift work. For women only, those working a 5x8 schedule had a higher prevalence of depressed mood, even after controlling for work content (very strong association). In conclusion, there was a link between 5x8 work (therefore including weekends and in connection with non-work life) and depressed mood in women. *[Note: the results for the female population in this study cannot be generalised to the entire employed population (males and females). Moreover, these results underline the presence of confounders, related in particular to the very content of the work to be performed* *and the psychosocial environment, and tend to suggest that shift work has an indirect effect on mood, mediated by certain intermediate factors related to the type of work].*

Ljosa *et al.* (2011), in a cross-sectional study undertaken among shift workers in the petroleum industry (specific population and work in extreme conditions), explored the association between individual factors and risk factors at work and psychological distress. The study showed that psychosocial risk factors at work (high quantitative demand, low level of social support, and high level of interference between work and private life related to shift work) were independently associated with distress at work. Shift work was only univariately associated with psychological distress. These results support the idea that shift work has no direct effects on mental health but rather indirect effects *via* its other effects on non-work life (work-family interference) and *via* exposure during shifts to increased psychosocial risk factors. *[Note: the study population was atypical since it lived on the platform (and therefore far from families) for two consecutive weeks, which may have had an effect itself, and makes it difficult to generalise these results to all shift workers]*.

Another study conducted by Srivastava in 2010 explored the relationship between stress factors, atypical working hours and mental health.

Shift workers had significantly higher scores than day workers for all variables related to stress and mental health. There was a correlation between stress and mental health for all employees (shift and day workers): the higher the stress level, the lower the level of mental health. Stress variables were almost all significantly correlated with negative effects on mental health. As for responsible factors for shift workers, the quantity of "stressors" in daily life and role conflicts at work were the main predictors of all mental health dimensions. Work-related stress factors (work overload and role conflicts and ambiguity in particular) played a major role in predicting effects on mental health for day workers. This study showed that shift work was a source of stress (at work and outside of work) and thereby had an effect on mental health.

The study by Wittmer and Martin (2010) focused on emotional exhaustion, the central component of burn-out, in mail-sorting employees of the postal service. It was original in that it dealt with workers having no contact with the public. Since interactions with the public can vary depending on the work shift in the service sector and have a direct effect on the emotional adjustment of employees, this study was able to control for the effect of this variable to more specifically assess the effects of work schedule. The study was undertaken in three different states in the United States. Data were collected through confidential questionnaires administered at the workplace, with a 90% response rate (total of 353 employees). All the employees had a fixed day, evening or night schedule, with a duration of around eight hours, often including Saturday or Sunday. The results showed that emotional exhaustion was greater for night workers than for day and evening workers. The analyses showed that night work acted as a modulator and amplified the negative effects of unfavourable working conditions (job demands) and work-family conflict on emotional adjustment but did not affect the effects of supervision quality (job resources). The results as a whole suggested that the factors that could lead to emotional exhaustion were exacerbated when workers had a night shift. The authors underlined that future studies should take into account the work schedule preferences of workers. In fact, in this study, the authors noted that 48% of night workers had filed a request to change schedules, despite a 10% salary bonus for night work. It is therefore possible that the imposed night schedule had a major impact on emotional exhaustion.

The study by Belkic *et al.* (2012) involved physicians. Shift/night work was considered in this study as a stress factor negatively influencing lifestyle, which could have repercussions especially for cardiovascular health and for certain cancers. The possibility of a gender effect, with women being more vulnerable (stronger association between stress factors and lifestyle), was also explored in this study, but no conclusions could be drawn due to the small sample size. Anaesthesiologists and surgeons had more risk factors (number of nights and number of hours worked) than other physicians. The greater the number of nights, the higher the "poor lifestyle" score. A prevention message was suggested by the authors: the organisation of night work (number of nights, free time between shifts, well organised relays with proper management by colleagues on days off) has an impact on at-risk behaviours. *[Note: even though this study investigated a very specific target (physicians) and a small sample (191 participants), the organisational avenues for prevention are valuable and should be explored in future applied research]*.

The study by Morikawa *et al.* (2014) investigated the effects of age in the relationship between work-related factors and alcoholism. The authors defined work-related factors as shift work and stress factors (Karasek's model). Two thousand seven hundred and eighty-eight employees in a Japanese factory were interviewed twice, at one-year intervals, about their alcohol consumption and potential depressive symptoms. This study's results showed that the frequency of heavy drinking increased with age. Regarding the type of work associated with the schedules, the study showed that blue-collar workers (who are shift workers) had a higher OR for heavy drinking than white-collar workers (who are day workers) for all age groups, especially among 20-29 year olds. In the other age groups, there were significant differences in ORs between blue-collar and white-collar workers but these were not related to shift work. The relationship between psychosocial risk factors and heavy drinking was different in the four age groups. This study underlined that the effects of shift work on addictive behaviour may be related to age. *[Note: minor methodological limitations should be highlighted: there may have been a bias related to the one-year period between the measurements for depression and exposure to stress factors and the questionnaires investigating addictive behaviours. Another possible bias was related to the different socio-economic statuses of the white-collar and blue-collar workers. In addition, the particular study population, with all the employees working for the same Japanese company (same context, same environment), makes it difficult to generalise the results].*

The study by Pai and Lee (2011) conducted in Taiwan indirectly explored the relationship between night work and psychological health by assessing the prevalence of physical and psychological violence (verbal abuse, sexual harassment) and post-traumatic stress in nurses. Data were obtained by post using carefully validated questionnaires completed by 521 nurses (78% response rate). The results showed that night work was associated with a higher risk of sexual harassment and that this type of psychological violence was associated with a high prevalence of severe post-traumatic stress symptoms. There was no significant association between night work and other forms of workplace violence. The authors considered that the increased risk of sexual harassment, mainly by patients, was caused by the low staff/patient ratio and the high percentage of time spent working alone during night shifts. *[Note: the study did not specifically focus on night work, which was assessed using a single question, and it is not certain that there was sufficient statistical power to determine the link between night work and sexual harassment at work (n = 67)]*.

The study by Picakciefe *et al.* (2012) focused on violence against nurses and its link to working conditions. The analysis relied on questionnaires on the type of work (shift or regular, night or day) and workplace violence, administered to 268 nurses in a Turkish hospital. The authors stated that 86% of the study's nurses had been exposed to violence and that the nurses involved in night work or shift work in the past year had been significantly more exposed to violence during their work shift than other nurses. According to the authors, certain individual characteristics (being a young woman for example) as well as certain work-related characteristics (being a beginner, having zero to 10 years of work experience, doing overtime work) increased the frequency of sexual violence. The logistic regression analysis showed that night work, having more than 21 years' experience as a nurse, and perceiving a sense of insecurity at the workplace were significant risk factors in exposure to workplace violence. Thus, certain work-related characteristics (especially lack of experience, isolation and overtime work) and certain individual characteristics (being a young woman) may modulate these violent behaviours. *[Note: the study population, of a modest size, and the non-validated questionnaires used were two methodological limitations of this study]*.

6.3.3.4 Assessment of the level of evidence

The review of the literature preceding 2010 and the national report published on the topic in 2012 (SFMT-HAS report, 2012) reported inconsistent results. Therefore, no conclusion can be drawn as to the effect of night work on mental health.

To summarise, 18 epidemiological studies out of the 20 analysed (published between 2010 and 2014) showed an association between night work (fixed or rotating shifts) and diminished mental health. This relationship involved the organisational characteristics of shift work (shift duration, number of nights, night work experience) in five studies, was linked to sleep impairment further to night work in another five studies, and seemed more indirect in the eight other studies and mediated by psychosocial risk factors related to the content and organisation of night work.

6.3.3.4.1 Epidemiological studies

The data show an association in the majority of studies, but not in all of them, especially not in the only longitudinal study, and it does not appear possible to exclude all the biases and confounding factors. Thus, after an analysis of the epidemiological studies, the experts conclude that the evidence supporting the existence of an effect of night work on mental health is limited (see Figure 20).

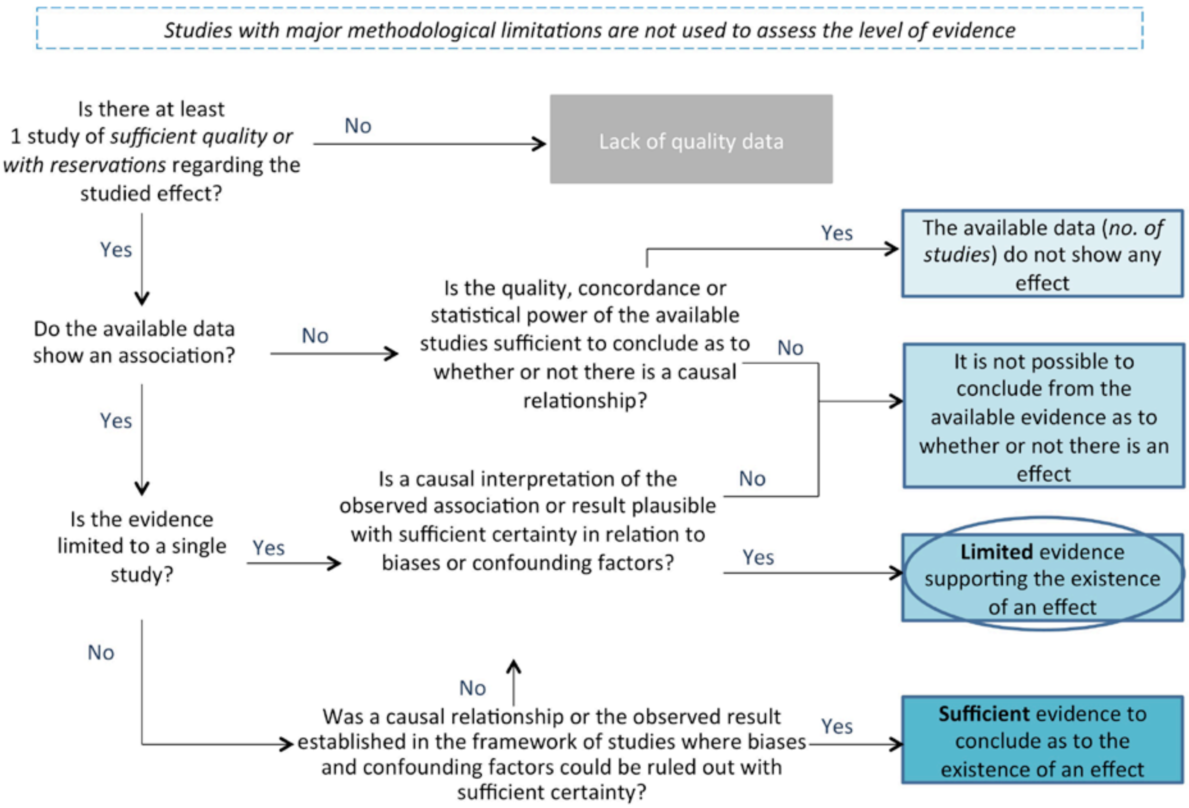


Figure 20: assessment of epidemiological studies dealing with psychological health

6.3.3.4.2 Experimental studies

A recent experimental study (Boudreau *et al.*, 2013) conducted with shift workers in the laboratory reported better mood quality when there was an increase in circadian synchronisation (between the internal biological clock and the sleep-wake schedule imposed by night work).

In healthy subjects, the experimental studies show that mood is influenced by complex interactions between the internal biological time (circadian phase) and the previous waking period. The studies also show that the nature of these interactions is such that modest changes in the synchronisation of the sleep-wake cycle can have major effects on subsequent mood (Boivin *et al.*, 1997). The link between disruption of the circadian system and psychiatric diseases has been confirmed by recent clinical studies, which show that in addition to cognitive and mood impairments (Gotlib and Joormann, 2010), depressed and bipolar patients have disrupted circadian rhythms, especially the wake-sleep cycle (McClung *et al.*, 2013) and the expression of clock genes in the brain (Li *et al.*, 2013).

Furthermore, irrespective of its effect on the circadian system, exposure to irregular non-24-hour light-dark cycles may also be responsible for mood disorders. Experimental studies in humans show that light regulates mood and cognition, directly *via* the ganglion cells that express melanopsin or indirectly through the circadian system (Chellappa *et al.*, 2014). From a clinical standpoint, continuous light exposure induces an antidepressant effect, both in animals and in humans (Iyilikci *et al*., 2009; Wirz-Justice *et al.*, 2013). In rodents, studies show that exposure to an abnormal day/night cycle (less than 24 hours) induces pseudo-depressive behaviour and impaired cognitive function (LeGates *et al.*, 2012; LeGates *et al.*, 2014).

Thus, the experimental studies in night workers, healthy subjects and animals suggest mutual interactions between circadian system disruption, an irregular light-dark cycle, and the psychiatric domain. These results provide evidence supporting the existence of an effect of night work on mental health.

6.3.3.4.3 Conclusion

Considering the evidence provided by the 20 epidemiological studies and by the experimental studies, the following diagram led the experts to conclude that night work has a "probable effect" on mental health in humans (see Figure 21).

<table>
<tr><td colspan="2"></td><td colspan="2">Evidence of the existence of the effect in experimental studies in humans or animals</td></tr>
<tr><td colspan="2"></td><td>Evidence supporting the existence of an effect</td><td>No evidence supporting the existence of an effect</td></tr>
<tr><td rowspan="5">Evidence of the existence of the studied effect in epidemiological studies</td><td>Sufficient evidence to conclude as to the existence of an effect</td><td colspan="2">Proven effect</td></tr>
<tr><td>Limited evidence supporting the existence of an effect</td><td>Probable effect</td><td>Possible effect</td></tr>
<tr><td>It is not possible to conclude from the evidence as to whether or not there is an effect</td><td rowspan="2">Possible effect</td><td rowspan="2">It is not possible to conclude from the available data as to whether or not the studied effect exists</td></tr>
<tr><td>Lack of quality data</td></tr>
<tr><td>The available data do not show any effect</td><td>It is not possible to conclude from the available data as to whether or not the studied effect exists</td><td>Probably no effect</td></tr>
</table>

Figure 21: classification of the effect of night work on psychological health

6.3.3.5 Discussion and research outlook

Night work seems to increase psychosocial risk factors and/or sleep disorders, which in turn may increase the risk of mental disorders. The consequence of this result is that controlling for confounding factors is essential to determine the nature of the effect of night work itself. As there are so many of these confounding factors, they are never all controlled in any one study. Future research should carefully control for the content and organisation of night work in order to neutralise biases related to psychosocial risk factors.

Another bias, which is particularly difficult to control, stems from the fact that clinically depressed people are probably not at work or have been transferred to day work (healthy worker effect). Moreover, it is likely that individuals who have symptoms of depression are less inclined to complete questionnaires. The effects of night work on mental health may therefore be underestimated. In fact, that was one of the conclusions of the only longitudinal study published between 2010 and 2014 (Thun *et al.*, 2014). The need for longitudinal studies with the measurement of mental health from when a night shift is accepted and with background career information seems essential to decide on an effect of night work *per se* on mental health.

6.3.4 Metabolic disorders and cardiovascular diseases

In this section, metabolic disorders and cardiovascular diseases are presented together, since their aspects are inter-dependent.

The following effects related to metabolic disorders are addressed: body mass index (BMI[41], an index enabling excess weight and obesity to be characterised), type-2 diabetes, dyslipidaemia and metabolic syndrome, which is a complex disease involving various metabolic disruptions. As for cardiovascular diseases, the issues of high blood pressure, stroke and coronary diseases are discussed.

6.3.4.1 Epidemiological studies on the effects of shift work including night work on metabolic disorders and cardiovascular diseases

Over the past few years, many epidemiological studies and some meta-analyses have been undertaken to assess the association between shift work including night work and the risk of metabolic disorders: obesity or excess weight, diabetes, hypertension, dyslipidaemia and metabolic syndrome. The majority of cross-sectional, case-control and cohort studies have investigated shift work including night work or involving the disruption of circadian rhythms. The main issues raised have concerned the role of shift work itself or of related factors in the existence or non-existence of risk, and the possibility of determining potential risk exposure thresholds.

The recommendations of the HAS on the monitoring of shift and/or night workers concluded that the analysis and summary of the literature demonstrate that shift and night work:

- are associated with an increase in the risk of lipid profile disruptions (NP3);
- are associated with an increase in body mass index (NP2);
- are associated with an increase in the risk of metabolic syndrome; this relative risk ranges from 1.46 to 5.10 depending on the study (NP2);
- are associated with an increase in the risk of cardiovascular disease; this relative risk ranges from 1.1 to 1.4 depending on the study (NP2);
- are associated with an increase in the risk of high blood pressure (relative risk ranging from 1.1 to 2) (NP3);
- are associated with an increase in tobacco use (NP3).

Still in the framework of the work undertaken by the HAS, and according to the experts, shift and/or night work can be considered a significant cardiovascular risk factor since it is associated with an increase in the prevalence of most known cardiovascular risk factors (lipids, weight, high blood pressure, smoking).

In most of the studies reviewed in this report, the assessment of exposure (the exact characteristics of shift or night work) remains highly imprecise, potential confounding factors related to metabolic disorders (eating habits and nutritional factors, smoking, socio-economic factors, etc.) are often imprecisely or not at all analysed, and the healthy worker effect, which needs to be considered for night work, is not taken into account. However, certain cross-sectional studies, retrospectively assessing exposure, enable more substantiated conclusions to be made as to the possible links between shift work and metabolic risks.

A few cohort studies and a few case-control studies nested within cohort studies, considered of good quality or with minor methodological limitations, were selected. Furthermore, two recent meta-analyses assessed the association between shift work including night work and

[41] Body Mass Index (BMI) is calculated by dividing body weight in kilograms by the square of the height in metres

the occurrence of metabolic syndrome or any of its components. The experts have presented the corresponding results below.

In total, 142 articles were selected based on their titles and abstracts (from over 260 publications).

In the end, more than 60 articles were identified by the experts as having sufficient relevance and methodological quality to contribute to the assessment of the effects of shift work including night work.

6.3.4.1.1 Metabolic effects

6.3.4.1.1.1 Weight gain and body mass index (BMI)

Roos *et al.* (2013) assessed, in a case-control study, the links between various working conditions (schedule, chemical and physical exposure, psychosocial conditions) and weight gain over a follow-up period of five to seven years in middle-aged municipal employees of the City of Helsinki (5786 women and 1313 men). Data were taken from the Helsinki Health Study (HHS) questionnaire survey. A questionnaire was sent by post to city employees between the ages of 40 and 60 from 2000 to 2002 and a follow-up survey was conducted in 2007. During the follow-up period, 26% of the women and 24% of the men reported weight gain of at least 5 kg. Night shift work, exposure to physical violence or threats, and hazardous exposure were moderately associated with a high risk of weight gain. After adjusting for age, night shift work was significantly associated with weight gain of 5 kg of more for women (OR = 1.43; [95% CI = 1.13-1.82]) and not significantly associated for men (OR = 1.29; [95% CI = 0.90-1.86]). Adjustments for other covariables did not significantly alter the results. *[Note: despite this study's strengths (large number of study subjects and very high response rate), there were limitations related especially to the self-reported data (in particular weight, schedule type, covariables, etc.) and the fact that eating habits were not taken into account].*

The team of Suwazono published two articles (Suwazono *et al.,* 2010a; Suwazono *et al.*, 2010b) dealing with a cohort of workers in a Japanese steel company. One article focused on the estimation of a benchmark dose (BMD) for the number of years of rotating shift work associated with an increase in BMI and its 95% lower limit (Tanaka *et al.,* 2010). The study investigated 7254 workers (4238 regular day workers and 2926 shift workers) receiving annual check-ups between 1991 and 2005. For workers in the 40-49-year age group, the minimum and mean values for years of rotating shift work inducing an increase in BMI of 7.5% or more were 18.6 and 23.0 years. For a BMI increase of 10% or more, these values were 16.9 and 19.4 years. For workers aged 50 or over, the corresponding values were respectively 22.9 and 28.2 years, and 20.6 and 23.6 years. Logistic regression showed a statistically significant increase in the risk of a 7.5% BMI increase (compared to the BMI when entering the cohort) after only four years of shift work including night work (OR = 1.49; [95% CI = 1.33-1.68]). The authors concluded that special attention should be paid to middle-aged workers having worked above the threshold number of years of shift work including night work.

Zhao *et al.* (2012) studied the effects of maintaining or changing work status between shift work and day work on BMI changes in a cohort of nurses and midwives (Nurses and Midwives e-cohort Study – NMeS). The general objective of this e-cohort study was to study health problems in nurses and midwives in Australia, New Zealand and the United Kingdom. Recruiting for the cohort started in April 2006 (study time S1) and lasted until April 2008 (study time S2). The authors compared workers keeping the same schedule (day or shift work) and workers changing schedules (day to shift work and *vice versa*) between times S1 and S2. Shift work could be ongoing or rotating, only at night, only in the evening, in the morning and evening, or in the evening and at night. Of the 2078 participants included between the ages of 21 and 70 years (mean age 43.95 years; standard deviation 9.48 years), 183 maintained day work during the follow-up period, 1194 maintained shift work, 270 switched from day work to shift work, and 431 switched from shift work to day work. Potential confounding factors (quality of diet, alcohol, smoking, physical activity, menopausal status, etc.) were specified at the start of the study. Over the follow-up period, the switch from shift work to day work was associated with a significant decrease in BMI; the maintenance of shift work and the switch from day work to shift work were associated with a significant increase in BMI. *[Note: in spite of its methodological limitations (potential selection biases related to electronic recruiting, health data reported instead of measured, high cohort attrition in relation to the over 10,000 workers recruited for the overall NMeS cohort, etc.), this study suggested that shift work has negative effects on BMI].*

In a secondary analysis conducted among 107,663 participants in the Nurses' Health Study (NHS) II, Pan *et al.* (2011) showed that rotating shift work including night work was associated with an increased risk of obesity and excessive weight gain (> 5% of the starting weight) during the follow-up period. In a multivariate analysis, each five-year increase was associated with an increase of 0.17 BMI units (95% CI = 0.14-0.19) and an increase of 0.45 kg in weight (95% CI = 0.38-0.53). The results therefore suggested an effect of rotating night shift work on the risk of type-2 diabetes in women, which appeared partly mediated by weight gain (see Figure 22).

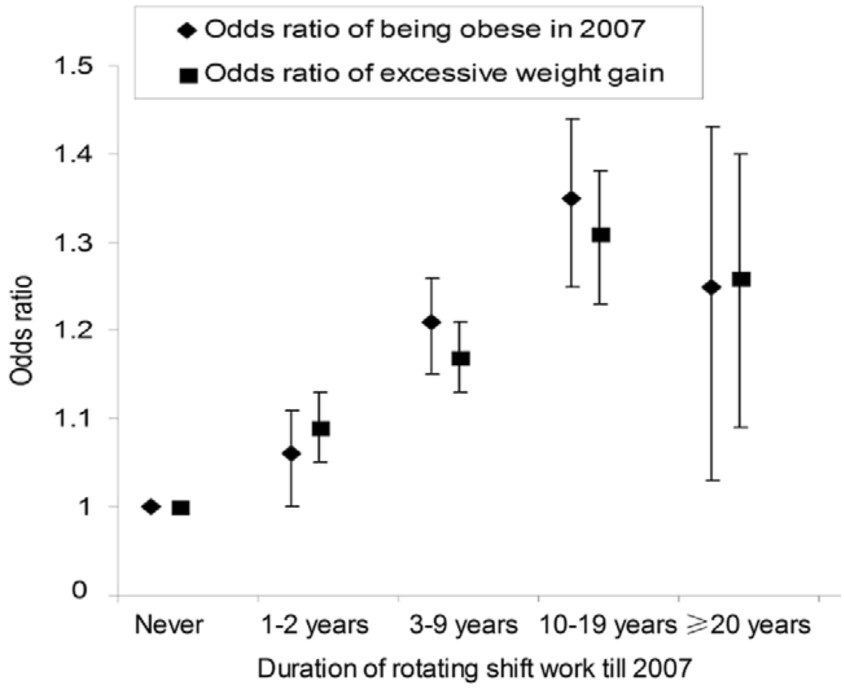


Figure 22: rotating night shift work and risk of obesity and weight gain in the Nurses' Health Study II

6.3.4.1.1.2 Type-2 diabetes

The prospective cohort study of Suwazono *et al.* (2010a) focused on the relationship between impaired glucose metabolism, assessed by measuring glycated haemoglobin (HbA1c), and shift work in 7104 Japanese workers in the same steel company monitored for 14 years with annual check-ups between 1991 and 2005. The aim was to calculate a BMD for the number of years of rotating shift work associated with relative increases in HbA1c during the observation period compared to the HbA1c level at study inclusion. For a population of workers aged 50 years or over (mean age 53 years), the minimum and mean values for the number of years of shift work were respectively 17.8 and 23.9 years for an increase of 15% or more in HbA1c, and 25.2 and 31.7 years for a more than 30% increase in HbA1c. Logistic regression showed a statistically significant increase in the risk of an HbA1c increase compared to the value when entering the cohort. The reported risks (ORs) ranged from 1.03 (95% CI = 1.02-1.04) per additional year of shift work including night work for an increase of more than 15% to an OR of 1.06 (95% CI = 1.04-1.08) for an increase of more 30%. The results indicated that special attention should be paid to workers of around 40 to 50 years of age, for whom cumulative shift work duration exceeds the benchmark doses corresponding to the various increases in HbA1c.

Oyama *et al.* (2012) undertook a retrospective cohort study among male employees of a Japanese company manufacturing innovative products based on chemistry and material sciences in four sectors: chemical products and fibres, houses and building materials, electronics, and medical/pharmaceutical sectors. The aim was to investigate the risk of impaired glucose tolerance related to shift work. Glucose intolerance was defined by an HbA1c level of above 5.9%. The study monitored 6413 employees under the age of 30 with no glucose intolerance during the first health exam for the company, over a period running from 1981 to 2009. The risk of developing impaired glucose tolerance was significantly higher for three-shift workers (hazard ratio (HR) = 1.78; [95% CI = 1.49-2.14]) and two-shift workers (HR = 2.62 [95% CI = 2.17-3.17]) (see Figure 23).

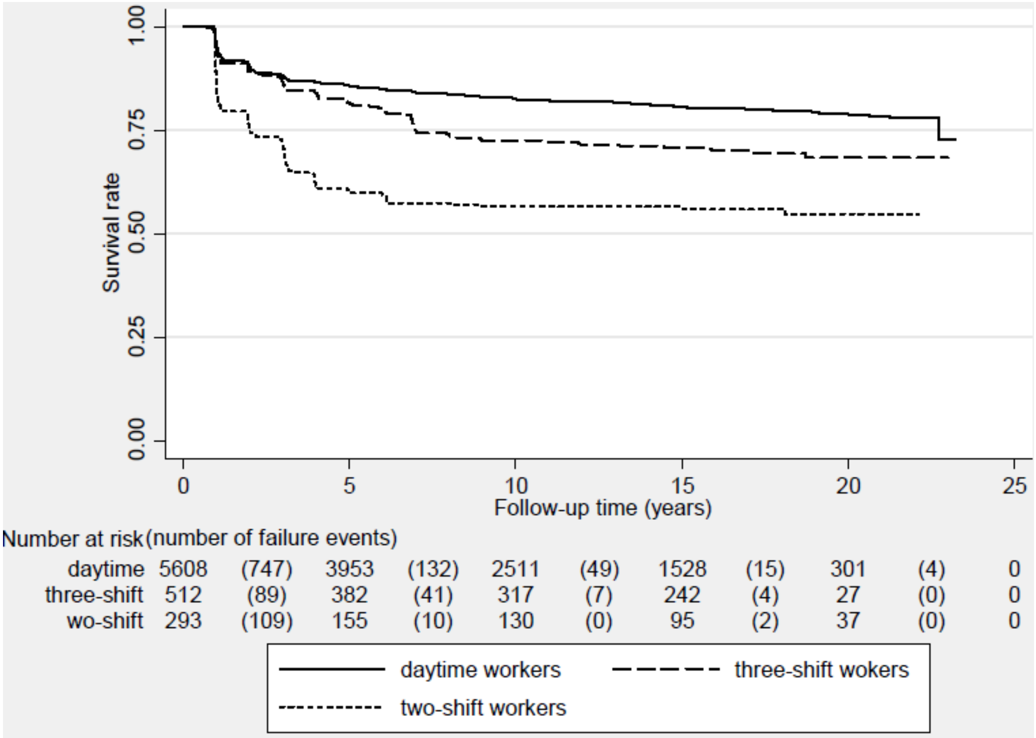


Figure 23: Kaplan-Meier survival curves for impaired glucose tolerance among shift workers according to type of work schedule (Oyama *et al.*, 2012)

The risk was even higher for workers with a normal and stable BMI during the follow-up period. Some potential confounding factors (alcohol, smoking, physical activity) were roughly taken into account in the study, but others were not considered (dietary intakes, family history of diabetes, educational level, socio-economic criteria, working conditions, etc.). However, two major points of this study should be underlined: the long cohort follow-up period, i.e. 9.9 years on average and up to 23 years, and the observation of an effect for workers with a normal BMI. The authors suggested that sleep disturbances may be responsible for impaired glucose metabolism.

Pan *et al.* (2011) conducted a cohort study on shift work and type-2 diabetes within two cohorts of American nurses from the Nurses' Health Study. They included 69,269 women from NHS I and 107,915 women from NHS II, and monitored them for around 20 years. All of the subjects were without diabetes, cardiovascular disease and cancer at inclusion. The authors compared nurses working night shifts, defined as at least three nights of work per month, and nurses who had never worked night shifts. The diagnosis of diabetes was self-reported by the participants and validated with an additional questionnaire. During the 18 to 20 years of follow-up, 6165 (NHS I) and 3961 (NHS II) incident cases of type-2 diabetes were recorded. The statistical analysis using the Cox proportional model, adjusted for diabetes risk factors, found a significant dose-response relationship between the duration of shift work including night work and the risk of type-2 diabetes in both cohorts. Two analytical models were used: the first adjusted for age and potential confounding factors (alcohol, smoking, physical activity, dietary intake, medications and hormonal treatments, and family history of diabetes) and the second included the same variables but also adjusted for BMI. In the first model, every five-year increase in the duration of rotating shift work with nights was associated with a 13% increase in the risk of diabetes (95% CI = 11%-14%) in the two cohorts combined. After adjusting for BMI, these increases were more than halved, but remained statistically significant. No significant interaction was found between rotating shift work including night work and baseline BMI.

Gan *et al.* (2015) conducted a meta-analysis of observational studies assessing the relationship between shift work and the risk of type-2 diabetes. The criteria set for including studies were as follows: shift work was the exposure variable considered and the outcome was type-2 diabetes, and the studies had to provide risk estimates with a 95% CI for the association between shift work and type-2 diabetes or provide sufficient information to enable their calculation. Two independent authors extracted data and assessed the quality of the studies, with resolution of disagreements by a third reader. If there were several publications on the same study, only that with the longest follow-up period was selected. Twelve studies (28 publications) were selected, including seven prospective cohort studies, one retrospective cohort study and four cross-sectional studies, including 226,652 participants of whom 14,595 had type-2 diabetes. Shift work schedules were classified as described in the original studies: rotating, irregular and unspecified, night, mixed and evening shift work. In some studies, the working hours were very long (12 hours): 6pm to 6am or 7pm to 7am (see Table 9).

Table 9: results of a recent meta-analysis of epidemiological studies on the risk of developing type-2 diabetes associated with shift/night work

Author (year) Number of studies	Study types and population	Number of risk estimates*	Definition of exposure	Pooled RR (95% CI)	I^2 heterogeneity
Gan *et al.* (2015) 11 studies	All studies	28	Shift work including night work (yes *vs* no)	1.09 (1.05-1.12)	40.9%, p=0.014
	Cohort studies	16	"	***1.12 (1.06-1.19)***	**52.9%, p=0.007**
	Cross-sectional studies	12	"	***1.06 (1.03-1.09)***	10.9%, p=0.339
	Men	15	Shift work including night work (yes *vs* no)	**1.37 (1.20-1.56)**	0%, p=0.547
	Women	9	"	**1.09 (1.04-1.14)**	**54.3%, p=0.025**
	Different schedules	4	Rotating schedule	**1.42 (1.19-1.69)**	13.4%, p=0.325
		6	Irregular or unspecified schedule	**1.06 (1.04-1.08)**	0%, p=0.601
		15	Fixed night schedule	**1.09 (1.04-1.14)**	37.6%, p=0.07
		2	Mixed schedule	1.40 (0.84-2.33)	0%, p=0.715
		1	Evening schedule	1.73 (0.85-3.52)	--

* The number of articles or studies was not indicated for the detailed analyses in the article by Gan *et al.* (2015); the 11 studies reported 28 risk estimates.

In seven of 12 studies, diabetes was confirmed by the medical record or by a physician. In the other studies, diabetes was self-reported, supplemented by a response to an additional questionnaire from a diabetes association. The confounding factors and variables controlled in the analysis changed depending on the study. The authors obtained an adjusted pooled risk for the association between shift work and type-2 diabetes of 1.09 (95% CI = 1.05-1.12; p = 0.014; I^2 = 40.9%); the pooled risk remained significant after the exclusion of a study with no adjustment for confounding factors.

The sub-group analyses showed a stronger association for men than for women. All of the shift work schedules, except for the mixed and evening shifts, were associated with a statistically higher risk of type-2 diabetes, compared to the fixed day schedules, with a significant difference between these shift work schedules ($p_{interaction} = 0.04$). The risk for rotating shift work was clearly higher than for other shift work groups (pooled risk = 1.42). Among the limitations of the meta-analysis, the authors mention varying definitions of shift work and diabetes in the original studies analysed, as well as limited information not enabling a dose-effect relationship to be analysed. In the end, this meta-analysis suggested that shift work is associated with a significantly increased risk of type-2 diabetes, particularly among rotating shift workers.

6.3.4.1.1.3 Dyslipidaemia

Suwazono *et al.* (2010b) undertook a case-control analysis nested within a prospective cohort of 6886 male employees (4079 permanent day workers and 2807 shift workers) of a Japanese steel company, who received annual check-ups between 1991 and 2005. The main objective of the study was to estimate a benchmark dose for the number of years of rotating shift work associated with a relative increase in serum total cholesterol (T-Cho; indicator of lipid metabolism). The authors described the minimum number of years of work associated with a 25%, 30%, 35% and 40% increase in T-Cho compared to initial T-Cho, with no statistically significant dose-response relationship. For a 5% probability, in middle-aged workers (40-49 years), the minimum and mean numbers of years of rotating shift work inducing a 20% increase in T-Cho were respectively 21.0 and 28.0 years. The benchmark doses gradually increased as a function of the percentage increase in T-Cho and reached, for a 45% increase in T-Cho, minimum and mean numbers of years of rotating shift work of 27.7 and 32.1. The results suggested that special attention should be paid to middle-aged workers having worked above the threshold number of years of shift work including night work. *[Note: the limitations of this study primarily involved some potential non-assessed confounding factors (diet, work experience before starting the study, etc.) and the lack of data on other lipid parameters (triglycerides, high- and low-density lipoproteins (HDL and LDL))].*

6.3.4.1.1.4 Metabolic syndrome

Metabolic syndrome is a collection of symptoms related to abdominal obesity for which there is a proven link to insulin resistance and increased cardiovascular risk. The association between abdominal obesity and type-2 diabetes was first described by Jean Vague[42] and the notion has since been confirmed by epidemiological studies. In the 1980s, several authors showed that insulin resistance was associated with various metabolic abnormalities (glucose intolerance, type-2 diabetes, dyslipidaemia) and high blood pressure. This led to the concept of syndrome X, proposed in 1988 by Reaven[43], characterised mainly by hyperinsulinaemia

[42] Vague J. La différentiation sexuelle, facteur déterminant des formes de l'obésité. *Presse Méd* 1947; 30:339-340.

[43] Reaven GM. *Role of insulin resistance in human disease*. Diabetes, 1988, 37, 1595–160.

and insulin resistance[44]. However, abdominal obesity was not a defining criterion for syndrome X. Several years later, metabolic (or dysmetabolic) syndrome was proposed as a single entity encompassing glucose-lipid abnormalities, high blood pressure and abdominal obesity. The notion that abdominal obesity and metabolic syndrome are associated with a higher risk of type-2 diabetes and the development of cardiovascular diseases gradually emerged based on the results of several epidemiological studies.

The International Diabetes Federation (IDF) considers that this syndrome is the driving force for the twin global epidemics of type-2 diabetes and cardiovascular diseases.

Since metabolic syndrome was first officially defined by a working group of the World Health Organization (WHO, definition revised in 1999), a number of other definitions have been proposed. The most broadly accepted definitions were formulated by the WHO, the European Group for the Study of Insulin Resistance, and the US National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III).

A new IDF consensus definition of metabolic syndrome was developed in 2005, identifying abdominal obesity as a central component; the 21 participants in the consensus included experts in the fields of diabetes, cardiology, metabolism, epidemiology and health policy from five continents. Its objective was to propose easy-to-use criteria taking ethnicity into account.

Waist circumference is a predominant and essential criterion. But the thresholds have been revised downwards: 94 cm for men and 80 cm for women in Europe versus 102 cm for men and 88 cm for women in the North American definition (ATP III). In addition, for the first time, these thresholds vary with ethnic origin and are even lower for Asians (see Table 10, Table 11 and Table 12).

Table 10: waist circumference, an ethnic-specific criterion[45]

Country or Ethnicity	**Waist circumference (cm) Threshold value (positive diagnosis if =)**	
	Men	**Women**
European *	94	80
South Asian (figures based on Chinese, Malaysian and Indian-Asian populations)	90	80
Chinese	90	80
Japanese	85	90
Ethnic South and Central American	Use South Asian values pending more specific data	
Sub-Saharan African	Use European values pending more specific data	
Middle East and Eastern Mediterranean	Use European values pending more specific data	

[44] Ferrannini E, Haffner SM, Mitchell BD, Stern MP. *Hyperinsulinaemia: the key feature of a cardiovascular and metabolic syndrome*. Diabetologia, 1991, 34, 416–422.

[45] Alberti KG, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, Fruchart JC, James WP, Loria CM, Smith SC Jr; *International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; International Association for the Study of Obesity*.

Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. Circulation. 2009 ; 120(16): 1640-5.

Table 11: definition of metabolic syndrome by NCEOP/ATP III, IDF 2005 and IDF 2009

	NCEP ATP III (2001)	IDF (2005)	IDF/AHA/NHLBI (2009)
	3 of the 5 following criteria:	waist circumference + 2 of the 4 other criteria	3 of the 5 following criteria
Elevated waist circumference	≥ 102 cm/men ≥ 88 cm/women	essential, with ethnic-specific thresholds; European origin ≥ 94 cm: men ≥ 80 cm: women	ethnic-specific thresholds, using the IDF 2005 thresholds for non-Europeans and allowing a choice between the IDF and NCEP/ATP III thresholds for those of European origin
Elevated TG[46]	> 1.5 g/L or treatment	> 1.5 g/L or treatment	> 1.5 g/L or treatment
Low HDLc[47]	< 0.40 g/L: men < 0.50 g/L: women	< 0.40 g/L: men < 0.50 g/L: women	< 0.40 g/L: men < 0.50 g/L: women
Elevated BP[48]	Systolic ≥ 130 mm Hg and/or diastolic ≥ 85 mm Hg or treatment	Systolic ≥ 130 mm Hg and/or diastolic ≥ 90 mm Hg or treatment	Systolic ≥ 130 mm Hg and/or diastolic ≥ 85 mm Hg or treatment
Elevated fasting glucose	≥ 1.1 g/L or treatment	≥ 1.0 g/L or treatment	≥ 1.0 g/L or treatment

Table 12: WHO definition of metabolic syndrome

WHO (1998)	Diabetes, impaired fasting glucose, impaired glucose tolerance or insulin resistance (HOMA) + 2 of the other criteria
Waist-to-hip ratio	> 0.90: men; > 0.85: women
High TG or low HDLc	TG > 1.5 g/L or HDL < 0.35 g/L: men; < 0.39 g/L: women
Urinary albumin excretion	> 20 µg/min
BP	> 140 / 90 mm Hg or treatment

46 Level of *triglycerides*

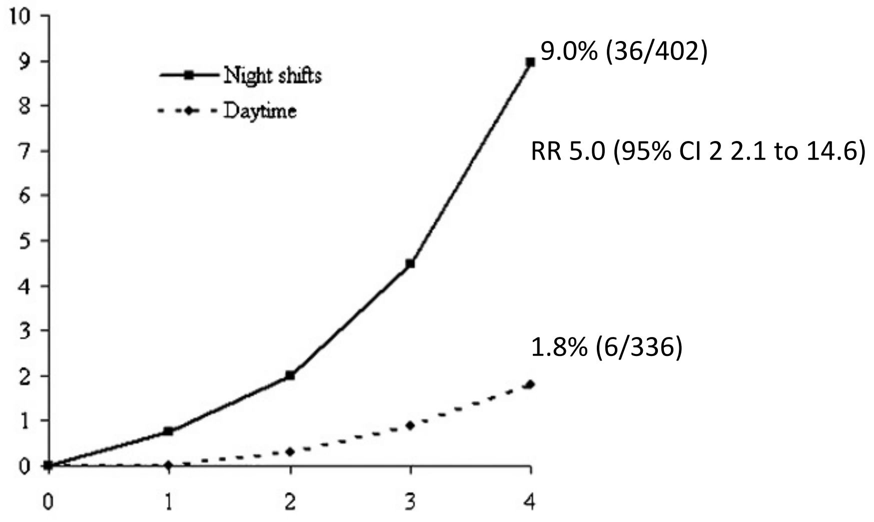
47 High-Density Lipoprotein Cholesterol

48 Blood pressure

Guo *et al.* (2013) undertook a cross-sectional study on shift work including night work and metabolic syndrome, with a retrospective assessment of exposure to shift work in a cohort of 26,382 retired workers in China (11,783 men and 14,599 women). They compared workers who had been engaged in shift/night work (rotating 2x12, 3x8 or 4x6 work, with all these shifts including night work) for at least one year to day workers (8am to 5pm). They found a significant relationship between the number of years of shift/night work and the risk of metabolic syndrome. In the multivariate analysis, the ORs for metabolic syndrome associated with 11-20 years and more than 20 years of shift/night work were respectively 1.14 (95% CI = 1.03-1.26) and 1.16 (95% CI = 1.01-1.31). A dose-response relationship was noted in the female population: a 10-year increase in the duration of shift/night work was significantly associated with a 10% increase in the OR for metabolic syndrome (95% CI = 1%-20%). In the entire cohort, shift work was significantly associated with an increased risk of hypertension (OR = 1.07; [95% CI = 1.01−1.13]), elevated waist circumference (OR = 1.10; [95% CI = 1.01−1.20]), and hyperglycaemia (OR = 1.09; [95% CI = 1.04−1.15).

Pietroiusti *et al.* (2010) studied the association between night shift work and the risk of metabolic syndrome in male and female nurses included in an annual health surveillance programme by occupational physicians in three large hospitals in Italy. The cohort study ran from the beginning of 2003 to the end of 2007. The subjects included were night shift workers, compared to day workers, with none of the components of metabolic syndrome at inclusion. Night shift work was defined as at least four days per month of fixed or rotating night shifts during the year on average. Day work was defined as regular work between 7am and 9pm for a least one year. The cumulative incidence of metabolic syndrome was 9% in night shift workers versus 1.8% in day workers (relative risk 5.0; 95% CI = 2.1-14.6) (see Figure 24: cumulative incidence of metabolic syndrome in night shift and day workers (according to Pietroiusti et al., 2010).

The annual incidence rate was 2.9% for night shift workers versus 0.5% for day workers (significant difference, log-rank test p = 0.001, Kaplan–Meier survival curves in both groups).



N. at risk

Night shift	402	387	365	332	298
Day-time	336	322	308	298	284

Figure 24: cumulative incidence of metabolic syndrome in night shift and day workers (according to Pietroiusti *et al.*, 2010)

A multiple Cox regression analysis showed that, of the selected variables (age, gender, smoking, alcohol, family history, physical activity and work schedule), the only predictors of the occurrence of metabolic syndrome were sedentariness and night shift work.

The meta-analysis by Wang (Wang *et al.*, 2014) included studies that were not of sufficient quality according to the method adopted by the Working Group. However, the quality of this analysis was deemed sufficient for its inclusion in the discussions on the assessment of the effect. This meta-analysis studied the risk of metabolic syndrome in relation to shift work including night work (night shift or rotating schedule covering the 12am to 5am period). According to the criteria set (sufficient data to calculate risk estimates with a 95% confidence interval and assessment of study quality by two independent readers), the authors included 13 eligible studies published between 2002 and 2011, including three cohort studies, one case-control study nested within a cohort, and nine cross-sectional studies, for a total of 2286 cases of metabolic syndrome, including 953 cases in Asians. Metabolic syndrome was defined in eight studies according to the NCEP ATP III criteria, in three according to the IDF criteria, and in one study according to the criteria of the Japan Society for the Study of Obesity (see Table 13).

Table 13: Results of a recent meta-analysis of epidemiological studies on the risk of developing metabolic syndrome associated with shift/night work

Author (year) Number of studies	Study types and population	No. of (case) studies	Definition of exposure	Pooled RR (95% CI)	P heterogeneity
Wang *et al.* (2014) 13 studies	All studies *Cohort and nested case-control* *Cross-sectional*	13 4 9	Shift work including night work (yes vs no) " "	**1.57 (1.24-1.98)** **2.03 (1.31-3.15)** **1.39 (1.08-1.80)**	**0.001** **0.071** **0.015**
	Cross-sectional studies	2	Duration of shift work including night work < 10 years ≥ 10 years	1.16 (0.62-2.15) **1.77 (1.32-2.36)**	0.651 0.936
	NCEP ATP III criteria	8	Shift work including night work (yes vs no)	**1.84 (1.45-2.34)**	0.371
	IDF criteria	3	Shift work including night work (yes vs no)	**1.57 (1.29-1.92)**	0.823
	Asian countries	5	Shift work including night work (yes vs no)	1.35 (0.92-1.99)	**0.020**
	Other countries (non-Asian)	8	Shift work including night work (yes vs no)	**1.65 (1.39-1.95)**	0.282
	Men	6	Shift work including night work (yes vs no)	**1.36 (1.03-1.81)**	**0.005**
	Women	3	Shift work including night work (yes vs no)	**1.61 (1.10-2.34)**	0.801

The adjusted pooled relative risk for metabolic syndrome related to night shift work was 1.57 (95% CI = 1.24-1.98), with significant heterogeneity between the studies ($p_{heterogeneity}$ = 0.001). When considering only case-control and cohort studies, the adjusted pooled relative risk was higher, calculated at 2.03 (95% CI = 1.31-3.15; ($p_{heterogeneity}$ = 0.07), than the pooled relative risk calculated from cross-sectional studies (pooled RR = 1.39; [95% CI = 1.08-1.80], $p_{heterogeneity}$ = 0.015).

Based on the available data from two studies (De Bacquer *et al.*, 2009; Tucker *et al.*, 2012), the authors obtained a dose-response relationship with a relative risk of metabolic syndrome of 1.77 (95% CI = 1.32-2.36) for 10 years or more of night shift work versus a non-significant relative risk of 1.16 (95% CI = 0.62-2.15) for less than 10 years (non-significant heterogeneity). Given the heterogeneity between the studies in the meta-analysis, analyses were undertaken by sub-group. They showed still-significant pooled relative risks that were higher with the NCEP ATP III criteria than with the IDF criteria, for women than for men, and for non-Asian countries than for Asian countries. The additional analyses excluding the Japanese study (Kawada et al., 2014) with specific Japanese criteria for metabolic syndrome showed results that remained significant. *[Note: generally speaking, the various criteria used to define metabolic syndrome are a potential source of study heterogeneity and can explain differences in risk depending on the criteria used].*

Specific effects on separate components of metabolic syndrome were reported in only six of the eligible studies. The calculated pooled risks were significant for obesity (1.66; [95% CI = 1.02-2.71]), hyperglycaemia (1.30; [95% CI = 1.16-1.46]), and high blood pressure (1.30; [95% CI = 1.17-1.44]), and non-significant for hypertriglyceridaemia and lowering of HDL cholesterol. Nonetheless, only studies considering metabolic syndrome as a whole were selected; studies exploring only one or more of its components, including lipids, were excluded from the meta-analysis. This may explain why no association was found here for triglycerides or HDL cholesterol. The limitations of this meta-analysis were especially related to varying definitions of night shift work depending on the study (at least one night shift per week for some, two or three rotating shifts per week for others, etc.). The lack of a consistent definition of night work in relation to shift intensity can lead to exposure classification biases and the dilution of effects in analyses aggregating studies. In addition, a majority of cross-sectional studies were considered here, having the healthy worker effect as a potential bias, leading to the potential under-estimation of the relationship between night shift work and metabolic syndrome. In this meta-analysis, the pooled relative risk appeared higher when only analytical case-control and cohort studies were taken into account. The level of adjustment for potential confounding factors for metabolic syndrome varied between studies and was also a potential source of heterogeneity. In the end, this was the first meta-analysis quantitatively showing a relationship between night shift work covering the 12am to 6am period and the risk of metabolic syndrome, as well as a potential dose-response relationship with a higher risk for workers with a longer cumulative duration of night work.

6.3.4.1.2 Cardiovascular effects

Over the past few decades, a growing number of epidemiological studies have shown that shift work including night work can be associated with long-term health effects, on the cardiovascular system in particular.

Most studies have examined the association between shift work and coronary diseases, but recent studies have also assessed the association with high blood pressure and other cardiovascular problems such as arrhythmia and changes to the blood vessel endothelium.

After preliminary sorting based on the review of the 140 abstracts of studies published up to August 2015, 68 publications were selected for analysis. In the end, 26 articles were identified as having sufficient relevance and methodological quality to contribute to the assessment of the effects of shift work including night work on cardiovascular function.

6.3.4.1.2.1 Early markers of cardiovascular dysfunction

6.3.4.1.2.1.1 Cardiac autonomic activity

Recent studies, all cross-sectional, indicate that shift work including night work can affect the cardiac autonomic nervous system, contributing to increased cardiovascular risk.

Heart rate variability (HRV) is one of the most reliable markers. Heart rate and its variability are influenced by the sympathetic and parasympathetic systems, and a decrease in variability and increase in heart rate are the result of an imbalanced autonomic system. In the normal population, autonomic activity has a circadian rhythm, with a prevalence of sympathetic activity during the day and of parasympathetic (vagal) activity during the night (Massin, 2000). A smaller ECG deviation and a shift to a higher low-frequency/high-frequency ratio (i.e. more sympathetic activity or less parasympathetic activity) are associated with cardiovascular diseases and related conditions such as metabolic syndrome and diabetes. Moreover, a decrease in vagal cardiac function accompanies and precedes the development of several risk factors. Elevated vagal activity is therefore an indicator of good autonomic regulation (Thayer, 2010; Koskinen, 2009; Perciaccante, 2006).

Kunikullaya *et al.* (2010) compared HRV in 36 night and 36 day employees of an outsourcing company providing telephone support. They were matched for age and gender. Night shift employees tended to show lower values for vagal activity and higher values for sympathetic activity as well as more sleepiness than day employees. However, HRV parameters did not vary significantly between day and night employees.

Lo *et al.* (2010) explored the effects of shift work on dynamic changes in autonomic control of HRV and systolic and diastolic blood pressure in 16 young nurses working the night shift and six others working the day shift. During the night shift, the nurses showed significant increases in vascular stress, with an average increase in systolic blood pressure of 9.7 mm Hg. Whereas HRV profiles returned to the baseline level after each shift, the systolic and diastolic blood pressure of the night shift workers did not completely return to baseline levels the following day off ($p < 0.001$).

Wong *et al.* (2012) studied HRV over two work days in a paramedic setting in day workers and night shift workers. Night shift workers reported higher job strain and had higher daily cortisol production, as well as reduced HRV and endothelial function, but the differences between the two groups were not statistically significant.

Souza *et al.* (2015) assessed, in a field study, HRV in 438 night shift workers. They observed that prolonged shift work was associated with a decrease in parasympathetic modulation and an increase in blood pressure, suggesting that shift work induces unfavourable changes in cardiac autonomic control.

The QT interval, which is the electrocardiographic expression of ventricular depolarisation and repolarisation, is an important clinical finding since a lengthened QT interval, corrected for heart rate (QTc), is a predictor of polymorphic ventricular tachycardia, which is associated with episodes of syncope, with possible progression to ventricular fibrillation and sudden death.

Meloni *et al*. (2013) measured the QTc interval in 216 healthy male workers, including 91 engaged in regular day work, 32 in 24-hour on-duty work shifts, and 93 in irregular six-hour on-call work shifts. With reference to day workers, the QTc interval was prolonged among the night workers in the two groups. The prevalence rate for a prolonged QTc, adjusted for age and obesity, was 2.2 times higher (95% CI = 1.2-4.2) in irregular six-hour shift workers, for whom conduction and repolarisation disorders were more commonly observed.

Mozos and Filimon (Mozos *et al*., 2013) studied the relationship between working time and the QT interval and the T wave (peak to end) in 60 shift workers during the morning, afternoon and night shifts. The QT and $T_{peak\text{-}end}$ intervals were prolonged during the night and morning shifts compared to the afternoon shift. QT and $T_{peak\text{-}end}$ interval prolongation was higher in hypertensive, obese and overweight individuals, smokers, and those with prolonged exposure to shift work.

6.3.4.1.2.1.2 Vascular inflammation

The possible role of inflammation in the relationship between shift work and the increased risk of cardiovascular diseases is not well understood. However, it has been suggested that the increase in the risk of several disorders associated with night shift work may be related to inflammatory processes resulting from sleep deprivation. Some earlier studies suggested that night shift work induces an increase in lymphocytes (Curti *et al.,* 1982) and leukocytes (Sookoian *et al.,* 2007).

