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## Metabolic disturbances in male workers with rotating three-shift work. Results of the WOLF study

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**Abstract Objectives:** The aim of the present study was to investigate the relationship between important metabolic risk factors for coronary heart disease (CHD) and type 2 diabetes in shift workers and day workers. **Methods:** Cross-sectional data from a sub-population in the WOLF study consisting of 665 day workers and 659 three-shift workers in two plants were analysed. **Results:** A higher proportion of shift workers than day workers had high triglyceride levels ( $\geq 1.7$  mmol/l), low levels of HDL-cholesterol ( $< 0.9$  mmol/l) and abdominal obesity (waist/hip ratio  $> 0.9$ ). The risk of low HDL-cholesterol was doubled in shift workers, (odds ratio (OR): 2.02, 95% confidence interval (95% CI): 1.24–3.28) after being adjusted for age, socio-economic factors, physical activity, current smoking, social support and job strain. High levels of triglycerides were also significantly associated with shift work (OR: 1.40, 95% CI: 1.08–1.83). The OR for abdominal obesity was 1.19, (95% CI: 0.92–1.56). The prevalence of hyperglycaemia (serum glucose  $\geq 7.0$  mmol/l) was similar in day and shift workers. No significant interaction was seen between shift work and abdominal obesity with regard to the associations with triglycerides and HDL-cholesterol. **Conclusions:** We found a significant association between shift work and lipid disturbances (i.e. low HDL-cholesterol and high triglyceride levels). We did not find any association with hyperglycaemia.

**Keywords** Shift work · Metabolic factors · Abdominal obesity · job strain

### Introduction

There is considerable evidence of an association between shift work and coronary heart disease (CHD) (Bøggild and Knutsson 1999). Metabolic disturbances could mediate a pathogenetic effect induced by a mismatch of circadian rhythm, behavioural changes or social stress (Knutsson and Bøggild 2000).

In a study on railway workers an increase in serum concentrations of cholesterol, glucose, uric acid and potassium was demonstrated (Theorell and Åkerstedt 1976). A number of epidemiological studies have shown that shift workers have higher serum concentrations of triglycerides, but the results have been inconsistent (De Backer et al. 1987; Knutsson et al. 1988, 1990; Lasfargues et al. 1996; Nakamura et al. 1997; Orth-Gomér 1983; Romon et al. 1992; Thelle et al. 1976). In a recent study metabolic risk factors such as high triglyceride levels, low HDL-cholesterol levels and obesity measured by body mass index (BMI) was observed to cluster among shift workers in both genders, particularly in women (Karlsson et al. 2001). Both low HDL-cholesterol and high serum triglyceride levels are risk factors for CHD, and therefore might account for an increased risk of cardiovascular disease seen in shift workers. The aim of the present study was to investigate the relationship between shift work and important metabolic risk factors for CHD and type-2 diabetes.

### Methods

#### Study population

The work, lipids and fibrinogen (WOLF) study, was intended to investigate the relationship between occupational conditions, including psychosocial and cardiovascular risk factors. The base-

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**Table 1** Shift schedules in the two paper and pulp manufacturing plants. Working hours: *M* morning work (6 a.m.–2 p.m.), *M12* morning work (6 a.m.–6 p.m.), *A* afternoon work (2 p.m.–10 p.m.), *N* night work (10 p.m.–6 a.m.), *N12* night work (6 p.m.–6 a.m.), *M* morning shifts when blood samples were taken, – not at work

Schedule	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
Plant A							
Week 1	–	–	–	–	N	N12	N12
Week 2	N	N	N	N	–	–	–
Week 3	A	A	A	A	A	–	–
Week 4	<u>M</u>	<u>M</u>	<u>M</u>	<u>M</u>	M	M12	M12
Week 5	–	–	–	–	–	–	–
Week 6	–	–	–	–	–	–	–
Plant B							
Week 1	A	A	A	N	N	N12	N12
Week 2	–	–	–	–	–	–	–
Week 3	N	N	N	A	A	–	–
Week 4	<u>M</u>	<u>M</u>	<u>M</u>	<u>M</u>	M	M12	M12
Week 5	–	–	–	–	–	–	–
Week 6	–	–	–	–	–	–	–

line examination was carried out during 1992 to 1998 in the Stockholm area and in two counties in the north of Sweden (Alfredsson et al. 2002).

