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The influence of occupational class and physical workload on working life expectancy among older employees

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ABSTRACT (ENGLISH)

Objective This study investigates the impact of physical workload factors and occupational class on working life expectancy (WLE) and working years lost (WYL) in a sample of older Finnish workers. **Methods** A 70% random sample of Finns in 2004 was linked to a job exposure matrix for physical workload factors and register information on occupational class and labor market status until 2014. Transitions between being at work, time-restricted work disability, unemployment, economic inactivity, disability retirement, retirement and death were estimated. A multistate Cox regression model with transition-specific covariates was used to estimate the WLE and WYL at age 50 up to 63 years for each occupational class and physical workload factor for men and women (N=415 105). **Results** At age 50, male and female manual workers had a WLE of 10.13 and 10.14 years, respectively. Among both genders, manual workers had one year shorter WLE at age 50 than upper non-manual employees. This difference was largely attributable to unemployment (men: 0.60, women: 0.66 years) and disability retirement (men: 0.28, women: 0.29 years). Self-employed persons had the highest WLE (11.08 years). Men and women exposed to four or five physical workload factors had about one year lower WLE than non-exposed workers. The difference was primarily attributable to ill-health-related reasons, including disability retirement (men: 0.45 years, women: 0.53 years) and time-restricted work disability (men: 0.23, women: 0.33 years). **Conclusions** Manual workers and those exposed to physical workload factors had the lowest WLE. The differences in WYL between exposure groups can primarily be explained by ill-health-based exit routes.

FULL TEXT

Headnote

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or five physical workload factors had about one year lower WLE than non-exposed workers. The difference was primarily attributable to ill-health-related reasons, including disability retirement (men: 0.45 years, women: 0.53 years) and time-restricted work disability (men: 0.23, women: 0.33 years).

Conclusions Manual workers and those exposed to physical workload factors had the lowest WLE. The differences in WYL between exposure groups can primarily be explained by ill-health-based exit routes.

Key terms Finland; occupation; older worker; physical workload factor; socioeconomic difference; work disability; working career; working years lost.

The European ageing population is already resulting in an older workforce as well as sustainability issues of social protection systems (1). The current division of time between employment and retirement is a major challenge for policies (2). Extending working life has therefore become a strategic objective in many European countries. In order to have effective policies to extend working life, a proper understanding of labor market dynamics of years in later life spent in work, retirement or other states is needed.

Labor market dynamics in later life differ across groups of workers. Particularly workers with a low occupational class and strenuous working conditions have a higher risk to exit paid employment, often through ill-health-related exit routes (3, 4). In general, adverse working conditions are associated with premature exit from paid employment (5). Longitudinal studies from different countries reported that unfavorable working conditions such as higher physical workload increased the risk of early retirement (6-9) and disability benefits (8, 10-12). Moreover, workers with a lower occupational class are more likely to have strenuous working conditions (10, 13).

Since both a low occupational class and physically demanding work increase the risk of exit from paid employment, it is relevant to quantify their impact on cumulative measures such as working life expectancy (WLE) and working years lost (WYL). WLE expresses the number of years that persons are expected to be in paid employment until they eventually leave the labor force for retirement (14). In the past decade, several studies have estimated the expected duration of working life (14-21). So far, differences in WLE have been studied according to gender, ethnicity, socioeconomic positions, working conditions and chronic diseases. Generally, men have a higher WLE than women and persons with a high education have a higher WLE than those with a low education (14, 18, 19). The gap measure WYL reflects the working time lost due to premature exit from paid employment through various exit routes such as disability benefits, unemployment etc (14). Studies differ in how many different states for WYL are included. Some studies have studied WYL only for disability benefits (22, 23), while other studies have included other labor market states, eg, unemployment and sickness absence (20).

So far, most studies on WLE and WYL have relied on prevalence-based methods, which are unable to incorporate the complexity of laborforce dynamics with many transitions between paid employment and nonemployment states (14, 24). In addition, most studies have ignored the possibility to return to paid employment after initial exit and, therefore, underestimate the WLE. Furthermore, many studies have not made the distinction between being employed and being present at work, thereby not fully capturing the WYL due to, for example, sickness absence. In this study, a multistate Cox regression model was used to capture the dynamic patterns among transitions in and out of being at work over a ten-year period. We were, therefore, able to estimate time spent in specific exit routes including ill-health-related exit routes. The aim of this study was to estimate WLE and WYL attributable to different reasons among Finnish workers aged 50-63 years according to gender, occupational class, and physical workload factors.

