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17 October 2023 02:27

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Characteristics of working hours and the risk of occupational injuries among hospital employees: a case-crossover study

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ABSTRACT (ENGLISH)

Objectives We investigated the association of working hours with occupational injuries in hospital shift work. Methods Registry data of occupational injuries of hospital employees from 11 towns and 6 hospital districts were linked to daily payroll data to obtain working hours for 37 days preceding the first incidence of the injury (N=18 700). A case-crossover design and associated matched-pair interval analysis were used to compare working hour characteristics for three separate hazard windows among the same subjects. Conditional logistic regression was used to calculate odds ratios (OR) with 95% confidence intervals (CI). Results We found an elevated risk of an occupational injury for workdays with evening shifts (OR 1.09, 95% CI 1.03-1.14) and workdays following night shifts (OR 1.33, 95% CI 1.17-1.52). After excluding commuting injuries, the risk increased during the evening shifts (OR 1.15, 95% CI 1.09-1.23) and the work days following night shifts (OR 1.44, 95% CI 1.24-1.69), but was no more significant during the morning shifts. Injury risk increased following a week of >5 morning shifts or >3 evening shifts, but did not increase according to the number of preceding night shifts or quick returns. The length of the work shift (OR 1.22, CI 1.06-1.42) - not the length of the weekly working hours - was associated with an increased risk. Conclusions The results indicate an increased occupational injury risk during the evening shifts and during work days following night shifts, with the risk increasing according to the number of evening but not night shifts.

FULL TEXT

Headnote

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Key terms fatigue; night work; registry data; shift work; shift worker; working time; work hour.

Approximately 20% of European employees and, in some industries, up to 38% of US employees work in shifts (1). Based on the EU Working Time Directive (2003/88/EC), shift work means any method of organizing work in shifts where workers succeed each other according to a certain pattern, entailing the need for workers to work at different times of the day. Shift rotation can be regular or irregular, and the shift rotation can be continuous or discontinuous in relation to weekends. In Europe, irregularly rotating working hours are frequent in health and social care sector, as well as in commerce, hotels, restaurants and catering, all sectors in which female workers dominate (1).

It has been estimated that the costs due to workrelated injuries amount to US$ 250 billion a year, which is approximately 1.8% of GDP in the US and 2.7-6.0% of GDP in countries like Norway, Sweden, Finland and Denmark (2). In Finland, there are over 125 000 occupational and commuting injuries annually, based on the obtained claims received by the Finnish Workers Compensation Center.

Compared to day work, night and shift work has been reported to be associated with an increased number of occupational injuries in the general population (3), and in industry, construction, mining (4, 5), and health and social care sectors (6-9). Changing the work schedule from day to nonstandard shift work may increase injury risk at work (10). Based on a recent review and meta-analysis of Fischer et al (4), the increased risk of occupational injuries was associated with night and evening shifts. Similarly, this review suggested an exponentially increasing risk for morning and night shifts, and an increase of risk beyond the 9th hour of duty (4). Recently, an association between a short time between the shifts (eg, <11 hours) and occupational injuries was found among Danish hospital workers (11, 12).

Sleepiness is regulated by the circadian and homeostatic factors and is considered to create an increased need for sleep or trouble staying awake (8, 13). Sleepiness is considered a mechanism underlying the increased risk of occupational injuries in shift work (13). As shown in many earlier studies, night shifts, early morning shifts, and a short time between consecutive shifts are associated with insufficient time to meet habitual need for daily sleep, as well as an increased sleepiness due to the requirement to stay awake at a physiologically incorrect time of the day (14-16). Shift work-related partial sleep deprivation may also accumulate over the days (17), causing impairments in alertness and cognitive performance (18).

There are several limitations in some of the earlier research examining the association of working hours with occupational injuries. In the systematic review by Fischer (4), 22 of the 24 studies on shift work and occupational injuries had cross-sectional designs that are sensitive to selection bias and residual confounding due to potential unadjusted confounders. Working during the night is associated with lower socioeconomic status, a higher physical work load, and obesity (19), all of which are associated risk factors and potential confounders for studies on occupational injuries. Several earlier studies on working hours and injuries have also been based on self-reported exposure, making them sensitive to information bias. Only few studies have utilized objective exposure data of working hours (8) and/or objective outcomes based on compensation claims (6, 20). Finally, most earlier studies on shift work and occupational injuries are based on industrial cohorts while high quality studies among nurses are rare (7).

Occupational injuries are common in hospital wards with a significance for both employee and patient safety (9, 21).

Methods

In order to provide additional evidence and fill several methodological gaps, we used a case-crossover design with a matched-pair interval analysis to study the associations of payroll based objective working hour characteristics with the risk of a registry-based occupational injuries among hospital employees.

Based on a unique personal identification number, we linked occupational injuries of the employees of the Finnish Public Sector (FPS) cohort study from the years 2000-2015 (N=18 700, employees with >1 injury) with the preceding objective payroll data for 37 days before the injury (figure 1). The FPS study is one of the largest on-going open cohort studies comprising all employees of ten Finnish towns (10-town study) and six hospital districts (Work and Health in Finnish Hospital Personnel study) (22). We excluded employees who had leisure-time injuries only, ie, no occupational injuries. Leisure-time injuries are not compensated by employers and are thus not systematically found in the database of the Finnish Federation of Accidents Insurance Institutions. We also excluded employees with injuries due to violence by patients (7.9%). Although these injuries are work-related, they are often due to patient behavior (ie, alcohol-related violence during night-time) and are not likely to be associated with employees, human factors or fatigue. Physicians (N=331) were excluded due to missing information on on-call work. Of the final sample, 91% (N=18 700) were women and 9% men, the mean age of the sample was 43 (standard deviation 16-71) years. The Ethics Committee of the Hospital District of Helsinki and Uusimaa approved the study (HUS 1210/2016).

Working hour data

The payroll-based working hour data were retrieved from a shift scheduling program Titania® used for shift scheduling and payroll in the municipal health and social sector in Finland (23). The employee data included personal identification number with information on age and sex, and the daily starting and ending times of the work shifts, including both the draft shift schedules and the final schedules used for payroll. The data included information on individual work and shift rota unit. The characteristics of the payroll based working hours are described in table 1, as reported also earlier (23, 24). Of the sample, 97% had morning, 66% had evening, and 23% had night shifts. Shift rotations with evening and night shifts were irregular, the order of the work shifts and free days varying from week to week. The shift rota tables of the employees were established for each three-week period in all hospital units separately, depending on the need for 24-hour services and patient work for each period. We classified the varying length and timing of the working hours into three shift categories: (i) morning (starting >03:00-<21:00 hours); (ii) evening (>3 hours >18:00-<02:00 and not categorized as a night shift); and (iii) night (>3 hours 23:00-06:00 hours) as described earlier (24). We also created categories for long work shifts (>12 hours), quick returns (<11 hours between two shifts) and long weekly working hours (>40, >48 or >55 hours/week) (23, 24).

Occupational injury data

Occupational injury data was obtained from the Finnish Federation of Accidents Insurance Institutions. In Finland, any costs (health costs, sickness absence, permanent damage) of occupational work-site and commuting injuries are compensated via a statutory insurance system; but injuries without any monetary costs are also required by law to be reported to the employer, who then passes on the information via the insurance companies to the Finnish Federation of Accident Insurance Institution. The injury data includes information on the date of the injury, categorization (work/commuting/leisure) and the reported external cause, location and type of the injuries (eg, falling, crashes, violence, physical load). The included leisure-time injuries are, however, only a small part of all leisure-time injuries in Finland, while occupational injuries are systematically included. Among the occupational injuries, 71% of the injuries take place during the working hours and 29% during commuting. Injuries due to sudden physical strain (29%), falling or slipping (24%), and sharp objects like needles (17%) are the most frequent.

Statistical methods

A case-crossover design was used to assess the association between a work-related injury and various characteristics of work shifts using a matched-pair interval approach. The case-crossover approach has been shown to be an efficient design to examine transient risk factors related to injury causation (25, 26). This within-subject design has the advantage of controlling the known and unknown confounders that are different between the subjects but do not vary over time. The case-crossover approach has been previously used to study the effects of sleep and working hours on traffic accidents (27).The effects of payroll-based irregular work hour characteristics on accidental injuries (12) and sickness absence (28) have been studied before using the case-crossover design.

The basic requirements for the case-crossover design in injury research are related to the requirements of the injuries being acute with a known onset time, the exposures being transient and the possibility of the injured cases to serve as their own control (29, 30). The hazard and control windows need to be selected a priori, and the control window needs to show variability (ie, transience) in the exposure. In this study, the requirements for the known exposure and outcome timing were fulfilled based on the register data of working hours (exposure) and the information on the timing of the occupational injuries (outcome) in relation to the work shifts of all days. The study question also satisfies the requirement that the exposures be intermittent and exhibit transient effects (ie, the case moves across periods of varying exposure), as there was high transience in the shift patterns of the workers. The shift rotation tables of employees were planned at health and social sector units for three-week periods in each unit

separately, hence the number of day, evening and night shifts as well as their order thus varying not only within the three week periods but also between the weeks.
In the matched-pair interval analysis, a pair of hazard and control intervals contributed by the same subject are compared. The injury risk was evaluated for three separate hazard windows: for the day of the injury, the preceding day of the injury day, and the seven preceding days of the injury day. Our hypothesis for the possible pathway from exposure of the working hours to the injury is based on increases in sleepiness during work shifts that interfere with the circadian and/ or homeostatic processes, such as morning and night shifts (31). Based on this, our first hazard window was taken from the same day on which the first injury was reported. A work shift may cause sleepiness during the following day, too, especially when there is insufficient opportunity to recover through sleep between the shift and the following day, such as in connection with night shifts and quick returns (17, 32, 33). For that reason, the second hazard window was selected one day after the exposure. Finally, it is possible that night shifts or other nonstandard work hour arrangements cause accumulation of sleepiness and impairments in cognitive performance, thus causing a progressive injury risk over several days (4, 18). To study this, the last hazard window included seven preceding days of the injury. We did not use longer periods, eg, one month, as the characteristics of the current shift system were balanced every three weeks. This means hazard windows of several weeks would have decreasing variability compared to one-week periods that differed more in relation to the length, timing and intensity of the working hours.
The hazard period for the date of the injury was defined as the calendar day including the morning or evening shift (00:00-24:00) or the end of the night shift (from 00:00-24:00, the night shifts starting mostly between 20:00-23:00 during the preceding date and ending at around 07:00 hours the following date). For night shifts, the hazard window following the night shift was the date after the end of the night shift. If the injury took place during a specific shift, it was coded as 1 ("yes"), otherwise the date was coded as 0 ("no"). The control window was always the same weekday including any work shift occurring seven dates earlier than the hazard window. If the control window one week earlier did not include any work shift, a new control window was looked for from the earlier week on the same weekday, up to the maximum of four weeks apart from the injury. If no control window was found during the preceding four weeks, the observation was assigned as missing.
For the hazard window of the preceding seven dates of the date of the injury, the control window consisted of the previous seven dates of the hazard window, starting from the same weekday as the hazard window. If the control window one week earlier did not include any work shifts, the control window was taken from the earlier week, etc. up to the maximum of four weeks before the injury. The first incidence of an occupational injury alone for each subject was considered. We estimated odds-ratios (OR) and 95% confidence intervals (CI) for the risk of injury in the hazard windows compared to the control window using conditional logistic regression analysis.
Results
Table 2 shows that there was a statistically significantly, elevated risk for an occupational injury during the morning (OR 1.06, 95% CI 1.01-1.11) and evening (OR 1.09, 95% CI 1.03-1.14) shift, but not during the night shift (OR 0.98, 95% CI 0.88-1.08). Using the preceding day as the hazard period, injury risk was not increased following a morning or an evening shift but was increased during a work shift following a night shift (OR 1.33, 95% CI 1.17-1.52). Specific shift combinations within the injury hazard windows showed for the most part non-significant associations with injuries, except for a decreased risk for the combination of a morning shift (during the preceding day of the start of the night shifts) and a night shift (OR 0.63, 95% CI 0.43-0.93), and a decreased risk for the combination of an evening and night shift (OR 0.69, 95% CI 0.48-0.99). Long work shifts with >12 hours were associated with an increased risk during the shift (OR 1.23, 95% CI 1.06-1.42).
Work-related injury risk was also estimated based on the number of morning, evening or night shifts during the preceding seven days (table 3). Having only 1 morning (OR 0.94, 95% CI 0.89-0.99) or 0 evening (OR 0.93, 95% CI 0.89-0.98) shifts during the seven days ending in an occupational injury was associated with a significant decrease in injury risk. However, the risk increased significantly following a week including >5 morning shifts (OR 1.12, 95% CI 1.07-1.18), or following a week including >3 evening shifts (OR 1.15-1.22) preceding the injury. For night shifts,

the risk was increased in the case of having only 1 night shift (OR 1.12, CI 1.01-1.23) during the preceding week, but became lower and insignificant according to a higher number of night shifts during the preceding week (table 3).

The number of quick returns during the preceding week was not significantly associated with the injury risk (OR 1.40, 95% CI 0.68-2.89 for two quick returns during the preceding week, table 4). Similarly, the length of the total weekly working hours of the preceding week was not associated with the risk for injury for the working weeks of >40 hours (OR 0.99, 95% CI 0.94-1.04, N=4570), for the working weeks of >48 hours (OR 1.00, 95% CI 0.92-1.08, N=1540), or for the working weeks of >55 hours (OR 1.01, 95% CI 0.91-1.13, N=926).

Since the etiology of work time and commuting injuries may be different, we conducted a sensitivity analysis on the association of different work shifts with occupational injuries excluding the smaller group of commuting injuries. The main results were similar to the combined data: the risk for occupational injuries was elevated during the evening shifts (OR 1.15, 95% CI 1.09-1.23, N=3173) and following the night shifts (OR 1.44, 95% CI 1.24-1.69, N=623). The risk for injuries was not statistically significant during the night shifts (OR 1.06, 95% CI 0.94-1.19, N=623) or during the morning shifts (OR 1.01, 95% CI 0.95-1.07, N=8159).

Discussion

This study of over 18 000 hospital employees with occupational injuries linked with comprehensive objective working hour data utilized a case-crossover design with a matched-pair interval analysis to investigate the associations of working hour characteristics with occupational injuries. The results indicate an increased injury risk following >5 morning shifts and following >3 evening shifts during the preceding week. For the night shift, the injury risk increased only during the following work shift but not according to the number of night shifts during the preceding week. The risk for occupational injuries increased during long work shifts.

We observed an association between the number of evening shifts and occupational injuries, with an increasing pattern in relation to the number of preceding evening shifts and the risk for injury. Since the observed risks for injuries between the morning, evening and nights shifts - as well as in between the different number of preceding work shifts - are not directly comparable, the results need to be interpreted with caution. However, the findings of the association of evening shifts and injuries does not seem to be in line with the meta-analysis of Fischer et al (4) but is consistent with the recent Danish payroll study (8, 12). The Danish study also found an increasing trend for the association between the number of evening shifts during the preceding week and the risk for injury. For the night shift, we found an increased risk for occupational injuries only during the days following the night shift but not during the night shift days. The Danish payroll study (8) found a similar association between the number of night shifts and injury risk, but this study did not differentiate injury risk for the periods during or following the night shifts. The Danish study focused also on the more serious injuries, based on database requiring contacts to emergency rooms, and studied the risk in relation to any injuries, whether taking place during working hours, commuting or leisure-time. The lack of information on leisure-time injuries in our study may have weakened the observed association between night shifts and the risk for occupational injuries. Injuries were more frequent following the night shifts, suggesting that they might take place also during free-time reserved for recovery.

We found that occupational injuries were most frequent following the weeks of only one night shift, and least frequent following the weeks with three night shifts. These findings are not consistent with earlier studies, most of them in industry (4). Occupational injury risk may be the highest during the first night shift due to higher odds for severe sleepiness, as found in several studies (14, 15, 34). On the other hand, insufficient sleep during the following night shifts may cause cumulative fatigue that can increase the risk for injury. We found that only night shifts, not the morning or evening shifts, were associated with occupational injuries following the shifts. This, however, may be due to the observed shorter sleep length after the night shifts, compared to average sleep length after the morning and evening shifts (16, 17).

The finding indicating occupational injuries were the most frequent following the week including 3 night shifts, but not following the week of >5 night shifts, cannot be explained by a lower cumulative sleep deprivation. The used case-crossover design compares exposure within individuals with the benefit of excluding bias due to the possible inter-individual differences. This means that the observed null findings in relation to the possible increased risk due to several night shifts are not biased due to individual differences. However, the lower observed risk among those having several night shifts may be due to having a smaller self-selected group of, for the most part, permanent night workers. The group having occupational injuries following >5 night shifts was smaller (N=111) than the group having the maximum of 3 (N=350) or only 1 (N= 912) night shift during the preceding week of the injury. The OR stratified according to the number of work shifts are thus not comparable to each other, particularly in a situation in which an employee performs many night shifts. Furthermore, we should not exclude the possibility that an increase in the number of consecutive night shifts in a non-selected group of irregularly rotating night shifts might cause an increase in the risk for occupational injuries (35, 36).

The reason for the increased risk for injuries during the evening shifts in hospital work is unclear. It is well known that sleepiness and fatigue in hospital work is lower during the evening than the night shifts, as shown also by us in the same population using a field study (16, 37). The evening shifts usually started at 13:00-13.59 while the night shifts most frequently started at 20.0020.59, being up to three hours longer than the evening shifts (24). Based on our earlier joined study, morning shifts accounted for 8% of all operational hours (by each hour of the shift), while evening hours made up 3% and night shifts only 1% (24). The need for workforce is thus much more limited in the evenings and especially during the nights, reflecting probably variation in work demands and the availability of the work force. The need for patient care and possibly also for safety-sensitive operations is the lowest during the nights, when most patients in hospital wards sleep. During the evenings, staffing level decreases remarkably from daytime, but it is possible that the work demands for each employee are high due to patients being awake and needing hospital care. We also found a small increased risk for the morning shifts that was not significant in the sensitivity analysis after excluding commuting injuries. This suggests that commuting, possibly due to travelling during the rush hours or eg, more slippery pavements in the early morning together with perceived sleepiness, could be the reason for the observed risk. The observed decreased risk for occupational injuries for the shift combination of a morning shift during the preceding day, and a night shift during the following day is supported by some earlier observations for a lengthened sleep, a high percentage of napping and a low number of dozing off in a morning-night shift combination (38).

We found that long shifts were associated with occupational injuries. On the other hand, the number of quick returns during the preceding week was not associated with the risk for injury. The findings that long work shifts are linked with occupational injuries is mostly supported by the earlier studies, reporting on the association of long working hours with decreased safety and lower quality of care (4, 21, 39). A short lapse of time between the shifts, normally the criteria being <11 hours according to the EU Working Time Directive, has been found earlier to be related to an increased risk for occupational injuries among hospital employees (12, 40, 41). For example, the Danish payroll data among hospital workers found a 39% increased risk for occupational injuries in quick returns compared to shift intervals of 15-17 hours, adjusted to year, season, age, sex and occupation. The risk decreased to 17% in the fully adjusted model (11). Quick returns with the length 6-8 hours were not associated with an increased risk in the full statistical model, the risk consisting mostly from quick returns of only 1-5 hours (split shifts). This would mean our results are not fully in disagreement with the Danish payroll study. However, we could not find significant associations between quick returns and the number of injuries. This may be due to the small number of quick returns in this sample, and possible interactions of quick returns with some other characteristics of working hours. For example, the percentage of short shift intervals correlated negatively (correlation coefficient 0.41) with long spells of consecutive night shifts in our earlier study (23).

The strengths of this study are the use of objective registry data for both daily working hours and occupational injuries and the benefit of having a large and representative sample of hospital employees without a loss of follow-up. Our results add to some earlier registry studies with the design of the study and the analysis of several working hour characteristics in three separate hazard windows in order to get a comprehensive overview of the detailed working hour characteristics relevant to occupational safety. The use of payroll data offers the advantage of having access to precise information without recall bias or attrition (23). The use of payroll data is also optimal for the analysis of irregular shift systems with transient working hours. The case-crossover approach used is highly appropriate when examining transient risk factors related to injury causation (25). Since the employees are compared to themselves, the design controls for all measured or unmeasured confounders that do not vary between the hazard and control windows. The design thus automatically controls for between-employee confounders, workrelated differences, and time of the year.

Overall, our study and the use of the case-crossover study design has some limitations (25). We could not control for the potential shift-dependent variation in work demands and tasks associated with the risk for injuries. The differences in occupational injury risk between the morning, evening and night shift days may be due to differences in work tasks. The exact time of the day of the injury was not known, but having the minutebased follow-up of the true working hours, we could locate the timing of the injuries to different times of the day. The OR for morning, evening and night shifts are not directly comparable due to the higher number of subjects, and possible self-selection. Since night shifts were less frequent than morning and evening shifts, as well as the shift combinations associated with night shifts, the probability of finding a hazard window from the preceding week was lower, decreasing the statistical power. This also increases the probability for confounding due to the possibility of individual differences changing over time (eg, a respiratory infection) between the control and hazard windows. However, we could decrease the bias by limiting the lag to a maximum of four weeks.

We had to exclude the leisure-time injuries due to the data not being representative of the study population. Since leisure-time injuries can also partly depend on preceding work shifts in addition to the occupational injuries (defined as injuries during working hours or commuting, according to the Finnish legislation). This is likely to attenuate the observed association of night shifts and the risk for injuries since we found a significantly increased risk especially after, but not during the night shifts. As for commuting injuries, albeit there is control of between-person confounders in this study design, one limitation is the control of within-person confounding which is still possible for multiple, correlated transient factors that change over time within a subject. For example, if a driver, feeling tired, uses concurrently a mobile phone (ie, distraction) while moving through hazardous road conditions, this confounding would be uncontrolled and could still be a threat to the internal validity (29). Finally, since the sample is based on hospital employees only, the results should not be directly generalized to other sectors. Future studies should use even large samples in order to stratify the results according to the different types and characteristics of the injuries.

Several practical conclusions can be made based on the obtained results. Preventive safety measures on irregular shift work arrangements should pay extra attention on evening shifts, which were shown to be the highest risk period for injuries. Long work shifts, long spells of consecutive evening shifts and single night shifts, which were shown to have an increased risk for occupational injuries, should be avoided or minimized if possible. Having a morning or evening shift during the preceding day of the starting time of the first night shift might offer possibly better recovery before the becoming spells of nights, as previously reported (38).

Acknowledgements

This work was supported by grants from the Finnish Work Environment Fund (no 114317) and NordForsk (74809).

Disclosure statement

The authors declare no conflicts of interest.

Sidebar

Härmä M, Koskinen A, Sallinen M, Kubo T, Ropponen A, Lombardi DA. Characteristics of working hours and the risk of occupational injuries among hospital employees: a case-crossover study. Scand J Work Environ Health. 2020;46(6):570-578. doi:10.5271/sjweh.3905

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Received for publication: 29 January 2020

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DETAILS

Subject:	Shift work; Sleep; Commuting; Working conditions; Personal identification numbers; Injuries; Violence; Night shifts; Statistical analysis; Risk; Evening; Workers; Working hours; Confidence intervals; Morning; Leisure; Employees; Nighttime; Occupational safety; Regression analysis; Occupational health; Health risks
Business indexing term:	Subject: Shift work Personal identification numbers Workers Working hours Employees
Location:	United States--US; Finland
Publication title:	Scandinavian Journal of Work, Environment &Health; Stockholm
Volume:	46
Issue:	6
Pages:	570-578
Publication year:	2020
Publication date:	2020
Section:	Original article
Publisher:	Scandinavian Journal of Work, Environment &Health
Place of publication:	Stockholm
Country of publication:	Finland, Stockholm
Publication subject:	Occupational Health And Safety
ISSN:	03553140
e-ISSN:	1795990X

Source type:	Scholarly Journal
Language of publication:	English
Document type:	Journal Article
DOI:	https://doi.org/10.5271/sjweh.3905
ProQuest document ID:	2464655007
Document URL:	https://www.proquest.com/scholarly-journals/characteristics-working-hours-risk-occupational/docview/2464655007/se-2?accountid=211160
Copyright:	Copyright Scandinavian Journal of Work, Environment &Health 2020
Last updated:	2020-11-27
Database:	Public Health Database

Maternal occupational exposure and congenital heart defects in offspring

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ProQuest document link

ABSTRACT (ENGLISH)

Objectives Congenital heart defects (CHD) are the most prevalent congenital anomalies. This study aims to examine the association between maternal occupational exposures to organic and mineral dust, solvents, pesticides, and metal dust and fumes and CHD in the offspring, assessing several subgroups of CHD. Methods For this case-control study, we examined 1174 cases with CHD from EUROCAT Northern Netherlands and 5602 controls without congenital anomalies from the Lifelines cohort study. Information on maternal jobs held early in pregnancy was collected via self-administered questionnaires, and job titles were linked to occupational exposures using a job exposure matrix. Results An association was found between organic dust exposure and coarctation of aorta [adjusted odds ratio (OR_{adj}) 1.90, 95% confidence interval (CI) 1.01-3.59] and pulmonary (valve) stenosis in combination with ventricular septal defect (OR_{adj} 2.68, 95% CI 1.07-6.73). Mineral dust exposure was associated with increased risk of coarctation of aorta (OR_{adj} 2.94, 95% CI 1.21-7.13) and pulmonary valve stenosis (OR_{adj} 1.99, 95% CI 1.10-3.62). Exposure to metal dust and fumes was infrequent but was associated with CHD in general (OR_{adj} 2.40, 95% CI 1.09-5.30). Exposure to both mineral dust and metal dust and fumes was associated with septal defects (OR_{adj} 3.23, 95% CI 1.14-9.11). Any maternal occupational exposure was associated with a lower risk of aortic stenosis (ORadj 0.32, 95% CI 0.11-0.94). Conclusions Women should take preventive measures or avoid exposure to mineral and organic dust as well as metal dust and fumes early in pregnancy as this could possibly affect foetal heart development.

FULL TEXT

Headnote

Objectives Congenital heart defects (CHD) are the most prevalent congenital anomalies. This study aims to examine the association between maternal occupational exposures to organic and mineral dust, solvents, pesticides, and metal dust and fumes and CHD in the offspring, assessing several subgroups of CHD.

Methods For this case-control study, we examined 1174 cases with CHD from EUROCAT Northern Netherlands and 5602 controls without congenital anomalies from the Lifelines cohort study. Information on maternal jobs held early in pregnancy was collected via self-administered questionnaires, and job titles were linked to occupational exposures using a job exposure matrix.

Results An association was found between organic dust exposure and coarctation of aorta [adjusted odds ratio (OR_{adj}) 1.90, 95% confidence interval (CI) 1.01-3.59] and pulmonary (valve) stenosis in combination with ventricular septal defect (OR_{adj} 2.68, 95% CI 1.07-6.73). Mineral dust exposure was associated with increased risk of coarctation of aorta (OR_{adj} 2.94, 95% CI 1.21-7.13) and pulmonary valve stenosis (OR_{adj} 1.99, 95% CI 1.10-3.62). Exposure to metal dust and fumes was infrequent but was associated with CHD in general (OR_{adj} 2.40, 95% CI 1.09-5.30). Exposure to both mineral dust and metal dust and fumes was associated with septal defects (OR_{adj} 3.23, 95% CI 1.14-9.11). Any maternal occupational exposure was associated with a lower risk of aortic stenosis (ORadj 0.32, 95% CI 0.11-0.94).

Conclusions Women should take preventive measures or avoid exposure to mineral and organic dust as well as metal dust and fumes early in pregnancy as this could possibly affect foetal heart development.

Key terms maternal characteristic; maternal exposure; metal gas; metal fume; mineral dust; mother; organic dust; pesticide; solvent; work.

Congenital heart defects (CHD) are the most prevalent congenital anomalies. Approximately 7 per 1000 pregnancies are affected by a CHD (1). Of these, >90% are live births, ~8% of the pregnancies are terminated because of CHD, and 1-2% are still births (1). Since the introduction of prenatal ultrasound screening, ~50% of critical CHD cases are detected prenatally, and this number continues to increase with improvements in ultrasound technology, recommendations, and training for foetal heart examination (2). Survival rates are also increasing due to improved surgical intervention and intensive care (3). Major CHD have a significant impact on children's physical and mental health in the shortand long-term (4, 5), making it important to identify modifiable risk factors to prevent CHD in offspring.

Both genetic and environmental factors are involved in the development of CHD. Chromosomal anomalies are found in 12% of the infants with CHD (6), and an increasing number of gene point mutations have been identified that cause isolated non-syndromic CHD (7). Having first-degree family members with CHD or a multiple pregnancy increases the risk of CHD in offspring by 1-10% (8). In addition, certain maternal illnesses (eg, maternal diabetes, phenylketonuria, rubella infec tion), exposure to specific medications during pregnancy (eg, anticonvulsants and higher doses of lithium), and high maternal weight increase the risk of CHD in offspring (8, 9). Lifestyle factors such as parental smoking and alcohol use can also increase the risk of CHD (8-10), while periconceptional folic acid supplementation decreases this risk (11). Other risk factors include exposure to environmental agents such as ambient air pollution, chemicals, and metals (12, 13).

Exposure to potential teratogenic agents can occur in the workplace. A recent meta-analysis found an association between maternal occupational exposure to solvents and CHD (14). In this meta-analysis, it was not possible to examine subgroups of CHD since the majority of studies selected included small numbers of cases. However, it is important to assess subgroups of CHD as defects differ in etiology and develop during different stages of embryogenesis. The aim of the present study was to examine the association between various types of maternal occupational exposures early in pregnancy and subgroups of CHD in the offspring.

Methods

Study design

Cases were selected from the European Registration of Congenital Anomalies and Twins Northern Netherlands (EUROCAT NNL). This registry collects data of infants born with a congenital anomaly in the three northern provinces of The Netherlands. In addition to live-born infants (up to 10 years of age at notification), EUROCAT NNL registers stillbirths, miscarriages, and terminated pregnancies affected by a congenital anomaly. EUROCAT NNL identifies eligible cases by active case ascertainment using hospital records, prenatal diagnosis records, and postmortem records. After parents give informed consent, they are asked to complete a questionnaire. Information is collected regarding the pregnancy, obstetric and medical history, demographic characteristics, use of medication, and occupation and lifestyle factors early in pregnancy (15).