More recently, Puttonen *et al.* (2011) investigated the relationship between shift work and systemic inflammation, indicated by elevated levels of circulating C-reactive protein (CRP) and leukocytes, in a cross-sectional sample of 1877 airline employees (1307 men and 840 women). In models adjusted for age and recent infectious diseases, CRP levels were significantly higher among male three-shift workers ($p = 0.002$) and slightly higher among male two-shift workers ($p = 0.076$). In women, the CRP level was higher for two-shift workers ($p = 0.028$). In the adjusted model (for smoking, education, alcohol consumption, physical activity and obesity), only the association between three-shift work and CRP was significant ($p = 0.021$), whereas leukocyte count was associated with two-shift work for men ($p = 0.020$) and three-shift work for women ($p = 0.044$).

As for inflammatory cytokines, Van Mark *et al.* (2010) reported no significant difference in serum concentrations of interleukin 6 (IL-6) or tumour necrosis factor (TNF-α) between shift workers and day workers, whose body mass indexes were similar.

In a study of two groups of 25 people working three night shifts and three day shifts consecutively, Khosro *et al.* (2011) demonstrated a statistically significant increase in IL-6, CRP, neutrophils, lymphocytes and platelets for night workers. TNF-α was also increased but the increase was not statistically significant.

6.3.4.1.2.1.3 Endothelial function and risk of atherosclerosis

Arterial stiffness is a pathological condition characterised by vascular lesions closely related to atherosclerotic disease. Increased arterial stiffness, indicated by high pulse wave velocity (PWV), is associated with an increase in cardiovascular events and mortality. Chen *et al.* (2010) studied the relationship between shift work including night work and the risk of atherosclerosis in a group of professional bus drivers by measuring brachial-ankle pulse wave velocity, body mass index, biochemical variables, and blood pressure. Long-term shift drivers had a higher PWV than regular and short-term shift drivers ($p < 0.01$). Age and diastolic blood pressure were positively associated with PWV. After adjusting for all variables, a 3.6 cm/s increase in flow was calculated for every year of shift driving. Tarzia *et al.* (2012) studied endothelial function (by measuring brachial artery dilation during post-ischaemic hyperaemia) and endothelium-independent function (in response to 25 mg of sublingual glyceryl trinitrate) in 20 healthy young doctors, with no cardiovascular risk factors, after a night of work and a night of sleep. Endothelial function was slightly altered after the night of work compared to the night of sleep, but it was not influenced by the number of hours of sleep during the night of work or by the duration of night work (12 months or less *versus* more than 12 months).

Atherosclerosis is now considered an inflammatory disease and pathophysiological studies have analysed the molecules involved in the interaction between endothelial vascular cells and the immune system. For example, resistin (an adipose tissue hormone) increases levels of "bad" cholesterol and promotes endothelial dysfunction by accelerating the accumulation of LDL in the arteries; circulating resistin is therefore a predictor of coronary atherosclerosis (Reilly *et al.*, 2005). Plasminogen activator inhibitor type 1 (PAI-1) may play a major role in the pathogenesis of human atherosclerosis and contribute to plaque progression and complications associated with plaque rupture (Hasenstab *et al.*, 2000). Burgueño *et al.* (2010) evaluated the circulating levels of four biomarkers of atherosclerosis (soluble CD40 ligand, monocyte chemotactic protein-1, resistin and PAI-1) in a sample of young adult men including 184 shift workers and 225 day workers. Rotating night shift workers had significantly higher circulating levels of resistin (6440 +/- 4510 pg/ml) than day workers (5450 +/- 3780 pg/ml), even after adjusting for age and blood leukocyte count ($p < 0.05$). The multiple regression analysis showed that plasma levels of resistin were significantly correlated with shift work ($p < 0.05$) and blood leukocyte count ($p < 0.01$), irrespective of age, BMI, waist-hip ratio, and insulin resistance. Moreover, the circulating levels of the three other markers were not significantly different between the two groups of workers.

Increased plasma levels of homocysteine are another potential cardiovascular risk factor, since they can influence endothelial dysfunction, oxidative stress, and atherogenic inflammation (McCully, 2009). Martins *et al. (*2003) observed a significant increase in plasma levels of homocysteine in 30 long-haul bus drivers engaged in shift work including night work, compared to 22 day workers matched for age and BMI. Similarly, Lavie and Lavie (2007) reported a significant increase in homocysteine levels in elderly shift workers with sleep disorders. Conversely, Copertaro *et al.* (2008) found no increase in the average plasma level of homocysteine in 30 night-shift nurses compared to 28 day nurses over an 18-month period, although the former had higher body weight and systolic blood pressure.

6.3.4.1.2.2 Coronary diseases (coronary ischaemia and myocardial infarction)

Fifteen years ago, a systematic review by Bøggild and Knutsson *(*1999) of 17 studies published between 1949 and 1998 (four cross-sectional and 13 analytical studies, including four case-control and nine cohort studies) reported an association between shift work including night work and cardiovascular diseases. On average, shift workers had a 40% increase in the risk of ischaemic heart disease compared to day workers. The authors selected the studies based on unspecified quality criteria involving in particular the temporal dimension of the study, adjustment for various confounding factors (age, gender, nationality, region, other job functions, social class), the selection process, exposure measurement, and statistical analysis. The authors considered there should be no adjustment for cholesterol, smoking or social support, considering these factors as mediators between shift work and cardiovascular diseases, rather than potential confounding factors.

The 17 studies gave very different risk estimates, from 0.4 to 3.6, with the majority ranging from 1 to 2. Five out of nine large-scale studies reported a risk estimate of around 1.4 but the four others found no association (see Figure 25). Of the four studies exploring the association with cumulative shift work duration, two observed a linear increase to 20 years of shift work, while the others found no exposure-response relationship. These results give the impression of highly heterogeneous studies from a methodological standpoint, probably due to selection biases, exposure classification biases, the cardiovascular diseases considered, and the appropriateness of the comparison groups used. Three studies explored the risk for women, and their results suggested that women have the same risk as men.

Several possible mechanisms were proposed to explain coronary disease in shift and night workers, including the disruption of circadian sleep-wake rhythms and cardiac regulation, chronic sleep deprivation, job stress, conflicts between working time and family and social life, and changes in cardiovascular risk factors (smoking, obesity, dyslipidaemia). The authors concluded that the risk of developing coronary diseases is probably multifactorial. However, the reviewed studies focused on worker behaviour and neglected other potential risk factors. The authors made several recommendations to improve future research, in particular the selection of appropriate reference groups, knowledge of risk factors for coronary diseases, the use of markers of atherosclerosis and haemostasis, consideration of the circadian rhythm of the biomarkers used, and a better definition of exposure to atypical hours.

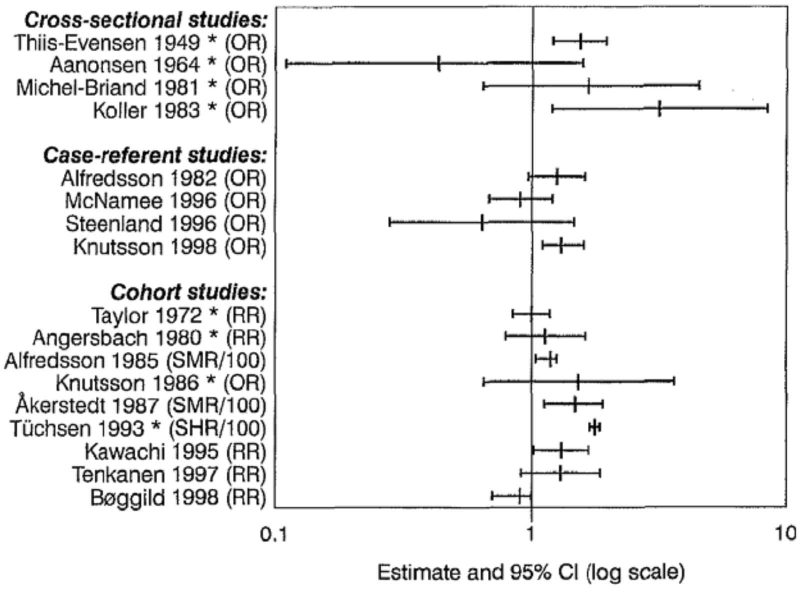


Figure 25: epidemiological studies, dealing with the relationship between shift work and cardiovascular diseases in humans, reviewed by Bøggild and Knuttson (1999)

Ten years later, Frost *et al.* (2009) published a new systematic analysis on ischaemic heart disease, based on 16 epidemiological studies published between 1972 and 2008. The authors concluded there was limited epidemiological evidence of a causal relationship, due to the heterogeneity of the studies. This analysis from 2009 included six new studies (two case-control and four cohort studies), plus ten studies (three case-control and seven cohort studies) already considered in the previous review by Bøggild and Knutsson. Seven of these studies used mortality data, six were based on incidence data, and one used both types of data.

The risks obtained in 14 of these studies (the two other studies considered cardiovascular disorders other than coronary diseases) ranged from 0.6 to 1.4 in 12 studies, whereas two reported higher risks of up to 2.35. Most of the studies based on deaths showed only a weak or no association, while the studies also considering non-fatal events showed modest positive associations. For the majority of the studies, the authors could not reasonably rule out selection (participation rate, healthy worker effect) and information (different exposure classifications and diagnostic criteria) biases.

Recently, a major meta-analysis of 34 studies published between 1983 and 2011, including more than two million people in total (11 prospective cohort studies, 13 retrospective cohort studies, and 10 case-control studies) was undertaken by Vyas *et al.* (2012). Ten studies considered myocardial infarction, 28 all coronary events, and two ischaemic stroke.

In the meta-analysis of the pooled data, shift and night work were associated with a statistically significant increase in myocardial infarction and coronary events. The pooled risks were significant with and without adjustment for other risk factors. All shift work schedules with the exception of evening shifts were associated with a statistically higher risk of coronary events (pooled risk of 1.41). Moreover, the prospective cohort studies reported a higher risk of coronary events (1.32) than the retrospective cohort studies (1.19) and the case-control studies (1.12). On the basis of the prevalence of shift workers in the adult working population in Canada (32.8%), the authors also attempted to estimate an attributable risk for shift work in the entire population, which was 7.0% for infarction and 7.3% for coronary events, for people employed in 2009 and 2010 (see Table 14).

The imprecise estimation of cardiovascular risk was possibly due to heterogeneity between studies, primarily related to considerable variations in the numbers of subjects taken into account, the follow-up period, a lack of information about exposure over several working periods, differences in adjustment for various risk factors, and heterogeneous descriptions of cardiovascular effects (which varied depending on changes in classification systems). It should also be noted that some of the studies examined in this review did not have shift and night work as their main objective but they assessed this risk as a competing or modifying factor for the effect, such as insomnia or job stress, or for groups of workers exposed to loud noise or chemical products with a cardiovascular impact.

Table 14: results of the meta-analysis of epidemiological studies on the risk of developing cardiovascular diseases associated with shift/night work

Author (year) Number of studies	**Study types and population**	**Number of (case) articles***	**Definition of exposure**	**Pooled RR (95% CI)** Adjusted RR	**I² heterogeneity**
Vyas *et al.*			Shift work including night work (yes *vs* no)		
(2009)	All studies	10	Myocardial infarction	**1.23 (1.15-1.31)**	0%
34 studies		28	All coronary events	**1.24 (1.10-1.39)**	85%
		2	Stroke	**1.05 (1.01-1.09)**	0%
	Prospective cohort studies	11	Coronary events	**1.32 (1.07-1.63)**	
	Retrospective cohort studies	8	Coronary events	**1.19 (1.06-1.34)**	
	Case-control studies				
		9	Coronary events	1.12 (1.00-1.25)	
	All the studies				
			Evening schedule	1.29 (0.69-2.41)	94%, p=0.43
			Irregular/unspecified schedule	**1.28 (1.01-1.63)**	92%, p=0.04
			Mixed schedule	**1.22 (1.08-1.38)**	46%, p=0.001
			Night schedule	**1.41 (1.13-1.76)**	36%, p=0.002
			Rotating schedule	1.21 (1.00-1.46)	71%, p=0.0495

Over the past few years, four other epidemiological studies have been published, including one case-control study and two cohort studies.

Carreon *et al.* (2014) evaluated coronary disease and cancer mortality in a cohort of 1874 people working between 1946 and 2007 in a chemical manufacturing plant who were exposed, among other things, to vinyl chloride, carbon disulphide and o-toluidine. Internal comparisons showed increased coronary disease mortality for people exposed to carbon disulphide for 90 days or more and to night shift work for four years (median for the examined population) or more compared to workers exposed to these two factors for less than four years (standardised rate ratio of 2.70). *[Note: this was a "small" study that aimed to explore the effects of exposure to some chemicals and shift work, with "rough" adjustment for some potential confounding factors but not taking into account known risk factors for coronary diseases (BMI, family history, diabetes, etc.). The mean duration of employment was very short (1.6 years) in this cohort and the authors did not produce a risk estimate associated with shift work alone].*

Hermansson *et al.* (2014) studied the association between shift work including night work and an increase in fatality after myocardial infarction (death within 28 days of onset) compared to day workers. Data were obtained from the study of 1542 cases (1147 men and 395 women) under the age of 65 in two regions of Sweden (SHEEP and VHEEP surveys). The ORs adjusted for age and fatality among shift workers (their definition included evening work and night work) were 1.63 (95% CI = 1.12-2.38) for men and 0.56 (95% CI = 0.26-1.18) for women. Adjusting for a high BMI, type-2 diabetes and high blood pressure in a multivariate regression model, the OR for male shift workers was 2.17 (95% CI = 1.46-3.23), whereas there was a slight decrease in risk for women (OR = 0.47). An analysis adjusting for physical inactivity, smoking, a low socio-economic level and high psychological demand with low decision-making latitude produced lower risks for men (OR = 1.65; [95% CI = 1.05-2.6]) and for women (OR = 0.38; [95% CI = 0.11-1.29]). *[Note: despite good data and statistical analysis quality, the definition of exposure to shift work (only the last five years, no description of the amount of night work, etc.) was rough and the possibility of a recall bias was strong because information about deceased people was obtained from the family, whereas surviving subjects completed the questionnaires themselves]*.

Gu *et al.* (2015) examined the association between rotating shift work and all causes of mortality in a prospective cohort study of 74,862 nurses in the United States (Nurses' Health Study) over a 22-year follow-up period. After adjusting for several other risk factors (age, alcohol, exercise, menopausal status, use of hormones, diet, smoking, BMI, education), the risk of cardiovascular mortality gradually increased with the increase in the number of years of exposure to night work: 1-5 years (OR = 1.02; [95% CI = 0.94-1.11]); 6-14 years (OR = 1.19; [95% CI = 1.07-1.33]); 15 years or more (OR = 1.23; [95% CI = 1.09-1.38]).

Park *et al.* (2015) examined history of cardiovascular diseases in the 12 months preceding the third survey on working conditions in South Korea, which involved 29,711 employees. After adjusting for several other risk factors (age, gender, education, salary, alcohol, smoking, job type, company size, working hours), night work was significantly associated with an increased risk of cardiovascular diseases (OR = 1.58; [95% CI = 1.11-2.25]), and the group of people with the largest number of cumulative nights had a maximum increase in risk (OR = 1.81; [95% CI = 1.19-2.74]). *[Note: in this survey, cardiovascular disease was defined only by a positive answer to the question "Have you had any cardiovascular disease in the past 12 months?". In addition, night work was unusually defined as at least two hours of work between 10pm and 5am, at least one night per month].*

6.3.4.1.2.3 High blood pressure

Regarding the effects of shift work with night work on high blood pressure, several studies have addressed this topic in recent years with mixed and inconclusive results. In most of the studies included in the aforementioned review by Bøggild and Knutsson (1999), no relationship was shown between shift work and high blood pressure.

Puttonen *et al.* (2010), who analysed 24 studies undertaken between 1994 and 2008, obtained mixed results for blood pressure levels in night shift workers. Cross-sectional epidemiological studies did not show any significant association between rotating shift work including night work and blood pressure: five studies reported similar levels in night and day workers, while two studies reported that former night shift workers had considerably higher blood pressure levels than day workers. Two longitudinal studies suggested that rotating shift work is a risk factor for an increase in blood pressure, while three other studies found no effect. One study suggested that longer exposure to night shift work increased the likelihood of developing high blood pressure in men over the age of 30, and another study suggested the development and progression of high blood pressure in male workers.

In 2011, Esquirol *et al.* (2011) undertook a systematic review of English-language literature dealing with the link between cardiovascular risk factors and night shift work published between 2000 and 2010. They examined 14 longitudinal studies, five of which were positive for a significant association, and 20 cross-sectional studies, of which five were positive, five uncertain and 10 negative. While acknowledging that the studies were fairly heterogeneous in terms of sample size, study type, assessment and classification methods, and control for confounding factors, the authors concluded there is a potential increase in the risk of developing high blood pressure in night shift workers, possibly influenced by exposure duration.

De Gaudemaris *et al.* (2011) analysed the relationship between blood pressure and risk factors related to work organisation in a total of 2307 nurses and 1530 nursing assistants in 214 work units in France (ORSOSA study). Systolic and diastolic blood pressure appeared to be significantly associated with age ($p < 0.001$) and excess weight ($p < 0.001$); night workers had a 2.5 mm Hg higher average level of systolic blood pressure ($p < 0.001$) than day workers. The authors concluded that poor relationships within teams are associated with higher levels of blood pressure in hospital workers.

Lieu *et al.* (2012) conducted a prospective cohort study (1991-2007) in black and white nurses participating in the Nurses' Health Study II who were non-hypertensive at baseline in 1991. During the 16 years of follow-up, they identified incident cases of hypertension in 580 black women out of 1510 (38%) and in 23,360 white women out of 94,142 (28%). In black women, the multivariate risk ratio for those who had worked rotating shifts for more than 12 months in the previous two years was significantly higher (HR = 1.81; [95% CI = 1.14-2.87]) than for those who had worked during the day. However, in white women, there was no increase in risk (HR = 0.99; [95% CI = 0.93-1.06]). *[Note: this study had some limitations: the hypertension diagnosis and rotating night work were self-reported]*.

In the same cohort of North American nurses (NHS I-II), Gangwisch *et al.* (2013) investigated the relationship between sleep duration and hypertension. After adjusting for several risk factors, the prevalence of hypertension was significantly higher for women sleeping five hours or less per night (OR = 1.19, [95% CI = 1.14-1.25]) than for those sleeping more than seven hours. Obesity acted as a partial mediator, but this was not the case for diabetes, hypercholesterolaemia, snoring, menopause, post-menopausal hormone therapy or shift work.

Gholami Fesharaki *et al.* (2014) undertook a 14-year historical cohort study involving 5331 male workers in a steel company in Iran. The association between shift work and systolic and diastolic blood pressure was studied after adjusting for BMI, age, work experience, marital status, smoking, and education. No significant association between work and blood pressure was observed in the three groups (day workers, weekly rotating shift workers and routinely rotating shift workers).

6.3.4.1.2.4 Ischaemic stroke

Four studies examined the potential association between shift work and ischaemic stroke. All these studies were published before 2010.

The aim of the register study of male workers in Finland, monitored from 1981 to 1994 (5.4 million person-years), by Virtanen and Notkola (2002) was to study the role of working conditions and social inequalities in cardiovascular disease mortality. According to the results, the elimination of unfavourable working conditions could reduce the number of all cardiovascular deaths by 8%, deaths from myocardial infarctions by 10%, and cerebrovascular deaths by 18%. The most influential working conditions seemed to be high workload, low control, noise, and shift work. Regarding stroke, rotating shift work slightly increased the risk compared to day work. Work schedules came from a job-exposure matrix based on the job title declared in two consecutive censuses: classification errors were therefore inevitable but could not be quantified.

Karlsson *et al.* (2005) examined the relationship between shift work and total and specific mortality from coronary heart disease, stroke and diabetes, in a cohort of 2354 shift workers and 3088 day workers in two Swedish pulp and paper plants. The cohort was monitored from 1952 to 2001 by linkage to the national Cause of Death Register. Total mortality was not higher for shift workers than for day workers, but shift workers had an increased risk of death from stroke with a standardised relative rate (SRR) of 1.56 (95% CI = 0.98-2.51), at the limit of statistical significance.

The study by Hermansson *et al.* (2007) was undertaken using a case-control study nested within two cross-sectional studies conducted from the register of the Northern Sweden Monitoring of Trends and Determinants in Cardiovascular Diseases (MONICA) study and the Västerbotten Intervention Programme for the prevention of cardiovascular diseases and diabetes. No statistically significant difference was observed between the 139 shift workers and the 469 day workers in terms of smoking, high serum triglycerides, high serum total cholesterol, job strain, or level of education. The results of the logistic regression analysis showed a slight difference, not statistically significant, for the risk of ischaemic stroke. The odds ratio for the risk of ischaemic stroke for shift workers was 1.0 (95% CI = 0.6-1.8) and was the same for men and women.

Another study was undertaken by Brown *et al.* (2009) in a cohort of 80,108 North American nurses (Nurses' Health Study) between 1998 and 2004, in which 1660 ischaemic strokes were recorded. After adjusting for several vascular risk factors, rotating night work was associated with a 4% increased risk of ischaemic stroke for every five years of additional work (relative risk = 1.04; [95% CI = 1.01-1.07]; $p_{trend} < 0.01$). Those with a history of more than 15 years of rotating night work had a substantially higher risk of ischaemic stroke (HR = 1.23, [95% CI = 1.01-1.50]) than those who had never worked the night shift.

In the end, three cohort studies and one nested case-control study are available, only one of which showed a statistically significant relationship between night shift work and stroke. The others, while showing a slightly positive trend, were not statistically significant. Also worth noting are some apparently inconsistent results, as in the study by Virtanen and Notkola, where there was an increased risk of stroke in men engaged in two day shifts but not in those engaged in three work shifts including night shifts.

It should also be pointed out that these studies all had methodological limitations already described for coronary disease and hypertension, especially as to the definition and quantification of shift work and adjustment for confounding factors.

6.3.4.2 Experimental studies in humans on the effects of shift work including night work on metabolic disorders and cardiovascular diseases

Some experimental studies in humans have been undertaken in a laboratory to assess the effects of circadian disruptions on metabolic and cardiovascular disorders. The numbers of study subjects were reduced, but the comparison groups were more balanced and the protocols were rigorous and controlled. Even though these laboratory protocols were different from the actual rhythms of shift workers, they provide insight into the mechanisms linking shift work to metabolic and cardiovascular disorders.

6.3.4.2.1 Metabolic effects

Buxton *et al.* (2012) assessed the effects of forced desynchrony between the circadian clock (24-hour period) and the sleep-wake rhythm (28-hour period) combined with sleep restriction (5.6 hours/day) for three weeks on men and women with no shift work experience in the three years preceding the study. This chronic desynchrony and sleep restriction protocol caused an 8% decrease in resting metabolic rate, an increase in circulating glucose concentrations (+14%) and a decrease in circulating postprandial insulin concentrations (-27%). Circadian cortisol and glucose rhythms were not modified between the first and third weeks of treatment and ghrelin and leptin rhythms were similar before and after treatment. There was no difference in response between young and older subjects or between men and women. All of these results suggest that the circadian desynchrony and sleep restriction protocol leads to hyperglycaemia consecutive to inadequate pancreatic compensation, in men and women regardless of their age.

Heath *et al.* (2012) assessed the effects of severe (4.7 per 28 hours) or moderate (7 per 28 hours) sleep restriction on snacking behaviour. Healthy young men (average age of 22) with no sleep disorders who had not been subject to daily disruptions (shift work or transmeridian travel) for at least three months before the study were subject to shift work for one week. This study's results showed that the frequency of sweet snack consumption was significantly higher in the subjects with severe sleep restriction than in those with moderate restriction and this frequency increased throughout the day. However, the frequency of consuming other types of snacks was the same for both sleep restriction conditions. This study was consistent with that of Hogenkamp *et al.* (2013), who assessed only the effects of sleep deprivation for one night on the amount of food ingested, showing that young men (23 years on average) deprived of a night of sleep had increased hunger and higher concentrations of ghrelin and tended to choose larger portion sizes. This study suggested that the increase in food intake (generally sweet) may be a compensatory homeostatic response to sleep deprivation, which is observed in shift work.

Leproult *et al.* (2014) measured the effects of circadian disruption for eight days in healthy men and women aged 21 to 39 on insulin secretion and sensitivity, and inflammation. Desynchronisation consisted in a forced sleep delay of 8.5 hours, four days out of eight; sleep deprivation (4 hours and 45 minutes per day) was applied to both the control and desynchronised groups. Individuals engaged in shift work or with sleep disorders were excluded. A significant decrease in insulin sensitivity was observed in both groups due to sleep restriction. However, insulin resistance and inflammation parameters were significantly higher for the desynchronised individuals, suggesting that circadian disruption can increase the risk of diabetes and inflammation, irrespective of sleep loss.

In 2014, McHill *et al.* (2014) studied the pathophysiological mechanisms that can link circadian disruption, nutrition and metabolic changes. The subjects were healthy individuals who had not been engaged in night work for at least one year and did not use any stimulants or psychotropic substances. Daily disruption was spread out over six days (two days of night activity, two days of daytime activity, and one day of night activity). During periods mimicking shift work, the individuals showed a decrease in daily energy expenditure as well as a decrease in energy expenditure after food intake. These phenomena may be a mechanism related to the risk of increased BMI and obesity observed during shift work including night work. This study also reported increased total daily fat utilisation on the first and second days of shift work, and reduced carbohydrate and protein utilisation on the second day. Ratings of hunger were reduced during shift work days despite a decrease in 24-hour levels of leptin and peptide-YY.

Lastly, Wehrens *et al.* (2010) compared the effects of one night of sleep deprivation followed by one night of recovery on postprandial metabolic responses (glucose, insulin, triacylglycerols and fatty acids) in male workers (aged 25 to 45) engaged in night work for at least five years (nine years on average) and those working regular hours (with no shift work experience). In both groups, the basal level of triacylglycerols was reduced after sleep deprivation, suggesting higher energy expenditure. The basal level of fatty acids was lower after the night of recovery. After the meal following the night of recovery, insulin and triacylglycerol levels were significantly higher and the level of fatty acids was significantly lower compared to the situation before the night of sleep deprivation, suggesting insulin insensitivity. Although there was no overall difference between the shift and non-shift workers, the non-shift workers generally had a higher basal level of insulin and lower fatty acids, and after the night of recovery, postprandial insulin levels were higher and fatty acid levels were lower.

6.3.4.2.2 Cardiovascular effects

McCubbin *et al.* (2010) studied the effects of simulated shift work on the blood pressure of young men and women (average age 23 years) with normal daytime activity and sleep, divided into two groups: at risk (family history) and not at risk for hypertension. The results obtained showed that simulated night work with sleep deprivation induced a significantly higher increase in blood pressure in at-risk people than in those with no family history. The authors concluded that night work with sleep restriction may contribute to poor blood pressure regulation in individuals with a family history of hypertension.

Kubo *et al.* (2011) assessed coronary microcirculation flow in young nurses (average age of 32) with no confirmed cardiovascular risks, by comparing night shift workers to regular day workers. Measurements were taken in the morning (9am) after a night of shift work or at the beginning of a regular day of work. Although the shift schedules were heterogeneous, the results showed that coronary microcirculation flow after the night of work was lower than after a regular night of sleep (3.8 +/- 0.6 *vs* 4.1 +/- 0.6; $p < 0.001$), indicating that coronary microcirculation was impaired after night shift work in nurses. Interestingly, the subjects who had hypercholesterolaemia or were smokers tended to have larger decreases in coronary microcirculation flow.

In an experimental study of two groups of 25 people working three night shifts and three day shifts consecutively, Khosro *et al.* (2011) demonstrated a statistically significant increase in several intravascular inflammatory factors, such as IL-6, CRP, neutrophils and lymphocytes, for night workers compared to day workers. TNF-α was also increased but the increase was not statistically significant.

Wehrens *et al.* (2012) conducted a laboratory study involving 11 experienced male night shift workers and 14 day workers matched for age, body mass index and cholesterol. There was no difference in the circadian phase between the two groups, but a significantly higher LF[49] / HF[50] ratio, significantly lower heart rate variance, and a trend for a lower percentage of endothelial flow-mediated dilatation were observed in shift workers.

6.3.4.3 Experimental studies in animals (rodents) on the effects of shift work on metabolic disorders and cardiovascular diseases

In biology, it is common to rely on experimental studies undertaken with laboratory animals (usually mice and rats) to understand the underlying mechanisms of biological functions and their disruption. It is well established that the mechanisms regulating the daily rhythms of biological functions are based on similar systems in mammals (see introductory sections). However, regarding the biological consequences, in particular for metabolic and cardiovascular systems, of shift work including night work, it is difficult to extrapolate the results of animal studies to humans since this work arrangement involves complex and interconnected notions. There are two main types of animal studies aiming to analyse the impact of circadian disruptions on metabolic function: shift work modelling and the disruption of molecular clocks.

[49] Low-frequency fluctuations, corresponding mainly to the sympathetic system.

[50] High-frequency or respiratory fluctuations, corresponding mainly to the parasympathetic system.

6.3.4.3.1 Modelling of shift work including night work

To understand the mechanisms involved in the metabolic and cardiovascular consequences of night shift work, there are four animal models that respectively use altered timing of food intake, the light-dark cycle, activity, and sleep. The last two parameters are particularly difficult to model in rodents (see Figure 26).

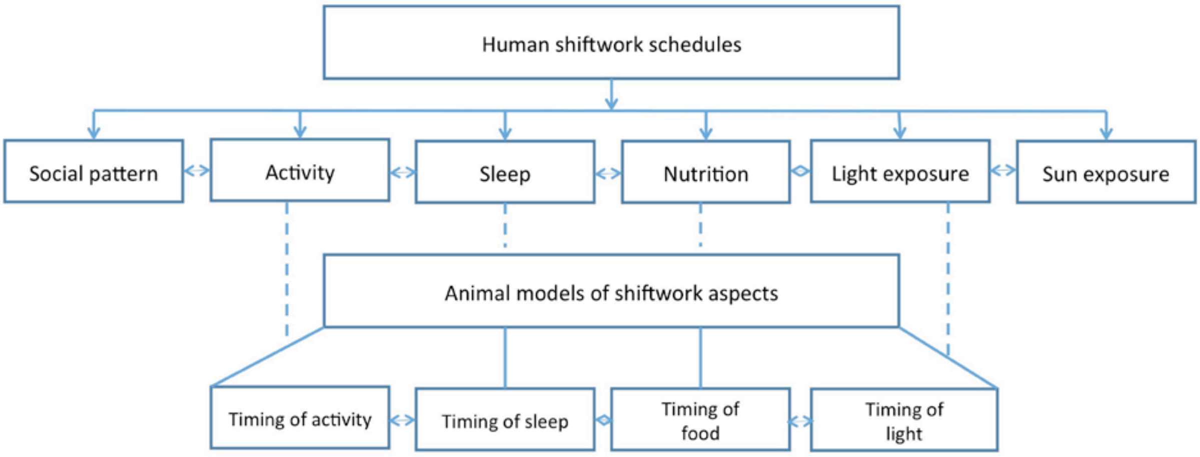


Figure 26: modelling of night shift work in animals (according to Opperhuizen *et al.,* 2015)

Altering the timing of food intake causes desynchronisation between the central clock in the suprachiasmatic nuclei and peripheral clocks (liver, pancreas, etc.). It should be noted that the food given to rodents is constant whereas shift workers have changes in the timing and composition of their food intake. Of the 11 recent animal studies described in the review by Opperhuizen *et al.* (2015), testing changes in feeding times (day instead of night), seven (64%) reported effects on body weight, either with an increase (3/11) or a decrease (4/11). One study tested the effects of a shift in feeding time combined with high-fat food and showed that mice gained more weight when fed in the resting phase than in the activity phase. Regarding the amount of food consumed, the majority of studies reported either a lack of effect (6/11) or a decrease (5/11). Similarly, the majority of studies reported no effects on glucose or lipid metabolism. The two studies recording blood pressure and heart rate reported a decrease in these parameters when the timing of food intake was changed. In all cases, it was reported that the expression of clock and metabolic genes was modified with shifted feeding.

The modification of light-dark schedules has a major effect on the central circadian clock instead of on secondary clocks (there have been few studies on the topic). The results of animal studies are difficult to interpret since various means have been used for the disruption of light-dark cycles: constant light, light and dark rhythms with different 24-hour periods, and phase shifting, but with varying directions (forward or backward), hours, frequencies and durations. In the seven studies described in the review by Opperhuizen *et al.* (2015) that tested exposure to constant light (a protocol known to abolish several daily rhythms), food intake was not modified, but in half of the studies, an increase in body weight was observed, with a clear difference between mice and rats, the latter being much less affected. However, a majority of studies (6/7) reported that glucose metabolism was modified. Nine studies in rats (5) and mice (4) analysed the effects of changing the light-dark cycle with varying parameters. The majority of the studies (86%) reported a change in glucose metabolism, but a change in body weight was reported in only five studies, with either an increase (4) or a decrease (1). Similarly, of the six studies that analysed food intake, half did not report any effects and the other half reported an increase (2) or a decrease (1).

Although it is difficult to model in rodents, altering the timing of activity or sleep was tested in some studies. Six studies in rats showed that forcing activity during the usual resting period resulted in an increase in body weight in half of cases (3/6); no changes in food intake were observed in four out of six studies, and the other two studies showed either an increase or a decrease. Various methods were used to modify the sleep-wake rhythm of rodents, with varying degrees of sleep restriction. Glucose metabolism was altered in the five reported studies, either with an increase (3) or a decrease (2). Results for body weight and food intake also varied considerably.

6.3.4.3.2 Disruption of molecular clocks

It is currently acknowledged that molecular (central and peripheral) clocks are involved in the regulation of carbohydrate and lipid metabolism. The aim of these studies was to analyse the impact of mutations in certain clock genes on metabolic function. A first series of studies was undertaken with knock-out (KO) animals for various clock genes in the entire body (Marcheva *et al.*, 2010; Wu *et al.*, 2010; Carvas *et al.*, 2012; Barclay, 2013). KO mice for the clock gene have a pronounced metabolic phenotype: they have a disrupted food intake rhythm and are hyperphagic, hyperlipidemic, hyperglycaemic, hypo-insulemic and obese. KO mice for the BMAL1 gene have reduced insulin levels, increased adiposity, glucose tolerance impairment and heavily reduced insulin sensitivity. Mutant mice for the Per2 gene have reduced fasting glucose, reduced hepatic glycogen content, increased blood concentrations of insulin and impaired gluconeogenesis. In mutant mice for the Cry1 and Cry2 genes, glucose homeostasis is also heavily impaired, particularly when they are fed a high-fat diet and rapidly become obese, probably by developing insulin resistance. In a second series of studies, the Cre-Lox technique was used to generate KOs in specific organs (Lee *et al.*, 2011; Jacobi *et al.*, 2015). For example, liver-specific BMAL1 KO mice have a phenotype suggesting a role of the hepatic clock in releasing glucose to the blood. Pancreas-specific BMAL1 KO mice show hyperglycaemia, reduced glucose tolerance and impaired insulin secretion. Lastly, adipose tissue BMAL1 KO mice eat more during their resting period and are obese.

To summarise, circadian disruptions, whether behavioural or molecular, often have metabolic effects on laboratory rodents, although the nature and extent of the effects are not always reproducible. Metabolic changes do not always affect body weight or adiposity. Lastly, it is important to note, when extrapolating effects to humans, that different results are achieved in studies with rats and mice, even when the same procedure is applied.

6.3.4.4 Assessment of effects

Overall, the level of evidence is increased with new studies for the causal relationship between shift work including night work and obesity, metabolic syndrome and its components, impaired glucose metabolism, type-2 diabetes, and cardiovascular diseases. A dose-effect relationship with the duration of shift work has been highlighted in several longitudinal epidemiological studies.

There are still limitations in the epidemiological studies related especially to the consensual definition of shift work, the imprecise assessment of exposure, and the consideration of various confounding factors and effect mediators; thus, the level of evidence provided by these studies is often limited.

The following sections propose a conclusion and classification for each of the major health effects studied, i.e.:

- obesity and excess weight;
- type-2 diabetes;
- dyslipidaemia;
- metabolic syndrome;
- coronary diseases;

- high blood pressure;
- ischaemic stroke.

Even though abdominal obesity and type-2 diabetes are components of metabolic syndrome, it is important to study them separately since by themselves they are major public health issues.

6.3.4.4.1 Obesity and/or excess weight

6.3.4.4.1.1 Epidemiological studies

Several of the studies analysed by the experts, in particular the case-control studies, showed a significant association between night shift work and weight gain or an increase in BMI. Few studies have considered abdominal obesity, which is related to cardiovascular risk in these patients and is the main component of metabolic syndrome.

The cohort study, in spite of its methodological limitations (potential selection biases related to electronic recruiting, health data reported instead of measured, high cohort attrition in relation to the over 10,000 workers recruited for the overall NMeS cohort, etc.), suggested that shift work has negative effects on weight gain.

It is interesting to note that a cohort study showed that switching from shift work to day work was associated with a significant decrease in BMI; however, this major reversibility criterion was mentioned in only one study.

The experts therefore considered that the evidence from the epidemiological studies is limited to conclude as to the existence of an effect (see Figure 27).

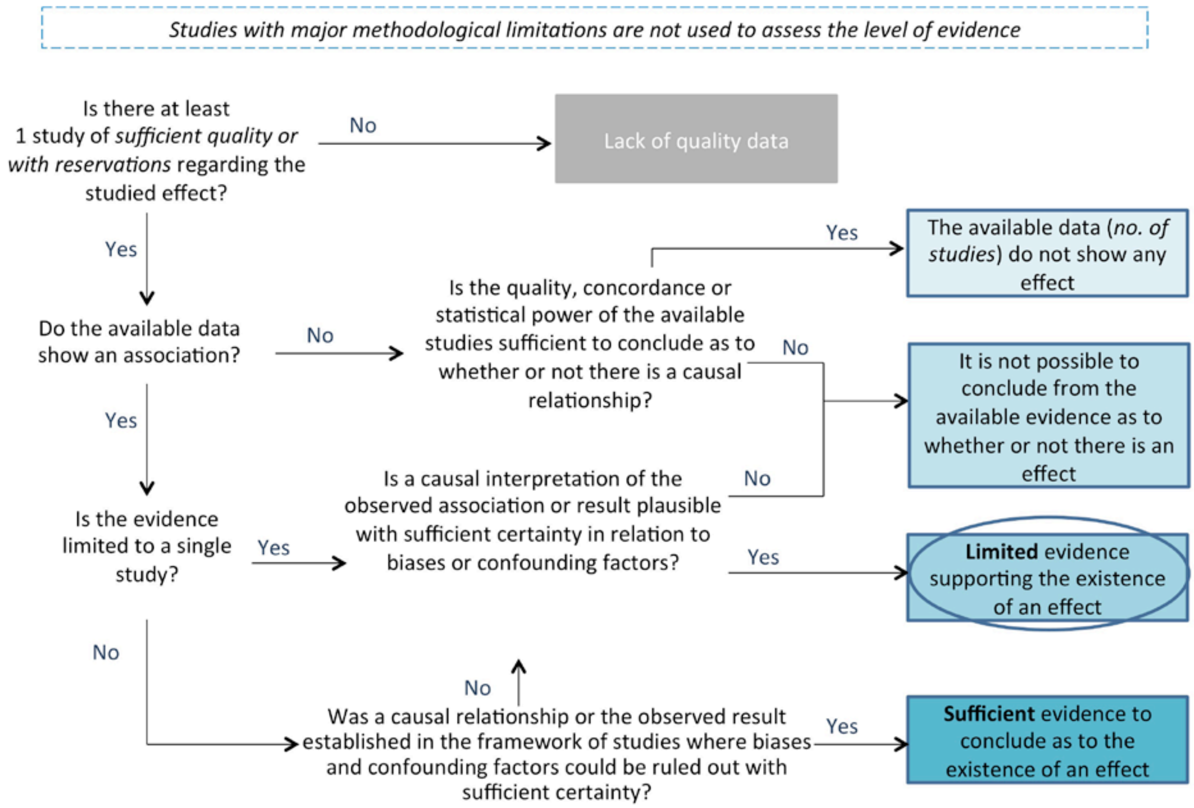


Figure 27: assessment of epidemiological studies dealing with obesity and/or excess weight

6.3.4.4.1.2 Experimental studies in humans and animals

Experimental studies in humans show that circadian disruption, whether or not it is associated with sleep deprivation, causes an increase in hunger and in the amount of (mainly sweet) food consumed. This effect may be a compensatory homeostatic response to sleep deprivation, which is observed with shift work. Moreover, energy expenditure tends to decrease. These phenomena may be a mechanism related to the risk of increased BMI and obesity observed during night shift work. Most animal studies mimicking a chronic shift in feeding time or light reported a change in body weight, especially when high-fat food was offered. Moreover, mice whose circadian timing is disrupted, either due to a total clock gene mutation or a BMAL1 gene mutation in adipose tissue, tend to be hyperphagic and obese.

Studies suggest that the increase in (generally sweet) food intake may be a compensatory homeostatic response to sleep deprivation, which is observed in shift work with night hours. These results suggest that the desynchrony/sleep restriction protocol leads to hyperglycaemia consecutive to inadequate pancreatic compensation, in men and women regardless of their age. These phenomena may be a mechanism related to the risk of increased BMI and obesity observed during shift work.

6.3.4.4.1.3 Conclusion

In accordance with the method adopted by the Working Group and considering the evidence provided by the epidemiological studies and the plausible mechanisms from the experimental studies, the experts conclude that night work has a probable effect on weight gain in humans leading to excess weight or obesity (see Figure 28).

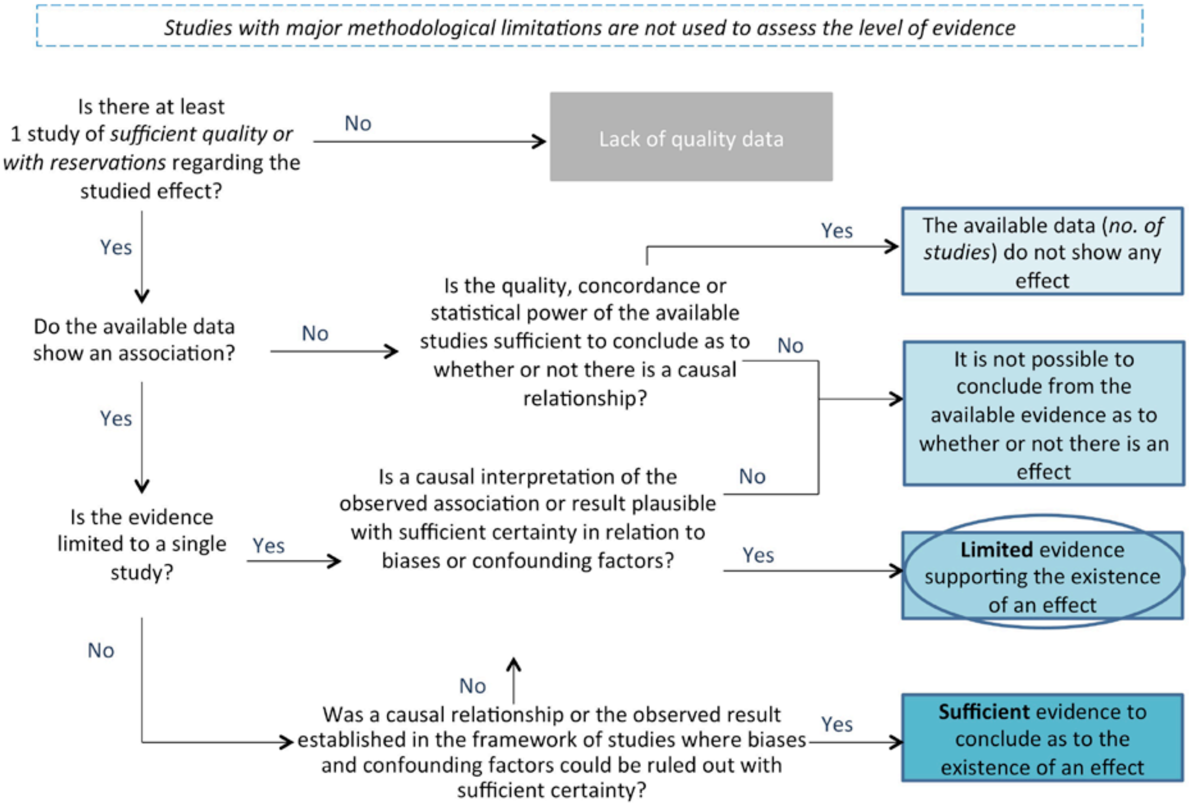


Figure 28: classification of the effects of shift work including night work on obesity

6.3.4.4.2 Type-2 diabetes

6.3.4.4.2.1 Epidemiological studies

The case-control studies showed a statistically significant increase in the risk of an increase in glycated haemoglobin (HbA1c), used for the assessment of impaired glucose metabolism.

A significant dose-response relationship between the duration of shift work with night hours and the risk of type-2 diabetes was shown in two cohorts analysed by the experts. Every five-year increase in the duration of rotating shift work with nights was associated with a 13% increase in the risk of type-2 diabetes. After adjusting for BMI, these increases were more than halved, but remained statistically significant.

Out of seven cohort studies, only three were positive.

In the different studies selected, risk coefficients were significant and showed that shift/night work was associated with a significantly increased risk of type-2 diabetes, particularly among shift workers with rotating hours. The major arguments for causality include a clear dose-effect relationship; however, the relative risks in the meta-analysis were fairly low compared to those found for the study of metabolic syndrome for example.

In addition, the fact that the classification of the diabetes criterion was not necessarily accurate since it was self-reported (no glucose testing) in several studies increased the identified limitations.

The experts therefore considered that the evidence from the epidemiological studies was limited to conclude as to the existence of an effect on type-2 diabetes or glucose metabolism (see Figure 29).

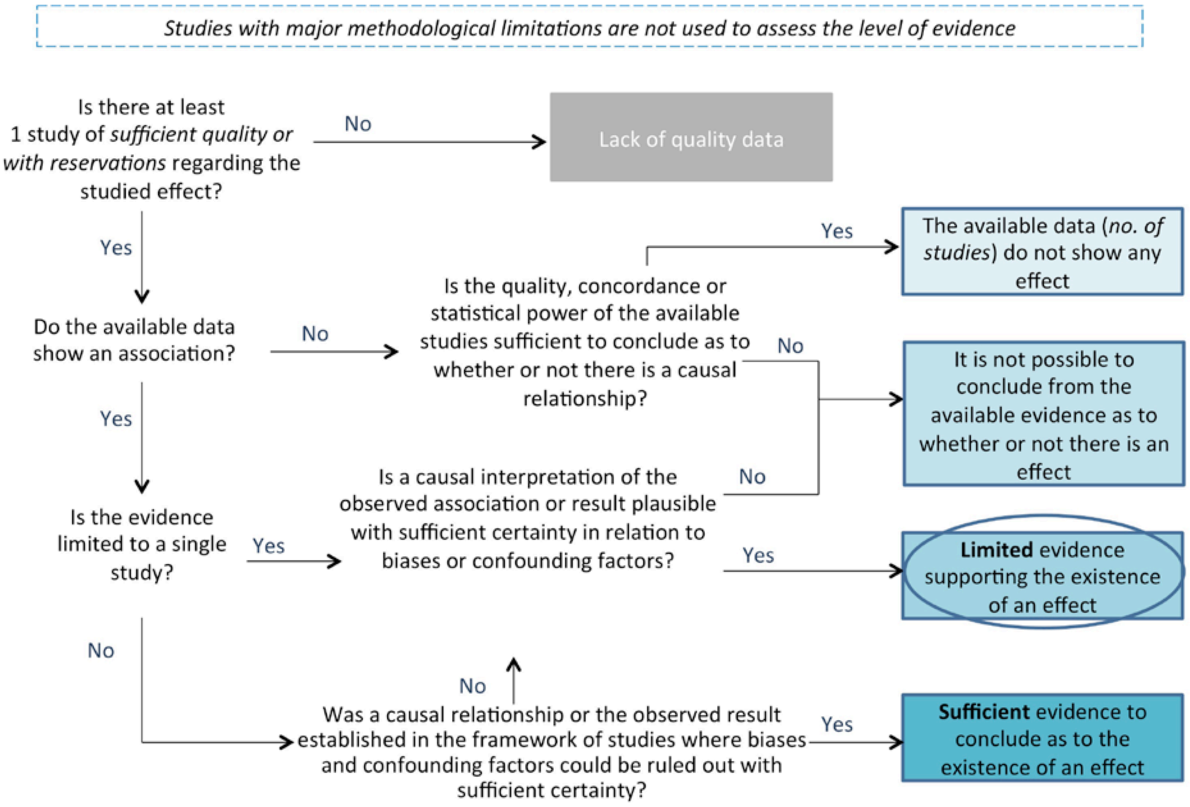


Figure 29: assessment of epidemiological studies dealing with diabetes or glucose metabolism

6.3.4.4.2.2 Experimental studies in humans and animals

On the mechanistic level, the effects of circadian disruption and/or sleep restriction on insulin resistance are plausible.

In the majority of studies testing the effect of circadian disruption in humans or animals, impaired glucose metabolism, as well as sensitivity to insulin, were observed. Moreover, mice with a clock gene mutation also showed impaired glucose and/or insulin metabolism.

6.3.4.4.2.3 Conclusion

In accordance with the method adopted by the Working Group and considering the evidence provided by the epidemiological studies and the plausible mechanisms from the experimental studies, the experts conclude that night shift work has a probable effect on glucose metabolism, with an increase in the risk of type-2 diabetes (see Figure 30).

		Evidence of the existence of the effect in experimental studies in humans or animals	
		Evidence supporting the existence of an effect	No evidence supporting the existence of an effect
Evidence of the existence of the studied effect in epidemiological studies	**Sufficient** evidence to conclude as to the existence of an effect	***Proven effect***	
	Limited evidence supporting the existence of an effect	***Probable effect***	***Possible effect***
	It is not possible to conclude from the evidence as to whether or not there is an effect	***Possible effect***	***It is not possible to conclude from the available data as to whether or not the studied effect exists***
	Lack of quality data		
	The available data do not show any effect	***It is not possible to conclude from the available data as to whether or not the studied effect exists***	***Probably no effect***

Figure 30: classification of the effect of shift work including night work on type-2 diabetes or impaired glucose metabolism

6.3.4.4.3 Dyslipidaemia

6.3.4.4.3.1 Epidemiological studies

Studies focused mainly on minimum and mean values for years of rotating shift work resulting in an increase in cholesterol.

Most of the epidemiological studies did not take into account the sub-fractions of cholesterol (HDL-C, LDL-C), or triglycerides, since total cholesterol itself was not the most relevant parameter. Given the methodological limitations and the few available studies taking these parameters into account, it is difficult to draw any epidemiological conclusions.

The results suggested that special attention should be paid to middle-aged workers having worked above the threshold number of years of shift work including night work.

The experts therefore considered that based on the evidence from the epidemiological studies, it is not possible to conclude as to whether or not there is an effect on dyslipidaemia (see Figure 31).

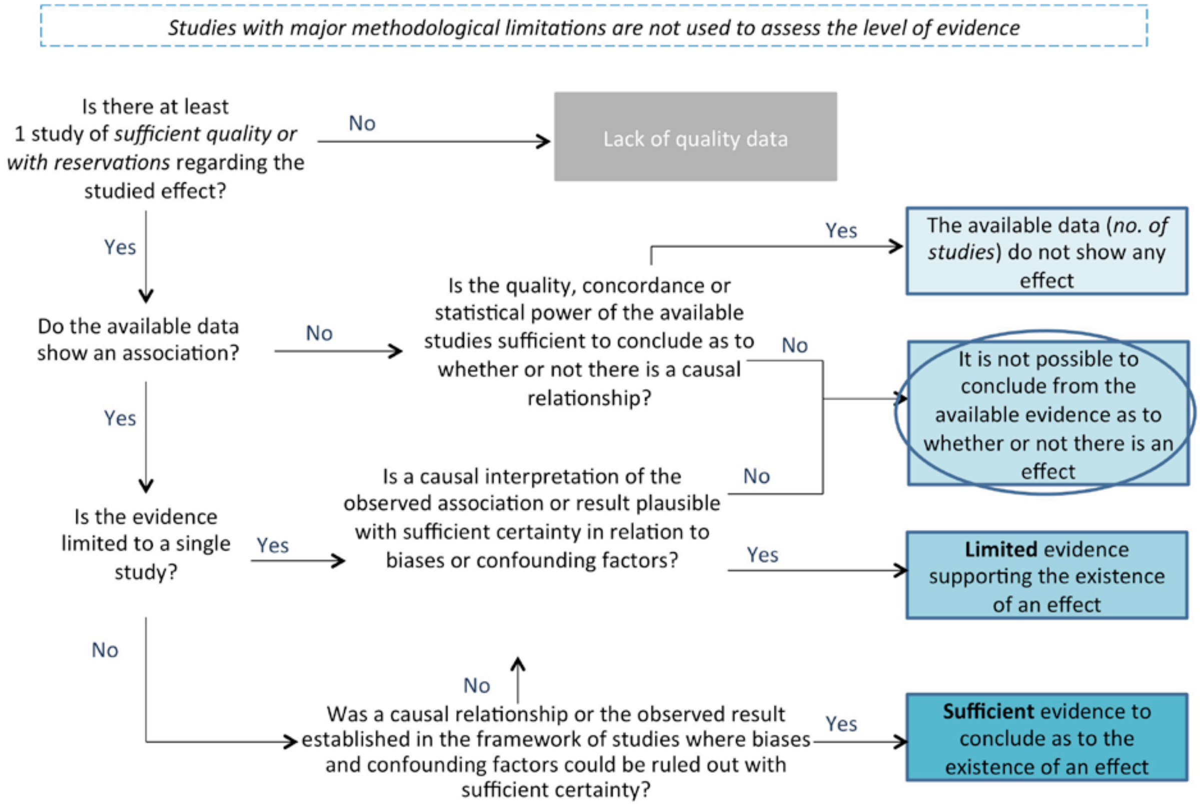


Figure 31: assessment of epidemiological studies dealing with dyslipidaemia

6.3.4.4.3.2 Experimental studies in humans and animals

Very few experimental studies have analysed the occurrence of dyslipidaemia in humans or animals. In a study in humans, workers with fixed hours generally had a lower basal level of fatty acids, while mutant mice for the clock gene are hyperlipidemic.

