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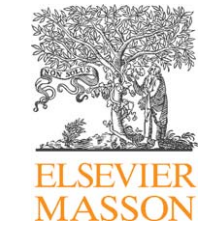

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REVIEW

Shift work and cardiovascular risk factors: New knowledge from the past decade

Le travail posté et les facteurs de risque cardiovasculaire : les nouvelles connaissances de ces dix dernières années

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Summary Cardiovascular diseases remain a major public health problem. The involvement of several occupational factors has recently been discussed, notably the organization of work schedules, e.g. shift work. To analyse the progress of knowledge on the

Abbreviations: ACTH, Adrenocorticotropic hormone; BMD, Benchmark duration; BMI, Body mass index; BP, Blood pressure; CLOCK, Circadian Locomotor Output Cycles Kaput; CRP, C-reactive protein; CVD, Cardiovascular disease; DBP, Diastolic blood pressure; HbA1c, Gycosylated haemoglobin A1c; HDL-C, High-density lipoprotein cholesterol; IDF, International Diabetes Federation; IGT, Impaired glucose tolerance; LDL-C, Low-density lipoprotein cholesterol; NCEP-ATP III, National Cholesterol Education Program Adult Treatment Panel III; OR, Odds ratio; SBP, Systolic blood pressure.

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factors;
Hypertension;
Body mass index;
Lipids;
Metabolic syndrome

relationship between cardiovascular risk factors and shift work. A review of English-language literature dealing with the link between cardiovascular factors and shift workers (published during 2000—2010) was conducted. Studies published in the past 10 years tend to document an impact of shift work on blood pressure, lipid profile (triglyceride levels), metabolic syndrome and, possibly, body mass index. However, the consequences on glucose metabolism are unclear. These results are not yet firmly established, but are supported by strong hypotheses. Some advice could reasonably be proposed to guide the clinical practitioner.

MOTS CLÉS
Le travail posté ;
Facteurs de risque cardiovasculaire ;
Hypertension artérielle (HTA) ;
Indice de masse corporelle (IMC) ;
Lipides ;
Syndrome métabolique

Résumé Les maladies cardiovasculaires demeurent un problème majeur de santé publique. Ainsi récemment, l'implication des plusieurs facteurs professionnels a été évoqué et notamment l'organisation des horaires de travail (travail posté). Analyser l'avancée des connaissances sur les relations entre le travail posté et les facteurs de risque cardiovasculaire. Une revue de la littérature anglaise traitant du lien les facteurs de risque cardiovasculaire et le travail posté a été menée durant la période de 2000—2010. Les études les plus récentes tendent à documenter des effets du travail posté sur la pression sanguine artérielle, sur le profil lipidique (notamment sur les taux de triglycérides), sur le syndrome métabolique et probablement sur l'indice de masse corporelle. Les conséquences sur le métabolisme glucidique restent à préciser. Les résultats ne sont pas encore strictement établit, mais plusieurs hypothèses physiopathologiques les supportent et des conseils pourraient être raisonnablement proposés aux praticiens.

Background

Among the various causes of mortality, deaths attributable to CVDs are the most widespread worldwide, and forecasts suggest they will still rank first in 2030 (World Health Statistics, 2008). The factors implicated in CVD have inspired the development of various prevention strategies over the past 40 years. Although some of these factors are well proven, others remain uncertain. Among those currently recognized, non-modifiable risk factors (e.g. age and gender) are set apart from modifiable ones (e.g. high BP, dyslipidaemia and diabetes). However, despite improvements in therapeutic management, people remain at risk of CVD. This poses the question as to whether undiscovered or unrecognized factors could have a role to play in better overall risk management.

Some occupational factors are now suspected to be related to CVD. Among them, the management of work schedules (shift work) is becoming an increasingly important one. Directive 93/104/EC broadly defines shift work as 'any method of organizing 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'. Typically, shift work can be performed in two shifts with a break in the late afternoon and on weekends (2×8), in three shifts with a break on weekends (3×8) or in four or five shifts to ensure working round the clock. This mode of operation may vary depending on the rotation cycle (number of days between two identical sequences), the direction of rotation (clockwise or counterclockwise) and the stability of the time slots planned (permanent night work). Shift work is therefore organized in a wide range of possible schedules. This way of managing work schedules contrasts with a more standard pattern ('daytime work pattern').

In the working world, shift work is a very common mode of operation to serve obvious economic and social goals. In the US, sources from the Bureau of Labor Statistics in 2004 stated that 15% of US employees did shift work. According to the fourth report on working conditions in Europe, issued in 2005, shift work represented an important mode of operation to address the economic circumstances of modern society (15—20%).

A link between shift work and cardiovascular disease has been hypothesized and highlighted increasingly in recent years, but cannot be firmly asserted. A meta-analysis of 17 studies, published in 1999, noted a 40% higher relative risk of CVD among shift workers compared to day workers, for both men and women [1]. A recently published overview of the literature focusing on ischaemic heart disease and based on 16 studies (1972—2008) did not conclude with certainty that shift work has an impact [2]. Broadly, similar results were seen recently from a 22-year period of follow-up of a Finnish cohort which analysed mortality due to coronary heart disease in both genders [3].

The difficulties in analysing to the consequences of shift work on cardiovascular risks remain for several reasons: heterogeneous definitions of shift work; heterogeneity in the confounding factors included in studies; and the pathological and physiological mechanisms considered. We wanted to contribute to this research by proposing a survey of the literature that deals with the impact of shift work on CVD risk factors during 2000—2010. Pertaining to the group of

factors deemed modifiable, the work schedules could, if firmly implicated, be a major target for public and individual efforts to prevent CVD.

Methods

Literature search

Searches were conducted using the following electronic bibliographies and repositories, to analyse the link between shift work and cardiovascular risk factors: PubMed, Cochrane library and Embase. The following key words were included as MeSH terms: shift work, night work shift workers, and night workers. Each of these was combined individually with the following: (1) cardiovascular risk factors; (2) hypertension; (3) BMI (obesity, overweight); (4) lipids (triglyceride, cholesterol, HDL-C); (5) diabetes; and (6) metabolic syndrome).

Selected articles

From a review published in 1999 [1], we have updated the knowledge of this field by including: (1) original articles published between January 2000 to December 2010; (2) written in English and published in an international peer-reviewed journal; and (3) concerning adult subjects. Review articles and those with no empirical results informing the link between shift work and cardiovascular risk factors were excluded.

Classification of articles

The publications were classified by cardiovascular risk factors. We have also described systematically the type of study (cross-sectional, longitudinal, prospective or retrospective), the number, age and gender of subjects examined, and their distribution between day workers and shift workers, and the type of shift work.

Our purpose was to classify how the different types of work schedules studied in these articles are associated with different cardiovascular risk factors, taking care of confounding parameters. Summary tables are available at the end of this overview, organized by study design in each category of cardiovascular factor and by year of publication.

Results

Included articles

Initially, 215 articles were recovered from the search of the three databases, but after reviewing titles and abstracts and removing duplicates, 74 articles remained and have been studied in this review (Fig. 1).

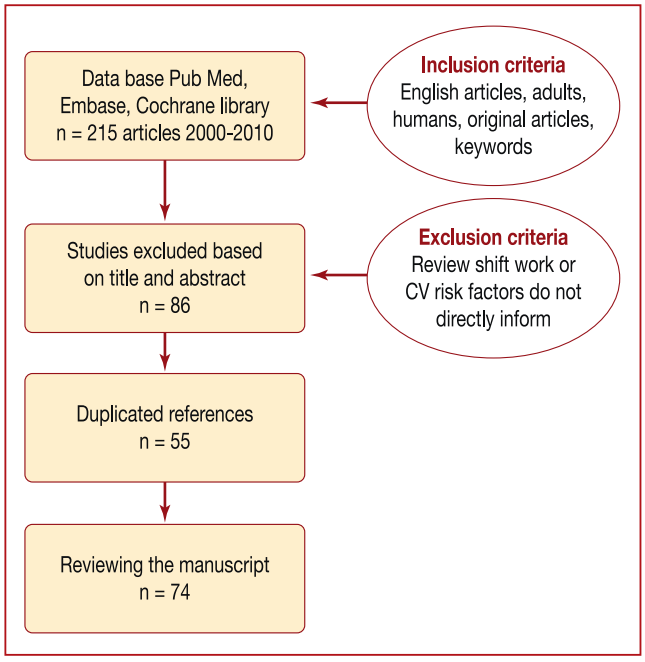

Figure 1. Studies included in this review.

Shift work and hypertension

The role of the working environment on the pathogenesis of hypertension is not clear, but are there any grounds for so-called 'idiopathic' hypertension (Table 1)? The review of the literature published in 1999 by Bøggild and Knutsson [1] showed no link between shift work and hypertension in most of the studies included. However, research carried out over the past decade, including more longitudinal studies and the use of the new hypertension definition (SBP > 140 mmHg and/or DBP > 90 mmHg and/or taking antihypertensive medication) tends to show an impact of shift work on threshold values of arterial BP.

Among workers in a Japanese steel factory, a significantly higher risk of developing hypertension (odds ratio [OR] 1.10, 95% confidence interval [CI] 1.01—1.20) has been found for shift workers compared to day workers [4]; and a higher risk of progression from mild to severe hypertension (OR 1.23, 95% CI 1.05—1.44) [5]. Moreover, some studies have implicated shift work as a possible cause for raised systolic or diastolic pressure [6—8], but this has not been confirmed by other longitudinal studies, based on baseline results or during the monitoring periods [3,9—14]. The disparities in these findings may relate to the way other co-variates or confounders, such as career development, have been handled in the analyses. Similarly, the findings of cross-sectional studies have been mixed: some report a link between shift work and BP [15,16], while others refute it [17—25].

Some authors have analysed the effects of shift work on hypertension, while taking into account age and duration of exposure. In one study, a higher risk was found among shift workers aged 40—49 years, but not in those aged 30—39 and 50—59 years, suggesting a 'healthy workers effect' [26]. A significant increase in arterial SBP was also noted in men aged > 30 years exposed to shift work over 1—10 years, but

Table 1 Relationship between shift work and hypertension or blood pressure variation.