Controls without congenital anomalies (nonmalformed controls) were selected from the Lifelines cohort. Lifelines is a three-generation cohort study following 167 000 participants over a 30-year period in the same geographical region as EUROCAT NNL. Lifelines participants were recruited through their general practitioners, and participants (18-65 years old) were also asked to invite their offspring and parents in order to create a three-generation cohort. Participants' children could participate if they were between 6 months and 18 years old. Parents of participating children completed a questionnaire regarding the pregnancy, their health during pregnancy, childbirth, and the child's health in the first six months of life (16).

Case and control definition

CHD cases were coded by trained registry staff according to the International Classification of Diseases 9th revision (ICD-9) until 2001 and according to ICD 10th revision (ICD-10) from 2002 onwards, using international EUROCAT guidelines (17, 18). Cases with heterotaxy syndrome or an underlying genetic, chromosomal, or syndromic condition were excluded, resulting in the selection of 1922 CHD cases born 19972013 (figure 1). Mothers with missing job information (N=400) or without a job (N=260) were excluded to avoid healthy worker bias.

Three of the study authors classified the remaining cases according to the Botto classification to account for the diversity of cardiac phenotypes and underlying developmental mechanisms. The Botto classification has been described previously (19). Briefly, morphologically homogeneous groups were produced for each cardiac phenotype, based on anatomy and developmental and epidemiologic evidence. The seven main heart defect groups were: conotruncal heart defects, atrioventricular septal defects (AVSD), anomalous pulmonary venous return (APVR), left ventricular outflow tract obstruction (LVOTO), right ventricular outflow tract obstruction (RVOTO), septal defects, and complex heart defects. A few cardiac malformations are not included in the Botto classification. In line with the classification described by Riehle-Collarusso and colleagues (20), cases with a bicuspid aorta valve were classified as LVOTO anomaly and cases with a vascular ring (vascular rings/slings, double aortic arch, right descending aortic arch, aberrant left subclavian artery, or pulmonary artery sling) were classified as conotruncal defects. Cases were excluded if they could not be classified (eg, coronary artery malformations, N=52) or constituted isolated patent ductus arteriosus (N=24). Additionally, CHD were classified as isolated defect (only the heart is affected) or as multiple defect (presence of cardiac and extra-cardiac malformations). Cases were also classified by the complexity of their cardiac phenotype: simple (anatomically discrete or well-recognized single entities), association (common, uncomplicated combinations of heart defects), and complex malformations (those not described as simple or association). If multiple siblings were affected by a CHD, one infant per family was randomly selected to avoid genetic correlation, resulting in exclusion of 12 cases. Overall, 1174 infants with CHD were included; 85.4% of these infants were live-born, 10.6% were live-born but died after birth, 2.6% were terminated pregnancies, 1.1% were stillborn infants, and 0.3% were miscarriages.

All participants from the Lifelines cohort bom 1997- 2013 (same years as the EUROCAT NNL cases) were selected as controls (N=12 494, figure 2). Only infants of which the biological mother was a Lifelines participant were included (N=12 331). We excluded 814 infants because one or more congenital anomalies were reported or information on congenital anomalies was missing. As with cases, mothers without a job or missing job information were excluded (N=3029) and only one infant per family was selected, resulting in exclusion of another 2886 infants. In total, 5602 children without congenital anomalies were included as the control group.

Exposure assessment

Two authors coded the mother's description of her job early in pregnancy using the International Standard Classification of Occupations 1988 (ISCO88) (21), without knowledge of case or study details. To translate ISCO88 codes into occupational exposure, the ALOHA+ job exposure matrix (JEM) was used. Occupational exposure was assigned based on six categories: organic and mineral dust, solvents, pesticides, metal dust and fumes, and gases and fumes. Those categories were combined into one category which is referred to as "any" exposure. All women exposed to one or more exposure categories were labelled as exposed to any exposure. This JEM assigns exposure intensity in three categories (no, low, and high exposure). Because "high" (intensity and probability) exposure did not occur often, the categories "low" and "high" were combined into "exposed". The ALOHA+ JEM is specifically built for use in general population studies (22, 23). However, in our female study population, there was a strong correlation of exposure to solvents with exposure to gases and fumes and to organic dust with gases and fumes (Spearman's rank correlation coefficient = 0.75 and 0.80, respectively). Therefore, the association of gases and fumes with CHD was not analyzed.

Statistical analysis

Baseline characteristics of mothers and infants were tabulated, and differences between cases and controls were tested for significance using Chi-square tests. The following covariates were assessed: child sex (male/ female), birth year (1997-2000, 2001-2004, 2005-2008, or 2009-2013), maternal age at delivery (15-19, 20-24, 25-29, 30-34, 35-39, or >40 years old), maternal body mass index (BMI) (self-reported pre-pregnancy weight and height for EUROCAT NNL cases and objective measurement at baseline visit for Lifelines controls) [underweight (<18.5 kg/m2), normal (18.5-24.9 kg/m2), overweight (25.0-29.9 kg/m2), or obese (>30 kg/m2)], maternal education level [low (primary school, lower vocational education, pre-vocational education), middle (secondary vocational education, general secondary education or pre-university education), or high (higher professional education or academic education)], maternal smoking and alcohol use, folic acid use (no/not during periconceptional period, yes/sometime during periconceptional period), and fertility problems [no, yes (selfreported fertility problems and/or fertility treatment)].

The association between maternal occupational exposure early in pregnancy and CHD was assessed using univariate and multivariate logistic regression analysis to estimate crude and adjusted odd ratios (ORcrude/ORadj). The multivariate logistic regression associations were adjusted for child sex, maternal age at delivery, maternal educational level, maternal BMI, smoking and alcohol use during pregnancy, folic acid supplementation, and fertility problems, based on Chi-square tests (table 1). Although the correlation between exposure to mineral dust and exposure to metal dust and fumes was negligible (Spearman's rank correlation coefficient = 0.08), exposure to metal dust and fumes contributes to mineral dust exposure. Consequently, additional analyses were performed with a combination of those exposures. Stratified analyses were performed for cases with isolated and multiple defects. In addition, a sensitivity analysis restricted to non-smoking mothers who did not report drinking alcohol early in pregnancy was performed to explore the effect of information bias introduced by selecting cases from EUROCAT NNL and controls from the Lifelines cohort. An exposure-response analysis was conducted for maternal occupational exposure and CHD in general. If <5 infants were exposed, data was not presented and OR were not estimated.

Results

Baseline characteristics differed between cases and controls (table 1). Infants born with a CHD were more often boys. Mothers of case infants had a lower maternal age at delivery, lower educational level, and lower BMI. As expected, they were also more likely to smoke or consume alcohol, used folic acid supplements less often, and had more fertility problems compared to mothers of controls.

In total, 37.6% of CHD infants and 35.6% of the control infants were exposed to any of the maternal occupational exposures early in pregnancy (table 2), and no association was found between any exposure and CHD in general. When examining any exposure and specific groups of CHD, we found an association for pulmonary (valve) stenosis in combination with ventricular septal defect (VSD) (ORadj 3.06, 95% CI 1.20-7.81). However, any exposure is also associated with a lower risk of aortic stenosis (ORadj 0.32, 95% CI 0.11-0.94).

When analyzing specific exposures, the most prevalent maternal occupational exposure was to organic dust, with approximately 30% of women exposed. Associations were found between organic dust exposure and coarctation of aorta (ORadj 1.90, 95% CI 1.01-3.59) and pulmonary (valve) stenosis in combination with VSD (ORadj 2.68, 95% CI 1.07-6.73). Mineral dust exposure was less common (10% of cases and 8% of controls) and was associated with CHD in general (ORadj 1.29, 95% CI 1.01-1.64). When analyzing mineral dust exposure in relation to specific CHD, we found an association with LVOTO defects (ORadj 1.75, 95% CI 1.06-2.89), particularly coarctation of the aorta (ORadj 2.94, 95% CI 1.21-7.13), and with RVOTO defects, especially pulmonary (valve) stenosis (ORadj 1.99, 95% CI 1.10-3.62). Approximately 25% of mothers were exposed to solvents and 2-3% to pesticides, but no associations between exposure to solvents or pesticides and CHD were found. Although the prevalence of exposure to metal dust and fumes was only 0.4% for controls and 1% for cases, we did observe an association between this exposure and CHD in general (ORadj 2.40, 95% CI 1.09-5.30). When mothers were exposed to mineral dust and metal dust and fumes, the association with CHD in general became stronger compared to exposure to mineral dust or metal dust and fumes alone (ORadj 2.92, 95% CI 1.23-6.92), and an association with septal defects was found (ORadj 3.23, 95% CI 1.14-9.11) (supplementary material, www.sjweh.fi/show_abstract. php?abstract_id=3912, table S1).

Stratified analysis by isolated and multiple defects included 1009 cases with isolated CHD and 165 cases with CHD and extra-cardiac malformations. The ORadj for isolated CHD were comparable to the total group of CHD (supplementary table S2). One additional association was observed when only isolated defects were included: exposure to metal dust and fumes was associated with septal defects (ORadj 3.06, 95% CI 1.14-8.23). The ORadj for multiple defects that include CHD showed no association for any of the exposures (supplementary table S3). Only a small number of cases were included in the stratified analyses for multiple defects, and most ORadj were not estimated due to sparse outcome and exposure data.

The analyses restricted to non-smoking mothers who did not report drinking alcohol early in pregnancy to explore the effect of information bias included 703 cases and 4622 controls (supplementary table S4), and the association between maternal occupational exposure to mineral dust and LVOTO anomalies was not observed. Due to few data it was not possible to explore specific subgroups of LVOTO anomalies in this sensitivity analysis.

An exposure-response analysis was performed for any exposure and CHD in general. The ORadj appeared to be non-significant but higher in the high exposure group only (ORadj 1.37, 95% CI 0.97-1.94; supplementary table S5).

Discussion

This study showed that infants with specific CHD were more likely to be exposed in utero to organic and mineral dust and metal dust and fumes at the workplace of mother compared with infants without malformations. Exposure to organic dust was associated with a two-fold increased risk of coarctation of aorta and a three-fold increased risk of pulmonary (valve) stenosis in combination with VSD. Organic dust includes exposure to smaller particles such as fungal and bacterial spores/ cells, pollen, viruses, or fragments of larger organisms including cotton and wood dust, flour, textile and paper fibers. All mothers exposed to organic dust were considered to be relatively low exposed. Almost two thirds of these women worked in health or personal care, another 15% worked as cleaners and 13% worked in agriculture or the food industry. Mineral dust exposure was associated with a two-fold increase in LVOTO defects in offspring, specifically coarctation of the aorta. Exposure to mineral dust exposure was also associated with a two-fold risk of RVOTO defects, specifically pulmonary (valve) stenosis. Mineral dusts are aerosols originating from minerals, such as from the soil, (nonfibrous) silica dusts, and coal. Of the 12% of women high exposed to mineral dust, 90% were working in agriculture/horticulture. Of the low-exposed women, 50% worked as cleaners and the rest in various jobs such as metal, electronics, plastics production and dairy and livestock production. Exposure to metal dust and fumes was associated with a two-fold increase of CHD in general. However, this result has to be interpreted carefully as only 1% of the women, mostly those working as machine and instrument operators/repairers, were occupationally exposed to metal dust and fumes. Exposure to mineral dust in combination with metal dust and fumes was associated with a three-fold increased risk of septal defects. We also found that infants affected by aortic stenosis were less likely to be exposed to any maternal occupational exposure compared to non-malformed controls. However, only five cases with aortic stenosis were included, and analyses for specific subgroups of exposure could not be performed. No specific job association was identified.

During their work, mothers may inhale mineral, metal or organic aerosols, which can pass through the lungs into the blood. These agents might consequently cross the placental barrier and have been found at the foetal side of the placenta (24). Occupational exposures - including to several organic, mineral, and metal compoundscan induce oxidative stress, which may induce teratogenesis via misregulation of critical pathways involved in foetal development (25).

Although the association between metal dust and fumes and CHD/isolated septal defects has to be interpreted with caution, previous studies have found increased risks. One study found an association between exposure to metals and specific septal defects (26). Two other studies showed that maternal occupational exposure to mineral oils, which are often used in the metal industry, increased the risk of isolated septal defects (27) and coarctation of the aorta (28). Another study using comparable methods did not show this association, but these estimates could have been imprecise as this study included less than five exposed cases (28). To our knowledge, no studies specifically examining organic or mineral dust have been reported.

Our results did not confirm the association between occupational exposure to solvents and CHD reported by a meta-analysis using similar occupational exposure assessment methods (14). It is possible that the difference is explained by the diversity of CHD included in the metaanalysis. One previous study assessing solvent exposure and specific types of CHD also showed no association (29), but another study found an association with peri membranous VSD and aorta stenosis (30). Our results on maternal occupational exposure to pesticides are in line with the meta-analysis, which also found no association with CHD (14). One previous study found an association between pesticide exposure and specific CHD, such as RVOTO defects, hypoplastic left heart syndrome, and tetralogy of Fallot (31). Unfortunately, our sample size was too limited to analyze these specific CHD.

Limitations

Occupational exposure assessment using the ALOHA+ JEM is done at job level, which could have resulted in misclassification of exposure. Circumstances at the workplace are often unpredictable and can vary within jobs, between workplaces and over time. It is also possible that women avoided certain exposures because they wanted to become pregnant or knew they were pregnant while performing a job that would normally come with these exposures. The limited number of exposed women could have resulted in high OR with large CI and restricted our ability to explore exposureresponse associations.

Because EUROCAT NNL does not collect data on non-malformed controls, controls were selected from Lifelines, and this approach introduced several limitations. EUROCAT NNL aims to investigate the prevalence and risk factors for congenital anomalies, and its questionnaire is focused specifically on risk factors for congenital anomalies. Lifelines collects data to obtain insight into healthy ageing, and specifically for children on neonatal and childhood diseases. Consequently, the Lifelines questionnaire includes items on a wide variety of risk factors. These differences could introduce information bias during assessment of the covariates. We assume that bias was not introduced for maternal occupational exposure as mothers were asked to report a description of their job early in pregnancy in both questionnaires, and recall bias is limited for self-reported jobs (32). After exploration of the effect of information bias in a sensitivity analysis, it seems that the effect of information bias is limited as only the association between maternal occupational exposure to mineral dust and LVOTO anomalies was no longer observed. Additionally, residual confounding due to maternal diabetes, paternal smoking, environmental exposures, or other occupational factors not covered by the ALOHA+ JEM could have been introduced since information regarding those risk factors was lacking.

Another major concern of using Lifelines is selection bias. Previous studies showed that some groups of individuals, for example those with a low socioeconomic status, are less likely to participate in population-based cohort studies

(33, 34). However, Lifelines is known to be representative of the population in the northern Netherlands, indicating selection bias might be low (35).

Strengths

A major strength of this study is the high quality of data from EUROCAT NNL, which registers detailed medical information for each case. Anomalies were coded by trained registry staff according to international coding guidelines (18). Case classification was performed under supervision of an experienced clinical geneticist and a pediatric cardiologist. Use of the Botto classification made it possible to create homogenous groups of CHD based on anatomy and developmental and epidemiological evidence (19). Another strength is that EUROCAT identifies eligible cases by active case ascertainment using various sources in the catchment area, and ~72% of the parents of a child affected by a CHD agreed to participate and responded to the questionnaire. A major strength of the JEM approach is that it limits the effect of recall bias on exposure status as well as differential misclassification of exposure when compared to selfreported exposure (22, 36).

Concluding remarks

This large population-based case-control study showed that maternal occupational exposure to organic dust, mineral dust, and metal dust and fumes early in pregnancy could possibly affect the development of the foetal heart. These exposures, with a prevalence of 1-30% at the workplace, were associated with a two- to threefold increase in LVOTO, RVOTO, and septal defects in this study. Despite the limitations of this study, women should be careful if they are exposed at work to mineral and organic dusts and metal dust and fumes in the months before and early in pregnancy.

Acknowledgement

We thank all those who are involved in providing and processing information to EUROCAT NNL, including the affected families, clinicians, health professionals, and registry staff. We wish to acknowledge the services of the Lifelines cohort study, the contributing research centers delivering data to Lifelines, and all the study participants. We thank Kate McIntyre of the University of Groningen, University Medical Center Groningen (UMCG), for editorial assistance.

Funding

Nynke Spinder was paid by the Graduate School of Medical Sciences (MD/PhD program), UMCG, Groningen, The Netherlands. EUROCAT NNL is funded by the Dutch Ministry of Health, Welfare and Sports. The Lifelines Biobank initiative has been made possible by funding from the Dutch Ministry of Health, Welfare and Sport, the Dutch Ministry of Economic Affairs, UMCG The Netherlands, University Groningen and the northern provinces of the Netherlands. The funding sources had no involvement in study design; analysis or interpretation of data; writing or submission of the manuscript.

Competing Interests

The authors report no conflicts of interest.

Protection of research participants

EUROCAT NNL and Lifelines operate within the scope of the Dutch Data Protection Act, according to the principles of the Declaration of Helsinki and in accordance with the research code of the UMCG, The Netherlands, and the Code of Good conduct. EUROCAT NNL did not require ethics committee approval to collect and store data according to the medical ethical committee of the UMCG in line with the act Medical Research involving Human Subjects. The medical ethical committee of the UMCG approved Lifelines. All parents and participants of EUROCAT NNL and Lifelines give informed consent before participation.

Sidebar

Spinder N, Bergman JEH, Kromhout H, Vermeulen R, Corsten-Janssen N, Boezen HM, du Marchie Sarvaas GJ, de Wall HEK. Maternal occupational exposure and congenital heart defects in offspring. Scand J Work Environ Health. 2020;46(6):599608. doi:10.5271/sjweh.3912

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Received for publication: 28 April 2020

DETAILS

Subject:	Pesticides; Pregnancy; Dust; Aorta; Defects; Heart; Fumes; Metals; Stenosis; Questionnaires; Families &family life; Miscarriage; Congenital defects; Offspring; Confidence intervals; Subgroups; Occupational exposure; Solvents; Coronary vessels; Exposure; Congenital anomalies; Classification; Occupational health; Veins &arteries; Ventricle; Pulmonary arteries; Ultrasonic imaging; Aortic stenosis
Location:	Netherlands
Publication title:	Scandinavian Journal of Work, Environment &Health; Stockholm
Volume:	46
Issue:	6
Pages:	599-608
Publication year:	2020
Publication date:	2020
Section:	Original article
Publisher:	Scandinavian Journal of Work, Environment &Health
Place of publication:	Stockholm
Country of publication:	Finland, Stockholm
Publication subject:	Occupational Health And Safety
ISSN:	03553140
e-ISSN:	1795990X
Source type:	Scholarly Journal
Language of publication:	English

Document type:	Journal Article
DOI:	https ://doi.org/10.5271/sjweh.3912
ProQuest document ID:	2464654645
Document URL:	https://www.proquest.com/scholarly-journals/maternal-occupational-exposure-congenital-heart/docview/2464654645/se-2?accountid=211160
Copyright:	Copyright Scandinavian Journal of Work, Environment &Health 2020
Last updated:	2023-06-27
Database:	Public Health Database

Causal inference and evidence-based recommendations in occupational health and safety research

Anonymous

ABSTRACT (ENGLISH)

In a recent editorial, British researchers concluded that, due to heterogeneity of shift working in longitudinal studies, it is too difficult to draw a firm conclusion about the risk of breast cancer, let alone about an exposure threshold for night shift work (2). Recently, a large-scale RCT found no effect of vitamin D intake on reduced risk of depression (8), despite numerous observational studies suggesting such an effect (9). [...]there are good reasons to treat results from observational studies with caution. The recommendation to stop asbestos production, which rather came too late than too early, was not based on RCT but observational studies on the multiple health-hazardous effects of asbestos (11). [...]when considering the evidence, researchers should not only consider the best evidence based on available data and their causal inference, but also the potential consequences of continuing current practice. Regarding single observational studies, VanderWeele lists eight considerations that increase confidence in the estimate, including longitudinal design; the quality of the assessment of exposure, outcome and confounders; flexible statistical modeling examining robustness to modelling decisions; and attempts to address unmeasured confounding.

FULL TEXT

In this issue of the Journal, a group of distinguished Nordic researchers, led by Anne Helene Garde and including four of our Associated Editors, present a discussion paper that originated from a workshop and provides detailed recommendations on night shift work (1). The recommendations are very clear: to protect workers' health, night shift schedules should have: (i) <3 consecutive night shifts; (ii) shift intervals of >11 hours; and (iii) <9 hours shift duration. For pregnant women, night work should be limited to one shift per week. The authors acknowledge that

under circumstances allowing better possibilities for daytime sleep, recommendations could be different.
The discussion paper is remarkable in that it provides clear and strong recommendations based on what the authors themselves call a "limited literature", thus a limited scientific evidence on the risk of shift work for cancer and other health and safety risks. In a recent editorial, British researchers concluded that, due to heterogeneity of shift working in longitudinal studies, it is too difficult to draw a firm conclusion about the risk of breast cancer, let alone about an exposure threshold for night shift work (2). Yet, both Nordic and British researchers seemed to agree that we should not postpone recommendations on best practice in shift work scheduling for reasons of lack of certainty on causal inference.
For the most important health and safety conditions the Nordic authors are concerned with - cancer, cardio-vascular disease, diabetes, injuries and pregnancy-related outcomes - the evidence relies on observational studies. Although longitudinal studies on shift work increasingly use register-based exposure information on working hours patterns, often based on payroll data that is linked with registers in healthcare (3, 4), these studies are still vulnerable to important biases, such as selection bias and residual confounding. There are several examples in the literature of well-conducted observational studies suggesting an effect of an exposure that subsequently was not corroborated in randomized controlled trials (RCT). One of the most famous examples is hormone replacement therapy (HRT) in post-menopausal women. Numerous observational studies suggested a protected effect of HRT with regard to risk of cardiovascular disease (5, 6), but when an RCT was finally conducted, it found the effect of HRT to be more harmful than beneficial (7). Recently, a large-scale RCT found no effect of vitamin D intake on reduced risk of depression (8), despite numerous observational studies suggesting such an effect (9). Thus, there are good reasons to treat results from observational studies with caution.
On the other hand, exercising caution does not mean that one should abstain from making recommendations when evidence is based on observational studies only, in the hope that this would keep one on the safe side of scientific scrutiny. There is no safe side. In accordance with Paul Watzlawick's famous quote that "one cannot not communicate" (10), it can be reasoned that not making recommendations is also a form of recommendation, the recommendation to continue business as usual. The recommendation to stop asbestos production, which rather came too late than too early, was not based on RCT but observational studies on the multiple health-hazardous effects of asbestos (11). Thus, when considering the evidence, researchers should not only consider the best evidence based on available data and their causal inference, but also the potential consequences of continuing current practice.
Fifty-five years ago, Sir Austin Bradford Hill published his famous nine viewpoints on causal inference in health research (12). As pointed out by Bradford Hill, as well as other scholars (13), none of the nine viewpoints (today mostly known as "criteria") ensures that an observed observation is causal, however, they still might be helpful in assessing the confidence whether or not a measure of association indicates a causal link between two variables. Today, causal inference remains an intensively discussed topic. In its December 2016 issue, the International Journal of Epidemiology published a series of articles, discussion papers and letters on causal inference in epidemiology, in particular on the merits and limitations of the counterfactual "potential outcome approach", which relies heavily on experiments whether induced by the researcher or natural changes in particular situations that may be interpreted as happening at random (14, 15). This approach has been criticized by proponents of a more "pluralistic approach" for a variety of reasons, among others that it limits causality to particular factors that are usually not widely generalizable (16, 17). Very recently (September 2020), in an opinion paper (18), the main proponent of the potential outcome approach, Tyler VanderWeele asked: "Can sophisticated study designs with regression analyses of observational data provide causal inferences?" The answer seem to be a cautious "yes". Regarding single observational studies, VanderWeele lists eight considerations that increase confidence in the estimate, including longitudinal design; the quality of the assessment of exposure, outcome and confounders; flexible statistical modeling examining robustness to modelling decisions; and attempts to address unmeasured confounding. Evidence then may evolve from accumulation of results from multiple high-quality studies, in particular if these have different designs that are subject to different biases (18).

The struggle on causal interpretation and subsequent evidence-based recommendations is also visible in the GRADE (Grading of Recommendations, Assessments and Evaluations) system, which rates the certainty of evidence and the strengths of recommendations in systematic reviews, for example in Scandinavian Journal of Work, Environment and Health articles (19-22). As GRADE has its origins in healthcare evaluation, its evidence assessment favors the RCT, and although the GRADE working group encourages applying GRADE to observational studies (23), the quality rating of observational studies always starts with "low quality", with possibilities for upgrading and downgrading, whereas the quality rating of RCT starts with "high quality". The recently developed "Navigation Guide" (24) - a methodology for synthesizing evidence in systematic reviews that evolved from environmental research but is now also applied in occupational health research (25, 26) - recommends a different approach, where the quality assessment of observational studies starts with "moderate" before the process of up- or downgrading (24).

The paper by Garde et al (1) is not a systematic review, it uses neither GRADE nor Navigation Guide methodology and does not grade the evidence. It is a discussion paper written by leading researchers in the field that base their conclusions and recommendations on their knowledge of the literature, including systematic reviews. Given that a substantial proportion of the workforce is exposed to some type of night shift work, this is a bold, but necessary, step. We are looking forward to further research, both original studies and reviews, corroborating or challenging the conclusions and recommendations of this discussion paper.

Sidebar

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DETAILS

Subject:	Shift work; Asbestos; Womens health; Risk management; Longitudinal studies; Breast cancer; Night shifts; Exposure; Vitamin D; Heterogeneity; Quality assessment; Inference; Cardiovascular disease; Occupational health; Confidence; Occupational safety; Mental depression; Statistical models; Risk reduction; Mathematical models; Health risks; Correlation analysis; Safety research
Business indexing term:	Subject: Shift work
Location:	Denmark
Publication title:	Scandinavian Journal of Work, Environment &Health; Stockholm
Volume:	46
Issue:	6
Pages:	554-556
Publication year:	2020
Publication date:	2020
Section:	Editorial
Publisher:	Scandinavian Journal of Work, Environment &Health
Place of publication:	Stockholm
Country of publication:	Finland, Stockholm
Publication subject:	Occupational Health And Safety
ISSN:	03553140
e-ISSN:	1795990X
Source type:	Scholarly Journal
Language of publication:	English
Document type:	Editorial
DOI:	https://doi.org/10.5271/sjweh.3929
ProQuest document ID:	2464654567
Document URL:	https://www.proquest.com/scholarly-journals/causal-inference-evidence-based-recommendations/docview/2464654567/se-2?accountid=211160

Upper-extremity musculoskeletal disorders: how many cases can be prevented? Estimates from the COSALI cohort

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ABSTRACT (ENGLISH)

Objective This study aimed to estimate the proportion and number of incident upper-extremity musculoskeletal disorders (UEMSD) cases attributable to occupational risk factors in a working population. Methods Between 2002-2005, occupational physicians randomly selected 3710 workers, aged 20-59, from the Pays de la Loire (PdL) region. All participants underwent a standardized clinical examination. Between 2007-2010, 1611 workers were re-examined. This study included 1246 workers who were free of six main clinically diagnosed UEMSD at baseline but were diagnosed with at least one of these UEMSD at follow-up [59% of men, mean age: 38 (standard deviation 8.6) years]. Relative risks and population-attributable fractions (PAF) were calculated using Cox multivariable models with equal follow-up time and robust variance. The total number of incident UEMSD in the PdL region was estimated after adjustment of the sample weights using 2007 census data. The estimated number of potentially avoidable UEMSD was calculated by multiplying PAF by the total number of incident UEMSD in PdL. Results At follow-up, 139 new cases of UEMSD (11% of the study sample) were diagnosed. This represented an estimated 129 320 incident cases in the PdL in 2007. Following adjustment for personal factors, 26 381 (20.4% of all incident UEMSD) were attributable to high physical exertion, 16 682 (12.9%) to low social support, and 8535 (6.6%) to working with arms above shoulder level. Conclusions A large number and important proportion of incident UEMSD may be preventable by reducing work exposures to physical exertion and working with arms above shoulder level as well as improving social support from co-workers/supervisors.