6.3.4.4.3.3 Conclusion

Considering the evidence provided by the epidemiological studies and the plausible mechanisms from the experimental studies, the experts conclude that night work has a possible effect on the risk of dyslipidaemia (see Figure 32).

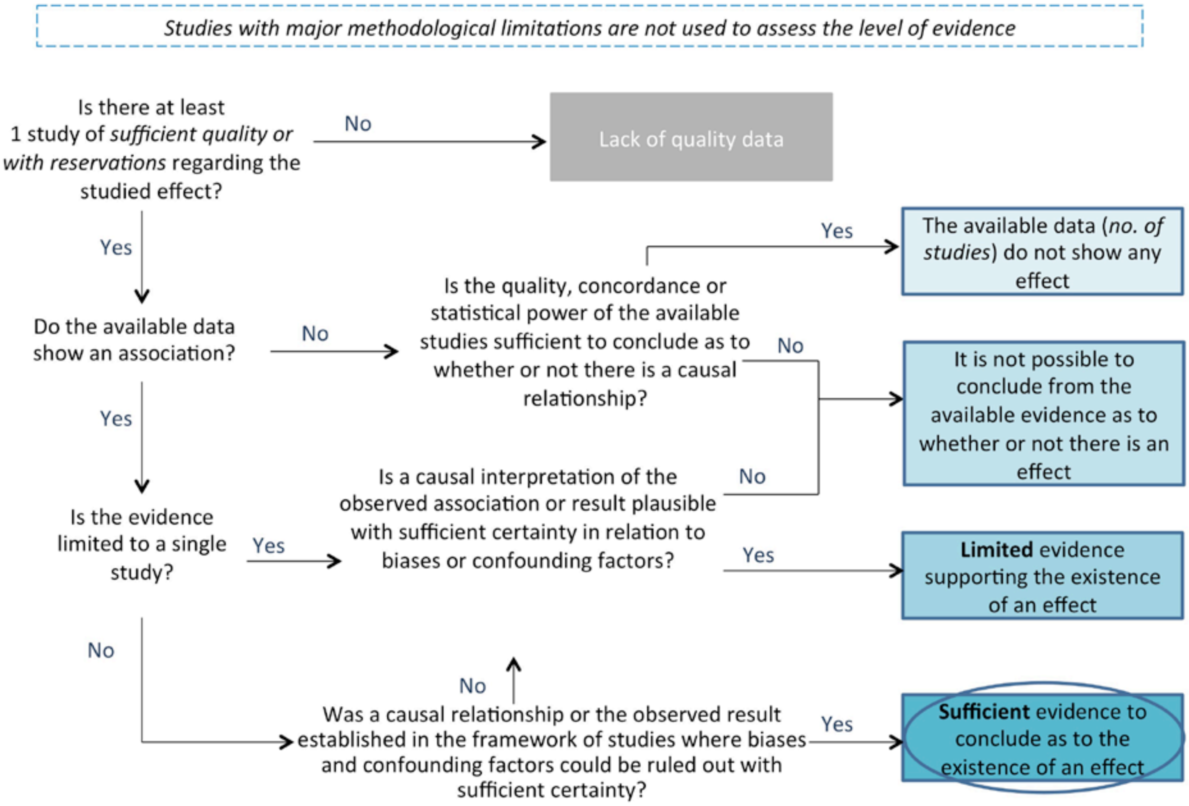


Figure 32: classification of the effect of shift work including night work on dyslipidaemia

6.3.4.4.4 Metabolic syndrome

6.3.4.4.4.1 Epidemiological studies

Most of the epidemiological studies are cross-sectional and the case-control studies nested within cohort studies provide arguments suggesting there is an association between shift work including night work and certain components of metabolic syndrome, especially when there are dose-response patterns. However, the conclusions and the level of evidence regarding the causality of these associations based solely on these studies in specific populations remain limited due to methodological limitations, relating in particular to absent or imprecise control for potential confounding factors or the healthy worker effect.

In addition, several cohorts were reviewed by the experts, some of which showed a higher incidence rate for metabolic syndrome for shift work including night work than for day work.

Lastly, the examined meta-analysis showed a quantitative relationship between night shift work covering the 12am to 6am period and the risk of metabolic syndrome, as well as a dose-response relationship with a higher risk for workers with a longer cumulative duration of night work.

In conclusion, even though studies cannot take all biases and confounding factors into consideration, the experts consider that there are strong arguments for causality and that the evidence cannot be simply classified as "limited". In the end, the epidemiological studies (cross-sectional, cohort and case-control) converge towards a sufficient level of evidence to show a causal relationship between shift work including night work and metabolic syndrome. A dose-effect relationship is commonly reported. Thus, regarding the epidemiological studies, the expert group considers the evidence is sufficient to conclude as to the existence of an effect (see Figure 33).

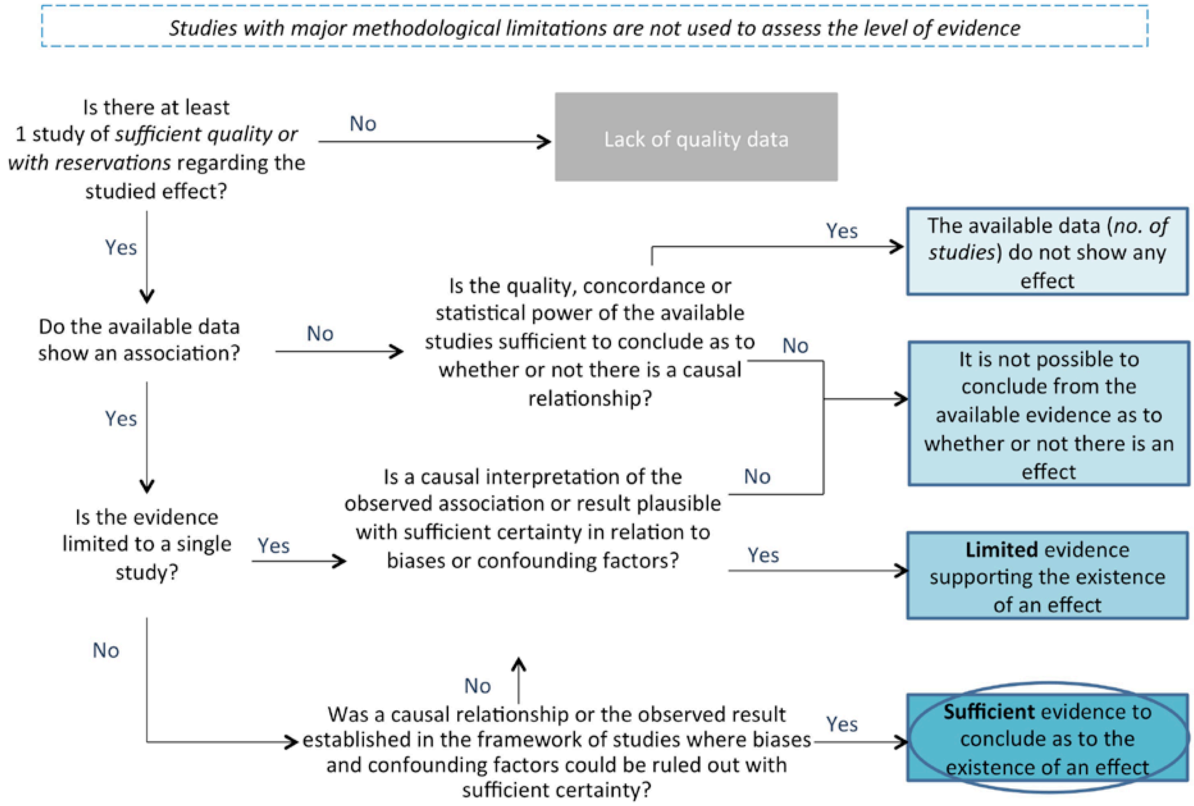


Figure 33: assessment of epidemiological studies dealing with metabolic syndrome

6.3.4.4.4.2 Experimental studies in humans and animals

Metabolic syndrome is a typically human chronic phenomenon; therefore, it is difficult to provide additional evidence with epidemiological studies in animals. However, studies show that some aspects of metabolic syndrome can be observed experimentally. For example, most animal studies report weight gain or increased adiposity and impaired glucose metabolism associated with a decrease in insulin sensitivity due to disruptions to the circadian system. Similarly, some experimental studies in humans report a higher level of sugar consumption and hyperglycaemia or an increase in insulin resistance.

On the mechanistic level, the effects of circadian disruption and/or sleep restriction are plausible here for metabolic syndrome.

Considering the effects, there is a plausible relationship between circadian disruptions and metabolic syndrome in humans.

6.3.4.4.4.3 Conclusion

In accordance with the method adopted by the Working Group and considering the evidence provided by the epidemiological studies and the plausible mechanisms from the experimental studies, the experts conclude that shift work including night work has a proven effect on the risk of metabolic syndrome (see Figure 34).

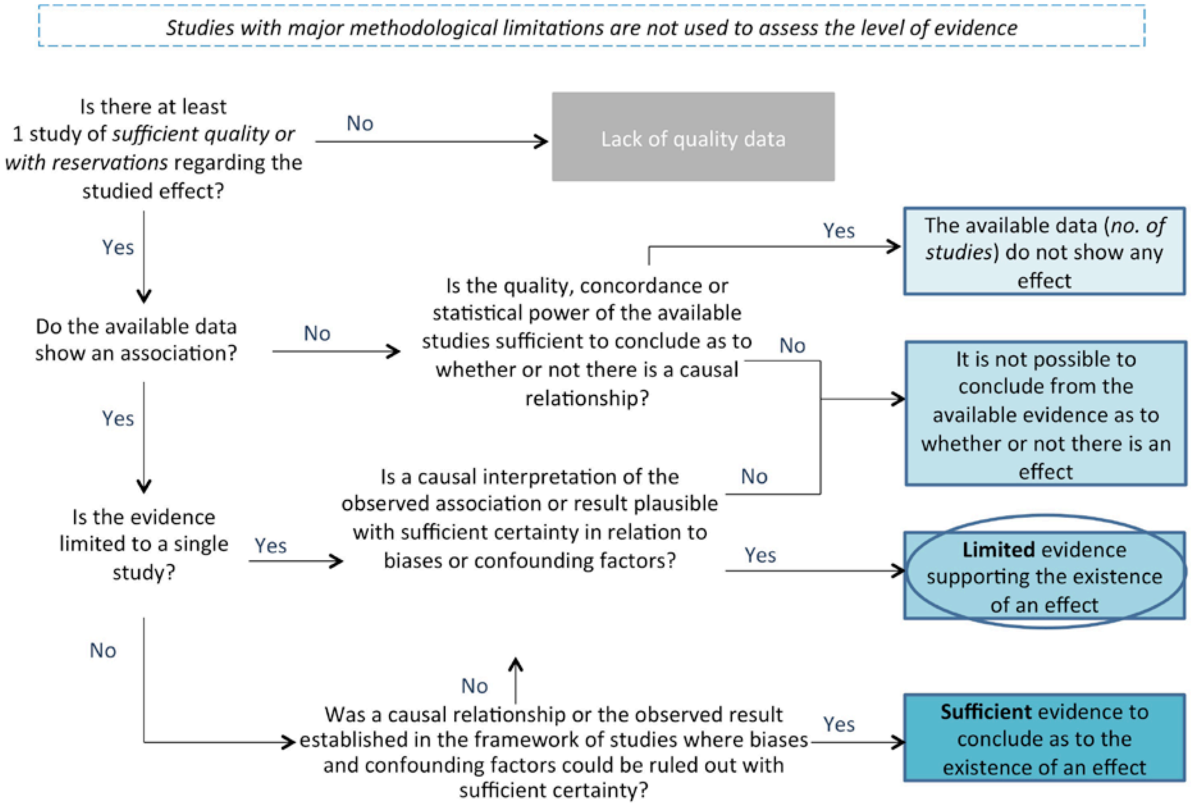


Figure 34: classification of the effect of shift work including night work on metabolic syndrome

6.3.4.4.5 Cardiovascular diseases

The literature describes the pathophysiological mechanisms that may explain the causal relationship between night shift work and cardiovascular diseases (see Figure 35; Puttonen *et al.,* 2010). These are mechanisms related to:

a) physiological stress, due to inflammation and coagulation processes, cardiac autonomic function, hormonal responses and blood pressure;
b) psychological stress, due to stressful working conditions, work-life conflicts, and recovery from work;
c) behavioural stress, due to impaired sleep quantity and quality and unhealthy lifestyle (smoking, poor nutrition, physical inactivity).

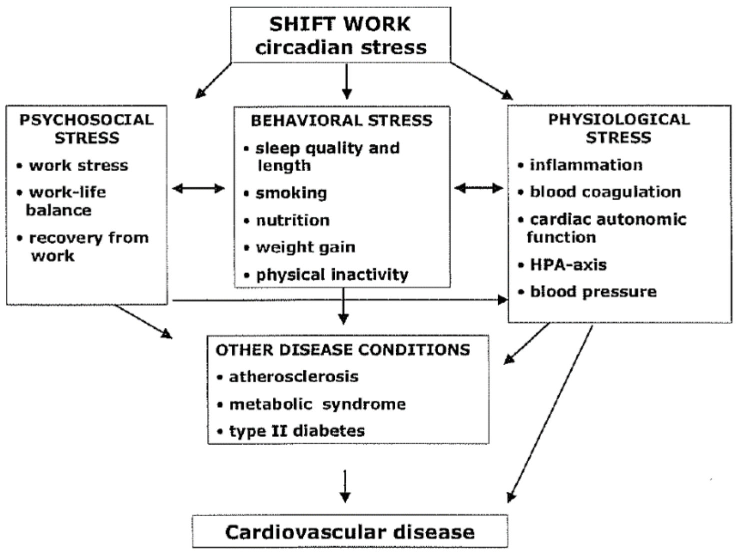


Figure 1. Model for pathways from shift work to cardiovascular disease.

Scand J Work Environ Health 2010, vol 36, no 2 **97**

Figure 35: model for the pathophysiological mechanisms involved in cardiovascular diseases related to shift work including night work (according to Puttonen *et al.*, 2010)

Based on the risk factors examined in the chapter on the effects on metabolism, and on the studies described in the above sections, on coronary disease in particular, as well as on high blood pressure and other vascular lesion and impairment factors, the association is plausible.

Nevertheless, it should be noted that most of the studies are affected by selection and information biases. These methodological limitations are related to the imprecise definition and quantification of exposure, the incorrect classification of cases and controls, the type of study (cross-sectional, longitudinal), the various groups/sectors examined, the diagnostic criteria, the reporting methods, the confounding and/or effect-mediating factors considered, and the "healthy worker effect" (in terms of ageing, recruitment, periodic medical surveillance).

Indeed, it is not always easy to establish a causal relationship between shift work and cardiovascular diseases, given their chronic, degenerative and multifactorial aetiology.

For example, ageing itself is a risk factor for cardiovascular disease but, when it is combined with night shift work, it can be underestimated in elderly workers due to the "sick shift-worker effect". This was demonstrated in a 13-year follow-up study of Finnish workers, where the relative risk of ischaemic heart disease was higher after five years of shift work than after 13 years (1.59 *versus* 1.34) (Virkkunen *et al.*, 2006). However, the "healthy worker effect" is due not only to the ageing of "survivors" but also to selection, when recruiting for shift work, and to the increased periodic medical surveillance (testing) of shift workers.

The same applies for smoking, since it has often been observed that the number of cigarettes smoked per day is higher for night shift workers than for day workers. Thus, smoking can become a mediator, and not only a confounding factor, for night shift work and cardiovascular diseases.

Furthermore, as stated in the section on metabolic disorders, obesity, dyslipidaemia, metabolic syndrome and diabetes, which are cardiovascular risk factors, are more common in shift and night workers than in day workers.

Referring to the data in the literature presented above, we can draw the following conclusions:

- the amount of convincing evidence suggesting an association between night shift work and cardiovascular disorders and diseases is increasing;
- several direct and indirect pathophysiological mechanisms are involved (chronobiological, behavioural, psychosocial);
- most epidemiological studies still have severe limitations in terms of the definition of shift work and job exposure;
- there is still significant heterogeneity between studies regarding diagnostic criteria and control for confounding factors.

Few experimental studies in humans and even fewer in animals have analysed the effects of time shifts or circadian disruptions on the cardiovascular system. A study showed that simulated night work with sleep deprivation induced a significantly higher increase in blood pressure in at-risk people than in those with no family history, and another study reported that coronary microcirculation was impaired after night work in nurses. The authors suggested that sympathetic tone may be higher or parasympathetic tone may be lower for shift workers, contributing to increased cardiovascular risk in these workers.

In conclusion, regarding the association between shift work including night work and cardiovascular diseases:

- considering the limited evidence provided by the examined epidemiological studies (see Figure 36), the effect of shift work including night work on coronary diseases (coronary ischaemia and myocardial infarction) is probable for humans (see Figure 37);
- the effect of shift work including night work on high blood pressure is possible for humans (see Figure 38 and Figure 39);
- the effect of night shift work on ischaemic stroke is possible for humans (see Figure 40 and Figure 41).

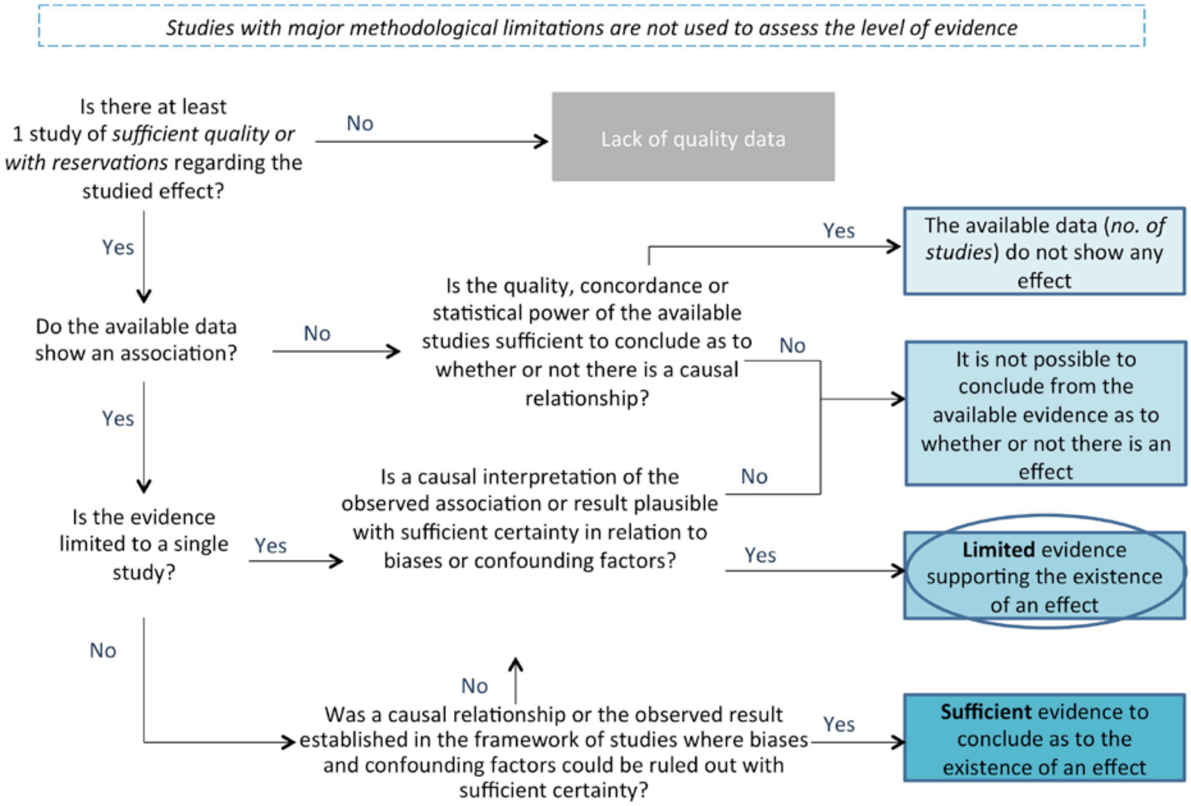


Figure 36: assessment of epidemiological studies dealing with coronary diseases (coronary ischaemia and myocardial infarction)

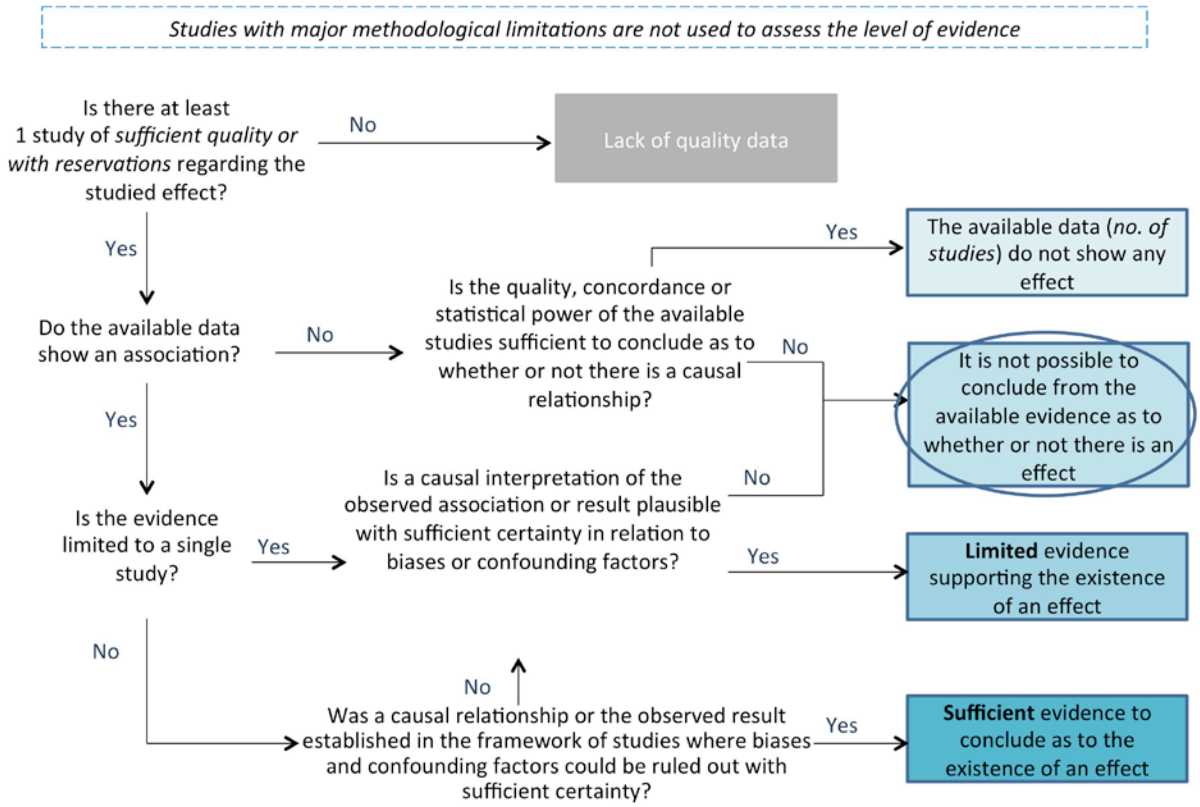


Figure 37: classification of the effect of shift work including night work on coronary diseases (coronary ischaemia and myocardial infarction)

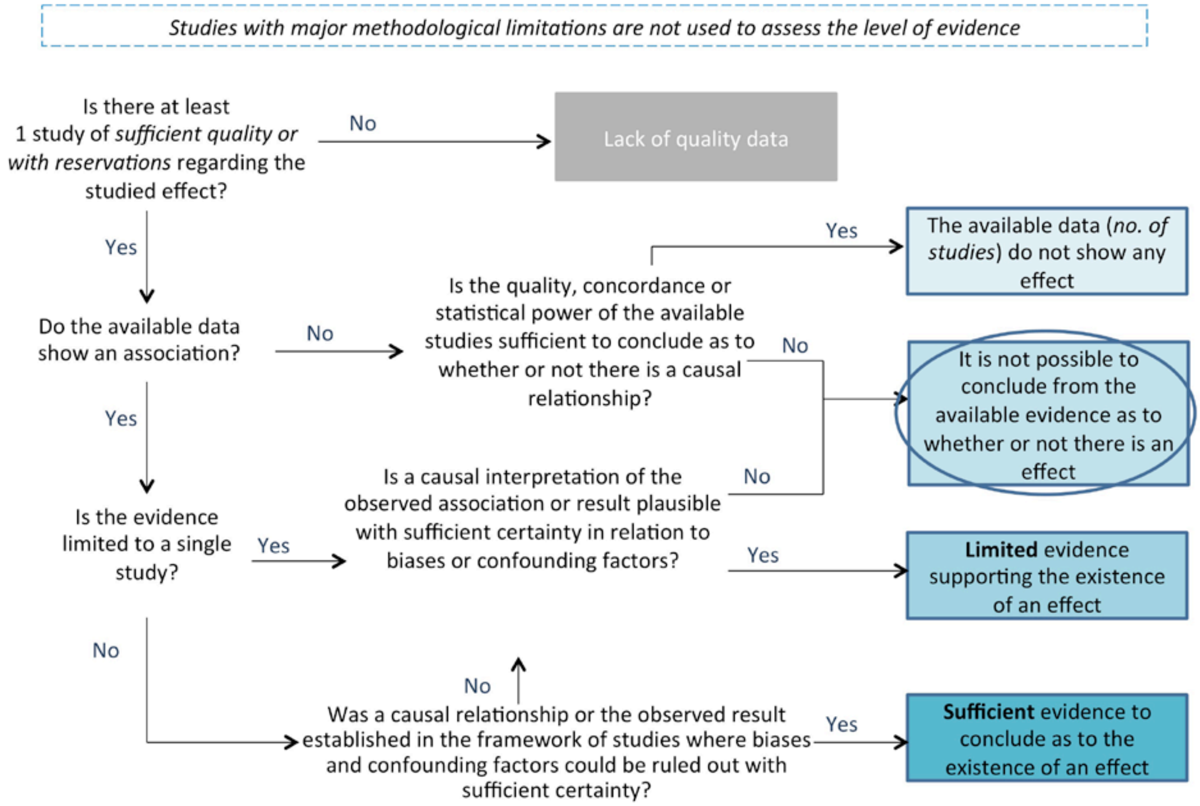


Figure 38: assessment of epidemiological studies dealing with high blood pressure

		Evidence of the existence of the effect in experimental studies in humans or animals	
		Evidence supporting the existence of an effect	No evidence supporting the existence of an effect
Evidence of the existence of the studied effect in epidemiological studies	**Sufficient** evidence to conclude as to the existence of an effect	*Proven effect*	
	Limited evidence supporting the existence of an effect	*Probable effect*	*Possible effect*
	It is not possible to conclude from the evidence as to whether or not there is an effect	*Possible effect*	*It is not possible to conclude from the available data as to whether or not the studied effect exists*
	Lack of quality data		
	The available data do not show any effect	*It is not possible to conclude from the available data as to whether or not the studied effect exists*	*Probably no effect*

Figure 39: classification of the effect of shift work including night work on high blood pressure

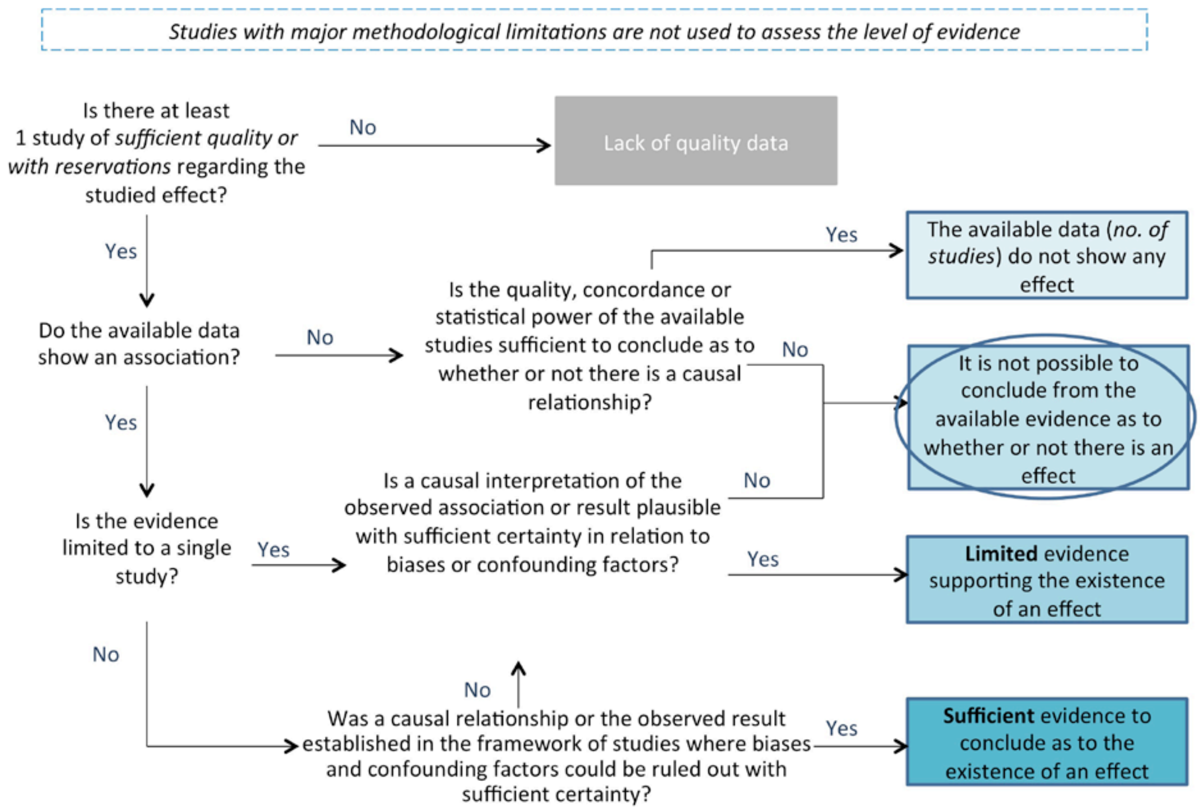


Figure 40: assessment of epidemiological studies dealing with ischaemic stroke

<table>
<tr><td colspan="2" rowspan="2"></td><td colspan="2">Evidence of the existence of the effect in experimental studies in humans or animals</td></tr>
<tr><td>Evidence supporting the existence of an effect</td><td>No evidence supporting the existence of an effect</td></tr>
<tr><td rowspan="5">Evidence of the existence of the studied effect in epidemiological studies</td><td>Sufficient evidence to conclude as to the existence of an effect</td><td colspan="2">Proven effect</td></tr>
<tr><td>Limited evidence supporting the existence of an effect</td><td>Probable effect</td><td>Possible effect</td></tr>
<tr><td>It is not possible to conclude from the evidence as to whether or not there is an effect</td><td rowspan="2">Possible effect</td><td rowspan="2">It is not possible to conclude from the available data as to whether or not the studied effect exists</td></tr>
<tr><td>Lack of quality data</td></tr>
<tr><td>The available data do not show any effect</td><td>It is not possible to conclude from the available data as to whether or not the studied effect exists</td><td>Probably no effect</td></tr>
</table>

Figure 41: classification of the effect of night work on ischaemic stroke

6.3.5 Cancers

6.3.5.1 Introduction

A group of experts convened by the International Agency for Research on Cancer (IARC) in 2007 considered that "shift work that involves circadian disruptions" was "probably carcinogenic" (Group 2A). This assessment based on studies published to date concluded there was "limited evidence in humans" and "sufficient evidence in animals" (IARC 2010; Straif *et al*,. 2007).

In this IARC publication, six of the eight epidemiological studies considered showed a modest increase in the risk of breast cancer in women who had worked at night, most often over long periods. The examined animal studies showed that changes to the circadian rhythm induced by various modes of manipulating the light-dark cycle or by the alteration of melatonin secretion had an impact on tumour development. Lastly, the pathophysiological mechanisms described by which "circadian disruption" may promote the development of malignant tumours included the consequences of light exposure at night (suppressing peak night-time melatonin concentrations), disruptions in the normal physiological function of the genes regulating circadian rhythm, and immunodeficiency related to sleep disorders (IARC, 2010).

Following the publication of the IARC monograph, there remained considerable uncertainty regarding the effects of night work on cancer risk. Since it was written in 2007, new epidemiological studies have been undertaken to assess the association between shift and/or night work and cancer risk. The aim of this current report is to update the assessment of the carcinogenic effects of night work in humans, taking into account all of the original epidemiological studies published up to 31 August 2015. It refers to a total of 24 epidemiological studies and five meta-analyses. The same publication can focus on several cancer sites. Table 15 below summarises the number of studies per cancer site:

Table 15: number of studies per cancer site.

	No. of cohort studies	No. of case-control studies	No. of meta-analyses
Breast cancer	8	16	5
Prostate cancer	5	3	
Ovarian cancer	3	1	
Lung cancer	3	2	
Pancreatic cancer	3	1	
Colorectal cancer	3	7	

Several studies on aircraft personnel (flight attendants and pilots) published in the past few years, dealing with breast cancer and prostate cancer in particular, examined workers with atypical work schedules but did not specifically assess the link between cancer and night shift work. These studies were excluded from this review since in the absence of information about work schedules, the observed effects cannot be directly attributed to shift work.

6.3.5.2 Epidemiological studies

6.3.5.2.1 Breast cancer

6.3.5.2.1.1 Epidemiological studies assessed in the IARC monograph (2007)

Eight published studies investigated the association between night shift work and breast cancer in women.

The first publications presented data from two cohorts of nurses in the United States (Nurses' Health Study 1 and 2) and one cohort of nurses in Norway (cohort of the Norwegian Board of Health). The two American studies showed a statistically significant increase of 36% to 79% in breast cancer risk in nurses with 30 and 20 years or more of shift work experience including at least three night shifts per month, after adjusting for the main confounding factors (Schernhammer *et al.,* 2001; Schernhammer *et al.,* 2006). The third study was a case-control study within a cohort based on the registry of nurses in Norway. Exposure to night work was determined based on the assumption that nurses were engaged in shift work if they were employed at infirmaries (with the exception of managerial and teaching jobs), whereas nurses not working at infirmaries were involved in day work only. The authors reported an OR of 2.21 (95% CI = 1.10-4.45) for nurses classified as night workers for at least 30 years compared to nurses working during the day (Lie *et al.,* 2006).

Two case-control studies nested within cohort studies reported an association between night work and breast cancer. A Norwegian study showed a non-significant increase in risk in female radio and telegraph operators working on merchant ships, primarily in post-menopausal women, with an OR of 4.3 after at least 3.1 years of night work (Tynes *et al.,* 1996). A Danish study based on the cross-referencing of national files (cancer registry, pension fund and population registry) compared the risk of breast cancer between women in business sectors with at least 60% night workers and those in sectors with less than 40%

night workers (data taken from a survey on living and working habits in 1976). The author reported a 50% to 75% increase in the risk of developing breast cancer for people with more than six months of night work (Hansen, 2001). In the United States, a case-control study reported an OR of 1.6 (95% CI = 1.0-2.5) for night work (working a night shift at least once a week), after adjusting for several confounding factors (Davis *et al.,* 2001).

Two articles reported negative results. A Swedish study was undertaken based on census data from 1960 and 1970 and cross-referencing with the data from the national cancer registry (Schwartzbaum *et al.,* 2007). Employees in business sectors in which at least 40% of workers had rotating hours were considered exposed to night shift work. The results did not show any risk of breast cancer in the exposed business sectors compared to those with a lower proportion of shift work *(the Working Group notes that the job-exposure matrix used to define exposure to shift work was developed based on survey data where an abnormally low proportion of participants had reported having a rotating schedule).* In the other negative study (O'Leary *et al.,* 2006), which was a case-control study, night work was defined as working in at least one job ending after 2am at least once a week. After adjusting for several confounding factors, no association between breast cancer and shift work was observed.

The IARC monograph also considered the results of a meta-analysis that showed a relative risk of 1.51 (95% CI = 1.36-1.68), calculated from the six aforementioned positive studies; the two negative studies had not been published at the time of the expert meeting in 2007 (Megdal *et al.,* 2005).

6.3.5.2.1.2 New epidemiological studies (published after 2007)

The epidemiological studies are summarised in the tables available in Annex 14

Cohort studies

Five cohort studies have been published since 2007.

In a prospective cohort study undertaken between 1996 and 2007 in 73,049 Chinese women in the Shanghai region, incident cases of breast cancer were identified in the local cancer registry (Pronk *et al.,* 2010). Of the women between the ages of 40 and 70 years, 717 had been diagnosed with invasive breast cancer. There was no significant increase in cancer risk in the women exposed to night work compared to the unexposed women. No increase in risk was observed, including for those who had worked at night for more than 20 years (HR = 1.0; [95% CI = 0.8-1.2]) or for more than 30 years (HR = 1.1; [95% CI = 0.9-1.5]). *[This was a first study in an Asian population where the incidence rate for breast cancer is lower than in a Caucasian population. The type of schedule was estimated using a job-exposure matrix and the definition of night work used was unusual (shift starting after 10pm at least three times a month), making it difficult to compare to the other published studies].*

A Swedish study (Knutsson *et al.,* 2013) examined the risk of breast cancer in a population of 4036 women participating in the WOLF (Work, Lipids, and Fibrinogen) longitudinal cohort study. Cancer cases were identified through cross-referencing with the Swedish cancer registry. In total, 94 women developed breast cancer during the follow-up period (with an average duration of 12.4 years). The risk of breast cancer in women working night shifts was significantly increased (hazard ratio or HR = 2.02; [95% CI = 1.03-3.95]) compared to women working during the day. In women under the age of 60, the HR was 2.15 (95% CI = 1.10-4.21). *[No analysis was given in relation to the duration of night work, and the type of schedule was determined by questionnaire, when recruiting for the cohort, between 1993 and 2003].*

A Dutch study (Koppes *et al.,* 2014) monitored a cohort from the general population of subjects who had participated in 14 labour force surveys between 1996 and 2009. Of the 285,723 participating women, 2531 were hospitalised for breast cancer during the follow-up period, of seven years on average. Occasional and permanent night work were not associated with the risk of hospital admission for breast cancer, which did not increase with the increase in the number of hours worked per week or the number of years in a job involving night work. These results were the same for nurses and for women with other occupations. *[This very large-scale study was undertaken by linkage to files with an imprecise assessment of night work and its frequency. The few confounding factors that were considered were roughly measured].*

A recent cohort study (Gu *et al.,* 2015) examined the association between night work and causes of mortality in 74,862 women participating in the US Nurses' Health Study. During the 22 years of follow-up (1988-2010), 14,181 deaths were documented, including 5413 cancer deaths. There was no significant association between rotating night work considered as a whole and breast cancer deaths, but an upward trend was noted for women with over 30 years of exposure (HR = 1.47; [95% CI = 0.94-2.32]). *[In this large-scale American cohort study, information about night work dated back to 1988, when the participants were asked specific questions, and any changes in work schedules occurring after 1988 were not taken into account, the overall effect of which was to reduce the risk estimate to the null value.]*

A last recent cohort study, undertaken in Sweden (Akerstedt *et al.,* 2015), analysed the data from a screening study from the Swedish Twin Registry. This analysis focused on twins born before 1959 who completed a questionnaire between 1998 and 2003, with breast cancer follow-up in the Swedish cancer and death registries. At the time of recruitment, there were 10,252 female day workers and 3404 people who had occasionally worked at night for at least one year. After an average follow-up period of 12 years, 463 cases of breast cancer were diagnosed. The statistical analysis adjusted for several potential confounding factors showed that the relative risk was increased, at the limit of statistical significance, after more than 20 years of night work (HR = 1.68; [95% CI = 0.98-2.88]). When follow-up was limited to diagnoses before the age of 61, the relative risk was slightly increased (HR = 1.77; [95% CI = 1.03-3.04]). Shorter exposure to night work showed no significant effects, suggesting that night work is associated with an increased risk of breast cancer in women, but only after relatively long-term exposure. *[This was an analysis of a cohort established for purposes other than the investigation of breast cancer, with a reasonable participation rate (74%). Night work was imprecisely defined, based on a question when recruiting. The time at which confounding factors were measured is not clear in the article].*

Case-control studies

The German GENICA study (Gene ENvironment Interaction and breast CAncer) was examined in two relevant publications. The first article compared 857 women newly diagnosed for breast cancer between 2000 and 2004 to 892 controls. Detailed information about employment and working hours was obtained during a phone interview (Pesch *et al.,* 2010). Fifty-six cases and 57 controls had worked at night, i.e. for the full period from 12am to 5am for at least one year. There was no significant difference in the incidence of breast cancer in women who had been engaged in shift work (OR = 0.91; [95% CI = 0.55-1.49]) or night work (OR = 0.96; [95% CI = 0.67-1.38]) compared to those who had never been involved in shift work. An increased risk, although not statistically significant, was observed in women who had worked more than 807 night shifts during their lifetime (OR = 1.73; [95% CI = 0.71-4.22]). For those who had been engaged in shift work for 20 years or more, the OR was 2.48 (95% CI = 0.62-9.99), whereas for those with 20 years or more since their last night shift, the OR was 0.61 (95% CI = 0.27-1.41). In the second article, the researchers explored the association between shift work and breast cancer by separately analysing 653 cancer cases with oestrogen-receptor-positive tumours (ER+) and 174 oestrogen-receptor-negative cancer cases (ER-) (Rabstein *et al.,* 2013). Overall, shift work and night work were not associated with an increased risk of cancer, regardless of the hormonal status of the tumours. However, night work for 20 years or more was associated with a significantly higher risk of ER- breast cancer (OR = 4.73; [95% CI = 1.22-18.36], based on four cases), and a high cumulative number of night shifts (more than 806 or more than 1055 shifts for systems with more than three nights per month) was associated with a non-significant increase in the risk of tumours (respectively OR = 2.34, based on seven cases, and OR = 2.11, based on six cases). *[Despite the satisfactory participation rates – over 67% – the study lacked power for the analysis of the duration of work due to the small number of cases and controls].*

Based on linkage between the Norwegian registry of nurses and the national cancer registry between 1990 and 2007, a case-control study nested in a cohort of nurses aged 35 to 74 matched 699 breast cancer cases with 895 controls (Lie *et al.,* 2011). Night work was defined as including work between midnight and 6am, even if the shift started earlier or ended later. The results of the multivariate statistical analysis showed ORs that were slightly, but not significantly, increased (between 1.1 and 1.4) in nurses who had worked three nights or more per month. Most of the significant results emerged for those who had had shift work schedules for more than five years, in particular with five consecutive nights or more (OR = 1.6; [95% CI = 1.0-2.4]), six consecutive nights or more (OR = 1.8; [95% CI = 1.1-2.8]), and seven consecutive nights or more (OR = 1.7; [95% CI = 1.1-2.8]). These results suggest that the risk of breast cancer may be related to a large number of consecutive nights, increasing circadian disruption. *[This was the first study reporting an increase in risk related to the number of consecutive nights of night work. The study included prevalent cases only, i.e. people who had not died from cancer since their diagnosis, and the authors did not rule out the possibility of a recall bias, since cases had a higher participation rate than controls].*

In a case-control study nested in a cohort of 18,551 women in the Danish military, born between 1929 and 1968, Hansen and Lassen identified, by linkage to files in the national cancer registry, 141 incident cases of breast cancer between 1990 and 2003 and compared them to 551 controls (Hansen et Lassen, 2012). The OR, adjusted for several personal and professional risk factors (including exposure to electromagnetic fields), was 1.4 (95% CI = 0.9-2.1) in women who had worked night shifts (at least one year between 5pm and 9am), compared to those with no night shift experience. The risk of breast cancer increased with the number of years of shift and night work (p_{trend} = 0.03) and with the cumulative number of night shifts (p_{trend} = 0.02). The highest risk was noted for workers in the highest tertile of cumulative exposure (OR = 2.3; [95% CI = 1.2-4.6]) and for those who had worked at least three nights per week for more than 14 years (OR = 2.5; [95% CI = 1.0-6.6]), whereas no increase in risk was detected for women working less than three nights per week. The strongest association was found in the group of women with a morning chronotype and high cumulative workload (OR = 3.9; [95% CI = 1.6-9.5]) compared to women with an evening chronotype. *[The participation rate was fairly low (around 60%) and deceased subjects were excluded from the study, but the sensitivity analyses still indicated that selection biases were unlikely].*

Another case-control study, undertaken within a cohort of 58,091 Danish nurses born between 1933 and 1970, explored the association between shift work and the incidence of cancer from July 2001 to June 2003 (Hansen and Stevens, 2012). A detailed interview on work schedules was conducted with the 310 cases identified from the Danish cancer registry and matched with four controls per case. In general, the nurses who had worked rotating shifts including night shifts had a significant increase in the risk of breast cancer (OR = 1.8; [95% CI = 1.2-2.8]) compared to the nurses who had always worked during the day. The risk was even higher for nurses who had worked permanent night shifts in addition to rotating night and day shifts (OR = 2.9; [95% CI = 1.1-8.0]). In another comparison, the nurses who had worked after midnight during more than 1095 shifts had twice the risk of developing breast cancer than those whose shifts ended before midnight (OR = 2.2; [95% CI = 1.5-3.2]). When various shift work systems were compared, day-night rotating shifts were associated with the highest risk (for 733 nights or more, OR = 2.6; [95% CI = 1.8-3.8]). *[The study had some limitations due to the low number of cases per shift work system and possible overlapping and errors in the classification of work schedules, since the interviews took place several years after exposure].*

A French study on night work, conducted between 2005 and 2008, compared 1232 cases of breast cancer and 1317 controls from the general population (Menegaux *et al.,* 2013). Exposure to night work was characterised in terms of total duration, the average number of nights per week, and night shift start and end times, and categorised as "overnight" (shift of six consecutive hours spanning the period from 11pm to 5am), "late evening" (shift ending between 11pm and 3am), or "early morning" (shift starting between 3am and 5am). The risk was higher for overnight workers (OR = 1.35; [95% CI = 1.01-1.80]), and then for late evening workers (OR = 1.25; [95% CI = 0.79-1.98]), whereas no association emerged with the early morning shift, compared to day workers. The risk was significantly higher for those who had worked at night for more than 4.5 years (OR = 1.40; [95% CI = 1.01-1.92]), especially for women who had worked less than three night shifts per week on average (OR = 2.09; [95% CI = 1.26-3.45]). Women involved in night work for more than four years before their first pregnancy had a significantly higher risk (OR = 1.95; [95% CI = 1.13-3.35]), which was even higher when the schedule included less than three night shifts per week (OR = 3.03; [95% CI = 1.41-6.50]). *[The result of higher risk for less than three nights of work per week on average conflicts with the results obtained in the two studies described above. This suggests that a rapidly rotating schedule ("less than three nights per week on average") may be riskier in terms of the disruption of circadian rhythms than permanent or slowly rotating night work ("more than three nights on average"); it is therefore not possible to reach a firm conclusion on rotation rate].*

Between 2009 and 2011, a population-based case-control study undertaken in Western Australia recruited 1205 incident cases of breast cancer and 1789 age-matched controls (Fritschi *et al.* 2013). A slight increase in risk, not statistically significant, was found for women who had been engaged in night shift work (OR = 1.16; [95% CI = 0.97-1.39]). The authors explored the effect of circadian desynchronisation, which they defined as high if the shift work system included more than four consecutive nights of forward rotation or more than six nights of backward rotation, medium if there were three or four nights of forward rotation or four to six nights of backward rotation, and low otherwise. When night work was performed in blocks of more than four consecutive weeks, the phase shift was considered less significant. A 22% increase in breast cancer risk, with a statistically significant dose-response relationship, was found for women who had worked with phase shift compared to those who had not worked with phase shift. *[This study had a good sample size, but a fairly low participation rate, of 57.8% for cases and 41.1% for controls. The results given according to the duration of night work or phase shift showed a higher risk in the category with the shortest duration of exposure, which conflicts with the results of several studies].*

Researchers grouped together breast cancer cases from two cities in Canada in order to examine the relationship between night work and cancer with 1134 cases and 1179 controls participating in a breast cancer screening programme who were matched for age (Grundy *et al.,* 2013). The association was significant for subjects with 30 years or more of shift or night work (OR = 2.21; [95% CI = 1.14-4.31]), and the results were similar for health workers and other occupations. No relationship was found for shorter durations of shift work and there were no apparent interactions with tumour hormone status. *[The participation rates were fairly low, from 49% to 59% depending on the city and the case or control status, and the work duration analysis was based on small population sizes (n=28 cases for 30 years or more)].*

A case-control study nested within a large cohort of female textile workers in Shanghai, China sought to verify if shift work modified the risk of breast cancer (Li *et al.,* 2015). This study included 1709 breast cancer cases and 4780 controls, and night work was defined as a shift with continuous work between midnight and 5am. No association was found between shift work including night work and breast cancer based on the number of years of night work or the number of nights worked. The authors suggested that the effect of shift work on breast cancer risk may be different for women of Asian origin and for those of Caucasian origin. *[This was a study with a sufficient population size (more than a hundred cases for each of the work duration strata). However, the follow-up period for the subjects was very short (five years for cases and 11 years for controls on average)].*

Another recent case-control study undertaken in China (Wang *et al.,* 2015) examined associations between night work and activities, daily sleep duration and daytime napping, and the risk of breast cancer in 712 women diagnosed with primary breast cancer, matched in five-year age groups with 742 healthy women examined in the same two hospitals in Guangzhou, between 2010 and 2012. Of the subjects, 33.0% of the cases and 26.2% of the controls reported having worked at night (OR = 1.34; [95% CI = 1.05-1.72]). A significant interaction was found between night work and sleep duration: sleep durations of six hours or less per day (OR = 1.83; [95% CI = 1.03-3.25]) and nine hours or more per day (OR = 3.69; [95% CI = 1.94-7.02]) were significantly associated with an increased risk of breast cancer in women who had worked at night. Daytime napping was associated with a reduced risk of breast cancer in night workers (OR = 0.57; [95% CI = 0.36-0.90]) but not in other workers. A stronger association between night work and breast cancer risk was observed in women whose tumours were positive for the oestrogen receptor and for pre-menopausal women. *[Approximate measurement of night work including the notion of "other night activities" with likely selection and classification biases, since the study focused mainly on sleep, and night work was documented by a very general question with no evaluation of quality or duration].*

Lastly, a case-control study based on a population from 10 regions of Spain evaluated the association between night work and various clinical types of breast cancer, taking chronotype into account (Papantoniou *et al.,* 2015). Occupational history was assessed in face-to-face interviews and shift work information was available for 1708 cases and 1778 controls, recruited from 2008 to 2013. Fixed or rotating shift work including night work was associated with a modest increase in breast cancer risk compared to day workers (OR = 1.18; [95% CI = 0.97-1.43]). The risk was higher for women with invasive tumours (OR = 1.23; [95% CI = 1.00-1.51]) and for oestrogen- and progesterone-positive tumours among pre-menopausal women (OR = 1.44; [95% CI = 1.05-1.99]). Chronotype was differentially associated with breast cancer depending on the duration and type of night work. *[Interesting study due to the detailed analysis taking into account factors that can be associated with shift work (e.g. chronotype, hormonal receptors) and the type of cancer, with some inconsistent results. The sub-groups were too small for a valid statistical comparison].*

Meta-analyses

As of 31 August 2015, five meta-analyses had been published since the release of the IARC monograph (He *et al.,* 2014; Ijaz *et al.,* 2013; Jia *et al.,* 2013; Kamdar *et al.,* 2013; Wang *et al.,* 2013). Their main findings are summarised in Annex 14.

These meta-analyses were all published recently and had a large number of studies in common since their documentary research strategies and inclusion and exclusion criteria were very similar. The end dates of the literature searches for these five meta-analyses ran from March 2012 to January 2014. Three of these meta-analyses estimated that the risk of breast cancer was approximately 20% higher in women who had worked at night than in women who had never worked at night (Kamdar *et al.*, 2013: eight studies; Jia *et al.*, 2013: 13 studies; He *et al.*, 2014: 15 studies). *[However, two of these meta-analyses included studies of flight attendants and did not provide risk estimates excluding these studies (Kamdar et al., 2013 and He et al., 2014), thus overestimating the risk associated with shift work including night work].*

Three meta-analyses produced pooled risks based on an incremental analysis of night/shift work duration. Two analyses showed 3% to 5% risk increases for every additional five-year period of night/shift work (1-2% for cohort studies and 6-9% for case-control studies) (Wang *et al.*, 2013; Ijaz *et al.*, 2014). He *et al.* (2014) reported a 16% increase per ten-year increase in the duration of night/shift work, including studies of flight attendants.

Two meta-analyses reported pooled risks based on the duration of night/shift work. Using women who had never been involved in night/shift work as the reference group, Kamdar *et al.* reported that the risk associated with less than eight years of night/shift work was higher (pooled risk = 1.13) than the risk associated with eight years or more of night/shift work (pooled risk = 1.04) when all studies were analysed together. When only studies in nurses were analysed, the opposite was found (pooled risk of 1.05 and 1.14 respectively) (Kamdar *et al.*, 2013) *[this may have been due to the higher risk for flight attendants with less than* *eight years of exposure, see* **Annex 14.***]*. The other meta-analysis reported a 15% higher risk for people who had been engaged in night or shift work for at least 15 years (Jia *et al.*, 2013). *[It is important to underline the limitations of such analyses since certain studies considered in these meta-analyses defined exposure thresholds based on the median duration of exposure while others categorised exposure levels: the compared analytical units were therefore not quite the same].*

In addition to presenting pooled risk estimates for night/shift work, the meta-analysis by He *et al.* (2014) also produced estimates for circadian disruption (associated with shift work, exposure to light at night, employment as a flight attendant, and short sleep duration).

In each of the meta-analyses, the authors mentioned inter-study heterogeneity in terms of the study populations, the definition of night/shift work, the methods for collecting exposure information, the classification of night/shift work duration, and adjustment for potential confounding factors.