Reference	Study type; years; recruitment	*n* gender (age [mean or range])	SW schedule	Adjustment parameters	BP parameters	Main results SW vs DW (OR [95% CI]) unless otherwise specified
Longitudinal studies						
Sakata et al., 2003 [4]	Prospective; 1991–2001; workers in Japanese steel company	3022 ♂ DW 2316 ♂ SW	3 × 8; irregular shift work: 5 days; 2 rest days; 5 evenings; 1 rest day; 5 nights; 2 rest days; clockwise rotation	Age, BMI, drinking and smoking habits, physical activity, TC, creatinine, γGTP, HbA1c, uric acid	Hypertension (SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg and/or treatment)	Increased risk of onset of hypertension (1.10 [1.01–1.20])
van Amelsvoort et al., 2004 [14]	1 y; nurses and incinerator plant workers	150 ♂ ♀ DW 227 ♂ ♀ SW	Counter-clockwise rotation (night, afternoon, morning); clockwise rotation (morning, afternoon, night)	Educational level, gender, age, JSI variables, variables under study at baseline	BP	No significant change in BP after 1 y in SW
Oishi et al., 2005 [5]	Prospective; 1991–2001; workers in Japanese steel company	1560 ♂ DW (40.3 y) 1381 ♂ SW (40.5 y) All had mild hypertension	3 × 8 irregular shift work: 5 days; 2 rest days; 5 evenings; 1 rest day; 5 nights, 2 rest days; clockwise rotation	Age, BMI, drinking and smoking habits, physical activity, TC, creatinine, γGTP, HbA1c, uric acid	Progression from mild hypertension (SBP 140–159 and/or DBP 90–99 mmHg); to severe hypertension (SBP ≥ 160 and/or DBP ≥ 100 mmHg)	SW significantly associated with progression from mild to severe hypertension (1.23 [1.05–1.44]) and severe diastolic hypertension (1.28 [1.07–1.52])
Kivimäki et al., 2006 [38]	Prospective; 2000–2004; nurses in 21 Finnish hospitals	1999 ♀ DW (45.3 y) 5038 ♀ SW (41.1 y)	3 × 8; 2 × 8; permanent nights	None	BP	Baseline BP NS; high BP in SW did not predict leaving organisation to get DW
Morikawa et al., 2007 [12]	Prospective; 1993–2003; Japanese factory workers	1993/2003: 712 ♂ DW/DW (36.4 y) 173 ♂ DW/SW (36.0 y) 210 ♂ SW/DW (36.2 y) 434 ♂ SW/SW (33.5 y)	2 × 8, 3 × 8; counter-clockwise rotation; non-continuous system (5 days, 5 nights, 5 evenings with 2 weekend rest intercalated); continuous system (3–4 days, 3–4 nights, 3–4 evenings and 1 rest day intercalated)	Age, BMI, smoking, alcohol, physical activity	Increase in SBP and DBP over 10 y	NS

Table 1 (*Continued*)

Reference	Study type; years; recruitment	*n* gender (age [mean or range])	SW schedule	Adjustment parameters	BP parameters	Main results SW vs DW (OR [95% CI]) unless otherwise specified
Virkkunen et al., 2007 [11]	Prospective; 1982—1999; industrial workers; Helsinki heart study, Finland	404 ♂ DW (52.5 y) 27 ♂ SW (52.6 y)	2 × 8; 3 × 8; irregular work, night work (without noise or physical workload)	None	BP during 8-year follow-up	SBP and DBP NS
Nabe-Nielsen et al., 2008 [13]	Prospective; 2004—2005; Danish social/healthcare assistants	1483 ♂ ♀ DW (35.1 y) 482 ♂ ♀ SW1 (36.3 y) 124 ♂ ♀ SW2 (36.6 y) 474 ♂ ♀ SW3 (33.6 y) 307 ♂ ♀ SW4 (33.6 y)	SW1: evenings; SW2: nights; SW3: 2 × 8 without night work; SW4: 2 × 8 and 3 × 8 with night work	Age, gender, education, cohabitation, general self-efficacy, years of school, former experience in the eldercare sector	Hypertension history	SW1 (1.04 [0.66—1.63]); SW2 (0.70 [0.27—1.82]); SW3 (1.26 [0.79—2.02]); SW4 (1.18 [0.68—2.05]); all vs DW
Suwazono et al., 2008 [6]	Prospective; 1991—2005; workers in Japanese steel company	3963 ♂ DW (35.8 y) 2748 ♂ SW (36.7 y)	3 × 8 irregular shift work: 5 days; 2 rest days; 5 evenings; 1 rest day; 5 nights; 2 rest days; clockwise rotation	Age, BMI, tobacco, alcohol, physical activity, TC, creatinine, γGTP, AST, HbA1c, uric acid	Increased SBP or DBP by ≥ 10%, ≥ 15%, ≥ 20%, ≥ 25%, ≥ 30%	≥ 10%: SBP (1.15 [1.07—1.23]); DBP (1.19 [1.11—1.28]); ≥ 15%: SBP (1.21 [1.12—1.31)]; DBP (1.22 [1.13—1.33]); ≥ 20%: SBP (1.15 [1.04—1.28]); DBP (1.24 [1.13—1.37]); ≥ 25%: SBP (1.20 [1.06—1.37]); DBP (1.16 [1.03—1.30]); ≥ 30%: SBP (1.23 [1.03—1.47]); DBP (1.04 [0.89—1.22])
Puttonen et al., 2009 [9]	Prospective; 1980—2001; Young Finns Study	668 ♀ DW 515 ♂ DW 831 ♀ SW 712 ♂ SW All 24—39 y	2 × 8; 3 × 8; regular evening or night work	Age	BP	No association with SBP or DBP

Table 1 (*Continued*)

Reference	Study type; years; recruitment	*n* gender (age [mean or range])	SW schedule	Adjustment parameters	BP parameters	Main results SW vs DW (OR [95% CI]) unless otherwise specified
De Bacquer et al., 2009 [8]	Cohort study; 1995—2003; BELSTRESS, Belgium	1220 ♂ DW (44.7 y) 309 ♂ SW (43.1 y)	2 or 3 rotating shifts	Age, WC, DBP, HDL-C	SBP/DBP ≥ 130/85 mmHg and/or treatment	(1.31 [1.04—1.66])
Lin et al., 2009 [7]	Retrospective cohort; 2002—2007; employees of electronic manufacturing company, Taiwan	125 ♀ DW (31.1 y) 160 ♀ past SW (34.7 y) 102 ♀ current SW (31.9 y)	2 × 8; 6 days, 3 rest days, 6 nights, 3 rest days; 12-h shifts	Smoking, age, insulin status, metabolic syndrome, job, physical activity, snack before sleeping	BP ≥ 130/85 mmHg or treatment at 5-y FU	Elevated BP: DW: 15.2%; past SW 34.4%; current SW: 37.3% (both $P < 0.05$ vs DW)
Pietrouisty et al., 2010 [10]	Prospective cohort, 2003—2007; nurses in 3 hospitals in Italy	336 ♀ ♂ DW (37.9 y) 402 ♀ ♂ SW (38.9 y)	Night or rotating shifts with ≥ 4 nights/month	None	Incidence of BP ≥ 130/85 mmHg or treatment	DW: 11.9%; SW: 11.2%; NS
Hublin et al., 2010 [3]	Cohort study; 1975—1981—2003; Finnish nationwide official register	7698/7838 ♂/♀ DW 108/224 ♂/♀ nights 509/701 ♂/♀ SW-DW 562/610 ♂/♀ DW-SW 962/930 ♂/♀ SW	From questionnaire: mainly DW; mainly SW; mainly nights	Age, marital status, social class, education, smoking, alcohol, hypertension, BMI, physical activity, life satisfaction, sleep length, use of hypnotics and/or tranquilizers, physical load of work, working place	Hypertension	Hypertension incidence not significantly different for both genders
Thomas & Power 2010 [37]	'1958 British birth cohort'	2710/1665 ♂/♀ DW 662/368 ♂/♀ nights 776/300 ♂/♀ mornings 2226/1357 ♂/♀evenings 1358/864 ♂/♀ weekends All 45 y	SW if ≥ 1/week outside 07:00—18:00; 4 types of SW: Summing the Number of shift work types (0—4) nights, mornings, evenings, weekends	Social class, total h per week, employee, physical activity, diet, smoking, alcohol, diabetes treatment	BP	NS for SBP and DBP for ♂ working several types of shift NS for SBP for ♀ in several types; lower DBP in ♀ type 4

Table 1 (*Continued*)

Reference	Study type; years; recruitment	*n* gender (age [mean or range])	SW schedule	Adjustment parameters	BP parameters	Main results SW vs DW (OR [95% CI]) unless otherwise specified
Cross-sectional studies						
Ohira et al., 2000 [32]	Japan	26 ♂ DW (32 y) 27 ♂ SW (31 y)	3 × 8; 2 days, 1 afternoon, 2 nights, 3 days off	BMI, alcohol, anger expression, physical activity	24-h ABP (mean BP during awake, asleep, non-work awake, work)	SBP significantly higher during awake and work periods; but no difference in DBP
Munakata et al., 2001 [33]	Nurses, Japan	18 ♀ SW (29 y)	2 days off, 2 nights, 1 day off, 2—3 days, 2 evenings	None	24-h ABP	SBP lower during night shift than day shift ($P = 0.01$); no difference in DBP
Ha et al., 2001 [28]	Workers in manufacturing firm	134 ♂ SW (29 y)	3 × 8; counter-clockwise rotation; 3 days in the same shift, 1 day off	Age, JSI, occupational history, past medical history, family history, smoking, alcohol consumption, interaction age × duration of SW	BP (measured at each of the 3 shifts) and SW duration	SBP and DBP associated with duration of SW ($P < 0.05$); BP fell morning to afternoon to night ($P = 0.031$)
Karlsson et al., 2001 [18]	VIP study, Sweden	9857 ♀ DW 9719 ♂ DW 4632 ♀ SW 3277 ♂ SW All aged 30, 40, 50 or 60 y	Any shift or weekend work	None	SBP ≥ 140 mmHg or DBP ≥ 90 mmHg or treatment	Prevalence of hypertension: NS except for men included in group 40 years old 15.5% sw/12.3% dw, $P < 0.01$
Kitamura et al., 2002 [30]	Factory employees with untreated hypertension	12 ♂ SW (53.6 y)	4 days, 2 days off, 4 nights	None	24-h ABP	Circadian BP pattern changed from dipper to non-dipper on 1st day of night shift; returns to dipper within a few days

Table 1 (*Continued*)

Reference	Study type; years; recruitment	*n* gender (age [mean or range])	SW schedule	Adjustment parameters	BP parameters	Main results SW vs DW (OR [95% CI]) unless otherwise specified
Nagaya et al., 2002 [26]	Gifu Prefectural Center; Health-check programme, Japan	2824 ♂ DW (47.1 y) 826 ♂ SW (45.6 y)	Any mandatory night work (permanent night workers excluded)	BMI, job, drinking, smoking, exercise Stratified by age classes	SBP ≥ 140 mmHg or DBP ≥ 90 mmHg or treatment	30—39 y (NS); 40—49 y (1.62 [1.17—2.24]); 50—59 y (NS)
Karlsson et al., 2003 [19]	WOLF study, Sweden	665 ♂ DW (44.3 y) 659 ♂ SW (44.2 y)	3 rotating shifts	None	SBP ≥ 140 mmHg or DBP ≥ 90 mmHg or treatment	DW: 21.1%; SW: 16.9%; $P = 0.052$
Murata et al., 2005 [24]	Copper-smelting plant, Japan	87 ♂ DW 153 ♂ SW	4-shift forward rotation system	BMI, HDL-C, TG, haemoglobin, haematocrit, smoking, drinking, age, work duration	SBP ≥ 160 mmHg or DBP ≥ 95 mmHg	(1.06 [0.50—2.22])
Ha & Park 2005 [27]	Nurses and blue-collar workers	134 ♂ SW (29.1 y) 226 ♀ SW (28.5 y)	3 × 8; irregular rotating shifts including mornings, evenings, nights	Smoking, drinking, physical activity, JSI	BP	♂ ≥ 30 y: SW duration associated with SBP ($P < 0.05$); ♀ < 30 y: SW duration inversely associated with DBP ($P < 0.05$)
Fialho et al., 2006 [29]	Medical residents in ER	56 ♂ ♀ DW and SW (25.4 y)	DW: common working day; SW: 24-h shift	None	Mean 24-h ABP	Higher SBP (117 vs 113 mmHg; $P < 0.05$) and DBP (73 vs 69 mmHg; $P < 0.05$)
Ghiasvand et al., 2006 [17]	Repairs workshop	266 ♂ DW (38.6 y) 158 ♂ SW (46.4 y)	Not normal daylight hours	None	SBP ≥ 140 mmHg or DBP ≥ 90 mmHg or treatment	DW: 11.7%; SW: 17.1%; NS
Sookoian et al., 2007 [22]	2005; factory workers in Buenos Aires	877 ♂ DW (34 y) 474 ♂ SW (36 y)	Clockwise rotation; 2 × 8; 4 days, 4 nights, 3 rest days, 2 days, 3 rest days, 4 days	None	Mean BP	Mean SBP: NS; mean DBP: DW: 78 mmHg; SW: 76 mmHg ($P = 0.04$)