FULL TEXT

Headnote

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Conclusions A large number and important proportion of incident UEMSD may be preventable by reducing work exposures to physical exertion and working with arms above shoulder level as well as improving social support from co-workers/supervisors.
Key terms cohort study; France; MSD; musculoskeletal disease; occupational risk factor; physical exertion; preventable case; prevention.
(ProQuest: ... denotes formulae omited.)
Upper-extremity musculoskeletal disorders (UEMSD) are among the leading causes of morbidity and work disability in the working population of industrialized and developing countries (1, 2). Today, these disorders are a major concern for occupational and public health due to the considerable human, social and occupational costs (2-4). According to Eurostat, MSD account for almost 60% of work-related problems and are, therefore, the main work-related disease in the European Union (5). In France, according to 2018 social health insurance data, UEMSD accounted for 80% (39 555 cases) of all occupational diseases (6).
Numerous epidemiologic studies in working populations have identified a wide range of personal and work-related risk factors associated with UEMSD (7-12). While some personal attributes (eg, age) cannot be modified by preventive or medical interventions, exposure to work-related factors can potentially be modified by workplace-based interventions (13-15). In order to target and prioritize risk factors for more effective interventions in the workplace, it would be useful to quantify the proportion and number of UEMSD cases that could be prevented if exposure to these factors were reduced to levels that minimize the risk of UEMSD. Such information may provide an estimate of the theoretically maximum potential impact of preventive programs in the workplace (16). Identifying the occupational risk factors of UEMSD with the greatest impact may help public health practitioners and policy-makers prioritize interventions that reduce exposure to these factors (17).
At the population level, the effect of a risk factor on a disease can be quantified by the computation of the population attributable fraction (PAF) by taking into account both the strength of the association between a risk factor and a disease and the prevalence of that risk factor within the population (18). Thus, the PAF provides an estimate of the proportion of cases that would not have occurred if the exposure to a risk factor was reduced or eliminated (19); and it is therefore relevant to decision-making in public health.
Although there is extensive literature providing evidence of the associations between UEMSD and exposures in the workplace, few studies have assessed the PAF in the general working population (20-25) and specifically exposed populations (26-28). Moreover, none of these studies has estimated the number of incident UEMSD cases attributable to occupational risk factors. Identifying potential modifiable risk factors that preventive interventions could target to avert the greatest number of cases would improve the prevention of UEMSD in the working population. Consequently, the objective of this study was to estimate, using the multivariable model we previously obtained (29), the proportion and number of incident UEMSD cases attributable to occupational risk factors in the working population of the French region of Pays de la Loire (PdL).
Methods

Study population

We used data from the COSALI cohort, a prospective study of MSD and their risk factors in the working population based on two successive surveys of workers from the PdL region (30, 31). The region accounts for about 6% of the French working population and its diversified socioeconomic structure is similar to that of France as a whole (30). Between 2002-2005, 83 occupational physicians (OP) (18% of OP in the region) volunteered to take part in the study. They selected 3710 workers (2161 men, 1549 women) at random (out of 184 600 under the surveillance of the 83 OP, 2.0%). More than 90% of the selected workers participated in this study (<10%: no shows, refusals, duplications). Women were slightly underrepresented in the sample (42% versus 47% in the region, P<0.001). Overall, the distribution of occupations in the sample was close to that of the regional workforce, except for the occupations not surveyed by OP (eg, farmers, shopkeepers, and selfemployed workers). Data on personal characteristics and working conditions were collected by a selfadministered questionnaire. The OP conducted a clinical examination of the participants using a standardized clinical protocol that strictly applied the methodology and clinical tests of the European consensus criteria to diagnose work-related UEMSD (WRUEMSD) (32). Each participating OP in charge of medical surveillance of salaried workers received guidelines describing the clinical protocol (including diagnostic criteria charts and photographs of clinical tests) and underwent a 3-hour training program to standardize clinical examinations. Between 2007-2010, the OP re-examined 1611 workers using the same procedure as the initial assessment [see (30, 31) for more details about the COSALI cohort].

This study received approval from France's Advisory Committee on the Processing of Information in Health Research ("CCTIRS") and the National Committee for Data Protection ("CNIL"), initially in 2001 and again in 2006. Each worker provided written informed consent prior to participation.

For the present study, 1228 of the workers included at baseline did not participate in the follow-up due to death, retirement, parental leave, long-term sick leave, unemployment, etc. Of the remaining 2482 participants, 23 refused to participate and 848 workers did not undergo the second clinical examination because they had no mandatory examination scheduled during the follow-up period. A comparison of baseline characteristics of workers who attended a follow-up (ie, second clinical examination) and workers who did not attend was described previously (29) and demonstrated that workers who did not attend a follow-up were significantly more likely to be younger, temporary workers or individuals with a short length of service at baseline.

Among the 1611 participants with a standardized clinical examination at follow-up, 226 had at least one UEMSD at baseline and were excluded from the present study. Out of the 1385 eligible participants, ie, free of UEMSD at baseline, 110 workers with missing data for exposure or UEMSD were excluded (figure 1). In addition, 29 workers were excluded in order to standardize the auxiliary variables data between the sample and the external source, ie, the 2007 French population census data of the PdL region, before applying the weighting method (the calibration approach). After exclusions among eligible participants, the final study sample for current analyses consisted of 1246 participants.

Outcome definition

Incident cases of UEMSD were defined as workers free of the six main clinically diagnosed UEMSD at baseline but who met the criteria for at least one of the disorders at follow-up. This definition was based on the European consensus criteria to diagnose WRUEMSD for health surveillance or epidemiologic studies (32). This consensus is intended to facilitate more consistent collection, recording and reporting of information on WRUEMSD across the European Union by providing evidence-based or consensus-based case definitions and criteria for their identification and categorization. The six main diagnosed UEMSD were: (i) rotator cuff syndrome, (ii) lateral epicondylar tendinopathy, (iii) carpal tunnel syndrome (CTS), (iv) ulnar tunnel syndrome, (v) flexor-extensor peritendinitis or tenosynovitis of the forearm-wrist region, and (vi) De Quervain's tenosynovitis. Details regarding measurement of these disorders have been previously described (31).

UEMSD risk factors

Only baseline factors retained as independent risk factors of UEMSD that were previously in the same sample (29) were assessed in this study.

Personal factors included sex, age divided into three categories (<35, 35-44 and >45 years) and overweight/ obesity [body mass index (BMI) >25.0 kg/m2 (33)].
Work-related biomechanical factors [assessed using the European consensus criteria (32)] included: high repetitiveness of tasks (>4 hours/day); repeated/ sustained posture with arms above shoulder level (>2 hours/day); repeated/sustained elbow movements (flexion/extension) (>2 hours/day); and wrist twisting movements (>2 hours/day). Concerning the exposure "repeated/sustained shoulder abduction", workers who responded "rarely (<2 hours/day)", "often (2-4 hours/ day)" or "always (>4 hours/day)" were defined as being at risk of this posture (30). The questionnaire presented awkward postures in picture form to facilitate workers' understanding and thus increase the validity of posture self-assessment (34). The perceived physical exertion was evaluated using the Borg Rating Perceived Exertion (RPE) scale (35), ranging from 6 (no exertion at all) to 20 (maximal exertion). RPE was dichotomized using the threshold (Borg RPE scale >13) proposed by the French National Research and Safety Institute for the Prevention of Occupational Accidents and Diseases (INRS cut-offs) (36).
Work-related psychosocial factors - high psychological demands and low social support - were assessed using the 26 items of the French version of the Karasek Job Content Questionnaire (JCQ) (37). Scores were dichotomized using the median values of the French national SUMER study to classify exposed and unexposed workers (38).
Statistical analysis
Analyses were conducted for the entire cohort, and a sex-stratified analysis was also performed to account for possible sex differences in occupational exposures (39, 40).
Assessment of risk factors and population-attributable fraction (PAF) estimate in the COSALI cohort
Using a Cox multivariable regression model with constant follow-up time for each subject and robust variance (41), relative risks (RR) and their 95% confidence intervals (CI) were estimated for incident UEMSD occupational risk factors after adjustment for personal risk factors (age, sex, and BMI) in the COSALI cohort.
To quantify the proportion of UEMSD incident cases attributable to each risk factor, PAF were estimated for each risk factor in the multivariable model in addition to a combined PAF of all occupational factors. Point estimates and 95% CI of the PAF were calculated using the method described by Spiegelman et al (42). The PAF estimate accounted for the prevalence of the exposure and RR of UEMSD risk associated with that exposure (42):
...
where t denotes a stratum of unique combinations of levels of all background risk factors which are not under study, t=1;...; T, and RR2t is the relative risk in combination t relative to the lowest risk level, where RR(2,t)=1. s indicates an index exposure group defined by each of the unique combinations of the levels of the index risk factors, that is, those risk factors to which the PAFapplies, s=1;...; S, and RR1s is the relative risk corresponding to combinations relative to the lowest risk combination RR11=1. The joint prevalence of exposure group s and stratum t is denoted by pst, and ...
The calculation of PAF is recommended for multifactorial diseases when some risk factors are unmodifiable or not expected to change after intervention (43). To facilitate the comprehension and interpretation of the PAF estimate, the lower limit of its 95% CI was set to zero when this lower limit was negative.
Estimated number of incident UEMSD attributable to occupational risk factors
To estimate the number of incident cases of UEMSD attributable to occupational risk factors in the PdL region, the calculation procedure was implemented in two steps. First, the study sample was weighted to provide estimates of incident UEMSD cases which were representative of the PdL working population, using data from the 2007 population census of the PdL region [conducted by the French National Institute of Statistics and Economic Studies (INSEE)]. A calibration on margins, proposed by Deville et al (44, 45), was used to take the characteristics of the PdL working population into account. The new weights were calculated using the following auxiliary variables (also called calibration variables): age, sex, occupational class and economic sector. These auxiliary variables were measured in both the COSALI cohort and the 2007 French population census, ie, their population distribution was known, and were correlated with the variable of interest, ie, incident UEMSD (according to Spearman's correlation test). The "linear" calibration method was used to calculate the new weights from the "Calmar" macro (calibration on

margins) developed by Sautory (46). With the calibration method, weights are assigned to all survey respondents in order to make the sample as representative as possible of the (inference) population. Over-represented groups then had a small weight and under-represented groups a large weight. The weighted sample (ie, with the new weights) is more representative of the working population of the PdL region, resulting in estimates with a lower bias than those that are unweighted. Furthermore, through the calibration method, potential improvements in the accuracy of the estimates can be expected (47).

At the second step, the estimated number of incident cases of UEMSD (and the variation range) attributable to risk factor was obtained by multiplying the PAF (and the 95% CI) by the projected number of incident UEMSD in the PdL region in 2007.

All statistical analyses were performed using the SAS software, version 9.4 (SAS Institute Inc, Cary, NC, USA).

Results

Study sample characteristics

Of the 1385 eligible participants with a standardized clinical examination at follow-up, a total of 1246 participants (734 (59%) men and 512 (41%) women) with a mean age of 38.2 (standard deviation 8.7) years at baseline were included in current analyses (figure 1). A comparison of characteristics and working conditions at baseline between the eligible participants included in the analyses and those excluded is provided in an additional file [see supplementary material, www.sjweh.fi/show_ abstract.php?abstract_id=3911]. Excluded participants did not differ in terms of BMI, diabetes mellitus and rheumatoid arthritis, but were significantly older than those included in analyses (P<0.001). They were more likely to: be women (P=0.036) and lower-grade whitecollar workers (P<0.001), work in trade and services sectors (P<0.001), be temporarily employed (P=0.006) or have a higher seniority level in their current job (P= 0.041). No difference was observed in working conditions under study. However, borderline differences exist for perceived physical exertion, repetitiveness of task, and use of vibrating tools.

Incident UEMSD diagnosed at follow-up

At least one of the six UEMSD was diagnosed at followup in 139 workers free from UEMSD at baseline (74 men and 65 women) corresponding to a projected number of 129 320 new UEMSD cases in the PdL region in 2007 (table 1). The incidence proportion of UEMSD observed in the PdL region did not significantly differ between sexes (10.3% for men versus 12.4% for women; P=0.287). The most common diagnoses at follow-up were rotator cuff syndrome (incidence proportion 6.5%), lateral epicondylar tendinopathy (incidence proportion 2.2%) and CTS (incidence proportion 2.0%). The estimate of the projected number of workers in the PdL with two or more UEMSD at follow-up was 19 404 (1.7%) workers.

Incident UEMSD risk factors

The RR for incident UEMSD associated with occupational risk factors in the multivariable model after adjustment for personal risk factors are shown in table 2. The following occupational exposures were positively associated with incident UEMSD: high perceived physical exertion (RR 1.52, 95% CI 1.06-2.17), working with arms above shoulder level (RR 1.57, 95% CI 1.04-2.39) and low social support at work (RR 1.41, 95% CI 1.03-1.92).

Concerning personal factors, age was associated with the incident UEMSD while the RR for female sex was at the limit of statistical significance.

PAF and estimated number of incident UEMSD attributable to risk factors

PAF associated with the incidence of UEMSD in the multivariable model were 20.4% (95% CI -1.1-40.1) for high physical exertion (Borg RPE scale >13), 6.6% (-3.5-16.4) for working with arms above shoulder level (>2 hours/day), and 12.9% (0.3-25.1) for low social support (table 3). Of the projected estimate of 129 320 incident UEMSD cases in PdL in 2007, an estimated 26 381 (variation range: 0-51 857) new UEMSD cases were attributable to high physical exertion, 16 682 (388-32 459) to low social support, and 8535 (0-21 208) new cases to working with arms above shoulder level. A high number of incident UEMSD [10 863 cases (0-30 778)] could be attributed to working with shoulder abduction despite the associated RR failing to reach the 5% statistical significance level. The projected number of incident UEMSD attributable to all occupational factors in the multivariable model was estimated at 53 021 (0-98 671) cases, representing 41.0% of all new UEMSD in the PdL region.

Sex-stratified analyses

Results from sex-stratified analyses suggest that the observed relationship between incident UEMSD and high physical exertion or low social support were primarily observed among men. The relationship observed between incident UEMSD and sustained or repetitive shoulder abduction or working with arms above shoulder level were primarily observed among women. Thus, the association of high physical exertion with incident UEMSD was only statistically significant (RR 2.38, 95% CI 1.41-4.04)] among men, while the association with low social support approached statistical significance (RR 1.42, 95% CI 0.92-2.17). Occupational exposure with shoulder abduction was only found to be positively associated with incident UEMSD (RR 1.75, 95% CI 1.05-2.93) among women, and the RR associated with working with arms above shoulder level approached statistical significance (RR 1.70, 95% CI 0.97-2.98) (table 2).

Of the projected total estimate of 60 133 UEMSD incident cases among male workers in the PdL region in 2007, 25 015 were attributable to high physical exertion, representing 41.6% of all new cases, while 8599 (14.3%) could be attributed to low social support (table 3). Similarly, of the projected 69 187 new UEMSD cases among women estimated in 2007, 12 315 cases (17.8% of all new UEMSD) were attributable to working with shoulder abduction while 5258 cases (7.6%) could be attributed to working with arms above shoulder level. In addition, the PAF among women for being overweight/ obese (a potentially modifiable factor) was 15.3% corresponding to 10 586 new UEMSD cases in the PdL region in 2007.

The PAF attributable to all occupational factors was estimated to be 59.7% among men and 42.5% among women, corresponding to 35 899 and 29 411 projected incident cases of UEMSD in the PdL region, respectively.

Discussion

Main findings

This study has estimated the number of incident cases of UEMSD attributable to occupational exposure factors in the working population of the French PdL region in 2007.

Considering occupational risk factors for incident UEMSD, our results showed that an estimated 26 381 incident cases, representing 20.4% of all new projected UEMSD cases in the PdL region in 2007, were attributable to high physical exertion, 8535 incident cases (6.6%) to working with arms above shoulder level, and 16 682 incident cases (12.9%) to low social support from coworkers and supervisors. Furthermore, a significant number of new UEMSD cases (N=10 863) could be attributed to working with shoulder abduction despite the associated RR did not reach the 5% statistical significance level.

Comparison with previous literature

To our knowledge, this is the first cohort study estimating the number of potential cases of UEMSD attributable to occupational risk factors in an entire working population.

The main occupational factor likely to lead to the highest number of incident cases of UEMSD was high physical exertion, associated with 26 381 cases (about 20.4% of incident UEMSD in the PdL working population). Approximately one in five incident UEMSD could theoretically be prevented by reducing exposure to physical exertion in the workplace. Previous studies carried out in Italy and the Netherlands (22, 23) reported that 28% of CTS cases and 25% of lateral epicondylar tendinopathy cases respectively, could be attributable to high physical exertion. Moreover, a recent narrative review showed that forceful exertion was a significant risk factor for all UEMSD (48). Meta-analyses have also revealed a significant relationship between shoulder disorders and hand force exertion, but with moderate evidence (11), and between CTS and force (10). In addition, a summary study based on three longitudinal MSD studies provided strong evidence for a relationship between lateral epicondylalgia and occupational exposure to high hand force (49).

Our study indicated the important contribution of awkward shoulder postures with a projected estimate of 8535 (6.6%) and 10 863 (8.4%) incident UEMSD attributable to working with arms above shoulder level and working with shoulder abduction respectively. This result is consistent with recent PAF estimates (15% for lateral epicondylar tendinopathy and 9% for shoulder disorders) associated with awkward postures in the working population (22) and a recent meta-analysis showing moderate evidence of a positive association between shoulder disorders and exposure to arm-hand elevation (11).

The present study estimated the projected number of incident UEMSD related to low social support at 16 682, representing 12.9% of all incident cases. Our PAF estimates are in line with the findings from the 2001 US National Research Council extensive review (27), which concluded that improving low social support of coworkers and supervisors in exposed workers could potentially reduce the risk for UEMSD by 28-52%. A multitude of psychosocial factors in the workplace, including poor social support, activate psychosocial stress. Stress then appears to initiate a sequence of physiological reactions, including biochemical reactions, which in the short term may increase muscle tension and, in the long term, may increase the risk of MSD (50). Therefore, an improvement in social support from superiors and colleagues may contribute to the reduction of this risk. Moreover, workers with low social support may be exposed to higher levels of biomechanical risk factors (51). Conversely, high social support may facilitate the cooperation between coworkers in performing strenuous manual tasks to minimize biomechanical exposure (52). In a previous metaanalysis, exposure to low social support in the workplace was positively associated with the onset of UEMSD (9). A systematic literature review showed that low social support at work may result in an increased occurrence of specific disorders at the elbow (12). Another systematic review by Kraatz et al (53) showed strong evidence for adverse effects of low social support on the onset of shoulder disorders. A meta-analysis of Lang et al (54) found positive associations between psychosocial work stressors, including low social support at work, and shoulder symptoms and upper-extremity symptoms, while another found low-quality evidence of no association for social support (11). However, this finding has been inconsistent with some previous studies. A prospective study found no associations between social support and incident UEMSD (lateral epicondylitis, rotator cuff tendinitis, CTS, tendinitis of forearm-wrist extensors and flexors) (55). Recently, a review reported limited evidence for a positive association between psychosocial factors including low social support and CTS in the workplace (56).

Concerning personal risk factors, sex and age are not modifiable factors. Among the potentially personal modifiable risk factors, the present study suggests that (in women) an important number of projected incident UEMSD could be attributed to high BMI (15.3% of all projected new cases) in the PdL female working population. This result is in line with a prospective cohort study of Italian workers reporting that about 30% of CTS cases may be attributable to being overweight/obese (23). These differences may reflect the gender division of work where men are more often exposed to jobs requiring high physical work load and forceful exertion (eg, in the construction sector) and women more often exposed to highly repetitive tasks with lower force exertion (eg, in assembly line work) (39, 40). Moreover, highly physically demanding jobs (eg, manual handling of heavy loads) require mutual help and social support from coworkers to collectively cope with job tasks and minimize biomechanical exposure (52).

Strengths and limitations

The present study has some limitations. Approximately 57% of workers included at baseline did not have a follow-up clinical examination. Within this participant group, 58% were no longer being monitored by any OP of the network because they had left their baseline jobs without informing their OP. In some cases, their OP refused to participate in the follow-up period. Moreover, the follow-up period coincided with the major economic crisis in the PdL region in 2008-2009, during which the regional salaried workforce declined by 3.4% (33.7% in temporary employment agencies) (57). The lowest participation rate in this study was among young or temporary workers or those with a short length of service at baseline (29). According to a study on the effects of drop out in a longitudinal study of MSD (58), the differences between the participants and the drop out subjects had a very modest influence on the RR for effects of occupational exposures. We therefore believe that there was no major selection bias associated with the quality of the follow-up.

Another limitation is the exposure assessment, which was based only on workers self-reporting. In spite of that, the use of standardized and validated questions may have ensured better quality of the self-reported exposure measures. Non-differential misclassification of exposures may have occurred due to workers' inability to precisely recall or describe their current work exposures among workers without symptoms. Nevertheless, due to the prospective design of the study, exposure information gathered prior to UEMSD diagnosis resulted in low risk of differential recall bias. To the extent that the risk of UEMSD is increased by cumulative physical exposures, our analyses may have underestimated the true contribution of work exposures to the incidence of UEMSD in our study population. This may be particularly the case for rotator cuff syndrome, since studies of work-related risk factors for shoulder pain have identified the length of time employed as a risk factor (59). The single and short window of follow-up in this study after a long follow-up period is another potential limitation. Workers may have had a UEMSD in the period between the first and second clinical examinations, but recover and do not have the UEMSD at follow-up. This may have resulted in an underestimation of the number of cases diagnosed.

The computation of the combined PAF assumes independence and the absence of interaction between individual risk factors. However, there may be an interaction between certain occupational risk factors. In such cases, the calculation of the combined PAF may lead to its over- or underestimation. Nevertheless, none of the interactions between occupational exposures explored previously was statistically significant (29). It should also be noted that the choice of thresholds used to define exposure levels can have an effect on PAF estimates (60). However, to avoid bias, we chose exposure definitions as close as possible to public health recommendations and those recommended in the scientific literature. The concept of PAF supposes a causal relationship between exposure and UEMSD (19). Moreover, a strong association between a risk factor and UEMSD, ie, a high RR, may correspond to a low or high PAF depending on the prevalence of exposure. This leads to very different public health consequences as the prevalence of exposure can vary considerably within populations that are separated in time and space (61). Thus, we assume that a reduction in occupational exposure at the working population level would lead to a reduction in the incidence of WRUEMSD and PAF estimates should therefore be interpreted with caution. Finally, it is possible that the 95% CI of the PAF includes the null value, despite the significance of the RR due to the use of nonlinear transformations to compute the 95% CI of the PAF (62). Even so, zero should be close to the 95% CI.

The use of a prospective cohort including a representative sample of the working population at baseline is a major strength of the present study (31). Secondly, outcomes were clinically assessed by trained OP using standardized procedures (31, 32). In addition, this study strictly applied the definitions of exposures proposed by the European consensus criteria document (32), except for the measure of exposure to forceful exertion which was assessed according to the rating of perceived exertion (35) and the INRS cut-offs (36).

Another strength is the formula used to estimate the PAF from multivariable regression models, allowing a non-biased computation of PAF estimates adjusted for covariates (19). Lastly, sophisticated weighting adjustment methods (44-46) for enhancing estimate accuracy were used to extrapolate the number of cases observed in the study sample to the whole working population. Furthermore, the "linear " calibration method used to calculate the new weights was the one that gave the lowest variance and range of weight ratios (new weights / initial weights). Indeed, it was chosen by considering the following criteria: lowest dispersion, smallest extent and general appearance of the distribution of the new weight distribution; the other calibration methods give calibrated estimators with the same asymptotic accuracy (44, 46).

Finally, estimating the number of incident cases of UEMSD in the working population of the PdL region is useful for comparing the population-level impacts of various risk factors on the incidence of UEMSD. Furthermore, these estimates provide additional input for the implementation of prevention programs that target and prioritize the modifiable risk factors with the greatest impact for more effective interventions to reduce the medical, economic and social impact of UEMSD in the workplace.

Concluding remarks

Following adjustment for personal factors, we have been able to estimate the proportion and projected number of new UEMSD cases attributable to occupational risk factors in the working population of the French PdL region. According to our findings, an important proportion and a large number of incident UEMSD in the workplace in the PdL region could potentially be prevented by reducing occupational exposures such as physical exertion, working with shoulder abduction, and improving social support from coworkers and supervisors. These findings highlight the magnitude of potentially modifiable and preventable occupational exposures in the incidence of UEMSD in the workplace.

Acknowledgments

We acknowledge the following OP who were involved in the sentinel network: Doctors Abonnat, Adam, Addou, Agullo, Ansaloni, Aubrun, Banon, Bardet, Barraya, Beaurepaire, Becquemie, Berthelot, Bertin, Bertrand, Bidron, Biton, Biziou-Fouere, Bizouarne, Boisse, Bonamy, Bonneau, Bouchet, Bouguer, Bourrut-Lacouture, Bourven, Bradane, Breton, Bricaud, Caillon, Camer, Cesbron, Chabot, Charlon, Chevalier, Chisacof, Chotard, Clement dit Pontieu, Compain, Coquin-Georgeac, Cordes, Cormier, Couet, Coutand, Da Costa, Dachert, Dadourian, Danielou, Darcy, Davenas, De Lansalut, De Lescure, Diquelou, Dopsent, Dubois, Dufrenne-Benetti, Dupas, Durand, Durand-Perdriel, Evano, Fache, Faline, Fontaine, Fosse, Frampas-Chotard, François, Garrabe, Gasseau, Giffard, Girard, Girardin, Guerin, Guessard, Guillaumin, Guillier, Guillimin, Guinel, Harinte, Harrigan, Hefti, Herrouet, Herson, Hervio, Hirigoyen, Houssin, Husquin, Jahan, Jarry, Jube, Kalfon, Kergresse, Khouri, Krai, Labraga, Laine, Laine-Colin, Lamotte, Lasnier, Laventure, Le Clerc, Le Dizet, Le Mauff, Lechevalier, Lecompte, Ledenvic, Leroux, Leroy-Maguer, Levrard, Levy, Ligeard, Logeay, Louineau, Lourtis, Lucas, Maeker, Maison, Mallet, Marquiset, Martin, Martin-Laurent, Mazoyer, Meritet, Meyer, Michel MC, Michel R, MigneCousseau, Moisan, Morvan, Mouchet, Moui, Nivet, Page, Parrot, Patillot, Perou, Pierfitte, Pinaud, Pineau, Pizzalla, Plessis, Plouhinec, Pocreaux, Prod'homme, Puichaud, Quince, Rabjeau, Raffray, Riberot, Riou, Robin, RobinRiom, Roesch, Rouault, Roussel, Roux, Russu, Saboureault, Schlindwein, Soulard, Souvre-Debray, Spiesser, Thomas, Thomasset, Thomson, Tillette, Treillard, Tripodi, Verrier, Voisin.

We also thank Anna Lloyd (University of Angers, Angers) for her proofreading of the English and valuable comments on the manuscript.

Funding

This project was supported by Santé publique France, the French national public health agency, Saint-Maurice, France (Grant 9/25/2002-5 "réseau expérimental de surveillance des troubles musculo-squelettiques") and the French National Research Program for Environmental and Occupational Health of Anses (Grant EST-2016/1/42). None of the mentioned sources of funding had any role in the design, analysis or writing of this article.

The authors declare no conflicts of interest.

Ethics approval and consent to participate

Each worker provided informed written consent to participate in this study, and the study received the approval of the French Advisory Committee on the Processing of Information in Health Research ("CCTIRS") and the National Committee for Data Protection ("CNIL").

Sidebar

Nambiema A, Bodin J, Fouquet N, Berstrais S, Stock S, Aublet-Cuvelier A, Descatha A, Evanoff B, Roquelaure Y. Upper-extremity musculoskeletal disorders: how many cases can be prevented? Estimates from the COSALI cohort. Scand J Work Environ Health. 2020;46(6):618-629. doi:10.5271/sjweh.3911

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Received for publication: 16 March 2020

DETAILS

Subject:	Population; Workers; Supervisors; Risk factors; Disorders; Public health; Disease prevention; Social interactions; Shoulder; Risk analysis; Physicians; Musculoskeletal diseases; Health surveillance
Business indexing term:	Subject: Workers
Location:	France
Company / organization:	Name: European Union; NAICS: 926110, 928120
Publication title:	Scandinavian Journal of Work, Environment &Health; Stockholm
Volume:	46
Issue:	6
Pages:	618-629
Publication year:	2020
Publication date:	2020
Section:	Original article
Publisher:	Scandinavian Journal of Work, Environment &Health
Place of publication:	Stockholm
Country of publication:	Finland, Stockholm
Publication subject:	Occupational Health And Safety
ISSN:	03553140

e-ISSN:	1795990X
Source type:	Scholarly Journal
Language of publication:	English
Document type:	Journal Article
DOI:	https://doi.org/10.5271/sjweh.3911
ProQuest document ID:	2464654382
Document URL:	https://www.proquest.com/scholarly-journals/upper-extremity-musculoskeletal-disorders-how/docview/2464654382/se-2?accountid=211160
Copyright:	Copyright Scandinavian Journal of Work, Environment &Health 2020
Last updated:	2023-02-28
Database:	Publ ic Health Database

Quality improvement activity in occupational healthcare associated with reduced need for disability retirement: A Bayesian mixed effects modelling study in Finland

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ProQuest document link

ABSTRACT (ENGLISH)

Objectives There is evidence that occupational healthcare (OHC) may improve employees' work ability. This research was designed to study whether common quality improvement (QI) activities in the OHC quality network (OQN) - a voluntary collaborative forum - can reduce the need for disability pensions. Methods The study population comprised employees under the care of 19 OHC units in Finland affiliated with the OQN. The association of 12 QI activities with new disability pensions during the years 2011-2017 was analyzed by Bayesian mixed effects modelling. Results Patients of OHC units affiliated with the OQN have fewer full permanent disability pensions [odds ratio (OR) 0.77, 95% credible interval (CI) 0.60-0.98] and full provisional disability pensions (OR 0.68, 95% CI 0.53-0.87) than patients of unaffiliated units. Of the studied QI activities, the measurements of intervening in excessive use of alcohol had the strongest association with the incidence of all disability pensions (OR 0.53, 95% CI 0.41-

0.68). Participation in the focus of work measurements and quality facilitator training was also associated with the reduced incidence of disability pensions (OR 0.84, 95% CI 0.71-0.98, and OR 0.92, 95 CI 0.84-0.99, respectively). Conclusions Affiliation with a quality network seemed to improve outcomes by reducing full disability pensions or replacing them by partial disability pensions. Some QI activities in the OQN were associated with a reduction of disability pensions.