6.3.5.2.1.3 Summary of the epidemiological studies on breast cancer

The assessment dealt with a total of 24 epidemiological studies on breast cancer undertaken in various countries, including the eight studies assessed in the IARC monograph. Of them, eight cohort studies and seven case-control studies nested in cohorts focused on nurses (six studies), radio operators, military personnel, textile workers and cohorts of employees identified in general population registries or employer files (six studies). We also analysed nine population-based case-control studies, including a wide range of occupations and business sectors with various work schedule characteristics. Of these 24 studies, 16 reported a statistically significant positive association between night work and breast cancer (see Annex 14. The five meta-analyses, based mainly on the same publications, had consistent results and reported a 12% to 20% increase in breast cancer risk in women having been engaged in night work (excluding studies based on flight attendants). This overall assessment should be put into perspective and interpreted in light of the strengths and weaknesses of each of these studies.

At the time of the preparation of the IARC report published in 2007, only eight studies were available. The methods used to assess exposure to night work were imprecise and varied from one study to the next. The main results in the group of nurses involved the total number of years of exposure with a rotating work schedule including at least three nights per month. Other studies used a definition of night/shift work based only on the likelihood of exposure depending on the sector of employment. Lastly, risk factors in breast cancer likely to play a confounding role were not always properly taken into account.

Considering the weaknesses in the measurement of exposure to night work, a group of experts that met in April 2009 proposed a list of relevant parameters to be specified in epidemiological studies likely to influence the desynchronisation of biological rhythms and therefore the risk of cancer. The proposed definition of night work was "at least three hours of work between midnight and 5am". It recommended collecting the following information: number of years of employment including night work, number of nights per month or per year, cumulative number of nights worked over an entire career, number of consecutive nights worked and number of days off, continuous or discontinuous night work (with or without weekends off), rotation direction and duration for rotating night shifts, shift start time and end time. It also recommended obtaining data from individuals regarding sleep quality and quantity, diet, exposure to light at night, and chronotype (Stevens *et al.,* 2011).

Although they did not generally achieve this level of detail, the studies published since 2007 have improved the characterisation of exposure to night/shift work. Two studies also focused on chronotype and explored whether associations between night work and breast cancer were different for subjects with a morning chronotype and those with an evening chronotype.

Despite this progress, there is still considerable heterogeneity in the definition of night work, and the exposure parameters considered vary from one study to the next. When the same exposure measurement is used, the results are not always consistent. For example, an increased risk of breast cancer associated with long durations of exposure to night work (20 or 30 years or more), reported in several studies, is not always observed, and some studies report the opposite, i.e. that risk increases for short exposure durations. Recent findings indicate that exposure to night work may be associated with certain specific sub-types of breast cancer (defined by the profile of tumour hormone receptors or menopausal status), but the data available to date are not sufficient to draw a conclusion. Lastly, it is important to underline that inter-study differences limit the scope of the meta-analyses, which should be interpreted with great caution.

6.3.5.2.2 Prostate cancer

All of the epidemiological studies are summarised in Annex 14. Two of these studies on prostate cancer were described in the IARC monograph (IARC, 2010).

6.3.5.2.2.1 Epidemiological studies assessed in the IARC monograph (2007)

A cohort study including 14,052 men from 21 regions of Japan, aged 40 to 65 years at baseline between 1988 and 1990, examined the risk of prostate cancer identified from cancer registries (Kubo *et al.,* 2006). A self-assessment questionnaire administered at inclusion, dealing with lifestyle and working conditions, determined the type of work performed: day work, night work, or rotating shift work. During the follow-up period, 31 cases of prostate cancer were recorded. Relative risks were 2.3 (95% CI = 0.6-9.2, based on three cases) for fixed night workers and 3.0 (95% CI = 1.2-7.7, seven cases) for rotating shift workers, compared to day workers. *[The main limitations of this study were the low number of cases, the short follow-up period (seven years on average after inclusion), and the lack of precision in the measurement of exposure to night work]*.

A case-control study based on a cancer registry of residents in north-eastern Ontario, Canada investigated 760 cases of prostate cancer, in individuals aged 45 to 85 at the time of diagnosis, between 1995 and 1998 (Conlon *et al.,* 2007). The cases were frequency-matched for age with 1632 controls. A postal questionnaire included questions about risk factors related to lifestyle and each job held for at least one year. Usual working hours were categorised as either daytime shift, evening/night shift, rotating shift, or other. The OR for prostate cancer in men who had been involved in rotating shift work was 1.19 (95% CI = 1.00-1.42). The analyses dealing with the duration of rotating shift work in years and the age when working the first rotating shift showed statistically significant relationships. *[The proportion of cases and controls classified in the category of rotating shift workers was particularly high and seemed unrealistic. The study's statistical power was limited.]*

6.3.5.2.2.2 New epidemiological studies (published after 2007)

Cohort studies

A register-based study investigating 2.1 million male employees included in the 1960 and 1970 population censuses in Sweden identified the number of incident cancers in the national cancer registry through to 1989 (Schwartzbaum *et al.,* 2007). Shift work and night work were estimated based on a job-exposure matrix established from data from annual surveys on working conditions in Sweden undertaken between 1977 and 1981 in which the proportion of participants reporting rotating shift work was abnormally low (3% of men). The standardised incidence ratio (SIR) for prostate cancer in men with occupations with at least 40% shift workers was 1.04 (95% CI = 0.99-1.10). *[The Working Group notes that the use of the job-exposure matrix to classify employees as night workers was highly unspecific and may have generated major classification errors for the exposure groups, potentially biasing the results]*.

In the United States, a study on prostate cancer mortality related to work schedule was undertaken in a large prospective cohort (Gapstur *et al.,* 2014). It involved 305,057 male volunteers recruited in 1982 and monitored for mortality until 2010. A total of 4974 men died of prostate cancer according to the death certificates. A self-administered questionnaire collected information on work schedule at inclusion in 1982; subjects were classified based on their work schedule (fixed day work, rotating shift work, fixed evening work, fixed night work, or "other"). Information about sleep duration and insomnia was also collected. The analyses did not show any association between prostate cancer mortality and work schedule (RR for rotating shift work versus fixed day work of 1.08 (95% CI = 0.95-1.22)). Short sleep durations (less than five hours) were associated with an increased risk of dying of prostate cancer compared to durations of seven hours per night, only in the first eight years of follow-up. *[This was a large-scale study on prostate cancer mortality, but it only took into account exposure at the time of inclusion, and not the total duration of work with atypical hours. Furthermore, the use of mortality data instead of incidence data is not satisfactory for a cancer whose case fatality is not very high].*

Lastly, a retrospective cohort study among employees in a chemical company investigated 12,609 workers involved in shift work for more than one year between 1995 and 2005 as well as 15,219 day workers (Yong *et al.,* 2014). Cancer incidence was recorded for the 2000 to 2009 period in the cancer registry of Rhineland-Palatinate, Germany; 191 cases of prostate cancer were identified in day workers (used as the reference category) and 146 cases in shift workers. The risk of prostate cancer was not higher for shift workers (RR = 0.93; [95% CI = 0.71-1.21]). *[The exposure classification method was highly imprecise and did not indicate the duration of exposure to shift work; exposure classification errors may have occurred in this retrospective cohort study and were assessed by the authors; a healthy worker effect may have occurred].*

Case-control studies

Parent *et al.* studied associations between night work and 11 cancer sites in men based on the data of the multi-site study in Montreal, which was a large-scale population-based case-control study undertaken between 1979 and 1985 (Parent *et al.,* 2012). For prostate cancer, the analyses covered 400 cases in individuals aged 35 to 70 at the time of diagnosis and 533 controls matched for age. Night work, determined for every job held during their careers, was defined as work including the 1am to 2am period for at least six months. The results showed that prostate cancer was almost three times more common in men who had worked at night than in men who had never worked at night (OR = 2.77; [95% CI = 1.6-3.92]). The analyses based on the cumulative duration of night work showed consistently high odds ratios, but with no exposure-risk relationship. The risk of prostate cancer was high regardless of the period when night work was performed (recent past in the last 20 years or distant past more than 20 years before). *[The Working Group notes that the high prevalence of night work among the cases of prostate cancer, i.e. a third of the subjects, is unrealistic. Moreover, the lack of a duration-response relationship and the excess risk for a large number of other cancer sites affect the credibility of the results and suggest possible methodological artefacts.]*

Papantoniou *et al.* undertook a population-based case-control study on prostate cancer and night work (Papantoniou *et al.,* 2014). It included 1115 cases of prostate cancer diagnosed in 11 hospitals in seven regions of Spain between 2008 and 2012, as well as 1562 population controls matched for age and region. Night work was determined using lifetime occupational history thanks to a questionnaire completed face-to-face; the type of shift work (permanent night or rotating) was identified and the duration of night work was calculated. Individual chronotype was also determined. The results showed that men who had worked at night had a risk (OR) of prostate cancer of 1.14 (95% CI = 0.94-1.37) compared to men who had never worked at night, and that ORs increased with the duration of exposure to night work. Overall, the risk was higher in subjects with an evening chronotype, but it was also high in men with a morning chronotype who had had long durations of exposure to night work. Lastly, night work was more strongly associated with prostate cancer with poor prognosis. *[This was the first study on night work related to prostate cancer including both a large number of subjects (achieving satisfactory statistical power) and an assessment of lifetime exposure to night* *work. Its results are consistent and support a possible link between prostate cancer and night work but should be confirmed by other studies of the same quality. The results on chronotype and the various types of prostate cancer should also be confirmed.]*

6.3.5.2.2.3 Summary of the epidemiological results on prostate cancer

The literature review focused on eight epidemiological studies with an individual assessment of exposure to night work or shift work (five cohort studies and three case-control studies considered of sufficient methodological quality), two of which had been taken into account in the IARC monograph (IARC, 2010). The cohort studies did not report any increase in the risk of prostate cancer associated with night work or shift work, with the exception of the first publication relating to a small Japanese cohort. In these cohort studies, the measurement of exposure to night work was generally not very precise, was based on a short period in the career of the subjects, or was evaluated from a jobs-exposure matrix responsible for classification errors. Among the three case-control studies, the results showed associations with durations of exposure or indices of cumulative exposure to night work. However, some of these results may have been related to methodological problems. The most recent study reporting links between night work and the advanced stages of prostate cancer, and studying the modifier effect of the chronotype, provided more convincing evidence, but should be underpinned by new studies (see **Annex 14.**).

6.3.5.2.3 Ovarian cancer

6.3.5.2.3.1 Review: studies evaluated by the IARC (through to 2007)

No studies on ovarian cancer were reported by the IARC in its monograph published in 2010 (IARC, 2010).

6.3.5.2.3.2 New epidemiological studies (published after 2007)

Three prospective cohort studies (Carter *et al.,* 2014; Gu *et al.,* 2015; Poole *et al.,* 2011) and one case-control study (Bhatti *et al.,* 2013) (all American) were published very recently.

Two articles involved studies on the health of nurses (Nurses' Health Study I and II, NHS I and NHS II). Poole *et al.* (2011) described an analysis of the association between the duration of shift work including night work and epithelial ovarian cancer incidence and deaths over a period of around 20 years based on data from the two cohorts of nurses. The data on shift work included, for the two cohorts, the number of years of shift work including at least three nights per month (according to preselected categories) at the time of recruitment; for the second cohort, this information was updated later on four occasions. The authors concluded there was no association between shift work and the risk of ovarian cancer in the two cohorts, whether individual or combined, because even though the risk tended to increase after 10 years of shift work, there was no clear exposure-response trend. *[The duration of shift work was estimated only once for the NHS I cohort in which 73% of ovarian cancers (524 cases) were identified. Cancers were reported by the subjects or their families and were then verified in medical records: it is possible that the identification of non-deceased cases was not complete].*

Gu *et al.* (2015) studied the association between shift work including night work and all-cause mortality in the NHS I cohort of 74,862 nurses. In this study of 425 cases, the risk of ovarian cancer mortality was not increased overall or depending on the number of years of shift work including night work during the 22 years of follow-up. *[The comment made on the estimation of shift work for the article by Poole et al. 2011 applies here as well].*

Carter *et al.* (2014) examined possible associations between some indicators of circadian disruption (atypical schedule, sleep duration at night, and monthly frequency of insomnia) and the risk of dying from ovarian cancer in a cohort study aiming to identify cancer risk factors (Cancer Prevention Study II). Over a 28-year follow-up period, 1289 ovarian cancer deaths were recorded, including 101 in rotating shift workers. Compared to fixed day work, shift work (rotating schedule including night work) was associated with a statistically significant risk of ovarian cancer death (RR = 1.27; [95% CI = 1.03-1.56]), and fixed night work was associated with a lower and non-significant increase in risk (RR = 1.12; [95% CI = 0.67-1.87]). No association was found with sleep duration or insomnia. *[Work schedule information was collected only once, at the time of recruitment in 1982, through a single question on current employment. It is therefore impossible to establish an exposure-response relationship with these data].*

In a population-based case-control study undertaken in western Washington State, Bhatti *et al.* (2013) evaluated exposure to night work based on employment history collected in a face-to-face interview. This good-quality study included a high number of cases (1101 cases of invasive tumours and 389 cases of borderline tumours[51]) whose employment history was compared to that of controls selected by random-digit-dialling. The analyses were adjusted for this cancer's main risk factors. The authors reported a statistically significant increase for the incidence of invasive (OR = 1.24; [95% CI = 1.04-1.49]) and borderline (OR = 1.48; [95% CI = 1.15-1.90]) epithelial ovarian tumours related to night work (midnight to 4am). There was no significant trend with cumulative exposure (no exposure-response relationship). The risk was slightly higher, but not significantly, in people with a morning chronotype than in those with an evening chronotype. *[This good-sized study was able to adjust the analysis for several potential confounding factors. However, there was no adjustment for the consumption of tobacco or exposure to asbestos, which are two recognised carcinogens for ovarian cancer].*

6.3.5.2.3.3 Summary of the epidemiological studies on ovarian cancer

To summarise, very few epidemiological studies have been published on the association between shift work including night work and ovarian cancer. The two studies conducted in cohorts of American nurses, of moderate quality, showed no association between night shift work and ovarian cancer. However, a cohort study and a case-control study, undertaken in a general population of women, reported a statistically significant increase in the risk of developing this cancer or dying from it in women reporting night shift work. Nevertheless, these two studies did not find any exposure-response relationship between the number of years of shift work including night work and ovarian cancer. All four studies had an imprecise measurement of exposure to shift work including night work, generally determined by questionnaire. Except in the study by Bhatti *et al.* (2013), adjustment for potential confounding factors was generally highly imperfect in the cohort studies.

6.3.5.2.4 Lung cancer

6.3.5.2.4.1 Review: studies evaluated by the IARC (through to 2007)

Only one study on lung cancer was reported in the IARC monograph (IARC, 2010) – that of Taylor and Pocock (1972), who studied cancer mortality in England and Wales in a cohort including 8603 male manual workers, monitored from 1956 to 1968. The study's subjects, employed by 10 different companies on 1 January 1956, were born before 1920 and had all been continuously employed in the same company for at least 10 years during the 1946-1968 period. Detailed information about all the jobs held since 1946 was obtained thanks to the companies' payroll records. Based on this information, the subjects were classified into three groups: day workers (n=3860), night shift workers (n=3188), and ex-shift workers (n=555). Follow-up began when each worker fulfilled the condition of continuous employment for 10 years. During the follow-up period, 1578 deaths were recorded, and the date and cause of death were determined from the death certificates. Standardised mortality ratios were calculated based on male mortality data for the general population in England and Wales. Excess lung cancer mortality was observed in night shift workers (94 cases observed

[51] A borderline ovarian tumour is on the borderline between a benign tumour and a malignant tumour.

vs 84.4 expected). *[The IARC working group noted that the study had been undertaken in a cohort of survivors and that the definition of shift work, which required at least 10 years of shift work with less than six months of interruption, may have underestimated the risk if there is an effect on mortality within less than 10 years].*

6.3.5.2.4.2 **New epidemiological studies (published after 2007)**

Two cohort studies (prospective (Gu *et al.*, 2015) and retrospective (Yong *et al.*, 2014)), one nested case-control study (Kwon *et al.*, 2015) and one population-based case-control study (Parent *et al.*, 2012) were recently published.

Cohort studies

Yong *et al.* (2014) undertook a retrospective cohort study among employees in a chemical company, investigating 12,609 workers involved in shift work for more than one year between 1995 and 2005 as well as 15,219 day workers. Cancer incidence was recorded for the 2000 to 2009 period in the cancer registry of Rhineland-Palatinate; 555 cases of cancer were identified in day workers (used as the reference category) and 518 cases in shift workers. Eighty-five cases of lung cancer were observed in this cohort: 39 cases in day workers and 46 in shift workers. The risk was not increased in shift workers when compared to day workers (HR = 0.93; [95% CI = 0.54-1.63]). *[Note, however, the low incidence of lung cancer in this population compared to the male population of Rhineland-Palatinate: SIR = 0.48 (95% CI = 0.34–0.66) in day workers].*

Gu *et al.* (2015) studied the association between night work and all-cause mortality in a prospective cohort study of 74,862 American nurses. During the 22 years (1988-2010) of follow-up, 14,181 deaths were documented, including 5413 cancer deaths. There was a modest increase in lung cancer mortality: 1342 lung cancer deaths were observed in this cohort (501 in nurses who had never worked at night and 841 in nurses who had worked at night). A significant exposure-response relationship (p = 0.05, multiple adjustments) for the increase in the risk of lung cancer death was observed in this cohort, with the highest risk after 15 years of exposure ($HR_{\geq 15\ years}$ = 1.25; [95% CI = 1.04–1.51]).

Case-control studies

In Canada, Parent *et al.* (2012) looked for evidence of an association between night work (defined as work between 1am and 2am for at least six months) and the risk of 11 common cancers in a population-based case-control study including 3137 men with an incident cancer (11 anatomic sites) and 512 controls. Based on 761 cases of lung cancer, a significantly higher risk was found in men who had worked at night than in men who had never worked at night (OR = 1.76; [95% CI = 1.25–2.47]). *[The initial objective of this study was to examine the relationship between chemical/physical exposure and cancer, not the effect of night work. Moreover, the lack of a duration-response relationship and the excess risk for a large number of other cancer sites suggest possible methodological artefacts].*

Kwon *et al.* (2015) conducted a case-control study nested within a cohort of 267,000 female textile workers in Shanghai, China. The incident cases of lung cancer (n=1451) identified during the follow-up period (1989-2006) were compared to an age-stratified sub-cohort of 3040 women. The results did not show a significant association between the risk of lung cancer and rotating night work. Further analyses taking into account tumour latency times of 10 and 20 years gave similar results. *[This was a study with a sufficient population size (more than a hundred cases for each of the work duration strata). However, the follow-up period for the subjects was too short (five years for cases and 11 years for controls on average)].*

6.3.5.2.4.3 Summary of the epidemiological studies on lung cancer

Whereas the studies analysed in the IARC monograph showed a slight upward trend for risk, the results of more recent studies were less conclusive and even inconsistent. One cohort study showed no increase, but reported low incidence, and the other indicated a significant exposure-response trend. Moreover, one case-control study showed an increased risk, but for a cumulative duration of less than five years, and the other reported a non-significant decrease in risk in Chinese women. Thus, the results of additional studies will be required before a conclusion can be made as to the potential association between shift work and lung cancer.

6.3.5.2.5 Pancreatic cancer

6.3.5.2.5.1 Review: studies evaluated by the IARC (through to 2007)

No studies on pancreatic cancer were reported by the IARC in its monograph published in 2010.

6.3.5.2.5.2 New epidemiological studies (published after 2007)

Two prospective cohort studies (Lin *et al.*, 2013; Gu *et al.*, 2015), one retrospective cohort study (Yong *et al.,* 2014) and one population-based case-control study (Parent *et al.*, 2012) were recently published.

Cohort studies

In Japan, Lin *et al.* (2013) specifically studied the association between fixed night work and rotating shift work and the risk of pancreatic cancer in a population-based prospective cohort study (the Japanese Cohort Collaborative Study), including 22,224 men who were 40 to 65 years of age at baseline (1988-1990), divided into three groups depending on the type of work (18,781 day workers, 1083 night workers, 2360 rotating shift workers) and monitored for a maximum period of 20 years. A total of 127 pancreatic cancer deaths were observed in this cohort over an average follow-up period of 18 years, and no significant association was found between night work or rotating shift work and the risk of pancreatic cancer death. *[However, the number of cancers was small (five cases among the 1083 night workers), and the follow-up period was relatively short].*

Gu *et al.* examined the association between night work and all-cause mortality in a prospective cohort study including 74,862 American nurses. During the 22 years (1988-2010) of follow-up, 14,181 deaths were documented, including 5413 cancer deaths of which 407 were pancreatic cancer deaths. No association was observed between night work and the risk of pancreatic cancer death, irrespective of the duration of night work ($HR_{\geq 15\ years}$ = 1.03; [95% CI = 0.70-1.51]).

Yong *et al.* (2014) undertook a retrospective cohort study among employees in a chemical company, investigating 12,609 workers involved in shift work for more than one year between 1995 and 2005 as well as 15,219 day workers. Cancer incidence was recorded over an average follow-up period of 10 years (2000 to 2009) in the cancer registry of Rhineland-Palatinate; 10 cases of pancreatic cancer were identified in day workers and 12 cases in shift workers. The risk was not increased in shift workers (HR = 1.05; [95% CI = 0.40-2.87]).

Case-control study

In Canada, Parent *et al.* (2012) looked for evidence of an association between night work (defined as work between 1am and 2am for at least six months) and the risk of 11 common cancers in a population-based case-control study including 3137 men with an incident cancer (11 anatomic sites) and 512 controls. Based on 94 cases of pancreatic cancer, a significantly higher risk was found in men who had worked at least one night shift than in men who had never worked at night (OR = 2.27; [95% CI = 1.24-4.15]). The analyses based on the cumulative duration of night work did not show any increase in risk, and the risk of pancreatic cancer seemed high only for night work performed within the 20 years prior to diagnosis (OR = 3.81; [95% CI = 1.75-8.28]), but the population was small.

6.3.5.2.5.3 Summary of the epidemiological studies on pancreatic cancer

None of the three cohorts showed an increase in the risk of pancreatic cancer death (or incidence for Yong *et al.,* 2014) in shift or night workers.

Only the case-control study by Parent *et al.* (2012) indicated an increase in the risk of pancreatic cancer incidence associated with night work, not related to the cumulative duration of night work, for night work performed within the 20 years prior to diagnosis.

6.3.5.2.6 Colorectal cancer

6.3.5.2.6.1 Review: studies evaluated by the IARC (through to 2007)

Only one study on colorectal cancer was reported in the IARC monograph (IARC, 2010), i.e. the prospective cohort of the Nurses' Health Study, including 78,586 American nurses in 1988 (Schernhammer *et al.*, 2003). The questionnaire included a question on the total number of years during which nurses had worked rotating night shifts at least three nights per month in addition to day or evening shifts in the same month. During the 1988-1998 period, 602 cases of colorectal cancer were identified based on 758,903 person-years. Compared to nurses who had never worked at night, those who had worked rotating night shifts at least three days per month for one to 14 years and for 15 years or more had multivariate-adjusted relative risks of 1.00 (95% CI = 0.84-1.19) and 1.35 (95% CI = 1.03-1.77), respectively.

6.3.5.2.6.2 New epidemiological studies (published after 2007)

Cohort studies

Yong *et al.* (2014) undertook a retrospective cohort study among employees in a chemical company investigating 12,609 workers involved in shift work for more than one year between 1995 and 2005 as well as 15,219 day workers. Cancer incidence was recorded for the 2000 to 2009 period in the cancer registry of Rhineland-Palatinate; 137 cases of colon and rectal cancer were identified in this cohort: 68 cases in day workers and 69 in shift workers. The risk was not increased in shift workers (HR = 1.33; [95% CI = 0.86-2.06]).

Gu *et al.* (2015) examined the association between night work and all-cause mortality in a prospective cohort study of 74,862 American nurses registered in the Nurses' Health Study. During the 22 years (1988-2010) of follow-up, 14,181 deaths were documented, including 5413 cancer deaths of which 464 were colorectal cancer deaths: 180 in nurses who had never worked at night, and 284 in those who had worked at night. The upward trend in the risk of colorectal cancer death observed in this cohort, which was significant when the analyses were simply adjusted for age, was no longer significant after multiple adjustments.

Case-control study

In Canada, Parent *et al.* (2012) looked for evidence of an association between night work (defined as work between 1am and 2am for at least six months) and the risk of 11 common cancers in a population-based case-control study including 3137 men with an incident cancer (11 anatomic sites) and 512 controls. Based on 439 cases, a significantly higher risk of colon cancer was found in men who had worked at least one night shift than in men who had never worked at night (OR = 2.03; [95% CI = 1.43-2.89]). The analyses based on the cumulative duration of night work showed a significant increase in risk for cumulative durations of less than five years (OR = 2.32; [95% CI = 1.47-3.68]) and more than 10 years (OR = 2.11; [95% CI = 1.13-3.94]), and for night work performed within the 20 years prior to diagnosis (OR = 2.50; [95% CI = 1.51-4.14]) or more than 20 years prior to diagnosis (OR = 2.08; [95% CI = 1.24-3.47]). Based on 236 cases, a significantly higher risk of rectal cancer was found in men who had worked at night at least once than in men who had never worked at night (OR = 2.09; [95% CI = 1.40-3.14]). The analyses based on the cumulative duration of night work showed a significant increase in risk for a cumulative duration of less than five years (OR = 2.58; [95% CI = 1.33-4.33]), and for night work in the recent past, within the last 20 years (OR = 2.27; [95% CI = 1.27-4.05]), as well as in the distant past, more than 20 years earlier (OR = 2.35; [95% CI = 1.32-4.20]).

6.3.5.2.6.3 Summary of the epidemiological studies on colorectal cancer

The studies looking for an association between night work and the risk of colorectal cancer provided conflicting results.

The incidence of colorectal cancer was increased for nurses who had worked at night for more than 15 years in the IARC evaluation (RR = 1.35; [95% CI = 1.03-1.77]) (Schernhammer *et al.*, 2003). This increase in risk was not found later (Gu *et al.*, 2015) for mortality in the same cohort (HR = 1.33; [95% CI = 0.97-1.83]), but there was limited power for curable cancers such as colon cancer.

The German retrospective cohort (Yong *et al.*, 2014) did not find this increase in incidence (HR = 1.33; [95% CI = 0.86-2.06]).

The incidence of colon (OR = 1.74; [95% CI = 1.22-2.49]) and rectal (OR = 2.09; [95% CI = 1.40-3.14]) cancer was significantly increased in the Canadian case-control study.

6.3.5.2.7 Other cancers

A few studies have analysed the risk associated with exposure to night work for all cancers or for certain cancers other than those discussed above.

6.3.5.2.7.1 Review: studies evaluated by the IARC (through to 2007)

The IARC working group analysed three studies reporting risk estimates for other cancer sites or for all cancers.

Taylor and Pocock (1972) studied mortality by cancer (all cancers, stomach and bladder cancer, and leukaemia) in England and Wales in a cohort including 8603 male manual workers monitored from 1956 to 1968. The study was described in the section on lung cancer. Higher than expected all-cancer mortality was observed for shift workers compared to the male population in England and Wales (SMR[52]=1.16; 95% CI = 1.02-1.32; 219 cases observed). An internal comparison between shift workers and day workers also showed a similar but not statistically significant risk (SMR=1.14; 95% CI = 0.94-1.38). Mortality observed in relation to the expected numbers for stomach (36/25.2) and bladder (7/6.6) cancer and leukaemia (2/3.7) revealed a non-significant increase in risk for stomach cancer only in shift workers.

[52] *Standardised Mortality Ratio*

An ecological cohort study, based on census data, included the entire Swedish population working 20 hours or more per week in 1960 and 1970 (Schwartzbaum *et al.*, 2007). In this study, having the same occupation in the two censuses taken 10 years apart indicated a non-negligible duration of exposure in the context of this job. The census data included individual information about social status and industry, but not about working methods. A job-exposure matrix was thus constructed to evaluate the proportion of shift workers in each occupation. It relied on the results of a survey taken in 1977-1981 in a sample of the Swedish population (n=46,438), which included information about their usual occupation and working methods. Shift work was defined as a schedule with three or more possible shifts per day, or work hours during the night at least one day during the week preceding the interview. Around 3% of the men and less than 0.3% of the women participating in the censuses were classified as having been involved in shift work, defined by work in industries in 1960 and 1970 where at least 40% of the survey participants reported such a work schedule. Cancers were monitored from 1971 to 1989, from the Swedish cancer registry, and SIRs[53] were calculated based on person-years of follow-up and specific national rates obtained from the same registry. Significantly higher risks were observed in men for kidney cancer, skin cancer and other or unspecified cancers, whereas there was no significant increase in the incidence of any cancers in women. The SIRs for cancers in men were all close to one during the 19 years of follow-up, with the exception of kidney cancer (1.14; [95% CI = 1.00–1.31]), skin cancer (1.20; [95% CI = 1.02–1.41]), and other unspecified cancers (1.27; [95% CI = 1.07–1.50]). For the sub-group of men participating in the 1970 census only, the SIR for thyroid cancer was high (1.35; [95% CI = 1.02–1.79]). The results changed very little when the shift work status was based only on the 1970 census or on other definitions of exposure. *[The poor classification of shift work invalidated this study]*.

The third study mentioned in the IARC monograph was a prospective cohort study based on the American Nurses' Health Study where 53,487 women with an intact uterus in 1988 answered a question on rotating night work (Viswanathan *et al.,* 2007). Follow-up until mid-2004 identified 515 cases of endometrial cancer, with a relative risk of 1.47 (95% CI = 1.03-2.10) for nurses with more than 20 years of rotating work. After stratifying by BMI, the relative risk was 2.09 (95% CI = 1.24-3.52) in the sub-group of obese nurses (BMI > 30 kg/m^2) with at least 20 years of rotating work, but there was no increase in nurses whose BMI was below 30 kg/m^2, regardless of the duration of night work.

6.3.5.2.7.2 New epidemiological studies (published after 2007)

Four studies, two of which investigated the same population, analysing all-cancer incidence or mortality associated with shift work, were recently published: an analysis of the prospective cohort of American nurses (Gu *et al.,* 2015), two analyses of the same retrospective cohort (Yong *et al.*, 2013, 2014), and a population-based case-control study (Parent *et al.*, 2012).

Yong *et al.* (2014) undertook a retrospective cohort study among employees in a chemical industry investigating 14,038 workers involved in shift work for more than one year between 1995 and 2005 compared to 17,105 day workers. Mortality was monitored from 2000 to 2009 based on death certificates; 207 cancer deaths were identified in day workers (used as the reference category) and 197 cancer deaths in night shift workers. The risk of cancer death was not increased in night shift workers after adjusting for alcohol and tobacco consumption (HR = 0.71; [95% CI = 0.56–0.91]). The study on cancer incidence (Yong *et al.*, 2014b), undertaken with the same cohort during the same period, monitored cancer incidence in the cancer registry of Rhineland-Palatinate, for a total of 555 cases of cancer in day workers and 518 cases of cancer in shift workers. The risk of cancer, all sites combined, was not higher for shift workers (HR = 1.04; [95% CI = 0.89-1.21]). However, the risk of oesophageal cancer was almost tripled (14 cases, HR = 2.85 [95% CI = 1.01-8.81]) and that of leukaemia was

53 *Standardised Incidence Ratio*

increased, but not statistically significantly, after adjusting for tobacco, alcohol and duration of employment (16 cases, HR = 2.74; [95% CI = 0.89-9.98]). The authors of these studies, working in the company's health department, mentioned that the rapid rotation system used in their factories may have explained why rotating work did not have any harmful effects.

In Canada, Parent *et al.* (2012) looked for evidence of an association between night work (defined as work between 1am and 2am for at least six months) and the risk of 11 common cancers in a population-based case-control study including 3137 men with incident cancer (11 anatomic sites) and 512 controls. A significantly higher risk was found in men who had worked at least one night shift than in men who had never worked at night, for bladder cancer (OR = 1.74; [95% CI = 1.22-2.49]) and non-Hodgkin's lymphoma (OR = 2.31; [95% CI = 1.48-3.61]). However, no exposure-response relationship was found.

Gu *et al.* (2015) examined the association between night work and all-cause mortality in a prospective cohort study of 74,862 American nurses. During the 22 years (1988-2010) of follow-up, 5413 cancer deaths were documented. There was no significant association between rotating night work and mortality for all types of cancers (HR = 1.08; [95% CI = 0.98-1.19]) or for each specific type of cancer other than lung cancer.

6.3.5.2.7.3 Summary

To summarise, the epidemiological studies investigating the association between shift work and the risk of all-cancer mortality or incidence obtained primarily negative results, with the exception of the early study by Taylor and Pocock (1972), reviewed in the IARC monograph, which reported a 16% increase in cancer deaths. As for the analyses by individual cancer site, some showed an increase in risk, but the results of the various studies were not consistent for all sites. The cancer sites for which an increase in risk was reported by at least two studies were the bladder, stomach and oesophagus. Certain associations did not persist when exposure durations or indices of cumulative exposure to night work were studied. Some of these results may have been related to methodological problems and further research is required before a conclusion can be drawn (see **Annex 14.**).

6.3.5.3 Summary of the experimental studies in animals

The results of the numerous experimental studies in animals played a major role in the IARC classification of "shift work that involves circadian disruption" in Group 2A (probably carcinogenic). The majority of studies showed that there was a statistically significant association between changes to circadian biological rhythms, induced by various modes of manipulating the light-dark cycle or melatonin secretion/absorption, and the development of tumours following the administration of carcinogenic substances or human tumour tissue grafts.

An in-depth review is given in IARC Monograph No. 98 (2007). The most important aspects are briefly summarised here, especially in terms of:

- modification of carcinogenesis by alteration of the light-dark environment and central circadian pacemaker function;
- effects of pinealectomy and modification of physiological melatonin levels on the development and/or growth of chemically induced or transplantable tumours;
- effects of melatonin administration on tumour growth (Table 16).

6.3.5.3.1 Modification of carcinogenesis by alteration of the light-dark environment and central circadian pacemaker function

The importance of the time of exposure to various light and dark periods in tumour development and growth was highlighted in several studies that examined the effects of:

- the chronic alteration of the circadian time of exposure to chemical carcinogens (e.g. Dimethyl-benzanthracene, *N*-nitroso-*N*-methylurea, Diethylnitrosamine, 1,2-Dimethylhydrazine, Azoxymethane) in rodents kept in 24-hour light-dark regimens;
- constant exposure to light or, conversely, constant darkness;
- induction of experimental jet lag or other modifications in light exposure regimens;
- suprachiasmatic nuclei ablation or experimental "clock gene" mutations;
- transplacental chemical carcinogenesis.

6.3.5.3.2 Effects of pinealectomy and physiological melatonin levels on the development and/or growth of chemically induced or transplantable tumours

Pinealectomy is used in experimental models to determine whether the suppression of nocturnal melatonin secretion, without affecting the endogenous clock, leads to the enhancement of tumour development and/or growth. It therefore indirectly verifies whether nocturnal melatonin secretion inhibits the process of oncogenesis.

In several types of tumours (undifferentiated, sarcomas, hepatocarcinomas, adenocarcinoma of the ovary, melanoma, uterine and breast cancer), pinealectomised animals have a significantly reduced average lifespan compared to controls, a considerably reduced tumour latency time, increased tumour volume, with a faster growth rate, and a higher frequency of metastatic foci.

6.3.5.3.3 Effects of physiological melatonin administration on tumour growth in animals

Most of the studies showed the oncostatic action of melatonin on tumour development and growth in experimental animal models. However, these studies were performed using pharmacological (not physiological) doses of melatonin. The nocturnal concentrations of melatonin *in vivo* were inhibitory to oncogenesis and were inferred from studies using pinealectomy as a technique for specifically eliminating the nocturnal melatonin signal and observing the stimulation of tumour development and growth. Only a handful of studies directly investigated the role of physiological, nocturnal concentrations of melatonin on experimental tumour growth *in vivo*, in the event of liver tumours and human cancer xenografts in rats, where there was an inhibitory effect on linoleic acid uptake in tumour cells, a significant decrease in H3-thymidine incorporation, and a decrease in the development of cancer.

In the past few years, several other studies have been undertaken on the topic, confirming the importance of circadian factors, relating to light-dark exposure, nocturnal melatonin secretion and genetic conditions, as factors contributing to tumour development and growth. Disruption of the circadian time structure and the rhythmic organisation of the host/cancer balance leads to the alteration of cellular circadian metabolism and tumour proliferation (see, for example, Blask *et al.,* 2011, 2014; Wu *et al.,* 2011; Xiang *et al.,* 2012, 2015; Yang *et al.,* 2009). Comprehension of these mechanisms may thus be essential for the rational development of new therapeutic and preventive approaches.

Table 16: results of experimental studies undertaken in animals evaluated in IARC Monograph No. 98 (2007)

Study type / *Experimental condition*	No exposure	Chemical initiation/ promotion models	Transplacental chemical carcinogenesis models	Tumour cell transplantation or graft	Positive / Total
Alterations in light exposure	2/3	5/6	1/1	10/10	**18/20**
Lesions to the suprachiasmatic nucleus				1/1	**1/1**
Chronic jet lag				2/2	**2/2**
Pinealectomy (melatonin suppression)		2/8		11/13	**13/21**
Clock gene mutations	1/1	1/2			**2/3**
Circadian timing of carcinogen administration		4/4			**4/4**
Administration of melatonin to experimental tumours				5/5	**5/5**
Total	**¾**	**12/20**	**1/1**	**29/31**	**45/56**

6.3.5.4 Mechanisms

Several assumptions, based on the results of animal or *in vitro* trials and studies in humans, have been proposed to explain the mechanisms by which night or shift work may be responsible for an increased risk of cancer. There are five possible mechanisms of carcinogenesis (see Figure 42 and Figure 43), which are not mutually exclusive. They are briefly described below (Fritschi *et al.*, 2011).

Circadian desynchronisation

The central biological clock located in the suprachiasmatic nuclei helps synchronise, in normal physiological conditions, the functioning of the cerebral structures and peripheral organs with the 24-hour day (the light-dark cycle, see Chapter 3). Changes in the sleep-wake rhythm and light-dark cycle can lead to the desynchronisation of peripheral functions and a phase shift with the central biological clock. Cell proliferation is one of the major processes regulated by the circadian system, and asynchrony in the cellular cycle is one of the characteristics of tumour tissue cells (Fu and Lee, 2003). This asynchrony may be promoted by disruptions in the sleep-wake rhythm.

Supporting this mechanistic assumption, several laboratory studies have shown that the clock genes that regulate circadian timing in the cells can act as tumour suppressors and that changes in the expression of these genes can play a role in the development and spread of cancer (Levi *et al.*, 2010). Other recent studies have shown that the circadian system and clock genes are very closely involved in cellular division and suggest that circadian desynchronisation may disrupt it (Feillet *et al.*, 2015). Lastly, in studies in animals, chronic jet lag profoundly disrupts the circadian molecular clock, several of whose transcription rhythms are suppressed in the suprachiasmatic nuclei, liver, lungs, and kidneys (Levi *et al.*, 2010). Overall, the results of all of these studies provide convincing evidence that the circadian system and clock genes are involved in cancer risk.

Several epidemiological studies have also reported associations between clock gene polymorphisms and the risk of breast cancer (Hoffman *et al.,* 2010; Zhu *et al.,* 2005; Zhu *et al.,* 2008), prostate cancer (Chu *et al.*, 2008; Zhu *et al*., 2009) and non-Hodgkin's lymphoma (Hoffman *et al.*, 2009; Zhu *et al.*, 2007), but the exact mechanisms by which these polymorphisms may influence cancer risk are not known. Recent studies also suggest that certain clock gene polymorphisms may interact with night work to increase the risk of breast cancer (Truong *et al.*, 2014).

All of this evidence strengthens the assumption that circadian desynchronisation, as occurring in people with atypical work hours, may lead to a loss of control over cell proliferation in the tissues and promote the development of cancer.

Exposure to light at night and suppression of melatonin production

Melatonin is a hormone produced by the pineal gland with 24-hour timing. In the absence of light, its production peaks during the night. Laboratory studies in animals suggest that melatonin is an inhibitor of tumour development, but this issue remains a subject of debate.

In vertebrates, the timing of melatonin production is regulated by the central circadian clock but is also influenced by light, *via* a neural pathway between the retina and pineal gland. Melatonin production is nocturnal, and it can be suppressed by exposure to light, partially or completely, depending on the intensity and spectrum of light and the duration of exposure. In working conditions at times usually dedicated to sleep, exposure to artificial light at night partly inhibits melatonin secretion and may therefore inhibit its anti-carcinogenic effects (Stevens *et al.*, 2014).

While it is clear that melatonin has oncostatic effects and that exposure to light at night reduces melatonin levels in laboratory studies undertaken in healthy volunteers, the link between cancer and melatonin suppression has not been proven. This assumption, also referred to as the "light at night" (LAN) theory, should therefore be confirmed by additional studies.

Sleep disorders

Shift workers with night hours experience sleep disorders with a significantly reduced sleep duration. Several possible biological models have been described to explain how sleep quality and quantity may influence the risk of cancer.

The most relevant model relies on the assumption of immunosuppression related to sleep disturbances, since sleep usually contributes to the proper functioning of the immune system. This immunosuppression mechanism suggests that individuals with impaired sleep quality have an increased risk of cancer related to immune deficiency. However, the impact of sleep disorders on cancer risk is difficult to examine in epidemiological studies, due to the many confounding factors to be taken into account, but this line of research should be explored.

Lifestyle factors

Night work is often associated with behaviours having a negative impact on health, such as tobacco or alcohol consumption, physical inactivity, and obesity. The link between these risk factors and cancer has been proven by several studies. While they can increase the harmful effects of night work on health, they cannot be considered as the single cause of increased cancer risk in exposed workers. In most of the epidemiological studies on the relationship between night work and cancer risk reviewed above, the confounding effects related to these factors were adequately taken into account.

Vitamin D deficiency

This assumption is based on the idea that night workers have fewer opportunities to be exposed to daylight and the sun. There is also evidence suggesting that sun exposure provides protection against colorectal, prostate and breast cancers and non-Hodgkin's lymphoma, by increasing vitamin D production (Kimlin *et al.*, 2007; van der Rhee *et al.*, 2009). This assumption has not yet been widely corroborated; only one study showed reduced vitamin D in night workers (Romano *et al.,* 2015).

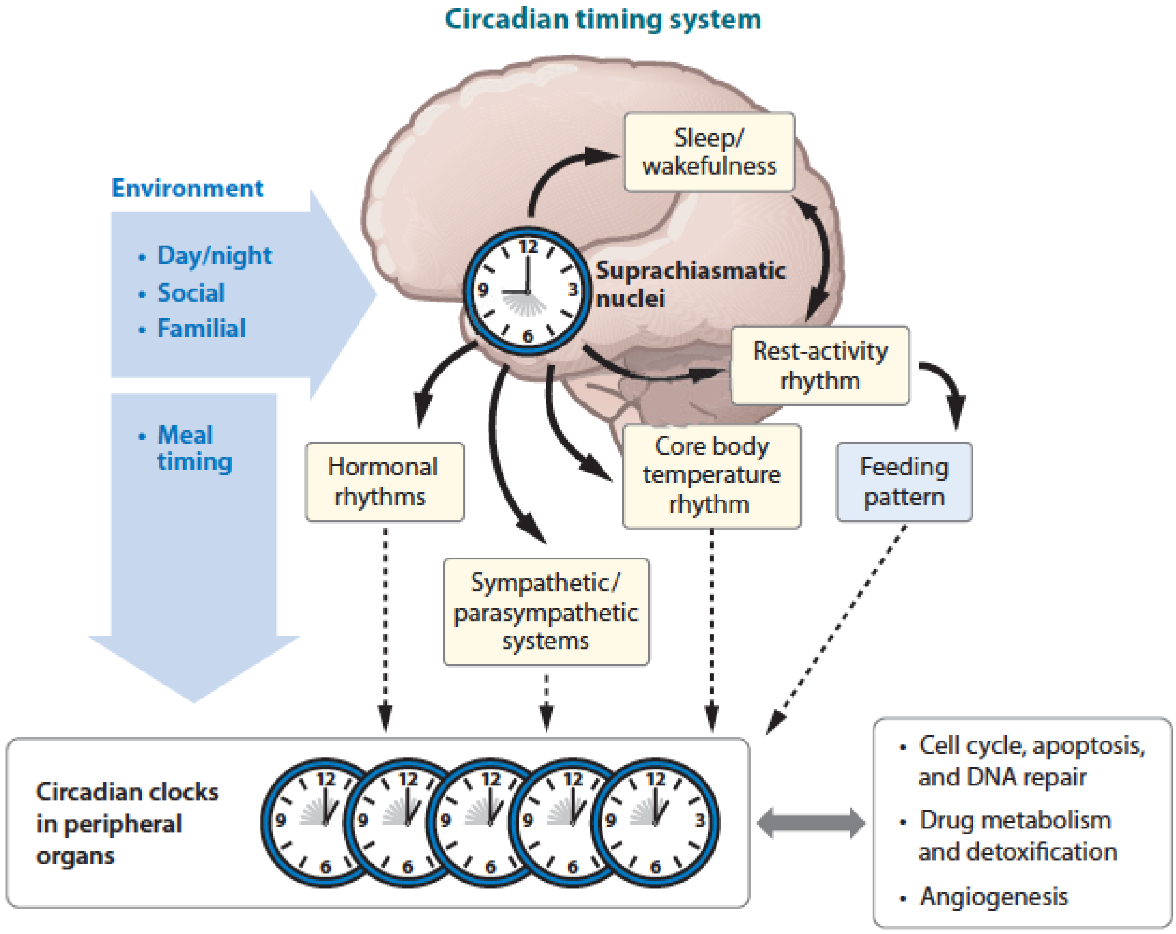


Figure 1

Schematic representation of the CTS. The CTS is composed of (*a*) a hypothalamic pacemaker, the suprachiasmatic nuclei SCN, (*b*) an array of SCN-generated circadian physiology outputs, and (*c*) molecular clocks in the cells of all peripheral tissues. Molecular clocks rhythmically control xenobiotic metabolism and detoxification, cell cycle, apoptosis, DNA repair, and angiogenesis over a 24-h period. The CTS is synchronized with time cues provided by light-dark cycles and other environmental factors. Circadian physiology outputs can also serve as CTS biomarkers.

Figure 42: figure summarising the five assumptions for the mechanisms of carcinogenesis (Levi *et al.,* 2010)

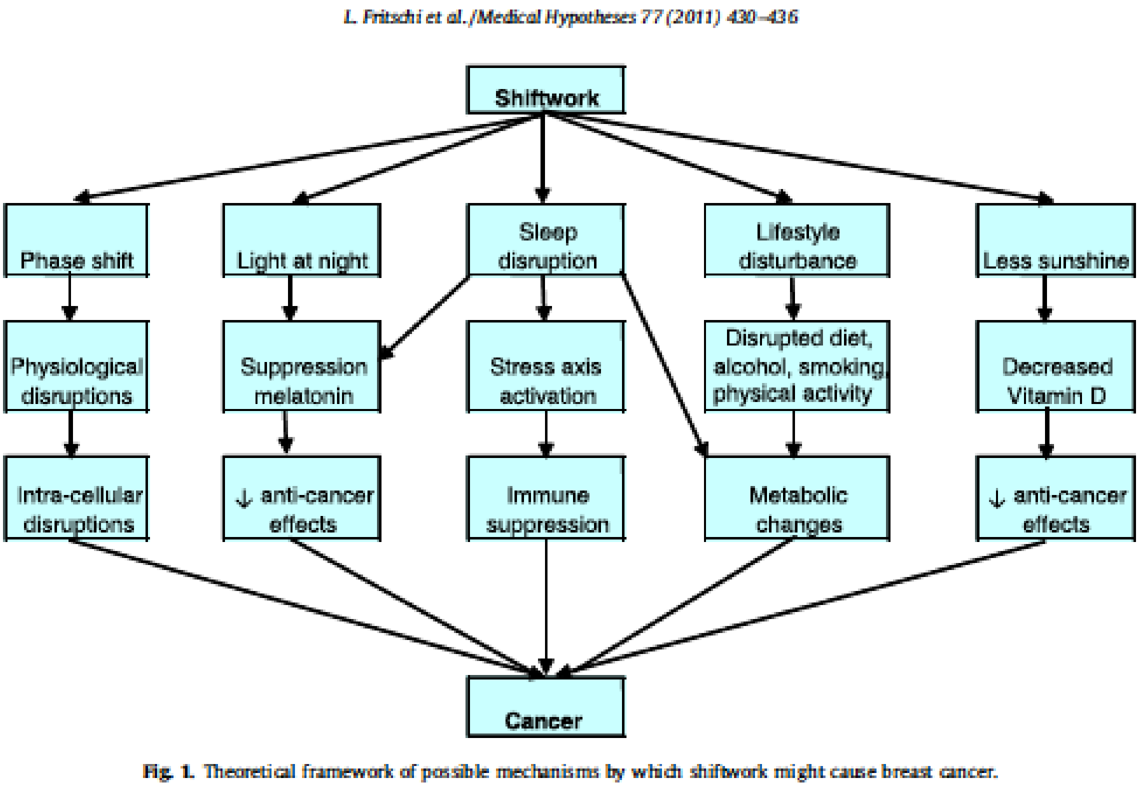


Figure 43: assumptions for the mechanisms of carcinogenesis (Fritschi *et al*., 2011)

6.3.5.5 Assessment of the level of evidence

6.3.5.5.1 Breast cancer

There are generally weak statistical associations between breast cancer incidence and exposure to night work, measured using various criteria. However, due to methodological difficulties and the lack of consistency between study results, it is not possible to provide a clear response regarding whether there is a causal link.

In particular, the expert group points out that due to the lack of standardisation in the measurement of exposure, it is not possible at this stage to draw a coherent picture of the risk of breast cancer in women involved in night/shift work. It acknowledges the progress made by studies published since the IARC report of 2007, which have improved the characterisation of exposure to night work, but without achieving the level of detail required to assess, in a satisfactory and reproducible manner, the circadian disruptions related to night work that are likely to increase the risk of cancer. It also notes that the assumption of an increased risk of breast cancer associated with long durations of exposure to night work (≥ 20 years), observed in earlier studies, has not always been confirmed. Lastly, it considers that the existence of residual confounding biases, related to certain occupational exposures or certain individual risk factors that are more common in night workers, which could explain some of the observed associations, cannot be completely ruled out.

Based on the analysed epidemiological studies, the expert group concludes that the evidence supporting an effect of work including night hours on breast cancer risk has been strengthened by the studies published since the IARC evaluation in 2007 but remains limited since it is not possible to exclude, with a sufficient degree of certainty, the existence of biases explaining the associations observed in the analysed studies (see Figure 44).

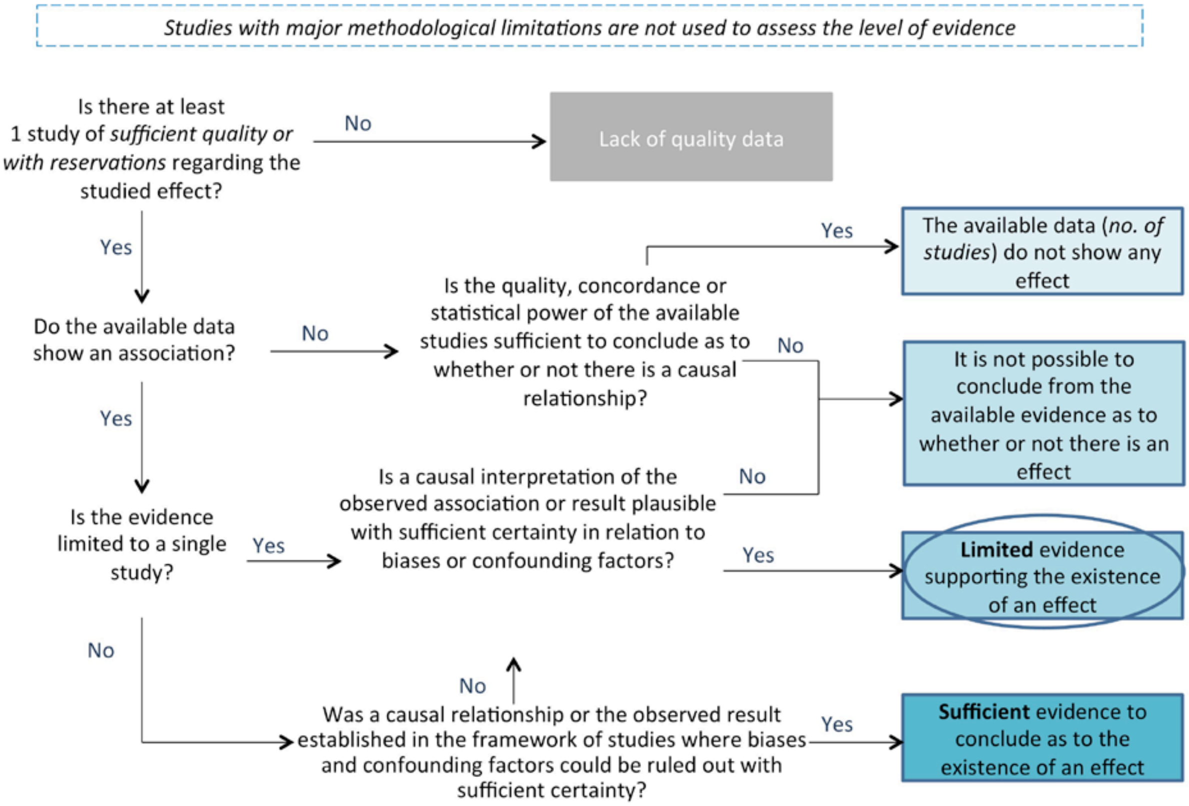


Figure 44: diagram for the assessment of epidemiological studies on breast cancer

6.3.5.5.2 Prostate cancer

On the basis of the available epidemiological studies, the expert group considers that the results suggest the possibility of an increased risk, but the evidence is insufficient; no conclusions can be drawn and the evidence will need be confirmed by further studies (see Figure 45).