Table 1 (*Continued*)

Reference	Study type; years; recruitment	*n* gender (age [mean or range])	SW schedule	Adjustment parameters	BP parameters	Main results SW vs DW (OR [95% CI]) unless otherwise specified
Copertaro et al., 2008 [21]	2005; hospital staff, Italy	77 ♂ ♀ healthcare DW (48.6 y) 70 ♂ ♀ healthcare SW (47.3 y) Subgroup: 41 ♀ DW nurses (45.8 y) 32 ♀ SW nurses (43.5 y)	SW healthcare 1—6 nights/month; nurses: 3 × 8; 1 day, 1 evening, 1 night, 2 rest days	None	BP	Overall: SBP and DBP NS. Nurses: SBP elevated ($P < 0.05$); DBP NS
Haupt et al., 2008 [25]	Study of Health In Pomerania (SHIP)	760/1052 ♂/♀ DW (61.5 y) 506/192 ♂/♀ SW (62.3 y)	Ever worked shifts/nights	None	SBP ≥ 140 mmHg or DBP ≥ 90 mmHg or treatment	DW: 52.8%; SW: 57.0%; NS
Nazri et al., 2008 [15]	Factory workers in Kota Bharu, Kelantan	72 ♂ DW (31.6 y) 76 ♂ SW (32.3 y)	2 × 8; alternating day- and night-time; 2 days, 2 nights, 3 rest days	BMI, nature of job	SBP ≥ 140 mmHg or DBP ≥ 90 mmHg or treatment	DW: 4.2%; SW: 22.4%; (9.1 [1.4—56.7]); $P < 0.001$
Lo et al., 2008 [31]	Nurses from municipal hospital, Taiwan	8 ♀ DW (27 y) 16 ♀ SW (27 y)	SW: day, evening, night	None	24-h ABP	SBP and DBP increased significantly during sleeping period after night/evening shift; SW associated with dipper/non-dipper status; BP not return to baseline after night shift ($P < 0.05$)

Table 1 (*Continued*)

Reference	Study type; years; recruitment	*n* gender (age [mean or range])	SW schedule	Adjustment parameters	BP parameters	Main results SW vs DW (OR [95% CI]) unless otherwise specified
Viitasolo et al., 2008 [36]	Airline company, Finland	84 ♂ SW: 40 changing to rapid forward rotation (47 y); 22 changing to flexible system (37 y); 22 staying on old system (44 y)	Old system: 3 evenings, 3 mornings, 3 nights, 2 rest days between each shift Rapid forward rotation:: morning, evening, night, 2 rest days; flexible system: direction and rotation comparable with? old system with 3 days off; possible change with rotas of the 3rd or 4th week	None	Mean SBP	SBP +6 mm Hg for flexible shift system, +2.5 mm Hg for rapid forward rotation; no change for old system; DBP NS for the 3 groups
Esquirol et al., 2009 [20]	Industrial plant, France	98 ♂ DW (48.8 y) 100 ♂ SW (46.5 y)	3 × 8; clockwise rotation; 1—2 mornings, 1—2 afternoons, 1—2 nights, 3—4 rest days	None	BP	SBP or DBP; NS
Sfreddo et al., 2010 [23]	Hospital nursing personnel, Brazil	276/35 ♀/♂ DW (33.1 y) 159/23 ♀/♂ night SW (36.4 y)	Night work	Age, gender, skin colour, marital status, y at school, tobacco, alcohol, sleeping hours, BMI	Hypertension: ≥ 140/90 mmHg or treatment; pre-hypertension: ≥ 120—139/ ≥ 80—89 mmHg	Hypertension or pre-hypertension (RR 1.0 [0.8—1.3])
Chen et al., 2010 [16]	Manufacturing factory, Taiwan	401 ♀ office workers (33.5 y) 220 ♀ DW (33.6 y) 656 ♀ day SW (34.9 y) 561 ♀ night SW (32.7 y)	Day SW: 07:00—19:00; night SW: 19:00—07:00; 2 days work, 2 days off	Age, smoking, drinking, educational level, duration of employment	SBP ≥ 130 mmHg or DBP ≥ 85 mmHg or treatment	DW (1.6 [0.8—3.0]); day SW (1.1 [0.6—2.1]); night SW (2.3 [1.2—4.4]); all vs office

♀: females; ♂: males; γGTP: gamma-glutamyl transpeptidase; 2 × 8: two shifts with a break in the late afternoon and on weekends; 3 × 8: three shifts with a break on weekends; ABP: ambulatory blood pressure; AST: aspartate transaminase; BMI: body mass index; BP: blood pressure; CI: confidence interval; DBP: diastolic blood pressure; DW: day workers; ER: emergency room; FU: follow-up; h: hours; HbA1c: gycosylated haemoglobin A1c; HDL-C: high-density lipoprotein cholesterol; JSI: job strain index; NS: not significant; OR: odds ratio; RR: risk ratio; SBP: systolic blood pressure; SW: shift workers; TC: total cholesterol; TG: triglycerides; WC: waist circumference; y: years.

these results have not been confirmed for women involved in shift work [27,28]. A first year of exposure to shift work seems to have no effect on arterial BP, in both genders combined [14].

Partial adjustment of the circadian rhythms of arterial BP could be an explanation, with insufficient decreases in arterial BP during a night awake and relative increases during a sleep period after night or evening work compared to sleep during the night for day workers. An evolving non-dipper status, complete or partially reversible after a day off, is recorded [29—33]. The measurement of heart rate variability for evaluating the cardiac autonomic function has been used in some studies. Modification of sympathetic system responses is probably involved under the influence of level of physical activity during the sleep-wakefulness cycle [34]. Twelve-hour night-shift work has been found to result in an elevated BP and heart rate, a decrease in heart rate variability, and a delay in BP recovery [35]. In the shift system, the individual flexibility of work hours seems to have a less deleterious effect on BP than rapid forward rotations [36]. Considering the sum of the number of shift work types worked at least once per week (night, evening, morning, weekend), the results only show an inverse relationship for DBP in women [37].

In summary, studies published in the past 10 years have highlighted a potential increase in the risk of developing hypertension for shift workers; and the duration of exposure could influence this link.

Shift work and lipid disturbances

The survey published by Bøggild and Knutsson [1] in 1999 identified 27 studies correlating shift work and lipid factors (Table 2).

Shift work and cholesterol

Up until 1999, most studies did not report any influence of shift work on total cholesterol. Similarly, various longitudinal studies from the past 10 years have not shown a connection between shift work and total cholesterol levels [4,5,12,14,38]. However, several reports from the same study population found a positive link between shift work and hypercholesterolemia or increase in total cholesterol level [39—41]. They suggested that a minimum of 20 years of exposure to shift work was required to result in a 5% risk of having a 20% increase in total cholesterol [40]. Most cross-sectional studies suggested no significant relationship between shift work and total cholesterol levels [20,22,25,42,43], with the exception of one study, where shift work increased levels for women aged 40, 50 or 60-years-old and for men aged 40-years-old [18]. Another study seemed to demonstrate a difference in the relationship for men and women, with shift work positively associated with total cholesterol levels in men $\geq$ 30 years of age, but negatively associated in women [27].

Regarding an association with levels of HDL-C, results of the studies conducted in the past 10 years are mixed. While some point to shift work having no impact on this parameter [7,9,14,16,22,42,43], others show an association either in certain age groups [26], in both genders combined [18,19,21], or after taking into account various confounding factors [8] or long duration of exposure (20 years) [20]. The few studies dealing with LDL-C agree unanimously that there is no correlation between shift work and LDL-C [9,14,20,22,43]. After the first year of exposure to shift work and the initial phase of adaptation, no change in lipids factors is apparent [14].

In summary, there is no clear association between shift work and levels of total cholesterol, HDL-C or LDL-C.

Shift work and hypertriglyceridaemia

Only four of the 12 studies reviewed in the meta-analysis conducted in 1999 [1] showed significantly higher values of triglycerides in shift workers. However, the studies conducted since then generally confirm that there is a risk of a higher triglyceride levels among shift workers [8,9,18—22,26,44]. However, three studies, including one conducted in Italy, did not confirm these results, and it is possible that the dietary habits or genetic factors in the Mediterranean area could be explanatory factors [7,42,43].

Alternatively, improvements in the organization of shift work could positively modify the disturbances of certain lipid factors. In one study, ergonomic changes in shift patterns for 6 months increased the levels of HDL-C, decreased the total:HDL cholesterol ratio and LDL-C compared with controls. Modifying the direction of rotation resulted in triglyceride levels falling by 4% in the clockwise rotation and increasing by 15% in the counterclockwise rotation [45].

In summary, an association between shift work and higher triglyceride levels is apparent.

Shift work and carbohydrate metabolism

Few studies have looked specifically at the impact of shift work on diabetes (Table 3). One of the longitudinal studies analysed the effect of shift work on type 2 diabetes [46]. This study showed no effect of shift work on type 2 diabetes among blue-collar workers, but highlighted a probable social class effect on type 2 diabetes between blue-collar shift workers and daytime white-collar workers [46]. Another longitudinal study showed that a shift worker has a 1.5-fold higher risk of hyperglycaemia ($\geq$ 1.20 g/L) or type 2 diabetes over a follow-up period of 6.6 years [8]. Sometimes, a higher risk was found in certain types of shift work (day-shift workers), but not in night workers [16]. Among a cohort of nurses, the link between the duration of shift work and diabetes disappeared when BMI was taken into account [47]. Furthermore, based on assay levels of glycosylated haemoglobin A1c (HbA1c), a Japanese cohort has suggested that shift work might be independent factor for type 2 diabetes [48,49]. In this population, exposure duration was included in the analysis by calculating the BMD, defined as the exposure corresponding to a certain percentage change in the risk indexed by elevation of HbA1c. Thus, for 50-year-old men, exposure to shift work for periods between 19—32 years corresponded to a 5% additional risk compared to day workers in the same age class [50].

Sometimes a link between shift work and hyperglycaemia has only been found in certain age classes and genders (e.g. women aged 60 years [18] or men aged 30—39 years [26]). IGT in shift workers has been reported in one study [42]. However, glycaemia and IGT are parameters

Table 2 Relationship between shift work and dyslipidaemia.