Method

Study population

For this study, we used a 70% random sample of the working-age population from the Finnish population census taken on the 31 December 2004. Persons aged 50-63 years belonging to the workforce on 1 January 2005 were eligible to the study. Persons who did not have an occupational class or an occupational job code were excluded (about 3%). The study population consisted of 415 105 persons (204 113 men and 210 992 women), who were followed from 1 January 2005 to 31 October 2014.

Social security system in Finland

Sickness absence is compensated after a waiting period of 10 full sickness absence days among wage earners and 1-4 days among self-employed persons, until a maximum of 300 days. Employers compensate wage earners for the waiting period. Part-time sick leave is a voluntary option for those who are incapable of performing their full duties, as determined by a physician, but who are able to work 40-60% of full time. The partial benefit is 50% of full benefit. A disability pension can be granted to an individual whose reduced work ability due to illness is medically confirmed. To receive a full disability pension, an individual's work ability needs to be reduced by >60%. A partial disability pension is granted if work ability is reduced by >40%. Both full and partial disability pension can be granted either on a temporary or permanent basis.

Eligibility to vocational rehabilitation from the earnings-related pension scheme is based on a medically confirmed threat of disability retirement within the next five years and on an expectation that work participation can be promoted and disability retirement postponed or prevented with vocational rehabilitation.

Unemployed job seekers receive unemployment benefits for either 300 days or 400 days depending on the length of previous employment. If the individual becomes unemployed after reaching the age of 58, the maximum is 500 days. After the basic unemployment benefit runs out, individuals can apply for labor market subsidies.

Since 2005, there has been a flexible statutory retirement age in Finland. During the time of this study, individuals could retire due to old age between the ages of 63 and 68 years. It was also possible to receive an early old-age pension at age 62. During the study period, a long-term unemployed (>500 days) person aged 60 could be granted an unemployment pension until reaching old-age retirement age. There are also special pensions for farmers.

Labor market states

During the period 2005-2014, the registers from the Finnish Centre for Pensions provided information on earnings-related pension periods, earning periods, unemployment periods, and vocational rehabilitation periods. Information on sickness allowance periods was obtained from the register of the Social Insurance Institution of Finland (Kela). Based on the period data on employment and benefit receipt, seven daily states were formed. Because states could take place simultaneously, we applied the following rules for state assignment:

- (i) Work: Individuals were defined as being at work if they had an earning period and did not receive any ill-health or unemployment related benefit at the same time. There were a few exceptions; individuals on parttime sickness absence were considered to be at work, since they were required to work part-time. Individuals with a partial disability retirement could work but did not have to. If partial disability retirees had an earning period, they were considered to be at work; if not, they were coded as being on time-restricted work disability.
- (ii) Time-restricted work disability: This state included full-time sickness absence, vocational rehabilitation due to medical reasons, temporary disability retirement and partial disability retirement (for those who did not have an earning period at the same time).
- (iii) Unemployment: This state included any type of unemployment benefit. If a person had an unemployment and earnings period at the same time, the state of unemployment overruled. This category also included unemployment retirement.
- (iv) Economic inactivity: This state included persons outside of the labor force for reasons other than retirement, eg, due to home care, studying or an unknown reason. This state also includes individuals who emigrated during the follow-up.
- (v) Disability retirement: This state included only permanent full disability retirement. From this state, only transitions to old-age retirement and death were allowed.
- (vi) Retirement: This state included old-age retirement and non-health-related types of early retirement. From this state only transitions to death were allowed.
- (vii) Death: Based on the mortality statistics.

Occupational class

Information on occupational class was obtained from the Finnish Longitudinal Employer-Employee Data (FLEED) of Statistics Finland. Four occupational classes were distinguished (i): upper non-manual employees, (ii) lower non-manual employees, (iii) manual workers, and (iv) self-employed.

Physical workload

Information on occupation at baseline was also obtained from FLEED during the last week of December 2004. The occupations were classified using the Classification of Occupations 2001 by Statistics Finland, which is based on the International Standard Classification of Occupations (ISCO-88). Heavy physical work (eg, lifting and carrying heavy loads, excavating, shoveling or hammering), kneeling or squatting at work (>1 hour a day), manual handling of heavy loads (lifting, carrying or pushing items >20 kg at least 10 times every day), working with hands above shoulder level (on average >1 hour per day) and awkward trunk posture (working in a forward bent posture >1 hour per day) were estimated with a gender-specific job exposure matrix (JEM) (25). The JEM provided the estimates for the likelihood of being exposed in the person's occupation. Based on previous research (25), the continuous JEM values (range 0-1) were dichotomized into non-exposed (<0.40), and exposed (>0.40 higher) workers. We calculated the total number of physical workload factors a person was exposed to and classified it into three categories: no exposure, 1-3 factors, and 4-5 factors.