FULL TEXT

Headnote

Objectives There is evidence that occupational healthcare (OHC) may improve employees' work ability. This research was designed to study whether common quality improvement (QI) activities in the OHC quality network (OQN) - a voluntary collaborative forum - can reduce the need for disability pensions.
Methods The study population comprised employees under the care of 19 OHC units in Finland affiliated with the OQN. The association of 12 QI activities with new disability pensions during the years 2011-2017 was analyzed by Bayesian mixed effects modelling.
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Conclusions Affiliation with a quality network seemed to improve outcomes by reducing full disability pensions or replacing them by partial disability pensions. Some QI activities in the OQN were associated with a reduction of disability pensions.
Key terms alcohol; depression; disability pension; health check-up; networking; pension; work ability.
(ProQuest: ... denotes formulae omited.)
Efforts are underway globally to improve the quality, coverage and security of healthcare (1). Quality improvement (QI) initiatives in healthcare aim at enhancing service delivery through process development (2). Such initiatives include activities that strive to improve existing processes or redesign processes altogether (2-4). Occupational healthcare (OHC) should focus on its core tasks, which are the promotion of healthy workplaces (5) and ensuring the health and work ability of employees (6, 7).
Processes intended to enhance and maintain employees' work ability should be established on evidencebased methods. Initiatives designed to reduce the risk of work-related disability can be particularly effective. These include general job modification, return-to-work coordination and organizational support (5), and targeted health check-ups for employees with work incapacities, followed by health-focused and workplace interventions addressing cases of musculoskeletal and mental disorders (8, 9). Reorganization of OHC services, including service coordination and rehabilitation after injuries, has been shown to reduce disability pensions (10). Multidomain interventions in the workplace including work adjustments, changes of role or work tasks, reductions in working hours, sabbaticals, physiotherapy and physical exercise may reduce the likelihood of disability pension (11). Early vocational rehabilitation can have the same effect (12). While depression is one of the main global reasons for disability, in Finland improvement and better organization of care are required before disability pension is granted due to depression (13, 14).
Disability retirement is predominantly caused by mental and musculoskeletal disorders (15). Other causes include cardiovascular diseases and accidents (15). Due to the ageing of the labor force (16), a lot of emphasis is put on the promotion of work participation and avoidance of early retirement (17). Predictive risk estimates have been developed for the prevention of chronic conditions (18). Once preventive activities have been implemented in OHC it can take a long time, even decades, for effects to be seen (19, 20). This means that outcome measures often cannot be used, thus process performance indicators are preferred in improvement measurements (19).

Often the results of OHC are assessed only by the resources employed and the number of patient visits because these are easy to measure. Instead, we should strive to measure the processes and their outcomes (eg, the reduction in the disability retirement). Measuring the performance of a process is more demanding and expensive than measuring the number of patient visits (2, 21) but gives more evidence of its effectiveness (4). Data on the performance of healthcare processes can be used to improve both the organization of care and clinical decision-making (22).

In addition to the evidence that OHC may improve the prevention of disabilities (8, 23) there is also evidence that networking may improve the quality and outcomes of healthcare, although this has not been studied in the field of OHC (24).

One of the major shared goals of employers, employees and OHC is the reduction of early retirement due to disability. Although much has been written about QI in healthcare, little is known about its impact in OHC on disability retirement. Therefore, we designed a study to find out whether the implementation of common QI activities in the occupational healthcare quality network (OQN) - a voluntary collaborative forum consisting of OHC service providers - reduces the need for disability retirement and which specific activities affect the outcomes. The study hypothesis was that common QI activities in the OQN are effective in reducing disability pensions.

Methods

The occupational healthcare quality network

At its foundation in 2011, the Finnish OQN had two goals: to reduce the rate of disability retirement, especially the full permanent disability pension, and lower the number of full disability pensions in favor of partial pensions. Conmedic, a nonprofit company that coordinates healthcare quality networks and facilitates the OQN, performed the data analyses of quality measurements. The members of the OQN support each other's development by exchanging material and information on best practices. Each OHC unit consists of occupational health physicians, occupational nurses, occupational physiotherapists and occupational psychologists. Since the foundation of the OQN, each unit has performed several of the common QI activities. The member units of the OQN have used the continuous quality development model in the development of processes (25) with repeated measurements of process indicators. This study included activity data from 19 OHC units across Finland that have been affiliated with the OQN either through the whole study period or for only a few years.

The study population and data

The outcome data covered the disability pensions of all Finnish municipality employees during 2005-2017 obtained from the pension registers of Keva, the largest pension provider in Finland which administers the pensions of public sector workers. The clients of the OHC units (municipalities) had to agree to the retrieval of data on disability retirements among their employees from Keva records. All the data from Keva were aggregated and anonymous with no possibility for an individual's identification.

The activity data were collected from January 2011 to December 2017, during which time the subset of OHC units affiliated with the OQN has varied. Regardless, the activity data of all participants was collected.

The study population consisted of all employees in the care of the 19 OHC units affiliated with the OQN between 2011 and 2017. The comparison population were all municipality employees in the care of nonaffiliated OHC units. The annual number of employees in the study population ranged between 32 239-38 438 and 445 628-487 921 in the comparison population during the period 2005-2017.

The 12 QI activities analyzed were: participation in (i) measurements of intervening in excessive use of alcohol; (ii) quality measurements of health check-ups; (iii) quality facilitator training; (iv) focus of work measurements; (v) resource measurements; (vi) quality network workshops; (vii) peer review training; (viii) quality measurements of depression care; (ix) advisory board of the OQN; (x) employee and employer satisfaction surveys; and reporting of (xi) QI plans for the coming year; and (xii) QI activities.

The focus of work measurements included measuring the following indicators in registers: proportion of the work done in preventive healthcare (following the classification of the National Pension Institution), proportion of all contacts directed to employees with musculoskeletal or mental disorders (which are the main reasons for early retirement), and the number of tripartite negotiations (employee with reduced work ability, employer and OHC) per year. The QI activities with their descriptions are presented in table 1.

We used the incidence of different disability pensions as outcome measures for the effects of QI activity in the OQN. The incident disability retirement was calculated by dividing the number of granted disability pensions by the number of insured employees at the end of each year. The definitions of the different pension benefits are described in table 2. We followed the STROBE guideline in the set-up of the study.

Statistical analysis

The statistical analysis was run by using a Bayesian generalized linear mixed model consisting of both fixed and random effects (26). The mixed-effect approach was chosen because it allows the modelling of employerspecific variability and yearly variability of data, thus rendering estimates that are representative of the overall effect of each fixed effect covariate of interest.

As there was no separate reference group to compare the activity data with, the units not affiliated with the OQN each year were used in the statistical model to estimate the effect of the covariates to the outcome. The random effects take care of adjusting for yearly variability as well as OHC-unit-specific variability, so that the fixed-effects estimates represent the overall effect of the study population.

Credible intervals (a Bayesian analogy to confidence intervals) are reported. Readers with no Bayesian background can follow the results in table 3 by interpreting the 95% credible intervals (95% CI) similarly as confidence intervals for odds ratios (OR).

The Bayesian model was implemented using Just Another Gibbs Sampler (JAGS) software (27) and data preprocessing was done in R (28). Each model was fitted to the data using four Markov Chain Monte Carlo (MCMC) chains (29) with a total length of 500 000 iterations. The first 20 000 iterations were discarded as a burnin. Thinning to every 100 iterations were used leading to 19 200 iterations stored for each model. The MCMC chains appear to have converged based on both visual inspection and Brooks-Gelman-Rubin Rhat-diagnostics (30). The Rhat-values were <1.006 for all covariates in the model. The Rhat-value 1.00 indicates the perfect convergence and all values <1.05 are acceptable.

Description of the model. The data has N observations where the index i runs over the rows of data. The response yi = (ki,ni) consists of the number of disability retirements k_i and number of employees n_i in OHC care during the year at row i. In addition, we utilized the 12 QI activities as indicators of participation in the OQN. We included the covariate "Affiliation with the Finnish Occupational Healthcare Quality Network", which indicates whether the OHC Emp(i) participated in any QI activity during Year(i), which also defines it as being affiliated with the OQN.

We generated five different models (marked #), each with different response covariates, but all within the same modelling setting. For each model, the response y_i ~Binom (p,,k_i) stands for #1 Full permanent disability pension, #2 Partial permanent disability pension, #3 Full provisional disability pension, #4 Partial provisional disability pension or #5 All granted disability pensions.

The probability $P(y_i = 1) = p_i$ of obtaining a disability retirement was modeled by the following equation:

...

In this equation, the parameter ß0 is a constant that defines the base level for retirement. Parameters bEmp and bYear are random effects for employer and calendar year, and the term fixed effects depends on the model. The presence of the random effect term bEmp [Emp(i)] factors in this model means that the measurements from the same employers in different years are more similar to each other than to those measured among the other employers. Respectively, bYearr [Year(i)] factor is the year-dependent effect of different years. The random effect terms follow Gaussian distribution:

...

Prior probability distributions. The prior probability distributions, which represent information regarding model parameters available prior to the analysis were as follows: For the constant and each fixed effect parameter, the N(0,1000) was used. For the variance parameters ... of the random effects ..., the inverse gamma distribution with parameters 0.001 and 0.001 was used.

Model selection. The models were selected according to the deviance information criteria (DIC) (31). After the model selection phase, each of the selected five models had a different number of covariates remaining. The model coefficients are transformed to OR using OR = exp(ß) where ßstands for fixed effect. The OR for fixed effects of all models are reported in table 3. Where a numerical value is not given (ns) the independent covariate has been excluded from the final model due to model selection. For example, in the model of "Full permanent disability pension", the only remaining fixed effects are affiliation with the Finnish OQN and participation in resource measurements.

Results

The mean age of the employees who were granted a disability pension in 2017 was 55.1 years in the study population while it was 54.1 years among all municipality employees. The number of different disability pension types granted during 2011-2017 are shown in figure 1. The number of full permanent disability pensions decreased from 31.7 grants /10 000 employees in 2011 to 13.6 grants /10 000 employees in 2017, while partial permanent disability pension and partial provisional disability pensions had a slightly increasing trend. The number of provisional pensions granted fluctuated during the period and peaked in 2008.

The affiliation of OHC units with the OQN is associated with a reduction in full disability pensions compared to the unaffiliated units, OR for full permanent disability pension 0.77, 95% CI 0.60-0.98 and for full provisional disability pension 0.68, 95% CI 0.53-0.87 (table 3). For all disability pensions, the association was not as strong as it was with full permanent disability pensions (OR 0.86, 95% CI 0.72-1.03).

Some of the QI activities appeared to be especially valuable in reducing disability retirement. Participation in the quality measurements of intervening in excessive use of alcohol was strongly associated with the reduction of all disability pensions (OR 0.53, 95% CI 0.41-0.68). The association with the partial permanent disability pensions was even stronger (OR 0.35, 95% CI 0.22-0.55). Participation in the quality measurements of health check-ups (HCU) was associated with the reduction of all disability pensions (OR 0.87, 95% CI 0.75-1.0). The association was especially strong with both types of partial disability pensions. Participation in the focus of work measurements associated also positively with the reduced incidence of total disability retirement (OR 0.84, 95% CI 0.71-0.98) as did participation in the quality facilitator training (OR 0.92, 95% CI 0.84-0.99) (table 3).

Some QI activities had negative associations with the reduction of incidence in disability pensions. Participation in the quality measurements of depression care was associated with an increased risk of total granted disability pensions (OR 1.27, 95% CI 1.05-1.51), participation in quality network workshops increased the OR, as did reporting the QI plans for the coming year and participating in the advisory board meetings (table 3).

The random effect variation was higher for employers (municipalities) random effects than for yearly random effects for all the models. The standard deviations for random effect of employers were 0.415 (95% CI 0.2660.628) in full permanent disability pension, 0.312 (95% CI 0.197-0.480) in partial permanent disability pension, 0.251 (95% CI 0.139-0.416) in full provisional disability pension, 0.551 (95% CI 0.276-0.873) in partial provisional disability pension and 0.264 (95% CI 0.172-0.400) in all disability pension together. The standard deviations for random effects of the study year were 0.241 (95% CI 0.119-0.426), 0.124 (95% CI 0.037-0.247), 0.144 (95% CI 0.072-0.25), 0.185 (95% CI 0.031-0.474), and 0.116 (95% CI 0.064-0.196), respectively. During the model selection process, covariates were dropped out from the model one at the time. Table 3 reports the OR for covariates included in the final models. DIC was used for model selection and final values are 957.3, 970.3, 1052.5, 564.6 and 25746.4, respectively.

Discussion

Our study showed that some QI activities had a positive association with the core outcome of OHC, namely reduction of early disability retirement. We found several improvement activities that were positively associated with work ability but also such that had negative associations. The activities with the strongest positive association with the reduction of early disability retirement were, in the order of their strength, participation in: (i) the quality measurements of intervening in excessive use of alcohol, (ii) the focus of work measurements and (iii) the quality facilitator training.

The affiliation of the OHC unit with the OQN showed a risk reduction of full permanent disability pensions and full provisional disability pensions while partial disability pensions did not differ from the comparison group. These findings might show that some full disability pensions have been replaced with partial disability pensions. We think that the results showed a change towards the intended targets of the OQN, namely, a reduction of full permanent disability pensions and shift to partial disability pensions.

Shifts from full to partial disability benefits, even in short-term sickness absences, have been shown to increase long-term work participation (32) and to bring social security savings (33). The shift towards partial disability benefits can be a way to break a downward spiral pattern found by a Danish study, in which a previous sickness absence was associated with the increased risk of work disability pension through a transition cycle: from work to sickness absence, from sickness absence to unemployment or to a disability pension (34).

We demonstrated a reduction in the granted disability retirements. This positive result may have been driven by the sum of all the QI activities, although it seems that some improvement activities have stronger effects than others. Earlier studies on the reduction of the need for disability retirement have shown the importance of broad multi-domain activities in the workplace in collaboration with OHC (10, 11). Such positive shifts often need multidisciplinary collaboration. In their systematic review, Cullen et al (8) showed that workplace-based return-to-work interventions and work disability management interventions helped workers with musculoskeletal and pain-related conditions and mental health conditions to return to work (8). The authors recommend that the interventions should include healthcare provision, service coordination and work accommodation components.

The QI activities affected the four disability pension types in different ways. The novel and surprising finding of this study was that participation in the quality measurements of intervening in excessive use of alcohol had such a strong association with the reduction of all disability pensions. One may speculate about the reasons why this activity was so effective. One explanation could be that healthcare workers find it difficult to discuss alcohol use. By participating in this activity, the management showed to the OHC personnel that intervening in risky use of alcohol is important. Studies have shown that excessive alcohol use is a strong driver of early retirement in Finland (35, 36). Screening, health advice and support to tackle alcohol-connected risk behavior are inexpensive especially when compared to disability retirement (37). There is also evidence that intervention at the workplace is effective in reducing problems related to excessive alcohol consumption (38).

Participation in the focus of work measurements, such as how diagnoses affect the patient flow, was associated with reductions in all types of disability pensions together. Such measurements can be difficult to make because the data are hard to find in patient and administrative records. The results regarding this activity may reflect this barrier and could show that units willing to perform the activity are also willing to make the necessary changes in patient flow.

The positive association we found concerning participation in the quality facilitator training was anticipated and could reflect the fact that deeper knowledge of the fundaments of QI may bring better results (39). Participation in the quality measurements of HCU had a weak association with the reduction in disability retirement. The reductions were mainly seen in the partial disability pensions. In Finland, HCU in OHC are targeted at employees who are in danger of prolonged sick leave and early retirement, those who are exposed to work hazards (such as chemicals and noise), and controls in 5- to 10-year intervals of the ageing. The first two types were the target group of our study. The associations we found may indicate that the activity has not led to major improvements in the processes that support work ability. However, some studies have found HCU to be a valuable component of Finnish OHC. The targeted HCU may work as triggers for interventions to address poor work ability (9, 40) while they can also work as interventions themselves (8). The health education given during HCU may have some effect in the prevention of occupational asthma and accidents (41). Moreover, health education may be even more important from the point of view that the risk factors found during HCU have predictive value of mortality for decades (20). On the other hand, while targeted HCU seem to be important, untargeted HCU in primary healthcare seem to have little or no effect on mortality or morbidity (42).

It appears that participation in the quality measurements of depression care was associated with an increased risk of all disability pensions. This finding is somewhat surprising since one would expect this measurement activity to show comprehensive interest in the mental health of employees. The result may, however, indicate an excessive presence

of mental problems and could reflect the findings of the systematic review of Cullen et al (8), which found that the traditional cognitive therapy methods used in OHC may be ineffective, and highlights the need for new work-focused cognitive behavioral interventions (8). Participation in quality network workshops, reporting the QI plans for the coming year, and participating in the advisory board meetings were also negatively associated with the reduction of disability pensions. It is important to recognize that not all changes result in improvement (4), but perhaps these activities do not have direct influence on the focus of work in the OHC unit.
The strengths of our study were that we were able to evaluate the association of several QI activities with the outcomes - ie, early disability retirement - and follow over a long period the main outcome of effective OHC, namely the prevention of early retirement. It seems that Bayesian mixed-effect modelling can be a feasible method in assessing the effect of multiple QI activities in healthcare.
The study had also weaknesses. Only the common QI activities of the OQN were included in the study. Several improvement activities of OHC based only in one unit were not included in the study. We did not include the results of resource or process measurements in the analysis of this study because of their high number. The OHC units have also participated in them at different times. Other limitations of this study were that the OHC units affiliated with the OQN may have had better OHC practices and greater interest to QI than the non-affiliated units even before the study. This could affect the results per se.
It is possible that the results of our study are not generalizable to all OHC units, not even within Finland. However, the results show the direction for further studies.
Concluding remarks
This study showed that OHC units reduced the numbers of disability pensions when affiliated with the quality network. Moreover, participation in the quality measurements of intervening in excessive use of alcohol, quality facilitator training, and the focus of work measurements may decrease the risk of work disability pension among employees of companies in the care of OHC units participating in these activities.
Acknowledgements
We extend our thanks to Keva for providing the data for this study, and especially to Katinka Lybäck, Head of Statistics at Keva, for her important advice and data collection.
Jarmo Kuronen has received grants from the Finnish Cultural Foundation and from Niilo Helander Foundation.
Conflicts of interest
Jarmo Kuronen works in a participating OHC unit. Klas Winell owns a quality improvement company. Juho Kopra and Kimmo Räsänen declare no conflicts of interest.
The grants from the Finnish Cultural Foundation and from Niilo Helander Foundation did not affect the study protocol, data set-up or reporting in any ways.
Ethical approval
An ethical review statement from a human sciences ethical committee is not required in this particular study, which is based solely on public information, registry and documentary data (43).
Sidebar
Kuronen J, Winell K, Kopra J, Räsänen K. Quality improvement activity in occupational healthcare associated with reduced need for disability retirement: A Bayesian mixed effects modelling study in Finland. Scand J Work Environ Health. 2020;46(6):630-638. doi:10.5271/sjweh.3901
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Received for publication: 18 September 2019

DETAILS

Subject:	Early retirement; Population; Collaboration; Bayesian analysis; Health care; Retirement; Estimates; Quality control; Modelling; Prevention; Employees; Alcohol use; Mental disorders; Disability pensions; Employers; Population studies; Statistical analysis; Quality improvement
Business indexing term:	Subject: Early retirement Employees Disability pensions Employers Quality improvement
Location:	Finland
Publication title:	Scandinavian Journal of Work, Environment &Health; Stockholm
Volume:	46
Issue:	6
Pages:	630-638
Publication year:	2020
Publication date:	2020
Section:	Original article
Publisher:	Scandinavian Journal of Work, Environment &Health

Place of publication:	Stockholm
Country of publication:	Finland, Stockholm
Publication subject:	Occupational Health And Safety
ISSN:	03553140
e-ISSN:	1795990X
Source type:	Scholarly Journal
Language of publication:	English
Document type:	Journal Article
DOI:	https://doi.org/10.5271/sjweh.3901
ProQuest document ID:	2464654381
Document URL:	https://www.proquest.com/scholarly-journals/quality-improvement-activity-occupational/docview/2464654381/se-2?accountid=211160
Copyright:	Copyright Scandinavian Journal of Work, Environment &Health 2020
Last updated:	2022-03-24
Database:	Public Health Database

The deterioration of mental health among healthcare workers during the COVID-19 outbreak: A population-based cohort study of workers in Japan

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ABSTRACT (ENGLISH)

Objectives This study compared the longitudinal change in the mental health of healthcare and non-healthcare workers during two months of the COVID-19 outbreak in Japan. Methods Data were derived from a prospective online cohort study of 1448 full-time employees in Japan. Participants were surveyed at baseline from 19-22 March

2020 (T1) and at follow-up from 22-26 May 2020 (T2). A self-administered online questionnaire was used to assess participants' fear and worry of COVID-19, psychological distress, and physical symptoms at T1 and T2. A series of generalized linear models were created to assess changes in outcomes between healthcare and non-healthcare workers. Demographic variables (ie, sex, age, marital status, child[ren], education, and residential area) were included in the models as covariates. Results A total of 1032 participants completed the follow-up questionnaire at T2 (follow-up rate, 72.6%). After excluding unemployed respondents (N=17), the final sample comprised 1015 full-time employees (111 healthcare and 904 non-healthcare workers). After adjusting for the covariates, psychological distress (and subscales of fatigue, anxiety, and depression) as well as fear and worry of COVID-19 increased statistically significantly more among healthcare than non-healthcare workers from T1 to T2. Conclusions Psychological distress, together with fear and worry of COVID-19, increased more among healthcare compared to non-healthcare workers during the COVID-19 outbreak. The study confirmed that healthcare workers are an important target for mental healthcare during the COVID-19 outbreak.

FULL TEXT

Headnote

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Conclusions Psychological distress, together with fear and worry of COVID-19, increased more among healthcare compared to non-healthcare workers during the COVID-19 outbreak. The study confirmed that healthcare workers are an important target for mental healthcare during the COVID-19 outbreak.
Key terms anxiety; depression; nurse; physician; SARS-Cov-2.

Poor mental health was reported among healthcare workers (HCW) during the COVID-19 outbreak of 2019-2020 (1-5). Recent systematic reviews of previous studies reported that HCW showed moderate-to-high levels of psychiatric symptoms such as anxiety, depression, insomnia (6), and acute and posttraumatic stress symptoms (7, 8) during the COVID-19 outbreak. Frontand second-line HCW, including not only physicians and nurses but also other allied healthcare professionals, manifested psychiatric symptoms (2, 9). These studies' findings suggest that HCW are major targets of mental healthcare (1, 6).

However, evidence showing that HCW developed poorer mental health compared to non-HCW in the COVID-19 outbreak is still limited. A study in China reported that HCW and non-HCW experienced similar levels of anxiety and depression, while HCW showed a poorer quality of sleep compared to non-HCW (10). This study may have underestimated the psychological effect of the COVID-19 outbreak on HCW because it was conducted in the early phase of the outbreak. Another study from China reported that the prevalence of depression and anxiety was greater among HCW compared to nonHCW (11). However, HCW have been known to suffer greater psychological distress compared to non-HCW even before the COVID-19 outbreak, which may be due to more stressful working conditions (12). To ascertain the influence of the COVID-19 outbreak on the mental health of HCW, in comparison with non-HCW, a longitudinal study is needed to observe their mental health status before and after the outbreak of COVID-19. To date, no such study has been reported.

In this two-month (mid-March to mid-May 2020) longitudinal follow-up study of full-time employees conducted during the first wave of COVID-19 outbreak in Japan, we assessed changes in fear and worry of COVID-19, psychological distress, and physical symptoms among HCW and non-HCW.

Methods

Study design, participants, and procedure

In February 2019, we assessed a prospective online cohort of full-time employees, stratified by sex and 10-year age groups (N=4120), who had participated in a large digital marketing research company survey of community-dwelling people across Japan. Through an invitation e-mail from the company, we further invited these respondents to participate in a baseline online survey for this study administered on 19-22 March 2020 (T1). The questionnaire was closed once the target sample (up to 1500 participants) was obtained or the answer deadline came. For this T1 survey, a total of 1448 participated; response rate: 35.1% (13, 14).

The flowchart of participant recruitment is shown in the supplementary material (www.sjweh.fi/show_abstract.php?abstract_id=3922) figure 1. Respondents at T1 were more likely to be single and have no children compared to non-respondents. Differences in sex, age, or psychological distress scores between these two groups were statistically non-significant. After excluding unemployed respondents (N=27), we followed the remaining 1421 respondents for two months and surveyed them again on 22-26 May 2020 (T2). There were no missing responses in the questionnaire. Respondents who participated both in T1 and T2 surveys were included in further analyses.

At the time of the baseline survey (T1), the number of people infected by COVID-19 had just begun to increase rapidly in Japan with 1046 reported COVID-19 cases and 36 deaths. On 16 April, the Japanese Government declared a state of national emergency, which continued until 25 May. At the time of the follow-up survey (T2), 16 581 COVID-19 cases and 830 deaths had been reported in Japan (15).

The Research Ethics Committee of the Graduate School of Medicine/Faculty of Medicine at the University of Tokyo approved this study [No. 10856- (3)].

Measurement variables

Global fear and worry about COVID-19. Global fear and worry about COVID-19 were assessed using a single item (13): "Do you feel anxiety about COVID-19?" Responses were rated on a 6-point Likert- scale ranging from 1="No, not at all" to 6="Yes, feel strongly."

Psychological distress and physical symptoms. Psychological distress and physical symptoms in the last 30 days were measured with 18- and 11-item subscales, respectively, of the Brief Job Stress Questionnaire (BJSQ) (16, 17). Five subscales of psychological distress assessed lack of vigor, anger-irritability, fatigue, anxiety, and depression. The physical symptoms scale assessed various somatic symptoms (eg, loss of appetite, headache). All items were rated on a 4-point Likert scale from 1="Never" to 4 - 'Almost always". The subscale scores were summed, with higher scores indicating greater distress or symptoms.

Demographic variables. Participants were asked about their occupations and whether they worked in healthcare facilities at T2. The response options included non-HCW (ie, general workers), HCW (ie, physicians, nurses/midwives), or other HCW (eg, pharmacists, clinical laboratory technicians) working in healthcare facilities, and HCW not working in healthcare settings (eg, public health centers, schools, or companies). We divided participants into two categories: all types of HCW (including both working and not working in healthcare settings) and non-HCW. We measured sex, age, marital status, having at least one child, educational attainment (>16 years), residential area (living in or outside a prefecture in which the government had declared a COVID-19 special emergency) as covariates in statistical analyses. We also collected information on industry and organization size at T1.

Statistical analysis

The mean change in scores of psychological distress and physical symptoms from T1 to T2 were compared between HCW and non-HCW (t-test for two independent groups). A general linear model with repeated measures using a first-order autoregressive (AR1) covariance matrix was used to estimate adjusted means of these outcomes between HCW and non-HCW, adjusting for the covariates (sex, age, marital status, having at least one child, education, and residential area). A differential change in the outcomes between the two groups was tested with a group^time interaction. Cohen's d was adopted to calculate crude and adjusted effect size (ES). Statistical significance was set as P<0.0071 (=0.05/7) for a two-tailed statistical test applying the Bonferroni's correction for the seven outcome variables. In addition, we conducted two sensitivity analyses. First, we conducted similar general linear model analyses with repeated measures using sampling weights to make the demographic distribution of sex, 10-year age groups, and occupation (HCW or non-HCW) of the sample comparable to that of the entire working population of Japan (see the supplementary table S1). Second, with dichotomizing fear and worry about COVID-19 into high (>4) and low (<3), prevalence of high fear and worry at T1 and T2 were compared between HCW and non-HCW (Fisher exact test). Multiple logistic regression was employed to estimate odds ratios (OR) and 95% confidence intervals (CI) of high fear and worry at T2 among HCW compared to non-HCW, adjusting for high fear and worry at T1 only and adjusting for high fear and worry at T2 and the covariates. SPSS 26.0 (IBM Corp, Armonk, NY, USA) Japanese version was used.

Results

A total of 1032 participants (72.6%) completed the follow-up questionnaire at T2. Compared to those lost to follow-up at T2, the completers were statistically significantly more likely to be engaged in the education industry sector. Differences in sex, age, psychological distress, marital status, or having a child(ren) at baseline between the two groups were statistically non-significant (data available upon request). We excluded respondents who became unemployed (N=17). The final sample consisted of 111 HCW and 904 non-HCW. Table 1 shows the characteristics of each group of participants. Two-thirds of HCW were female, while the male-to-female ratio was close to 1 among non-HCW. Among HCW, most participants (55%) were healthcare workers other than physicians and nurses/midwives. HCW also included those who worked in non-clinical settings (28%).

The mean scores of fear and worry of COVID-19, psychological distress and its subscales, and physical symptoms were similar for HCW and non-HCW at T1 (table 2). Fatigue increased from T1 and T2 statistically significantly more among HCW than among non-HCW (P=0.005 <0.0071 with the Bonferroni's correction). After adjusting for the covariates, the scores of total psychological distress and fatigue, anxiety, and depression subscales increased statistically significantly more among HCW compared to non-HCW (P= 0.002, 0.002, 0.003, and 0.006, respectively, all P<0.0071 with the Bonferroni's correction). The global fear and worry of COVID-19 also increased more among HCW compared to non-HCW, although the difference was not statistically significant (P=0.049 >0.007). The estimated ES was greater for total psychological distress, as well as fatigue, anxiety, and depression (0.243-0.323 in Cohen's d) than for fear and worry of COVID-19 (0.202).

Weighting the sample to make the demographic distribution comparable to the entire working population of Japan did not change the patterns observed in the non-weighted analyses described above in general (supplementary table S1). However, only fatigue increased statistically significantly more among HCW compared to non-HCW after adjusting for the covariates (P=0.003, P<0.0071 with the Bonferroni's correction); otherwise, the difference was statistically non-significant. Prevalence of high fear and worry about COVID-19 increased from T1 to T2 both among HCW and non-HCW (supplementary table S2). Multiple logistic regression showed that HCW had a marginally statistically significantly higher OR of having high fear and worry at T2, after adjusting for the fear and worry at T1 and the covariates (adjusted OR 1.94, 95% CI 0.97-3.88, P=0.063).

Post-hoc statistical power calculation

To statistically test (t-test) the T2-T1 difference in change scores of psychological difference between HCW (N=111) and non-HCW (N=904), with small effect size (0.2 in Cohen's d), the statistical power was estimated as 0.634, with an alpha of 0.05.

Discussion

Mean scores of fear and worry of COVID-19, psychological distress and its subscales, and physical symptoms at baseline were similar between HCW and non-HCW. However, most indicators deteriorated among HCW during the COVID-19 outbreak while they remained the same or even improved among non-HCW. In particular, after adjusting the covariates, psychological distress and its subscale of fatigue, anxiety, and depression increased statistically significantly more among HCW compared to non-HCW during the COVID-19 outbreak.