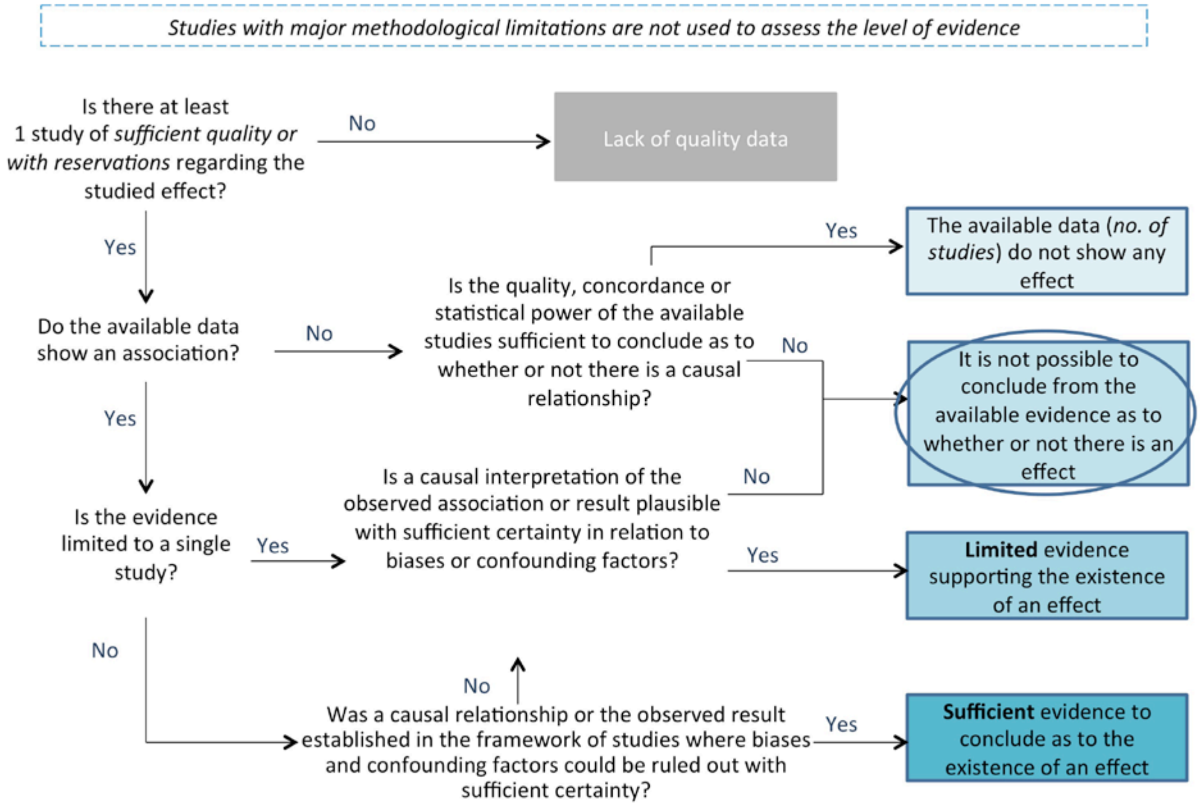


Figure 45: diagram for the assessment of epidemiological studies on prostate cancer

6.3.5.5.3 Other cancers

On the basis of the available epidemiological studies, the expert group considers that it is not possible to conclude from the available evidence as to whether night work has an effect on other types of cancer (see Figure 46).

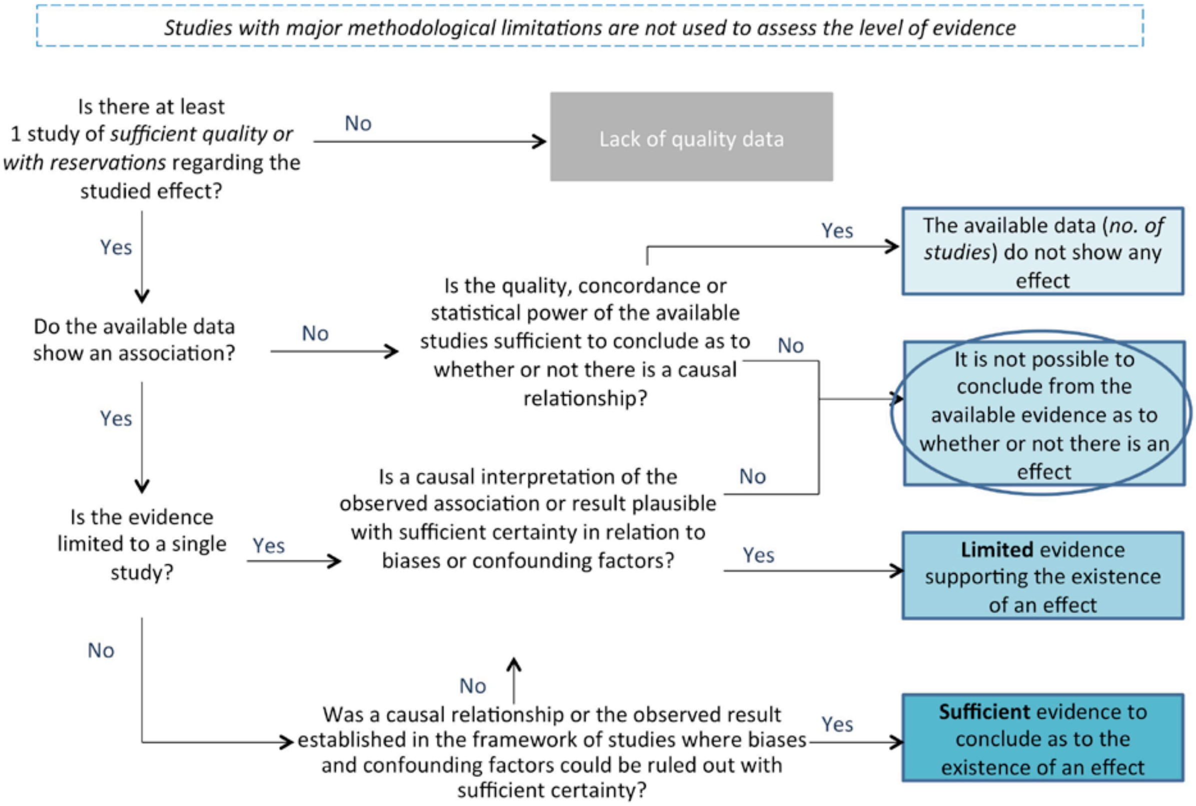


Figure 46: diagram for the assessment of epidemiological studies on other cancers

6.3.5.5.4 Conclusion

The expert group conducted a critical analysis of the epidemiological studies on the risk of cancer related to work including night hours. On this basis, it considers that there is information supporting an effect of night work on the risk of breast cancer, with limited evidence, and that it is not possible to conclude as to an effect for other cancer sites based on the available studies.

The expert group also considered the results of experimental studies in animals examining the links between disruptions caused to the circadian rhythm and the development of cancer, but did not critically analyse them. It acknowledges the existence of pathophysiological mechanisms that may explain the carcinogenic effects of disruptions to the circadian rhythm.

Based on the results of the epidemiological studies analysed and the results of experimental and biological studies, the Working Group concludes that night work has a probable effect on the risk of cancer (see Figure 47).

<table>
<tr><td colspan="2" rowspan="2"></td><td colspan="2">Evidence of the existence of the effect in experimental studies in humans or animals</td></tr>
<tr><td>Evidence supporting the existence of an effect</td><td>No evidence supporting the existence of an effect</td></tr>
<tr><td rowspan="5">Evidence of the existence of the studied effect in epidemiological studies</td><td>Sufficient evidence to conclude as to the existence of an effect</td><td colspan="2">Proven effect</td></tr>
<tr><td>Limited evidence supporting the existence of an effect</td><td>Probable effect</td><td>Possible effect</td></tr>
<tr><td>It is not possible to conclude from the evidence as to whether or not there is an effect</td><td rowspan="2">Possible effect</td><td rowspan="2">It is not possible to conclude from the available data as to whether or not the studied effect exists</td></tr>
<tr><td>Lack of quality data</td></tr>
<tr><td>The available data do not show any effect</td><td>It is not possible to conclude from the available data as to whether or not the studied effect exists</td><td>Probably no effect</td></tr>
</table>

Figure 47: diagram for the assessment of the effect of night work on cancer risk

6.3.6 Health effects not analysed in this report

Health effects not selected for the detailed analysis have, however, been described in this section, based on recent summaries and reports. Reproduction and pregnancy, as well as the link between gastrointestinal diseases and night work, have been widely studied, including by the French National Authority for Health (see HAS, 2012). A considerable number of articles are indeed available on this subject, but few publications have appeared since 2010. Lastly, few data are available on the effects associated with the immune system or the effects relating to the interaction between pharmacology and night work.

6.3.6.1 Gastrointestinal diseases

The literature search based on the equation established by the Working Group regarding the effects of night shift work on the gastrointestinal tract targeted 11 publications between January 2010 and December 2013. Three confirmed the negative effect of night shift work on the gastrointestinal tract, especially involving irritable bowel syndrome in nurses and nursing assistants (Nojkov *et al.*, 2010; Kim *et al.*, 2013) and gastrointestinal problems in Iranian petrochemical employees working 12-hour shifts (Choobineh *et al.*, 2012).

Meal times are major synchronisers of human life, having both a physiological and social content. Although shift workers do not significantly modify their total energy intake, they change the time and frequency and sometimes the content of their meals (more fats and carbohydrates in many cases), which are often eaten cold and during short breaks (snacking).

After sleep disorders, digestive disorders are most commonly described by night shift workers (20% to 75% *versus* 10% to 25% of day workers), since they are connected to phase shifts between meals and the normal circadian phases of gastrointestinal functions (such as gastric, pancreatic and biliary secretion, enzymatic activity, intestinal motility, the rate of nutrient absorption, and the hormones that regulate hunger and satiety) and changes in the quality and composition of foods (more pre-packed foods and carbonated beverages) (Lennernas *et al.,* 1994).

There are many surveys documenting that gastrointestinal disorders are more common in night shift workers than in day workers. These disorders vary, including changes in bowel habits (mainly constipation), digestion problems (flatulence and pyrosis), and more serious disorders such as chronic gastroduodenitis, peptic ulcer, and irritable bowel syndrome. These disorders were primarily reported in the past in several epidemiological studies, most of which were cross-sectional and not homogeneous in terms of the diagnostic methods used (questionnaires, clinical reports, insurance data, x-ray exams, endoscopy) and control for confounding factors (smoking, age, socio-economic status) (Colquhoun *et al.,* 1996; Knutsson, 2003).

A Japanese study on peptic ulcer (Segawa *et al.,* 1987), covering around 12,000 workers in several sectors, and the combination of x-rays and endoscopy, showed a doubling of the relative risk of peptic ulcer in night shift workers compared to day workers (2.38% *versus* 1.03% for gastric ulcer, and 1.37% *versus* 0.69% for duodenal ulcer). Moreover, some studies have shown that infection with *Helicobacter pylori* (which is considered the main cause of ulcer) is more common in night shift workers than in day workers, which is probably a sign that shift work impairs natural gastric defences (Zober *et al.,* 1998; Pietroiusti *et al.,* 2006).

A recent systematic review (Knutsson and Boggild, 2010) of 20 epidemiological studies on the association between night shift work and gastrointestinal diseases reported positive associations in four of six studies for gastrointestinal disorders, five of six studies for peptic ulcers, two of three studies for functional intestinal disorders, one study for gastro-oesophageal reflux, one of two studies for chronic inflammatory digestive diseases, and one of two studies for digestive cancers. However, the authors criticised the lack of control for confounding factors (age, smoking, socio-economic status, medications) in the studies, the lack of cohort and longitudinal studies, the lack of systematic questioning on digestive disorders, and the use of declarative data on work schedules.

The few retrospective studies undertaken often found conflicting results regarding disorders of the gastrointestinal tract in shift workers including night workers compared to day workers, due to a strong self-selection effort for night shift workers. In some cases, disease incidence among night shift and day workers was the same, but was higher for night workers transferred to day work for health reasons. In some studies, the prevalence of peptic ulcer was two to eight times higher in night shift workers than in day workers. In addition, the period between the start of work and the diagnosis of peptic ulcer was significantly shorter in night workers: however, it should be noted that over the past few years, new diagnostic techniques and the ability to better define specific therapies have helped reduce cases of chronic gastroduodenal disease.

The conclusions of the HAS report specified that four of six studies found a positive association between digestive symptoms and shift work, and five of six studies reported a moderate increase in the risk of ulcer in shift workers (relative risk close to 2 depending on the study).

The data remained insufficient to draw a conclusion as to functional intestinal disorders, gastro-oesophageal reflux, and chronic inflammatory bowel diseases.
In conclusion, shift and/or night work was associated with a moderate increase in the risk of peptic ulcer and digestive symptoms (NP 4).

The HAS stated that signs of functional dyspepsia and ulcer syndrome are the clinical phenomena to be monitored for gastroenterological disorders. It also indicated that specialised care is recommended when necessary.

6.3.6.2 Immune diseases

The literature search based on the equation established by the Working Group regarding the effects of shift work including night work on the immune system targeted 28 publications between January 2010 and December 2013. Of these 28 publications, 11 were relevant for the investigation of this effect.

These publications included work by a Swedish team (Hedström *et al.*, 2011) who investigated the link between multiple sclerosis and night shift work for the first time. In fact, the environment plays a major role in the aetiology of multiple sclerosis. Two population-based case-control studies were undertaken. The first study included 1343 incident cases and 2900 controls, and the second included 5129 prevalent cases and 4509 controls. The rate of multiple sclerosis was compared between groups that had been exposed to night shift work and those that had never been exposed, for various age groups. In both studies, there was a significant association between night shift work at a young age and the development of multiple sclerosis (OR = 1.6; [95% CI = 1.2-2.1] in the incidence study and OR = 1.3 [95% CI = 1.0-1.6] in the prevalence study). In the incidence study, the OR for multiple sclerosis was 2.0 (95% CI = 1.2-3.6) for those that had been exposed to night shift work for at least three years before the age of 20, compared to those that had never been exposed. The OR for the corresponding comparison in the prevalence study was 2.1 (95% CI = 1.3-3.4). The observed associations between night shift work at a young age and the development of multiple sclerosis in two independent studies strengthened the idea of an actual association. The consequences of night shift work such as circadian disruption, sleep deprivation and the disruption of melatonin secretion may promote inflammatory responses and thus be part of the mechanisms underlying this association. Experimentally in humans, sleep deprivation, even limited to one night, led to immune profile alterations (TNF alpha, CRP, cytokines, associated with changes in cortisol levels) (Faraut *et al.*, 2013).

A recent publication by the same team (Hedström *et al.*, 2015) studied the risk of multiple sclerosis based on age when first exposed to night shift work to attempt to see if the results were reproducible. A case-control study including 2337 cases and 4904 controls was undertaken. The OR related to the development of multiple sclerosis was 1.5 (95% CI = 1.2-1.8) for people who had started night shift work before the age of 20. This association was less pronounced (OR = 1.2; [95% CI = 1.1-1.4]) in populations who had started night shift work at the age of 20 or later. Thus, the effects of night shift work were more pronounced in subjects exposed at a young age, irrespective of the duration of shift work and the onset of the disease. These results suggest that young adults are more vulnerable to the risk of developing multiple sclerosis when exposed to night shift work.

6.3.6.3 Fertility, reproduction, pregnancy

Effects on female reproductive health

Most of the articles identified explored harmful effects in women, primarily in relation to pregnancy or the menstrual cycle. Female reproduction rhythms are partly controlled by the circadian system. Studies have suggested that women working night shifts are more likely to have altered ovulation patterns (and therefore fertility problems). Moreover, in pregnant women, night shift work may increase the risk of pregnancy complications and affect foetal well-being, due firstly to the mother's fatigue related to sleep deprivation and secondly to the disruption of hormonal circadian rhythms and the mother's sleep.

In its 2012 report, the HAS analysed five meta-analyses on night and/or shift work and effects on pregnancy (Quansah *et al.*, 2010; Croteau *et al.*, 2007; Bonzini *et al.*, 2007; Mozurkewich *et al.*, 2000; Bonzini *et al.,* 2011) and two prospective cohort studies on pregnancy outcomes (Niedhammer *et al.*, 2009; Abeysena *et al.*, 2009). Four of the meta-analyses found a positive association between night shift work and spontaneous abortion and premature delivery, and a probable association between night shift work and low weight for gestational age. However, a prospective cohort study did not find any association between night shift work and low birth weight (< 2.5 kg and < 3 kg), premature delivery or low weight for gestational age. In its report, the HAS concluded that shift and/or night work can be associated with a moderate increase in the risk of spontaneous abortion (relative risk ranging from 1.44 to 1.69 according to the meta-analyses)[54], premature delivery (relative risk ranging from 1.18 to 1.24 according to the meta-analyses), and intrauterine growth restriction (relative risk close to 1.1 according to the meta-analyses). The HAS indicated that further studies are required regarding the risk of low birth weight and recommended avoiding shift work and night work for pregnant women from 12 weeks of amenorrhoea (Article L 1225-11: pregnant workers and those who have recently given birth benefit from protective measures: at their request or at the written request of the occupational physician, they shall be assigned to a day shift throughout the duration of their pregnancy in particular, with no decrease in their compensation).

Below we present the results of the main publications published after 2010. The meta-analysis by Bonzini *et al.* (2011) studied the association between night shift work and preterm delivery, low birth weight, low weight for gestational age, and preeclampsia. This meta-analysis focused on 36 articles (17 for preterm delivery, 10 for low weight for gestational age, six for low birth weight, and three for preeclampsia or gestational hypertension). The meta-analysis concluded there was a relative risk of 1.03 for preterm delivery (95% CI = 0.93-1.14), 1.27 for low birth weight (95% CI = 0.93-1.74), and 1.12 for low weight for gestational age (95% CI = 1.03-1.22). The main limitation of this study was that shift work was not clearly defined. The mechanisms involved in the effects of shift work on pregnancy are poorly understood.

The review by Van Melick *et al.* (2014) studied the association between night shift work and the risk of preterm birth. Sixteen studies were included in this meta-analysis; eight were deemed of high quality and the eight others were deemed of moderate quality. An association between night shift work during pregnancy and the risk of preterm birth was found (OR = 1.04; [95% CI = 0.9-1.2]) but was statistically marginal. The authors indicated there was a lack of good-quality data on pregnancy complications for each trimester, especially the third trimester. The size of the study samples decreased considerably given the decrease in exposure to shift work in women as pregnancy progressed. Therefore, no robust conclusions can be drawn.

Effects on male reproductive health

As for females, male reproduction rhythms are partly controlled by the circadian system, and melatonin is thought to influence sperm physiology (Ortiz *et al.*, 2011).

Only two articles were found: a case-control study reported a link between night work and infertility (male infertility was defined as the act of consulting in a fertility clinic with no female factors of infertility; El-Helaly *et al.*, 2010) whereas a longitudinal study found no relationship between shift or night work and sperm quality measured by several criteria (semen volume,

[54] The HAS underlined that this statement was associated with a level of evidence of 2, i.e. it was founded on a scientific presumption provided by studies with an intermediate level of evidence.

concentration, morphology, and DNA fragmentation, Eisenberg *et al.*, 2015). Therefore, no conclusions can be drawn.

7 Traumatic injuries, accidentology

7.1.1 Introduction

Knowledge provided by the human and social sciences (ergonomics, sociology, psychology, etc.) as well as analytical methods in accidentology have evolved considerably, in particular following the many studies on human reliability and ergonomics that explain the mechanisms of interaction between human and organisational safety factors.

Analysing causes of accidents by the "human and organisational safety factors", used primarily in industrial safety, also provides relevant information for better understanding the complexity of the work situations that contribute to accidents and the interaction of human and organisational factors, as may be the case with night work.

Although this cannot be applied to the analysis of all occupational accidents, it can help avoid diagnoses that are over-simplistic because they are often based on partial analyses focusing on behavioural factors concerning the actors, rather than on causes of occupational accidents potentially involving major risks: organisation of work, design of equipment and work stations, management, working constraints and conditions, levels of regulated and managed safety, individual and collective means of regulating activity, *etc*.

All these essential factors to consider when analysing the work can include elements that vary greatly between situations of regular day work and shift work including night hours, for the same occupation, position or work process.

In addition, the elements of the work itself, whether exposure factors or modulators of the risk levels associated with shift or night work, cannot be understood on the same level as the individual human or behavioural factors that determine the adaptation strategies used to manage the risks contributing to accidents in these work situations, with the strategies themselves being subject to great variability.

For example, the strategies adopted by operators to maintain wakefulness or a sufficient level of vigilance, the time taken and the means used to anticipate risks, correct errors and protect themselves, as well as the procedures more generally, differ depending on their age, physiological parameters, experience, etc.

The contribution made by collective bodies, which is often inadequately analysed or estimated in studies, is of major importance: detection and correction of individual errors, help limiting the effects of individual variations in state, exchanges and capitalisation of experience with the introduction of shared professional rules, etc. Thus, any organisational changes liable to weaken these bodies or isolate the workers present an obstacle to occupational safety and lead to an increase in the risks contributing to accidents in shift or night work.

The same is true when the prescribed organisational systems are not sufficiently coordinated with the actual knowledge and the complexity of the work situations as perceived by the operators and collective bodies. Preventing risks of accidents related to night work, in particular occupational accidents involving safety, must therefore include a detailed ergonomic analysis of the work situations concerned, from every aspect (conceptual, organisational, human, etc.).

The epidemiological studies summarised in this chapter, which examine the links between shift or night work and the risk of an occupational accident, are useful for making estimates about the overall level of risk contributing to occupational accidents, providing descriptive statistics, and identifying elements related to the forms of shift or night work they may take into account and that may be key factors at a population level. This is the case, for example, with the vigilance problems and cognitive disorders resulting from various forms of shift work, which act as intermediary factors in the causality between the work and the risk.

Nevertheless, these same epidemiological studies remain limited in their ability to provide conclusions, because they cannot take into account all the elements relating to the work and activity that emerge from a detailed observational qualitative analysis of the work situations themselves. They can only therefore provide inevitably limited information for estimating the causality between night work and accidental risk, and for recommendations on prevention.

For this chapter on accidentology, the experts therefore combined the two bibliographical methods: for the human and social sciences and for epidemiology – preferred for the analysis of the chapters on the health effects – with a rigorous analysis of the scientific publications.

This chapter brings together the main relevant studies, review articles or study reports published before 2010 and selected by the experts, as well as an analysis of more recent studies (2010-14) identified by a keyword search using the *Scopus* search engine.

7.1.2 Accident rates and night work or shift work including night work

Well before a pathology becomes established, the very short-term effects of night work, whether fixed or rotating, can be seen on the levels of vigilance and physical, cognitive or psychomotor performance. An initial period of sleepiness – the longest – occurs around the normal bedtime and reaches a peak a few hours later (i.e. around five o'clock in the morning on average in people usually working during the day). The second peak of sleepiness occurs around twelve hours later (i.e. between 2pm and 4pm on average in people usually working during the day): this is the "wave of fatigue", more specifically the increase in sleepiness, at the start of the afternoon. The change in these rhythms (their phase and therefore the hours) is altered when people work at night (Chaumont *et al.*, 1979; Reinberg *et al.*, 1979; Vogel *et al.* 2012). This decline in vigilance and cognitive performance during night work is perfectly illustrated by the major industrial disasters which, for the most part, occurred at night [Chernobyl (1.23am), Three Mile Island (4am), Bhopal (12.30am), Exxon Valdez (12.04am)], with all being – at least partly – ascribed to human and organisational factors that resulted in an impaired level of vigilance and cognitive functioning (Mitler *et al.*, 1988; reviewed in Reinberg *et al.*, 2015).

The analyses of these major accidents highlighted the influence of the decline in vigilance and cognitive capacities related to the night work on the operators' mental representations: the difficulty in mentally generating an adequate representation of the state of a system is exacerbated if the operator is in an isolated situation or lacks an immediate deputy, as can be the case with night work.

Organisational and contextual problems with work therefore have a broad influence on the behavioural and physiological characteristics of individuals. In this framework, an individual's characteristics will help them "adapt" or not, with an underlying risk of decompensation; these are not then "risk factors" but modulators of effects.

Moreover, although similar in theory, work carried out at night is in fact not quite the same as that carried out during the day. There is therefore a variation in the actual work carried out at night in the same way as the physiological characteristics of individuals (vigilance levels, in particular) vary over the hours of the day and night.

Several questions therefore arise in the framework of this chapter:

- Are occupational accidents more numerous at night?
- Are occupational accidents more serious at night?
- Are occupational accidents occurring at night due to physiological disorders such as fatigue-related loss of vigilance, to the specific content and conditions of night work, or to a combination of these factors, with fatigue and its consequences (sleepiness, loss of vigilance) constituting an intermediate mechanistic factor of the occupational accident?

7.1.3 The indicators used

Let us begin with the concept of indicator. In France, under the terms of Article L.411-11 of the Social Security Code (CSS), "an occupational accident is considered to be, regardless of the cause, an accident arising due to or in the course of work, to any person employed or working in any capacity or in any place whatsoever, for one or more employers or company managers". For it to be an occupational accident, three conditions must be fulfilled; there must be an unusual circumstance that resulted in an immediate or deferred injury; this accident occurred in the course of or due to the work; and a link can be established between the injuries suffered and the accident reported. Any accident occurring during and at the place of work is presumed to be an "occupational accident" (source: INRS).

In France, four indicators are typically used to calculate and monitor the change in the risk level for an activity or sector:

- Frequency index (FI) =
  (number of accidents giving rise to a first compensation payment/workforce) x 1000.
- Frequency rate (FR) =
  (number of accidents giving rise to a first compensation payment/hours worked) x 1,000,000.
- Severity rate (SR) =
  (number of days lost through temporary incapacity/hours worked) x 1000.
- Severity index (SI) =
  (sum of the rates of permanent incapacity/hours worked) x 1,000,000.

It should be emphasised, however, that many studies do not use these "French" indicators, but use others that are sometimes specific to the country of the observed populations, or established specifically for the needs of the study.

7.1.4 The available data

7.1.4.1 French institutional data

In addition to its prevention, pricing and compensation missions, each year the Occupational Risk Directorate (DRP) of the National Health Insurance Fund for Salaried Workers (CNAMTS) collects and publishes detailed statistics on accidents in the workplace, commuting accidents and occupational diseases. We contacted the DRP, which provided us with the only existing sector study on the time of occurrence of occupational and commuting accidents (CNAMTS, 2009). However, it was not possible to exploit this sector study by the CNAMTS (2009) on the time of occurrence of occupational and commuting accidents in 2008: the scope of analysis for accidents occurring during the day was not limited to the same activities as those leading to accidents at night. Thus, for example, for a given establishment, which could have constituted the analysis framework, there may be more staff during the day than at night, carrying out quite different tasks.

Note however that the HAS (HAS, 2012) stated that with regard to occupational accidents, five international studies had been identified and their analysis suggested that shift and/or night work seems to be associated with an increased risk of occupational accidents and absences from work (NP4). It was reiterated, however, that this needed to be confirmed in a French context. Lastly, again according to the HAS and to the literature, shift and/or night work can be associated with an increased risk of traffic accidents and near-accidents (NP3).

7.1.4.2 European data

European statistics on occupational accidents, Eurostat (SEAT[55]) come from administrative data that have been collected annually since 1994 (following a pilot data collection scheme in

[55] Eurostat is the Statistical Office of the European Union.

1993). The SEAT data are based on reports of occupational accidents submitted to public (Social Security) or private insurance organisations, or labour inspectorates, depending on the systems in the Member States. The most recent SEAT data relate to the 1999 reference year for the final data, and to 2000 for a few aggregate estimates[56]. European social statistics on occupational accidents and health problems associated with night and shift work reveal the following figures for 1999:

NB: The risk indicator of an occupational accident is the incidence rate = (number of occupational accidents occurring during the year/number of people in employment in the reference population) x 100,000.

Table 46 – Relative incidence rate of accidental injuries at work by frequency of night work, age and severity
EU-11+HU, 1999, all NACE branches, most recent accidental injury only ([1]), EU mean rate = 100 for each severity

	Total	25-34 years	35-44 years	45-54 years	55-64 years
			All accidents with or without days' absence from work		
Total	100	118	94	81	83
Usually work at night	143	175	142	86	165
Sometimes work at night	149	156	162	126	158
Never work at night	93	110	85	78	76
			More than 3 day's absence		
Total	100	117	100	80	79
Usually work at night	116	103	128	84	185
Sometimes work at night	151	169	169	127	177
Never work at night	95	115	92	76	68
			2 weeks' absence or more		
Total	100	106	110	80	85
Usually work at night	109	67	160	47	124
Sometimes work at night	144	158	154	136	191
Never work at night	96	106	102	78	78

Data not available for D, E, IRL, L and UK.
([1]) Only accidental injuries occurred during the past 6 months by employees that answered directly to the survey and in the framework of the main job for the reference week of the LFS (respectively of the 2nd or 3rd quarter 1999 depending on the countries).

Figure 48: Relative incidence rate of accidental injuries at work according to the frequency of night work, the age of employees and the severity (in number of days of absence), Eurostat.

Figure 48 above shows that the figures relating to the number of accidents or number of days of absence are higher for people usually working at night than for those working at night sometimes or not at all. There is also a decrease in the number of accidents or days of absence as a function of age.

[56] The SEAT project was implemented in application of Directive 89/391/EEC(1) on the introduction of measures to encourage improvements in the safety and health of workers at work, in which Article 9, paragraphs (c) and d) establish the obligation for the employer to keep a list of occupational accidents resulting in a worker being unfit for work for more than three days, and draw up, in accordance with national laws and/or practices, reports on occupational accidents suffered by his workers.

Complete method available from http://ec.europa.eu/eurostat/documents/3217494/5638417/KS-BP-02-002-3A EN.PDF/6ba12a97-1d41-40cd-abfa-7a65c6e65587.

Table 45 – Relative incidence rate of accidental injuries at work by frequency of shift work, age and severity
EU-11+HU, 1999, all NACE branches, most recent accidental injury only (1), EU mean rate = 100 for each severity

	Total	25-34 years	35-44 years	45-54 years	55-64 years
			All accidents with or without days' absence from work		
Total	100	117	93	80	87
Usually work shift work	148	172	140	113	178
Sometimes work shift work	136	151	155	95	133
Never work shift work	89	104	80	74	71
			More than 3 day's absence		
Total	100	118	99	78	79
Usually work shift work	138	138	158	112	161
Sometimes work shift work	130	105	166	104	148
Never work shift work	92	115	83	71	64
			2 weeks' absence or more		
Total	100	105	110	80	81
Usually work shift work	135	114	182	109	163
Sometimes work shift work	129	96	169	109	170
Never work shift work	92	105	92	74	66

Data not available for D, E, IRL, L, FIN and UK.
(1) Only accidental injuries occurred during the past 6 months by employees that answered directly to the survey and in the framework of the main job for the reference week of the LFS (respectively of the 2nd or 3rd quarter 1999 depending on the countries).

Figure 49: Relative incident rate of accidental injuries at work according to the severity (in number of days of absence), the frequency of shift work and the age of employees (EU mean rate = 100 for each severity)

Similarly, Figure 49 above shows that the figures relating to the number of accidents or number of days of absence are higher for people usually working shifts than for those working shifts sometimes or not at all. There is also a decrease in the number of accidents or days of absence as a function of age.

Moreover, based on an analysis of occupational accidents in the EU between 1998 and 1999, Dupré[57] stressed that one of the factors aggravating the risk of accident was difficult working conditions such as shift or night work, and quantified it at +46%.

7.1.5 Literature analysis

The analysis of the international studies shows a panel of contrasting results, sometimes contradictory depending on the indicator used, but also due to the variability of the methodologies used, the diversity and complexity of the work situations considered, and the multifactorial nature of the occupational accidents.

However, the figures clearly suggest that shift and/or night work is associated with an increased accident rate (Salminen, 2010).

What about frequency?

The Canadian cross-sectional study by Wong *et al.* (Wong *et al.*, 2011) examined the risk of occupational accidents (OAs) according to the type of shift work practised. The frequency of OAs decreased in Canada between 1996 and 2006, but this decrease was not observed in shift/night workers. The proportion of errors was greater among night workers (5.9%), shift workers (3.9%) and workers subject to other atypical hours (3.1%) compared to day workers (2.9%). One of the biases identified was that night and shift work is more physical, but the risk of OAs remained higher among night and shift workers even after adjusting for this

[57] Dupré D., 2001, Statistiques en bref – Thème 3 – 16/2001 – Les accidents du travail dans l'UE 1998-1999 [Statistics in Brief – Theme 3 – 16/2001 – Occupational Accidents in the EU 1998-1999].

factor. This study also showed a difference between men and women: the excess risk of accident attributed to rotating and night shifts was 11.3%, and this excess risk was higher in women (14.4%) than in men (8.2%). This increased OA risk among women was particularly high in shift workers and can be explained in part by less predictable work schedules. The limitation of this type of large-scale study (reports from a national cohort comprising a very large number of companies) is that it is unable to take into account the differences in jobs practised, in particular here between men and women, or to ensure the consistency of practices in terms of compensation method.

The Canadian study by Mustard *et al.* (Mustard *et al.*, 2013) focused on the time of occurrence of occupational accidents between 2004 and 2008 in Canada. The analysis was carried out using data from two administrative sources of information:

- the Ontario workplace safety and insurance board (n = 458,141);
- the emergency department.

In particular, these statistics provide information on the date and time of the occupational accident and the cause of the injury. The results showed an increased risk of accidents or diseases with work carried out in the evening, at night, and early in the morning. The risk was observed equally with those performing manual work and in non-manual workers. In addition, the number of emergency department visits was three times higher between 4pm and five in the morning, with a peak between midnight and 2am. The same increased risk was observed for claims for health insurance coverage. The study showed that the risk of an accident at night was higher in those over 24 years of age (than those aged 15-24 years), and in women, all ages combined. Overall, the fraction of claims for reimbursement attributed to injuries during evening and night shifts was twice as high in women (12.5%) as in men (5.8%). This study indicated that not all visits to the emergency department gave rise to claims for coverage (40% less).

Some studies have also considered, in addition to the diurnal or nocturnal nature of the job, the effect of the successive number of nights, the length of the shifts, breaks during work, and changing from one shift to another.

Folkard and Tucker, in a review article on the question of accidents associated with night work, reported that both productivity and safety were reduced at night (Folkard and Tucker, 2003). They emphasised the importance of considering the successive number of night shifts, the length of the shift and the number of breaks allocated, to reduce accidents. For example, a 12-hour night shift that benefits from several rest breaks appears safer than an 8-hour night shift with only one.

After selecting more than 7000 articles, Wagstaff and Lie (Wagstaff and Lie, 2011) reported the results of 14 studies (selected for their high quality and relevance to the subject of accidentology). These studies all emphasised the deleterious effect of shift work on safety: indeed, all indicated at least one result unfavourable to safety associated with shift work. The analysed studies also showed the critical effects of long shifts (more than eight hours). It was also stated that night work in rotation increases the risk of accidents, whereas fixed night shift work seems more protective.

A recent comprehensive review on the question of occupational accidents identified shift/night work and shift duration as risk factors for occupational accidents (Salminen, 2010). Working for more than 12 hours, for example, doubles the risk of accidents. Afternoon and night teams are at increased risk of OAs in industrialised countries (in particular, a significant increase in the risk was noted in the United States), whereas the situation is reversed in developing countries, with an increase in OAs for morning teams. The authors explain these results by the absence of supervisors in the afternoon and night teams in these developing countries, and therefore a potential under-reporting of OAs.

Chiu and Tsai (Chiu and Tsai, 2013) examined the impact of different work schedules on sleep complaints and minor accidents during work or leisure time. This cross-sectional study resulted from a national survey conducted among 18,794 people in Taiwan. The results showed that long shifts (>8h) constitute a risk factor for insomnia, excessive daytime sleepiness, and minor accidents. After adjustment for confounding factors, the analysis indicated that switching from the evening to the night shift presents a significant excess risk of sleepiness and minor accidents compared to the fixed day shift. In this study, the night shift was not associated with more insomnia, sleepiness or minor accidents.

Again in relation to shift duration, de Castro *et al.* (de Castro *et al.*, 2010) in the Philippines studied the association between mandatory overtime, shift work and the risk of work-related injuries or illnesses, in a sample of 655 nurses. They showed that atypical working hours and mandatory overtime were risk factors for injury and absence from work, regardless of the duration of the work (or additional jobs). After adjustment for weekly working hours, shift length and demographic variables, shifts other than those in daytime hours were associated with work-related injuries and illnesses. The frequency of mandatory overtime was also associated with work-related injuries, illnesses and absences from work of more than two days caused by an occupational accident or work-related illness.

Folkard and Hill (2001) highlighted the deleterious effect of consecutive nights. The risk of accident increased in the context of successive nights of work, rising by 15% on the second night, 30% on the third and 50% on the fourth. Modelling of existing data estimated the risk on the sixth and eighth nights to be 200% and 250%.

The study by Hopcia *et al.* (Hopcia *et al*., 2012) investigated occupational accidents for consecutive and cumulative shifts. This was a cross-sectional study conducted with 502 hospital staff. It showed that the risk of occupational injury/accidents increased with the number of consecutive shifts, per week and/or per month, and with the number of cumulative hours, in particular when these shifts involved night work. The increased risk was observed when the number of cumulative hours during the previous 7 days increased, when the total number of night shifts of more than 4 hours carried out in the previous 7 days was three or more, and when the number of hours worked at night was more than 36 per week. The increased risk of injury was further accentuated if the number of hours or shifts were accumulated over a month (and not over 7 days): in particular when the number of night shifts increased.

A difference in the occurrence of accidents according to the work cycle has also been noted. Thus, the study by Violanti *et al.* (Violanti *et al.*, 2012) explored the risk of injury according to the working hours and the work activity level in 419 police officers. In this study, night work increased the relative risk (adjusted for age) of an occupational accident by 72% compared to the day shift (by 66% compared to the afternoon shift). The increased risk of occupational accidents was higher on the first day of night work (69% compared to day work), decreased on day 2, and remained stable on days 2, 3 and 4, but remained at least twice as high during night shifts compared to day and afternoon shifts. In this study, the physical activity involved in the night work represented an additional increased risk of occupational accident.

The longitudinal study by Wong *et al.* (Wong *et al.*, 2014) followed workers for six years to study the risks of OAs according to types of shift work and changes in the shift schedules. The OAs were compiled from the compensation system; minor accidents were not therefore included in this analysis. This study showed that employees working exclusively on day shifts had the fewest OAs, compared to other types of schedules.

This study also showed that the number of OAs was higher when the worker changed shift system – switching from work during the day to atypical hours but also switching from atypical hours to work during the day – and among those who remained on atypical hours. Note that the differences persisted after controlling for the content of the work. There were nuances between the genders: women were slightly more exposed to accidents when working atypical hours and when there were changes to their shift system. Here, more than the shift system in itself, it would seem to be the change from one system to another that increased the OAs, which may require a re-examination of other dimensions of the work situation (integration/training for the position, for example) that goes beyond a single physiological issue such as loss of vigilance associated with a change in sleep patterns, for example. This study does not, however, specify whether the access to compensation following an OA was identical in all jobs. If this is not the case, that could indicate a bias.

Kantermann *et al.* (Kantermann *et al.*, 2013) examined the direction of rotation of the shift teams. This was a retrospective analysis of 578 occupational accidents occurring over a 5-year period in a Belgian steel mill among a population of 730 workers subject to either a clockwise or anti-clockwise rotation direction. The results indicated that the accident rate did not differ significantly between clockwise or anti-clockwise rotations. In both types of rotation, a significantly higher rate of accidents was noted in the morning shifts compared to the night shifts. This could be related to the shift starting early (6am) and to the fact that morning shifts require the most intense work.

On the whole, these recent studies show a higher frequency of accidents during night work.

What about severity?

After a literature search based on key words (*Scopus*), surprisingly, very few studies listed between 2010 and 2014 addressed the issue of severity of OAs. This section is therefore largely based on earlier work.

The previous observations made by the INRS (INRS 2013), which drew on a review of studies in accident rates at work (Queinnec, 1992), showed a lower frequency of accidents during night work, whereas on the other hand the severity rate increased. Indeed, in his book, (Quéinnec *et al., 1992)* drew on three earlier studies: "Generally speaking, the various studies carried out in the field have led to the conclusion that the accident frequency rate decreases during the course of the night shift while the severity rate increases" (Kubler 1956; Leconte *et al.*,1988).

This result was also found by Ong *et al.* (Ong *et al.* 1987), who showed more serious injuries during the night shift – whereas the frequency of the OAs was reduced – than during morning and afternoon shifts in a steelworks in Singapore.

In 1994, Smith *et al.* published a study analysing 4645 injuries at work and showed an increase in the frequency of injuries at night (with a gradient: morning – afternoon – night). The authors also stressed the influence of the nature of the work, and identified an increase in the severity of injuries in certain types of work (Smith *et al.*, 1994).

Ogiński *et al.*, (Ogiński *et al.*, 2000) conducted a study of accident typologies in a steel mill in Poland over 38 years. They reported that the frequency of OAs did not vary according to the shifts (morning, afternoon, night) but that the night accidents were more severe, with this severity being assessed according to the number of days of absence consecutive to the accident.

The study by Violanti *et al.* (Violanti *et al.* 2013) aimed to determine whether long-term absences resulting from occupational accidents depended on the type of shift work. This was a cross-sectional study among 419 police officers in the United States. In this study, night work was associated with an increased risk of accidents. Long-term absences (>90 days) were greater following accidents that took place among police officers working night shifts compared to those working day shifts, as well as for night shifts versus afternoon shifts. The study also revealed that even short-term absences (1, 5, 15, 30 days) were increased in police officers working night shifts compared to day shifts.

In a study concerning fatal accidents, Williamson and Feyer (Williamson and Feyer, 1995) showed that in 1020 fatal occupational accidents occurring from 1982 to 1984 in Australia, the mortality rate was twice as high at night compared to the day.

Horwitz and McCall (Horwitz and McCall, 2004) carried out a study on the basis of claims for compensation by workers in Oregon from 1990 to 1997, in order to examine differences in the claims of hospital employees (n=7717) according to the shift position. The average number of days of absence for shift workers was higher for night shifts (46) than for evening (39) or day (38) shifts. Out of 10,000 employees, the rate of injuries for day shifts was estimated at 176 (95% CI = 172-180), compared with 279 (95% CI = 257-302) for the night shift and 324 (95% CI=311-337) for evening shifts. Hospital employees working evening and night shifts were thus found to be more at risk than workers in the day team with regard to injuries at work. In addition, night shift workers reported more serious accidents, judging by the length of the work absences as measured by disability leave. The authors emphasised that the workforce present and differences in work content according to the teams can also influence the risk of OAs.

However, and regarding the severity of OAs, Horwitz and McCall demonstrated the importance of the indicator used to address the concept of severity of an OA. Their results showed that the average number of days of recovery following an injury occurring at night was greater than the average number of days of recovery for injuries occurring during the day or evening. If another potential indicator of injury severity were considered, i.e. the average overall cost of coverage (including not only compensation for the days of absence from work but also the medical costs and costs related to disability and to vocational (re)training), they found no difference between the different work shifts, which led them to conclude that the severity of the injury was not increased. This questions the relevance of the indicator used to address the concept of severity of an OA, an aspect that will be discussed at the end of the chapter.

The study by Barsky (Barsky, 1992), conducted in Canada in six automotive plants, showed a reduced severity of injuries at night and in the afternoon shift compared to the morning shift.

The Australian study by Loudoun (Loudoun, 2010) analysed more than 5000 occupational accidents in the construction sector. This was a cross-sectional study that compared the frequency and severity of occupational accidents in young people and more experienced workers during the day and night shifts. The assumption was that night work increased the risk of occupational accidents, especially for young people. The results showed that young people (19-24 years) had an increased risk during the night shift. On the other hand, the study revealed no difference in the severity of the OAs.

In conclusion, among the 11 studies identified, which were often old (the 10 studies published before 2010 had been selected by the experts) and which addressed the concept of accident severity, a majority (8 out of 11) showed increased severity of OAs during the night shift.

Road risk (road accidents, commuting accidents)

Since the publication by Folkard in 1997 (Folkard, 1997) of the theory of "*Black Time*" (increased risk of traffic accidents at night for diurnal individuals), studies have shown that atypical working hours have an impact on road risk (reviewed in Philip and Akerstedt, 2006). An increased risk of traffic accidents and near-accidents has been reported, with these risks being greater when travelling to the morning shift and returning home after a night shift (Musa, 2013).

In the recent report by the HAS (HAS, 2012), it was concluded that "shift and/or night work can be associated with an increased risk of traffic accidents and near-accidents (with a low level of evidence, NP3). The estimated risk is close to 2 for accidents and varies for near-accidents between 1.84 [1.06-3.20] and 5.9 [5.4-6.3] depending on the studies".

Five recent studies (2010-14) explored the effects of night/shift work on commuting accidents by firstly examining the link with sleep disorders that can result from work in atypical hours (Ohayon *et al.,* 2010; Fruchtman *et al.,* 2011; Swanson *et al.*, 2012; Ftouni *et al.* 2013) and errors at work (Asaoka *et al.*, 2013):

In the United States, Ohayon *et al.* (Ohayon *et al.*, 2010) studied the effects of the organisation of work on sleep duration, excessive sleepiness, sleep attacks, traffic accidents, and domestic or occupational accidents on a sample of 3345 individuals aged 18 years and over, representative of the general population of the State of New York. The results of this study showed that compared to other types of work organisation, night work or day-evening-night rotation was strongly associated with short sleep duration, excessive sleepiness in situations requiring heightened attention, sleep attacks and an increase in the risk of traffic accidents.

In Israel, Fruchtman *et al.* (Fruchtman *et al.*, 2011) used a questionnaire to assess fatigue and sleep deprivation and their main consequences on a sample of 76 volunteer residents of a university hospital centre. The results of this study indicated that for these residents, the weekly duration of work was around 70 hours and the duration of sleep, usually around 6 hours per night, was reduced to 1.1 +/- 0.5 hour during a 24-hour on-call shift. Seventy-one per cent of residents reported having driven a vehicle after a shift, and 40.7% of drivers reported having felt sleepy when driving during the previous month. Eighteen and a half per cent of the residents had had a car accident after a shift during their residency, with sleepiness at the wheel being strongly associated with the risk of a car accident when driving home after a shift. These effects are possibly attributable to night work via the increased fatigue and sleepiness.

Swanson *et al.* (Swanson *et al.*, 2012) studied the risk of accidents among 1000 American drivers, of whom 68 worked at night. The purpose was to assess the association between the number of hours worked per week and night work, and drowsy driving, falling asleep while driving, and accidents due to sleepiness. The results showed that working more than 40 hours per week was associated with more drowsy driving, but not with falling asleep while driving or the risk of accidents. Night workers with or without sleep/sleepiness disorders reported drowsy driving at least once a week more often than day workers. Falling asleep while driving in the previous year appeared more frequent in night workers with symptoms, whereas no difference was noted for the frequency of accidents in this past year (although an under-reporting bias related to the declarative method of collection and to social desirability was mentioned). This study showed that both a large range of weekly hours and shift work were risk factors for drowsy driving and thus potentially for road accidents.

Lastly, Ftouni *et al.* (Ftouni *et al.,* 2013) focused on 27 nurses working at night or on shifts and studied 369 of their commutes (car driving). The purpose was to compare sleepiness during the commutes before and after a night shift, using objective and subjective measurements, and to examine the association between the sleepiness measurements and the incidents reported while driving. The results showed significantly higher subjective and objective sleepiness during the journeys after a night shift. The increase in objective sleepiness (eye measurement), but not that of subjective sleepiness, was associated with an increase in adverse driving events. The relative risk of dangerous driving events was 8 times higher after the night shift. As for the relative risk of inattention, this was 3 times higher after the night shift. Dangerous events were also more frequent if the worker had been awake for more than 16 hours at the time of the journey.

The study by Asaoka *et al.* (Asaoka *et al.*, 2013) focused on factors associated with shift work disorder in 1198 nurses (mostly women) working rapid-rotation shifts in Japan. In this study, shift work disorder (even if it was defined from questionnaires assessing insomnia and sleepiness, and not according to the criteria of the American Academy of Sleep Medicine) increased in prevalence in line with the exposure to night work (in number of years). The study reported that the risk of errors (procedures), near-misses and accidents (traffic, occupational accidents) was increased among nurses suffering from this disorder. A logistic regression analysis indicated that the factors predictive of shift work disorder were the number of hours worked per month, the number of night shifts worked per month and the chronotype (more frequent among evening chronotypes).

The five studies cited in this paragraph suggest an indirect link between shift/night work and road risk *via* problems of sleepiness or sleep disorders. All the studies concurred as to an unfavourable influence of shift/night work on the risk of road accidents.

7.1.6 Conclusion

The studies examined in the framework of this chapter show that there is generally an increased frequency and severity of accidents during night work or shifts including night work. In the analysis performed, in addition to the physiological mechanisms involved (sleepiness, sleep debt, circadian disruption), a number of elements appear in the studies and should be taken into account in the risk of accidents at work: organisational, environmental (working conditions) and managerial factors.

The question of frequency

The general trend that emerges from the in-depth analysis of the publications is that atypical working hours are harmful with regard to safety at work. Indeed, all the recent studies (2010-14) selected, apart from one – which focused on minor accidents at work and during leisure time (Chiu *et al.*, 2013) – have shown an increase in the number of occupational or commuting accidents at night or when working certain 3x8 shifts (mainly morning shifts), or when changing shifts.

The majority of studies analysed reported an increase in accidents, an increased risk of OAs during the night, and reduced safety (Wong *et al.,* 2014; Wong *et al.*, 2011; Salminen, 2010; De Castro *et al.*, 2010; Violanti *et al.*, 2012; Wagstaff *et al.*, 2011; Folkard and Tucker, 2003). This fact persists even when the studies are careful to control for the type of job practised – physical or not, manual or not (Wong *et al.*, 2011; Mustard *et al.*, 2013; Wong *et al.,* 2014). The study by Violanti *et al.* (2012) showed that physical workload was a factor increasing the risk for night workers, and Smith *et al.* (1994) also stressed the influence of the nature of the work, and identified an increase in the severity of injuries in certain types of work.

Some publications also suggested that women may be more prone to nocturnal OAs than men (Wong *et al.,* 2014; Wong *et al.*, 2011 Mustard *et al.*, 2013), as well as young workers, when this factor is included in the analysis (Mustard *et al.*, 2013). Other studies emphasised the positive role of breaks in the work, which may reduce accidents (Folkard and Tucker, 2003; Tucker *et al.*, 2003; Sallinen, 2014) and may be even more beneficial if taken in the form of a nap (see Chapter 9) (Uehli *et al.*, 2014).

Some authors stressed the influence of the length of the work shifts (Salminen, 2010): long shifts (more than eight hours) may be detrimental from the point of view of accidents (Wagstaff *et al.*, 2011) and may even promote an increase in minor OAs (Chiu *et al.*, 2013). Overtime was also identified as one of the factors influencing occupational accidents during the night (Castro *et al.*, 2010).

Regarding shift work, a single study focused on the frequency of OAs according to the direction of rotation – clockwise or anticlockwise – without finding a clear difference (Kantermann *et al.,* 2013). It should be noted however that the influence of the direction of rotation has been shown in recent studies on certain biological functions (cognition, vigilance, sleep), with a clockwise rotation being more favourable to evening chronotypes and an anticlockwise rotation more favourable to morning chronotypes (Vetter *et al.*, 2015).

An increase in occupational accidents during changes from one shift to another was identified in certain studies (Wong *et al.,* 2014; Chiu *et al.,* 2013), or during a change in the shift system: from daytime work to atypical hours, or the reverse (Wong *et al.,* 2014).

Two studies stressed that the risk of accidents at night increased with successive nights of work (Folkard and Hill, 2001; Hopcia *et al.*, 2012) and one study showed that there were more occupational accidents at the beginning of the work cycle (Violanti *et al.*, 2012).

The question of severity

Turning to the severity of occupational accidents (assessed most of the time according to the number of days of absence from work following the accident), most of the studies considered, although older, showed greater severity in accidents occurring at night (Ong *et al.*, 1987; INRS ED 5023, 2013; Oginski *et al.*, (2000); Violanti *et al. (*2013), Horwitz and

McCall (2004)). Among the studies selected, only one was concerned with fatal workplace accidents, indicating a mortality rate twice as high at night compared to the day (Williamson and Feye, 1995).

One study reported an increase in the severity of injuries with certain types of work (Smith *et al.*, 1994).

Two studies found no difference in the severity of OAs between night shifts and day shifts (Barsky *et al.*, 1992; Loudoun, 2010). We should emphasise one aspect of the study by Horwitz and McCall (2004), who found an increased severity of OAs during the night based on the number of days of recovery following the accident, but did not find this same phenomenon when taking the average overall cost of health insurance coverage as a potential indicator of injury severity.

The studies examined in the framework of this chapter support an association between night work or shift work including night work and the accident rate, even if this association is probably not direct and can involve intermediate mechanistic factors such as sleepiness, reduced vigilance, and decrease in cognitive and psychomotor performance.

Road accidents

Most of the studies on this subject showed a greater risk of road/commuting accidents associated with shift/night work. Shift/night work is often described as being responsible for short-duration sleep and "sleep debt", and as a risk factor for sleepiness (see Sections 6.3.1 and 6.3.2). In this respect, shift/night work could be associated with a greater number of road accidents.

7.1.7 Discussion and research outlook

7.1.7.1 Primarily descriptive studies

An initial observation is needed: in many of the studies analysed here, the "occupation" and the "content of the work" are seldom controlled. However, the work carried out by operators in the course of the night may not be exactly the same as that carried out in the day, the organisation can vary, as can the conditions of execution. This is why the very nature of the work is an essential element to be considered, in particular in the accident registry.