Statistical analyses

Multistate Cox regression model. First, based on the information on daily transitions between states, transition rates were assessed in order to calculate the WLE and WYL. Individuals could move between states over time. The multistate model was composed of the previously mentioned six states and death, with death as the absorbing state. In the model, individuals with disability retirement could only move to retirement or death, and individuals in the retirement state could only move to death. A total of 27 possible transitions remained, for which a transition matrix was constructed (figure 1). Calculations were censored at 63 years, and the estimated WLE and WYL is thus based on the transitions from age 50 until 63.

Following Robroek et al (14), the R package *mstate* developed by Putter (26) was used to estimate cumulative transition rates and transition probabilities based on the multistate models. Analyses were performed separately for men and women. For each of the 27 transitions, occupational class and exposure category of physical workload were defined as covariates (27, 28). Using age as the underlying time axis, a Cox proportional hazards model was fitted to estimate the transition rates between states. We applied the Markov assumption that transition rates were only dependent on the current state. The baseline transition hazards were used to calculate transition probabilities for each of the possible transitions in the model. The baseline hazard was adjusted with the estimated hazard ratios (HR) by the Cox analysis.

WLE and WYL The estimated transition probabilities in the multi-state model were used to calculate the expected length of stay (ELOS) in a specific state, given the current state (ELOS function in the *mstate* R package). We set the time horizon for the ELOS at age 63 and used the transition probabilities from the starting time (age 50 years). WLE is defined here as the number of years in the work state, conditional on being in the workforce at age 50. Bootstrapping was used to calculate the uncertainty around the expected length of stay. Bootstrapping consisted of resampling from the study population with replacement. The ELOS is calculated on the bootstrapped population, this was repeated 100 times. The lower and upper bound of the ELOS were estimated as the 2.5th and 97.5th percentile of the bootstrapped ELOS. The total WYL due to being outside of work were calculated as the difference between the potential work years until the age of 63 years (ie, 13 years) and the WLE at age 50. A sensitivity analysis for physical workload was conducted excluding the self-employed since this group had the highest WLE but also a high physical workload.

Results

Men were more frequently exposed to physical workload factors than women, especially to manual handling of heavy loads, working with hands above shoulder level and heavy physical work (table 1). Male lower and upper non-manual employees were rarely exposed to physical workload factors, while this was more common among women in these occupational classes. Self-employed workers were often exposed to multiple physical workload factors. Overall, men were more often exposed to four or five physical workload factors than women (24.8% and 13.8%, respectively, figure 2).

Table 2 shows the WLE at age 50 and WYL for each occupational class, separately for men and women. The WLE

for men and women was 10.13 and 10.14 years, respectively. For both genders: (i) the WLE was around 10.50 years among upper level employees and 9.51 years among manual workers, with a gap of one year between these occupational classes; (ii) the largest WLE was found for the self-employed, slightly above 11 years; (iii) a total of 3.49 years of being at work was lost, of which 44% was due to ill-health-related reasons (time-restricted work disability, disability retirement, or death).

There were small differences in WYL between men and women. Women lost slightly more years due to timerestricted work disability and retirement, and men lost slightly more years due to disability retirement and death. Absolute occupational class differences in WYL between upper non-manual employees and manual workers were largest for unemployment (men: 0.60, women: 0.66 years) and disability retirement (men: 0.28, women: 0.29 years). Table 3 shows WLE and WYL for the different groups by the number of physical workload factors, separately for men and women. The difference in WLE between persons not exposed and persons exposed to four or five physical workload factors was 0.90 years for men and 0.98 years for women. Compared to persons with no exposure to physical workload factors, persons with exposure to 4 or 5 physical workload factors lost most years due to disability retirement (men: 0.45, women: 0.53 years) and time-restricted work disability (men: 0.23, women: 0.33 years). When analyzing each physical workload factor separately, the largest difference in WYL between exposed and non-exposed workers was for physical heaviness (men: 0.83 years, women 0.93 years) (figure 3). For each factor of physical workload, time-restricted work disability and disability retirement had the largest contributions to the WYL. The analysis of the influence of physical workload on WLE within each occupational class showed consistent differences of 0.48-0.72 years between exposure to four or five physical workload factors versus no exposure (table 4). When comparing the most advantaged group (upper non-manual employees with 0 exposures) and the most disadvantaged group (manual workers with four or five exposures), the difference in WLE was 1.56 for men and 1.59 for women. The WYL were attributable primarily to disability retirement in both genders, but also unemployment (both genders) and time-restricted work disability (women).