Reference	Study type; years; recruitment	*n* gender (age [mean or range])	SW schedule	Adjustment parameters	Lipid parameters	Main results SW vs DW (OR [95% CI]) unless otherwise specified
Longitudinal studies						
Sakata et al., 2003 [4]	Prospective; 1991–2001; workers in Japanese steel company	3022 ♂ DW 2316 ♂ SW	3 × 8; irregular shift work: 5 days, 2 rest days, 5 evenings, 1 rest day, 5 nights, 2 rest days; clockwise rotation	None	Mean TC at baseline	NS
van Amelsvoort et al., 2004 [14]	1 y; nurses and incinerator plant workers	150 ♂ ♀ DW 227 ♂ ♀ SW	Counter-clockwise rotation (night, afternoon, morning); clockwise rotation (morning, afternoon, night)	Educational level, gender, age, JSI variables, variables under study at baseline	Mean TC, HDL-C, LDL-C at baseline and 1 y	LDL-C:HDL-C lower ($P = 0.004$); TC, LDL-C and HDL-C NS
Oishi et al., 2005 [5]	Prospective; 1991–2001; workers in Japanese steel company	1560 ♂ DW (40.3 y) 1381 ♂ SW (40.5 y)	3 × 8; irregular shift work: 5 days, 2 rest days, 5 evenings, 1 rest day, 5 nights, 2 rest days; clockwise rotation	None	Mean TC at baseline	NS
Kivimäki et al., 2006 [38]	Prospective; 2000–2004; nurses in 21 Finnish hospitals	1999 ♀ DW (45.3 y) 5038 ♀ SW (41.1 y)	3 × 8; 2 × 8; permanent nights	None	Self-reported high TC	At baseline: NS; high TC was not a predictor of leaving organisation to find day work
Morikawa et al., 2007 [12]	Prospective; 1993–2003; Japanese factory workers	1993/2003: 712 ♂ DW/DW (36.4 y) 173 ♂ DW/SW (36.0 y) 210 ♂ SW/DW (36.2 y) 434 ♂ SW/SW (33.5 y)	2 × 8; 3 × 8; counter-clockwise rotation; non-continuous system (5 days, 5 nights, 5 evenings with 2 weekend rest intercalated); continuous system (3–4 days, 3–4 nights, 3–4 evenings and 1 rest day intercalated)	Age, BMI, smoking, alcohol, physical activity	Mean TC over 10 y	NS

Table 2 (*Continued*)

Reference	Study type; years; recruitment	*n* gender (age [mean or range])	SW schedule	Adjustment parameters	Lipid parameters	Main results SW vs DW (OR [95% CI]) unless otherwise specified
Biggi et al., 2008 [44]	Prospective; 1976—2007; Milan	157 ♂ DW (42.3 y) 331 ♂ SW (47.0 y)	Permanent nights	Study period, job, age, lifestyle variables	TG > 150 mg/dL; TC > 200 mg/dL	High TG and high TC more common in night workers
Dochi et al., 2008 [41]	Prospective; 1991—2005; steel company, Japan	3263 ♂ DW 2247 ♂ SW	Clockwise rotation; 3 × 8; 5 days, 2 rest days, 5 evenings, 1 rest day, 5 nights, 2 rest days	Age, tobacco, alcohol, physical activity, BMI, laboratory data	TC ≥ 5.7 mmol/L	(1.1 [1.00—1.21])
Lin et al., 2009 [7]	Retrospective cohort; 2002—2007; electronic manufacturing company, Taiwan	125 ♀ DW (31.1 y) 160 ♀ past SW (34.7 y) 102 ♀ current SW (31.9 y)	2 × 8; 6 days, 3 rest days, 6 nights, 3 rest days; 12-h shifts	Smoking, age, insulin status, metabolic syndrome, job, physical activity, snack before sleeping	HDL-C < 40 (♂) or < 50 (♀) mg/dL; TG ≥ 150 mg/dL at 5-y FU	High TG: DW 9.6%; past SW 8.1%; current SW 11.8% (NS); low HDL-C: DW 11.2%; past SW 11.3%; current SW 14.7% (NS)
Dochi et al., 2009 [39]	Prospective; 1991—2005; steel company, Japan	4079 ♂ DW (36.2 y) 2807 ♂ SW (36.9 y)	Clockwise rotation; 3 × 8; 5 days, 2 rest days, 5 evenings, 1 rest day, 5 nights, 2 rest days	Age, tobacco, alcohol, physical activity, BMI, laboratory data	TC raised from baseline	≥ 20% (1.16 [1.07—1.26]); ≥ 25% (1.16 [1.05—1.28]); ≥ 30% (1.11 [0.98—1.25]); ≥ 40% (1.30 [1.07—1.58])
Puttonen et al., 2009 [9]	Prospective; 1980—2001; Young Finns Study	668 ♀ DW 515 ♂ DW 831 ♀ SW 712 ♂ SW All 24—39 y	2 × 8; 3 × 8; regular evening or night work	Age	Mean LDL-C, HDL-C, TG at baseline	LDL-C and HDL-C both NS; TG (♀: 1.26 vs 1.14; $P = 0.042$; ♂: 1.69 vs 1.48; $P = 0.017$)
De Bacquer et al., 2009 [8]	Cohort study; 1995—2003; BELSTRESS, Belgium	1220 ♂ DW (44.7 y) 309 ♂ SW (43.1 y)	2 or 3 rotating shifts	Age, WC, DBP, HDL-C	TG ≥ 220 mg/dL; HDL-C < 40 mg/dL	Low HDL-C (1.42 [1.02—1.99]); high TG (1.53 [1.22—1.92])

Table 2 (*Continued*)

Reference	Study type; years; recruitment	*n* gender (age [mean or range])	SW schedule	Adjustment parameters	Lipid parameters	Main results SW vs DW (OR [95% CI]) unless otherwise specified
Suwazono et al., 2010 [40]	Prospective; 1991—2005; steel company, Japan	4079 ♂ DW (36.2 y) 2807 ♂ SW (36.9 y)	Clockwise rotation; 3 × 8; 5 days, 2 rest days, 5 evenings, 1 rest day, 5 nights, 2 rest days	Age, tobacco, alcohol, physical activity, BMI, creatinine, GGT, AST	TC raised from baseline; BMD and BMDL were calculated	≥ 20% (1.03 [1.02—1.04]); ≥ 45% (1.13 [1.09—1.09]); threshold y for SW at 5% risk of increased TC: age 40—49 y: ≥ 21 y; age ≥ 50 y: 22.7 y
Cross-sectional studies						
Karlsson et al., 2001 [18]	VIP study, Sweden	9857 ♀ DW 9719 ♂ DW 4632 ♀ SW 3277 ♂ SW All aged 30, 40, 50 or 60 y	Any shift or weekend work	Age, socioeconomic group	TG > 1.7 mmol/L; HDL-C < 1.0 mmol/L (♀) or < 0.9 mmol/L (♂); mean TC	Low HDL-C: ♀ (1.26 [1.03—1.53]), ♂ (1.15 [0.96—1.38]); high TG: ♀ (1.13 [1.02—1.25]), ♂ (1.12 [1.01—1.24]); higher TC in SW for ♀ at age 40, 50, 60 y ($P < 0.05$) and ♂ at 40 y ($P < 0.05$)
Nagaya et al., 2002 [26]	Gifu Prefectural Center; Health-check programme, Japan	2824 ♂ DW (47.1 y) 826 ♂ SW (45.6 y)	Any mandatory night work (permanent night workers excluded)	BMI, job, drinking, smoking, exercise]	TG ≥ 1.7 mmol/L; HDL-C < 1.04 mmol/L Stratified by age classes	40—49 y: high TG (1.65 [1.26—2.16]); 50—59 y: low HDL-C (0.59 [0.36—0.93]); all other associations NS
Karlsson et al., 2003 [19]	WOLF study, Sweden	665 ♂ DW (44.3 y) 659 ♂ SW (44.2 y)	3 rotating shifts	Age, socioeconomic group, current smoking, physical activity, low social support, JSI	TC > 6.4 mmol/L; HDL-C < 0.9 mmol/L; TG ≥ 1.7 mmol/L;	TC > 6.4 mmol/L: DW 28.1%; SW 19% ($P < 0.0001$); HDL-C < 0.9 mmol/L: (2.03 [1.18—3.48]); TG ≥ 1.7 mmol/L: (1.40 [1.08—1.83])
Di Lorenzo et al., 2003 [42]	Chemical industry, Italy	134 ♂ DW (48.9 y) 185 ♂ SW (48.7 y)	3 × 8; counter-clockwise; 2 nights, 2 afternoons, 2 mornings, 3 rest days	None	Mean TC, HDL-C, TG	All NS

Table 2 (*Continued*)

Reference	Study type; years; recruitment	*n* gender (age [mean or range])	SW schedule	Adjustment parameters	Lipid parameters	Main results SW vs DW (OR [95% CI]) unless otherwise specified
Ha & Park 2005 [27]	Nurses and blue-collar workers	134 ♂ SW (29.1 y) 226 ♀ SW (28.5 y)	3 × 8; irregular rotating shifts including mornings, evenings, nights	Smoking, drinking, physical activity, JSI, BMI	Mean TC	♂ ≥ 30 y: TC elevated with SW duration (ß = 9.72; $P < 0.05$); ♀ ≥ 30 y: (ß = −2.82; $P < 0.05$)
Sookoian et al., 2007 [22]	2005; factory workers in Buenos Aires	877 ♂ DW (34 y) 474 ♂ SW (36 y)	Clockwise rotation; 2 × 8; 4 days, 4 nights, 3 rest days, 2 days, 3 rest days, 4 days	None	Mean TC, HDL-C, LDL-C, TG	SW had elevated TG ($P = 0.003$); TC, HDL-C, LDL-C all NS
Lavie & Lavie 2007 [43]	Electric company, Israel	207 ♂ DW (55.1 y) 154 ♂ SW (56.3 y)	6 mornings, 3 afternoons, 3 nights; 1–2 rest days intercalated	Age, sleep disturbed	Mean TC, HDL-C, LDL-C, TG	All NS
Haupt et al., 2008 [25]	Study of Health in Pomerania (SHIP)	760/1052 ♂/♀ DW (61.5 y) 506/192 ♂/♀ SW (62.3 y)	Ever worked shifts/nights	None	Mean TC, LDL-C:HDL-C	LDL-C:HDL-C higher in SW (3.0 vs 2.9; $P < 0.05$); TC NS
Copertaro et al., 2008 [21]	2005; hospital staff, Italy	77 ♂ ♀ healthcare DW (48.6 y) 70 ♂ ♀ healthcare SW (47.3 y) Subgroup: 41 ♀ DW nurses (45.8 y) 32 ♀ SW nurses (43.5 y)	SW healthcare 1–6 nights/month; nurses: 3 × 8; 1 day, 1 evening, 1 night, 2 rest days	None	Mean HDL-C or TG	Overall, SW had lower HDL-C ($P < 0.05$) and higher TG ($P < 0.01$). In nurses, SW had lower HDL-C (NS) and higher TG (NS)
Esquirol et al., 2009 [20]	Industrial plant, France	98 ♂ DW (48.8 y) 100 ♂ SW (46.5 y)	3 × 8; clockwise rotation; 1–2 mornings, 1–2 afternoons, 1–2 nights, 3–4 rest days	None	Mean TG, TC, LDL-C, HDL-C	In SW: decreased HDL-C ($P < 0.028$); elevated TG ($P < 0.039$); TC and LDL-C NS

Table 2 (*Continued*)

Reference	Study type; years; recruitment	*n* gender (age [mean or range])	SW schedule	Adjustment parameters	Lipid parameters	Main results SW vs DW (OR [95% CI]) unless otherwise specified
Chen et al., 2010 [16]	Manufacturing factory, Taiwan	401 ♀ office workers (33.5 y) 220 ♀ DW (33.6 y) 656 ♀ day SW (34.9 y) 561 ♀ night SW (32.7 y)	Day SW: 07:00—19:00; night SW: 19:00—07:00; 2 days work, 2 days off	Age, smoking, drinking, educational level, duration of employment	TG ≥ 150 mg/dL or 1.295 mmol/L; HDL < 40 mg/dL or 1.695 mmol/L	High TG (vs office): DW (0.9 [0.5—1.8]); day SW (1.7 [0.9—3.1]); night SW (0.7 [0.4—1.5]); low HDL-C (vs office): DW (1.1 [0.7—1.8]); day SW (0.9 [0.6—1.4]); night SW (0.7 [0.4—1.1])

♀: females; ♂: males; 2 × 8: two shifts with a break in the late afternoon and on weekends; 3 × 8: three shifts with a break on weekends; AST: aspartate transaminase; BMD: benchmark duration; BMDL: lower confidence limit of benchmark duration; BMI: body mass index; BP: blood pressure; CI: confidence interval; DW: day workers; FU: follow-up; h: hours; GGT: gamma-glutamyl transpeptidase; HDL-C: high-density lipoprotein cholesterol; JSI: job strain index; LDL-C: low-density lipoprotein cholesterol; NS: not significant; OR: odds ratio; SW: shift workers; TC: total cholesterol; TG: triglycerides; WC: waist circumference; y: years.