Few studies have incorporated the question of the nature of the work performed in their analyses. One study showed that physical workload was a factor increasing the risk for night workers (Violanti *et al.,* 2012). Another stressed the influence of the nature of the work, and identified an increase in the severity of injuries with certain types of work (Smith *et al.*, 1994). Three studies reported an increased risk of occupational accidents during night shifts, whether or not the job was manual (Mustard *et al.*, 2013) or physical (Wong *et al.*, 2011), or after controlling for the content of the work (Wong *et al.,* 2014).

7.1.7.2 Differences in the characterisation and coverage of occupational accidents depending on the country

The methodology adopted to carry out this expert appraisal was based on an international literature search. In the same way that the definition of night work varies according to the countries considered and constitutes a methodological difficulty in itself, the analysis of international studies raises the question of the difference between the systems for recognising and compensating an occupational accident, which may vary according to the country. To take an example: if we consider Air France and KLM, now combined within the same group, there are significant discrepancies related to the difference in qualifying an accident between France and the Netherlands. Thus, barotitis media and back pain, recognised as occupational accidents in France and accounting for around 40% of reported occupational accidents at Air France, are recorded as sick leave by KLM, in accordance with Dutch legislation. This places indicators that are difficult to compare within the same group

(RSE, 2009). These differences in characterisation and coverage of OAs in Europe are illustrated in a report by Eurofound (1989).

7.1.7.3 The question of under-reporting

The absence of an administrative or managerial structure at night raises the pressing question of under-reporting of OAs. In France, employers are obliged to report to the National Health Insurance Fund (CPAM) any accident leading to bodily injury of an employee during working time and at the place of work, regardless of its severity, within 48 hours of the date on which they became aware of this accident's occurrence. They may not prejudge as insignificant the nature of the injury to avoid reporting an accident, no matter how minor (CSS, Art. L. 441-2).

However, some accidents that may be recognised as OAs are not reported to the CPAM, either by the employer (to avoid an increase in contributions for the OA/OD risk) or by the victim (who did not notify management because they were not present at night, or through fear of dismissal or retaliation). This under-reporting is likely to be even greater for "relatively" minor OAs, which are more easily concealed by the employer or the victim, and for which the compensation provided by the legislation on OAs is seen by the victim as marginal. Thus, the report by the Bonin Commission assessed that the number of OAs with absence from work in 2009 was under-reported by over 100,000, on the basis of the CNAMTS data compared with those of the DARES's 2009 Sumer survey (see Table 17). However, it reduced this gross figure to 56,000 to take account of workers having suffered multiple accidents, and eventually came to an estimate of 40,000 under-reported OAs by applying a 30% deduction to correct statistical uncertainties related to the survey sampling. Regarding accidents without absence from work, the same data indicated the under-reporting of 249,000 accidents without absence for 2009.

Table 17: Extract from the Bonin report, 2014[58]

Table 4: Results of the DARES 2009 Sumer survey

	Accidents with absence from work*	Accidents without absence from work
Estimated number of AFW for 2008 – DARES survey CNAMTS field	756,500	545,000
Number of AFW for 2008 recognised by the CNAMTS (2008-2009)	701,253	296,506
CNAMTS (2008-2009) / DARES 2009 survey	92.7%	54.4%

Sources: CNAMTS 2008-2009; 2009 Sumer survey (DARES)

** after correction for workers having suffered multiple accidents*

This notion of under-reporting is also addressed in international publications. For example Mustard (2013), in Canada, suggested that under-reporting concerned up to 40% of OAs at night, and explained that it was possible because of the absence of management and administrative structures at night. This notion of under-reporting of more minor accidents was also mentioned in a report concerning practices in Italy (Costa, 1991).

The under-reporting of OAs occurring at night is a non-negligible bias when assessing the reality of the links between night/shift work and the accident rate. Indeed, the majority of studies analysed in this chapter focused on analysing serious OAs – i.e. those giving rise to

[58] http://www.securite-sociale.fr/IMG/pdf/rapport_sous-declarato_atmp_10_07.pdf.

a report – *via* the number of days of absence, the number of visits to the emergency department, and cases where compensation was obtained.

7.1.7.4 The indicator of severity of the occupational accidents

The earlier reviews of accident rates related to night and shift work concluded as to a greater severity of occupational accidents during night shifts ("atypical hours" dossier on the INRS website, INRS ED 5023, 2013) and a reduced frequency. However, it is clear from the literature analyses carried out in this chapter that while the severity is indeed increased, so is the frequency.

The importance of the indicator used to consider an occupational accident as "serious" should be stressed. France, like a great many other countries, opts for an indicator based on the number of days of absence from work. The work by Horwitz and McCall (2004) is interesting in the sense that it questions the relevance of the chosen criteria.

Thus, they showed that the average number of days of recovery (and therefore absence from work) after an injury occurring at night is greater than that of an injury occurring during the day. But they also stated that if another potential indicator of injury severity were considered, i.e. the average overall cost of coverage (including not only compensation for the days of absence from work but also the medical costs and costs related to disability and to vocational (re)training), there is no difference between day and night.

The classic indicators "frequency rate" and "severity rate" were also discussed in a report by the DARES (DARES, 2009), which stated that it is *"simplistic to consider OAs with absence from work as more "serious" for physical health than OAs with medical care but without absence from work. Employee victims of an OA, which would normally result in a reduced number of days off, may continue working if their presence in the establishment is necessary (for example, for maintaining the business). These OAs are then recorded as OAs with treatment but without absence from work. Associated with the under-reporting of OAs, this constitutes a supplementary bias in the measurement of OAs with absence from work."* Thus, "serious" accidents could in reality be more numerous than they seem.

7.1.7.5 Specific populations studied

Most of the studies found in the international literature focused on populations from very specific occupations (police, nurses, etc.): these are occupations, which in France, fall under public service, rather than private law. On the one hand, the access to compensation and the reporting conditions can be different, and on the other, speech may be freer in occupations afforded better protection by civil servant status, hence the difficulty in extrapolating the results to other populations. Analysing accidents only based on reports may not be sufficient in all professional contexts. However, this methodological issue was rarely addressed in the studies analysed. In this respect, analyses of real work and activity, as proposed by the ergonomic approach, is one way of reinforcing understanding of the links and mechanisms at work between night and/or shift work and accidents (see the introduction to this chapter).

7.1.7.6 Gender effect

Three studies described an excess risk of accidents for women during night work (Wong *et al.,* 2011; Wong *et al.,* 2014; Mustard *et al.,* 2013). However, the protocols used in the studies are such that it is not possible to go further in the understanding of potential causes: one study identified issues related to the anticipation of schedules, for example, but it cannot be ruled out that this increased risk reflects the exercise of different occupations.

Similarly, a longitudinal gender analysis of data on claims at the CNAMTS was recently published by the ANACT[59] and identified several findings: while occupational accidents fell overall between 2001 and 2012, they increased significantly for women. Since 2001,

[59] French National Agency for the Improvement of Working Conditions

commuting accidents have been on the decline for men but increasing for women. This study with respect to gender, by risk and by sector, showed that the differences noted in the area of claims by women and men largely related to differentiated exposure associated with distinct occupations (ANACT publication 2014). This gender effect during atypical working hours should be refined in future research.

7.1.7.7 Shift changes

The concept of increased claims during shift changes, regardless of the type, was found in two studies (Wong *et al.*, 2014 and Chiu *et al.*, 2013) and deserves to be explored in future research. Indeed, if this period of fragility is confirmed, it would be beneficial to deploy specific prevention measures.

7.1.7.8 Absence of a precise characterisation of exposure

Lastly, a comment made frequently in this report again concerns the lack of a precise description of the shift/night system: besides the fact that the very definition of night work differs from one country to another, comparisons are generally made between a group working "atypical hours" in the broad sense (grouping together fixed night teams, 3x8, 2x8, on-call, *etc*., with the direction of the rotations varying from one study to another, along with the frequencies of rotations, the length of the shifts and the recovery plans) and a group working daytime hours. More detail in the characterisation of exposure would improve understanding of the links between shift/night work and the effect studied, regardless of which kind.

8 The work itself as a modulator of the impact of shift work including night work

The effects of night and shift work on the health of employees subjected to it are not unambiguous or systematic. They depend on a combination of factors based on the employees' individual, social and family characteristics, the characteristics of the work, and the work situation. These multiple factors will modulate, i.e. reduce or amplify, the effects of night shift work on employee health. This chapter focuses on the work, the working environment and the nature of the work, and shows how these characteristics can combine with night shift work. It also describes the individual and collective strategies adopted by the employees concerned by these time constraints, in order to achieve their work objectives.

As with the study of the health effects, the experts began by conducting a keyword search using the Scopus search engine (www.scopus.com).

Then, as with Chapter 5, it was ultimately decided to draw on the specific knowledge and skills of the specialised experts. In order to support their findings, the experts used all the publications they deemed useful to cite, besides those already identified, "giving priority to those of key importance, of good quality, or those that posed interesting and new questions". The criteria for the inclusion of articles were therefore based on the experts' specific knowledge and skills (see Chapter 5).

8.1 Working environment and work context

8.1.1 Night work: a specific work context

Although work can take place at any time in the 24-hour period, the conditions for carrying it out at night may not be the same as during the day. There are many reasons for this. The requirements regarding level of production or service rendered can vary depending on the time of day, thereby implying a different kind of work: a production line that runs at a slower rate at night, fewer prescriptions for patients who are sleeping or anxious in hospital wards, or an assembly line that only operates at night to deal with malfunctions and maintenance activities.

When production and service conditions are identical (stable ammonia production over 24 hours in a chemical plant, for example), the organisational context differs almost systematically: there are often far fewer staff at night, management can be scaled down or even totally absent, support or peripheral services are generally closed, and the environment is far quieter.

In the hospital sector, several studies have described the specificity of the night work context, with nursing staff most often isolated, and no doctors on site to whom they can refer in case of need. The tasks of the nurses and care assistants differ, with fewer technical treatments, more interpersonal contact and increased patient monitoring. In light of this specificity, the studies show that the caregivers redefine their own objectives and priorities in their action goals during the night shift (Toupin, 2009).

This specific night work context is conducive to resting and sleeping, when the demands of the tasks fluctuate. It can also foster learning and taking on responsibility, in cases where work objectives can only be achieved when taking on tasks that span beyond one’s job description.

8.1.2 Transport conditions

Transport conditions, namely public transport frequency or the road environment, as well as the feeling of safety or insecurity during the commute between home and the workplace, should be taken into account in the working conditions for shift work that includes night hours. The infrequent rate of public transport early in the morning and late in the evening or night lengthens commute time and makes it more complex (several different modes of transport may be needed), thereby reducing the time available for sleep and recovery. These transport conditions have an even greater impact when the employee lives further away from the place of work.

A feeling of insecurity on public transport and during the commute may also worry the workers. Thus, women in particular may feel obliged to opt for longer night shifts, to avoid starting after 10pm and finishing before seven in the morning. This then ensures that the commute between home and the workplace is facilitated by more frequent public transport and takes place in a context of safety (see the recent report by the High Council for Gender Equality, HCElfh, 2015).

8.2 Nature of the work and requirements of the hours: combined effects?

8.2.1 Shift work: an observed accumulation with other forms of time constraint

The French national surveys on working conditions (Section 2.4) revealed that employees subjected to shift and/or night work also accumulated more constraints regarding the rhythm of work. Thus, 86% of those who worked at night also worked on Saturdays, and 72% on Sundays. They often accumulated several schedule constraints: irregular weeks, absence of a weekly 48-hour rest period, hours determined exclusively by the company without any change possible. Twenty-five per cent of them experienced long working days of more than 11 hours (compared to 17% of employees as a whole). Night work was often also accompanied by rotating shifts. Similarly, more of these night workers (7%) experienced a working day divided into two separate periods of more than three hours, compared to other workers (3%). Twenty per cent of night workers did not have a meal break (compared to 13% of employees working daytime hours).

8.2.2 Shift or night work: an accumulation of hardship factors

Shift work including night work has non-negligible consequences for employees because of the existence of time conflicts that affect their health, family and social life, but also the work itself in terms of safety and reliability.

Overall, the scientific studies tell us that the frequency and severity of the pathologies developed can be modulated according to the duration of the hours worked, the age of the employees, their personal characteristics and family situation, but also according to the specific characteristics of the working hours. Authors encourage consideration of all these aspects, in order to measure, as precisely as possible, the effects of shift and night work on the health of those who are subject to it. However, surprisingly, one field does not seem to have attracted the attention it deserves: the nature of the work carried out by the employees. *Working hours* are often reduced to the question of the *hours,* and rarely extended to that of the *work*. This reducing of work situations solely to their time dimension presents a risk, however, because the effects – in particular on health – produced by desynchronisation are not specific, and could be the result of other work constraints inherent to the occupational situation.

Thus, sleep disturbance, gastrointestinal disorders and cardiovascular disease associated with the practice of shift work could also be the product of other occupational demands such as physical or mental hardship, or environmental conditions. This has led some authors, on completion of their work, to insist on the need to consider the content of the work (Gadbois and Quéinnec, 1984; Rutenfrantz and Knauth, 1986; Kogi, 1996; Pavageau, 2005; Prunier-Poulmaire, 1997). However, a retrospective review of 310 publications from five international symposia on night and shift work that took place between 1985 and 1993 showed that only 10% of them examined the question of combined effects resulting from the interaction between the demands of the tasks and the type of working hours practised (Prunier-Poulmaire, 1997).

This lack of interest in the work content is especially surprising since national surveys tell us that, in addition to their atypical hours, night shift workers accumulate other severe professional constraints: obligation to rush their work, lack of autonomy in the work and lack of means to carry it out, absence of meal breaks, etc. Thus, "all other things being equal", more employees regularly working atypical hours (57.5% compared with 44%) reported that their jobs involved at least three physical hardship factors or that they were subject to at least three vigilance constraints (DARES, *Premières Synthèses* – March 2009 – No. 22.2). They were also more frequently exposed than other employees to verbal and/or physical abuse in the context of their work.

Regarding employees who work at night, according to the "Working conditions" survey of 2013, they described conditions that were on average considerably more difficult than the others: this finding was broadly stable compared to 2005 (DARES Analyses, August 2014 – No. 062). They reported, for example, that they were subject to at least three vigilance constraints (44.3% compared to 27.3% of day workers); these included not taking their eyes off their work, having to read small letters or figures, examine very small objects, and pay attention to visual and audible signals that were difficult to detect. More employees working at night (47.3% compared to 30.5%), "all other things being equal", reported that their work involved at least three physical hardship factors among the following: long and frequent walking, heavy loads, postures that were painful or tiring over time, requirement to stand for long periods, painful or tiring movements, subjected to shaking or vibration, inability to hear someone two or three metres away, or exposure to toxic substances in the working environment (see also Section 2.4).

In this respect, it seems important to consider the cyclical variation in the human body's susceptibility to hazards in the physical environment: the human body's greater fragility in the course of the night makes it especially vulnerable to aggression (noise, heat, toxic agents, *etc*.). Thus, in addition to its specific effects, night shift work can contribute to the development of occupational pathologies due to the body's greater vulnerability at night. The development of long shifts, such as 2x12, has given new meaning to the need to consider the content of the work, in particular from the perspective of the duration of exposure to toxins (Knauth, 1993).

But besides this chrono-toxicological perspective, a few studies have stressed the existence of a combination of occupational factors that can interact adversely on health. Thus, as early as 1986, Frese & Semmer hypothesised that the state of health of shift workers did not solely depend on the organisational arrangements of the hours. They conducted a questionnaire survey among 3346 workers in 104 different companies in the paper and ceramics industries. This questionnaire consisted of 10 questions on the demands of the working environment:

- 6 on psychological stress;
- 9 on psychosomatic complaints;
- 4 on nervousness – mental stress;
- 10 on the state of health.

The analyses of covariance they performed helped confirm the role of night shift work in psychosomatic disorders and mental stress, enabling the authors to reaffirm the deleterious role of shift work independently of that relating to the demands of the tasks. But they also discovered that psychological and environmental stress were directly correlated with psychosomatic complaints, mental stress and changes in the state of health. They concluded that the stress resulting from the demands and characteristics of the work situation could add to the negative effects of shift work.

On completion of their work, Pokorski *et al.* (1987) came to the conclusion that the stress caused by night shift work may be severely aggravated when other stress factors related to the working environment or its organisational arrangements were present in the work situation. They therefore support the analyses developed previously by Teiger *et al.* (1981) in their survey of rotary printer operators.

Bortkiewicz *et al.* (1987) also concluded, at the end of their work, that the actual nature of the work performed may induce a state of fatigue independently of the working hours practised. Estryn-Behar *et al.* (Estryn-Behar *et al.,* 1990) hypothesised that differences in health status between nurses and care assistants working under a system of identical hours may relate to the specificities of each of the two occupations.

Cervinka (Cervinka, 1993) conducted a study of 31 workers doing night shifts in a cement plant. In her approach, she considered the environmental and psychosocial stress of workers by means of six questions relating to time pressures and professional responsibilities. She concluded by showing that stress factors inherent in the exercise of the job acted independently from the stress associated with the working hours practised, and may therefore have a specific influence.

These results reinforce the findings of a German study on current and former shift workers in 24 chemical plants (Kiesswetter and Seeber, 1995), which revealed that the effects of working hours and those of environmental and psychosocial stress factors were combined, leading to the effects of time conflicts, the nature of the work and its conditions of execution being considered jointly.

Costa *et al. (*Costa *et al.,* 1990) conducted a study on 52 workers in the food industry working semi-continuous 3x8 shifts, and 52 nurses working 3x8 shifts. This study relied on the distribution of a questionnaire that focused on the employees' family situation, sleep, state of health and working conditions (workload, monotony, meaning of work, *etc*.). They confirmed the health effects of shift work including night work but also the effects of the characteristics of the occupational activity: the degree of motivation prompting employees to work shifts was not the same among the nurses and the food industry workers. While night work was regarded as legitimate by the nurses, the workers saw the shift work including night work as being imposed on them, which affected their state of health.

The results of a study conducted by questionnaire (but also based on 39 observations of the work and on individual interviews) with 650 staff of 41 French customs brigades (Prunier-Poulmaire *et al.*, 1998) showed, by means of logistic regression analyses on 302 employees, that task demands had effects on perceived health (as felt by the individuals) that were of the same nature and sometimes the same magnitude as those attributable to night shift work. For example, interpersonal difficulties with users had effects on sleep that were as large as those caused by shift work: OR of 4.1 compared to 3.5 for the practice of 4x6 and 5.5 for the practice of 3x8. The same was true for appetite disorders: OR of 2.5 compared to 2.7 for the practice of 4x6 and 3.5 for the practice of 3x8. The findings were the same for cardiovascular diseases or high blood pressure: OR of 2.2 compared to 3.1 for the practice of 3x8. Similarly, experiencing monotonous or physically demanding work was accompanied by sleep disorders, affecting both the quality and duration of sleep. The findings of this study showed that the effects observed were the result of not only biological and social desynchronisation but also the specific demands of the tasks performed in the course of the work. *[Note: health was estimated subjectively in this study,* via *questionnaires. The impact on objective health, for example on the cardiovascular system or hypertension, may be different.)*

Pavageau (Pavageau, 2005; Pavageau, 2006) found similar results from a study carried out on 617 prison officers (questionnaires, observations of activity and interviews, multivariate analyses): the content of the work seemed to adversely affect the health of the prison guards. In this situation, he stressed the key role of the feeling of insecurity and the arduous nature of the detention. These two conditions were involved in respectively 63% and 53% of 19 situations tested, whereas the "hours" condition only exerted an influence in 32% of situations.

This study therefore supports the assumption that *"the time constraint may not explain everything regarding the state of health of shift workers"* (Teiger, 1989; Barthe *et al.,* 2004) and that it is in fact the joint effects of the hours and the work that affect health.

More specifically, the state of health of shift/night workers seems to be more accurately the product of the effects of the working hours practised, the controls that these employees establish in the area of their lives outside work, and the effects arising from the nature and demands of the work performed. Pavageau (Pavageau, 2006) and Prunier-Poulmaire (Prunier-Poulmaire, 2015) insist on the idea according to which the constraints of the hours and the demands of the tasks may be not only additive but potentiated.

In conclusion, these different studies provide important insights for building knowledge of the combined effects of shift work including night work and the demands of the tasks. Indeed, whether they compare variations in workload over 24 hours, or assess changes in the body's reactions to constant external aggression, all these developments testify to the fact that the content of the work is not without consequences for the person executing it, and to the importance of further examining the effects it produces in addition to those generated by the working hours.

All these studies stress the importance of not disregarding effects specific to the demands of the tasks and their conditions of execution. From this point of view, ergonomic analyses of the work and an examination of the actual activity are essential pathways to understanding.

8.3 Individual and collective controls established by the people concerned

Shift and/or night workers, like any other workers, will seek to achieve their objectives throughout their work shift, taking into account the physiological changes induced by the circadian destabilisation they undergo. And in virtually every case, the objectives set will be achieved, the deadlines will be met, without any errors, any fall in productivity, and with a quality of work equivalent to that performed during the day.

A series of studies conducted mainly in ergonomics shows how men and women subject to circadian variations to their psychophysiological functions manage to achieve their work objectives, in their everyday work. They show the construction and implementation of controls, which are manifested in the work activity itself by a qualitative and quantitative reorganisation of the work performed, a reorganisation that can be seen at both individual and collective levels (Barthe *et al.*, 2004).

It should be noted that few studies have examined possible variations in the work activity in night shifts, whose demonstration would imply firstly adopting an ergonomic approach centred on the actual work activity, and secondly obtaining the means to observe this activity, mainly at night.

8.3.1 Controls associated with a specific work activity according to the morning, afternoon and night shifts

An initial series of studies conducted with process controllers working rotating shifts (3x8) sought to identify whether or not circadian rhythmicity was maintained, by comparing work activity during the morning, afternoon and night shifts.

In a chemical plant (Terssac *et al.*, 1983), the monitoring activity of manufacturing process controllers involves obtaining information relating to the state of the process. The operators obtain this information from zones located on wall panels, on a synoptic view and on a signalling device. An analysis of changes in the direction of the controllers' gaze on the different zones revealed that the distribution of how information was obtained underwent a quantitative variation according to the work shift considered, despite production over the three shifts remaining stable. During the afternoon shift, the rate of information collection was highest, it fell to its minimum level during the night shift and was at an intermediate level during the morning shift. This result, which reflects the rhythm of the monitoring activity with a maximum in the afternoon and a minimum at night, was corroborated in the same situation, after the control room had been computerised (Andorre and Quéinnec, 1998), but also in other process control situations: in a cement plant (Christol *et al.*, 1979), in a water treatment plant (Dorel, 1982) and in nuclear power plants (Chabaud *et al.*, 1988, Prunier-Poulmaire *et al.*, 2011).

Based on a more detailed analysis of the work activity, supervision strategies specific to the work shift were identified among the manufacturing process controllers of the aforementioned chemical plant (Terssac *et al.*, 1983). The controllers collected the information according to three different methods: they consulted a particular zone on an *ad hoc* basis (*ad hoc* information collection strategy), they limited consultation to a few precise zones, which were scanned one after the other in the same direction (scanning strategy); or they developed associations between several information zones, implying changes in the scanning direction (reading strategy). The results showed firstly that *ad hoc* information collection constituted the most common monitoring strategy. The relative frequency at which the three strategies were established differed according to the work shift. *Ad hoc* information collection predominated in the morning, the afternoon shift was characterised by an increase in procedures of associations between several zones (reading), and the night shift by a monitoring activity limited to a few zones that were consulted according to the last strategy identified (scanning).

This same work situation was analysed after the introduction of a computer system that led to information being accessed via pages on a screen (Andorre and Quéinnec, 1998). These screen pages (more than 500 in total) were grouped into five main categories: synoptic views, functional groups, histories, alarm pages and other pages. The consultation profiles relating to the five categories of screen pages varied according to the controller's work shift: the morning shift (4am-midday) was characterised by a greater proportion of requests for functional groups (screen pages that display the results of an action), the afternoon by an increase in requests for alarm pages (screen pages that locate a disruption), and the night (8pm-4am) saw operators consult proportionately more synoptic views (pages that provide an overview of the process status).

Thus, the supervision strategy adopted in the morning was a reactive strategy, whereas at night the operators implemented a strategy that anticipated changes in the process parameters.

Lastly, a study that focused on analysing the forms of coordination between process controllers in a metallurgical plant (Van Daele and de Keyser, 1991) also showed a variation in collective activity according to the work shift in question. Three forms of coordination were distinguished: by division of tasks, by division of goals and by mutual adjustment. While the form of coordination by division of tasks dominated during the day shifts, coordination by mutual adjustment was observed at night. It can then be assumed that the chronobiological constraints associated with night work lead the operators to implement a reorganisation of the work activity, also at a collective level.

8.3.2 Individual and collective controls during the course of the night shift to maintain and improve the reliability of work

Demonstrations of a rhythmic pattern of behaviours from the comparison between day and night shifts are relatively well-established. Other studies show that variations in work activity can also be seen during the night shift.

For example, in the customs service (Prunier-Poulmaire *et al.*, 1998), officers will tend to perform controls in sites that pose the greatest danger at the start of the night shift. They will also group together tasks involving reflection, precision and decision-making at the start of the shift, and then alternate others that are more physical and require less attention. This strategy allows them to maintain vigilance and break the monotony of certain tasks.

Through experience, shift and night workers develop a precise knowledge of the variations of their physiological functioning and can precisely identify the times during their shift when their vigilance levels will be lowest and therefore when the work will be more difficult to manage (Toupin *et al.,* 2014). Studies therefore show that from the start of the night shift, workers will anticipate the fatigue and sleepiness to come.

For example, from the start of the shift, nurses will ensure that they have the medical prescriptions needed to manage any possible night anxiety in patients. They will also arrange to tour the ward as early as possible, in order to see a maximum number of patients awake and thus obtain an accurate representation of the state of their health, in order to better plan the night to come (Toupin, 2012; Pueyo *et al.,* 2011)

The objective is to build a comprehensive representation of the situation in the past, present and future in order to anticipate and allow room for manoeuvre, so as to better cope with any unforeseen events that could occur during the most difficult hours of the shift.

Regardless of this forward planning, sleepiness can directly affect the work activity the moment it occurs. During a peak of fatigue, operators will then transfer non-priority tasks, move around less and communicate with each other less. If the demands of the job do not enable the employees to bring forward or defer certain tasks, then adjustments in how they perform them and changes in their operating procedures can be observed.

For example, in the hospital sector (Barthe and Quéinnec, 2005), during the night shift (which lasts around 12 hours), nurses and childcare assistants in the team at a neonatology department have to provide four periods of care for the babies in the department (every 3 hours, from 8pm to 5am). While the requirements are almost identical during these work periods, the results show a difference in the actual duration of the care according to the shift. The care period that begins at two in the morning is shorter (50 min on average) than the other three periods during the night shift (90 min on average). Qualitative analyses revealed that the staff adopted specific strategies for cleaning and feeding the children during the care period at around 2am, which explain the observed reduction in the actual working time. Indeed, when the baby's health allowed it, certain secondary activities such as nappy changing were deferred, and feeding the children with an infant bottle was often replaced by feeding via a stomach tube. These adjustments enabled staff to work more quickly – feeding a child using a tube takes around a fifth of the time needed when using a bottle – and to achieve their objectives. The consequences of these changes in care strategies in the middle of the night aim both to combat the decline in vigilance suffered by the staff at this time, and to anticipate the accumulation of fatigue occurring at the end of the night shift. Thus, the team members had the chance to take some rest before the final care period of the night shift, so as to be able to combat the accumulation of fatigue. These strategies also helped preserve the patients' sleep while also meeting the feeding and care objectives.

Collective reorganisations also occur within teams, in order to cope with the demands of the work, while collectively managing individual variations in vigilance. Dorel and Quéinnec (1980) showed, in process control at a drinking-water plant, a collective reorganisation of the monitoring work aimed at giving as many responsibilities as possible to the operator benefiting from three days of rest following the night shift, thereby preserving the second operator, who has to come back to work the following night. In the aforementioned neonatology department, the nurses and childcare assistants helped each other in order to mutually reduce their workload and provide technical assistance or specific skills at certain times of the shift (Barthe, 2000). More specifically, when tasks requiring maximum concentration, such as attaching a drip to a premature infant, had to be carried out at three in the morning, they then worked systematically in pairs, for greater safety and convenience for the patient. They also organised their activity jointly so as to allow themselves individual moments of rest. A study conducted in a steelworks on the rolling-mill work station revealed that the two operators, who are expressly required to alternate the roles of roller and operator every hour, in fact took turns to fulfil these two roles simultaneously (Guérin and Noulin, 1984). Thus, the operators preferred to increase their workload momentarily in order to obtain frequent periods of free time to regain their energy or to rest. This redistribution of labour was observed in all three shifts covering the 24 hours, but the periods of recovery it enabled are especially important during the night shift, when the microsleeps they allow contribute to maintained vigilance.

Lastly, in the customs brigades, there was an informal division of tasks between the officers: it can be seen that those who began the night cycle took on the most difficult and dangerous tasks (such as questioning offending users), which require great self-control, careful listening, unfailing patience and high concentration (Prunier-Poulmaire, 1997).

These strategies adopted by workers on rotating and night hours, in work and outside work, help control the risks in terms of work, personal life and health. But they are not always sufficient. The readjustments observed in actual work to anticipate variations in sleepiness – transfers of tasks, mutual assistance and rest – are only possible when there is room for manoeuvre in the work situation. This is not always the case. Updating the individual and collective control processes at play in the work activity and in one's personal life is a prerequisite to the co-construction of measures aimed at controlling the risks to work and health (Barthe, 2015).

9 Means of preventing the existing risks associated with shift work including night work

This chapter addresses prevention of the risks associated with shift work including night work firstly in its legislative and regulatory dimension, and then by identifying the existing means of prevention documented in different media, based on an analysis of scientific publications. This is therefore a list of the means of prevention reported by the literature rather than a list of the means recommended by the Working Group. In fact no analysis was conducted of the effectiveness of the means of prevention listed below.

As with the study of the health effects, keyword searches were initially performed using the Scopus search engine, to provide a literature base. The experts drew from this base all the publications they considered relevant.

As with the other chapters dealing with aspects relating to the human and social sciences, for this chapter on the means of prevention, the Working Group proposed adopting a particular adapted method based on the specific knowledge and skills of the specialised experts. In order to support their findings, the experts used all the publications they deemed useful to cite, "giving priority to those of key importance, of good quality, or those that posed interesting and new questions".

9.1 Prevention of occupational risks

9.1.1 The employer's legal obligations

In their occupational activity, employees are exposed to risks of various natures, which may cause their health to deteriorate. Employers have a duty to eliminate or reduce these risks, to ensure employee safety and protect their physical and mental health. The French Labour Code imposes an obligation of means and results on employers (Art. L.4161-1 of the Labour Code).

In order to implement appropriate preventive measures, employers have a guide to the nine general principles of prevention listed by the Labour Code:

- avoid the risks;
- assess the risks that cannot be avoided;
- combat the risks at their source;
- adapt the work to the person (design of work stations, choice of equipment, and working and production methods), with the aim being primarily to limit work that is monotonous or performed at a pre-determined rate;
- take account of developments in technology;
- replace what is hazardous by something that is safe or less hazardous;
- plan for prevention by incorporating it in a coherent whole: technology, work organisation, working conditions, social relations, the influence of environmental factors;
- take collective protective measures and give them priority over personal protective measures;
- give employees appropriate instructions.

Employers are bound by a general safety obligation in respect of workers, and must conduct an occupational risk assessment, which must be recorded in a specific document: the "single document on occupational risk assessment, or DUER" (Articles R. 4121-1 to R. 4121-4 of the

Labour Code). The list[60] of 52 hazards and risks drawn up by the Ministry of Labour[61] includes *night work* and *work in successive rotating teams*.

Besides the requirement to apply the regulatory provisions, since November 2010, the employer must also take measures to prevent arduous work (Article L.4121-1 of the Labour Code). The 10 risk factors selected to define arduous work[62] also include *night work* and work *in successive rotating teams* under the constraints related to "rhythms of work likely to leave sustainable, identifiable and irreversible traces on worker health" (Article L.4121-3-1 of the Labour Code).

9.1.2 Types of prevention: primary, secondary, and tertiary

The World Health Organisation (WHO) defines health as *"a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity",* and prevention as "*the series of measures taken to avoid or reduce the number and severity of accidents and diseases*". It proposed the distinction, now taken for granted, between three types of prevention: primary, secondary and tertiary, which actually correspond to successive states of a disease (Flageolet, 2008).

Primary prevention refers to the series of acts intended to reduce the incidence of a disease, i.e. to reduce the occurrence of new cases; secondary prevention refers to the series of acts intended to reduce the prevalence of a disease, i.e. to detect a disease before the onset of symptoms, so as to be able to intervene and delay or cease its progression, i.e. to reduce the duration of its evolution. Tertiary prevention refers to the series of acts intended to reduce the prevalence of chronic disabilities or relapses within the population, i.e. to reduce functional disabilities due to the disease.

Health prevention for employees at work is also broken down according to the WHO's three types of prevention, enabling a distinction to be made in the actions to be implemented by employers:

- in primary prevention, the actions consist in avoiding occurrence of the risk, removing its causes in the organisation of the work, or mitigating its effects. The actions of primary prevention focus on the risk factors, aiming to combat the risk at its source. Primary prevention aims to promote an occupational environment that is not conducive to accidents or disease. Primary prevention actions also involve informing all the employees likely to be affected of the potential risks;
- in secondary prevention, the measures involve identifying the health problem at its earliest stage and applying fast and effective treatment to limit the adverse consequences. Thus, the actions involve information intended for the employees concerned on the means available to best "withstand" these risks. The actions here are therefore focused on the employees and the tools that can help them manage the difficulties associated with the risks identified in the work;
- In tertiary prevention, the actions enable the monitoring and support of employees in a poor state of health, and also seek reparation.

The Labour Code, *via* the general principles of prevention, encourages primary prevention. Primary and collective prevention strategies are *a priori* more effective and more enduring than those of secondary and tertiary prevention: by acting on the causes, primary prevention has a lasting impact (Brun, 2007).

The means identified for preventing risks associated with night and shift work are presented in this chapter based on this categorisation of prevention.

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[60] List with operational significance proposed by the Ministry of Labour to help companies prevent occupational risks.

[61] http://www.travailler-mieux.gouv.fr/Dangers-et-Risques.html.

[62] http://www.travailler-mieux.gouv.fr/Quels-sont-les-facteurs-de-risques.html.

9.2 Primary prevention of the risks associated with shift/night work

Primary prevention of the risks associated with shift and night work will seek to eliminate night and shift work and, if this is not possible, will seek to mitigate the effects in the work situation and in the entire professional life. The actions of primary prevention focus on the risk factors.

The literature reports several levels of action that can be investigated jointly to minimise or mitigate the risks associated with night and shift work (Barthe, 2015), (Toupin, 2014):

- modification of the shift system, so that it minimises circadian desynchronisation and sleep disturbance, promotes recovery of employees' sleep debt, and enables them to better reconcile their personal and professional lives;
- actions targeting the working conditions and work content, to avoid amplifying the effects of night and shift hours on the employees;
- action involving career paths and human resources management, in order to control the duration of exposure of employees.

9.2.1 Acting on the shift system

9.2.1.1 Eliminate and restrict night work

Applying the principles of primary prevention, night work should be eliminated, or the number of people working these hours should be reduced. It should be reiterated that "for employees as a whole, the use of night work must remain exceptional and be justified by economic or social requirements specified in an agreement (extended collective branch convention or agreement, or company or establishment agreement), concluded before its establishment or its extension to new categories of employees (Articles L. 3122-32 and 3122-33 of the Labour Code)".

To reduce, restrict or even eliminate shift work including night work, the issue will then be to assess whether or not the targeted results can be achieved by organising the work in other ways.

A few examples of questions that may be asked:

- rather than operate production lines during the night, would it be possible to opt for an organisation that is equally effective in terms of production but less harmful to health? For example, by doubling the line and then operating them simultaneously during the day?
- is it absolutely necessary to make certain support teams work at night (maintenance, cleaning or other support teams), would their work not be as effective during the day?
- is it possible to operate certain technologies or computer systems continuously throughout the night without the on-site presence of numerous systems controllers?
- is it socially necessary to operate catering, sales and other services around the clock?
- *etc.*

Optimising the organisation of night work is the result of a compromise between collective (organisational, social, health and economic) and personal (psychological, health, social, family) factors.

9.2.1.2 Adjust the time system for shift and night work

Even if it should be considered systematically, it is not always possible to eliminate or significantly reduce shift or night work. The problem that then arises is how to adjust the shift system so that it interferes as little as possible with people's biological structure and psychophysiological and family balance, thereby reducing the risks to health and well-being.

9.2.1.2.1 As a preamble: a complex subject and an intervention methodology requiring consultation with those primarily affected

The organisation of a new shift system is a very sensitive issue that requires careful examination, both at a general, collective and individual level and taking into account individual chronobiological, sleep and domestic factors.

The impact of the disrupted rhythms induced by the hours requires a systemic and multifactorial approach (see Chapters 3 and 5 of this report). Indeed several dimensions relating to both the characteristics of the individual (biological clock, age, social and family life, *etc*.) and those of the work (salary and bonuses, work content, hardship factors, *etc*.) are concerned by the question of shift and night hours and may together affect employee health. Thus, any recommendations made regarding the shift system in place will affect both the work situation, the conditions of its execution, its organisation and the spheres of the employees' personal lives.

For example, moving the time that the morning shift starts from 4am to 6am, in order to delay the time the employee has to wake up, thus reducing sleep debt and increasing sleep quality (REM sleep phase preserved), has implications for organisation of the work and subsequently for the employees.

Here are two of them:

- implications on the time that the morning shift ends. If the length of the shift is still 8 hours, the morning shift will end later, at 2pm instead of midday (6am-2pm), and this will impact the times of the afternoon and night shifts (2pm-10pm and 10pm-6am respectively); this change, rather favourable from a physiological perspective, may become unfavourable from the point of view of the employee's personal life because it will reduce the number of possible lunches with family, evenings out, social encounters, *etc*.
- implications on the content of the work. Tasks originally planned for the beginning of the afternoon shift (between midday and 2pm) will now take place at the end of the morning shift. This may be work that is too demanding for the end of a shift or that may require the implementation of tools to foster continuity of these tasks over the two shifts; this change will then have to be accompanied by a reorganisation, a redistribution of tasks between the morning and afternoon shifts.

A change in the shift system (in this case the time that the shift begins) requires an analysis of the situation as a whole, taking into account the shifts covering the 24 hours, the work that is performed, and the point of view of the employees, as well as the establishment of an intervention approach involving all the actors. According to the European Foundation for the Improvement of Living and Working Conditions (Corlett, 1988)*: "It is difficult to deal with the problems associated with the adaptation of shiftwork and night work unless these forms of work are placed in their context".*

From the organisational point of view, new modes of rotation often provide technical support for the reorganisation of production, mainly due to the adoption of new technologies or changes in the organisation of the work. Technical innovations often lead to changes in tasks and workload and, therefore, the schedule for performing the work (Quéinnec, 1985; De Terssac, 2004).

From the employees' point of view, changes in the organisation of working time often conflict with their lifestyles and free time, in particular regarding the domestic aspects of family and social life. These problems can be resolved satisfactorily by a careful analysis of the work characteristics (Kogi, 1995); (Jeppesen, 2000); (Knauth and Hornberger, 2003); (Knauth *et al.,* 2006).

The methodologies advocated by the work of Eurofound (Corlett, 1988), as well as that of Quéinnec, although written more than 20 years ago, are still relevant methodological guides.

They proposed guidelines for intervening in the shift system, which they explained as criteria defining the shift system accompanied by an indication of the knowledge acquired and the social practices in terms of advantages/disadvantages. According to these authors, four conditions are essential for ensuring that the guidelines really prepare actions to transform the working conditions of shift and/or night workers:

- establish a clear policy to improve the life of shift workers;
- involve all the actors in the choice to be negotiated;
- consider several modes of temporal organisation rather than just one;
- introduce flexibility in the choices so they can be revised in light of their results.

They establish principles relating to the temporal organisation of work:

- there is no single solution. There is no "right" solution for organising shift and night work, men and women obey circadian rhythms that promote activity during the day and rest at night;
- there is no absolute determinism of technology on the temporal organisation of work. In industry, the wider use of shift work is encouraged by the need to amortise equipment with the increase in the length of its use;
- temporal organisation requires choices to be made. These relate to the shift system in place, the arrangements for assigning employees within this timetable, and the design of the operation of the facilities and the work to be performed;
- there is an interaction between different areas. It is impossible to define an option in one area without considering the consequences in the others;
- the temporal organisation of work necessarily involves contradictions. Any change in hours is likely to be positive from a certain point of view and negative from another. The advantages and disadvantages should then be jointly assessed;
- it is necessary to find a compromise, which will be developed, negotiated, implemented and assessed with the people whose work situation will be affected;
- this negotiated compromise is by definition temporary, and is likely to change over time.

This methodology was partly adopted by Eurofound, which in 1988 published a book entitled "*Adapting Shiftwork Arrangements*", co-authored by Corlett, Quéinnec and Paoli.

This book presents:

- adaptation options to mitigate the effects of shift work: a reduction in work duration, an improvement in the working environment (appropriate canteen, transport and healthcare services), an increase in flexibility, moving the hours at which a shift begins, fairly rapid forward rotation systems, and automation of work stations at night;
- as well as a methodology to be put in place to introduce the change: necessary participation of interested parties, development of a follow-up policy, possible questioning of solutions that were mutually acceptable at a particular time in the past, plurality of adopted solutions, information for all, the indispensable condition of real participation and the continuation of scientific research on the subject.

9.2.1.2.2 Characterisation of the shift system

Some studies have stated that the organisation of the shift system (see Section 2.3 of this report for a list of the characteristics of a shift system) can be improved: some indicate that well-organised rotation cycles can be less harmful to health, and can improve worker satisfaction and productivity.

As mentioned previously, many organisational analyses (Knauth, 1993; Knauth, 1996; Knauth, 1998) have shown that no single shift system is "optimal" or "better" than the others in general, but that each system should be planned and adopted taking into account the specific working conditions and the demands of the tasks, as well as the social and personal characteristics of the workers concerned.

Some of the means of prevention cited by authors (Corlett, 1988; Monk, 1992; Wedderburn, 1994; Colquhoun, 1996; Kogi, 1998; Kogi, 2001; Pallesen *et al.,* 2010; Knauth *et al.*, 2003) are presented in the following paragraphs. It should be noted that the various recommendations detailed below have not been assessed, they are based on a reduced number of sufficiently controlled scientific studies (particularly with biases taken into account).

9.2.1.2.3 Number of consecutive night shifts

The studies agree that one or two consecutive nights are probably less disadvantageous in terms of the employee's biological rhythms, whereas after 4-6 successive nights there may be a significant change in phase and a flattening of circadian rhythms, requiring several rest days to achieve resynchronisation (Haus and Smolensky, 2006; Sallinen and Kecklund, 2010; Härmä, 2000). Thus, on this basis, several authors seem to advocate a maximum of three consecutive nights, to avoid affecting circadian rhythmicity, even if these aspects need further investigation.

9.2.1.2.4 Frequency, rotation speed and duration of rest periods

Two prospects were mentioned by Folkard with a view to avoiding or minimising any phase change in biological rhythms (Folkard, 1992; Folkard, 2008):

a) maintain, as much as possible, the adjustment of biological rhythms to the phase change imposed by night work through permanent night work or a job that rotates at a slow speed. In reality, this prospect is impractical since the rest days prevent any long-term adjustment of the biological clock. In addition, permanent fixed night work is only advised in conditions of specific needs and must be accompanied by reinforced medical supervision (HAS, 2012);

b) avoid the change in phase of biological rhythms through rapid rotation, to avoid subjecting the body to the strain of endless adjustments and readjustments of the biological clock, and therefore avoid the states of circadian desynchronisation. Some studies have suggested that it would be easier to obtain immediate recovery with a rapidly-rotating shift system, whereas by increasing the number of consecutive nights (slow rotation), there would be a gradual accumulation of sleep deprivation and fatigue, which the worker could not fully recover from even with a day of complete rest (Akerstedt, 2003). The meta-analysis by Pilcher *et al.* (Pilcher *et al.*, 2000), which analysed 36 studies, suggested the opposite; the results suggest that total sleep time is shortest with night work and rapid rotations (< 4 days), and that long rotations reduce total sleep time less than rapid rotations. At this stage, for sleep and recovery, it must therefore be considered that there is no consensus at the international level on the recommendation. Some authors also mention the importance of positioning the rest days at specific times so that they offer the most benefits in terms of recovery. In particular, so that they give maximum opportunity for the realignment of circadian rhythms: to this end, they should be placed mainly after the night shifts (Kurumatani *et al.,* 1994; Barton *et al.,* 1995) and to a lesser extent after the morning shifts. Again, however, there is no consensus.

Note that the number of teams alternating on the shifts during the rotation cycle directly determines the number of rest periods. Changing to the fifth team in the continuous systems in place in France in the 1980s (5x8 instead of 4x8), combined with the decline in work duration, enabled rest days for employees to be added for each cycle, time that helped facilitate the partial recovery of accumulated sleep debt, family gatherings and social and/or personal life.

9.2.1.2.5 Direction of rotation

Teams performing shift work may take over from each other either:

- in a clockwise direction or "rotation with a phase delay" (for example, working two shifts in the morning, followed by two shifts in the afternoon, followed by two night shifts);
- in an anticlockwise direction or "rotation with a phase advance" (night/afternoon/morning).

As indicated by many experimental studies conducted in conditions of total isolation, from a chronobiological point of view, clockwise rotation may be preferable, because the circadian rhythmicity of the biological functions has an internal period slightly longer than 24 hours (Arendt, 1998). The body may therefore adapt better to a lengthening rather than a shortening of the period, as in the case of "jet-lag", passing rapidly through several time zones, which determines major adaptation problems with flights heading east, in an "anticlockwise" direction, rather than going west, or "clockwise" (Wegmann,1985; Reinberg, 2003).

This concept, correct at the population level, is not necessarily true at the individual level. Although the endogenous period of the biological clock is on average longer than 24 hours in humans (Duffy *et al.,* 2011), which enables better circadian adaptability to a clockwise rotation and a time difference when travelling west, on average, this endogenous period is shorter than 24 hours in around 25% of the population, and these individuals, who are usually early-to-bed/early-to-rise types, more easily tolerate a time difference when travelling east and anticlockwise rotations (Vetter *et al.,* 2015). The concept of chronotype could therefore prove to be a major individual factor in tolerance to different rotating shifts, the direction of the rotations, and their frequency.

Studies conducted in a real situation generally show that clockwise rotations generate fewer problems, regarding physical or psychological well-being and sleep, for shift workers (Barton *et al.,* 1995; Tucker *et al.*, 2003; Härmä *et al.*, 2000). This better acceptance of clockwise rotations is reported as being particularly evident among ageing employees: fewer sleep-related complaints and a positive action on certain markers of inflammation (Viitasalo *et al.,* 2015). The results of another study, conducted in a company and based on physiological measurements, support this finding, namely higher morning and night cortisol rates, associated with poor sleep quality, were found in employees on anticlockwise rotations (Vangelova, 2008).

A longitudinal study (follow-up at 32 months) on 95 employees on clockwise rotations and 681 employees on anticlockwise rotations described an increased need for recovery and poorer overall health among the employees on anticlockwise rotations. In addition, fewer "work-family life" conflicts and better sleep quality were found in employees on clockwise rotations (van Amelsvoort *et al.,* 2004).

In a literature review identifying 26 publications between October 2005 and November 2006, Bambra *et al.* (Bambra *et al.,* 2008) identified three types of organisational actions with a positive impact on health and work/family life balance; one of these was the change from an anticlockwise to a clockwise rotation (the other two were moving from a slow rotation to a rapid rotation, and participating in the planning of rotations).

Lastly, in a recent literature review (Neil-Sztramko *et al.,* 2014), seven interventions concerned the change in direction of rotation (six anticlockwise to clockwise, and one in the other direction). The follow-up ranged from four weeks to one year. Three studies showed a beneficial effect of the change in direction of rotation (from anticlockwise to clockwise) on sleep quantity or quality (Hakola and Härmä, 2001; Hakola *et al*., 2010); Härma, 2000) but this effect was not observed in the other three publications (Knauth, 1998; Orth-Gomér, 1983; Viitasalo *et al.,* 2008). The authors noted the fairly low quality of the studies exploring sleep. One study showed a positive effect of the change in direction of rotation on risk factors (cholesterol, triglycerides, blood pressure).

Despite a trend found in the studies of better acceptance of clockwise rotations, this rule should be carefully validated by future studies, in which the chronotypes of employees have been identified, exposure to shift work well characterised, and the effects precisely quantified, before generalising this in the company environment.

9.2.1.2.6 The times at which shifts begin and end

Regarding the morning shift, the earlier it begins, the more the total duration of sleep is reduced, and the more the sleep at the end of the night, naturally rich in REM sleep, is shortened. Ingre *et al.* (Ingre *et al.,* 2008) showed that with a morning team, sleep length was a function of the morning shift start time. Other authors have concluded that delaying the start of the shift by one hour would improve prior sleep and reduce daytime sleepiness (Rosa *et al.,* 1996).

In addition, the duration of the commute between home and the workplace often amplifies this amputation of sleep duration. Some authors recall that the need for consecutive recovery from sleep and fatigue may therefore lead to an increased risk of errors and accidents due to excessive daytime sleepiness (Rosa *et al.,* 1996; Akerstedt *et al.*, 2010).

For night shifts, the times at which they start or finish determine the duration of the work performed at night and therefore the magnitude of circadian rhythm disruption, sleep debt and the need for recovery from fatigue.

9.2.1.2.7 Duration of work shifts: avoid long shifts

It is often recalled that the length of the shift should be adjusted to both the workload during the shift, and also its positioning in the 24-hour period. Thus, a long shift during the day is more in phase with the circadian rhythmicity of biological functions (better synchronised with the biological day) than a long night shift. Several authors reiterate that, in any case, the occasions on which shifts exceed 8 hours should be minimised (Axelsson *et al.,* 1998; Rosa 1995; Yamada, 2001; Ferguson *et al.*, 2012), in particular when they include night work.

As a general rule, it is advisable to define the duration of the shift according to the workload and nature: whether it is mainly physical or mental. Thus, long shifts are probably better tolerated if the physical effort is not high (administrative work, light physical work with appropriate rest breaks) and if there is no exposure to toxic substances. Besides the duration of the shift, the debate should also focus on the conditions for carrying out the work during the shift.

Faced with a real increase in the establishment of 12-hour shifts in companies and hospitals – most of the time without questions being asked about occupational health or safety – a group of occupational health stakeholders recently published a compendium of their findings and produced a summary of the literature (Weibel, 2014). Weight gain, and increased risk of error, occupational or commuting accidents, addictive behaviour, musculoskeletal disorders and back pathologies were the most frequently documented side effects of long shifts compared to 8-hour shifts. Workers on long shifts are obliged to choose between health and family availability, most often to the detriment of their health. Twelve-hour shifts aggravate adaptation difficulties when there is a failure to take into account the physical and mental load of the work and the benchmarks that help give meaning to the work. An organisation based on long shifts should only be adopted in cases of absolute necessity, while complying with rest times, breaks and the amplitude of days, and taking account of recommendations that limit the negative effects (Weibel, 2014). Furthermore, 2x12 h shift systems (like any other clockwise system) can differ greatly depending on the other organisational elements with which they are combined: the number of employees, whether or not they are able to sleep (or rest) during the shift, means of transmitting information between the different teams, *etc*. may all alleviate some of the disadvantages of long 12-hour shifts. The establishment of long shifts, and their effects, can only therefore be considered from a systemic analysis of the work, taking into account the other organisational elements mentioned above, the content of the work, and the characteristics of the people concerned (Barthe, 2009).

9.2.1.2.8 Rotation cycles and the distribution of days off: importance of predictability and regularity

In continuous shift work, the rest days at the end of the cycle do not always coincide with the weekend, a period of the week with great social value. Some authors argue that regularity and predictability, combined with a certain degree of flexibility controlled by the worker, can compensate for this problem and enable more satisfactory management of leisure time, family time and social commitments (Costa *et al.,* 2004; Kogi, 2004).

A study conducted on the childcare efforts of 30 telephone operators, mothers of young children subjected to hours that were atypical, irregular and unpredictable, showed that these childcare efforts (actions seeking a childcare solution to cover their work periods) averaged 4 per week and, for some of them, could be as many as 18 times per week (Prevost, 2001). The employees sought predictability, they wanted advance notification of their hours, regularity in their hours, and for their rest days to fall at the end of the week (Messing *et al.,* 2014).

9.2.1.2.9 Shift handover: a shift overlap time that favours continuity

Continuity of activities, whether production or service, is ensured by 2, 3 or 4 shift rotations, over the 24 hours. The shift handover is considered to be the period when one team, called the outgoing team, is replaced by another, the incoming team.

The shift handover can be planned in the organisation of the work, with a prescribed overlap between two consecutive shifts, which enables the teams to meet.

Grusenmeyer (Grusenmeyer, 1995; Grusenmeyer, 1997) formalised the concept of shift handover based on industrial sites running continuously: a nuclear power station and paper pulp manufacturer. She distinguished between the time for passing on instructions, the time taken for the incoming team to take over, and the time taken for the outgoing team to "disconnect". Her work showed the process of adjusting and sharing functional representations between the incoming and outgoing operators at the time of shift handover, and its importance to reliability.

Le Bris *et al.* (Le Bris *et al.,* 2012) analysed the activity of team leaders on an aircraft final assembly line and showed that the type of shift handover (notes with meeting *vs* notes without meeting) had an impact on the content of transmissions. Unsurprisingly, the analysis showed that when there was a "meeting", the content of the exchanges was more detailed, and that oral exchanges during the meeting enabled the incoming and outgoing team leaders to validate their assumptions, update the representation they had of the work situation, and work together. It is therefore a guarantee of reliability. For shift work, the shift handover is an important time for coordination, updating representations on the situation, and transferring responsibilities.