For the purpose of this article, a sub population of individuals employed in two paper and pulp manufacturing plants in the north of Sweden, with complete laboratory data, were selected. Grinding, barking, boiling, bleaching and paper manufacturing were typical job types among shift workers. Typical jobs among day workers were electrical and mechanical maintenance, laboratory work, and office work.

The data collection from these two plants started in September 1996 and ended in December 1997. All permanently employed individuals ( $n=1,695$ ) were invited to participate. Of these, 1,590 men and women took part in the study, with a total rate of participation of 94%.

The exposure for day or shift work was obtained from the WOLF questionnaire. Only 24 women worked shifts, therefore all women ( $n=190$ , both day and shift workers) were excluded and the analyses were restricted to men.

Also excluded were 29 men who reported that they had diabetes, and nine individuals who had not answered the specific question about diabetes disease. Thirty-eight men who worked two shifts, roster work, or other types of work schedules, were excluded.

After these exclusions 665 day workers and 659 three-shift workers remained. Of the shift workers, 149 worked at plant A and 510 at plant B. The three-shift schedules were quite similar in the two plants (Table 1).

#### Data collection

The investigation was performed in close co-operation with the occupational health units of the participating plants. Specially trained nurses from the occupational health service carried out the medical examination, which included blood sampling and measurement of height, weight, waist/hip ratio and blood pressure. The study participants answered a questionnaire that covered a wide range of factors, including working conditions, physical activity, education and health. The medium time taken to fill in the questionnaire was 45 min. Afterwards, the subjects were asked to return for a 45-min counselling session, during which the results of the health examination were discussed. The participants were often offered pertinent advice, sometimes scheduled for a follow-up visit, and occasionally referred to the occupational health doctor or to a general practitioner.

Body weight was measured with the participant wearing light indoor clothing, and was recorded to the nearest kilogramme. Height was measured to the nearest centimetre, with the subject wearing no shoes. Blood pressure was measured in the participant's right arm while he was in the supine position after a 5-min rest. Two measurements were taken within 1 min, and the mean of the two measurements was used as the recorded blood pressure.

Subjects were asked to fast for 9 h before blood samples were taken and clinical examination was carried out. The timing of blood sampling was adjusted to interfere as little as possible with the production process and was carried out on weekday mornings from Monday to Thursday between 6 and 6.45 a.m. in shift workers and between 7.30 to 9.30 a.m. in day workers. All shift workers started the morning shift at 6 a.m. after a weekend off duty, when they underwent the blood sampling procedure (Table 1).

Triglycerides, cholesterol, glucose, HDL-cholesterol and gamma-glutamyltransferase were determined enzymatically. HDL-cholesterol was measured after precipitation with phosphotungstic acid and magnesium chloride. Serum glucose was measured with an enzymatic calorimetric test.

An immunological test based on electro-chemiluminescence techniques was used for the measurement of serum insulin.

HbA1c and lipoprotein were determined by an immuno-turbidimetric method, and fibrinogen was measured by a spectrophotometric test.

All blood analyses were carried out in the same laboratory (CALAB Medical Laboratories AB, Stockholm, Sweden). The laboratory is accredited by the Swedish Board for Accreditation and Conforming Assessment (SWEDAC).

Hypertension was defined as a systolic blood pressure  $\geq 160$  mmHg or a diastolic blood pressure  $\geq 90$  mmHg, or as the patient's being currently in receipt of medical treatment for hypertension.

Body mass index (BMI) was calculated as weight (kg) divided by height (m) squared. Those with BMI  $\geq 30$  were classified as obese.

Abdominal obesity was defined as waist/hip ratio  $> 0.9$ .

The level of triglycerides was defined as being raised when concentrations were  $\geq 1.7$  mmol/l, and the level of HDL-cholesterol as being low when concentrations were  $< 0.9$  mmol/l. Ln-transformation was used for the calculation of linear regression models.

Hyperglycaemia was defined as a fasting glucose level  $\geq 7.0$  mmol/l in serum.