Table 3 Relationship between shift work and carbohydrate metabolism.

Reference	Study type; years; recruitment	*n* gender (age [mean or range])	SW schedule	Adjustment parameters	Diabetes parameters	Main results SW vs DW (OR [95% CI]) unless otherwise specified
Longitudinal studies						
Sakata et al., 2003 [4]	Prospective; 1991–2001; workers in Japanese steel company	3022 ♂ DW 2316 ♂ SW	3 × 8 irregular shift work: 5 days, 2 rest days, 5 evenings, 1 rest day, 5 nights, 2 rest days; clockwise rotation	None	HbA1c at baseline	DW 4.65 ± 0.51%; SW 4.63 ± 0.47%; NS
Morikawa et al., 2005 [46]	Prospective; 1993–2001; workers in factory, Japan	Blue-collar workers: 1099 ♂ DW (35.3 y) 228 ♂ SW 2 × 8 (33.5 y) 499 ♂ SW 3 × 8 (33.7 y) White-collar workers: 1041 ♂ DW (33.7 y)	2 × 8 non-continuous system; day and evening shifts. 3 × 8 counter-clockwise; non-continuous system: 5 days, 5 nights, 5 evenings; continuous system: 3–4 days, 3–4 nights, 3–4 evenings; rest days intercalated	Age, BMI, family history, smoking, drinking, physical activity	HbA1c ≥ 6.1%	Blue-collar SW vs DW: 2 × 8 (1.73 [0.85–3.52]); 3 × 8 (1.33 [0.74–2.36]); blue vs white collar: DW (1.19 [0.66–2.16]); 2 × 8 (2.01 [1.00–4.34]); 3 × 8 (1.61 [0.88–2.97])
Oishi et al., 2005 [5]	Prospective; 1991–2001; workers in Japanese steel company	1560 ♂ DW (40.3 y) 1381 ♂ SW (40.5 y)	3 × 8 irregular shift work: 5 days, 2 rest days, 5 evenings, 1 rest day, 5 nights, 2 rest days; clockwise rotation	None	HbA1c at baseline	NS
Suwazono et al., 2006 [49]	Prospective; 1991–2005; workers in Japanese steel company	3203 ♂ DW (35.1 y) 2426 ♂ SW (37.4 y)	3 × 8 irregular shift work: 5 days, 2 rest days, 5 evenings, 1 rest day, 5 nights, 2 rest days, clockwise rotation	None	HbA1c ≥ 6.0% or diagnosis by hospital physicians	Higher rate for SW (7.4 vs 5.7/1000-person y]); (1.35 [1.05–1.75]); $P = 0.021$
Kivimäki et al., 2006 [38]	Prospective; 2000–2004; nurses in 21 Finnish hospitals	1999 ♀ DW (45.3 y) 5038 ♀ SW (41.1 y)	3 × 8; 2 × 8; permanent nights	None	Self-reported diabetes at baseline	NS; but diabetes was predictive of leaving organisation to find day work (51.83 [1.01–3.32])

Table 3 (*Continued*)

Reference	Study type; years; recruitment	*n* gender (age [mean or range])	SW schedule	Adjustment parameters	Diabetes parameters	Main results SW vs DW (OR [95% CI]) unless otherwise specified
Morikawa et al., 2007 [12]	Prospective; 1993—2003; Japanese factory workers	1993/2003: 712 ♂ DW/DW (36.4 y) 173 ♂ DW/SW (36.0 y) 210 ♂ SW/DW (36.2 y) 434 ♂ SW/SW (33.5 y)	2 × 8; 3 × 8; counter-clockwise rotation; non-continuous (5 days, 5 nights, 5 evenings, 2 weekend rest intercalated); continuous (3—4 days, 3—4 nights, 3—4 evenings, 1 rest day intercalated)	Age, BMI, smoking, alcohol, physical activity	HbA1c	NS over 10 y
Kroenke et al., 2007 [47]	Prospective; 1989—1997; Nurses' health study II, US	62,574 ♀ (29—46 y in 1993)	Rotating night-shift work for 1 ≤ 12 months, 1 ≤ 2, 2 ≤ 5, 5 ≤ 10, ≥ 10 y	Model 1: age, family history diabetes, work hours, JSI, job support, work characteristics, tobacco, alcohol, diet Model 2: also BMI, smoking, obesity, physical activity, nutrition intake	Cases T2D 1993—1999 (≥ 1 classic symptoms and/or FPG 7.8 mmol/L and/or RPG 11.1 mmol/L) and/or treatment	Higher risk of T2D with longer exposure to shift work (model 1: $P = 0.001$; model 2: $P = 0.30$)
Nabe-Nielsen et al., 2008 [13]	Prospective; 2004—2005; Danish social/healthcare assistants	1483 ♂ ♀ DW (35.1 y) 482 ♂ ♀ SW1 (36.3 y) 124 ♂ ♀ SW2 (36.6 y) 474 ♂ ♀ SW3 (33.6 y) 307 ♂ ♀ SW4 (33.6 y)	SW1: evenings; SW2: nights; SW3: 2 × 8 without night work; SW4: 2 × 8 and 3 × 8 with night work	Age, gender education, cohabitation, general self-efficacy, years of school, former experience in the eldercare sector	Diabetes prevalence	SW1 (0.88 [0.46—1.70]); SW2 (0.98 [0.29—3.31]); SW3 (0.95 [0.47—1.90]); SW4 (0.74 [0.30—1.80])
Biggi et al., 2008 [44]	Prospective; 1976—2007; Milan	157 ♂ DW (42.3 y) 331 ♂ SW (47.0 y)	Permanent nights	None	Glycaemia > 110 mg/dL and mean level	Glycaemia > 110 mg/dL: DW 3.8%; SW 5.1%; mean glycaemia: DW 87.3 mg/dL; SW 85.1 mg/dL

Table 3 (*Continued*)

Reference	Study type; years; recruitment	*n* gender (age [mean or range])	SW schedule	Adjustment parameters	Diabetes parameters	Main results SW vs DW (OR [95% CI]) unless otherwise specified
De Bacquer et al., 2009 [8]	Cohort study; 1995—2003; BELSTRESS, Belgium	1220 ♂ DW (44.7 y) 309 ♂ SW (43.1 y)	2 or 3 rotating shifts	Age, WC, DBP, HDL-C	Glycaemia ≥ 120 mg/dL	(1.56 [1.18—2.05])
Lin et al., 2009 [7]	Retrospective cohort; 2002—2007; electronic manufacturing company, Taiwan	125 ♀ DW (31.1 y) 160 ♀ past SW (34.7 y) 102 ♀ current SW (31.9 y)	2 × 8; 6 days, 3 rest days, 6 nights, 3 rest days; 12-h shifts	Smoking, age, insulin status, metabolic syndrome, job, physical activity, snack before sleeping	Glycaemia ≥ 100 mg/dL	Development of hyperglycemia within 5 y: DW 10.4%; past SW 12.5%; current SW 18.6% (NS)
Suwazono et al., 2009 [48]	Prospective; 1991—2005; workers in Japanese steel company	4219 ♂ DW (36.3 y) 2885 ♂ SW (36.8 y)	3 × 8 irregular shift work: 5 days, 2 rest days, 5 evenings, 1 rest day, 5 nights, 2 rest days; clockwise rotation	Age, BMI, tobacco, alcohol, physical activity, TC, creatinine, γGTP, AST, HbA1c, uric acid	Increased HbA1c vs baseline	≥ 10% (1.35 [1.26—1.44]); ≥ 15% (1.29 [1.19—1.40]); ≥ 20% (1.23 [1.11—1.37]); ≥ 25% (1.19 [1.03—1.36]); ≥ 30% (1.14 [0.95—1.37])
Suwazono et al., 2010 [50]	Prospective; 1991—2005; workers in Japanese steel company	4219 ♂ DW (36.3 y) 2885 ♂ SW (36.8 y)	3 × 8 irregular shift work: 5 days, 2 rest days, 5 evenings, 1 rest day, 5 nights, 2 rest days; clockwise rotation	Age, BMI, tobacco, alcohol, physical activity, TC, creatinine, γGTP, AST, HbA1c, uric acid	Increased HbA1c vs baseline; BMDL/BMD expressed	SW ≥ 50 y: BMDL/BMD for 5%: ≥ 15%: 17.8/23.9 y; ≥ 20%: 15.7/18.7 y; ≥ 25%: 18.9/22.7 y; ≥ 30%: 25.2/31.7 y
Cross-sectional studies						
Karlsson et al., 2001 [18]	VIP study, Sweden	9857 ♀ DW 9719 ♂ DW 4632 ♀ SW 3277 ♂ SW All aged 30, 40, 50 or 60 y	Any shift or weekend work	None	Diabetes: FPG ≥ 7.0 mmol/L and/or OGTT ≥ 12.2 mmol/L and/or history stratified by age classes	Diabetes NS; FPG ≥ 7.0 mmol/L NS; OGTT NS (excepted for SW vs DW ♀ aged 60 y; $P < 0.05$)
Nagaya et al., 2002 [26]	Gifu Prefectural Center; Health-check programme, Japan	2824 ♂ DW (47.1 y) 826 ♂ SW (45.6 y)	Any mandatory night work (permanent night workers excluded)	BMI, job, drinking, smoking, exercise	Glycaemia ≥ 7.0 mmol/L or treatment, stratified by age	30—39 y (6.75 [1.31—56.1]); 40—49 and 50—59 y (NS)

Table 3 (*Continued*)

Reference	Study type; years; recruitment	*n* gender (age [mean or range])	SW schedule	Adjustment parameters	Diabetes parameters	Main results SW vs DW (OR [95% CI]) unless otherwise specified
Karlsson et al., 2003 [19]	WOLF study, Sweden	665 ♂ DW (44.3 y) 659 ♂ SW (44.2 y)	3 rotating shifts	None	Glycaemia $\geq$ 7.0 mmol/L; HbA1c $\geq$ 5.3%	Both NS
Di Lorenzo et al., 2003 [42]	Chemical industry, Italy	134 ♂ DW (48.9 y) 185 ♂ SW (48.7 y)	3 $\times$ 8 counter-clockwise; 2 nights, 2 afternoons, 2 mornings, 3 rest days	BMI, class of working age, TG, insulin	Glycaemia; OGTT	Glycaemia NS; OGTT higher SW (492 vs 477 mg/dL; $P < 0.05$); covariance analysis NS
Ha & Park 2005 [27]	Nurses and blue-collar workers of manufacturing firm	134 ♂ SW (29.1 y) 226 ♀ SW (28.5 y)	3 $\times$ 8; irregular rotating shifts including mornings, evenings, nights	Smoking, drinking, physical activity, JSI	Glycaemia	SW duration: NS
Lavie & Lavie 2007 [43]	Electric company, Israel	207 ♂ DW (55.1 y) 154 ♂ SW (56.3 y)	6 mornings, 3 afternoons, 3 nights, 1—2 rest days intercalated	Age, sleep disturbed	Glycaemia	NS
Sookoian et al., 2007 [22]	2005; factory workers in Buenos Aires	877 ♂ DW (34 y) 474 ♂ SW (36 y)	Clockwise rotation; 2 $\times$ 8; 4 days, 4 nights, 3 rest days, 2 days, 3 rest days, 4 days	None	Glycaemia; insulin; HOMA index	Glycaemia NS; insulin decreased ($P = 0.02$); HOMA decreased ($P = 0.003$)
Haupt et al., 2008 [25]	Study of Health in Pomerania (SHIP)	760/1052 ♂/♀ DW (61.5 y) 506/192 ♂/♀ SW (62.3 y)	Ever worked shifts/nights	None	Diabetes	DW 12.1%; SW 14.6% (NS)
Copertaro et al., 2008 [21]	2005; hospital staff, Italy	77 ♂ ♀ healthcare DW (48.6 y) 70 ♂ ♀ healthcare SW (47.3 y) Subgroup: 41 ♀ DW nurses (45.8y) 32 ♀ SW nurses (43.5y)	SW healthcare: 1—6 nights/month; nurses: 3 $\times$ 8; 1 day, 1 evening, 1 night, 2 rest days	None	Glycaemia	NS