In some cases, while this handover time is neither formalised nor paid by the company or establishment, it is nevertheless possible to see the incoming operators arrive well before their shift starts, and the outgoing operators remaining well beyond the end of their shift. This informal overlap, solely at the initiative and discretion of the incoming operator, demonstrates the importance they attach to this meeting and the exchanges it enables. Nor is it infrequent for incoming operators to call their colleagues after they have returned home, because they remember an event they have not informed them of, or are concerned about the change in the status of production or of a patient.

The shift handover is an important time for coordination, updating representations on the situation, and transferring responsibilities. These authors (Le Bris and Grusenmeyer) reiterate that the shift handover helps avoid any break in the succession of teams, by enabling the coordination of activities and the monitoring of hazards, in particular. The possibility of a meeting between the incoming and outgoing teams, allowing for verbal exchanges, is a guarantee of reliability and contributes to the prevention of occupational risks.

It therefore seems important to encourage formal sharing time between the teams by organising sufficient overlap time between rotating shifts, to ensure the continuity, quality and reliability of the work produced.

9.2.1.2.10 Enabling recovery during the shift: rest and naps during the night shift

Scientific research that has studied the effects of nocturnal naps on night operators, using performance tests and self-assessment scales, emphasises the positive effects of resting during the night shift.

Smith and Wilson in "Shiftwork: Health, Sleep and Performance" compared in their study two groups of intensive care nurses during night shifts (9pm-8.30am): the first group was made up of nurses who had the opportunity to take a nap in the middle of the night, the second, nurses who did not. The results showed that at the end of the night shift, the nurses who had taken naps performed better in a test of logical reasoning and had a better mood level than those who had not slept. Another comparative study, conducted with the process controllers of two chemical companies (Matsumoto and Harada, 1994), one having introduced nighttime naps lasting two hours, the other not, showed a beneficial impact of nocturnal naps, not on the subjective state of the operators at the end of the night, but on their level of fatigue during the rotation cycle.

In a laboratory situation, many studies, performed with sleep-deprived subjects, have tested the effects of napping on performance and vigilance, according to its position in the 24 hours and its duration (Tassi *et al.*, 1994). They emphasise the importance of anchor sleep, i.e. taken regularly at the same time to foster the normal periodicity of biological rhythms (MINORS *et al.*, 1987). The only disadvantage of night naps, which is expressed unanimously, concerns their negative consequences on performance immediately after waking up, due to the phenomenon of sleep inertia (Dinges, 1992). This phenomenon is particularly true for long naps, it does not exist for short naps (15-20 min), as has been shown in the company environment by Bonnefond *et al. (*Bonnefond *et al.,* 2001).

Smith-Coggins *et al.* (Smith-Coggins *et al.,* 2006) showed that naps improved the performance of a simulation task. In this study, 49 health professionals (doctors and nurses) were divided into two groups and worked for three successive nights. Only the first group were able to take a 40 min nap at three o'clock in the morning. The results showed that the staff who had slept had faster reaction times, fewer vigilance failures and assessed themselves as less fatigued and sleepy at the end of their night shift. In addition, in a simulated work task, installing an intravenous drip, staff who had benefited from a nap inserted the catheter more quickly than those who were not given the chance to sleep.

Ruggiero *et al.* (Ruggiero and Redeker, 2014), in a systematic review on the effects of naps on sleepiness and performance, identified 13 relevant studies (studies comparing napping and absence of napping in the laboratory or in the field). One single study was a randomised controlled trial (Smith-Coggins *et al.,* 2006). Most found that despite a short period of sleep inertia immediately after the naps, they helped reduce sleepiness and improve performance during the night shift. Scheer *et al.* (Scheer *et al.,* 2008) stressed that it would be preferable to plan for a recovery period after a nap, especially at night. They stated that a planned nap during work may increase total sleep duration and reduce the harmful health effects of sleep deprivation (cardiovascular, cancer, gastric ulcers) as well as performance deficits and sleepiness. Most of the studies tested naps of 20-40 minutes starting between 2am and 3am (for reasons of feasibility in the field). In these conditions, the introduction of a nap had a positive influence on sleepiness, in certain vigilance tests (PVT, see the description of this test in the section on cognitive performance) and on performance (Smith *et al.,* 2007). Naps had a beneficial effect on sleepiness and reaction times for a period of 15 to 225 minutes after the end of the nap episode (Lovato *et al.,* 2009). The authors stressed that these short naps are not sufficient to compensate for the sleep debt caused by night work. In studies where this has been measured, naps did not disturb daytime sleep and, in the majority of cases, performance was not affected by sleep inertia.

It should be noted that in many work situations, naps during the night shift are neither formalised nor authorised. Even when tolerated, conditions do not always allow staff to sleep (unsuitable premises, lack of beds, vague distribution of tasks, *etc*.) and only rest is possible.

These rest periods must be understood as quiet episodes, to be distinguished from moments of relaxation, discussion, and meals with colleagues. Akerstedt and Landström (Akerstedt, 1998) considered that these rest periods could enable night operators to recover and restore their levels of vigilance in a similar way to naps. In addition, the effects on sleepiness of rests taken during night shifts have been demonstrated, but in terms of safety and efficiency at work, nothing has yet been clearly confirmed (Tucker, 2003).

Lastly, there is the question of whether or not a nap can be taken in the work situation. A study conducted in a hospital where five members of the healthcare team were able to rest or sleep during the night shift showed that the episodes of rest and naps, taken spontaneously, were dependent on the demands of the night. During quiet nights, the healthcare staff took more periods of rest and naps between their monitoring rounds than during busy nights.

Even if at present additional studies are needed to determine the ideal duration and positioning of naps to minimise the effects of sleep debt on sleepiness and performance, most studies show a beneficial effect of naps. In terms of feasibility, taking short naps during work clearly seems to be a promising prevention option, to consider on a case-by-case basis, depending on the demands of the work. Indeed, such naps can only be established after a prior detailed analysis of the work. This involves conditions relating to the demands and rhythms of the work, the staffing levels, and the possibility of handing over responsibilities within the work team.

9.2.2 Acting on the work itself in order to limit the effects of shift and night work

Besides adapting the shift system, prevention teams can simultaneously put in place measures to act on the work situation itself, to try and limit the risks. These measures are sought based on a precise knowledge of the work to be performed during these hours and the individual and collective control processes at play in the work activity and in the workers' personal lives (see Chapter 8).

9.2.2.1 Acting on the other occupational risks

Workers subject to situations of rotating and night shifts often have more difficult working conditions. The last study by the DARES showed that in 2012, night workers suffered more frequent time constraints: 87% also worked in the evenings and 72% of them also worked on Saturdays, on a regular basis. For 89% of night workers, the hours were determined and imposed by the company without any changes possible (Algava, 2014). They were also subject to more organisational constraints, with a requirement to be versatile, limited freedom to make decisions, and no possibility of autonomy in relation to the time constraints for carrying out their tasks. Their work involved more physical hardship and vigilance factors, such as, for example, "the requirement to stand for long periods or remain in another tiring or painful posture", "long or frequent walking", "the inability to take their eyes off their work", or "having to pay attention to brief visual or audible signals" (Algava, 2014). The analyses performed for this expert appraisal report, based on Sumer data (see Section 2.4), confirm this accumulation of hardship factors. They show harsher working conditions for employees working night and atypical hours than for workers with standard hours, regardless of sex. This is reflected by greater time pressure, increased adaptability, less autonomy, risks and consequences of errors regarded as more serious for safety, with more frequent physical or sexual abuse than for employees working standard hours.

Another example of occupational risks other than those from shift and night work is that employees exposed to certain toxic substances are more vulnerable at night, due to the fact that metabolic rates and biological effects vary according to the different times of day (Haus *et al.*, 2006; Smolensky and Reinberg, 1990).

Thus, prevention and measures focused on the other occupational risks present in work situations involving rotating and night shifts: stricter time constraints, painful postures, sustained attention, lack of autonomy, risk of abuse or exposure to toxic substances, would improve the working conditions and therefore the health of people working under these shift conditions.

9.2.2.2 Acting on the content of the work: nature of the tasks and increased room for manoeuvre

All the studies reported in Chapter 8 based on the analysis of the work activity of people working rotating and night shifts show that a debate is needed on the nature of the tasks prescribed during the shifts. This mainly involves designing tasks compatible with the workers' functional capacities (physical and cognitive), in particular by taking care to reduce constraints relating to work rate, physical effort, attention, memory, etc. For example, ensuring that the most demanding or dangerous tasks are completed in the first few hours of the night shift and conversely, avoiding monotony and therefore lack of attention, and sleepiness. It may also be possible to consider reorganising certain night tasks – or even transferring some of them to the day – and offering breaks that are carefully distributed throughout the work shift.

Similarly, these studies reveal the anticipation strategies adopted by the operators during night shifts in light of the experience they have of how their biological state evolves (Toupin, 2012; Toupin, 2014; Pueyo *et al.* 2011). In prevention, enabling operators to anticipate can introduce room for manoeuvre, giving maximum flexibility to the way instructions are implemented. This can also lead to a reflection on the tools providing a global and synthetic view of the situation in the past, present and future, technological tools, organisational tools (e.g. meeting during shift handovers), *etc*.

9.2.2.3 Promoting the collective dimension of the work: numbers in the teams

The work collective is also a significant help in managing fatigue related to working hours. Reinforcing night teams can then be a solution to compensate for the effects of these hours on reliability, safety and health. In addition to the cooperation and communication made possible to manage fatigue related to the hours, a sufficient workforce in the teams working atypical hours would enable adjustments such as the introduction of naps during the night shifts. The nighttime nap, which is a practice rarely considered in France, nevertheless has beneficial effects on the level of sleepiness and fatigue, on mood, on some cognitive functions of the operators, but also on the risk of error. The establishment of such naps requires a prior detailed analysis of the work and involves conditions relating to the demands and rhythms of work, the staffing levels, and the skills present.

9.2.2.4 Promoting the reconciliation of the different spheres of life

In addition to the studies presented in Chapter 5 of this report, on the links between social and family life and rotating and night shifts, the work situation itself can prevent or promote management of the implications of atypical hours on life outside work. For example, women working as cleaners in the evening, who call their children in the evening during their breaks to help with homework, give instructions on the evening meal, but also to tell their children to go to bed (Abbas, 2009). Managing the private sphere during work reflects a "dual presence" at family and professional level, which makes strong demands on affective and cognitive resources (Vogel, 2003). When this management is hampered by the work it can be a source of impairment to health over a longer or shorter period; it can also have a negative impact on the result of the work.

Controlling the risks associated with atypical working hours also means promoting reconciliation between the hours, work and personal life. There needs to be a debate on the tools to foster this management: the possibility of phoning from the place of work, teleworking, *etc*. Compromises should also be found in consultation with key stakeholders regarding the choice of hours, the predictability of the schedule, the options for modes of childcare, public transport, or mobility from one type of shift to another depending on the family situation.

To summarise, the studies reiterate that the organisation of shift working time can minimise the disruption of biological rhythms and social life. The indications identified from the literature (but not validated by the Working Group) are as follows:

- reduce night work as much as possible;
- adopt rapid rotation regimes, in order to limit the number of consecutive night shifts, so as to disrupt circadian rhythms and sleep as little as possible;
- limit night shifts to three consecutive shifts;
- generally opt to rotate shifts in a clockwise direction (morning/afternoon/night), because it follows the natural periodicity of most individuals' biological circadian rhythms (except for morning chronotypes for whom an anticlockwise rotation may be less detrimental) and in order to benefit from longer rest periods between shifts;
- do not start the morning shift too early, in order to limit sleep debt and avoid excessive daytime sleepiness;
- do not finish too late in the evening, in order to limit family desynchronisation.
- encourage the greatest possible number of weekends of rest ;
- adjust the length of the shift according to the physical and mental load of the tasks;
- consider shifts lasting 9 to 12 hours only in specific cases (light work, adequate breaks, no exposure to toxic substances, no night work);
- preferably arrange the rest days after the night shift, to promote faster recovery from fatigue and sleep debt;
- insert appropriate breaks during the shift, leaving sufficient time for meals and short naps;
- organise sufficient overlap time between the shifts and therefore between the teams to enable the transmission of oral information that enhances the quality of the work, safety and reliability;
- increase the room for manoeuvre and temporal flexibility of tasks so that people can organise themselves during the shift to manage their psychophysiological variations;
- promote the collective dimension of the work during night shifts (collective debates and exchanges between teams at the stage when the organisation of night work is being planned), which ensures reliability, safety, and preservation of health;
- promote the reconciliation of the different spheres of life.

The aspects mentioned above may differ in their weight and influence. Thus, the solutions should be considered according to various factors, such as the activity sector, labour relations, union representation, the characteristics of the company population (for example mostly women, ageing employees), the geographical location of the company, the socio-economic level of the employees, the organisation of transport and social services. In addition, consultation, and collective exchanges between the teams at the stage when the organisation of night work is being planned, are essential prerequisites.

9.2.3 Acting on the career paths

9.2.3.1 Duration of exposure, health and shift work

Employees rarely practice shift and night work throughout their whole lifetimes. In France, in 2011, the mean duration of exposure to night work was 15 years, and the median duration was 13 years (Bahu, 2012). At the European level, the number of employees doing night and shift work in 2010 declined gradually with age, both for men and women (Eurofound, 2012).

The links between the duration of exposure to occupational constraints, such as shift and night work, and the state of health are complex, since employees suffering from the most serious health problems in the short or medium term have "left" these constraining hours (reassignment to the day shift, resignation, exiting the labour force, or even death), while more resistant employees may keep their shifts, and their hours, for many years. Some studies show very significant excess risks in certain chronic pathologies after as few as 5 years of shift work, including a part at night, others after 10 years or more, so there is no determinable threshold from a scientific point of view, given the multiple factors modulating exposure and effects. Bourget-Devouassoux and Volkoff (Bourget-Devouassoux, 1991) showed, from the results of INSEE's "*Living Conditions*" survey, that the morbidity rate of workers in the 40-64 years age group was higher among former shift workers now working regular day shifts than among current shift workers. The morbidity rate was calculated from four indicators: chronic disease, symptoms perceived in the last 3 weeks, work interruptions lasting at least 3 weeks, and hospitalisation in the last 12 months, on a sample of 2879 workers. Current shift workers had a morbidity indicator close to those who had never been exposed. This is the "healthy worker" effect established as early as 1959 in Danish plants (Aanonsen, 1959). The health consequences of shift and night work are very often masked by a selection effect: employees working at night tend to return to normal hours when major health disorders become apparent.

Hence the importance of examining the entire career path in order to better assess the effects of shift and night work on health.

9.2.3.2 Career paths and age management

The "Health and career path" survey by the Directorate for Research, Studies, Evaluation and Statistics (DREES) focused on the career trajectories and health of nearly 14,000 employees. It showed that people in their fifties exposed to physical constraints in their professional careers, including night work (night work, repetitive work, physically demanding work or exposure to toxic products) were less healthy than people of the same age who had never been exposed (DREES, 2011). For night work, 31% of people aged between 50 and 74 years exposed to night hours for 5 to 14 years reported that they were "limited in their usual activities", compared to 22% of people who had never been exposed (Bahu, 2012).

While few studies have addressed the problems of work-related strain throughout the entire working life, the fact remains that the existence of difficult working conditions requires specific measures to be taken. In companies that have held a debate on the employment of seniors, the implementation of new human resources management (HRM) practices that incorporate age-related collective management can be observed. These practices are based firstly on traditional tools for jobs and skills management planning, in order to define patterns of career paths, and secondly on a more systematic debate on working conditions and their effects (in terms of potential risks for health, but also the risk of obsolescence of skills). They attempt to take account of the diversity of the employees' capabilities, aspirations and skills by structuring clear and socially acceptable rules.

Thus, in a report for the COCT (Steering Committee on Working Conditions) of 2012, the French National Agency for the Improvement of Working Conditions (ANACT) advocated several options to pursue on preventive action with regard to the ageing of workers:

- overall improvement of working conditions. This limits the effects of work-related strain, broadens the room for manoeuvre when assigning employees of different ages, and increases the opportunities to develop preservation strategies;
- actions "targeted" at personnel with capacity limitations. These limitations are not specific to an age group, but their statistical link with age has been established. The question then arises as to how to establish a reserve of less arduous work situations that could be occupied by personnel suffering from the sequelae of accidents or disabling conditions of varying severity;
- adapting career paths, in such a way as to limit long-term exposure to disadvantageous constraints, while encouraging consistent paths that enable experience to be built up. While it is accepted that developing this experience implies both variety in the situations experienced – avoiding professional stagnation – and

"breathing" time conducive to the deployment of personal and collective reflections on these situations, the importance of an "ergonomic" approach (in the sense of an optimal arrangement of the work resources and situations) is underlined, not only for each situation, but in how they are linked together.

Related to the particular case of night/shift work, these courses of action imply the possibility of a temporary or permanent return to day shifts, and therefore an organisation of work that enables employees to "exit" shift and/or night work temporarily, or permanently.

9.3 Secondary prevention of risks associated with shift and night work

It should be remembered that in secondary prevention, the measures involve identifying the health problem at its earliest stage and applying fast and efficient treatment to limit adverse consequences. Thus, the actions involve information intended for the employees concerned on the means available to deal with these risks. The actions here are therefore focused on the employees and the tools that can help them manage the difficulties related to the risks identified in the work. Adopting measures that can reduce the adverse consequences of night work can enable employees to adapt them to their own specific preferences and social and family constraints.

9.3.1 Measures for the promotion and protection of health

9.3.1.1 Sleep and vigilance

9.3.1.1.1 Sleep hygiene

The lack of sleep suffered by night and shift workers largely originates from their difficulty getting sleep of sufficient quality and duration when they sleep during the day. Applying the principles of sleep hygiene, already used in the treatment of insomnia and recommended in the HAS report on night work (HAS, 2012), could help improve diurnal sleep, even if they have not yet been tested systematically in night workers. Sleep hygiene refers to a set of behaviours, environmental conditions and other factors associated with sleep that are under an individual's control and that can be adjusted to improve sleep. In general, sleep hygiene recommendations are intended to reduce behaviours that interfere with good sleep, and strengthen those that promote it. Clinicians agree in recommending at least the following four rules to patients with insomnia (Stepanski and Wyatt, 2003):

- maintain a regular sleep schedule;
- avoid caffeine, alcohol and nicotine in the hours before bedtime;
- adapt the sleep environment (light, temperature, noise, appropriate bedding);
- exercise (except in the hours before bedtime).

Although a regular sleep schedule is not possible for night workers, in particular if they work rotating shifts, the other three rules remain relevant. Caffeine has a stimulating effect that can disrupt the worker's sleep several hours after it is last consumed. It is therefore recommended that night workers only use caffeine at the beginning of their shift and do not drink coffee during the last 5 hours of work if they plan to go to bed shortly after their return home (HAS, 2012). This recommendation may be particularly important for older workers whose daytime sleep is even more sensitive to the disruptive effects of caffeine (Carrier *et al.,* 2009).

Alcohol is often used before bedtime to facilitate sleep. However, the sedative and anxiolytic effects that help a person fall asleep are cancelled out by the negative effects on sleep quality that make the sleep fragmented, agitated and ineffective (Ebrahim *et al.*, 2013).

Adapting the sleep environment is the primary recommendation to facilitate daytime sleep for night workers. Indeed, as they have to sleep during the day, their environment is often particularly unfavourable to sleep, due to the presence of light, noise and a higher ambient temperature. A study showed that 15% of shift workers developed sleep disorders if they had good housing conditions, compared to 73% if their housing did not offer silence and isolation during their daytime sleep (Aanonsen, 1964).

Regarding exercise, the regular practice of physical activity seems to have a beneficial, albeit moderate, effect on sleep by increasing its duration as well as the proportion of most healing stages of sleep (Driver *et al.*, 2000). However, high-intensity exercise should be avoided in the two hours before bedtime.

9.3.1.1.2 Timing of the main sleep episode

According to Akerstedt, most night workers choose to go to bed in the morning, when returning home from work (Akerstedt, 1998). This is also what is most often recommended to workers. Several authors have stated that if there is no adjustment of the biological clock to night work, the circadian propensity to wakefulness increases rapidly during the course of the day, limiting the person's ability to remain asleep (Foret and Benoit, 1974) (Akerstedt, 1984). Thus, experimental studies show that the later a person goes to bed, the shorter the duration of their diurnal sleep (Akerstedt *et al.*, 1982a; Czeisler *et al.*, 1980). The duration of the main sleep episode would therefore be longer if the worker went to bed in the morning, as early as possible after returning from work, which is not always compatible with the requirements of parental life, since this time corresponds to when children need to be woken up and get ready for school. However, a minority of night workers choose from the outset to have their main sleep episode in the afternoon and the evening, before starting their night shift (Dumont *et al.,* 2001). This strategy may have the advantage of restoring a similar "rest-work-leisure" sequence to that of day workers, and seems to be favoured especially by workers with a morning chronotype, who find it more difficult to sleep in the morning and stay awake in the evening (Natale *et al.,* 2003). As the chronotype tends more towards the morning upon ageing, it is possible that this strategy is more suitable for older workers, but this hypothesis has not yet been tested in the field. Laboratory studies suggest that having the main sleep episode in the afternoon and the evening would reduce sleepiness and improve performance during the night shift (Horowitz *et al.*, 2001; Santhi *et al.*, 2005; Santhi *et al.*, 2008), mainly by reducing homeostatic sleep pressure, since the duration of wakefulness between the end of the sleep episode and the start of the night shift is shorter (similar to that of day workers when starting work in the morning).

9.3.1.1.3 Naps

A favoured way of increasing total sleep duration is the taking of naps in addition to the main sleep episode. Naps can be taken either in the workplace, when this is possible and accepted, or at home. The fears associated with the use of naps in the workplace are firstly that they can affect the duration or quality of the main sleep episode, and secondly that they are followed by a period of so-called "sleep inertia", during which levels of vigilance can be extremely low. Most of the studies that have tested the effects of naps in night workers have assessed the effects of naps taken at the workplace on different indicators of vigilance and performance, and have shown a beneficial effect.

Another option available to the worker is to take a nap at home during the day in addition to their main sleep episode. Few studies have been conducted in the field to assess the effectiveness of this strategy. However, in a retrospective study, a nap before the night shift was significantly associated with increased vigilance and a reduction in accidents among police officers, mainly due to the decline in homeostatic sleep pressure (Garbarino *et al.*, 2004). Another study also showed that a nap in the evening, before the first two of a series of four night shifts, improved performance and reduced sleepiness, particularly in combination with caffeine consumption (Schweitzer *et al.*, 2006). As well as lengthening the duration of sleep per 24 hours during a series of night shifts, the nap can also be used preventively during the day preceding the first night shift. Laboratory studies suggested that a 2-hour nap during the afternoon preceding a night of sleep loss effectively reduced sleepiness during the night (Dinges *et al.*, 1987). In fact, the results of this study even suggested that the preventive nap before the night of sleep loss may be more effective at reducing nocturnal sleepiness than the nap taken during the night.

9.3.1.2 Pharmacological aids

9.3.1.2.1 Caffeine

Caffeine is the means used most often by night workers to increase their levels of vigilance during the night. Laboratory studies show that caffeine may reduce night sleepiness and increase performance, and its preventive use prior to the increase in sleepiness may be even more effective than its use for reducing sleepiness that is already elevated (Akerstedt *et al.*, 2009). However, studies on the ground are rare. One study measured the effects of 4 mg of caffeine administered 30 minutes before the beginning of the night work, and found a beneficial effect on nighttime vigilance, as well as increased efficiency in combination with a nap (Schweitzer *et al.*, 2006).

A Cochrane review published in 2010 (Ker *et al.*, 2010) identified the studies that had tested caffeine's potential to increase vigilance and prevent accidents and errors among night workers. Out of the 13 randomised studies included in the analysis, two assessed the effect of caffeine on errors and found a significant decrease in errors with caffeine, compared to a placebo. The 11 studies that assessed the effects on cognitive performance found significant beneficial effects on thinking capacity, memory and attention. While it is impossible to conclude as to the effects of caffeine on the risk of errors or accidents, the stimulating effects of caffeine on cognitive functions appear to be quite clear. The authors pointed out, however, that the research data were mainly collected in young subjects in simulation studies and that it is therefore difficult to determine whether the observed results could apply on the ground to real night workers, or to older workers.

The stimulating effect of caffeine, whether it comes from coffee, energy drinks or other sources, continues for several hours. As mentioned in the section on sleep hygiene, workers should therefore avoid its consumption in the last 5 hours of work if they want to prevent negative effects on their sleep after returning home (HAS, 2012).

9.3.1.2.2 Melatonin

As the hormone melatonin has sleep-inducing properties, it may have the potential to foster daytime sleep. A Cochrane review covering only the randomised controlled studies published up to September 2013 assessed nine studies that tested the effects of melatonin on daytime sleep in night workers (Liira *et al.*, 2014). The results suggested that taking melatonin (1 to 10 mg) extended the duration of daytime sleep by 24 minutes on average, without any effect on sleep latency or any side effects. The results did not show any dose-response relationship. However, the studies were assessed as being of low quality because most focused on a small number of subjects and on the short-term (one week or less). According to a more comprehensive review (Smith *et al.*, 2012), melatonin may modestly increase sleep duration and quality, particularly in people who have the greatest difficulty sleeping during the day, in agreement with the experimental studies (Wyatt *et al.*, 2006).

Melatonin also has chronobiotic properties, enabling it to act on the synchronisation of the circadian clock. The times of administration have opposite (and more modest) effects to those of exposure to light. Taking melatonin in the morning (before daytime sleep) may promote a delay in the clock, which is desired to promote daytime sleep at the beginning of the day, whereas taking melatonin in the afternoon promotes an advance, which is desired when the sleep episode takes place later in the day, before the night shift. However, the clock delay induced by melatonin administered in the morning has not been observed in all studies (Lockley, 2007). On the other hand, in the only randomised controlled trial conducted in night workers, with a daily dose of 0.5 mg at bedtime during a series of 7 consecutive nights of work, the circadian adjustment proved to be very low (Sack, 1997). Moreover, the chronobiotic effect sought involved administration of melatonin at a precise biological time, which is not exactly known in workers on night or rotating shifts. The chronobiotic property of melatonin is therefore difficult to implement in practice.

Lastly, as the decrease in melatonin secretion is one of the proposed hypotheses for the mechanisms that can connect night work and cancer, the administration of melatonin supplements as a preventive measure could be considered. However, its involvement in carcinogenesis has not been clearly established (see Section 6.3.5), and its preventive effects on cancer risk have not been demonstrated (Bonde *et al.*, 2012). In addition, the possibility of adverse effects from the regular intake of melatonin cannot currently be excluded, since its long-term effects have not been documented, and some of its properties, in particular its proinflammatory effects, could be harmful to certain people or in the presence of autoimmune disease (Kostoglou-Athanassiou, 2013). Melatonin is not approved in France for the treatment of shift work disorder (SWD).

9.3.1.2.3 Medication

Drugs such as modafinil and armodafinil are sometimes prescribed in some countries to improve the vigilance of workers suffering from shift work disorder (SWD). Three randomised controlled studies were analysed in the 2014 Cochrane review on pharmacological interventions in night workers: one on modafinil and two on armodafinil (Liira *et al.*, 2014). Both drugs appear to modestly increase vigilance and decrease sleepiness in workers suffering from SWD. Several side effects have however been reported: severe skin reactions, headaches, nausea and increase in blood pressure. Unlike the American Academy of Sleep Medicine, which recommends the use of these drugs for night workers (Morgenthaler *et al.*, 2007), the authors of the Cochrane review consider that modafinil is associated with only a slight benefit and frequent side effects. These drugs have not been tested in night workers not suffering from SWD, but the merits of the chronic use of drugs in healthy night workers seem questionable. These drugs, approved in some countries, are not approved in France and Europe for the treatment of shift work disorder (SWD).

Sleeping pills can help with daytime sleep (Walsh *et al.*, 1995), but the two randomised controlled studies on the hypnotics (zopiclone and lormetazepam) included in the 2014 Cochrane review (Liira *et al.,* 2014) were of low quality and did not seem to show an effect on the quality and duration of daytime sleep.

9.3.1.3 Adjusting circadian rhythms by controlled exposure to light

As the light-dark cycle is the main environmental indicator used by the circadian clock to synchronise itself, controlled exposure to light could theoretically be used to facilitate the circadian adjustment of night workers to their shifts. It has been known since the 1990s that the circadian clock can be completely resynchronised in a few days by exposing individuals to high-intensity light for the entire night (Czeisler *et al.*, 1990). A series of laboratory studies have shown that circadian synchronisation to simulated night work was significantly promoted by an increase in light during the work shift (Baehr *et al.* 1999; Boivin *et al.*, 2002). Some studies have however reported that the increase in light intensity during the night shift was more effective among evening rather than morning chronotypes, and that it could even be counterproductive in morning chronotypes (Revell *et al.,* 2006).

Recently, a series of experimental studies in humans have shown that it was not necessary to expose people continuously to bright light, but that intermittent exposure (Rimmer *et al.*, 2000; Gronfier *et al.*, 2004; Gronfier *et al.*, 2007) or more moderate light intensity (Martin *et al.*, 1998) could have the same resynchronisation properties. Other promising chronobiological approaches have been studied in the laboratory. A number of studies have shown that decreasing the light intensity in specific wavelengths at certain times of the day, *via* optical filters (glasses), could promote the quality of sleep, and vigilance during the work shift (Sasseville *et al.*, 2009; Smith *et al.*, 2012; Rahman *et al.*, 2013). However, given the small populations examined in these studies, these results need to be replicated before optical filters can be recommended. Moreover, the use of these glasses, for example when returning home after a night shift, could increase sleepiness while driving (Lockley, 2007), a risk that should be assessed.

In a recent review of interventions conducted on the ground, (Neil-Sztramko *et al.*, 2014) 12 studies were identified that measured the effects of controlled exposure to light and dark: 7 studies that used protocols of intermittent exposure to bright light, 4 studies that combined exposure to bright light with the wearing of glasses filtering blue light, and one study that assessed only the effects of wearing glasses filtering blue wavelengths. Among all these interventions, the light intensities ranged from 200 to 10,000 lux and the accumulated exposure time from 10 minutes to 6 hours. The variables most often measured were sleep quality (7 positive and 3 negative) and circadian markers: melatonin (4 positive studies, 3 negative), cortisol (1 positive and 1 negative) and body temperature (2 positive and 1 negative). The results obtained therefore differed very widely and no conclusions can be drawn because of the heterogeneity of the protocols used for the exposure to light (duration, intensity, time, intermittent or continuous) and the measured parameters (sleep quality, melatonin, cortisol, temperature, *etc*.). Similarly, the wearing of filter glasses was not controlled for, and varied according to the working hours of the participants and the commute duration after work.

It should be noted that the circadian adjustment (circadian resynchronisation) is not immediate after a change of shift and can only be achieved in a few days, if conditions (mainly exposure to light and dark) are favourable. This circadian adjustment can only therefore be considered for fixed shifts, or slow rotations, but not for quick rotations. Even with fixed shifts and slow rotations, the relevance of a complete circadian resynchronisation could be challenged on the basis that the night workers become desynchronised again once they return to a day shift or go on leave (Rajaratnam and Arendt, 2001). This is the complaint of oil platform workers, whose periods of night work (in a protected environment) are long enough (14 to 21 consecutive nights) to produce a circadian adjustment. They become synchronised with their night work, but are then desynchronised at the beginning of their rest period. Controlled exposure to light has been used successfully in this population to accelerate their readaptation to daytime life (Thorne *et al.*, 2010). Complete resynchronisation therefore requires repeated adjustments at each schedule change. Even if this has not been demonstrated, it has been suggested that these repeated changes to the internal time of the biological clock could be more harmful to health than the desynchronisation itself (Haus *et al.*, 2006). This assumption should be viewed with caution until it has been demonstrated.

It is possible that a partial adjustment is a good compromise to facilitate greater stability of the circadian system. In simulation studies, a partial adjustment was obtained by combining intermittent bright light at night with the wearing of glasses filtering blue light after work (Smith *et al.*, 2012), or by changing the profile of exposure to light during the day (Dumont *et al.*, 2009). This approach has not yet been tested on the ground in night workers, and the degree of partial adjustment that may be most favourable to health still needs to be determined.

Thus, even if simulation studies in the laboratory show that an increase in light intensity during the night shift, or a reduction at other times (for example in the morning), are favourable to circadian clock synchronisation and better sleep quality, the fact that the studies on the ground have not systematically observed these positive effects suggests that practical implementation is not obvious. At this stage, the best application parameters have not yet been determined and studies on the ground are still too fragmented to be able to derive any clear recommendations on the prevention of health problems among shift and night workers using controlled exposure to light. Other adequate studies on the ground are needed, with sufficient populations, well documented exposure to night work, and well quantified effects with validated scales and relevant biological markers.

9.3.1.4 Behavioural interventions: sporting activity and diet

Night work has an impact on lifestyles, including the practice of physical activities and diet (Atkinson *et al.,* 2008).

Night work, whether fixed or rotating, restricts the opportunities for physical exercise and participation in team sports. In addition, it is particularly difficult for a tired and sleep-deprived worker to commit to the regular practice of physical activity.

Food consumption may also be modified by night work. Firstly, the normal habits of family meals are disrupted, and secondly, appetite and food preferences can be altered by lack of sleep and circadian desynchronisation. For example, a recent study showed an increase in the consumption of high-fat foods after a simulation of night work (Cain *et al.*, 2015), and the increase in food intake during sleep deprivation has been well established (Spiegel *et al.*, 2004).

Behavioural interventions designed to improve the physical activity and eating habits of night workers could improve their health, particularly their metabolic and cardiovascular functions, and thus reduce the risk of cardiometabolic disorders.

The HAS report reiterates that shift and/or night workers should be informed about the importance of maintaining three meals per 24 hours, according to the advice of the 2006-2010 French National Health and Nutrition Programme (PNNS), in particular regarding the frequencies of consumption of food groups.

Very few randomised controlled studies have been conducted on the ground. In a review published in 2014 (Neil-Sztramko *et al.*, 2014), two studies were analysed. The first tested a physical activity programme for nursing staff. The results showed an improvement in sleep duration with varying results on the subjective quality of sleep. Exercise improved respiratory capacity and strength, but had no effect on the phase of the circadian clock. The second tested a weight loss programme in factory workers. This programme led to a decrease in body mass index and blood pressure, and an increase in the level of physical activity and fruit consumption. A recent study assessed the effect of a one-year nutrition programme with dietary supervision offered to 235 night workers, on permanent or rotating shifts (Gusto *et al.*, 2015). This structured intervention improved behaviour associated with the consumption of sweet products, water and salt, and significantly increased recreational physical activity while reducing daily energy intakes. This type of intervention therefore has real potential to improve the health of night workers and reduce the harmful effects of their work schedules.

9.3.2 Monitoring of exposed employees

Individual monitoring of employees' state of health is carried out within occupational health departments, whose "sole mission is to avoid any impairment of worker health due to their work". It involves conducting specific medical examinations, in the framework of medical check-ups for "fitness" that can only be performed by the occupational physician. These examinations enable a link to be established between the employee's health and their professional situation[63].

These medical visits are of different types[64];

- the pre-recruitment medical examination. This is mandatory for any employee hired by a company, and must take place before the date of recruitment or at the latest before expiry of the trial period. The pre-recruitment medical examination has several purposes: it allows the doctor to ensure that the employee is medically fit for their job, to propose possible adjustments to the job or assignment to other jobs, to determine

[63] Fantoni-Quinton S, Czuba C. La Réforme Santé Travail [Occupational Health Reform]. ISTNF, 2012.

[64] Legal note of the CISME. Suivi individuel de l'état de santé des salariés [Individual monitoring of employees' state of health]. CISME; September 2014.

whether the employee is suffering from a condition that could be dangerous to others, to inform them about any risks specific to the job and the necessary medical monitoring, and to make them aware of the means of prevention applied;

- periodic medical examinations which, in theory, take place at least every two years. They help ensure that medical fitness for the job is maintained, and provide information on the medical consequences of exposure to the work and the necessary monitoring;
- "on demand" medical examinations are also provided for and can be requested by the employer or employee;
- examinations for "pre-resumption" and "resumption" of work.

The "pre-resumption" visit is mandatory for any employee who has been absent from work for more than three months. It is organised by the occupational health department and carried out by the occupational physician, but takes place on the initiative of the general practitioner, the medical adviser of the social security organisations, or the employee. The purpose of this visit is to recommend adjustments and adaptations for the job, recommendations for reclassification, or vocational training to facilitate reclassification.

The "resumption" visit is required after an employee has been absent for at least 30 days due to an occupational accident, or non-occupational illness or accident. And also, without any concept of duration, after maternity leave or an absence due to an occupational disease. Its purpose is to issue the notice of fitness to resume work, and also to give recommendations on adjustments or adaptations for the job, or reclassification of the employee. It also provides an opportunity to examine any proposals that may have been made by the employer, to adjust or adapt the job following the pre-resumption visit.

Specifically concerning night work, the Labour Code provides for specific protective provisions for individual medical monitoring. The employee concerned must be examined by the occupational physician before they can be assigned to their shift. If the doctor finds that the employee's state of health is compatible with night work, they then issue a medical fitness certificate. The night-working employee will be seen again every 6 months at a periodic medical visit, in the context of the enhanced medical surveillance (Articles L. 3122-42 and R. 3122-18 to R. 3122-21 of the French Labour Code).

For shift work, there is no such specific legal provision. Shift workers benefit from medical supervision under the conditions established by the Labour Code: pre-recruitment examination (Articles R. 4624-10 to R. 4624-14) and then periodic examinations at least every two years[65].

In addition, during these visits, the occupational physician may refer to the "Recommendations of good practice for the medical-professional surveillance of shift or night workers", established by the French National Authority for Health (HAS) in 2012. These are based on a professional agreement within a working group, following the opinion of a study group, and were developed in accordance with the HAS's methodology. They specify the different health effects that may be caused by these work rhythms, according to the levels of scientific evidence found in the literature. They state for each of these effects the clinical elements to be monitored during the medical visits, the clinical or paraclinical assessment tools that can be used, the recommended frequencies of their use, and the recommended measures or countermeasures. For example, the doctor can ask the employee about any possible sleep disorders, assessing their sleep time over 24 hours. To help with this, they may ask the employee to complete a sleep diary, during the first visit and then repeatedly if there are new complaints or in the framework of the follow-up. In the event of sleep

[65] INRS. ED 5023 "Le point des connaissances sur : Les horaires atypiques de travail" [Review of knowledge on atypical working hours]
http://www.inrs.fr/accueil/produits/mediatheque/doc/publications.html?refINRS=ED %205023.

disorders, they may advise the employee to maintain a minimum sleep time, take short naps, avoid stimulants, *etc*[66].

Lastly, during these visits, besides the effects on health, the occupational physician should also attempt to investigate the impact of night and/or shift work on the working conditions and quality of life. These consequences are generally mixed: indeed, these types of work organisation may include adaptations and advantages such as having more free time, or better remuneration; but on the other hand, the working conditions may be more difficult because these employees are often subject to other time constraints (work on Sundays, long days, etc.), as well as to other occupational exposure. They also feel a lack of professional recognition as well as professional and social isolation. The latter is accentuated by frequent difficulties reconciling social and family life: phase shift with regard to school rhythms, spouse's schedules, transport timetables[67].

However, it may be that following these various visits, the occupational physician finds that the employee is unfit for night and/or shift work.

This concept of unfitness is legally defined in such a way that it can only be decided by the occupational physician, who then becomes the key contact person for the employer and the employee. Unfitness is a very specific status, governed by law, which can only be declared after an examination of the employee's job, a study of the working conditions in the company, and two medical examinations two weeks apart, possibly combined with additional examinations (Article R. 4624-31 of the Labour Code). During this procedure, the occupational physician has to propose "individual measures such as job transfers or transformations, justified by considerations relating mainly to age, physical strength, or the workers' state of physical and mental health" (Article L. 4624-1 of the Labour Code). The employer is then required to reclassify the employee declared unfit, whether or not their unfitness is of occupational origin, and must therefore take into account the written conclusions of the occupational physician, and their suggestions regarding the employee's ability to exercise another existing task in the company (Articles L. 1226-2 and L. 1226-10 of the Labour Code). This mission of the occupational physician for professional reclassification is also exercised throughout the duration of the worker's employment contract, and therefore outside the unfitness procedure described above. The occupational physician will then instead make proposals on adapting the job. Specifically concerning night work, the Labour Code stipulates that night workers shall be given priority for the assignment of a day job (Articles L. 3122-37 and L. 3122-43) if that is what they wish.

However, in order to suggest adaptations to the job and/or reclassifications, the occupational physician needs knowledge of the work sites, working conditions and occupational risks, as well as the jobs that are performed there. To do this, the Labour Code stipulates that they shall have free access, either on their own initiative or at the request of the employer, to the CHSCT or staff representatives (Article R. 4624-3 of the Labour Code). To better carry out these workplace study and analysis actions, the occupational physician can obtain help from members of their multidisciplinary occupational health team (nurse, occupational health assistant, ergonomist, psychologist, technician or chemical engineer, *etc*.). This then enables them, according to the expertise requirements and the specialities, to mobilise different IPRPs (specialists in prevention of occupational risks), who will help better understand the

[66] HAS: Surveillance médico-professionnelle des travailleurs postés et/ou de nuit [Medical-professional monitoring of shift and/or night workers]. May 2012. Références en Santé au Travail. September 2012. No.131.

[67] CESE: "Le travail de nuit : impact sur les conditions de travail et de vie des salariés" ["Night work: impact on working conditions and the life of employees"] 2010.

different dimensions of the job(s) concerned. However, before these actors can intervene, the occupational physician must first have obtained the employer's agreement[68].

The dialogue between the employer, the employee and the occupational physician thus seems to be indispensable for achieving the priority objective of this approach: keeping the person concerned in employment[69].

9.4 Monitoring of the employee as part of tertiary prevention

It should be remembered that in tertiary prevention, the actions primary enable the monitoring and support of employees in a poor state of health, and also seek reparation and maintenance of employment.

French regulations require employees who work at night to undergo periodic medical surveillance every 6 months (Articles L. 3122-42 and R. 3122-18 to R. 3122-21 of the Labour Code). This is because employees who work at night are liable to develop health problems connected with these types of hours, in particular sleep disorders.

Thus, during the occupational health medical visit, the occupational physician (or even the occupational nurse acting by delegation) will endeavour to find any signs and symptoms that could suggest intolerance to night work. Since 2012, this monitoring has relied on recommendations, established from scientific data, and validated and certified by the French National Authority for Health, which indicate the specific elements to be screened for (HAS, 2012).

To demonstrate the existence of sleep disorders, it is recommended that the employee be questioned about the duration and quality of their sleep: chronic sleep debt, onset insomnia, sleep maintenance insomnia and early awakening, and discomfort from environmental factors (noise, light) (Léger *et al.,* 2009). On the basis of the information collected, an assessment of the chronotype using the "Horne and Ostberg Questionnaire" should provide some insight to understanding any disorders. At this level, moving on to the "Spiegel" sleep questionnaire and keeping a sleep diary can be useful for confirming the employee's complaints.

The doctor will then seek the existence of sleepiness by questioning the employee directly and also using the "Epworth" questionnaire. Investigating any occupational or commuting accidents may also provide indirect evidence on this same subject.

Then, a clinical examination involving measurement of biometric parameters and objective signs (weight, heart rate, blood pressure, cardiopulmonary auscultation, investigation of digestive symptoms, existence of musculoskeletal pains, etc.) will later help assess the employee's general condition and the potential impacts that sleep disorders may have on this condition.

Depending on the information collected, the occupational physician will assess the existence (and severity) of a sleep disorder. They may then decide on "first level" care, if it seems to them that the disorder is not yet very significant. This will mainly consist of individual advice on sleep and a healthy lifestyle (maintaining a minimum sleep duration of 7 h per 24 hours, taking naps of less than 30 minutes, organising a favourable daytime sleep environment, adapting diet, limiting consumption of stimulants, maintaining physical activity, etc.). More regular monitoring may be proposed: for example, an additional visit after 2-3 months to see

[68] Fantoni-Quinton S, Czuba C. La Réforme Santé Travail.[Occupational Health Reform]. ISTNF, 2012.

[69] Wurtz E, Fantoni Quinton S. La place du médecin du travail dans le processus de reclassement du salarié déclaré inapte à son poste de travail. [The role of the occupational physician in the process to reclassify an employee declared unfit for their job.] Archives des Maladies Professionnelles et de l'Environnement. 2015; 76: 279-283.

whether the advice has had an effect, and to ensure that the employee's state of health has not deteriorated.

On the other hand, if the occupational physician's diagnosis identifies any sleep and/or vigilance disorders that have an impact on the employee's general state of health (and therefore on safety), they will then be guided towards specialist help. This will preferably be in a sleep medicine department where a precise personalised diagnosis can be made. Depending on the results of this examination, and on the change in the employee's state of health, sick leave can be prescribed, and when it has come to an end, at the work resumption visit, the advisability of keeping the same job or changing to a day shift should be discussed.

In any case, these disorders will need to be linked back to the employee's working conditions, by questioning them in detail about their schedule, their hours (their duration), and their rest periods. An investigation about the job itself should be performed to search for any possible "anomalies" or malfunctions in terms of work organisation. Proposals for improvement can then be made to avoid the persistence of the disorders and prevent the emergence of the same disorders in other colleagues working on the same team.

This individual care can therefore, in addition to caring for the employee's health, contribute to initiating and implementing a broader approach to preventing disorders related to night work in companies (INRS, 2013).

10 Conclusions and recommendations of the working group

10.1 Conclusions

In France, while there are an abundance of precise regulations relating to night work, there is no exact definition of shift work, with or without night hours, in the French Labour Code. Accordingly, shift work is not covered by a specific section of this Code, but is subject to disparate provisions, because of its implications.

Night work is still very much an exceptional provision, whose use is strictly regulated. It must also be justified by a need to ensure the continuity of economic activity or services of social value. It cannot be implemented without collective bargaining.

It concerns many members of the French population. In 2012, 15.4% of employees, or 3.5 million people, worked at night, regularly or occasionally. This is a million employees more than in 1991, with this increase affecting women in particular. The national surveys stressed that the working conditions of these employees are more difficult than for others: they are subjected to more numerous physical hardship factors, greater time pressure, and more frequent tensions with their colleagues or the public.

Many studies have investigated the effects on health (and more rarely on family and social life) of shift work including a part at night, and the analysis of the results, in the framework of this expert appraisal, has revealed the following conclusions:

Regarding the aspects relating to social and family life:

Shift work including night work places limitations on social life because of the temporal mismatch between the shift worker's rhythm of life and that of society as a whole (limited opportunity for leisure, sporting or cultural activities carried out alone, reduced network of contacts and friends). There may also be consequences relating to couples' relationships: limited time for meeting and sharing, changes to marital relations and sex life, and the emergence of role conflicts that are felt more acutely by the spouses than by the employees themselves. Research into the impact of shift work on relations between workers and their children shows a decrease in the frequency and duration of family interactions and in the perceived quality of parenthood, and a deterioration in the nature and quality of parental functions.

Regarding the health effects of night work/shift work including a part at night:

Concerning the non-carcinogenic effects

The Working Group concluded that shift/night work has a **proven effect** in humans on:

- sleepiness;
- sleep quality and the reduction of total sleep time;
- the occurrence of metabolic syndrome.

The Working Group concluded that shift work including night work has a **probable effect** in humans on:

- psychological health;
- cognitive performance;
- obesity and weight gain;
- type-2 diabetes;
- coronary diseases (coronary ischaemia and myocardial infarction).

The Working Group concluded that shift work including night work has a **possible effect** in humans on:

- dyslipidaemia;
- high blood pressure;
- ischaemic stroke.

In addition, the experts concluded that shift work including night work led to increased accident rates (frequency and severity).

Concerning the effects related to the risk of cancer

The Working Group considered that the epidemiological studies provide globally consistent results supporting an increased risk of breast cancer, with limited evidence.

The evidence provided by the epidemiological studies is not sufficient to reach a conclusion about prostate cancer, despite the results of a small number of studies showing an association. The results for the other cancer sites are insufficiently documented and no conclusions can be drawn.

Ultimately, based on the results of epidemiological studies on night work/shift work including night hours, and experimental studies in animals on disruptions to the circadian rhythm, the Working Group concluded that night work has a probable carcinogenic effect.

10.2 Recommendations

10.2.1 Recommendations for preventing the risks associated with exposure to night work

The Working Group reiterates that the health risk assessment concluded as to the existence of a number of possible, probable and proven human health effects of shift work including night hours.

In application of the principles of primary prevention, night work should be eliminated, or the number of people working these types of hours should be reduced. It should be reiterated that *"for employees as a whole, the use of night work must remain exceptional and be justified by economic or social requirements specified in an agreement (extended collective branch convention or agreement, or company or establishment agreement), concluded before its establishment or its extension to new categories of employees (Articles L. 3122-32 and 3122-33)"*.

In addition, the Working Group notes the existence of various means of prevention aimed at reducing the impact of night shift work on the health of the employees concerned. Some of these means of prevention may warrant more in-depth study:

- reduce night work as much as possible;
- encourage the greatest possible number of rest weekends;

- increase the number of rest days and preferably arrange them after the night shift, to enable a faster recovery from fatigue and lack of sleep;
- adjust the length of the night shift according to the arduous nature of the tasks (physical or mental load, etc.) and their conditions of execution (physical or environmental ambiance of the work);
- adjust the nature of the tasks to the workers' functional capacities (physical and cognitive), in particular by taking care to reduce constraints relating to work rate, physical effort, attention, memory, *etc*.;
- shorten rather than lengthen the duration of night shifts, in order to avoid combining the negative effects of circadian desynchronisation with those of sleep pressure and debt;
- promote access to and security of transport after the night shift (carpooling, company bus, *etc*.);
- insert appropriate rest breaks during the shift, leaving sufficient time to encourage short naps, and improve the rest conditions;
- organise sufficient overlap time between the shifts and therefore between the teams to enable the transmission of oral information that enhances the quality of the work, safety and reliability;
- give employees the option of organising their tasks and leave them room for manoeuvre in deciding on their chronological order according to the fluctuation of their cognitive and physical capabilities;
- promote the collective dimension of the work, in order to limit worker isolation, enable quality social support, increase the reliability of the system and avoid errors;
- when designing shift and night work schedules, take care to conciliate the different spheres of life (life at work and life outside work) on which the employees' state of health also depends;
- insist on the importance of fostering good quality sleep at home;
- encourage better lighting conditions to ensure greater vigilance during the shift and improve sleep quality at home: increase light during the night shift, and then sleep in the dark;
- get personnel involved in drawing up shift work systems;
- reduce the other occupational constraints and risks (time-related, organisational, physical, physical agents, etc.);
- avoid starting the morning shift too early, in order to limit sleep debt and avoid excessive daytime sleepiness;
- avoid finishing too late in the evening, in order to limit family desynchronisation;
- hold a debate on the numbers in the night work teams and on the characteristics of the employees who comprise them (skills and know-how).

Lastly, the Working Group reiterates that anything that reduces desynchronisation and sleep debt is favourable in principle, but that prudence should be exercised in the general recommendations, firstly due to inter-individual variability (chronotype, sex, age, *etc*.), and secondly because of elements of work organisation that may be favourable for one job but may prove unfavourable for a team in another job. Some other means of prevention, listed in the chapter on the subject in this report, currently suffer from a lack of consensus in the scientific community, either because of a lack of studies or contradictory results. These are listed below:

- limiting the number of consecutive night shifts: there is no consensus on an acceptable number of nights;
- adopting rapid rotation regimes in order to limit the number of consecutive night shifts could be favourable to sleep, but unfavourable to circadian rhythmicity: there is no consensus on the best frequency to adopt;
- rotating the shifts in a clockwise direction (morning/afternoon/night) seems favourable for most workers because it follows the internal periodicity of the circadian biological rhythms and enables them to benefit from longer rest periods between shifts; however this may not apply to morning chronotypes (because their circadian period is shorter and they tend to go to bed earlier and wake up earlier) for whom an anticlockwise rotation may be less detrimental: there is no consensus on the best direction of rotation;
- promoting wakefulness and vigilance;
- promoting naps during the night shift, and at home (for example before beginning the night shift).

Regarding the career path, the Working Group recommends:

The Working Group endorses the recommendations of the French National Agency for the Improvement of Working Conditions (ANACT) and advocates several options to pursue on preventive action with regard to the ageing of workers:

- overall improvement of working conditions. This limits the effects of work-related strain, broadens the room for manoeuvre when assigning employees of different ages, and increases the opportunities to develop preservation strategies;
- actions "targeted" at personnel with capacity limitations. These limitations are not specific to an age group, but their statistical link with age has been established. The question then arises of how to establish a reserve of less arduous work situations that could be occupied by personnel suffering from the sequelae of accidents or disabling conditions of varying severity;
- adapting career paths, in such a way as to limit long-term exposure to disadvantageous constraints, while encouraging consistent paths that enable experience to be built up. While it is accepted that developing this experience implies both variety in the situations experienced – avoiding professional stagnation – and "breathing" time conducive to the deployment of personal and collective reflections on these situations, the importance of an "ergonomic" approach (in the sense of an optimal arrangement of the work resources) is underlined, not only for each situation, but in how they are linked together.

10.2.2 Recommendations concerning possible directions for scientific research

For experimental studies

The Working Group reiterates that:

- there are too few experimental studies in humans;
- nocturnal animal models (in particular rats and mice) are unsuitable for assessing the effects of night/shift work. As mentioned previously, animal studies are usually conducted in rodents that are nocturnal and sensitive to light, very different from diurnal animals and human beings. It is not possible to reproduce the equivalent of night or shift work in nocturnal animals;
- the majority of animal studies are carried out on males (to avoid interference from hormonal cycles);

- there is often a failure to systematically take modulators (such as age, sex and chronotype) and environmental influences into account.