All cut-off values of the analyses of BMI, waist/hip ratio (abdominal obesity), HDL-cholesterol, triglycerides, hyperglycaemia and hypertension are in accordance with the metabolic syndrome suggested by the WHO consultant group (Alberti and Zimmet 1998).

Insulin was measured in milli-units per litre and dichotomised. High insulin values were defined as fasting values  $> 13$  mU/l. HbA1c values  $> 5.3\%$  were considered as being abnormal.

Values of fibrinogen  $\geq 3.7$  g/l were considered as being unfavourable, and levels of lipoprotein(a)  $> 0.30$  g/l were defined as being raised. A gamma-glutamyltransferase level  $> 1.30$   $\mu$ kat was defined as being abnormal.

Length of education was used as a proxy for socio-economic situation. Low education was defined as  $\leq 9$  years (primary school), middle as 10–12 years (high school) and high education as  $> 12$  years of schooling (university studies).

Leisure-time physical activity was assessed by the question "How often do you exercise?" and the respondents were asked to include if they were physically active when getting to and from work, for example by walking or cycling. The variable was categorised according to the response alternatives: never, seldom, sometimes, or on a regular basis. Smoking status was based on the question "Are you a current smoker?" and dichotomised into the groups "yes" or "no". Snuff use was based on the question "Are you a current snuff user?" and dichotomised into the groups "yes" or "no".

Job strain was measured by a Swedish modification of a questionnaire originally developed by Robert Karasek (Theorell et al. 1998). To measure psychological demands we used five items each with four response alternatives (scoring 1–4). By adding up the sums of these scores, ranging from the minimum score of 5 to the maximum score of 20, we formed an index of psychological demands. An index of decision latitude was formed in a similar way, based on six items. Both psychological demands and decision latitude were split into two groups around the median value. The group that reported a combination of high psychological demands and low decision latitude constituted the job-strain group.

Social support in the work place was measured by the question 'What is your working environment like?' The following response options were presented:

- There is a calm and pleasant atmosphere at my work place.
- There is a good spirit at my work place.
- My workmates support me.
- My workmates accept that I can have a bad day.
- I get on well with my superiors.
- I get on well with my workmates.
- I find it easy to discuss matters freely with my workmates.

Each response alternative was: agree completely, generally agree, generally disagree, and disagree completely. Each alternative was given a specific value, and on the basis of these questions an index was formed. In the analysis the subjects were split into two groups around the median value and defined as having either low or high social support.

The Research Ethics Committee of the Karolinska Institute approved the study.

#### Statistical methods

We used Pearson's chi-square test and Student's *t*-test to compare proportions and continuous variables, respectively. Multiple logistic regression was used in multivariate analyses, and linear regression for analyses of continuous variables. All data analysis was carried out with software SPSS, version 10.0.

## Results

Mean age was similar in shift and day workers (44.3 vs 44.2), but the age distribution differed somewhat (Table 2). The median age for day workers was 46 years and for shift workers was 44 years. Higher education was more common among day workers. Tobacco use and physical activity were similarly distributed between the groups. Job strain was more prevalent among shift workers.

Lipoprotein(a), which is genetically influenced, and GGT and fibrinogen did not differ between shift and day workers.

**Table 2** Demographic, behavioural and basic biochemical characteristics of the study population

Characteristic	Shift		Day		<i>P</i>
	(%)	( <i>n</i> )	(%)	( <i>n</i> )	
Age groups (years)					
20–30	9.0	59	15.6	104	
31–40	30.0	198	18.2	121	
41–50	32.8	216	35.6	237	
51–60	25.8	170	28.6	190	
> 60	2.4	16	2.0	13	< 0.001
Total	100	659	100	665	
Plant A	47.5	149	52.5	165	
Plant B	50.5	510	49.5	500	0.35
Education level					
< 10 years	31.3	206	25.3	168	
10–12 years	65.1	429	62.9	418	
> 12 years	3.6	24	11.9	79	< 0.001
Leisure-time physical activity					
Never	3.7	24	2.9	19	
Seldom	25.3	166	25.9	165	
Sometimes	46.0	302	42.6	282	
Regularly	25.1	165	29.6	196	0.27
Smoking and snuff-taking status					
Current smoker	14.4	95	16.0	106	0.43
Current snuff taker	30.7	201	28.6	189	0.41
Lipoprotein(a) <sup>a</sup>	22.8	150	23.5	156	0.76
Fibrinogen <sup>b</sup>	7.4	48	6.8	45	0.67
Gamma-glutamyltransferase <sup>c</sup>	5.3	35	5.0	33	0.77
Job strain	32.4	209	11.5	75	< 0.001
Low social support	57.2	369	53.0	344	0.13