This study demonstrated that HCW were more likely than non-HCW to develop psychological distress during the COVID-19 outbreak. The findings are consistent with previous cross-sectional studies indicating that HCW showed a high prevalence of anxiety, depression, and other psychiatric symptoms (2, 6, 7, 11), suggesting that HCW experienced poor mental health during the COVID-19 outbreak. The patterns were similar but statistically significant only for fatigue when the sample weight was applied to make the demographic distribution of the present sample comparable to that of the entire working population of Japan. This is probably attributable to a reduced statistical power caused by applying the sample weighting to the limited size of the sample. This longitudinal study provides more compelling evidence that the mental health of HCW declined during the COVID-19 outbreak, not just because of their prior working conditions, and that the degree of deterioration was greater for HCW than for non-HCW. Among non-HCW, psychological distress and physical symptoms did not change, although their fear of COVID-19 increased slightly. The finding is consistent with a previous longitudinal study conducted in China showing that stress, anxiety, and depression were stable in a general sample during a spike in the number of COVID-19 cases (18). However, those who experienced greater stress due to COVID-19 may have been more likely to be lost to follow-up, which could lead to an underestimation of the effect of COVID-19 on mental health among non-HCW. It is also plausible that some potentially vulnerable groups, such as people with chronic conditions or disabilities, may have experienced a deterioration of mental health during the COVID-19 outbreak (19), which could have been masked in the analysis of the entire non-HCW sample.

Limitations

This study has several limitations. The number of HCW in this sample was small (N=111). HCW participating in an internet survey may have been biased. The distributions of sex and age in this sample represented the working population of Japan. The findings were similar when the sample was weighted to make the sex- and age-distributions comparable to that of the entire working population of Japan. However, the sample may still be biased in terms of some other demographic characteristics, such as education and income. These possibilities may limit the generalizability of the findings. Our sample of HCW included only a few physicians and nurses/midwives. Therefore, our findings may not be generalized to these professionals. Moreover, the sample consisted only of full-time employees. Furthermore, we did not ask HCW participants whether they were in charge of the treatment of COVID-19 patients, which is an important predictor of posttraumatic stress among HCW (2, 8, 20). We also did not ask about important characteristics of work settings, such as clinics or hospitals, where the HCW worked. Nevertheless, most HCW reported that they worked in large organizations, which could have been hospitals. The study sample also included HCW working in laboratory facilities or industries related to the manufacturing of medical equipment, which may have resulted in an underestimation of the effect of the COVID-19 outbreak. Furthermore, we did not consider whether the respondents tested positive for COVID-19 at any point in the study. Lastly, we did not measure posttraumatic stress as a unique indicator of mental health among HCW during the COVID-19 pandemic (2, 8, 9).

Concluding remarks

The two-month longitudinal study revealed that psychological distress among HCW deteriorated during the early months of the COVID-19 outbreak in Japan. The study suggests that mental healthcare should be available to HCW working in diverse environments.

Disclosure

Approval of the research protocol: This study was approved by the Research Ethics Committee of the Graduate School of Medicine/Faculty of Medicine at the University of Tokyo, No. 10856- (3).

Online informed consent was obtained from all participants with full disclosure and explanation of the purpose and procedures of this study. We explained that their participation was voluntary and that they could withdraw consent for any reason simply by not completing the questionnaire.

Conflict of interest

The authors report no conflicts of interest.

Funding

This work was supported by internal funds of the Department of Mental Health, Graduate School of Medicine at the

University of Tokyo.
The sponsors had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; or the decision to submit the manuscript for publication.

Sidebar

Sasaki N, Kuroda R, Tsuno K, Kawakami N. The deterioration of mental health among healthcare workers during the COVID-19 outbreak: A population-based cohort study of workers in Japan. Scand J Work Environ Health. 2020;46(6):639-644. doi:10.5271/sjweh.3922

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Received for publication: 16 June 2020

DETAILS

Subject:	Polls &surveys; Mental health; Demographic variables; Severe acute respiratory syndrome coronavirus 2; Generalized linear models; Health care; Medical personnel; Questionnaires; Fear; Health facilities; COVID-19; Outbreaks; Nurses; Fatigue; Age; Residential areas; Employees; Mental depression; Coronaviruses; Neighborhoods; Midwifery; Population studies; Statistical models; Education; Anxiety; Cohort analysis
Business indexing term:	Subject: Employees
Location:	China; Japan
Publication title:	Scandinavian Journal of Work, Environment &Health; Stockholm
Volume:	46
Issue:	6
Pages:	639-644
Publication year:	2020
Publication date:	2020

Section:	Short communication
Publisher:	Scandinavian Journal of Work, Environment &Health
Place of publication:	Stockholm
Country of publication:	Finland, Stockholm
Publication subject:	Occupational Health And Safety
ISSN:	03553140
e-ISSN:	1795990X
Source type:	Scholarly Journal
Language of publication:	English
Document type:	Journal Article
DOI:	https://doi.org/10.5271/sjweh.3922
ProQuest document ID:	2464654035
Document URL:	https://www.proquest.com/scholarly-journals/deterioration-mental-health-among-healthcare/docview/2464654035/se-2?accountid=211160
Copyright:	Copyright Scandinavian Journal of Work, Environment &Health 2020
Last updated:	2023-08-22
Database:	Public Health Database

Association between asbestos exposure and pericardial and tunica vaginalis testis malignant mesothelioma: a case–control study and epidemiological remarks

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ABSTRACT (ENGLISH)

Objectives The purposes of this study are to describe the epidemiology of pericardial and tunica vaginalis testis mesothelioma and assess the role of asbestos exposure for these rare diseases. Methods Based on incident pericardial and tunica vaginalis testis mesothelioma cases collected from the Italian national mesothelioma registry (ReNaM) in the period 1993-2015, incidence rates, survival median period and prognostic factors have been evaluated. A case-control study has been performed to analyze the association with asbestos exposure (occupational and non-occupational) for these diseases. Results Between 1993 and 2015, 58 pericardial (20 women and 38 men) and 80 tunica vaginalis testis mesothelioma cases have been registered with a mean annual standardized (world standard population as reference) incidence rates of 0.049 (per million) in men and 0.023 in women for the pericardial site, and 0.095 for tunica vaginalis testis mesothelioma. Occupational exposure to asbestos was significantly associated with the risk of the diseases [odds ratio (OR) 3.68, 95% confidence interval (CI) 1.85-7.31 and OR 3.42, 95% CI 1.93-6.04 in pericardial and tunica vaginalis testis mesothelioma, respectively]. The median survival was 2.5 months for pericardial and 33.0 months for tunica vaginalis testis mesotheliomas. Age was the main predictive factor for survival for both anatomical sites. Conclusions For the first time in an analytical study, asbestos exposure was associated with pericardial and tunica vaginalis testis mesothelioma risk, supporting the causal role of asbestos for all anatomical sites. The extreme rarity of the diseases, the poor survival and the prognostic role of age have been confirmed based on population and nationwide mesothelioma registry data.

FULL TEXT

Headnote

Objectives The purposes of this study are to describe the epidemiology of pericardial and tunica vaginalis testis mesothelioma and assess the role of asbestos exposure for these rare diseases.

Methods Based on incident pericardial and tunica vaginalis testis mesothelioma cases collected from the Italian national mesothelioma registry (ReNaM) in the period 1993-2015, incidence rates, survival median period and prognostic factors have been evaluated. A case-control study has been performed to analyze the association with asbestos exposure (occupational and non-occupational) for these diseases.

Results Between 1993 and 2015, 58 pericardial (20 women and 38 men) and 80 tunica vaginalis testis mesothelioma cases have been registered with a mean annual standardized (world standard population as reference) incidence rates of 0.049 (per million) in men and 0.023 in women for the pericardial site, and 0.095 for tunica vaginalis testis mesothelioma. Occupational exposure to asbestos was significantly associated with the risk of the diseases [odds ratio (OR) 3.68, 95% confidence interval (CI) 1.85-7.31 and OR 3.42, 95% CI 1.93-6.04 in pericardial and tunica vaginalis testis mesothelioma, respectively]. The median survival was 2.5 months for pericardial and 33.0 months for tunica vaginalis testis mesotheliomas. Age was the main predictive factor for survival for both anatomical sites.

Conclusions For the first time in an analytical study, asbestos exposure was associated with pericardial and tunica vaginalis testis mesothelioma risk, supporting the causal role of asbestos for all anatomical sites. The extreme rarity of the diseases, the poor survival and the prognostic role of age have been confirmed based on population and nationwide mesothelioma registry data.

Key terms epidemiology; Italy; national registry; rare disease.

Malignant mesothelioma (MM) is a neoplasm of mesothelial cells, and the International Agency for Research on Cancer (IARC) has firmly established the causal role of asbestos (1-3). Despite international health institutes' and agencies' recommendations (4-7), currently 2 000 000 tons of asbestos per year are still produced worldwide (8, 9). Pericardial and tunica vaginalis of testis (TVT) MM accounted for around 1% of cases in the available MM case series (10-13). Incidence and survival for these forms have seldom been reported. The surveillance, epidemiology, and end results (SEER) program from the US National Cancer Institute provided evidence of mean annual standardized incidence rates, in 1973-2013, for pericardial MM of 0.35 and 0.36 (per 10 million person-years) in men and women, respectively, and of 0.54 for TVT MM (14).

The causal role of asbestos exposure in pericardial and TVT MM aetiology has been considered as plausible, but no epidemiological analytical study ever tested the asbestos (or other putative risk factors) role for these diseases (11, 12, 15, 16). Italy is one of the countries more widely involved in the current epidemic of asbestos-related diseases due to the large use of asbestos in the past and the number of exposed individuals among workers (and in the general population) until the asbestos ban issued in 1992 (17-20). In this context, a permanent and mandatory epidemiologic surveillance system on MM is active, based on a national MM registry (Registro Nazionale dei Mesoteliomi, ReNaM in Italian). ReNaM aims are to provide estimates of MM incidence at national population level to assess and record asbestos exposures of cases and identify any possible underestimated or unknown source of asbestos contamination.

This study aims to (i) describe incidence and survival for pericardial and TVT MM cases detected by ReNaM and (ii) assess the association with asbestos exposure using a case-control design.

Methods

Incidence and survival analyses

ReNaM is an epidemiological surveillance system characterized by a network of regional operating centers [Centri Operativi Regionali (COR) in Italian] gradually established by all 20 Italian regions. Case series from Calabria, Sardinia and Molise are available but these regions still cannot ensure completeness of registration. Reporting is compulsory, but COR also actively search and register incident MM cases at the healthcare services that diagnose and treat most cases (pneumology and chest surgery units as well as pathology units). Completeness of registration is periodically checked by surveys, using regional current health sources, pathology units, hospital admissions and mortality registries. According to ReNaM guidelines (21) and as extensively described elsewhere (22), cases are classified as "definite" (histological confirmation of diagnosis, possibly completed by immunohistochemical characterization, and confirmation by imaging and clinical diagnosis), "probable" (usually, cytological diagnosis and confirmation by imaging and clinical diagnosis) or "possible" MM (clinical diagnosis with positive imaging). The occupational and residential history and information on lifestyle habits are obtained using a standardized questionnaire administered by trained interviewers to cases or their next of kin. COR assess both occupational and non-occupational exposure to asbestos. Occupational histories are coded using the Italian standard classifications of industry and occupation. In each COR, experts carry out the exposure assessment in cooperation, if necessary, with the industrial health and safety units of local health authorities. Lifetime asbestos exposure is classified as "occupational" (definite, probable, possible) or "non-occupational" (familial, environmental, other non-occupational - such as leisure-time-related activities), according to the ReNaM guidelines (21). "Unlikely" exposure is assigned to subjects for whom information is inadequate or asbestos exposure could be reasonably ruled out.

Actually, ReNaM has collected cases with a diagnosis of MM from 1993-2015. Pericardial and TVT MM cases were extracted and analyzed for the whole period. Age and gender standardized incident rates have been calculated using the world, European (as proposed by Eurostat in 2013) and Italian (2011 census) populations as standard populations. The distribution and the extent of person-years of observations is reported in the supplementary material (www.sjweh.fi/show_abstract. php?abstract_id=3895) table S1. Survival was estimated by the Kaplan-Meier method, and Cox's proportional hazard regression has been used to assess the role of prognostic factors separately for pericardial and TVT MM. The predictive variables in the final Cox's multivariate model were gender (men and women), age at diagnosis (categorized as follows: <64, 65-74, >75 years old), calendar period of diagnosis (1993-

2003 and 2004-2015), diagnosis level of certainty (definite, probable and possible MM) and morphology (epithelioid, biphasic, fibrous, unspecified MM). The reference modality was the first for all predictive variables in the model. The model's goodness-of-fit to empirical data was assessed by the log likelihood test.

Case-control study

We conducted a case-control study using (i) pericardial and TVT MM cases registered by ReNaM in the period 1993-2015, during which coverage of the Italian population progressed as previously described, and (ii) two sets of controls recruited in two earlier case-control studies: a population-based study on pleural mesothelioma and a hospital-based study on cholangiocarcinoma.

We only used controls who had completed the questionnaire. The distribution of controls by gender, age, year of birth, and region of residence is described in table S3. The first set of controls was taken from a multicentric unpublished population-based case-control study on pleural mesothelioma (called MISEM), performed in five Italian regions (Apulia, Lombardy, Piedmont, Tuscany, and Veneto). Controls were frequency-matched to cases by gender and age and randomly sampled from residents aged 20-89 years in 2012 (Apulia, Piedmont, Tuscany and Veneto) and 2014 (Lombardy). Interviews were performed in 2014-2015 and the participation rate was 48.4%. The second set of controls was taken from a hospital-based unpublished case-control study on cholangiocarcinoma performed in Emilia-Romagna region (called CARA) in which controls were enrolled and interviewed in 2014-2016, and that was an evolution of a previous epidemiological study (23). Participation rate was almost complete. Both sets of controls were interviewed using the same standardized ReNaM questionnaire and assessment of asbestos exposure was performed following ReNaM guidelines.

We calculated odds ratios (OR) and 95% confidence intervals (CI) of pericardial and TVT MM for lifetime asbestos exposure (occupational, familial, environmental, and leisure activity related) using "unlikely" asbestos exposure as reference. To avoid sparse data problems, we fitted conditional regression models using age categories (<55, 55-59, 60-64, 65-69, 70-74, 75-79, and >80 years) as the adjustment set (24). For pericardial MM, we calculated gender-specific and -adjusted analyses. Sensitivity analyses were performed by applying the following restrictions to cases: (i) only cases from the six regions which enrolled control subjects (table S4); (ii) only cases with definite diagnosis (table S5); (iii) only cases diagnosed in 2000-2015 (table S6); 4) only subjects born before year 1950 (table S7). Finally, we performed specific analyses by economic sectors of exposure. Statistical analyses were performed with Stata version 15, 2017 (StataCorp, College Station, TX, USA).

Results

Incidence and survival analyses

Between 1993 and 2015, 58 pericardial MM cases (38 and 20 in men and women, respectively) and 80 TVT MM were registered in ReNaM (table 1). The mean age at diagnosis was 61.8 [standard error (SE) 2.4] years and 61.4 (SE 3.1) in men and women, respectively, for pericardial MM and 66.7 (1.8) for TVT MM. The gender ratio for pericardial cases (male versus female) was 1.95, ranging from 1.5 in 1993-2003 to 2.6 in 2004-2015. The majority of cases were born before year 1950 in both sites and genders. Histological confirmation was obtained for 87.7% of cases; for 17 cases, only cytology or positive imaging were available. The epithelioid form is predominant in both anatomical sites (37.9% in pericardial cases and 52.5% in testicular cases). Incidence analyses, reported in supplementary table S2, confirm the extreme rarity of these diseases. Mean annual standardized incidence rates for pericardial MM in the overall period 1993-2015 were 0.080 (x 1 000 000 inhabitants) in men and 0.036 in women, using the European standard population as reference (0.049 and 0.023 if world population was used). Pericardial MM incidence rates were higher in 1998-2003 for both genders (0.067 and 0.039 in men and women, respectively, with world population standardization), but no reliable temporal trend analysis was possible. TVT MM mean annual incidence rates were 0.095, with the peak in the same period (0.116 in 1998-2003).

The median survival of pericardial MM was 2.5 (SE 1.0) months; 6.8 (SE 0.6) for females and 1.4 (SE 0.6) for males. For TVT MM cases, the median survival was 33.0 (SE 7.8) months. Results of Cox's proportional hazard model for pericardial MM survival showed that older subjects (>75 years) had a hazard risk equal to 3.52 (95% CI 1.45-8.51), with respect to subjects <65 years (table 2a and figure 1a). Pericardial mesothelioma cases with sarcomatoid morphology presented a risk of 1.42 (95% CI 0.53-3.80, P-value 0.6), but this finding, although established in pleural and peritoneal mesothelioma, has to be considered with extreme caution due to the small sample size. Similar findings have been obtained for TVT MM, with a more favorable prognosis for younger patients, (table 2b and figure 1b). Asbestos exposure has been assessed for 113 out of 138 (81.9%) MM cases included in this study, after a direct (56/113=49.6%) or indirect (to a next of kin) interview (57/113=50.5%) (table 1). Occupational exposure to asbestos (definite, probable or possible) was present for 61.9% of interviewed subjects (70/113), with differences by gender and site (23.6% in females pericardial MM, 75.0% in males pericardial MM and 66.2% in TVT MM). The economic sectors more frequently associated with asbestos exposure were construction, steel mills, metal-working industry, textile industry and agriculture. Asbestos exposure in this last sector in Italy has been previously described in ReNaM reports, due mainly to the maintenance of rural buildings containing asbestos.

Case-control study

We included 45 cases (28 men, 17 women) of pericardial MM and 68 cases of TVT MM. There were 929 controls (593 men, 336 women). There were 74 subjects exposed to asbestos (27 pericardial MM and 47 TVT MM) and occupational exposure was largely predominant (70 MM cases). Considering pericardial MM, an overall significant risk was found for occupational asbestos exposure (OR 3.68, 95% CI 1.85-7.31), with relevant gender difference (OR 5.52, 95% CI 2.14-14.2 and OR 1.99, 95% CI 0.606.63 in men and women, respectively) [table 3]. The low number of non-occupationally exposed cases (two cases) leads to statistically unstable risk estimates. The OR of occupational exposure to asbestos for TVT MM risk was 3.42 (95% CI 1.93-6.04). The overall OR of pericardial MM for asbestos-exposed subjects (either occupational or non-occupational) were 1.79 (95% CI 0.95-3.34) and 2.25 (95% CI 1.30-3.90) for pericardial and TVT MM, respectively (data not shown). Sensitivity analyses gave comparable results (tables S7-7), whereas the analyses by economic sectors did not show specific risks.

Discussion

As a legacy of the massive use of asbestos until the 1992 ban, Italy is today one of the countries most affected by asbestos-related diseases. Thanks to a long-term epidemiological surveillance of MM incidence, which covers the Italian population almost completely, our study provides - to our knowledge for the first time - a comprehensive nationwide picture of pericardial and TVT MM epidemiology. Furthermore, this is the first analytical epidemiological study to evaluate the risk related to asbestos exposure for these rare diseases, showing a significant association between occupational asbestos exposure and both pericardial and TVT MM incidence, supporting the evidence that asbestos cause MM in all anatomical sites.

Pericardial and TVT MM are such extremely rare diseases that incident rates are seldom estimated at the population level. Such a low incidence level prevents exercises of correlation between past asbestos consumption, as a proxy of exposure, and incidence, similar to those performed for pleural and pericardial mesothelioma (25, 26). In asbestos-exposed cohorts, disease rarity prevents any meaningful analysis. Even at the national level, it is very difficult to discuss the epidemiology of pericardial and TVT MM. In Italy, previous cases reports by specialized cancer registries have been published for pericardial and TVT MM at regional (11, 27, 28) and national level (29). Potential risk factors for pericardial MM, other than asbestos exposure, have been suggested in some case reports or literature reviews: therapeutic ionizing radiation exposure, smoking, chemotherapeutic treatment and history of cardiovascular diseases (11, 16, 30, 31), but no epidemiological study has ever tested these hypotheses. Hydrocele, inguinal hernia or infection and trauma, ionizing radiation and tobacco smoking have been supposed as potential risk factors for TVT MM without experimental or epidemiological confirmations (16, 32). Most of the studies do not contain any information about asbestos exposure. A review of 27 case reports on pericardial MM showned that a third of the patients were exposed to asbestos (33); Guney and colleagues (34) reviewed 74 cases of TVT MM and found that 34.2% of patients presented a history of asbestos exposure. Recently, the need to include the assessment of ionizing radiation or radiotherapy for MM cases registered by ReNaM has been discussed according to the putative role in mesothelioma risk (35).

The main strength of this study is the presence in Italy of a systematic active search of MM over the whole national territory, with standard criteria for case identification, diagnosis classification and evaluation of the occupational, environmental and familial history of affected people, obtained by the means of a structured individual questionnaire. The temporal and territorial extent of the Italian surveillance system comprises >1000 million of person-years of observations. Mesothelioma epidemiological surveillance systems, comparable to Italian experience for information completeness, exposure assessment and territorial coverage, are rare and - to the best of our knowledge - currently present only in Australia, France and South Korea (36-39). Notwithstanding the old age at diagnosis and the large period of recruitment for pericardial and TVT MM cases, the majority of diagnoses were confirmed by histology (78% and 95% respectively). The completeness and quality of diagnosis in ReNaM have been confirmed by comparison with the Italian cancer registries (40). The interview rate was 85% for TVT MM and 78% for pericardial MM, even despite the poor prognosis. All cases and controls included in case-control study have been interviewed using the ReNaM questionnaire, occupational histories were coded with the same classifications of industry and occupation, and exposure was assessed according to the same protocol.

Some limitations of this study have to be considered. Cases of pericardial and TVT MM used in this study have been extracted by ReNaM archives. ReNaM methods in detecting, classifying and coding MM cases have been repeatedly published in the literature (20, 41). ReNaM is collecting MM cases across Italy, but the activity of its regional operating centers did not begin at the same time and this could have biased our study given the inhomogeneous territorial distribution of industrial and natural sources of asbestos exposure. Exposure assessment was qualitative, and the ability to identify the modalities of asbestos exposure effectively was not fully consistent among regional registries despite the use of a shared structured questionnaire. The percentage of collected exposure histories varied between 45-95% among regions. Furthermore, the possible lack of homogeneity among COR in classifying and coding diagnoses and exposures (according to the national guidelines) has to be considered. Finally, as generally is the case with specialized registries, potential over-reporting could be a concern for ReNaM. Limitations of the case-control study is that control samples refer to previous studies conducted between 2012 and 2015 with a temporal mismatch with MM cases (1993-2015). The incomplete time coverage of controls was partially compensated by being age-matched and the fact that we considered lifetime asbestos exposure, which is likely to be fairly constant after the 1992 asbestos ban in Italy, even if the amount of asbestos-containing materials removed after the ban was consistent and could introduce a bias that is difficult to assess. Furthermore, lifetime occupational asbestos exposure among male cases and controls showed little variation except for those born on or after 1960. Sensitivity analyses with temporal restrictions (only period 2000-2015 and only subjects born before 1950) were in line with the results of the main analysis (tables S5 and S6). Geographical coverage of controls was also incomplete, with controls enrolled only from Apulia, Lombardy, Piedmont, Tuscany, Veneto and Emilia-Romagna regions. These regions were (and still are) among the most industrialized areas in Italy, and it is highly plausible that lifetime asbestos exposure is higher in the population living in these regions than in other regions that did not provide controls. Case-control sensitivity analyses, restricted to the six regions which enrolled control subjects, yielded ORs that were comparable with those found in the main analysis. Finally, the qualitative reconstruction of exposure and the contemporary use of chrysotile and amphiboles in many occupational settings in Italy did not allow for any separate analysis between different varieties of asbestos fibers.

In conclusion, this study provided further evidence of the extreme rarity of pericardial and TVT MM, with a mean annual incidence rates in Italy <1 case per 10 million person-years. Survival analyses confirmed the very poor prognosis for pericardial MM and the prognostic role of age for both pericardial and TVT MM (more favorable for younger patients). Finally, for the first time, our analytical epidemiological study showed an association between asbestos exposure and pericardial and TVT MM risk, supporting the causal role of asbestos for MM of all anatomical sites.

Acknowledgments

The authors thank all COR personnel who were involved in the epidemiological surveillance of MM incidence and the asbestos exposure assessment.

Competing interests

Dario Consonni, Carolina Mensi, Dario Mirabelli and Corrado Magnani served as consultants for the court in trials concerning asbestos-related diseases.

Funding statement

INAIL (Italian Workers Compensation Authority) partial supported and funded this work: research triennial plan of action 2016-2018, project BRIC n.59. The units of epidemiology or occupational health hosting the COR belong to the National Health Service and are financed by their health authorities.

Ethics approval

As reporting of malignant mesothelioma to the National Mesothelioma Registry (ReNaM) is compulsory by law (277/1991 and 81/2008), ethics approval is not required for cases. The MISEM and CARA studies (used for control analyses) were approved by the following institutional review boards: Comitato Etico Interaziendale, AOU San Giovanni Battista di Torino and AO CTO/ Maria Adelaide, Torino, Italy and Comitato Etico del Policlinico di Sant'Orsola, Bologna, Italy

Sidebar

Marinaccio A, Consonni D, Mensi, C, Mirabelli D, Migliore E, Magnani C, Di Marzio D, Gennaro V, Mazzoleni G, Girardi P, Negro C, Romanelli A, Chellini E, Grappasonni I, Madeo G, Romeo E, Ascoli V, Carrozza F, Angellilo IF, Cavone D, Tumino R, Meslis M, Curti S, Brandi G, Mattioli S, Iavicoli S, ReNaM Working Group. Association between asbestos exposure and pericardial and tunica vaginalis testis malignant mesothelioma: a case-control study and epidemiological remarks. Scand J Work Environ Health. 2020;46(6):609-617. doi:10.5271/sjweh.3895

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Received for publication: 3 February 2020

DETAILS

Subject:	Asbestos; Population; Womens health; Mesothelioma; Epidemiology; Thoracic surgery; Gender; Survival; Questionnaires; Hospitals; Medical prognosis; Age; Confidence intervals; Occupational exposure; Exposure; Occupational health; Health risks; Regions; Rare diseases
Location:	Italy; United States--US

Publication title:	Scandinavian Journal of Work, Environment &Health; Stockholm
Volume:	46
Issue:	6
Pages:	609-617
Publication year:	2020
Publication date:	2020
Section:	Original article
Publisher:	Scandinavian Journal of Work, Environment &Health
Place of publication:	Stockholm
Country of publication:	Finland, Stockholm
Publication subject:	Occupational Health And Safety
ISSN:	03553140
e-ISSN:	1795990X
Source type:	Scholarly Journal
Language of publication:	English
Document type:	Journal Article
DOI:	https://doi.org/10.5271/sjweh.3895
ProQuest document ID:	2464653991
Document URL:	https://www.proquest.com/scholarly-journals/association-between-asbestos-exposure-pericardial/docview/2464653991/se-2?accountid=211160
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Last updated:	2023-06-28
Database:	Public Health Database

A longitudinal study on the association between quick returns and occupational accidents

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ABSTRACT (ENGLISH)

Objective This study aimed to investigate how change in the number of quick returns [(QR) <11 hours between consecutive shifts] longitudinally is associated with risk of occupational accidents among nurses. Methods Two-year follow-up data from 1692 nurses participating in the Survey of Shiftwork, Sleep and Health among Norwegian nurses (SUSSH) (mean age 40.2, standard deviation 8.3 years, 91% female) were used. Negative binomial regression analyses were conducted to investigate the association between changes in the number of QR after two years and occupational accidents, controlling for demographics, work factors, and occupational accidents at baseline. Results An increase from having no or a moderate number of QR (1-34 per year) from baseline to the two-year follow-up assessment was associated with an increased risk of occupational accidents, compared to experiencing no change in the number of QR. Those with a moderate number of QR at baseline who experienced an increase after two years had an increased risk of causing harm to patients/others [incident rate ratio (IRR) 8.49, 95% confidence interval (CI) 2.79-25.87] and equipment at work (IRR 2.89, 95% CI 1.13-7.42). Those who had many QR (>34 per year) at baseline but experienced a reduction after two years had a reduced risk of causing harm to themselves (IRR 0.35, 95% CI 0.16-0.73) and patients/others (IRR 0.27, 95% CI 0.12-0.59). Conclusion A fairly consistent pattern was demonstrated in which changes in the number of QR over the two-year follow-up period was associated with a corresponding change in the risk of occupational accidents.

FULL TEXT

Headnote

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Conclusion A fairly consistent pattern was demonstrated in which changes in the number of QR over the two-year follow-up period was associated with a corresponding change in the risk of occupational accidents.

Key terms fatigue; nurse; occupational injury; sleep; sleepiness; shift work; shift worker.

Twenty-three percent of employees in European countries reported having at least one quick return [(QR) <11 hours of rest between two consecutive work shifts] in the last month (1). QR are associated with short sleep duration, increased daytime sleepiness and fatigue (2, 3). This is assumed to be the central mechanism for the empirically supported link between QR and risk of injury and occupational accidents (4-7). In a study where objective data on exposure to QR (payroll data) was linked to national records of injuries (N>60 000), it was demonstrated that QR were associated with a 39% higher risk of injury compared to having 15-17 hours off between shifts (4). Based on the same register data, it was shown that QR are primarily associated with occupational injuries, rather than injuries that occur during commutes or leisure time (7). In a recent study based on a cross-sectional survey, QR were associated with a higher risk of nurses reporting causing harm to themselves, patients/others, and equipment at work (6). However, the temporal relationship between QR and accidents and injuries has yet to be investigated, specifically whether a reduction or an increase in the number of QR over time are associated with a corresponding change in the risk of such incidences.

Accordingly, the aim of the present study was to investigate how a reduction or an increase in the number of QR over time are associated with the risk of nurses reporting occupational accidents. We hypothesized that a reduction or an increase in the number of QR over time would be associated with a corresponding decrease and increase in the risk of occupational accidents.