Table 3 (*Continued*)

Reference	Study type; years; recruitment	*n* gender (age [mean or range])	SW schedule	Adjustment parameters	Diabetes parameters	Main results SW vs DW (OR [95% CI]) unless otherwise specified
Esquirol et al., 2009 [20]	Industrial plant, France	98 ♂ DW (48.8 y) 100 ♂ SW (46.5 y)	3 × 8; clockwise rotation; 1—2 mornings, 1—2 afternoons, 1—2 nights, 3—4 rest days	None	Glycaemia	Glycaemia decreased ($P < 0.041$)
Chen et al., 2010 [16]	Manufacturing factory, Taiwan	401 ♀ office workers (33.5 y) 220 ♀ DW (33.6 y) 656 ♀ day SW (34.9 y) 561 ♀ night SW (32.7 y)	Day SW: 07:00—19:00; night SW: 19:00—07:00; 2 days work, 2 days off	Age, smoking, drinking, educational level, duration of employment	Glycaemia ≥ 5.5 mmol/L	DW (1.9 [1.0—3.8]); day SW (2.5 [1.1—4.3]); night SW (1.7 [0.8—3.6]); all vs office

♀: females; ♂: males; γGTP: gamma-glutamyl transpeptidase; 2 × 8: two shifts with a break in the late afternoon and on weekends; 3 × 8: three shifts with a break on weekends; AST: aspartate transaminase; BMD: benchmark duration; BMDL: lower confidence limit of benchmark duration; BMI: body mass index; CI: confidence interval; DW: day workers; FPG: fasting plasma glucose; FU: follow-up; h: hours; HbA1c: glycosylated haemoglobin A1c; HOMA homeostasis model Assessment IGT: impaired glucose tolerance; JSI: job strain index; NS: not significant; OGTT: oral glucose tolerance test; OR: odds ratio; RPG: random plasma glucose; SW: shift workers; T2D: type 2 diabetes; TC: total cholesterol; WC: waist circumference; y: years.

often included in publications describing the impact of shift work on cardiovascular risk factors. Considering these parameters, most studies have not found any significant difference between shift work (or its duration) and day work [4,5,7,12,13,19,21,22,25,27,38,43], while in a minority of studies, shift work is related to a reduced mean glycaemia level [20,44].

In summary, the consequences of shift work on glucose metabolism are not yet well defined.

Shift work and overweight

Two approaches have been used in the literature to address the impact of working schedules on body weight (Table 4). The first concerns the comparison of risk across various threshold values of BMI. Taking into account overweight or obesity (defined as BMI ≥ 25 or $\geq 30\,kg/m^2$, respectively) or abdominal obesity (waist circumference), some studies have found a significantly positive link with the management of work schedules. In 2006, the prevalence of obesity in a cohort of 5038 shift workers and 1999 day workers was 9.6 and 8.5%, respectively ($P < 0.004$) [51]. Risk of obesity or central obesity has also been found to be higher in permanent night workers (12-hour shifts) [16], but not in rotating shift workers [8].

In two cross-sectional studies, Karlsson et al. have shown a significant 1.4-fold higher risk of obesity among male and female shift workers in an analysis of the VIP study [18], but these results were not confirmed using data from the WOLF study, taking into account a number of important confounding factors such as tobacco consumption and physical activity [19].

The second approach uses the same parameters as continuous variables, without threshold values. The results are somewhat at odds with the previous analyses. Higher waist circumference or BMI are related to shift working in some studies [21,22,42,44,52—56], but the opposite was found in some [4,5], while no association was found in others [20,57].

Finally, several studies have been looked at a relationship between BMI increase or weight gain and duration of exposure to a shift work pattern. Sometimes, a positive link has been found [12,57,58], but this has not been confirmed by other studies, after 1 year's exposure [14] or 1—10 years' exposure [27].

In summary, most of longitudinal studies indicate an impact of shift work on increased BMI. However, in view of the results of other studies, it is difficult to assert this link.

Shift work and metabolic syndrome

Metabolic syndrome has been variously defined [59,60], and the definition is, of course, crucial to unravelling the underlying pathophysiological processes (Table 5). A positive link between shift work and some cardiovascular risk factors has been described by two cross-sectional studies at the beginning of century [18,26]. A definition drawn up in 2001 by the NCEP-ATP III has been used in three cross-sectional studies of shift workers: the first concerned subjects working in 2×8 shifts [22] and the others 3×8 shifts [20,21]. Thus, in 2007 [22], the risk of metabolic syndrome was 1.5 times higher among shift workers, taking into account age and physical activity. The second study dealt with 152 hospital staff (doctors, nurses and auxiliaries), including 70 involved in shift work, and this showed no significant differences in the prevalence of metabolic syndrome using the NCEP-ATPIII definition [21]. However, with the use of a new IDF score, which takes into account almost the same parameters but with different weights, the prevalence of the metabolic syndrome was 37.1% among shift workers and 20.8% among day workers ($P < 0.05$) [21].

The third study provided some additional clarification of the risk of metabolic syndrome (NCEP-ATPIII), regardless of factors such as age, physical activity (during and outside work), food intake (quantitative, qualitative), stress constraints at work, consumption of alcohol and tobacco [20]. The risk was twice as high for 3×8 male shift workers compared to male day workers, but no significant risk was obtain using the IDF score [20]. These results are corroborated by three recent prospective studies [7,8,10]. Indeed, although the authors of these studies were unable to incorporate dietary factors, they showed a significantly independent link between shift work and the development of metabolic syndrome after a follow-up time between 4 and 8 years, taking into account to several confounding factors. One of them specifically examined the link between metabolic syndrome and shift work in women [7]. The authors confirmed that day—night and shift work rotation accelerated the progression of metabolic syndrome over 5 years [7]. One cross-sectional study of night shift workers who worked 12-hour shifts found no relation with metabolic syndrome, but the values used to define lipid thresholds seem to need more explanation [16].

In summary, recent studies add weight to the notion that, after taking into account several confounding factors, there is a link between shift work and the metabolic syndrome.

Shift work and physical inactivity

Physical inactivity is a modifiable risk factor of CVD. It is often included in studies as a relevant adjustment factor, measured by either quantitative or qualitative questionnaires. The physical activity considered here is often that performed during leisure time. However, it appears that physical activity performed during work time should also be included. Thus, the monitoring of 26,643 hypertensive Finnish people for 20 years revealed a reduced risk of dying from cardiovascular diseases that depended on physical activity at work, taking into account age, standard of education, behavioural habits, BMI, SBP, cholesterol level, and physical activity outside work (in leisure time and while travelling) [61].

Shift workers often seem to engage in greater physical activity during work [8,13,20,22,62], but when this is incorporated as a confounding factor, it does not alter the link between shift work and the other cardiovascular risk factors examined. Similarly, the level of leisure-time physical activity generally does not differ between day and shift workers [5,14,19], except in a few publications in which the sedentary are over-represented among shift workers [4,63], highlighted the difficulties of social organization encountered by shift workers.

Table 4 Relationship between shift work and being overweight.

Reference	Study type; years; recruitment	*n* gender (age [mean or range])	SW schedule	Adjustment parameters	Overweight parameters	Main results SW vs DW (OR [95% CI]) unless otherwise specified
Longitudinal studies						
Yamada et al., 2001 [52]	Nested-case; 1996—1999; plant employees, Japan	192 ♂ SW (31.1 y)	3 × 8 in 1996 change to 12-h shift in 1997	None	BMI	BMI increased 1996 to 1998 (22.9 to 23.2 kg/m2; $P < 0.01$) after change
Sakata et al., 2003 [4]	Prospective; 1991—2001; workers in Japanese steel company	3022 ♂ DW 2316 ♂ SW	3 × 8; irregular shift work: 5 days, 2 rest days, 5 evenings, 1 rest day, 5 nights, 2 rest days, clockwise rotation	None	BMI at baseline	BMI lower in SW ($P < 0.01$)
van Amelsvoort et al., 2004 [14]	1 y; nurses and incinerator plant workers	150 ♂ ♀ DW 227 ♂ ♀ SW	Counter-clockwise rotation (night, afternoon, morning) or clockwise rotation (morning, afternoon, night)	Educational level, gender, age, JSI variables, variable under study at baseline	Gain in weight, BMI, WHR over 1 y of shift work	Weight:—0.98 vs +0.43 kg ($P < 0.003$); BMI:—0.13 vs +0.13 kg/m2 ($P < 0.004$); WHR:—0.0093 vs—0.0052 (NS)
Oishi et al., 2005 [5]	Prospective; 1991—2001; workers in Japanese steel company	1560 ♂ DW (40.3 y) 1381 ♂ SW (40.5 y)	3 × 8; irregular shift work: 5 days, 2 rest days, 5 evenings, 1 rest day, 5 nights, 2 rest days, clockwise rotation	None	BMI at baseline	BMI lower in SW ($P < 0.005$)
Kivimäki et al., 2006 [51]	Prospective; 2000—2004; nurses in 21 Finnish hospitals	1999 ♀ DW (45.3 y) 5038 ♀ SW (41.1 y)	3 × 8; 2 × 8; permanent nights	None	BMI ≥ 30 kg/m^2	More obesity in SW (9.6% vs 8.5%; $P < 0.004$); obesity factors as predictors of change SW to DW (0.88 [0.56—1.38])

Table 4 (*Continued*)

Reference	Study type; years; recruitment	*n* gender (age [mean or range])	SW schedule	Adjustment parameters	Overweight parameters	Main results SW vs DW (OR [95% CI]) unless otherwise specified
Morikawa et al., 2007 [12]	Prospective; 1993—2003; Japanese factory workers	1993/2003: 712 ♂ DW/DW (36.4 y) 173 ♂ DW/SW (36.0 y) 210 ♂ SW/DW (36.2 y) 434 ♂ SW/SW (33.5y)	2 × 8; 3 × 8; counter-clockwise rotation; non-continuous (5 days, 5 nights, 5 evenings, 2 weekend rest intercalated); continuous (3—4 days, 3—4 nights, 3—4 evenings, 1 rest day intercalated)	Age, BMI, smoking, alcohol, physical activity	BMI increase over 10-y FU	DW/SW vs DW/DW (1.08 vs 0.62 kg/m2; $P < 0.05$); SW/SW vs DW/DW (0.89 vs 0.62 kg/m2; $P < 0.05$)
Biggi et al., 2008 [44]	Prospective; 1976—2007; Metropolitan area in Milan	157 ♂ DW (42.3 y) 331 ♂ SW (47.0 y)	Permanent nights	None	BMI	Significant influence of night work was observed in Higher BMI in SW
Suwazono et al., 2008 [54]	Prospective; 1991—2005; workers in Japanese steel company	4328 ♂ DW (36.6 y) 2926 ♂ SW (36.8 y)	3 × 8; irregular shift work: 5 days, 2 rest days, 5 evenings, 1 rest day, 5 nights, 2 rest days, clockwise rotation	Age, drinking, smoking, physical activity	Increase in BMI	≥ 5% (1.02 [1.01—1.04]); ≥ 7.5% (1.04 [1.03—1.06]); ≥ 10% (1.06 [1.04—1.08])
De Bacquer et al., 2009 [8]	Cohort study; 1995—2003; BELSTRESS, Belgium	1220 ♂ DW (44.7 y) 309 ♂ SW (43.1 y)	2 or 3 rotating shifts	Age, WC, DBP, HDL-C	WC ≥ 94 cm	(1.12 [0.88—1.42])
Cross-sectional studies						
Geliebter et al., 2000 [58]	Nurses, nurse's aides, security personnel, hospital US	36 ♀ day SW 49 ♀ late SW	Late shift = evening and night work	None	Weight change	Weight gain in late SW: +4.3 kg ($P < 0.02$)
Karlsson et al., 2001 [18]	VIP study, Sweden	9857 ♀ DW 9719 ♂ DW 4632 ♀ SW 3277 ♂ SW All aged 30, 40, 50 or 60 y	Any shift or weekend work	Age, socioeconomic factors	BMI ≥ 30 kg/m2	♀ SW (1.39 [1.25—1.55]); ♂ SW (1.44 [1.27—1.64])