<sup>a</sup>Lipoprotein > 0.30 g/l

<sup>b</sup>Fibrinogen > = 3.7 g/l

<sup>c</sup>Gamma-glutamyltransferase > 1.30 µkat/l

**Table 3** Prevalences of metabolic risk factors among male day and shiftworkers in the WOLF study

Characteristic	Day worker		Shift worker		<i>P</i>
	(%)	( <i>n</i> )	(%)	( <i>n</i> )	
Triglycerides ≥ 1.7 mmol/l	25.1	167	32.5	214	0.003
HDL-cholesterol < 0.9 mmol/l	3.9	26	7.6	50	0.004
Hypertension <sup>a</sup>	21.1	140	16.9	111	0.052
BMI ≥ 30	14.3	95	15.0	99	0.705
Waist/hip ratio > 0.9	62.9	416	69.5	457	0.012
Hyperglycaemia <sup>b</sup>	2.0	13	2.0	13	0.981
HbA1c > 5.3%	10.5	70	8.1	53	0.124
Fasting insulin > 13 mU/l	10.3	67	9.1	58	0.489
Total cholesterol > 6.4 mmol/l	28.1	187	19.0	125	0.000

<sup>a</sup>Systolic BP > 160 mmHg, diastolic BP ≥ 90 mmHg or subject using anti-hypertensive drugs

<sup>b</sup>Fasting serum glucose ≥ 7.0 mmol/l

A higher proportion of shift workers had hypertriglyceridaemia, low HDL-cholesterol levels and increased waist/hip ratio (Table 3). The mean value of serum insulin in day workers was higher than in shift workers (8.2 vs 7.5 mmol/l, *P* < 0.05). The proportion of fasting glucose ≥ 7.0 mmol/l, was 2%, identical in both day and shift workers.

The prevalence of hypertension was higher among day workers, although not statistically significant.

**Table 4** ORs (obtained through multiple logistic regression) of low HDL-cholesterol levels, obesity, and high triglyceride levels associated with shiftwork. Results of multiple logistic regression

Parameter	Low HDL-cholesterol levels		High triglyceride levels		Abdominal obesity	
	OR	95% CI	OR	95% CI	OR	95% CI
Shiftwork <sup>a</sup>	2.02	1.24–3.28	1.43	1.13–1.82	1.34	1.07–1.69
Shiftwork <sup>b</sup>	1.85	1.13–3.07	1.41	1.11–1.80	1.34	1.05–1.70
Shiftwork <sup>c</sup>	1.81	1.10–2.99	1.39	1.09–1.78	1.30	1.02–1.67
Shiftwork <sup>d</sup>	1.79	1.09–2.96	1.39	1.09–1.79	1.28	0.99–1.64
Shiftwork <sup>e</sup>	1.83	1.10–3.06	1.39	1.08–1.78	1.27	0.98–1.63
Shiftwork <sup>f</sup>	2.03	1.18–3.48	1.40	1.08–1.83	1.19	0.92–1.56

<sup>a</sup>Crude OR<sup>b</sup>OR adjusted for age<sup>c</sup>OR adjusted for age and socio-economic group<sup>d</sup>OR adjusted for age, socio-economic group, physical activity and current smoking<sup>e</sup>OR adjusted for age, socio-economic group, physical activity, current smoking, and low social support<sup>f</sup>OR adjusted for age, socio-economic group, physical activity, current smoking, low social support and job strain

The crude odds ratio (OR) for low HDL-cholesterol levels among shift workers was twice that of day workers (OR: 2.02, 95%CI: 1.24–3.28). The OR estimate slightly decreased when adjusted for age and socio-economic factors (OR: 1.81, 95%CI: 1.10–2.99) (Table 4). The further inclusion of physical activity and smoking did not alter the OR, but when social support and job strain were included in the logistic regression model, the estimate increased to 2.03 (95%CI: 1.18–3.48).