Methods

Study design

We used data from the Survey of Shiftwork, Sleep and Health (SUSSH) among Norwegian nurses. The SUSSH cohort was initiated in the winter season of 2008/2009, and members of the Norwegian Nurses Organisation (N=6000) were asked to participate. They were randomly selected from five different strata based on number of years since they qualified as a nurse. We invited 1200 nurses from each of the following five strata: 0-1.0, 1.1-3.0, 3.1-6.0, 6.1-9.0, and 9.1-12.0 years since completing the degree, respectively; and 600 invitations were returned due to wrong addresses. Finally, 2059 nurses responded (response rate=38% [2059/5400]). Later in 2009, 2741 newly graduated nurses were invited to join the cohort, of which 905 agreed (response rate=33%). These two groups formed the baseline cohort of the SUSSH, for which there since have been annual data collections. The present study used data from the 2016 (N=1841; response rate=66%) and the 2018 (N=1698; response rate=66%) waves.

The survey questionnaire was sent to each nurse's home address by letter (with two reminders to nonresponders), together with a prepaid return envelope. Participation was voluntary, and the Regional Committee for Medical Research Ethics in Western Norway (No. 088.88) and the Norwegian Data Inspectorate (08/01235/ IUR) approved the study protocol.

Questionnaires

Information about the participants' sex and age was assessed in 2008/09 (participants' age in 2018 was calculated based on that information). Relationship status and child care responsibility (in the household; yes/no) were assessed in 2018. Participants were asked about their percentage of full time equivalent (FTE) in 2018, which had the four response categories: <50%, 50-75%, 76-90% and >90%.

Shift work. Exposure to QR was assessed both in 2016 and 2018 with the open-ended question: "Over the past 12 months, how many times have you had <11 hours free between two consecutive shifts?" Exposure to night shift was assessed in 2018 with the question: "How many night shifts have you worked in the last 12 months?"

Occupational accidents. Three items assessing the number of self-reported occupational accidents were constructed for the purpose of the SUSSH cohort (6, 8) and included in both the 2016 and 2018 surveys. The questions were open-ended and phrased as follows: "How many times during the last year have you: 1) Experienced occupational accidents that you felt were your fault, causing harm to yourself? 2) Experienced occupational accidents you felt were your fault, causing harm to patients/others? 3) Experienced occupational accidents you felt were your fault, causing harm to equipment?"

Statistical analysis

SPSS Statistics (version 25 for Macintosh, IBM, Armonk, NY, USA) was used to run GLM negative binomial regression in order to investigate the relationship between changes in number of QR from 2016 to 2018 and occupational accidents in 2018. The number of participants in the different analyses varied due to missing data. Occupational accidents are generally rare events with a mean close to 0 (skewed distribution), in which negative binomial regression had the best model fit. We separated between those who had no QR, a moderate number (1-34), and a high number (>34) in 2016, which created three groups approximately equal in terms of number of participants. Further, for each of these three groups, as a measure of change in number of QR the last year in 2016 to the number of QR the last year in 2018, we separated between those who had no change in the number of QR ("no change"; allowing for a margin of +/-4 QR for the "no change" category), those who had a reduction in the number of QR ("reduction"), and those who had an increase in the number of QR ("increase"). Thus, change in QR over the two-year assessment period was included as a categorical variable in the analyses. Crude models were tested, as well as models adjusting for sex, age, relationship status, having children in the household, percentage of FTE, number of night shifts the last year in 2018, and occupational accidents the past year at baseline. The rationale for including this list of confounders was that they define some of the basic elements of an individual's life and work situation, all of which have been found to account for part of the variance of occupational accidents in previous research (eg, 6, 8).

Some participants (N=9) reported having >150 QR during the last year. These figures were deemed erroneous and replaced by 150, as we considered this the maximum number of QR one person can possibly have in one year. Results are presented as log counts and exponential parameter estimates [Exp (B)] with 95% confidence intervals (CI). Exp(B) is referred to as incidence rate ratios (IRR) in this paper. An alpha level of 0.05 was set to indicate statistical significance. Missing values were treated as invalid in the analyses.

Results

Descriptive statistics of demographics, work factors and occupational accidents are reported in table 1. Descriptive statistics of occupational accidents across subgroups in this study are presented in the supplementary material (www.sjweh.fi/show_abstract. php?abstract_id=3906) table S1.

The results from the negative binomial regression analyses in terms of incidence rate ratios (IRR) are reported in table 2 (log counts are reported in the supplementary material table S2). Those who had no QR and those who had a moderate number (1-34) at baseline - and experienced an increase in QR over the two-year assessment period - demonstrated an increased risk of causing harm to patients/others and equipment, compared to those in the no-change group. Those who had a high number of QR (>34) at baseline and experienced a reduction in QR over the assessment period, demonstrated a reduced risk of accidents compared to those in the no-change group.

Discussion

This paper presents results from a two-year follow-up study investigating the risk of occupational accidents among nurses when experiencing a change in the number of QR in the work schedule. Overall, the results showed a fairly consistent pattern in which an increase in the number of QR was associated with an increased risk of accidents, while a decrease was associated with a reduced risk of accidents.

An increase in the number of QR over the two-year assessment period was associated with relative risks for work related accidents of 2.89-8.49 compared to those who did not change the number of QR. This suggests a considerable increased risk of occupational accidents as the number of QR increases. These findings are by and large in line with previous studies demonstrating an association between QR and injuries and occupational accidents (4-7). However, a unique pattern in this study was that an increase in the number of QR primarily increased the risk of accidents that involved causing harm to patients/others and equipment, rather than causing harm to oneself. It is unclear why there was no increased risk of causing harm to oneself; although we can speculate that the threshold for classifying something as harmful to oneself may be higher compared to what one considers harmful to others. Furthermore, for those who had many QR at baseline and experienced a reduction in the number of QR over the assessment period, the risk of causing harm to oneself and patients/ others was significantly reduced. These findings seem reasonable since those who had a high number of QR at baseline had more than twice the reduction in QR over the two-year assessment period than those with a moderate number of QR.

The current study is the first to demonstrate that an increase or decrease in the number of QR over time is associated with a corresponding increase and decrease in the risk of occupational accidents. This takes us one step further towards probing the causal link between QR and occupational accidents. However, it will be necessary to demonstrate this association in a randomized controlled trial (eg, by reducing QR in one condition) before a causal link can be established.

The strengths of the SUSSH cohort include the relatively large sample size, the longitudinal design, and the homogenous sample, reducing the influence from occupational confounders. However, considering that there were relatively few nurses who reported having QR in this study (27.6% in 2016 and 24.5% in 2018), the subgroups that were created based on changes in the number of QR over time were relatively small, which raises the probability of false discoveries and inflated effect size estimations. Still, the validity of the results is supported by the fact that the outcomes were fairly consistent across the analyses. The small subgroups entail limitations in terms of statistical power. Another limitation concerns the uncertainty related to the representativeness of the findings, considering the relatively low response rate in the first wave of the SUSSH survey (9), and the subsequent dropout that has followed over the cohort period. It is a limitation that the study only included self-reported measures of exposure and outcome variables, which may have caused recall bias or social desirability bias. Additional limitations with the SUSSH cohort and the assessments included in the present study are discussed in more detail elsewhere (eg, 6, 10, 11).

Acknowledgements

The Regional Committee for Medical Research Ethics in Western Norway (No. 088.88) and the Norwegian Data Inspectorate (08/01235/IUR) approved this study.

Informed consent was obtained from all participants included in the study.

The study was partly funded from Nordforsk, Nordic Program on Health and Welfare (74809). The authors declare no conflict of interest.

Sidebar

Vedaa Ø, Harris A, Waage S, Bjorvatn B, Thun E, Buchvold HV, Djupedal ILR, Pallesen S. A longitudinal study on the association between quick returns and occupational accidents. Scand J Work Environ Health. 2020;46(6):645-649. doi:10.5271/sjweh.3906

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Received for publication: 6 February 2020

DETAILS

Subject:	Shift work; Risk management; Sleep; Accidents; Regression analysis; Demographics; Age; Confidence intervals; Occupational accidents; Injuries; Nurses; Occupational safety; Demography; Statistical analysis; Risk reduction; Correlation analysis; Longitudinal studies
Business indexing term:	Subject: Shift work Occupational accidents
Publication title:	Scandinavian Journal of Work, Environment &Health; Stockholm
Volume:	46
Issue:	6
Pages:	645-649
Publication year:	2020
Publication date:	2020
Section:	Short communication
Publisher:	Scandinavian Journal of Work, Environment &Health
Place of publication:	Stockholm
Country of publication:	Finland, Stockholm
Publication subject:	Occupational Health And Safety
ISSN:	03553140
e-ISSN:	1795990X

Source type:	Scholarly Journal
Language of publication:	English
Document type:	Journal Article
DOI:	https://doi.org/10.5271/sjweh.3906
ProQuest document ID:	2464653982
Document URL:	https://www.proquest.com/scholarly-journals/longitudinal-study-on-association-between-quick/docview/2464653982/se-2?accountid=211160
Copyright:	Copyright Scandinavian Journal of Work, Environment &Health 2020
Last updated:	2023-03-06
Database:	Public Health Database

How to schedule night shift work in order to reduce health and safety risks

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ABSTRACT (ENGLISH)

This paper aims to provide scientifically based recommendations on night shift schedules that reduce health and safety risks. As outlined in figure 1, night shift schedules included night shift intensity (number of night shifts per unit time), consecutive night shifts (number of night shifts in a row), permanent night shift work (primarily or only night shifts), shift intervals (time between shifts), direction of rotation (typically forward, eg, D → E → N, or backward rotation, eg, N → E → D) and shift duration (number of hours in a shift). In this paper, the term "circadian disruption" is used in a broad sense to cover the changes in the circadian rhythm such as amplitude, duration, and timing of biological rhythms and objective or subjective proxies of changed circadian rhythm. Circadian disruption may, depending on intensity and duration, be caused by a number of factors: light-at-night, altered sleep-wake cycle (disturbed sleep), and other behaviors that alter the peripheral clocks.

FULL TEXT

Headnote

Key terms: cancer; cardio-metabolic disease; circadian disruption; health; injury; night shift; night shift work; night work; pregnancy; risk; safety; schedule; shift work; shift work schedule; shift worker; sleep duration; sleep quality; sleepiness

This Discussion Paper provides scientifically based recommendations on night shift schedules, including consecutive shifts, shift intervals and duration, which may minimize health and safety risks.

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Refers to the following texts of the Journal: 2013;39(4):325-334 2018;44(4):394-402 2018;44(4):403-413 2018;44(4):385-393 2019;45(3):256-266 2019;45(2):166-173 2020;46(4):446-453 2020;46(6):570-578 2020;46(6):645-649 2010;36(2):121-133 2015;41(3):268-279 2012;38(4):380-390

The following article refers to this text: 2020;46(6):554-556

of cancer have been published. Furthermore, the risk of other adverse health outcomes, such as cardiovascular disease, diabetes, injuries and pregnancy-related outcomes, have also been associated with night shift work. The increasing amount of studies on shift work, health and safety has prompted requests from policy-makers, employers and employees for scientifically based recommendations on specific ways to schedule night shift work in order to reduce health and safety risks, which extend previous recommendations on breast cancer to other outcomes.

This paper aims to provide scientifically based recommendations on night shift schedules that reduce health and safety risks. As outlined in figure 1, night shift schedules included night shift intensity (number of night shifts per unit time), consecutive night shifts (number of night shifts in a row), permanent night shift work (primarily or only night shifts), shift intervals (time between shifts), direction of rotation (typically forward, eg, D ^ E ^ N, or backward rotation, eg, N ^ E ^ D) and shift duration (number of hours in a shift). The a priori selected health and safety outcomes were cancer, cardio-metabolic disease, injuries and pregnancy-related outcomes, such as miscarriage and pregnancy-related hypertension and pre-eclampsia. These outcomes were selected because of severity of the disease/event and prior knowledge of studies expected to be informative. Furthermore, short term physiological effects related to circadian disruption, inadequate sleep duration and quality, fatigue and sleepiness were considered as possible mechanisms linking night shift work to health and safety risks and considered for further evidence in the formulation of the given recommendations.

Methods

Working within different fields of night shift work and health and safety research and performing epidemiological, observational or experimental studies, 15 experience shift work researchers participated in a 3-day workshop held in January 2020 in Denmark. Prior to the workshop, the participants identified the most relevant scientific literature on the associations and possible mechanisms between night shift work and health and safety within their main research area. After the workshop, a supplementary literature search was performed in PubMed. Furthermore, studies included in recent systematic reviews were checked for relevant information. Cohort and case-control studies and meta-analysis that assessed two or more doses or categories of a night shift schedule were included. Cross-sectional studies and studies that solely compared night shift work with day or non-night work, eg, ever/never night, were excluded. The recommendations were based on the literature on night shift schedules and the a priori selected outcomes. Evidence on short-term physiological effects was used to substantiate the recommendations.

Results

Short-term physiological effects of night shift work on health and safety risks

Circadian disruption. Circadian rhythms in physiological functions are pivotal for survival (5). They are primarily synchronized to the light-dark cycle by light exposure through the eyes, which excites the intrinsically photosensitive retinal ganglion cells (ipRGC). The ipRGC are connected to the suprachiasmatic nucleus (SCN) located in the hypothalamus (6). Virtually all cells in the body have molecular clocks that are normally synchronized by the master clock in the SCN. Projections from the SCN innervate the sympathetic nervous system and other structures such as the pineal gland, which regulates downstream peripheral oscillators via humoral, endocrine, and neural signals, resulting in a coherent time organization of bodily processes for optimal performance (7). Melatonin is a hormone mainly produced in the pineal gland under direct control of the circadian timing system. Thus, melatonin production is controlled by the light-dark cycle exposure, and its plasma concentration signalizes this to virtually all organs and tissues. Therefore, melatonin is essential to maintain the internal circadian synchronization and regulate the sleep-wake cycle.

In this paper, the term "circadian disruption" is used in a broad sense to cover the changes in the circadian rhythm such as amplitude, duration, and timing of biological rhythms and objective or subjective proxies of changed circadian rhythm (8). Circadian disruption may, depending on intensity and duration, be caused by a number of factors: light-at-night, altered sleep-wake cycle (disturbed sleep), and other behaviors that alter the peripheral clocks (9).

Night shift workers are exposed to light-at-night, which has earlier been proposed as one of the exposures linked with breast cancer through suppression of melatonin (10). Light-at-night is associated with lower levels of melatonin in both experimental (11-13) and observational studies of night shift workers compared with day workers (14, 15). Animal studies show that alterations in the light-dark schedule suppress melatonin (3). Furthermore, some prospective cohort studies indicate that women with higher levels of morning urinary melatonin metabolites have a modestly lower risk of breast cancer (16, 17).

For optimal biological efficiency, key circadian rhythms must maintain a certain phase relation to one another and follow an internal order (7). Because different organ tissues, biological systems and cells change their rhythms with different speed, desynchronization between internal circadian rhythms may develop as a consequence of night shift work (18). Experimental evidence shows that the internal desynchronization leads to an accelerated growth of human breast tumor xenografts in mice (19). The degree of desynchronization may depend on type of night shift schedules, eg, suppression of melatonin and changes in cortisol rhythms were influenced by the number of increasing number of consecutive night shifts among Danish male police officers (20).

Sleep duration and quality. Night shift workers normally sleep during the day, which is associated with short sleep duration, insomnia symptoms such as premature awakening and non-restorative sleep, and a reduction in stage 2 and rapid eye movement (REM) sleep compared with other shifts and days off (21-23). It is likely that components of the shift schedule, for example number of days off, intensity of night shift work, and frequency of quick returns and early morning work, contribute to chronic short sleep duration and insomnia (24). If the night shift worker suffers from shift work disorder, defined as having shift work-related sleep problems and/ or excessive sleepiness, one would assume that the sleep disturbances are chronic. The prevalence of shift work disorder is higher among night shift workers than shift workers who alternate between day and evening work, and shift work disorder is also positively correlated with frequency of night shifts in the shift schedule (25, 26).

Chronic short sleep duration (<6 hours per day), particularly when associated with insomnia complaints, has been associated with cardiovascular disease and type-2 diabetes (27, 28) and could be a mechanism linking night shift work with these adverse health outcomes. It has also been hypothesized that short sleep duration may increase cancer risk and that long sleep may reduce breast cancer, but findings are inconsistent (29). However, to the best of our knowledge, no prospective study has evaluated whether shift work disorder or chronic short sleep duration among night shift workers increase the risk of developing cardio-metabolic diseases and cancer.

Fatigue and sleepiness. Fatigue and sleepiness, particularly related to sleep restriction, have been suggested as plausible mechanisms linking night shift work and injury through impaired performance and alertness (30). Sleepiness, defined as increased sleep pressure, has been shown to rise while working during the night and may depend on the night shift schedule. The most consistent result is that sleepiness is most profound on the first night shift in both experimental and observational studies (31-38). Also, slowly backward-rotating shift systems (which have several consecutive shifts and sometimes short shift intervals) have been found to be associated more strongly with sleepiness on night shifts than fast forward-rotating systems (39). Furthermore, there are indications that alertness and performance are impaired on 12-hour night shifts compared with 8-hour shifts (40, 41), although later studies did not find such an effect on sleep or sleepiness (39).

Taken together, night shift work has several short-term physiological effects: circadian disruption is introduced, levels of melatonin are modestly suppressed, circadian rhythms are desynchronized, sleep duration is reduced, and sleepiness is increased. The short-term physiological effects appear to depend on how the night shifts are scheduled (20, 25, 26, 31-38). The short-term physiological effects are suggested to link night shift work to acute safety risks and possibly long-term health effects, although studies specifically addressing whether these acute effects serve as mediators of long-term health and safety risks are lacking.

Scheduling of night shift work and risk of cancer, cardio-metabolic disease and injuries

Studies of night shift intensity, consecutive night shifts, shift intervals, and duration of shift in relation to risk of cancer, cardio-metabolic disease and injuries are summarized in tables 1-3. In table 4, results from studies on pregnancy-related outcomes are presented.

Intensity of night shifts. Intensity of night shift work, which is often operationalized as number hours or night shifts per unit of time, has been suggested as important parameter in epidemiological studies (2, 42). Studies have used different measures of intensity, eg, night shift hours per week (43), lifetime mean night shifts per month (44), mean number of night shifts per week in periods with night shift work (45, 46) (table 1). Due to the large variation in the used metrics and exposure time windows, the consistency of results across studies cannot be evaluated, although generally, high intensity appears to be associated with higher risk of breast cancer (43, 45, 46), hypertension (47) and diabetes (44), but not injuries (48) (table 1).

Number of consecutive night shifts. Number of consecutive night shifts, ie, the number of night shifts in a row represents a specific case of intensity. Working >5 consecutive night shifts for >5 years has been associated with higher risk of breast cancer in nurses from Norway (49). Similarly, female military employees who had >3 consecutive night shifts for >6 years had higher breast cancer risk (45). Working >6 consecutive night shifts have been associated with a higher risk of prostate cancer, particularly in combination with long shifts, among permanent night but not rotating shift workers (50). In a meta-analysis based on eight studies mostly in industry, the risk of occupational injuries was studied on the first, second, third and fourth consecutive night shift. It was found that the risk increased with increasing number of consecutive night shifts and was highest on the fourth consecutive night shift (51). However, among hospital employees, the number of occupational injuries increased only in connection with one night shift during the past week (52). This finding can be explained by sleepiness being most profound on the first night shift as observed in both experimental and observational studies (31-38). Thus, the risk for injuries in relation to the number of consecutive night shift may depend on other shift characteristics, but at least in industry the risk has been shown to increase after three consecutive nights. Taken together, the results indicate that a maximum of three consecutive night shifts implies a lower risk of accidents and possibly cancer compared with more than three consecutive night shifts.

There are examples of night shift schedules, which involve many consecutive night shifts, eg, work on offshore oil platforms (7-14 consecutive nights) and work at remote places like Spitsbergen (21 consecutive nights), which show that circadian adaptation to night shift work appears to happen within days when it comes to subjective and objective measures of sleep (53-55) and cortisol rhythm (56). It is, however, not possible from the current literature to assess the long-term health and safety risk in these types of work settings. Thus, in special cases, eg, oilrigs and other isolated workplaces with better possibilities to adapt to daytime sleep, additional or other recommendations may apply.

Permanent night shift work, Permanent night shift work is characterized by having primarily or only night shifts and therefore many night shifts per week or month. It has been argued that employees with permanent night shift work adjust to day time sleep and therefore do not experience circadian disruption. However, only a very small minority of permanent night shift workers show complete adjustment of their endogenous circadian rhythm to night shift work (56, 57). We assume permanent night shift workers have health risks that are similar to workers on rotating night shift work with the addition of the potential effect of high intensity and number of consecutive night shifts. Because permanent night shift work is relatively rare, most of the existing studies that have included this work schedule are underpowered. Yet, permanent night shift work is associated with risk of breast and prostate cancer in some studies (50, 58) but not others (59, 60). The scheduling of permanent night shift work varies in duration of shifts, number of consecutive shifts and shift intervals. For this reason, the health risk associated with permanent night shift work per se cannot be evaluated without more detailed exposure information. Indeed in a study including such details, risk of prostate cancer was only higher among permanent night shift workers with long shifts and >6 consecutive night shifts (50).

Shift intervals, Shift intervals of <11 hours between two shifts (quick returns) have been associated with an increase in injuries (61, 62). Furthermore, evidence of a 5% increase in injuries for each hour less between two shifts has been shown (61). The results further indicate that the risk of injuries may be particularly increased after a quick return following a night shift (52, 61). In addition, a reduction in the number of annual quick returns reduced the risk, whereas an increase was associated with increased risk of self-reports of causing harm to one-self or patients/others (62). The available studies on shift intervals and occupational injuries indicate that risk of injury is reduced when quick returns are reduced and shift intervals are >11 hours (table 2).
Direction of rotation, In animal studies, the central circadian cycle is quicker to adjust when mimicking forward-rotation schedules, eg, D ^N, than backward rotation, eg, N ^D, and re-entrainment of most variables is slower for phase advance than phase delay (7). In several reviews, it has been concluded that shifting from backwards to forward rotation improves sleep (24, 39, 63), and an intervention study shows that fast forward rotation was associated with lower triglyceride and serum glucose and mean systolic blood pressure (64). Furthermore, forward rotation usually implies longer breaks (>24 hours) when changing from one type of shift to another, whereas backward-rotation systems often imply breaks corresponding to only the duration of the shifts, and therefore may have quick returns (65). Taken together, forward-rotating schedules appear to have the most advantages. However, a few studies with prostate cancer as an outcome, which address direction of rotation and the selected outcomes, found no associations (50, 66). For this reason, the risks of forward and backward rotation in relation to cancer, cardio-metabolic diseases and injuries cannot be evaluated based on the current literature.
Duration of night shifts. A meta-analysis based on four studies found that risk of injury was increased with shifts lasting 10 versus 8 hours (51). A register study of hospital employees reported an increased risk for occupational injuries in shifts lasting >12 hours (52). A large study with pooled data from case-control studies with complete work history in five countries, found a higher risk of breast cancer in pre-menopausal (but not post-menopausal) women working night shifts lasting >10 hours compared with women working night shifts lasting <8 hours (46). Night shifts lasting >10 hours were associated with higher risk of prostate cancer, particularly when part of permanent night shift work and >6 consecutive night shifts (50). These results support that risk of injury and possibly cancer are reduced with night shifts schedules, which have shifts with a maximum duration of 9 hours (table 3).
Pregnancy-related outcomes. Melatonin is also produced in the placenta (67) and may play a pivotal role in proper placenta function and parturition (68, 69). Meta-analyses of several large high-quality prospective studies indicate that the risk, if any, of preterm birth and growth restriction due to night shift work is marginal (70). The evidence with respect to miscarriage has been more limited but has indicated a higher risk especially with permanent night shift work (71). Knowledge regarding risk of pregnancy-related hypertension has been limited (71). Recently, a large nationwide cohort study of health professionals using payroll data, including exact working hours during pregnancy, found a dose-dependent higher risk of miscarriage in women working >2 night shifts the previous week (72). In the same cohort, the risk of calling in sick within two days following night shifts was higher throughout pregnancy independent of individual factors and time-invariant confounders (73), and - among night shift workers - the risk of hypertensive disorders of pregnancy, including pre-eclampsia, grew with increasing number of consecutive night shifts, particularly among obese women (body mass index >30 kg/m2) (74). The results support that, in order to reduce risk of miscarriage, pregnant women should have no more than one night shift in a week (table 4).

Recommendations and concluding remarks

We concluded that schedules that reduce circadian disruption may reduce cancer risk, particularly breast cancer, and schedules that optimize sleep duration and quality and reduce fatigue may reduce the occurrence of injuries. These changes in short-term physiological effects are generally achieved with fewer consecutive night shifts, sufficient shift intervals, and shorter night shift duration. Yet, sleepiness and possibly injury risk may be increased during the first night shift.
Based on the limited, existing literature, we recommend that in order to reduce the risk of injuries and possibly breast cancer, night shift schedules have (i) <3 consecutive night shifts, (ii) shift intervals of >11 hours and (iii) <9 hours shift duration.

In special cases, eg, oilrigs and other isolated workplaces with better possibilities to adapt to daytime sleep, other recommendations may apply.

Finally, in order to reduce risk of miscarriage, pregnant women should have no more than one night shift in a week. The risk associated with intensity, permanent night shift work and direction of rotation could not be evaluated based on the included studies. However, high intensity appeared to be associated with higher risk of breast cancer, hypertension and diabetes, and knowledge from physiological and experimental studies are in favor of forward rotation.

Generally, major knowledge gaps were observed and the number of studies on specific night shift schedules in relation to risk of cancer, cardio-metabolic diseases and injuries is limited. Concerning cancer, the majority of studies are related to breast cancer and, to some extent, prostate cancer. There is little evidence that results from these studies are transferable to other cancer types or from one sex to the other. Nor is it known if the short-term physiological effects per se are associated with long-term health and safety risk.

There are individual differences in response to night shift work, eg, according to age and chronotype (ie, how the circadian system embeds itself into the 24-hour day). Advanced ageing is associated with earlier chronotype (75), alterations in circadian rhythmicity and sleep-wake homeostasis (76), and higher morbidity and mortality in general. Ageing is, however, not associated with higher sleepiness in general (77) or in relation to sleepiness in night shift work (78). Due to the earlier chronotype and decreased sleep efficiency, sleeping especially after the nights shifts is curtailed (79). Besides the night shifts, also quick returns are associated with increased risk for sleep problems and fatigue among those aged >50 (80).

The present recommendations are related to the selected night shift schedules deemed relevant for health and safety. However, there are scheduling components related to night shift work that were not covered by the expert group - such as shift start and finish times and employees' control over night shift work. Also, the specific characteristics of night shift schedules were treated as if they were independent. However, the characteristics are highly correlated, eg, longer shift duration often implies fewer shifts and therefore more recovery time. More research is needed to establish how the different schedule characteristics interact and affect health and safety risks and if specific combinations imply a particularly higher or lower risk to health and safety. To make this possible, future etiological studies on shift work and health need to be based on precise and preferably repeated information on exposure combined with long, preferably registry-based follow-up. The use of register-based exposure information on working hours, like payroll data, is recommended if a sufficient proportion of working life is covered (81).

Although not systematic, the review of the literature aims to reduce bias in the selection of articles by employing a bibliographic search strategy and having a clear strategy for selection of papers. Several of the presented studies are based on hospital workers in the Nordic countries. Therefore, studies from other countries and sectors should be performed to take into account, eg, traditions regarding organization of night shift work, contextual factors such as working conditions and latitude-dependent exposure to sunlight over the year, work tasks, and the organization of the health care and welfare system.

Sleepiness is most profound on the first night shift. Accordingly, sleepiness is an inevitable consequence of working at night, no matter how night shifts are scheduled as long as employees change to night-time sleep during days off. Therefore, the concept of fatigue risk management, covering also sleepiness countermeasures other than optimal shift scheduling (eg, use of prior-sleep-wake data, fatigue detection technologies, and fatigue proofing strategies) has been introduced (82). Indeed, there are other ways to counteract the adverse health and safety risks of night shift work than through shift scheduling. At workplace level, fatigue risk management (82), lighting conditions (83) and self-rostering according to personal preference (84, 85) could be applied. There is some research supporting countermeasures at the individual level, such as bright light, melatonin, naps, use of stimulants, as a means to improve adaptation to night shift work (86). However, there is so far little evidence that such countermeasures reduce the long-term health consequences of night shift work (86). Lastly, other outcomes such as work-life balance and social well-being (87), productivity and patient safety may be relevant to consider when scheduling night shifts.