Table 4 (*Continued*)

Reference	Study type; years; recruitment	*n* gender (age [mean or range])	SW schedule	Adjustment parameters	Overweight parameters	Main results SW vs DW (OR [95% CI]) unless otherwise specified
Parkes 2002 [57]	Offshore personnel on 17 oil and gas installations, UK	787 ♂ day SW 787♂ day—night SW	Day SW: 12-h shifts; 14 days, 14 rest days; day-night SW: alternating periods of day and night shifts: 7 nights, 7 days, 14 rest days	None	BMI	BMI and shift pattern NS; age predicted BMI for day SW; exposure predicted BMI for day—night SW
Di Lorenzo et al., 2003 [42]	Chemical industry, Italy	134 ♂ DW (48.9 y) 185 ♂ SW (48.7 y)	3 × 8 counter-clockwise; 2 nights, 2 afternoons, 2 mornings, 3 rest days	Class of working age, age, class of working age × age, insulin	BMI, WHR	Elevated BMI in SW ($P < 0.01$); WHR NS
Karlsson et al., 2003 [19]	WOLF study, Sweden	665 ♂ DW (44.3 y) 659 ♂ SW (44.2 y)	3 rotating shifts	Age, socioeconomic group, current smoking, physical activity, low social support, JSI	Obesity (BMI ≥ 30 kg/m2); WHR > 0.9	Prevalence of obesity NS; WHR (1.19 [0.92—1.56])
Ishizakiet al., 2004 [53]	1997; metal products factory workers, Japan	3658 ♂ DW 585 ♂ SW	3 × 8	Age, matrimony, sedentary job, exercise, smoking, worksite support, job control	BMI and WHR	BMI: β = 0.506; $P = 0.001$; WHR: β = 0.011; $P = 0.001$
Ha & Park 2005 [27]	Nurses and blue-collar workers	134 ♂ SW (29.1 y) 226 ♀ SW (28.5 y)	3 × 8; irregular rotating shifts including mornings, evenings, nights	Age, educational level, job type, smoking physical activity	BMI	NS relation between SW duration (1—10 y) and BMI in ♀ and ♂
Sookoian et al., 2007 [22]	2005; factory workers in Buenos Aires	877 ♂ DW (34 y) 474 ♂ SW (36 y)	Clockwise rotation; 2 × 8; 4 days, 4 nights, 3 rest days, 2 days, 3 rest days, 4 days	None	BMI, WC, WHR	SW: elevated BMI ($P < 0.02$) and WHR ($P < 0.001$); WC NS

Table 4 (*Continued*)

Reference	Study type; years; recruitment	*n* gender (age [mean or range])	SW schedule	Adjustment parameters	Overweight parameters	Main results SW vs DW (OR [95% CI]) unless otherwise specified
Copertaro et al., 2008 [21]	2005; hospital staff, Italy	77 ♂ ♀ healthcare DW (48.6 y) 70 ♂ ♀ healthcare SW (47.3 y) Subgroup: 41 ♀ DW nurses (45.8 y) 32 ♀ SW nurses (43.5 y)	SW healthcare: 1—6 nights/month; nurses: 3 × 8: 1 day, 1 evening, 1 night, 2 rest days	None	WC	Overall: 95.8 vs 91.5 cm ($P < 0.01$); nurses: 94.8 vs 91.5 cm ($P < 0.01$)
Esquirol et al., 2009 [20]	Industrial plant, France	98 ♂ DW (48.8 y) 100 ♂ SW (46.5 y)	3 × 8; clockwise rotation; 1—2 mornings, 1—2 afternoons, 1—2 nights, 3—4 rest days	None	BMI, WHR	Both NS
Di Milia & Mummery 2009 [56]	Coal industry and regional university, Australia	201 ♂ ♀ SW (41.6 y) 145 ♂ ♀ DW (41.6 y)	2 days, 1 rest day, 2 nights, 4 days off	None	BMI	28.10 vs 26.19 kg/m2 ($P < 0.001$); long work hours implicated
Burgueño et al., 2010 [55]	Factory in Buenos Aires	255 ♂ DW 184 ♂ SW	Clockwise rotation; 2 × 8; alternating day/night, 12-h shifts; 4 days, 4 nights, 3 rest days, 2 days, 3 rest days, 4 days	None	BMI, WC, WHR	BMI: 27.0 vs 26.2 kg/m2 ($P = 0.024$); WHR 0.94 vs 0.92 ($P = 0.00001$); WC: 93.4 vs 91.4 cm ($P = 0.018$)
Chen et al., 2010 [16]	Manufacturing factory, Taiwan	401 ♀ office workers (33.5 y) 220 ♀ DW (33.6 y) 656 ♀ day SW (34.9 y) 561 ♀ night SW (32.7 y)	Day SW: 07:00—19:00; night SW: 19:00—07:00; 2 days work, 2 days off	Age, smoking, drinking, educational level, duration of employment	BMI ≥ 25 kg/m2, WC ≥ 80 cm	High BMI (vs office): DW (1.3 [0.8—2.2]); day SW (1.5 [0.9—2.4]); night SW (2.7 [1.6—4.5]); high WC: DW (1.4 [0.8—2.4]); day SW (1.4 [0.8—2.5]); night SW (2.9 [1.7—5.1])

♀: females; ♂: males; 2 × 8: two shifts with a break in the late afternoon and on weekends; 3 × 8: three shifts with a break on weekends; BMI: body mass index; CI: confidence interval; DW: day workers; FU: follow-up; h: hours; JSI: job strain index; NS: not significant; OR: odds ratio; SW: shift workers; WC: waist circumference; WHR: waist-to-hip ratio; y: years.

Table 5 Relationship between shift work and metabolic factors.

Reference	Study type; years; recruitment	*n* gender (age [mean or range])	SW schedule	Adjustment parameters	Metabolic syndrome parameters	Main results SW vs DW (OR [95% CI]) unless otherwise specified
Longitudinal studies						
De Bacquer et al., 2009 [8]	Cohort study; 1995—2003; BELSTRESS, Belgium	1220 ♂ DW (44.7 y) 309 ♂ SW (43.1 y)	2 or 3 rotating shifts	Age, WC, DBP, HDL-C	IDF score	(1.46 [1.04—2.07])
Lin et al., 2009 [7]	Retrospective; 2002—2007; employees of electronic manufacturing company, Taiwan	125 ♀ DW (31.1 y) 160 ♀ past SW (34.7 y) 102 ♀ current SW (31.9 y)	2 × 8; 6 days, 3 rest days, 6 nights, 3 rest days; 12-h shifts	Smoking, age, insulin status, metabolic syndrome, job, physical activity, snack before sleeping	MetS if ≥ 3 of: WC > 90 (♂) or > 80 (♀) cm; BP ≥ 130/85 mmHg or treatment; NCEP-ATPIII; glycaemia ≥ 100 mg/dL; HDL-C < 40 (♂) or < 50 (♀) mg/dL; TG ≥ 150 mg/dL	Development of MetS in 5 y: DW 5.6%; past SW 6.9%; current SW 15.7% ($P < 0.05$); risk of MetS: past SW (0.7 [0.2—2.4]); current SW (3.5 [1.3—9.0])
Pietroiusti et al., 2010 [10]	Prospective cohort; 2003—2007; nurses in 3 hospitals, Italy	336 ♀ ♂ DW (37.9 y) 402 ♀ ♂ SW (38.9 y)	Night or rotating shifts with ≥ 4 nights/month	Age, gender, physical activity, alcohol, tobacco, family history	MetS (NCEP-ATPIII)	HR 5.10 (95% CI 2.15—12.11)
Cross-sectional studies						
Karlsson et al., 2001 [18]	VIP study, Sweden	9857 ♀ DW 9719 ♂ DW 4632 ♀ SW 3277 ♂ SW All aged 30, 40, 50 or 60 y	Any shift or weekend work	Age	Number of CV risk factors: BMI ≥ 30 kg/m2; SBP ≥ 160 mmHg, DBP ≥ 90 mmHg or treatment; TG > 1.7 mmol/L	ORs for: $N = 1$: ♀ 1.06*; ♂ 0.99 (NS); $N = 2$: ♀ 1.20*; ♂ 1.30*; $N = 3$: ♀ 1.71*; ♂ 1.63*
Nagaya et al., 2002 [26]	Gifu Prefectural Center; Health-check programme, Japan	2824 ♂ DW (47.1 y) 826 ♂ SW (45.6 y)	Any mandatory night work (permanent night workers excluded)	BMI, job, drinking, smoking, exercise	Number of CV risk factors: SBP ≥ 140 mmHg, DBP ≥ 90 mmHg or treatment; TG ≥ 1.7 mmol/L or treatment; glycaemia ≥ 7 mmol/L or treatment; HDL-C < 1.04 mmol/L Analysis stratified by age	40—49 y: $N \geq 1$ (1.45 [1.12—1.88]); $N \geq 2$ (1.48 [1.08—2.02]); $N \geq 3$ (1.42 [0.67—2.87]); 50—59 y: $N \geq 1$ (0.73 [0.55—0.98]); $N \geq 2$ (0.59 [0.40—0.87]); $N \geq 3$ (0.75 [0.32—1.57])

Table 5 (*Continued*)

Reference	Study type; years; recruitment	*n* gender (age [mean or range])	SW schedule	Adjustment parameters	Metabolic syndrome parameters	Main results SW vs DW (OR [95% CI]) unless otherwise specified
Sookoian et al., 2007 [22]	2005; factory workers in Buenos Aires	877 ♂ DW (34 y) 474 ♂ SW (36 y)	Clockwise rotation; 2 × 8; 4 days, 4 nights, 3 rest days, 2 days, 3 rest days, 4 days	Age, physical activity	NCEP-ATP III score	NCEP-ATP III score (1.51 [1.01—2.25])
Copertaro et al., 2008 [21]	2005; hospital staff, Italy	77 ♂ ♀ healthcare DW (48.6 y) 70 ♂ ♀ healthcare SW (47.3 y) Subgroup: 41 ♀ DW nurses (45.8 y) 32 ♀ SW nurses (43.5 y)	SW healthcare 1—6 nights/month; nurses: 3 × 8; 1 day, 1 evening, 1 night, 2 rest days	None	NCEP-ATPIII and IDF scores	NCEP-ATPIII NS; IDF score: overall 37.1% vs 20.8% ($P < 0.05$); in nurses: 40.6% vs 17.1% ($P < 0.05$)
Esquirol et al., 2009 [20]	Industrial plant, France	98 ♂ DW (48.8 y) 100 ♂ SW (46.5 y)	3 × 8; clockwise rotation; 1—2 mornings, 1—2 afternoons, 1—2 nights, 3—4 rest days	Age, alcohol, smoking, JSI, physical activity, dietary parameters	NCEP-ATP III and IDF scores	NCEP-ATP III (2.33 [1.04—5.23]); IDF (0.95 [0.51—1.78])
Chen et al., 2010 [16]	Manufacturing factory, Taiwan	401 ♀ office workers (33.5 y) 220 ♀ DW (33.6 y) 656 ♀ day SW (34.9 y) 561 ♀ night SW (32.7 y)	Day SW: 07:00—19:00; night SW: 19:00—07:00; 2 days work, 2 days off	Age, smoking, drinking, educational level, duration of employment	NCEP-ATP III score	DW (1.8 [0.7—4.2]); day SW (2.1 [0.9—4.8]); night SW (1.8 [0.7—4.3]); all vs office

♀: females; ♂: males; 2 × 8: two shifts with a break in the late afternoon and on weekends; 3 × 8: three shifts with a break on weekends; BMI: body mass index; BP: blood pressure; CI: confidence interval; CV: cardiovascular; DBP: diastolic blood pressure; DW: day workers; h: hours; HDL-C: high-density lipoprotein cholesterol; HR; hazard ratio; IDF: International Diabetes Federation; JSI: job strain index; MetS: metabolic syndrome; NCEP-ATPIII: National Cholesterol Education Program Adult Treatment Panel III; NS: not significant; OR: odds ratio; SBP: systolic blood pressure; SW: shift workers; TG: triglycerides; WC: waist circumference; y: years.
$P < 0.0001$.