Crude OR for high triglyceride levels in shift workers compared with day workers was 1.43 (95%CI: 1.13–1.82). Age, socio-economic group, smoking, physical activity, social support, and job strain, did not confound this association.

The crude OR for abdominal obesity among shift workers was 1.34 (95%CI: 1.07–1.69). After adjustment for age, socio-economic status, smoking, physical activity, social support, and job strain, the OR decreased to 1.19 (95%CI: 0.92–1.56).

In order to assess differences between ages, we divided the workers into young ( $\leq 50$  years) and old ( $> 50$  years) groups. When adjustment were made for age, socio-economic group, physical activity and smoking, shift work was a predictor for abdominal obesity only in young shift workers (OR: 1.39, 95%CI: 1.05–1.85 vs OR: 1.11, 95%CI: 0.66–1.86). Contrariwise, in subjects older than 50 years, the OR for low HDL-cholesterol levels was stronger than in young subjects (OR: 3.20, 95%CI: 1.19–8.65 vs OR: 1.56, 95%CI: 0.89–2.85).

To test for interaction effects we used continuous variables. The reason for this was because of an unexpected finding: no lean shift worker had an HDL-concentration below the cut point ( $< 0.9$  mmol/l). Linear regression models using shift work and abdominal obesity as independent variables and ln-triglycerides and HDL-cholesterol as dependent variables did not yield significant interaction terms (beta =  $-0.307$  for HDL and beta =  $0.568$  for ln-triglycerides).

## Discussion

According to the results of this study shift workers have higher serum levels of triglycerides and lower serum levels of HDL-cholesterol than day workers. In addition, abdominal obesity was more frequently found among young shift workers. However, after adjustment for confounding factors, the OR became insignificant.

Our findings on increased concentration of triglycerides among shift workers are consistent with those of a number of previous studies. One possible explanation to this triglyceride increase could be an altered metabolism of lipids secondary to shift work. This interpretation is supported by findings of Hampton et al. (1996). We have found nine studies on triglycerides in shift workers published in international journals. Eight of these provided information on sampling procedures (fasting state or not, clock time) (De Backer et al. 1987; Knutsson et al. 1988, 1990; Lasfargues et al. 1996; Nakamura et al. 1997; Orth-Gomér 1983; Romon et al. 1992; Thelle et al. 1976). Five out of eight studies demonstrated increased concentrations of triglycerides in shift workers compared to day workers (Knutsson et al. 1988; Lasfargues et al. 1996; Nakamura et al. 1997; Orth-Gomér 1983; Romon et al. 1992). In four of these studies fasting samples were taken in the morning (Knutsson et al. 1988; Nakamura et al. 1997; Orth-Gomér 1983; Romon et al. 1992). In the other studies the information on these variables is incomplete. In other words, the inconsistencies in the study of the triglyceride–shift work association could be due to differences in blood sampling procedures. Triglyceride concentration in serum has a circadian variation, with its maximum value occurring at 3–4 a.m., and its minimum at noon (Rivera-Col et al. 1994). The drawing of blood at different times in day workers and shift workers could exaggerate or diminish differences in mean values between the two groups. Even if the blood samples were drawn at the same time, the two groups could differ with regard to “circadian time”. The induction of a phase shift of circadian rhythm in

shift workers could result in differences in mean concentration of triglycerides compared to day workers. Such difference would not be due to metabolic impact. Our study is also affected by this problem. The average time difference between blood sampling in day workers and shift workers was 2 h. However, the assumption that there is no phase shift of circadian rhythm in shift workers would explain only 50% of the measured difference in triglycerides. (Rivera-Col et al. 1994).