Acknowledgement
NordForsk, Nordic Program on Health and Welfare [grant number 74809] partly funded the writing of this paper.
Sidebar
Received for publication: 4 May 2020
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DETAILS

Subject:	Physiology; Shift work; Diabetes; Luminous intensity; Injuries; Sleep and wakefulness; Pregnancy; Night shifts; Sleep; Breast cancer; Schedules; Insomnia; Workers; Fatigue; Circadian rhythms; Clocks; Metabolic disorders; Melatonin; Safety; Cardiovascular disease; Nighttime; Disruption; Circadian rhythm; Light; Metabolites; Endocrine system; Health risks
Business indexing term:	Subject: Shift work Workers
Location:	Denmark
Publication title:	Scandinavian Journal of Work, Environment &Health; Stockholm
Volume:	46
Issue:	6
Pages:	557-569
Publication year:	2020
Publication date:	2020
Section:	Discussion paper
Publisher:	Scandinavian Journal of Work, Environment &Health
Place of publication:	Stockholm
Country of publication:	Finland, Stockholm
Publication subject:	Occupational Health And Safety
ISSN:	03553140
e-ISSN:	1795990X
Source type:	Scholarly Journal
Language of publication:	English
Document type:	Journal Article

DOI:	https://doi.org/10.5271/sjweh.3920
ProQuest document ID:	2464653168
Document URL:	https://www.proquest.com/scholarly-journals/how-schedule-night-shift-work-order-reduce-health/docview/2464653168/se-2?accountid=211160
Copyright:	Copyright Scandinavian Journal of Work, Environment &Health 2020
Last updated:	2021-12-14
Database:	Public Health Database

Psychosocial job strain and polypharmacy: a national cohort study

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ProQuest document link

ABSTRACT (ENGLISH)

Objectives Psychosocial job strain has been associated with a range of adverse health outcomes. The aim of this study was to examine the association between psychosocial job strain and prospective risk of polypharmacy (the prescription of >5 medications) and to evaluate whether coping strategies can modify this risk. Methods Cohort study of 9703 working adults [mean age 47.5 (SD 10.8) years; 54% female] who participated in the Swedish Longitudinal Occupational Survey of Health (SLOSH) at baseline in 2006 or 2008. Psychosocial job strain was represented by job demands and control, and measured by the Swedish version of the demand-control questionnaire. The outcome was incidence of polypharmacy over an eight-year follow-up period. Information on dispensed drugs were extracted from the Swedish Prescribed Drug Register. Logistic regression was used to estimate the association of job strain status with polypharmacy, adjusted for a range of confounders. Results During the follow-up, 1409 people developed polypharmacy (incident rate: 20.6/1000 person-years). In comparison to workers with low-strain jobs (high control/low demands), those with high-strain jobs (low control/high demands) had a significantly higher risk of incident polypharmacy (OR 1.40, 95% CI 1.04-1.89). The impact of high-strain jobs on developing polypharmacy remained among those with covert coping strategies (ie, directed inwards or towards others) but not among those with open coping strategies (ie, primarily directed toward the stressor). Conclusions Workers in high-strain jobs may be at an increased risk of polypharmacy. Open coping strategies may reduce the negative impact of psychosocial job strain on risk of polypharmacy.

FULL TEXT

Headnote

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Key terms coping; epidemiology; job control; job demand; occupational stress; stress.

Polypharmacy, the use of multiple medications by one individual, is increasing worldwide among those with multimorbidity (1). Polypharmacy has been highlighted as a key focus area by the World Health Organization in their global strategy to optimize medication use without harm (2). While there is no standard definition for polypharmacy, the most common is the concurrent use of >5 medications by a single individual (3). Although prescription drug use is highest among older people, the prevalence of polypharmacy has increased across all age groups over the last decade. In the US, the prevalence of polypharmacy increased from an estimated 8.2% in 1999-2000 to 15% in 2011-2012. Among those 20-39 years of age, the prevalence was 3.1% and 15% among 40-64-year olds (4). In 2015-2016, 60% of US adults aged 40-59 used >1 prescription drugs, and 15% used >5 (5). In Sweden, the prevalence of polypharmacy increased from 17% in 2006 to 19% in 2014 in the general population. The rate of polypharmacy was 8.5% among those <60 years (6). With growing medication use among those of working age, the contribution of working life to polypharmacy warrants further investigation.

Polypharmacy is associated with a range of adverse outcomes including inappropriate medication use, poor adherence, medication errors and drug interactions (7). Polypharmacy has also been linked to increased health care costs, and increased risks for hospitalization and mortality (1, 8). While a range of sociodemographic and socioeconomic risk factors for polypharmacy have been investigated (9), there is a paucity of research on the role of the psychosocial work environment (10). To date, no studies have investigated the association between psychosocial work stress and future risk of polypharmacy.

The psychosocial work-environment has been widely studied in terms of job strain - a situation with high psychological demands or pressures combined with low control in meeting those demands - and is assumed to be a risk factor for physical and mental health (11). Job strain has been reported to be associated with a range of adverse health outcomes including depression (12), cardiovascular disease (13, 14), diabetes (15), hypertension (16, 17), sleep disturbance (18), and musculoskeletal disorders (19, 20). Coping, defined as ongoing cognitive and behavioral efforts to manage psychological stress (21), may be employed to reduce the negative consequences of work stress. Coping may be broadly categorized into problem-focused (active efforts to resolve a problem) or emotion-focused (aims to reduce emotional discomfort) (22) and coping strategies may be primarily directed towards the stressor (open coping) or directed inwards or towards others (eg, family or friends) (covert coping) (23, 24). Coping has been previously found to have a moderating effect in the association between psychosocial work stress and various health and psychological outcomes (25-27). While certain strategies may be more beneficial than others, there remains a lack of clarity regarding coping's moderating role between job strain and a broader range of health outcomes.

The aim of this study was to examine the association between psychosocial job strain and prospective risk of polypharmacy (the use of >5 medications) and to evaluate whether coping strategies can modify this risk.

Methods

Study population

This was a data linkage study based on participants in the Swedish Longitudinal Occupational Survey of Health (SLOSH), an ongoing study of an approximately nationally representative sample of the Swedish working population (www.slosh.se) (28). Since 2006, a mailed self-completion questionnaire with two versions has been distributed biennially. Recipients who were in paid work >30% of full-time answered one version and recipients who temporarily or permanently worked <30% of full-time answered the other version. Statistics Sweden carried out the data collection, and a submitted response to the survey confirmed informed consent. The questionnaire asked extensive information on occupation, psychosocial work environment, work organization, health, and health-related complaints. The overall response rate to the questionnaires was 65% in 2006 (5985 respondents; 5141 to the 'worked >30% of full-time' and 844 to the 'worked <30% of full-time' questionnaire) and 61% in 2008 (11 441 respondents; 9756 to the 'worked >30% of full-time' and 1685 to the 'worked <30% of full-time' questionnaire) (28).

This study included participants who worked >30% of full-time when entering SLOSH in the year 2006 (N=5141) or 2008 (N=5170). Thus, there were a total of 10 311 individuals in gainful employment at baseline [mean age 47.8 (SD 10.8) years; 54% female]. We defined baseline as the first six months in 2006 and 2008 for the two cohorts, respectively. All the dates of study entry fell within this range. Prevalent cases were those who had polypharmacy during these six months. After excluding prevalent polypharmacy cases (>5 drugs, N=197) and people with missing occupational information (N=411), 9703 participants were included in the analytical sample.

Exposure

Psychosocial job strain was represented by job demands and control, and measured by the Swedish version of the demand-control questionnaire (DCQ) in SLOSH. The DCQ is widely used and has satisfactory psychometric properties (29, 30). Psychosocial demands at work were measured with five questions: (i) do you have to work very fast? (ii) Do you have to work very intensively? (iii) Does your work demand too much effort? (iv) Do you have enough time to do everything? (v) Does your work often involve conflicting demands? Job control was represented by decision authority and skill discretion and was assessed by six items from the DCQ: (i) do you have a choice in deciding how to do your work? (ii) Do you have a choice in deciding what you do at work? (iii) Do you have the possibility of learning new things through your work? (iv) Does your work demand a high level of skill or expertise? (v) Does your work require ingenuity? (vi) Do you have to do the same thing over and over again? These items were quantified on a scale from 1="yes, often" to 4="no, hardly ever/never". Except for answers to question 4 of the demands dimension and question 6 of the control dimension, the responses to the other nine questions were converted into 1="no, hardly ever/never" to 4-'yes". Response scores for job demands and job control were averaged, respectively. Thus, the response scores were presented in an ascending fashion (ie, higher scores referred to higher control/ demands). Following Karasek's job strain model (11), we combined job control and demands into four categories of job strain: low-strain jobs (low demands, high con- trol); passive jobs (low demands, low control); active jobs (high demands, high control); and high-strain jobs (high demands, low control). Psychosocial job strain was assessed at baseline only as it has been previously shown that levels of job demands and control remain relatively unchanged over time in the SLOSH cohort (31).

Outcome

The main outcome was the incidence of polypharmacy over an eight-year follow-up period. Information on dispensed drugs were extracted from the Swedish Prescribed Drug Register. This register contains data with unique patient identifiers for all prescriptions dispensed by pharmacies to the whole population of Sweden. Information on medication included the exact date of drug purchasing, drug name, dosage and quantity. All drugs were classified according to the anatomical therapeutic chemical (ATC) classification system (32). Polypharmacy was defined as the prescription of >5 medications and "excessive polypharmacy" was defined as the prescription of >10 medications. Data on drugs dispensed every quarter from the date of study entry were extracted and used to calculate quarterly polypharmacy outcomes each year over an eight-year period. The assessment of polypharmacy was based on the current drug use the last day of each quarter, by using a point prevalence method described previously (33).

Covariates

Characteristics were assessed by age and gender. Socioeconomic variables included the highest level of education (categorized into elementary, high school and university) and occupational class (blue- or white-collar worker). Age, gender and education were derived from national administrative registers and occupational class from the survey question: "To which occupational category do you belong?" with responses: (i) worker, (ii) clerical, (iii) line manager, and (iv) other. The first response was categorized as blue-collar worker and the remaining as white-collar worker. The presence of chronic diseases was derived from linked data from the National Patient Register which contains information for all inpatient and specialized outpatient visits in Sweden. All chronic diseases were defined according to International Classification of Diseases, 10th revision (ICD-10), and grouped into broad categories of chronic conditions, as previously reported (34).

The questions on coping were based on a questionnaire originally developed for a US study on high blood pressure but later adapted for the Swedish working population, which has been tested extensively (24, 35). Information about coping strategies in 2006 was collected by the question: "During the last two years when you felt steamrolled or unfairly treated by your manager/ managers or workmates, how have you reacted?" In 2008, this was changed to two separate questions: "How do you usually react if you are unfairly treated or get into conflict with a supervisor/manager?" and "How do you usually react if you are unfairly treated or get into conflict with a workmate?" In response to these questions there were four possible options that were graded on a scale, with 1=always to 4=never: (i) immediately made clear and clearly shown my feelings, (ii) suggested a compromise or other solution, (iii) kept quiet and brooded over it, and (iv) taken it out on my family/those closest to me. The first two responses represented open coping strategies, whilst the last two represented covert coping strategies. A sum score of coping strategies was calculated, ranging from 8-32, with higher scores representing more open coping strategies (24). Responses for the separate questions in 2008 were averaged. We further dichotomized scores using the median score for men and women separately.

Statistical analysis

Baseline characteristics across job strain categories and between people with and without polypharmacy were compared using Chi-square (x2) or one-way ANOVA followed by pairwise comparison with Bonferroni correction. Logistic regression was used to estimate the odds ratios (OR) and 95% confidence intervals (CI) for the association ofjob demands, job control and job strain status with polypharmacy. Logistic regression analyses were deemed more appropriate than Cox regression, as exact follow-up time to polypharmacy occurrence could not be determined (based on quarterly time points) and Cox proportionality assumptions did not hold across analyses.

Job control and job demands were treated as continuous variables first to examine linear associations with the outcome. To explore nonlinear associations, we created indicator variables for job control and job demands, respectively, using quartile distribution in men and women, separately. This was done to take into consideration gender differences in reporting perceived stress. The results from the quartile analyses revealed that the job controls and demands had different thresholds for polypharmacy, and the thresholds were similar between men and women. Thus we dichotomized job control (1 st quartile versus 2nd-4th quartile) and demands (1st and 2nd quartile versus 3rd and 4th quartile), respectively, and created the four job strain categories, with low strain as the reference group. Statistical interactions between job strain status and coping strategy, as well as potential effect modifiers such as sex, age, education, lifestyle factors, health status, and social support at work, were tested by introducing interaction terms in the model. In the case where a sta- tistically significant interaction was detected, stratified analysis was further conducted to compare polypharmacy risks across strata.

All analyses were first adjusted for age, sex and follow-up time, and additionally controlled for potential confounders. Variables that were significantly associated with polypharmacy and job strain, including occupational class, education and number of chronic diseases, were kept in the model in order to obtain the independent effect of job strain on polypharmacy. Collinearity tests showed that the variance inflation factor (VIF) for all the covariates was <1.26, with a mean value of 1.15, indicating the fully adjusted model should not have collinearity problems and the regression estimates from such a model should be stable. Sleep quality, depressive symptoms, and lifestyle factors were not significantly associated with polypharmacy or job strain and thus excluded from the analysis. A description of these covariates is provided in the supplementary material (https://www.sjweh.fi/show_abstract.php?abstract_id=3914).

Several sensitivity analyses were carried out. First, we excluded people taking any drugs at baseline to include participants who were relatively healthier. Second, we redefined the outcome as multiple/repeated polypharmacy over the follow-up period. This was done in order to lower the risk of false positive polypharmacy and also evaluate chronicity of polypharmacy. Third, we repeated the analysis by excluding 185 individuals who were <26 years because the occurrence of polypharmacy was uncommon (<2.17%). We also performed stratified analysis by age <55 versus >55 years because the younger participants had a lower rate of polypharmacy (<15.58°%) than the older participants (>21.68%). Fourth, we performed stratified analysis by occupation because both men and women work to a very large extent in Sweden, the labor market is quite gender segregated horizontally (men and women tend to have different occupations). Therefore, gender differences in demands and control could be due to actual differences between the jobs that men and women tend to do rather than the differences in reporting style as mentioned before. Finally, we used active job as a reference group as this has been reported in the occupational health literature and in studies of other health outcomes.

All reported P-values were two-sided, and P<0.05 was considered statistically significant. Data were computed using Stata SE 14.0 (StataCorp LP, College Station, TX, USA).

Ethical considerations

This study was conducted with the approval of the Regional Research Ethics Board in Stockholm. Data were coded and anonymized before statistical analyses.

Results

A total of 9703 participants were followed up to 31 December 2014 [mean follow-up time 7.1 (SD) 2 years]. Baseline characteristics of the study population by job strain status are summarized in table 1.

During the follow-up, 1409 (14.5%) people developed polypharmacy (prescription of >5 medications, incident rate: 20.6/1000 person-years). Incidence of polypharmacy varied across age groups: 19-39 years (N=113, 4.64%), 40-49 years (N=266, 9.79%), 50-54 years (N=230, 15.58%), 55-59 years (N=343, 21.6%), and 60-68 years (N=457, 30.5%). Of those with incident polypharmacy, 103 individuals developed excessive polypharmacy (prescription of >10 medications). As the incidence of excessive polypharmacy was low, we decided to run analyses focusing on polypharmacy. Baseline characteristics of the study population by polypharmacy outcome status are summarized in table 2. Those participants who developed polypharmacy were older and less educated, had greater number of chronic diseases and were less likely to use covert coping strategies.

The most prevalent medications contributing to polypharmacy at follow-up were beta blockers (ATC code: C07A), lipid modifying agents (C10A), antithrombotic agents (B01A), antidepressants (N06A), hypnotics and sedatives (N05C), drugs for peptic ulcer and gastrooesophageal disease (A02B), opioids (N02A), calcium channel blockers (C08C), angiotensin-converting enzyme (ACE) inhibitors (C09A), and other analgesics (N02B).

Compared with low job control, workers with high job control had a lower risk for polypharmacy (OR 0.74, 95% CI 0.59-0.92); however, there was no association between job demands and polypharmacy (table 3). In comparison to workers in active jobs, those in highstrain jobs had a significantly higher risk of incident polypharmacy (OR 1.40, 95% CI 1.04-1.89) (table 4).

In the sensitivity analysis, we found similar results among individuals >26 years (high-strain jobs: OR 1.41, P=0.025), in stratified analysis by age (age <55, highstrain jobs: OR 1.42, P=0.081 and age >54, high-strain jobs: OR 1.40, P=0.164), and in stratified analysis by occupation (among blue-collar workers, high-strain jobs: OR 1.30, P=0.239 and among white-collar workers, high-strain jobs: OR 1.52, P=0.062). When using active jobs as the reference group, results remained similar in fully adjusted models (high-strain jobs: OR 1.57, 95% CI 1.15-2.16).

We detected a statistically significant interaction between coping strategy and high-strain jobs. After stratifying by coping strategy, the effects of high job strain on developing polypharmacy remained in those with covert coping strategies (OR 1.61, 95% CI 1.04-2.48) (figure 1). However, no association was observed among those with open coping strategies. Similar results were observed after excluding individuals younger than 26 years, among those with covert coping strategies (high-strain jobs: OR 1.63, P=0.026) and among those with open strategies (high-strain jobs: OR 1.19, P=0.52). Among white-collar workers, passive jobs were associated with an increased risk of polypharmacy in those with covert coping strategies (OR 1.95, P=0.026). When using active jobs as the reference group, high-strain jobs (OR 2.05, 95% CI 1.32-3.21) and passive jobs (OR 1.79, 95% CI 1.15-2.79) were significantly associated with polypharmacy in those with covert coping strategies. No association was found for those with open coping strategies.

These results did not remain significant in other sen- sitivity analyses, when participants taking any drugs at baseline were excluded, and when the occurrence of multiple/repeated polypharmacy was used as the outcome (supplementary tables S1 and S2). In sensitivity analysis 2, active jobs were associated with an increased risk of polypharmacy compared to low-strain jobs (OR 1.99, 95% CI 1.07-3.72) in those with open coping strategies.

Discussion

Our study found that when compared with workers in low-strain jobs, high-strain jobs were associated with an increased risk of polypharmacy. After stratifying by coping strategies, this association remained only in those with covert coping strategies.

Previous studies have found job strain to be associated with a range of individual chronic diseases (12, 13, 15, 18) and shorter health expectancy (36). However, to our knowledge, no previous studies have looked at the association between job strain and polypharmacy. Polypharmacy indicates clinically significant medical conditions and symptoms requiring pharmacological intervention and provides a marker of multimorbidity and disease severity. However, polypharmacy may also indicate potential overuse of medications, including inappropriate or problematic medications and combinations. In such situations, the harms of medications may outweigh the intended benefits (1).

Our study found that high control at work was associated with a lower risk of polypharmacy, while job demands alone did not have a significant impact. This is in line with previous studies of other health outcomes including cardiovascular disease (13), mental health (37) and dementia (38). Our finding highlights the importance of control at work despite level of demands, suggesting that workers who are allowed to make decisions or utilize skills to manage work demands have lower levels of stress and thus avoid multiple medication use.

In our study, we found that compared with lowstrain jobs, those with high-strain jobs were at greater risk for developing polypharmacy. These associations remained after adjusting for a range of potential confounders, including occupational and health conditions, suggesting a direct association between job strain and polypharmacy. Low-strain jobs are theoretically ideal jobs, being the most relaxed, and were used as the comparator in our main analysis. Conversely, high-strain jobs, where low control is combined with high demands, represent stressful work situations, thus placing workers at risk of adverse health events. We used active jobs as a reference group in our secondary analysis. Active jobs are highly demanding jobs that allow the employee to decide when they do their work. As a result of the high level of decision latitude, employees do not experience their job as stressful, despite it being very psychologically demanding (11). Interestingly, both high-strain and passive jobs were associated with an increased risk for polypharmacy compared to active jobs in those with covert coping strategies. Passive jobs, where low control is combined with low demands, can be demotivational to workers as their skills and self-efficacy are underutilized and diminished (39). Under stimulation at work may also be recognized as a source of stress, similar to overstimulation (40). Thus, passive jobs can also lead to chronic stress. Passive jobs have previously been demonstrated to be associated with disability, multimorbidity and other outcomes (41, 42).

There are potential physiological mechanisms that may explain the observed association between psychosocial job strain and polypharmacy. Firstly, chronic stress may lead to neuroendocrine dysregulation of the hypothalamic-pituitary-adrenal axis, which in turn induces changes in the immune and inflammation systems and consequently the development of several chronic conditions and polypharmacy (12, 43, 44). These processes have been conceptualized as allostatic load (45). Work stress has also been linked to a range of disease risk factors including increased adiposity, systemic inflammation, and altered metabolic profile (46). Secondly, stress has been identified as a significant feature of several mental illnesses, including depression (12, 44), which may explain increased use of medications, especially psychotropics. Finally, stress may also lead to unhealthy lifestyle behaviors, such as smoking, heavy alcohol consumption, and physical inactivity (47, 48), which may also be implicated in the development of cardiometabolic diseases and polypharmacy. However, we found no significant interaction between lifestyle factors and job strain in our study.

Coping strategies appeared to moderate the association between psychosocial job strain and polypharmacy. In our study, more open styles of coping ameliorated the association between job strain and polypharmacy, with the association remaining only in those with more covert coping strategies. Previous studies have demonstrated that covert coping with unfair treatment at work is associated with an increased risk of cardiovascular disease (23, 24). Work-related stress in the presence of covert coping may also increase risk for oesophageal and gastric cancers (49). This highlights the important interaction between a stressful work environment and an individual's response to it. It is postulated that poor coping strategies can result in psychophysiological tension and the development of illness (24), which in turn may lead to polypharmacy. In subgroup analysis by occupational class, passive jobs were associated with an increased risk of polypharmacy among white-collar workers with covert coping strategies. This may reflect poor health behaviors and coping such workers (50).

The impact of high-strain jobs on polypharmacy disappeared when we took into account any drug use at baseline and repeated occurrences of polypharmacy at follow-up. This may suggest that the influence of job strain on polypharmacy is greatest in those with underlying chronic health problems but may not be long lasting. Interestingly, active jobs were associated with repeated occurrences of polypharmacy among workers with open coping strategies, suggesting potential stress from active jobs. More studies are warranted to clarify the underlying mechanisms.

The most commonly used medications contributing to polypharmacy reflect the treatment of medical conditions previously found to be associated with job strain including cardiovascular disease (beta blockers, lipid modifying agents, antithrombotics, ACE inhibitors), mental disorders (antidepressants, hypnotics and sedatives), gastroesophageal disease (drugs for peptic ulcer and gastro-oesophageal disease), and musculoskeletal and pain disorders (opioids and other analgesics).

However, previous studies investigating the association between job strain and specific medication use have been inconsistent. A previous study demonstrated that psychological work demands were associated with the purchase of antihypertensive medication in women (51). Exposure to low job control and high job demands was associated with subsequent psychotropic medication use, including antidepressants and anxiolytics, in a previous study (52). Another study found that men with high job strain had an increased risk of future antidepressant medication use (53). A cross-sectional study found an association between high job strain and self-reported benzodiazepine use (54). Conversely, other previous studies have found no significant association between job strain and psychotropics, including antidepressants (55).

Our study findings highlight the need for organizations and workplaces to optimize psychosocial work conditions in order to potentially reduce future risk of ill health and subsequent polypharmacy. Policies to empower workers to adopt better and more open coping strategies to mitigate this risk should be encouraged. Future studies should look at other types of working conditions, as well as the interplay between different medication classes. Strategies to manage psychosocial job strain at work should be further explored. As working conditions continue to evolve, and multimorbidity and complex drug regimens become more common with an aging population, such strategies will be of great importance to ensure a healthy and sustainable workforce.

This study has strengths and limitations. Strengths lie in the large, representative sample of Swedish workers. The prospective study design allowed a temporal association between psychosocial job strain and incident polypharmacy to be explored; however, causality cannot be concluded. Medication outcomes and medical comorbidity data were ascertained from national registers that were complete, thus avoiding any potential attrition or recall bias. However, data on psychosocial work environment and covariates were self-reported, which may lead to misclassification and response bias. Non-response varied from 35-39%; as occupational status is unknown among non-responders, it is difficult to determine whether respondents represent the overall Swedish working population. However, it was previously shown that, in general, those who were women, younger, married, university educated and born in Sweden were more likely to respond to the SLOSH questionnaires (28). Thus, this may impact the generalizability of our findings. We did not consider non-prescription medications such as those obtained over-the-counter, thus we may have underestimated incidence of polypharmacy. The measure of coping used in this study was relatively crude and other factors could explain the observed associations, such as personality traits or other personal characteristics underlying coping patterns (24). Additionally, this measure relates mainly to unfair treatment or conflicts at work and may not be optimal for other types of work stress. In addition, the large internal missing rate of the coping questions (13%) is a potential weakness. Although we adjusted for a range of important covariates, we cannot exclude the possibility of bias due to unmeasured confounding.

Concluding remarks

Workers of high-strain jobs may be at an increased risk of polypharmacy. Open coping strategies may reduce the negative effects of psychosocial job strain on risk of polypharmacy.

Acknowledgements

The authors are grateful to all colleagues and coworkers at the Stress Research Institute for providing data for this study as well as all participants in SLOSH. The study was supported by the Swedish Council for Working Life and Social Research (FORTE), #2019-01120, #2005-0734 and The Swedish Research Council (VR), #825-2009-6192, #2013-1645, #2015-06013, #2017-00624 and #2018-02998. The first author is supported by a NHMRC-ARC Dementia Research Development Fellowship (APP1107381).

The authors declare no conflicts of interest.

Sidebar

Tan ECK, Pan K-Y, Magnusson Hanson LL, Fastbom J, Westerlund H, Wang H-X. Psychosocial job strain and polypharmacy: a national cohort study. Scand J Work Environ Health. 2020;46(6):589-598. doi:10.5271/sjweh.3914

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Received for publication: 3 April 2020

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DETAILS

Subject:	Occupational stress; Population; Work environment; Investigations; Age; Coping; Polypharmacy; Employment; Drug use; Questionnaires; Occupational health; Prescription drugs; Risk; Cohort analysis
Business indexing term:	Subject: Occupational stress Work environment Employment
Location:	Sweden; United States--US
Publication title:	Scandinavian Journal of Work, Environment &Health; Stockholm
Volume:	46
Issue:	6
Pages:	589-598
Publication year:	2020
Publication date:	2020
Section:	Original article
Publisher:	Scandinavian Journal of Work, Environment &Health
Place of publication:	Stockholm
Country of publication:	Finland, Stockholm
Publication subject:	Occupational Health And Safety
ISSN:	03553140
e-ISSN:	1795990X
Source type:	Scholarly Journal
Language of publication:	English
Document type:	Journal Article
DOI:	https://doi.org/10.5271/sjweh.3914
ProQuest document ID:	2464653045
Document URL:	https://www.proquest.com/scholarly-journals/psychosocial-job-strain-polypharmacy-national/docview/2464653045/se-2?accountid=211160
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Last updated:	2023-02-27

Shift work relationships with same- and subsequent-day empty calorie food and beverage consumption

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ABSTRACT (ENGLISH)

Objectives Shift work may contribute to unhealthy eating behaviors. However, the evidence is built mainly on comparisons of eating behaviors between shift and non-shift workers. Growing research has suggested daily experiences and exposures may contribute to daily fluctuations in peoples food consumption. The purpose of this study was to examine within-person associations between shift work and same- and subsequent-day empty calorie food/beverage consumption. Methods This was a 14-day intensive longitudinal study using ecological momentary assessment. A convenience sample of 80 hospital registered nurses working a rotating shift in Taiwan completed a 21-item food checklist assessing their empty food/beverage consumption (ie, fast/fried food, sweet and salty snacks, sugar-sweetened beverages) four times at random daily. Daily shift work (ie, day, evening, or night shift) was derived from the registry-based work schedule. Three-level mixed-effects regression models were employed for hypothesis testing. Results A total of 77 participants with 2444 momentary assessments were included in the final analysis. The results suggested that participants on night compared to day shifts had higher likelihoods of fast/fried food intake [adjusted odds ratio (ORadj) 1.7, 95% CI 1.2-2.6] and sugar-sweetened beverage consumption (ORadj 1.5, 95% CI 1.0-2.1). However, there were no significant associations between shift work and subsequent-day empty calorie food/beverage consumption. Conclusions Night shift work is associated with same-day increased empty calorie food/beverage consumption among workers. Strategies that help to prevent unhealthy eating behaviors on night shifts may help to reduce rotating shift workers empty calorie food/beverage consumption and ultimately improve their health.

FULL TEXT

Headnote

Objectives Shift work may contribute to unhealthy eating behaviors. However, the evidence is built mainly on comparisons of eating behaviors between shift and non-shift workers. Growing research has suggested daily experiences and exposures may contribute to daily fluctuations in peoples food consumption. The purpose of this study was to examine within-person associations between shift work and same- and subsequent-day empty calorie food/beverage consumption. Methods This was a 14-day intensive longitudinal study using ecological momentary assessment. A convenience sample of 80 hospital registered nurses working a rotating shift in Taiwan completed a 21-item food checklist assessing their empty food/beverage consumption (ie, fast/fried food, sweet and salty snacks, sugar-sweetened beverages) four times at random daily. Daily shift work (ie, day, evening, or night shift) was derived from the registry-based work schedule. Three-level mixed-effects regression models were employed for

hypothesis testing. Results A total of 77 participants with 2444 momentary assessments were included in the final analysis. The results suggested that participants on night compared to day shifts had higher likelihoods of fast/fried food intake [adjusted odds ratio (ORadj) 1.7, 95% CI 1.2-2.6] and sugar-sweetened beverage consumption (ORadj 1.5, 95% CI 1.0-2.1). However, there were no significant associations between shift work and subsequent-day empty calorie food/beverage consumption. Conclusions Night shift work is associated with same-day increased empty calorie food/beverage consumption among workers. Strategies that help to prevent unhealthy eating behaviors on night shifts may help to reduce rotating shift workers empty calorie food/beverage consumption and ultimately improve their health.

Key terms circadian rhythm; eating behavior; food consumption; ecological momentary assessment; shift worker.

To provide around-the-clock services, many industries (eg, healthcare) utilize shift work to extend their operational hours "24/7 (1). In general, shift work refers to work that requires workers to be on duty between 18:00-06:00 hours (2). Globally, shift workers account for approximately 20-25% of the workforce (3, 4). Moreover, in the US, two thirds of shift workers engage in rotating shift work (4), defined as periodically working different shifts (2).

Previous studies have found shift work, particularly rotating shift work, to be associated with increased risk of chronic diseases (eg, type 2 diabetes) (5, 6). Exposure to artificial light at night and changed sleep-wake cycle due to shift work may disrupt workers circadian rhythm and adversely affect shift workers health. Disrupted circadian rhythm has been linked to desynchronized appetite hormones (eg, decreased leptin) (7), which may increase appetite and food consumption (8). In addition, it has been documented that shift work may contribute to reduced insulin sensitivity (9) and decreased glucose tolerance (10), and in turn increased risk of type 2 diabetes (11, 12).

Empty calorie food/beverage consumption (ie, foods and beverages high in solid fats or added sugars and low in nutrients) (13) has also been linked to an increased likelihood of the aforementioned chronic diseases (14, 15). Shift work may play a role in between-person differences in empty calorie food/beverage consumption (16, 17). Relative to working on regular day shifts, research has found working on non-day shifts (ie, evening or night shifts) was related to higher intake of sweetened foods (17, 18) and sweetened beverages (18, 19). Thus, empty calorie food/beverage consumption, may be one of the pathways by which evening and night shift work increases chronic disease risk (20). Furthermore, research suggested that there may be a joint association of rotating shift work and unhealthy lifestyle (eg, low dietary quality) with increased type 2 diabetes risk (21).