Shift work and tobacco consumption

Most studies dealing with the effects of shift work on CVD risks include tobacco consumption as a confounding factor. Active tobacco consumption is often higher among shift workers [1,9,14,64,65]. Also, the risk of starting to smoke in one study was 1.5 times higher in the 2 years after starting shift work compared to day workers [66]. Smoking status varies according to the different patterns of shift work: being a smoker is significantly related to being permanently assigned to an evening or night shift, while being an ex-smoker is related to the 2×8 or 3×8 work patterns [13]. We should not forget that an increase in the weekly number of working hours significantly reduces the possibility of quitting smoking [67], and any deterioration in the social environment within the company could exacerbate tobacco consumption [68].

Shift work and other cardiovascular risk factors

The implications of the inflammatory process and thrombogenesis are currently considered in explanatory factors of cardiovascular events in patients with a metabolic syndrome [69]. Few studies have reported the influence of shift work on markers of inflammation. However, one study showed a stimulation effect of shift work (2×8) on leukocyte counts with or without metabolic syndrome, regardless of age, education, tobacco consumption and physical activity [22]. In the same population, endothelial dysfunction was also investigated, and it was found that the levels of resistin were significantly higher in shift workers [55].

Homocysteine and CRP have been studied in a population of 207 day workers and 154 shift workers [43]. Plasma levels of homocysteine were higher in shift workers > 40 years old with sleep disturbances (mean 19.5 μmol/L; one third had pathological levels [> 15 μmol/L]) compared to younger shift workers without sleep disturbances, or to daytime workers [43]. This agreed with earlier results from Martin et al. [70]. In a more recent study, a higher level of homocysteine was found among shift workers compared to day workers (11.6 ± 3.4 vs 10.6 ± 2.7 μmol/L; $P < 0.05$) [21]. The authors discussed two possible hypotheses: the interaction between homocysteine and the consumption of tobacco and coffee (known to increase homocysteine) and the relationship between homocysteine and insomnia (disturbances of the circadian rhythm), occupational stress and food habits [21].

Among the few studies that have measured and taken CRP or fibrinogen into account, most have shown no link with shift work [19,43,63], except for one study, which found elevated levels of CRP for some types of shift work in men [37].

Another approach, assessing brachial ankle pulse wave velocity measurements, has shown that the arteriosclerosis risk could be raised in shift workers [71]. Furthermore, a study conducted in a young population (24—39 years' old), 515 male day workers and 712 male shift workers, showed a higher risk of presenting preclinical atherosclerosis (ultrasound technology) among the latter group after adjusting for psychosocial, behavioural, anthropometric and biological parameters [9]. The risk of having carotid atheromatous plaques and tunica media thickening was twice as high in shift workers [9]. The changes in intima media thickness seem to occur relatively early after exposure to shift work (1—5 years) [25].

Discussion

The past 10 years have been enriched by longitudinal studies with large numbers of subjects included, and cross-sectional studies that have taken into account many confounding and explanatory factors.

Epidemiological difficulties

The difficulties in comparing these studies result from the use of several definitions of shift work, which may comprise multiple operating patterns (3×8, 2×8, fixed night schedules) or different rotating systems, with various consequences on health. This heterogeneity among shift patterns makes it difficult to generalize the results. Therefore, we must consider shift work patterns as entities with consequences on specific risk factors. Listed under the general term 'shift work', different ways of managing work schedules can influence the results obtained on the prevalence of CVD. These commentaries were underlined by several teams whose listed some questions to resolve in future research, such as considering the consequences on CVD of each type of shift work, the direction of rotation, rhythms of shift, and exposure duration [72,73].

The 'healthy worker' effect is one of the theories put forward to explain the absence of a link between shift work and CVD, as the impact of shift work is underestimated among such people. Indeed, maintaining individuals selected for their state of health in this type of job position could distort the results of studies, suggesting likely resurgence of CVD among ex-shift workers [74]. However, although this hypothesis is often mentioned, few studies have directly analysed this selection process. A prospective study conducted during 2000—2004 in 5038 nurses working in shifts (3×8, 2×8, fixed night schedule) and 1999 nurses working during the day did not reveal any difference in the prevalence of CVD (myocardial infarction, angina, hypertension) between those who had left their jobs and those who continued [38]. Neither CVD nor cardiovascular risk factors (e.g. hypertension, high cholesterol, obesity) are decisive for discontinuing shift work for daytime work. However, having diabetes and the cumulative number of cardiovascular risk factors were associated with a higher risk of leaving shift work for day work (OR 1.83, 95% CI [1.01—3.32] and OR 2.21, 95% CI [1.12—4.39], respectively) [38]. Furthermore, the risk of disability retirement due to CVD is not significantly different for various types of working patterns, except for women who transferred from day work to shift work [3]. Although the available studies have only shown that some cardiovascular risk factors are a reason to change from shift to day work, other factors could influence this decision, e.g. maladaptive sleep or disturbed rhythms of social or family life. Thus, these factors could interfere and explain the healthy worker effect described in some age classes by some authors [18,19].

Another factor is a possible selection effect when people are recruited: only those free of cardiovascular disease will be assigned to shift work. The opportunity to specifically study this potential distortion appeared in a recent longitudinal study including 2870 newly hired Danish students completing their training as assistant health counsellors [13]. Hypertension and diabetes were not found to affect the assignment of staff to any particular pattern of work [13]. Thus, the hypothesis of the implication of cardiovascular risk factors as a criterion for recruiting staff is often mentioned, but not actually demonstrated.

Pathophysiological hypotheses

Various pathophysiological hypotheses have been formulated to try to explain the influence of shift work on cardiovascular diseases. These are based on one of the first explanatory models, transcribed by Taylor and Francis in 1980 [75]. These hypotheses have recently been discussed and supplemented by Puttonen et al. [63] and Mosendane et al. [76]. The most currently quoted assumptions include: desynchronised circadian rhythms, sleep disturbances, variety of food intakes, psychosocial stress and social inequalities. Studies on shift work and the metabolic syndrome, taking into account many potentially explanatory factors (e.g. behaviour and stress), suggest that shift work could be an independent confounding factor. This strengthens the argument for desynchronization of circadian rhythms. Regarding cardiovascular risks, factors such as food habits, physical inactivity and stress could play a potentiating role. Therefore, incipient atherosclerosis and increases in shift workers could potentially result in biological disturbances and/or alterations of gene expression. Genetic factors may also be involved in the mechanisms that link the disturbances of circadian rhythms and the cardiovascular system [77]. The diurnal variations of the cardiovascular system under environmental stimuli are the result of a complex process involving extracellular (neurohumoural factors) and intracellular (circadian-regulated genes) factors. These could consist of a series of transcriptional modulators that would enable the cell to identify the parts of the day and to anticipate certain stimuli. The expression of some genes in the heart oscillates with circadian rhythmicity. In pathological situations, the expression of genes (CLOCK) in the heart and vessels would be affected, disrupting the heart's ability to adapt to external stimuli and possibly accelerating tissue damage. The alterations in circadian rhythm noted in the shift worker could therefore potentially alter gene expression and impact on cardiovascular disease. To our knowledge, only one study has looked into this field of research [78], suggesting a potential interaction of serotonin transporters and CLOCK gene variation on the genetic susceptibility to develop metabolic syndrome in rotating shift workers.

In addition, sleep disorders (notably short sleep) have often been suggested to explain the impact of shift work on lipids, BMI and diabetes, supporting the need to be careful about sleep patterns among shift workers [79—83]. This disruption of the circadian system might explain some of the hormonal abnormalities found in several studies, of cortisol or ACTH [84—86] or melatonin [87].

Among the explanatory factors for lipid disturbances, nutritional intake is most often cited. However, quantitative or qualitative nutritional intake does not seem to a discriminating factor in shift work [88—90]. By contrast, the chronological distribution is different [20,91—93]. Based on a review of publications dealing with the impact of food habits on shift work, a guidebook of dietary advice for shift workers has recently been published [94].

Some authors have suggested that the effect of shift work on mortality rate after myocardial infarction or several CVD risk factors could be mitigated by social class [38,66]. Occupational stress has been suggested as a potential explanatory factor of the link between CVD and shift work. A literature review by Härmä [95] on stress and working hours concluded that, because of the tasks they are assigned, shift workers have a lower level of latitude control and a higher level of psychological constraints (which contributes to a high level of occupational stress) or an imbalance in the effort—reward ratio in the working environment. These parameters could play a mediating role in the occurrence of CVD. Puttonen et al. have discussed all the explanatory mechanisms that are probably involved in the relationships between stress, shift work and CVD [63]. Stress is a strong determinant that should be integrated into futures studies.

Limitations

We only included articles written in English, thus potentially omitting interesting articles published in other languages. This choice was guided by the difficulties of understanding other languages, thus increasing the risk of misinterpretations; and the fact that the references included are in an international language used by most readers. The choice of the search strings could also constitute a limitation of this review.

Conclusions

Studies published in the past 10 years suggest an impact of shift work on some cardiovascular risk factors. Moreover, several intricate pathophysiological hypotheses support the effect of shift work on cardiovascular disease: disruption of circadian rhythms, sleep disturbances, behaviour factors (diet, alcohol and tobacco) and occupational stress. Thus, our advice for clinical physicians would be:

- during the patient's consultation, it might be useful to include questions about organization of work schedules and their tolerance of such schedules (i.e. tolerance of sleep disturbance, dietary habits, etc.);
- as shift work could play a role in increasing arterial BP, BP should be measured regularly. It is also important to take into account the period of work before the measurement of BP, and check the result after a day of rest;
- shift schedule could promote metabolic syndrome, particularly by increasing hypertriglyceridaemia. Regular biological screening and anthropometric measurements could reasonably be proposed in shift workers in order to detect lipid or carbohydrate metabolism abnormalities or weight gain early;

- some advice could be given to shift workers about cardiovascular risk prevention (e.g. diet, physical activity, tobacco and alcohol consumption);
- a close collaboration between occupational health practitioners and clinical physicians should allow better management of cardiovascular risk factors and CVD in shift workers. In some patients, particularly those resistant to drugs, a change to day work could be proposed.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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