In this study, shift workers had a lower HDL-cholesterol concentration than day workers did. The relative risk of low HDL-cholesterol levels was more pronounced in older shift workers ( $\geq 50$  years of age). HDL-cholesterol also has a circadian variation, which is roughly opposite to that of triglycerides, reaching a minimum at approximately 4 a.m. and a maximum at noon (Rivera-Col et al. 1994). In a similar fashion to triglycerides, the sampling procedures might influence comparisons between shift workers and day workers. In the present study blood sampling was carried out around 2 h earlier in shift workers. This time difference would explain approximately 25% of the observed difference in levels of HDL-cholesterol (Rivera-Col et al. 1994). Only three studies have studied HDL-cholesterol in shift workers. (Costa et al. 1990; De Backer et al. 1987; Romon et al. 1992) Two of these reported no difference (Costa et al. 1990; Romon et al. 1992), but in one study (De Backer et al. 1987) lower HDL-cholesterol levels were seen among both three-shift workers and workers with a heterogeneous system consisting of 24 h work, 24 h off, 24 h work and 48 h off. However, in one of these the time of blood sampling was not reported (Costa et al. 1990).

For men aged 50 years or younger we found a significant association between shift work and abdominal obesity. One possible explanation for this finding could be that shift workers contract abdominal obesity at a younger age than day workers do. In older age groups abdominal obesity is common in both shift workers and day workers. Previous results on obesity in shift workers have yielded contradictory results. We are aware of seven studies that found no difference in anthropometric measurements in shift workers compared with day workers (Burse 1990; Cesana et al. 1985; Costa et al. 1990; De Backer et al. 1987; Knutsson 1989; Orth-Gomér 1983; Romon et al. 1992). Nakamura et al. (1997) did not find differences in BMI, but reported waist/hip ratios that were significantly higher in three-shift workers than in day workers. However, the authors did not adjust for age and socio-economic status. In a Swedish cross-sectional study crude data showed correlation between shift work and waist/hip ratio, but no adjustments were made for socio-economic status (Rosmonds et al. 1996). A Danish study found weight gain in a population that worked shifts, although it disappeared after adjustment for socio-economic factors (Bøggild et al. 1999). In a Dutch study a significant association was found between shift work and BMI, and between shift work and waist/hip ratio (van Amelsvoort

et al. 1999). The results were adjusted for a number of confounding variables including educational levels.

Two cohort studies of nurses demonstrated a positive correlation between shift work and BMI (Kawachi et al. 1995; Niedhammer et al. 1996). A Swedish cross-sectional study showed a significant increase in BMI among shift workers compared with day workers, when adjustment was made for age and educational level (Karlsson et al. 2001).

A recent study by Parkes showed that "age but not duration of day exposure, predicts BMI for day workers, while for shift workers (day-night workers) duration of shift exposure is the major predictor, age per se contributing relatively little" (Parkes 2002).

Dietary aspects are not explored in this study but in a thesis by (Lennernäs 1993) it was concluded that two-shift and three-shift work has a negligible impact on total dietary intake, dietary quality or coffee/tea consumption, but causes a redistribution of food intake to the night in three-shift workers.

In this study we found no indication of higher blood pressure among shift workers than day workers. Hypertension is one of the important cardiovascular risk factors in the metabolic syndrome cluster and also initiated the metabolic syndrome discussion. However, many later epidemiological studies have shown a closer association between disturbances in the insulin-glucose axis and dyslipidaemia and low fibrinolytic activity than between the insulin-glucose axis and blood pressure (Lindahl et al. 1996).

Blood-pressure comparisons between day and shift work have been measured in many previous studies, with inconsistent results (Bøggild and Knutsson 1999). The measurement of blood pressure is inherently difficult in studies relating to shift work. Most published studies are based on casual blood-pressure measurements and have not taken into account its circadian variation. More studies that use 24-h measurements are needed.

No previous study has compared shift and day workers with respect to insulin levels. It has been shown that insulin secretion has a circadian rhythm, rising during the day and falling during the night (Boden et al. 1996). Furthermore, the metabolic response to eating could vary with circadian rhythm. During late evening the insulin response to the intake of food is greater than in the morning (Hampton et al. 1996; Ribeiro et al. 1998). In our study we have shown that day workers have higher mean concentration of serum insulin. One possible explanation for this finding is that blood was taken 2 h later in day workers and thus was affected by the individuals' circadian rhythms.