Recent studies have shown that empty calorie food/ beverage consumption can vary day-to-day or moment-by-moment based on experiences or environmental context (eg, stress, shift work), suggesting that empty calorie food/beverage consumption may vary not only between but also within persons (22, 23). Additionally, people's experiences and exposures on a given day may influence their behaviors on the subsequent day (23, 24). Cain et al (2015) observed that participants consumed more high-fat foods on the morning after being exposed to a simulated night shift (24). This indicates that a person's empty calorie food/beverage consumption may differ depending on their shift work that day or the previous. Yet, no study has examined how changes in work schedule timing relate to within-person daily fluctuations in empty calorie food/beverage consumption.

Building on prior research, the purpose of this study was to examine contributions of shift work to within-person variations in daily empty calorie food/beverage consumption using an intensive longitudinal study design (25) and ecological momentary assessment (EMA). Two hypotheses on within-person associations were tested: (i) on days when working evening or night shifts, empty calorie food/beverage consumption will be higher compared to days when working day shifts, and (ii) on days when working evening or night shifts, empty calorie food/ beverage consumption will be higher on the subsequent day compared to days when working day shifts.

Methods

Sample

Our target population was rotating shift (ie, a monthly work schedule including at least two shifts timings such as day and night shifts) workers. A convenience sample of registered nurses working in the Taiwan accredited hospitals (26) was recruited using electronic flyers shared on social media platforms (eg, Facebook). Inclusion criteria were as follows: (i) Taiwanese registered nurse working full-time (ie, 40 hours per week), (ii) 20-65 years old, (iii) working on rotating shifts in the hospital for >6 months and in the next 30 days, and (iv) no intention to leave the nursing profession in the next month. Exclusion criteria were: (i) having no smartphone or having a smartphone but no access to internet services, (ii) unwilling or unable to provide registry-based work schedule, (iii) working in an administrative position such as Dean or Head Nurse, and (iv) pregnant.

We recruited 80 registered nurses working in hospitals in Taiwan between October 2018 and January 2019; 1 dropped out of the study before the first EMA survey was sent. Our goal was to preserve as much of the sample as possible, but we recognized some people really did not participate. Thus, we excluded those whose participation was effectively zero. Our main interest was within-person associations between shift work and empty calorie food/beverage consumption. Therefore, we excluded participants with an EMA response rate <10% (ie, <6 completed EMA surveys) or <10% of possible valid EMA survey days (ie, a valid day was considered those in which >2 daily EMA surveys were completed) (N=2). As a result, the analytic sample comprised 77 participants. Only EMA surveys with complete data were included in the analysis. The detailed information related to data collection and exclusion is displayed in figure 1.

Study design and procedure

This was an intensive 14-day longitudinal study (25) using EMA (ie, a research approach that assesses participants' behaviors or experiences in the natural environment in real-time) (27) with three phases: baseline visit, consecutive 14-day EMA data collection period, and post visit (approximately two weeks after the baseline survey). During the baseline survey visit, we (i) obtained written informed consent; (ii) administered a questionnaire, (iii) provided instructions for EMA surveys, including how and when to answer an online survey in the REDCap system on the smartphones and what to do when there was downtime in this system; and (iv) collected the published work schedule during the past 30 days and the prospective work schedule for the next 30 days.

During the 14-day EMA data collection period, empty calorie food/beverage intake, work schedule, and potential confounders were collected using the EMA surveys. The EMA sampling method can be roughly divided into two categories: event-based sampling (ie, collecting data when an event occurs) and time-based sampling (ie, collecting data over time) (27). In this study, the EMA sampling method was time-based. Participants were signaled to complete the EMA survey using a provided survey link by either text message or e-mail four times per day at random during the following time blocks: 03:00-09:00, 09:00-15:00, 15:00-21:00, and 21:00-03:00 hours. Based on a participant's anticipated shift schedule and wake-sleep pattern, these four time blocks were adjusted as required. Most survey signals were sent via text message, with a text reminder every 15 minutes if there was no response from the participant. The survey was available for an hour after the initial text message was sent. If the participant did not complete the survey within an hour, the survey was closed and recorded as missing. Due to an unforeseen technical problem in which the messaging system had regular maintenance downtime each day (ie, 13:00-16:00 hours local time), an email survey signal was sent during that period using the Qualtrics system.

During the post visit, we administered a survey related to changes in shift schedules over the prior two weeks and provided compensation for participation of up to approximately US$30 in cash. The Institutional Review Boards (IRB) at the University of Illinois at Chicago (No. 2018-0950) and National Taiwan University Hospital (No. 201712216RIND) approved this study.

Measures

Shift work

Shift work was a day-level measure. It was assessed based on the time when a participant started their work shift (ie, day, evening, night) (28), documented on the published work schedule. We operationally defined night shifts as shifts with working hours covering 24:00-08:00 hours.

Empty calorie food/beverage consumption

Consumption of empty calorie foods/beverages was a moment-level variable. It was assessed four times per day with a 21-item checklist based on the following question: "Since the last signal, have you consumed or used any of the following items? (Please check all that apply)." The 21-item food checklist was created based on the top sources of empty calorie foods/beverages reported in the 2003-2006 National Health and Nutrition Examination Survey

(NHANES) (29), the 1993-1996 Nutrition and Health Survey in Taiwan (NAHSIT), and the 2005-2008 NAHSIT (30). Based on the food/beverage items listed in the food frequency questionnaire employed in the NAHSIT (31), the aforementioned 21 food/beverage items were grouped into the following categories: fried/fast food, sweet snack foods (ie, candy, chocolate, cookies, brownies, doughnuts, cakes, pastries, pies, jelly, puddings, sweetened shaved ice desserts or ice cream, popcorn), salty snacks (eg, chips), and sugar-sweetened beverages (ie, carbonated beverages, sugar-added processed juice, lactic acid drinks, sports drinks, instant powered drinks, chocolate beverages, and tea with added-sugar and/or toppings). Each category was analyzed as a separate outcome variable. Because of the right skewed distributions of empty calorie food/beverage consumption variables, we dichotomized these as "none" and "at least one". Namely, reporting at least one item in a food/ beverage category was considered consumption of that food/beverage category during the a given time block. Because salty snack consumption was reported in <5% of the surveys, sweet snack and salty snack consumption were combined as sweet and salty snack food consumption in the analysis.

Covariates

Time-varying covariates. The time-varying covariates in this study included emotions, stress, daily working hours, number of completed EMA surveys per day (range 1-4), and the sequence of EMA survey day (ie, the 1st, the 2nd, ..., or the 14th day).

Emotions were assessed four times per day using the ten-item International Positive and Negative Affect Schedule Short Form (I-PANAS-SF) (32) and four items from the affect subscale of the University of Wales Institute of Science and Technology (UWIST) mood scale (33, 34). In response to the question, "How have you been feeling since the last time you completed a survey?", items from the I-PANAS-SF (32) were assessed on a five-point Likert scale (ie, never, seldom, sometimes, often, always), while items on the UWIST (33, 34) were assessed on a four-point Likert scale (ie, definitely not, slightly not, slightly, definitely). Measures of positive emotions and negative emotions were constructed by summing scores of the seven positive affect items (range 7-33) and the seven negative affect items (range 7-33), respectively.

Stress was assessed with a single item in the tense arousal UWIST subscale: "stressed" (33, 34). As described above, this item was assessed on a four-point Likert scale from "definitely not " to "definitely ". Daily working hours were assessed based on the record in the published work schedule.

Time-invariant covariates. Assessed as part of the baseline survey, time-invariant covariates were person-level measures that included the following: age (in years), gender, educational attainment, marital status, family responsibility (ie, being as a main caregiver for kids or disabled persons in their family), and per capita household income. Other person-level covariates included body mass index (BMI) derived from self-reported height (cm) and weight (kg), health conditions (eg, medical history), smoking and tobacco use, occupational history such as year(s) of working as a registered nurse and history of rotating shift work (in years), and work unit (eg, surgical, medical ward, or intensive care unit).

Analysis

Descriptive statistics. STATA 15 (Statacorp, College Station, TX, USA) was employed for data analysis. Descriptive statistics were employed to describe participants' characteristics (eg, demographics), daily shift work, momentary empty calorie food/beverage intake (ie, fried/fast food, sweet and salty snacks, and sugar-sweetened beverages), and other time-varying covariates. In addition, momentary empty calorie food/beverage consumption was presented by shift timing: day, evening, or night shift.

Inferential statistics. Three-level mixed-effects logistic regression models were employed to test associations between shift work and three categories of empty calorie food/beverage consumption: fried/fast food, sweet and salty snack foods, and sugar-sweetened beverages. We employed backward selection methods based on results of a likelihood ratio test (significance level: 0.05) to select the most parsimonious model for each outcome. If a variable met the criterion for inclusion as a covariate in any model, it was included in models for all outcomes. As a result, the identified moment-level covariates were emotions and stress level; the day-level covariates were the number of complete EMA surveys and the sequence of EMA survey days. The identified person-level covariates were age, BMI, educational attainment, family responsibility, and health conditions.

To test our first hypothesis, we regressed empty calorie food/beverage consumption on same-day shift work (ie, predictor) and the identified time-varying and time-invariant covariates. To test our second hypothesis, we regressed empty calorie food/beverage consumption on prior-day shift timing, same-day shift timing, and the identified covariates.

Mixed-effects regression models are comprised of two components: fixed and random effects. For time varying variables, the effects can be divided into two components: within- and between-person effects (35). In this study, given a sample size of 77, we focused on the within-person effects that captured how changes in a time-varying independent variable in a person (ie, the deviance of person i at time t from the mean level/ proportion of person i across time) contributed to that person's variations in a dependent variable, accounting for that person's mean level/proportion of that variable across time (35).

Sensitivity analysis

Our primary strategy involved matching intake in a 24-hour calendar day to shift timing that same calendar day. This approach can capture intake prior to the start of a shift, particularly on evening shifts. However, it is possible that shift work affects subsequent day intake only. As a result, for working days, we tested the sensitivity of results by matching the start of a 24-hour consumption window to the start of a shift. After limiting to those observations that met this criterion, 2031 momentary observations were included in the sensitivity analysis.

It is possible that the effects of shift work on salty snacks differ from its influences on sweet snacks. Therefore, we also tested the sensitivity of results of snack food consumption by removing salty snack consumption from "sweet and salty snack consumption". The influences of shift work on sweet and salty snacks were analyzed in separate models.

Results

Descriptive statistics

After excluding observations with incomplete data, a total of 2444 EMA surveys nested within 961 person-day observations and 77 participants were included. Overall, each participant was followed for 12.5, standard deviation (SD) 2.3 days. The average number of EMA surveys per person-day was 2.5 (SD 1.0). Sample characteristics are presented in table 1. Out of the 961 person-day observations, 23.8% were day shifts, 22.0% were evening shifts, 22.3% were night shifts, and 32.0% were off-duty days. The average hours per working day were 8.2 (SD 0.4) hours. As shown in table 2, participants reported consuming fried/fast food at 16.1% of the signals, sweet and salty snack foods at 32.2% of signals, and sugar-sweetened beverages at 34.8% of signals.

Inferential statistics

Table 3 shows crude and adjusted associations between shift work and same-day empty calorie food/beverage consumption. After adjusting for covariates and accounting for a person's usual conditions of shift work, working night shifts was associated with a 70% increase in the likelihood of fried/fast food consumption [adjusted odds ratio (ORadj) 1.7, 95% confidence interval (CI) 1.2-2.6] and a 50% increase in the likelihood of sugar-sweetened beverage consumption (ORadj 1.5, 95% CI 1.0-2.1).

Table 4 shows crude and adjusted associations between shift timing and subsequent-day empty calorie food/beverage consumption. In the crude and adjusted models, shift work was not significantly associated with the likelihood of subsequent-day empty calorie food/beverage consumption.

Sensitivity analysis

Results in the sensitivity analysis were consistent with those presented in table 3 and table 4 (see supplementary material, www.sjweh.fi/show_abstract.php?abstract_ id=3903, table S1). Compared to day shifts, the likelihood of fried/fast food consumption and sugar-sweetened beverages intake were higher on night shifts. In terms of sweet and salty snack consumption, the results were similar when salty snacks were removed from the snack food measures (supplementary table S2).

Discussion

This is the first study to examine dynamic within-person associations between shift work and workers' empty calorie food/beverage consumption. We found that working night shift versus day shift was associated with higher likelihoods of reporting same-day fried/fast food consumption and sugar-sweetened beverage consumption. No associations were found between empty calorie food/beverage consumption and prior-day shift work.

Consistent with de Assis et al's findings (17), we did not find significant influences of evening shifts on empty calorie food/beverage consumption. Our findings suggested that, on night-shift-working days, the likelihood of fried/fast food consumption and sugar-sweetened beverage intake were higher than on day-shift-working days. There are multiple possible explanations for this finding. First, working night shift is often contrary to a person's biological clock, which may result in increased risk of circadian disruption (7) and further contribute to imbalanced secretion of appetite-hormones, such as decreased leptin (7, 36) or increased ghrelin (7, 37). Decreased leptin and increased ghrelin have been linked to increased appetite and food consumption (38). This may also explain why we did not observe increased empty calorie food/beverage consumption on evening shift compared to days working on day shift because circadian disruption is less likely.

Second, the food environment (eg, food availability) has been linked to a person's snack food consumption (22). Bonnell et al (16) reported that rotating shift workers consumed a greater proportion of discretionary snack foods on night compared to day shifts. When examining workers' food choices, accessibility of food was one of the major themes of increased discretionary snack food consumption (16). However, it was noteworthy that there were no significant associations between shift timing and sweet and salty snack consumption in this study. With the exception of fast food restaurants and convenience stores, most food outlets in Taiwan are closed when people are working at night. It is possible that fast/fried food and sugar-sweetened beverages were more accessible on night shifts, relative to sweet and salty snacks. As a result, ciations between shift timing and sweet and salty snack consumption were masked. Additional studies considering the food environment may help to understand if the environment may influence the relationships of shift work and daily empty calorie food/beverage consumption.

Third, night shift workers may consume unhealthy foods (eg, sweetened snacks) to stay awake during their night shifts (39, 40). A qualitative study of 12 registered nurses observed that some nurses consumed high sugar foods and sugar-sweetened beverages to prevent or to cope with their fatigue (41). In this study, we observed that 79.5% (676 out of 850) of participants' sugar-sweetened beverage consumption were caffeinated (eg, cola, tea). It is possible that the increased likelihood of sugar-sweetened beverage consumption in this study was related to participants' coping strategies for fatigue from night shifts.

Additionally, shift work may reduce workers' time available for food preparation (16) or consumption (39). Shift workers tend to purchase and consume something that is easy and quick to prepare (16). Therefore, it is also possible that increased consumption of empty calorie foods/beverages on night shifts is related to decreased time availability for food preparation or consumption on night compared to day shifts.

We found no associations between shift work and subsequent day empty calorie food/beverage consumption. To our knowledge, no study has investigated the dynamic effects of shift work on workers' next-day empty calorie food/beverage consumption. Shift work may disrupt workers' circadian alignment (7), which may further imbalance the appetite hormones (eg, ghrelin). Previous studies suggested increased pre-prandial levels of ghrelin were associated with greater appetite or food consumption during that meal (38). These findings are consistent with the possibility that the effect of appetite hormones on food intake is transient instead of long-term.

Implications for interventions

To improve workers' health behaviors, multi-level interventions (eg, organizational, individual) are recommended (42, 43). At the organizational level, the food environment has been noted as one of the main reasons for unhealthy food consumption among night shift workers (16). Since most food outlets that offer healthier foods at the workplace are closed at night, creating an environment where all workers have greater access to healthier nutrient-dense foods (ie, salad, fruit, non-fat milk) and less access to unhealthy foods or beverages (44) may help to decrease shift workers' empty calorie food/beverage consumption on days working night shifts.

Because previous studies have suggested that unhealthy food consumption (ie, discretionary snacks, sugar-sweetened beverages) may be a coping strategy for fatigue on night shifts (39-41), reducing fatigue from shift work may be beneficial for shift workers' dietary quality. At the organizational level, providing workers a proper break during night shifts, adequate staffing, and workload balance are recommended for the management of fatigue (45). At the individual level, programs that help people develop better coping mechanisms for fatigue (eg, regular exercise, combination of sleep hygiene and light exposure education) (46) may reduce shift workers' fatigue. In addition, shift workers tend to consume caffeine (eg, cola, coffee, tea) to promote alertness on night shifts (45). Therefore, replacing the source of caffeine intake (eg, from cola to nonsweetened tea or coffee) and educating workers about healthier snack foods (eg, nuts, seeds) as an alternative to promote alertness may reduce the possibility of sugarsweetened beverage consumption on night shifts.

Strengths and limitations

This study has several strengths. First, this is the first study to examine within-person associations between shift work and empty calorie food/beverage intake. Second, the prospective intensive longitudinal design using EMA methodology helped to assess participants' empty calorie food/beverage consumption in real-time, which reduced the chance of recall bias and increased ecological validity. Momentary assessments also allowed testing of short-term effects of shift work. For instance, we could examine whether shift work influenced sameor subsequent-day behavior. In addition, records from published work schedules were employed to assess participants' exposure to shift work, which reduced participants' recall bias of work schedules.

This study's limitations should also be considered. First, the findings of this study may not be generalizable to all rotating shift workers due to the use of a convenience sample of nurses. Participants in this study were relatively young. The healthy work effect (ie, workers who cannot adjust to shift work may choose not to work on rotating shifts) (47) might also introduce selection bias and affect the generalizability of the findings.

Second, a food checklist was employed to assess participants' empty calorie food/beverage consumption instead of using 24-hour dietary recalls or food records, which may also contribute to misleading findings. For instance, people may report the same number of empty calorie food/beverage items; however, the portion size or number of servings they consumed may differ.

Third, to capture each participant's shift work pattern, each participant was requested to respond to the EMA survey for 14 days, which may increase their burden and result in overall low response rates. The EMA survey response rate was 56.3%, which is lower than preferred (48) and might hinder the validity of study findings, especially when those observations were not missing randomly. Future studies investigating the feasibility and acceptability of an EMA study among shift workers may contribute to the application of EMA methodologies in this population. In addition, it is possible that workers were unable to respond to an EMA survey due to high work demands (49, 50). Workers often eat when they have time during work. Incorporating event-based EMA surveys during working hours and signal-based EMA surveys during non-working hours or off-duty days may help to better capture shift workers' food intakes and prevent missing surveys during working hours.

However, in this study, completed EMA surveys from participants were relatively evenly distributed across different shift timings (day: 229, evening: 211, night: 214, off-duty: 307), reducing concern that responses were mainly collected during certain types of shift timings. By asking participants' empty calorie food/beverage consumption since the last time they completed an EMA survey, it may also help to capture participants' intake if they had missed any EMA surveys.

Concluding remarks

Findings in this study revealed that shift work might influence same-day empty calorie food/beverage consumption. Shift work is unavoidable for certain types of industries (eg, healthcare, protective services). Thus, interventions that help to prevent unhealthy eating while working night shifts may be beneficial for rotating shift workers' health.

Acknowledgements

The authors sincerely thank all participants for their contributions to this study. We also thank the Active Living Research program of the University of California, San Diego, for the loan of the accelerometer equipment used in this study. The authors acknowledge Dr. Judith Shiao and Dr. Yue-Liang Guo for their enormous assistance in data collection for this study.

Financial support

This study was supported by two research awards from the Sigma Theta Tau International Honor Society of Nursing, Alpha Lambda Chapter, and the UIC College of Nursing PhD Student Research Award.

Conflict of Interest statement

The authors have declared that they have no conflict of interest.

Sidebar

Lin T-T, Park C, Kapella MC, Martyn-Nemeth P, Tussing-Humphreys L, Rospenda KM, Zenk SN. Shift work relationships with same- and subsequent-day empty calorie food and beverage consumption. Scand J Work Environ Health. 2020;46(6):579-588. doi:10.5271/sjweh.3903

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Received for publication: 3 March 2020

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DETAILS

Subject:	Shift work; Beverages; Smartphones; Working conditions; Workers; Food consumption; Eating; Regression analysis; Regression models; Food intake; Chronic illnesses; Sweet taste; Night shifts; Nighttime; Circadian rhythm; Food; Schedules; Occupational exposure; Correlation analysis; Eating behavior
Business indexing term:	Subject: Shift work Smartphones
Location:	United States--US; Taiwan
Publication title:	Scandinavian Journal of Work, Environment &Health; Stockholm
Volume:	46
Issue:	6
Pages:	579-588
Publication year:	2020
Publication date:	2020
Section:	Original article
Publisher:	Scandinavian Journal of Work, Environment &Health
Place of publication:	Stockholm
Country of publication:	Finland, Stockholm
Publication subject:	Occupational Health And Safety
ISSN:	03553140
e-ISSN:	1795990X
Source type:	Scholarly Journal
Language of publication:	English
Document type:	Journal Article
DOI:	https://doi.org/10.5271/sjweh.3903
ProQuest document ID:	2464652768
Document URL:	https://www.proquest.com/scholarly-journals/shift-work-relationships-with-same-subsequent-day/docview/2464652768/se-2?accountid=211160

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Citation style: APA 6th - Annotated with Abstracts - American Psychological Association, 6th Edition

Härmä, M., MD PhD, Koskinen, A., B.A., Sallinen, M., PhD., Kubo, T., PhD., Ropponen, A., PhD., & Lombardi, D. A., PhD. (2020). Characteristics of working hours and the risk of occupational injuries among hospital employees: A case-crossover study. Scandinavian Journal of Work, Environment & Health, 46(6), 570-578. doi:https://doi.org/10.5271/sjweh.3905

Objectives We investigated the association of working hours with occupational injuries in hospital shift work. Methods Registry data of occupational injuries of hospital employees from 11 towns and 6 hospital districts were linked to daily payroll data to obtain working hours for 37 days preceding the first incidence of the injury (N=18 700). A case-crossover design and associated matched-pair interval analysis were used to compare working hour characteristics for three separate hazard windows among the same subjects. Conditional logistic regression was used to calculate odds ratios (OR) with 95% confidence intervals (CI). Results We found an elevated risk of an occupational injury for workdays with evening shifts (OR 1.09, 95% CI 1.03-1.14) and workdays following night shifts (OR 1.33, 95% CI 1.17-1.52). After excluding commuting injuries, the risk increased during the evening shifts (OR 1.15, 95% CI 1.09-1.23) and the work days following night shifts (OR 1.44, 95% CI 1.24-1.69), but was no more significant during the morning shifts. Injury risk increased following a week of >5 morning shifts or >3 evening shifts, but did not increase according to the number of preceding night shifts or quick returns. The length of the work shift (OR 1.22, CI 1.06-1.42) - not the length of the weekly working hours - was associated with an increased risk. Conclusions The results indicate an increased occupational injury risk during the evening shifts and during work days following night shifts, with the risk increasing according to the number of evening but not night shifts.

Spinder, N., M.D., Bergman, Jorieke E H,M.D., PhD., Kromhout, H., PhD., Vermeulen, R., PhD., Corsten-Janssen, N., Boezen, H. M., . . . de Walle, Hermien E K, PhD. (2020). Maternal occupational exposure and congenital heart defects in offspring. Scandinavian Journal of Work, Environment & Health, 46(6), 599-608. doi:https://doi.org/10.5271/sjweh.3912

Objectives Congenital heart defects (CHD) are the most prevalent congenital anomalies. This study aims to examine the association between maternal occupational exposures to organic and mineral dust, solvents, pesticides, and metal dust and fumes and CHD in the offspring, assessing several subgroups of CHD. Methods For this case-control study, we examined 1174 cases with CHD from EUROCAT Northern Netherlands and 5602 controls without congenital anomalies from the Lifelines cohort study. Information on maternal jobs held early in pregnancy was collected via self-administered questionnaires, and job titles were linked to occupational exposures using a job exposure matrix. Results An association was found between organic dust exposure and coarctation of aorta adjusted odds ratio (ORadj) 1.90, 95% confidence interval (CI) 1.01-3.59] and pulmonary (valve) stenosis in combination with ventricular septal defect (ORadj 2.68, 95% CI 1.07-6.73). Mineral dust exposure was associated with increased risk of coarctation of aorta (ORadj 2.94, 95% CI 1.21-7.13) and pulmonary valve stenosis (ORadj 1.99, 95% CI 1.10-3.62). Exposure to metal dust and fumes was infrequent but was associated with CHD in general (ORadj 2.40, 95% CI 1.09-5.30). Exposure to both mineral dust and metal dust and fumes was associated with septal defects (ORadj 3.23, 95% CI 1.14-9.11). Any maternal occupational exposure was associated with a lower risk of aortic stenosis (ORadj 0.32, 95% CI 0.11-0.94). Conclusions Women should take preventive measures or avoid exposure to mineral and organic dust as well as metal dust and fumes early in pregnancy as this could possibly affect foetal heart development.

Causal inference and evidence-based recommendations in occupational health and safety research. (2020). Scandinavian Journal of Work, Environment & Health, 46(6), 554-556. doi:https://doi.org/10.5271/sjweh.3929

In a recent editorial, British researchers concluded that, due to heterogeneity of shift working in longitudinal studies, it is too difficult to draw a firm conclusion about the risk of breast cancer, let alone about an exposure threshold for night shift work (2). Recently, a large-scale RCT found no effect of vitamin D intake on reduced risk of depression (8), despite numerous observational studies suggesting such an effect (9). ...]there are good reasons to treat results from observational studies with caution. The recommendation to stop asbestos production, which rather came too

late than too early, was not based on RCT but observational studies on the multiple health-hazardous effects of asbestos (11). ...]when considering the evidence, researchers should not only consider the best evidence based on available data and their causal inference, but also the potential consequences of continuing current practice. Regarding single observational studies, VanderWeele lists eight considerations that increase confidence in the estimate, including longitudinal design; the quality of the assessment of exposure, outcome and confounders; flexible statistical modeling examining robustness to modelling decisions; and attempts to address unmeasured confounding.

Nambiema, Aboubakari,M.Sc, M.P.H., Bodin, J., PhD., Fouquet, N., PhD., Bertrais, S., PhD., Stock, Susan, MD,M.Sc, F.R.C.P.C., Aublet-Cuvelier, A., . . . Roquelaure, Yves,M.D., PhD. (2020). Upper-extremity musculoskeletal disorders: How many cases can be prevented? estimates from the COSALI cohort. Scandinavian Journal of Work, Environment & Health, 46(6), 618-629. doi:https://doi.org/10.5271/sjweh.3911

Objective This study aimed to estimate the proportion and number of incident upper-extremity musculoskeletal disorders (UEMSD) cases attributable to occupational risk factors in a working population. Methods Between 2002-2005, occupational physicians randomly selected 3710 workers, aged 20-59, from the Pays de la Loire (PdL) region. All participants underwent a standardized clinical examination. Between 2007-2010, 1611 workers were re-examined. This study included 1246 workers who were free of six main clinically diagnosed UEMSD at baseline but were diagnosed with at least one of these UEMSD at follow-up 59% of men, mean age: 38 (standard deviation 8.6) years]. Relative risks and population-attributable fractions (PAF) were calculated using Cox multivariable models with equal follow-up time and robust variance. The total number of incident UEMSD in the PdL region was estimated after adjustment of the sample weights using 2007 census data. The estimated number of potentially avoidable UEMSD was calculated by multiplying PAF by the total number of incident UEMSD in PdL. Results At follow-up, 139 new cases of UEMSD (11% of the study sample) were diagnosed. This represented an estimated 129 320 incident cases in the PdL in 2007. Following adjustment for personal factors, 26 381 (20.4% of all incident UEMSD) were attributable to high physical exertion, 16 682 (12.9%) to low social support, and 8535 (6.6%) to working with arms above shoulder level. Conclusions A large number and important proportion of incident UEMSD may be preventable by reducing work exposures to physical exertion and working with arms above shoulder level as well as improving social support from co-workers/supervisors.

Kuronen, J., M.D., Winell, K., PhD., Kopra, J., PhD., & Räsänen, K., PhD. (2020). Quality improvement activity in occupational healthcare associated with reduced need for disability retirement: A bayesian mixed effects modelling study in finland. Scandinavian Journal of Work, Environment & Health, 46(6), 630-638. doi:https://doi.org/10.5271/sjweh.3901

Objectives There is evidence that occupational healthcare (OHC) may improve employees' work ability. This research was designed to study whether common quality improvement (QI) activities in the OHC quality network (OQN) - a voluntary collaborative forum - can reduce the need for disability pensions. Methods The study population comprised employees under the care of 19 OHC units in Finland affiliated with the OQN. The association of 12 QI activities with new disability pensions during the years 2011-2017 was analyzed by Bayesian mixed effects modelling. Results Patients of OHC units affiliated with the OQN have fewer full permanent disability pensions odds ratio (OR) 0.77, 95% credible interval (CI) 0.60-0.98] and full provisional disability pensions (OR 0.68, 95% CI 0.53-0.87) than patients of unaffiliated units. Of the studied QI activities, the measurements of intervening in excessive use of alcohol had the strongest association with the incidence of all disability pensions (OR 0.53, 95% CI 0.41-0.68). Participation in the focus of work measurements and quality facilitator training was also associated with the reduced incidence of disability pensions (OR 0.84, 95% CI 0.71-0.98, and OR 0.92, 95 CI 0.84-0.99, respectively). Conclusions Affiliation with a quality network seemed to improve outcomes by reducing full disability pensions or replacing them by partial disability pensions. Some QI activities in the OQN were associated with a reduction of disability pensions.

Sasaki, N., M.D., Kuroda, Reiko,M.D., PhD., Tsuno, K., PhD., & Kawakami, Norito,M.D., PhD. (2020). The deterioration of mental health among healthcare workers during the COVID-19 outbreak: A population-based cohort

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