The Working Group recommends:

- prioritising experimental studies in diurnal animal models and humans;
- promoting experimental studies, both in males and females;
- studying the effects of co-exposures and environmental influences in the experimental studies;
- clearly defining the model of shift/night work and the types of tasks performed;
- assessing the effect of key modulators such as age, sex and chronotype;
- including night workers in experimental laboratory studies and taking their experience in this type of work into account.

For epidemiological studies

The Working Group reiterates:

- the many methodological limitations identified during the analysis of the epidemiological studies, in particular in terms of characterisation and duration of exposure, or taking confounding factors and the "healthy worker" effect into account;
- the fact that modulators of effects and differences in the content and organisation of work between night and day shifts are not adequately taken into account;
- the uncertainties that persist concerning the effects of shift/night work on some cancers and other little-studied diseases.

Accordingly, the Working Group recommends:

- implementing studies to gain a better understanding of the effect of co-exposures and interactions between night/shift work and other risk factors;
- taking care to better characterise exposure in epidemiological studies, using standardised questionnaires (IARC workshop 2009, Stevens 2011), incorporating the following parameters as much as possible:
    - the type of shift work (continuous or semi-continuous);
    - the time that the shift begins and ends;
    - the duration of the shifts considered;
    - the type of system (rotating or fixed);
    - the speed and direction of rotation;
    - the regularity or irregularity of the rotation cycle;
    - the cumulative duration of the shift work;
    - the number and position of rest periods between shifts.

It is also important to assess factors related to the workers' professional lives or lives outside work, such as the quantity and quality of sleep, diet, commute duration between home and the workplace, exposure to light during the night, chronotype, and duration of exposure to these working hours.

The Working Group also recommends:

- obtaining a better characterisation of the populations: age at the time of the study, age when starting the shift work including a part at night or the number of years of exposure, sex, family situation (number and age of children), chronotype, duration of sleep during and outside the work period, profiles of exposure to light, etc.;
- ensuring that confounding factors are better taken into account: considering the main confounding factors and factors specific to the effect considered;
- favouring longitudinal studies (cohort or case-control) in order to better understand the causal relationship, and how the healthy worker effect and the dose/response relationship (thresholds) are taken into account. It would be interesting, in longitudinal studies, to measure mental health from the moment the night work is accepted;
- in the large general cohort studies under way, integrating information on the characterisation of exposure, of populations, and the taking into account of confounding factors.

With regard to the studies on cancer, it also recommends:

- that the associations between night work and breast cancer should, as far as possible, be studied separately in women working in varied industry sectors, in order to assess the possible effects of different systems of working hours and the possible role of the characteristics of the work, in different professional situations (and other environmental exposure);
- precisely characterising the sub-groups of individuals (menopausal status, breast cancer tumour receptors). In the immediate future, the Working Group recommends taking initiatives to conduct a grouped analysis of the existing studies by characterising exposure consistently from the available data. Such an analysis would make it possible to stratify individuals by sub-group while maintaining a satisfactory statistical power.

For studies on the secondary means of prevention

Considering the lack of consensus on:

- the preferable direction of rotation (clockwise/anticlockwise);
- the acceptable number of consecutive night shifts;
- the frequency of rotations (fast/slow) that is least detrimental to the physiology;
- the best chronobiological approaches for fostering circadian synchronisation and the quality of wakefulness and sleep;
- the use of melatonin;
- the effectiveness of pharmacological approaches;
- the optimal parameters of exposure to light (the best lighting conditions);

the Working Group recommends conducting experimental studies in the laboratory and in actual conditions, including subjective and quantitative assessments of the impact of night work (on the amplitude and phase of the circadian system, sleep, sleepiness, cognition, metabolism, cardiovascular diseases, immunity, exposure to light), making it possible to:

- assess the effect of the direction of rotation (clockwise/anticlockwise), and the link between the effect and the chronotype of individuals;
- clarify the acceptable number of consecutive night shifts;

- determine the frequency of rotations (fast/slow) that is least detrimental to the body and to the well-being of individuals;
- determine rapidly (the same day) and precisely the phase of the circadian system (internal clock), in order to be able to optimise the effectiveness of the chronobiological approaches mentioned above (and determine the ideal time to increase and decrease exposure to light favourable to synchronisation of the circadian system);
- determine optimal times for administering melatonin for its sleep-inducing and circadian clock synchronising effects. As these times are dependent on the internal clock of individuals, it will be necessary to precisely determine the phase of their circadian system (see above point);
- assess the relevance and effectiveness of pharmacological approaches to promote synchronisation of the circadian system (melatonin) and increase vigilance during the shift (caffeine, stimulating compounds, etc.);
- assess the chronobiological approaches confirmed as effective in the laboratory for fostering circadian synchronisation and improving the quality of vigilance and sleep: naps before and during the night shift, increase in the intensity of light during the shift, avoidance and reduction of exposure to "non-visual" light in the morning or during the day, optimal times for light therapy.

For the other types of studies

Considering:

- the difficulty of quantifying the change in sleep time;
- the lack of consensus on the definition of fatigue;
- the difficulties encountered by the WG in accessing data, in particular on occupational accidents and commuting accidents;

the Working Group recommends:

- quantifying impaired sleep using quantitative approaches (actigraphy, polysomnography);
- developing studies on fatigue, in order to obtain a better metrological assessment of fatigue, as well as scales suited to the different types of fatigue: physical, cognitive, psychological;
- conducting studies on accidentology at work, with a methodology that would make it possible to jointly analyse the content of the work and the "timing" aspects of accidents: time of occurrence, shift concerned, its place in the rotation, etc.;
- conducting studies to understand the determinants of the under-reporting of occupational accidents at night, from the perspective of both employers and employees;
- examining in greater detail the link between night work and the severity of occupational accidents.

For studies on the socio-economic impact of night shift work

Considering:

- the absence of data on the social and economic cost of night shift work;
- the results of studies on family and social life;

the Working Group recommends:

- implementing sociology and economics studies on the social and economic cost of night shift work, in order to put into perspective the economic benefits gained and the social costs incurred (occupational accidents, occupational diseases, absenteeism, staff turnover rate) both at company and society level (negative externalities of shift work including night hours);
- expanding the framework of analysis to the entire family unit and not being limited to exclusively studying the effects on the workers themselves: accentuating research on the impact of night shift work on family life (relationships with partners and children, schooling of children, etc.);
- developing studies on women working shifts including at night, as well as single-parent families;
- continuing scientific work on the social life of night shift workers in order to shed light on the social impact of working these hours.

For ergonomic and qualitative studies

Considering:

- the need to distinguish the effects of the working hours practised from the specific requirements of the profession itself, to understand their respective impacts on health and personal life;
- the need to take into account the actual rotations and the reality of the work performed, rather than focusing solely on what is planned and authorised;
- the need to understand the adjustments made by people to manage the impacts of shift work including night work on their health and personal life;
- the few studies in ergonomics, sociology and, more generally, the human and social sciences on the subject;

the Working Group recommends:

- continuing work to precisely characterise the work situations, working conditions, the content and requirements of the tasks of shift and night workers;
- carrying out qualitative studies in work situations based on real work, with various shift systems (2x12h, etc.);
- conducting studies or action research to assess the organisational means of prevention for shift and night work (collective work, naps, tools promoting work/family reconciliation, etc.).

10.2.3 Recommendations for organising research and expert appraisal work

Considering:

- the limited research in the area of night work regulations in France;
- the many determinants of the potential risks associated with shift/night work;
- the socio-economic importance of the work;
- the shortage of funding for qualitative research;

the Working Group recommends:

- promoting research in the fields of sleep regulation and biological rhythms, the disorders induced by the circadian desynchronisation linked to night work/shift work with night hours, and sleep debt;
- given the multiple factors mediating the effects of shift/night work on health: fostering collaborative and multidisciplinary work through consultation with chronobiologists, sleep specialists, doctors (general practitioners, occupational physicians, specialists), epidemiologists, ergonomists, economists, representatives and preventionists from business, etc.;
- considering a method of funding research that involves the different social actors while preserving the independence of the research;
- encouraging collaboration between businesses and research laboratories to better study the health effects of atypical hours and shift work including night work on large populations (able to investigate both the overall impact of shift/night work and the specific impact of certain professions) while complying with professional ethics and preserving the independence of the research;
- promoting the availability of data from studies conducted in companies (internal reports/grey literature) to researchers, in order to enhance knowledge on the effects of this type of time organisation in an actual work context – consider a process for anonymising companies if there are concerns about the organisation's structure being revealed. Data collection methods should be available to enable their quality and limitations to be judged;
- because the employees' state of health is a product of the combined effects of the shift work, the requirements of the tasks and their conditions of execution, scientific studies should be undertaken to discern precisely what is caused by the time constraints and what results from the requirements of the work being performed – the consequences of either may be not only additive but may also possibly potentiate one another
- promoting and fostering action research in companies in order to implement and assess organisational means of prevention;
- due to the multiple symptoms of shift/night workers, who often accumulate several disorders (gastric, cardiovascular, etc.), work should be initiated to identify the precise role played by the taking of medication. The possibility cannot be ruled out that trying to reduce one of the health effects of night shift work (turning to sleep medication to reduce sleep disorders, for example) leads to an acceleration in the emergence of another disorder (gastric disorders for instance, which are one of the side effects of sleeping pills). This would help promote studies on adapting the treatment of shift or night workers' disorders while taking the chronobiological aspects into account.

The collective expertise appraisal report was validated by the Working Group on 26 January 2016 and by the Expert Committee on 15 March 2016.

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ANNEXES

Annex 1: request letter

—> DERA2
+ copie M. Telle-Lamberton

2011 -SA- 0088

Syndicat CFTC
La Vie à Défendre

COURRIER ARRIVE
28 MARS 2011
DIRECTION GENERALE

COURRIER REÇU LE
28 MAR. 2011
2011-028

Paris, le 22 mars 2011

ANSES
Monsieur Marc MORTUREUX
Directeur Général
27-31 avenue du Général Leclerc
94701 MAISONS ALFORT Cedex

OBJET : Saisine CFTC n° 1 - État des connaissances sur l'influence des horaires atypiques, notamment le travail de nuit, sur la santé des travailleurs.

Monsieur le Directeur Général,

La CFTC est soucieuse d'un haut niveau de protection des salariés et, plus largement, de l'environnement.

Le Centre international de recherche sur le cancer (IARC/CIRC) a ajouté le travail de nuit posté à la liste des agents « probablement cancérogènes » (groupe 2A). Selon l'agence, le travail de nuit augmenterait le risque de cancer dans des proportions modestes mais néanmoins réelles.

L'avis rendu par les experts du CIRC s'appuie notamment sur une série d'études épidémiologiques réalisées auprès d'infirmières travaillant de nuit et d'hôtesses de l'air soumises à de fréquents décalages horaires.

Ces professionnels sont confrontés à des horaires atypiques, le travail de nuit n'étant qu'une composante de leurs missions. Il nous paraît intéressant de vérifier si ce constat ne s'étend pas à tous les travailleurs soumis à des horaires atypiques susceptibles de perturber l'horloge biologique interne qui régule l'alternance des périodes de veille et de sommeil, sans pour autant être toujours qualifiés de « travail de nuit ».

.../...

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Confédération Française des Travailleurs Chrétiens
13, rue des Écluses Saint-Martin - 75483 Paris Cedex 10 - T/ 01 44 52 49 00 - F/ 01 44 52 49 18 - www.cftc.fr
Membre de la Confédération Européenne des Syndicats et de la Confédération Syndicale Internationale

Par exemple, nous pouvons notamment citer les hôtesses de caisse des commerces de détail ouvert régulièrement jusqu'à 22 heures, le travail posté en équipes alternantes, les serveurs en restauration ouverte à la clientèle le soir tard, les travaux publics effectués aux heures de moindre affluence, etc.

Dans ce contexte, nous sollicitons votre agence pour procéder à une évaluation des risques sanitaires pour les professionnels exposés à des horaires atypiques, notamment ceux soumis à un travail de nuit habituel, qu'il soit régulier ou non.

Dans cette attente, nous vous prions, Monsieur le Directeur Général, de recevoir l'expression de nos salutations distinguées.

Jacques VOISIN
Président

Annex 2: legislation on night work in the European Union Member States

Council Directive 93/104/EC of 23 November 1993 amended by Council Directive 88/2003/EC of 4 November 2003 concerning certain aspects of the organisation of working time.

Article 8: Length of night work.

"Member States shall take the measures necessary to ensure that normal hours of work for night workers do not exceed an average of eight hours in any 24-hour period".

Table 18: Presentation of the legislation on night work in the European Union Member States

Country	Maximum length of night work (in hours)	Legislation
Austria		**Working Time Act, as amended to BGBl. I No 124/2008** **Working Time Act, §12a(1)(2), as amended to BGBl. I No 124/2008** According to this Federal Act, "night" is the period between 10pm and 5am. **Working Time Act, §12a(1)(2), 12b(2)** According to this Federal Act, the term "night worker" refers to any person working: 1. regularly, or 2. unless otherwise provided for under a collective agreement, at least 48 nights in a calendar year, at least three hours during night time. **By way of derogation from §12a (1-2),** the following definitions are applicable for the coverage of the health examination: 1. "night" means the period between 10pm and 6am; 2. "night worker" refers to any person working regularly or at least 30 nights in a calendar year, at least three hours during night time.
Belgium	**8**	**Labour Act of 16 March 1971, as amended to 20 July 2011** **Labour Act, §§ 35** All workers are generally prohibited from being engaged in night work. Night work is authorised in certain specified sectors such as hotels and catering, the media, energy, medical facilities, transport, baking, and cleaning. Night work can be included in shift work, for tasks that require a continuous work rhythm and in companies where products or materials deteriorate rapidly. **Labour Act, § 35** Night work is work performed in the period from 8pm to 6am.

Country	Maximum length of night work (in hours)	Legislation
Bulgaria	**7**	**Labour Code as amended to 29 June 2012** **Labour Code, §140** The normal daily duration of night work in a five-day week is no more than seven hours. The normal weekly duration of night work in a five-day week is no more than 35 hours.
Cyprus	**7**	**Organisation of Working Time Law,** **Law 63 (1)/2002, as amended to Law 15 (1)/2007** **Organisation of Working Time Law, §2** Night work refers to work performed between 11pm and 6am. A night worker is a person who works at least three hours of his daily working time in the period between 11pm and 6am for at least seven consecutive working days, or who is likely to work, during night time, at least 726 hours of his annual working time.
Croatia	**8**	**Labour Act as amended to the Act of 20 May 2011** **Labour Act, §48(1)(5)** "Night work": work performed between 10pm and 6am and, for agriculture, between 10pm and 5am. "Night worker": worker who, on the daily basis of his work schedule, works, during night time, at least three hours of his working time or who, during the calendar year, works, during night time, at least one-third of his annual working time.
Czech Republic	**8**	**Labour Code No 262 as amended to 2012** **Labour Code, §94** A night worker cannot work more than eight hours over a period of 24 consecutive hours. If this is not possible for operational reasons, the employer shall arrange a normal weekly working time such that the daily duration of shift work does not exceed eight hours on average over a period of 26 consecutive weeks. **Labour Code, §78(1)(k)** "Night work": work performed in the period from 10pm to 6am. "Night worker": any employee who, during night time, works on average at least three hours of his working time over a period of 24 consecutive hours, at least once a week.

Country	Maximum length of night work (in hours)	Legislation
Denmark	**8**	Some flexibility is provided enabling collective agreements or company agreements to have different definitions of "night time" within the prescribed minimum limits of the directive. **Act No. 896 of 24 August 2004** for employees who are not covered by collective agreements, providing for at least equivalent rights **Ministry of Employment Act No. 896 of 24 August 2004 to partially implement the Working Time Directive** "Night work": work performed for a period of at least seven hours that must include the period from 12am to 5am. Unless otherwise agreed, the night work period covers the interval from 10pm to 5am. Night workers shall not perform more than eight hours of work per day on average over a four-month reference period. Where night work involves particular risks or heavy physical or mental strain, employees shall not work more than eight hours during a 24-hour period. "Night worker": worker who normally performs at least three hours of work during the night work period or who performs at least 300 hours of night work during a 12-month period. **Working Time Act, § 26** If night work is particularly hazardous or very physically or mentally straining, the maximum limit of daily working time is set at eight hours.
Estonia	**8**	**Employment Contracts Act, as amended to 4 June 2012** **Working and Rest Time Act, as amended to 11 February 2003** **Working and Rest Time Act, §19(1)** **Employment Contracts Act, §45(1), (5)** "Night work": work performed between 10pm and 6am. "Night worker": employer who works, during night time, at least three hours of his daily working time, or one-third of his annual working time.
Finland	**7**	**Working Hours Act No 605/1996, as amended to Act No 164/2005 §26, as amended to Act No 991/2010:** "Night work": work performed between 11pm and 6am. An employer must notify the labour protection authorities of regular night work, when the said authorities so request.

Country	Maximum length of night work (in hours)	Legislation
France	**8**	**Labour Code, §§ L 213-11, L3122-29, L3122-31 (Decree No 42/2006 and consolidated on 9 November 2009)** "Night work": any work performed between 9pm and 6am. An alternative period of nine consecutive hours, between 9pm and 7am, including the interval between 12am and 5am, can replace this period by a collective agreement, company agreement or establishment agreement. Night worker: any worker who performs, as part of his usual work schedule, at least three hours of night work, at least twice a week, or a minimum number of hours of night work during a reference period by agreement. The duration of night work must not exceed eight hours. An upper limit can be authorised by collective agreements or in exceptional circumstances by the Labour Inspectorate.
Germany	**8/10**	**Hours of Work Act, as amended to 31 October 2006.** **Hours of Work Act, §2(3)-(5), §7(1)** Night work: any work involving more than two hours of work performed during night time (between 11pm and 6am). In bakeries and pastry shops, it is defined as work performed during the period between 10pm and 5am. Collective agreements or individual employment agreements can define that night time starts between 10pm and 12am. Night workers are those who: (1) generally work at night as part of rotating shift work; or (2) work at night at least 48 days per year. **Hours of Work Act, §6(2)** Collective agreements or individual employment agreements can define that night time starts between 10pm and 12am. The daily working time of night workers cannot exceed eight hours. This limit can be extended to 10 hours at most, provided that the daily working time does not exceed eight hours on average over a period of one calendar month or four weeks. This reference period can be modified by a collective or company agreement.
Greece	**8**	**Presidential Decree, 88/1999 §2, 8, 9, 11** Night work is work performed during the period between 10pm and 6am.
Hungary	**8**	**Labour Code, Act 1/2012** **Labour Code, §113(4)** Night work must not exceed eight hours for employees working in conditions posing health risks. **Labour Code, I§89** "Night work": work performed between 10pm and 6am.

Country	Maximum length of night work (in hours)	Legislation
Ireland	**9**	**Organisation of Working Time Act, §16(1) as amended to Act No 29/2003** **Organisation of Working Time Act, §16(1)** "Night work": work performed in the period from midnight to 7am; "Night worker": employee who normally works at least three hours of his daily working time during night time and who works during night time for at least 50% of his working time in a year. **Organisation of Working Time Act, §16** A night worker (worker normally working at least three hours of his daily working time between midnight and 7am) must not work more than eight hours when his work involves particular risks or heavy physical or mental strain. For all other night workers, the working time is eight hours on average over a stipulated reference period (two months or more according to the provisions of a collective agreement).
Italy	**7**	***Legislative Decree 28 April 2003 n. 66*** Night work is work performed for at least seven hours including the period between 12am and 5am. A "night worker" is any worker who works at least three hours of his normal working time between 12am and 5am, or who works, between 12am and 5am, part of his normal working time as defined by the provisions of specific collective agreements. The daily working time of night workers cannot exceed eight hours on average per 24-hour period, unless the provisions of a collective agreement provide for a longer work duration, but also a longer reference period (more than 24 hours). *To be considered a "night worker", an employee must work at night at least 80 days per calendar year.*
Latvia	**8**	**Labour Law as amended to 21 September 2006.** **Labour Law, §138(1)(2)** Night work is work performed for more than two hours during the period between 10pm and 6am (for children, work performed between 8pm and 6am). A night worker is a person who generally works at night as part of shift work or for at least 50 days per calendar year.
Lithuania	**8**	**Labour Code as amended to Act No XI-1219 of 9 December 2010** **Labour Code, §§154(1)-(2)** Night work is work performed between 10pm and 6am when at least three hours of work are performed in this interval.
Luxembourg	**8**	**Labour Code, Official Journal of 29 August 2006, No 149, as amended to 18 August 2012** **Labour Code, § L211-14 (Act of 19 May 2006)** Work performed between 10pm and 6am. Workers who perform, during night time, at least three hours of their working time or those who, under a collective agreement, are likely to work at night for at least a quarter of their annual working time.

Country	Maximum length of night work (in hours)	Legislation
Malta	**8**	**Organisation of Working Time Regulations, Legal Opinion No 247 of 2003, as amended to Legal Opinion No 427 of 2007** **Organisation of Working Time Regulations, §2** "Night work": work performed in the period between 10pm and 6am. A "night worker" is any worker who: (a) normally works at least three hours of his daily working time during night time; or (b) works more than 50% of his annual working time at night, or in some cases to a lesser extent as defined by an applicable collective agreement.
The Netherlands	**10**	**Working Hours Act (*Arbeidstijdenwet, Atw*), as amended and in effect to 9 June 2009** **Working Hours Act §5:8.2** **Working Hours Decree, §4.9:2** If shift work is performed during night time, working time must not exceed 10 hours per shift and 40 hours per week on average (60 hours at most per week) over a reference period of 16 weeks, provided that night work is performed at least 16 times during this period. Collective agreements can stipulate that employees work 40 hours on average over a reference period of 52 weeks, provided that unforeseeable circumstances or the nature of the work justify the fluctuations in workload, leading employees to work more than 40 hours per week on average over a period of 16 weeks, and that the work cannot be reasonably organised in another manner, or else if the employee is primarily responsible for supervising other workers on the employer's behalf. **Working Hours Decree, §4.7:1, 4.7** **Working Hours Act §5:8.6-9** During the period running from Friday 6pm to the following Monday 8am, night working time will be 10 hours at most, and may be extended to 11 hours at most on two occasions provided that night work is followed by a rest period of at least 12 consecutive hours and that these provisions are defined in a collective agreement. Over a period of 52 weeks, the employer must guarantee that the employee will benefit, at least 26 times, from a period of non-work between midnight on Saturday and midnight on Sunday.
Poland	**8**	**Labour Code, 262/2006** **Labour Code, §78 (k)** Night work is work performed during night time. Night time is the period between 10pm and 6am. **Labour Code, §94** An employee working at night as part of shift work must not work more than eight hours over a period of 24 consecutive hours.

Country	Maximum length of night work (in hours)	Legislation
Portugal	**8**	**Labour Code (*Lei* 7/2009)** **Labour Code, §223(1,2)** Night work is work performed in the period between 12am and 5am. Night workers are employees who perform at least three hours of their working time during night time. Collective agreements can define the period of night work: if there is no agreement, this period is between 10pm and 7am.
Romania	**8**	**Labour Code, Act No 53/2003, as amended to 31 December 2008** **Labour Code, § 125, §125(3)** Night work is work performed between 10pm and 6am. An employer that often turns to night work must inform the Territorial Labour Inspectorate.
Slovakia	**7**	**Labour Code of the Slovak Republic of January 2012** **Labour Code, §98(1)(2)** Night work is work performed between 10pm and 5am. A night worker is any employee who: a) performs work requiring regular performance at night, to the extent of at least three consecutive hours, or b) is liable to work at night, for a minimum of 500 hours per year.
Slovenia		**Employment Relationships Act, No 42/2002, as amended to Act No 103/2007** **Employment Relationships Act, §149, 150(1)** "Night work": work performed between 11pm and 6am. "Night worker": any employee who works at night at least three hours of his daily working time or at least one-third of his full annual working time. **Employment Relationships Act, §§151, 158** In a period of four months, the working time of a night worker may not exceed on average eight hours a day. Branch collective agreements may stipulate that the average time limitation is extended to six months. The working time of a night worker may not exceed eight hours a day when according to the risk assessment there is a higher risk of injuries or damage to health.
Spain	**8**	**Royal Decree No 1/1995 enacting the Workers' Charter as amended to Act 35/2010** **Royal Decree No 1 enacting the Workers' Charter, §36(1)** Night work is work performed between 10pm and 6am. Night workers are employees who perform work for at least three hours during the night period or one third of their working day.

Country	Maximum length of night work (in hours)	Legislation
Sweden **[amended]**	**8**	**Working Hours Act as amended to Act No 428/2005** **Working Hours Act, §13a** The term "night worker" refers to those who normally perform at least three hours of their working shift during the night or will probably perform at least one third of their annual working time during the night. The term "night" refers to the period between 10pm and 6am. Working time for night workers (between 10pm and 6am) may not exceed an average of eight hours during a reference period of at most four months.
United Kingdom	**8**	**Working Time Regulations of 1998, §6(1), (7) and (8) as amended to the Working Time Regulations of 2009 (S.I. 2009/1567)** Some flexibility is provided enabling collective agreements or company agreements to have different definitions of "night time" within the prescribed minimum limits of the directive. A night worker's hours of work in any reference period shall not exceed an average of eight hours for each 24 hours. However, an employer shall ensure that no night worker whose work involves particular risks or heavy physical or mental strain works for more than eight hours in any 24-hour period. **Working Time Regulations of 1998, §2(1)** "Night time" means a period of no less than seven hours that includes the period between midnight and 5am, determined by a relevant agreement or, in default of such a determination, the period between 11pm and 6am. A night worker is a worker who, as a normal course, works at least three hours of his daily working time during night time or is likely, during night time, to work at least such proportion of his annual working time as may be specified for the purposes of these Regulations in a collective agreement or a workforce agreement; for the purpose of paragraph (a) of this definition, a person works hours as a normal course if he works such hours on the majority of days on which he works.

Annex 3: summary table of work identified internationally

Table 19: summary table of work identified internationally

Identification			Identification of work		
Organisation	**Country**	**Type of document**	**Link**	**Date**	**Description of the work**
IARC		Monograph report	http://monographs.iarc.fr/ENG/Monographs/vol98/mono98-8.pdf	2007	IARC prepared a monograph on shift work, and the careers of painters and firefighters (Volume 98 (804 pp)). Regarding shift work involving night work (nurses in night teams, for example), the evidence of carcinogenicity associated with this type of work in humans was limited. However, sufficient evidence of carcinogenicity was observed in laboratory animals, suggesting that the disruption of the internal clock may play a role. The Working Group thus came to the following general conclusion: shift work disrupting the circadian cycle is probably carcinogenic to humans (Group 2A).

Identification			Identification of work		
Organisation	**Country**	**Type of document**	**Link**	**Date**	**Description of the work**
NIOSH (National Institute for Occupational Safety and Health)	United States	Report	http://www.cdc.gov/niosh/docs/2004-143/pdfs/2004-143.pdf	2004	"Overtime and Extended Work Shifts: Recent Findings on Illnesses, Injuries and Health Behaviors" Report summarising 52 other reports on the associations between long working hours and the occurrence of diseases or deterioration in performance. This report describes the results and methods used in these studies.
		Scientific publications			NIOSH published various studies dealing with the effects of shift work on the reproductive system (menstrual cycles, pregnancy complications, miscarriages, premature births, etc.)
Harvard Medical School and Harvard School of Public Health	United States		epidemiological studies		Interview with Eva Schernhammer (medical epidemiologist specialising in night work) by the ANSES Working Group Publication in January 2015 of a cohort studying the effects of night work in nurses (http://www.ajpmonline.org/pb/assets/raw/Health%20Advance/journals/amepre/AMEPRE_4276-stamped-010515.pdf)
CCHST (Canadian Centre for Occupational Health and Safety)	Canada	Guidance document	http://www.cchst.com/oshanswers/ergonomics/shiftwrk.html updated in November 2010		A document intended for employers and employees that lists a number of questions and answers about shift work: Can shift work cause cancer? What are the effects on circadian rhythms? What are some strategies for improvement? What are some organisational approaches? etc.

Identification			Identification of work		
Organisation	**Country**	**Type of document**	**Link**	**Date**	**Description of the work**
IRSST	Canada	Report	_	1988	"The persistent effects of night work on sleep and vigilance in a population of female former night workers". A questionnaire-based survey was undertaken among 479 nurses and nursing assistants. Of them, 15 were observed in a laboratory while sleeping.
		Report	http://www.irsst.qc.ca/media/documents/PubIRSST/RR-162.PDF	2001	"Effects of 12-hour rotating shift work on the health and safety of operators in an oil refinery"
		Report	http://www.irsst.qc.ca/-projet-prevention-par-la-phototherapie-des-troubles-d-adaptation-au-travail-de-nuit-0096-0340.html	2002	"Prevention of physiologic maladaptation to night-shift work by phototherapy"
		Report	http://www.irsst.qc.ca/media/documents/PubIRSST/R-659.pdf	2010	"Rotating shifts for police officers: study on complementary preventive approaches for fatigue reduction"

Identification			Identification of work		
Organisation	**Country**	**Type of document**	**Link**	**Date**	**Description of the work**
HSE (Health and Safety Executive, UK)	United Kingdom	Guide for employees and employers	http://www.hse.gov.uk/pubns/priced/hsg256.pdf	2009 2006	"Managing shift work: Health and safety guidance" This book is for employers, safety representatives, trade union officials, employees, regulators and other stakeholders. It explains employers' legal duties to assess risks associated with shift work. It aims to improve understanding of shift work and its impact on health and safety by providing advice on risk assessment, design of shift-work schedules and the shift-work environment.
		Other guides and documents of interest	http://www.hse.gov.uk/humanfactors/topics/fatigue.htm		
Health and Social Care Information Centre	United Kingdom	Result of a survey, HSE (Health Survey for England) 2013	http://www.hscic.gov.uk/catalogue/PUB16076/HSE2013-Ch6-sft-wrk.pdf	2013	Section presenting the results of a 2013 HSE (Health Survey for England) survey showing differences in health between people working at night and those with standard working hours

Identification			Identification of work		
Organisation	**Country**	**Type of document**	**Link**	**Date**	**Description of the work**
SUVA (Swiss Society for Occupational Medicine)	Switzer-land			2009	Occupational medicine memo The memo reviews typical problems associated with night work: - Sleep disorders and fatigue - Cardiovascular disease - Digestive problems, peptic ulcer - Night work and pregnancy - Cancer It also presents the medical examination for night workers
National Research Centre for the Working Environment, Denmark (NRCWE)	Denmark		http://www.arbejdsmiljoforskning.dk/en/projekter/skiftarbejde-og-helbred/formaal	2013-2016	Development of a project aiming to strengthen scientific knowledge in order to recommend the best possible organisation of work. The following effects are studied: • incidence and duration of sick leave • mental health • pregnancy complications and foetal death These effects were chosen because there are scientific indications linking them to shift work; however, the evidence remains limited. These three effects all have personal and societal consequences. Knowledge of these effects is essential when organising work.
Federal Institute for Occupational Safety and Health (BAuA)	Germany	Research project	-	2002	"Nutritional state of night shift workers" - study of a population of around 500 people between 1997 and 1999.

Identification			Identification of work		
Organisation	**Country**	**Type of document**	**Link**	**Date**	**Description of the work**
		Report	http://www.baua.de/de/Publikationen/Fachbeitraege/Gd59.html;jsessionid=666C17F7D28B0B3B57904C3BB7A5DB75.1_cid353	2010	"The effects of extended working hours on health and social well-being" The results show that an increase in the number of weekly hours of work increases the risk of health problems and reduces the time for social exchanges.
		Ongoing	http://www.baua.de/en/Research/Research-Project/f2355.html?nn=4947596	2016	Determination of the actual light exposure from natural and artificial sources with regard to circadian effects in shift-working employees – Joint project between the Federal Institute for Occupational Safety and Health (BAuA) and Public Health England (PHE).
		Ongoing	http://www.baua.de/en/Research/Research-Project/f2338.html?nn=4947596	Ongoing Planned end: 2018.04.30	"Occupational risk factors for cardiovascular diseases - prospective analysis of the Gutenberg Health Study (GHS)" A prospective cohort study (association between exposure factors and cardiovascular diseases) on various factors including night work is ongoing.

Identification			Identification of work		
Organisation	**Country**	**Type of document**	**Link**	**Date**	**Description of the work**
RIVM	The Nether-lands	Report	http://www.rivm.nl/dsresource?objectid=rivmp:76353&type=org&disposition=inline&ns_nc=1	2012	"Night work and health effects: A literature update" The association between night work and the development of conditions such as (breast) cancer, heart disease and obesity remains uncertain. Epidemiological studies that investigate the incidence of these conditions in night workers compared to day workers give inconsistent results as well as having limitations. This report's recommendations gave rise to research work (on the influence of smoking, alcohol and diet) and the collection of data on working hours. More research into the possible effects of night work and the related mechanisms should be undertaken to determine whether preventive measures are required to limit the health effects of night work.

Identification			Identification of work		
Organisation	**Country**	**Type of document**	**Link**	**Date**	**Description of the work**
		Report	www.rivm.nl/en/Documents_and_publications/Scientific/Reports/2014/maart/Shift_work_and_metabolic_risk_factors_A_literature_overview	2013	"Shift work and metabolic risk factors: A literature overview" RIVM conducted a literature review, commissioned by the Ministry of Social Affairs and Employment of the Netherlands. Certain results are inconsistent, which may be due to considerable heterogeneity in the types of shift work investigated (night shifts, evening shifts and rotating shifts), the study population, and factors that can influence this relationship (smoking, alcohol intake, activity, and food intake). Furthermore, RIVM wants to better understand the quality of the corresponding studies (for human studies) and thus have a better idea of the evidence supporting the relationship between shift work and metabolic effects. These results will be subject to a scientific review. Moreover, RIVM more closely examined all studies in animals (animal models for shift work). This opinion was recently accepted by Frontiers in Pharmacology.
Health and Safety Authority (Ireland)	Ireland			2012	Guidance for Employers and Employees on Night and Shift Work. The document reviews the main effects of night work - the necessary assessment of the related risks - advice for employees - review of the regulations - the procedure for evaluating night and shift work (tools, techniques and related questionnaires)

Annex 4: questionnaire for the international consultation

International consultation – Night work, shift work and other atypical working schedules and health

The French Agency for Food, Environmental and Occupational Health & Safety (ANSES) is undertaking an international consultation to know what approaches other countries may be using to conduct assessments of the impact of night work, shift work and other atypical working schedules on health.

Since IARC has classified shift work with circadian disruption as Group 2A, *probably carcinogenic to humans*, workers in France are more and more concerned about this topic. ANSES is undertaking a risk assessment of the health risks for professional populations exposed to atypical working hours especially night work and shift work.

To support its risk assessment on this topic, ANSES created a working group gathering experts from different countries who are specialized in the relevant domains of interest (chronobiologist, sleep specialist, oncologist, epidemiologist, occupational physicians, sociologists, *etc*.).

The aim of the present consultation is to gather information on national activities and ongoing work on a number of related issues, in various countries (focusing on Europe and North America). Given your institution's work in this domain, we are contacting you today to request any information you may have on one or more of the following issues:

- ***<u>Health impact or health risk assessment</u>***
- ***<u>Existing statistical data</u>***
- ***<u>Public policy, regulatory framework and societal context</u>***

Below is a list of specific questions relating to each of these three issues.

Once the work is completed, the resulting report, including the international consultation, will be made public on our website (www.anses.fr).

We would be very grateful if you could get back to us as soon as possible (preferably by the end of February 2015). We also welcome any suggestions you may have for further contacts in your country or from other countries or regions who may be able to provide us with relevant information.

Questions

⇨ ***Health impact or health risk***:

Are health impact assessments of night work, shift work and other atypical working schedules conducted by your institution or other institutions in your country/region/province? If yes, could you provide us with details on how they are conducted: by a working group of experts, research team, *etc*.? What is the schedule for completing the work? …

- ⇨ Are atypical working schedules a subject of major concern in your institution?
- ⇨ Which health effects do you explore? (cancer, sleep, metabolic disorders, addiction, *etc*.)
- ⇨ Did you prioritize which health effects are studied? If yes, what was your approach for prioritization?
- ⇨ What are the short- and/or long-term research needs relating to exposure to night work, shift work and other atypical working schedules of the general population identified in your country/region/province?

⇨ ***Existing statistical data***

Are data available in your country describing the proportions and/or number of workers facing night work, shift work and other atypical working schedules?

If yes, could you provide details (or refer us to a document) on how these data were collected?

⇨ ***Public policy, regulatory framework and societal context***

- Is this topic high on the agenda of the ministry of labour?
- What is the current regulatory framework about night work, shift work and other atypical working?
- Is there a public policy commitment to assessing the impact of night work, shift work and other atypical working?
- Is there pressure from workers' unions on policy-makers regarding this issue?

Annex 5: summary table on the international consultation

Table 20: Summary table on the international consultation

Organi-sation	**Country**	**Data**	**Health effects**	**Ongoing work and/or research**	**Future work**	**Recommendations/ issues to be addressed**
RIVM	The Nether-lands	The available data come from a national survey on work performed annually (*Enquête Beroepsbevolking*, EBB)	RIVM is focusing on the following health effects: breast cancer, metabolic disorders, immune function and infection. They are using experimental animal models to determine causal relationships and rule out factors related to lifestyle. There is also research work on biomarkers for circadian disruption.		RIVM is also working on the development of a national platform to compile and share knowledge of night/shift work with various stakeholders (employers, employees, public authorities). A Working Group of the Health Council of the Netherlands is preparing a review of the possible means of intervention to reduce the health effects of shift work. Three mechanisms are being explored: - circadian disruption, - sleep disturbance, - lifestyle disruption. Academics are currently working on the mechanisms of circadian disruption in animal models.	The main recommendations include: 1) better define shift work especially in order to better define and quantify exposure (review under preparation by Langenbergen *et al*.); 2) determine causal relationships between shift work and health effects; 3) identify relevant biomarkers for circadian disruption.

Organi-sation	Country	Data	Health effects	Ongoing work and/or research	Future work	Recommendations/ issues to be addressed
HSE	United Kingdom	HSE co-financed work undertaken with the German government, bringing together international experts, to determine how to measure shift work and improve epidemiological studies. In addition, data are being collected to identify the number of workers involved in shift work (through the Labour Force Survey, LFS).	HSE considers that fatigue is the key effect, since it can cause other negative health effects. A study undertaken by Oxford University focuses on breast cancer and cardiovascular diseases due to the high incidence of these diseases and growing interest in them.	A group created in 2004 recommended clarifying the association between shift work and breast cancer. It also recommended modifying population surveys to incorporate specific aspects on shift work experience. A study entitled "Shift Work and Disease" was entrusted to Oxford University in order to take advantage of the "Million Women Study" and a cohort of 63,000 men and women. This study focuses on breast cancer and cardiovascular diseases but the review of the epidemiological studies shows that no conclusions can be drawn.		HSE is currently focusing its research on the confirmation that shift work is related to the development of major diseases, such as breast cancer and cardiovascular diseases. HSE hopes to be able to improve knowledge of the possible mechanisms and better understand the role of work-related factors and lifestyle factors in the development of health problems related to shift work. If the link between shift work and the risk of serious diseases is confirmed, the longer-term research needs will be to identify professional groups who are the most at-risk and develop preventive measures to mitigate the risk.

Organi-sation	Country	Data	Health effects	Ongoing work and/or research	Future work	Recommendations/ issues to be addressed
BAUA	Germany	Work schedules are studied in micro-samples of people at the national level for people working full-time, people working part-time, and people involved in shift work.			A longitudinal study has been planned to assess the social, psychological and physiological consequences of permanent night work.	

Organi-sation	Country	Data	Health effects	Ongoing work and/or research	Future work	Recommendations/ issues to be addressed
NIOSH	United States	There is a study in progress dealing with police officers in Buffalo, New York. Data were collected from 1994 to 2014 on a daily basis by recording the type of work and working hours. NIOSH scientists are collaborating to collect data in the framework of various studies, including: The Harvard Nurses Study, the National Health Interview Survey (NHIS) and the REGARS (Reasons for Geographic and Racial Differences in Stroke) project.	NIOSH is undertaking a systematic review of cohort studies investigating risk factors for the development of cancer for the working population in the United States. NIOSH published various studies dealing with the effects of shift work on the reproductive system (menstrual cycles, pregnancy complications, miscarriages, premature births, etc.) NIOSH is studying the health effects of atypical working hours on transport professionals (truck drivers in particular). The health effects that are being explored include cancers, metabolic disorders, addiction, diabetes, fatigue, sleep, high blood pressure, cardiovascular diseases, and cholesterol levels.			NIOSH would like to investigate the following questions that have been raised: • Do night work and rotating night work have the same health effects? • Is there a dose-response effect related to the duration or frequency of shift work? • Are some effects transient? Do they disappear once shift work has been stopped? The following research needs have been highlighted: • Validation of self-reported shift-work data • Influence of Body Mass Index (BMI) • How does night work affect appetite, diet and exercise? • What is the best shift length (less than 8 hours, 8 hours, 12 hours)? • Duration of rest periods between shifts • Role of individual susceptibility and

Organi-sation	Country	Data	Health effects	Ongoing work and/or research	Future work	Recommendations/ issues to be addressed
						chronotype • How do atypical working hours affect the performance of truck drivers (accidents, injuries, near-accidents and chronic diseases in the road transport sector) • Influence of shift work on the disruption of circadian rhythms and the development of several types of chronic diseases • Recommendations aiming to prevent the disruption of circadian rhythms for professionals in highly exposed occupations such as those in the sectors of health, public services, the police, and fire departments.

Organi-sation	Country	Data	Health effects	Ongoing work and/or research	Future work	Recommendations/ issues to be addressed
Occupa-tional Cancer Research Centre (OCRC)	Canada	There are data describing the number and proportion of shift workers in Canada. These data were calculated by CAREX Canada. It was estimated that 13% of Canadian employees are regularly involved in shift work or night work. Around 21% of Canadian workers have atypical working hours (evening work, fragmented schedule, work on demand, etc.).	The effects studied by OCRC are breast cancer and prostate cancer. OCRC also focuses on chronic diseases such as cardiovascular diseases and diabetes.	A monitoring study on shift work and breast cancer is in progress with the aim of determining the proportion of breast cancer cases that can be attributed to shift work.		The following short-term research needs have been highlighted by this organisation: - obtain data from a current study to describe the professions and industries in which shift work occurs; - inform workers of the health effects of shift work. Long-term needs: - undertake cohort studies to assess the link between breast cancer and shift work
HSA	Ireland	No interest in shift work demonstrated by this organisation				

Organi-sation	**Country**	**Data**	**Health effects**	**Ongoing work and/or research**	**Future work**	**Recommendations/ issues to be addressed**
FIOH	Finland	The data come from Cochrane studies.	The most commonly studied health effects are sleep disruption, sleepiness, breast cancer, and cardiovascular problems.	Cochrane reviews are in progress on the prevention of sleep disruption and sleepiness. There is another Cochrane review on means of preventing injuries related to shift work.		

Annex 6: articles selected for cognitive effects and vigilance

Refer to the digital Annex available on the ANSES website (www.anses.fr).

Annex 7: articles not selected for cognitive effects and vigilance

Table 21: articles not selected for cognitive effects and vigilance

Author	Date	Comments
Diez	2011	Major methodological limitations
Gregory	2010	Major methodological limitations
Haire	2012	Major methodological limitations
Kageyama	2011	Major methodological limitations
Namita	2010	Major methodological limitations
Radun	2011	Major methodological limitations
Safari	2013	Major methodological limitations
Tanaka	2012	Major methodological limitations
Van Den Heuvel	2010	Major methodological limitations
Amirian 2	2014	Major methodological limitations
Asaoka	2012a	Not relevant for the studied effect
Asaoka	2012b	Not relevant for the studied effect
Chiu	2013	Not relevant for the studied effect
Christmas	2013	Not relevant for the studied effect
Culpepper	2010	Not relevant for the studied effect
Di Milia	2012	Not relevant for the studied effect

Eldevik	2013	Not relevant for the studied effect
Ftouni	2013	Not relevant for the studied effect
Gibson	2010	Not relevant for the studied effect
Grishin	2012	Not relevant for the studied effect
Kato	2012	Not relevant for the studied effect
Mansukhani	2012	Not relevant for the studied effect
McClelland	2013	Not relevant for the studied effect
Niu	2011	Not relevant for the studied effect
Oldenburg	2013	Not relevant for the studied effect
Pagnamenta	2012	Not relevant for the studied effect
Parkes	2012	Not relevant for the studied effect
Rajaratnam	2011	Not relevant for the studied effect
Ruutiainen	2013	Not relevant for the studied effect
Sadeghniiat-Haghighi	2011	Not relevant for the studied effect
Saksvik-Lehouillier	2012	Not relevant for the studied effect
Sessler	2011	Not relevant for the studied effect
Swanson	2012	Not relevant for the studied effect
Vennelle	2010	Not relevant for the studied effect
Violanti	2012	Not relevant for the studied effect
Wagstaff	2011	Not relevant for the studied effect
Veddeng	2014	Not relevant for the studied effect

Han	2014	Not relevant for the studied effect

Annex 8: articles selected for effects on psychological health

Refer to the digital Annex available on the ANSES website (www.anses.fr).

Annex 9: articles not selected for effects on psychological health

Table 22: studies not selected for psychological health

Author	Date	Comments
Bjorvatn	2012	Not relevant to the issue raised
Chae	2013	Not relevant to the issue raised
Chatti	2010	Major methodological limitations
De Vargas	2011	Major methodological limitations
Kageyama	2011	Not relevant to the issue raised
Kakeda	2011	Not relevant to the issue raised
Karhula	2013	Not relevant to the issue raised
Kim	2013	Not relevant to the issue raised
Lopes	2010	Not relevant to the issue raised
Mollart	2013	Major methodological limitations
Navamar Jaromi	2011	Not relevant to the issue raised
Riboldi	2012	Not relevant to the issue raised (literature review)
Shy	2011	Major methodological limitations
Ulas	2012	Not relevant to the issue raised
Wilsmore	2013	Not relevant to the issue raised
Wu	2010	Major methodological limitations
Burgueno	2010	Not relevant to the issue raised

Author	Date	Comments
Courtney	2013	Major methodological limitations
McCarty	2013	Not relevant to the issue raised
Sahraian	2010	Not relevant to the issue raised
Archer	2011	Major methodological limitations
Flo	2014	Not relevant to the issue raised
Luca	2014	Major methodological limitations
Hemamalini	2014	Major methodological limitations
Chang	2014	Major methodological limitations

Annex 10: articles selected for effects on sleep

Refer to the digital Annex available on the ANSES website (www.anses.fr).

Annex 11: articles not selected for effects on sleep

Table 23: studies not selected for effects on sleep

Author	Date	Comments
Swanson	2011	Major methodological limitations
Shy	2011	Major methodological limitations
Yeung	2014	Major methodological limitations
Kormpeli	2012	Major methodological limitations
Hansen	2011	Major methodological limitations
Huth	2013	Major methodological limitations
Archer	2011	Major methodological limitations
Fallis	2011	Major methodological limitations
Thorne	2010	Major methodological limitations
Kato	2012	Major methodological limitations
Tremaine	2011	Major methodological limitations

Annex 12: articles selected for metabolic disorders and cardiovascular diseases

Refer to the digital Annex available on the ANSES website (www.anses.fr).

Annex 13: articles not selected for metabolic disorders and cardiovascular diseases

Table 24: studies not selected for metabolic disorders and cardiovascular diseases

Author	Date	Comments
Anjum	2012	Review
Antunes	2010	Review
Barf and Scheurink	2011	Review
Bass and Takahashi	2010	Review
Bayon	2014	Review
Buss	2012	Review
Cannizzaro	2012	Major methodological limitations
Canuto	2013	Review
Chatti et al	2010	Major methodological limitations
Chung & Yang	2011	Major methodological limitations
Crispim	2011	Major methodological limitations
Diez et al	2011	Major methodological limitations
DiMilia	2013	Major limitations but useful for discussion
Diene	2012	Review
Ekmekcioglu	2011	Major methodological limitations
Escobar-Córdoba	2011	Major methodological limitations
Esquirol	2011	Review

Author	Date	Comments
Faraut	2013	Review
Ferreira	2012	Animal experiment
Fonken	2010	Animal experiment
Gale	2011	Major methodological limitations
Gamble	2013	Major methodological limitations
Garaulet M	2010	Review
Gooley	2014	Review
Ha et al	2012	Review
Han	2011	Major methodological limitations
Harris	2010	Major methodological limitations
Husse	2012	Animal experiment
Huth	2013	Major methodological limitations
Ika	2013	Major methodological limitations
Hwang	2012	Major methodological limitations
Hwang (2)	2012	Major methodological limitations
Hwang and Hong	2012	Review
Ioja	2012	Review
Itani	2011	Major methodological limitations
Järvholm	2013	
Jensen	2014	Review

Author	Date	Comments
Johnston	2014	Review
Kamata	2011	Major methodological limitations
Kawabe	2014	Major methodological limitations
Kawada	2010	Major methodological limitations
Kim	2013	Major methodological limitations
Kirthana	2010	Major methodological limitations
Kobayashi	2012	Major methodological limitations
Laugsand	2011	Major methodological limitations
Lee	2013	Major methodological limitations
Leenars	2012	Major methodological limitations
Li	2011	Major methodological limitations
Marqueze	2013	Major methodological limitations
Mohebbi	2010	Major methodological limitations
Moy	2010	Major methodological limitations
Nabe-Nielsen	2011	Major methodological limitations
Özbay		Cannot be evaluated (abstract only)
Peery	2013	Review
Poulsen	2014	Major methodological limitations
Rakshit	2014	Review
Rose	2011	Review

Author	Date	Comments
Sancini	2012	Not relevant
Sarrafi-Zadeh	2012	Review
Sathananthan	2010	Review
Sfreddo	2010	Major methodological limitations
Shimada	2011	Major methodological limitations
Singh	2012	Review
Tobaldini	2013	Not relevant
Uetani	2011	Major methodological limitations
van Drongelen	2011	Review
Vyas	2012	Review
Wang	2011	Review
Wirth	2014	Major methodological limitations
Young	2013	Major methodological limitations
Zhao	2011	Major methodological limitations
Zhao 2	2012	Major methodological limitations
Zimmerman	2012	Review
Zmrzljak and Rozman	2012	Review

Annex 14: articles selected for the cancer effect

Refer to the digital Annex available on the ANSES website (www.anses.fr).

Annex 15: articles not selected for the cancer effect

Table 25: studies not selected for the cancer effect

Author	Date	Comments
Langley	2012	Major methodological limitations
Li	2014	Major methodological limitations
Mirick	2013	Major methodological limitations
Wang	2015	Major methodological limitations
Arent	2012	Major methodological limitations
Qiu	2012	Major methodological limitations
Reszka	2013	Major methodological limitations

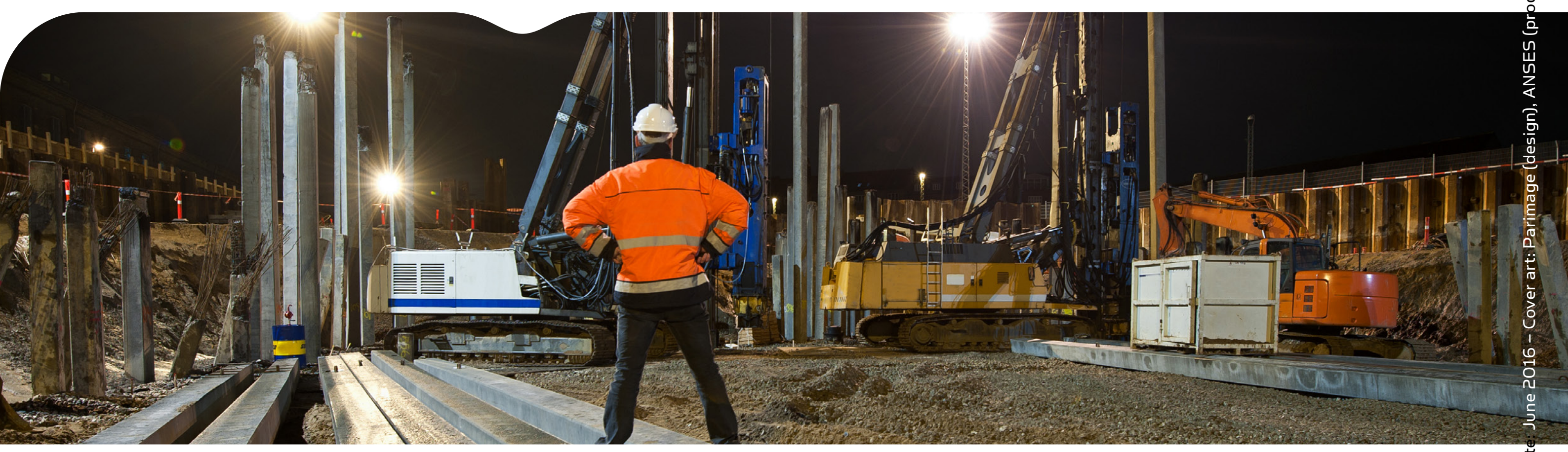
Annex 16: articles not selected for traumatic injuries, accidentology

Table 26: articles not selected for traumatic injuries, accidentology

Author	Date	Comments
Arakawa	2011	Major methodological limitations
Akhtar	2011	Not relevant
Amiri		Major methodological limitations
Amirian	2014	Major methodological limitations
Bohle	2010	Not relevant
Chimamize	2013	Not relevant
Dhande	2011	Not relevant
Gourni	2012	Not relevant
Lucidi	2013	Major methodological limitations
Maghsoudipour		Major methodological limitations
Musa	2013	Not relevant (review)
Pagnamenta	2012	Not relevant
Parkes		Not relevant (review)
Postnova	2013	Not relevant
Radun	2011	Major methodological limitations
Riboldi	2012	Not relevant (review)
Slogar		Not relevant (review)

Swanson	2011	Major methodological limitations
Uehli	2014	Not relevant
Vennelle	2010	Not relevant
Wagstaff	2011	Not relevant (review)
Zhao	2010	Not relevant (review)

Notes



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