Individuals with previously known diabetes mellitus were excluded from the analyses. The diagnosis of hyperglycaemia in the present analyses is, therefore, based only on serum glucose levels  $\geq 7.0$  mmol/l. We found the same prevalence of hyperglycaemia in both day workers and shift workers. These results are consistent with a recent cross-sectional study (Karlsson et al. 2001). In contrast, Kawachi et al. (1995) reported that in

a prospective study of female nurses the prevalence of diabetes tended to increase with years spent working shift. Mikuni et al. (1983) found that diabetes was more common in male three-shift workers than in day workers. There are few studies of diabetes and shift work, and differences in design may explain the inconsistencies in their findings.

In the study of a chronic disease such as diabetes, a cross-sectional study design could underestimate the "true" prevalence of diabetes in shift workers. A selection bias could occur if shift workers are transferred to daytime work when it is discovered that they are diabetics. In this study we have tried to reduce this effect by excluding individuals answering "Yes" on the question 'Do you have diabetes?'

Cross-sectional study designs do not have the same limitations when biochemical outcomes such as triglycerides and low HDL-cholesterol levels are studied, as these findings are often observed before obvious clinical manifestations occur. Hence a selection process similar to that for diabetes is less likely for these outcomes. Non-differential misclassifications of outcome that underestimate the risk and blur differences between the exposure groups is less likely, because all blood samples are analysed at the same laboratory.

The main advantages with this study are the high rate of participation and the high validity of the exposure data.

In conclusion, we found significant differences in the levels of HDL-cholesterol and triglycerides between shift workers and day workers. We also found anthropometric differences, indicating that abdominal obesity was more common among young shift workers. The profile of lipids among shift workers does indicate an association between shift work and the metabolic syndrome. However, our data on insulin and glucose do not support the hypothesis that shift work is a risk factor for diabetes. Further studies are needed to investigate whether shift work is a causal factor for diabetes.

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## References

- Alberti GMM, Zimmet PZ (1998) Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: Diagnosis and classification of diabetes mellitus. Provisional report of a WHO consultation. *Diabet Med* 15:539–553
- Alfredsson LS, Hammar N, Fransson EIM, de Faire UH, Hallqvist J, Knutsson A, Nilsson T, Theorell T, Westerholm P (2002) Job strain and major risk factors for coronary heart disease. Baseline results from the Wolf study. *Scand J Work Environ Health* 28:238–248
- Boden G, Ruiz J, Urbain J-L, Xinhua C (1996) Evidence for a circadian rhythm of insulin. *Am J Phys*: E246–E252
- Bursey RG (1990) A cardiovascular study of shift workers with respect to coronary artery disease risk factor prevalence. *J Soc Occup Med* 40:65–67
- Bøggild H, Knutsson A (1999) Shiftwork, risk factors and cardiovascular disease. *Scand J Work Environ Health* 25:85–99
- Bøggild H, Suadicani P, Hein H, Gyntelberg F (1999) Shiftwork, social class and ischaemic heart disease in middle aged and elderly men; a 22 year follow up in the Copenhagen male study. *Occup Environ Med* 56:640–645
- Cesana G, Panza G, Ferrario M, Zanettini R, Arnoldi M, Grieco A (1985) Can glycosylated hemoglobin be a job stress parameter? *J Occup Med* 27:357–360
- Costa G, Betta A, Uber D, Alexopoulos C (1990) Estimate of coronary risk in a group of Italian shiftworkers. In: Costa G, Cesana G, Kogi K, Wedderburn A (eds) *Shiftwork: health, sleep and performance*. Lang, Frankfurt am Main, pp 363–369
- De Backer G, Kornitzer M, Dramaix M, Peeters H, Kittel F (1987) Irregular working hours and lipid levels in men. In: G Schling, H Mörl (eds) *Expanding horizons in atherosclerosis research*. Springer, Berlin, pp 217–224
- Hampton SM, Morgan LM, Lawrance N, Anastasiadou T, Norris F, Deacon S, Ribeiro D, Arendt J (1996) Postprandial hormone and metabolic responses in simulated shiftwork. *J Endocrinol* 151:257–267
- Karlsson B, Knutsson A, Lindahl B (2001) Is there an association between shift work and having a metabolic syndrome? Results from a population based study of 27 485 people. *Occup Environ Med* 58:747–752
- Kawachi I, Colditz G, Stampfer M, Willet W, Manson J, Speizer F, Hennekens C (1995) Prospective study of shiftwork and risk of coronary heart disease in women. *Circulation* 92:3178–3182
- Knutsson A (1989) Shiftwork and coronary heart disease. *Scand J Soc Med Suppl* 44:1–36
- Knutsson A, Bøggild H (2000) Shiftwork and cardiovascular disease: review of disease mechanisms. *Rev Environ Health* 15:359–372
- Knutsson A, Åkerstedt T, Jonsson BJ (1988) Prevalence of risk factors for coronary artery disease among day and shift workers. *Scand J Work Environ Health* 14:317–321
- Knutsson A, Andersson H, Berglund U (1990) Serum lipoproteins in day and shiftworkers: a prospective study. *Br J Ind Med* 47:132–134
- Lasfargues G, Vol S, Cacès E, Le Clésiau H, Lecomte P, Tichet J (1996) Relations among nightwork, dietary habits, biological measures, and health status. *Int J Behav Med* 3:123–134
- Lennernäs MAC (1993) *Nutrition and shiftwork*. Thesis, Uppsala University, Sweden
- Lindahl B, Asplund K, Eliasson M, Evrin P-E (1996) Insulin resistance syndrome and fibrinolytic activity: the Northern Sweden MONICA study. *Int J Epidemiol* 25:1–9
- Mikuni E, Ohoshi T, Hayashi K, Miyamura K (1983) Glucose intolerance in an employed population. *Tohoku J Exp Med* 141 [Suppl]:251–256
- Nakamura K, Shimai S, Kikuchi S, Tominaga K, Takahashi H, Tanaka M, Nakano S, Motohashi Y, Nakadaira H, Yamamoto M (1997) Shiftwork and risk factors for coronary heart disease in Japanese blue-collar workers: serum lipids and anthropometric characteristics. *Occup Med* 47:142–146
- Niedhammer I, Lert F, Marne M-J (1996) Prevalence of overweight and weight gain in relation to night work in nurses' cohort. *Int J Obes* 20:625–633
- Orth-Gomér K (1983) Intervention on coronary risk factors by adapting a shift schedule to biologic rhythmicity. *Psychosom Med* 45:407–415
- Parkes K (2002) Shift work and age as interactive predictors of body mass index among offshore workers. *Scand J Work Environ Health* 28:64–71
- Ribeiro D, Hampton S, Morgan L, Deacon S, Arendt J (1998) Altered postprandial hormone and metabolic responses in a simulated shiftwork. *J Endocrinol* 158:305–310

- Rivera-Col A, Fustes-Arderiu L, Diez-Noguera A (1994) Circadian rhythmic variation in serum concentrations of clinically important lipids. *Clin Chem* 40:1549-1553
- Romon M, Nuttens M-C, Fievet C, Pot P, Bard J, Furon D, Fruchart J-C (1992) Increased triglyceride levels in shift workers. *Am J Med* 93:259-262
- Rosmonds R, Lapidus L, Björntorp P (1996) The influence of occupational and social factors on obesity and body fat distribution in middle aged men. *Int J Obes Relat Metab Disord* 20:599-607
- Thelle D, Førde O, Try K, Lehman E (1976) The Tromsø heart study. *Acta Med Scand* 200:107-118
- Theorell T, Åkerstedt T (1976) Day and night work: changes in cholesterol, uric acid, glucose and potassium in serum and in circadian patterns of urinary catecholamine excretion. *Acta Med Scand* 200:47-53
- Theorell T, Tsutsumi A, Hallqvist J, Reuterwall C, Hogstedt C, Freedlund P (1998) Decision latitude, job strain and myocardial infarction: a study of working men in Stockholm. The SHEEP Study Group. Stockholm heart epidemiology program. *Am J Public Health* 88:382-388
- van Amelsvoort L, Schouten E, Kok F (1999) Duration of shift-work related to body mass index and waist to hip ratio. *Int J Obes* 23:973-978