The sensitivity analysis, excluding the selfemployed, showed a larger difference than the main analysis in WLE between exposed and non-exposed workers (supplementary table S1, www.sjweh.fi/show_abstract.php?abstract_id=3919). Workers who were not exposed to physical workload factors had 1.34 years (men) and 1.04 years (women) higher WLE than those exposed to four or five factors. Absolute differences in WYL between the groups were largest for disability retirement (men: 0.61, women: 0.59 years), followed by unemployment for men (0.43 years), and time-restricted work disability for women (0.37 years).

Discussion

This study utilized longitudinal register data from 2005 to 2014 to estimate WLE at age 50 in the Finnish workforce overall as well as by occupational class and exposure to physical workload factors. Overall, the estimated WLE at age 50 was 10.1 years with no gender difference. Both male and female upper non-manual employees had a one year longer WLE at age 50 than manual workers, and self-employed workers had the highest WLE. Workers exposed to four or five physical workload factors also had a lower WLE than non-exposed workers, with a larger difference among women (0.98 years) compared to men (0.90 years). Differences in WYL between manual workers and upper non-manual employees were largest for unemployment (men: 0.60 years, women: 0.66 years). The difference between workers with exposure to multiple physical workload factors and non-exposed workers was largest for disability retirement (men: 0.45 years, women: 0.53 years).

Some previous studies have examined socioeconomic differences in WLE or WYL in Finland (15, 19, 22), and other countries (14, 20, 21). The absolute values reported in the studies are not directly comparable due to differences in definitions of working life, study populations, study periods, statutory retirement ages, and estimation methods. For instance, WLE has previously been based on time spent in paid employment instead of time actually being present at work (eg, 14, 18.). This is an important distinction as the latter excludes employment periods during which a person is on sick leave. Furthermore, the definition of being at work may vary depending on whether time-restricted work disability with part-time employment is defined as work or work-related disability. Likewise, crucial assumptions pertain to selection and definition of included states. Nevertheless, the findings of the current study are in line with

previous studies with regard to the lowest WLE in most disadvantaged groups, such as among persons with a low education, manual workers and those with physically demanding work (eg, 14, 15, 19-22.). These findings ask for prevention of premature exit from paid employment due to ill health among older workers with physically demanding work.

This study showed differences in WLE across occupational classes among both men and women. Manual workers had a WLE of 9.5 years at the age of 50, while upper non-manual employees had a WLE of 10.5 years, resulting in a one year difference. In a previous study on WLE in Finland, using the classical Sullivan method on repeated cross-sectional information from 1989-2012, much larger differences between upper non-manual and manual employees were reported throughout the study period, with differences of 3.65 years for men and 3.63 years for women in the last year (15). A primary reason for the difference in the results between the above mentioned study and the current one is likely the selection of the study population. The current study excluded those who were outside the workforce at baseline, resulting in a healthier study population particularly in physically demanding occupations. Additionally, Leinonen et al (15) examined employment participation until the end of working careers, ie, beyond the limit of age 63, as is used in the current study. Another study from the authors indicated that manual workers quit paid employment more often at the first possible age of retirement, whereas upper non-manual employees extended their working lives to an older age (29). Finally, Leinonen and colleagues measured labor market status only at the end of each year (15).

No gender differences were seen in WLE. The current study had a selected study population, ie, those who were in the workforce at age 50 because our focus was on the effect of physical work exposures. This may explain why no gender differences were found in contrast to previous Finnish findings, which showed longer WLE at age 50 among women compared with men (15, 16).

Traditional research in occupational health focuses on questions such as "what is the increased risk of workers with a high physical workload to exit paid employment?" (11) or "to what extent does physical workload explain occupational class inequalities in disability retirement for older workers?" (30). Our study adds a cumulative measure over the remaining working life course to the previous body of knowledge. WYL due to a range of states are calculated for different occupational classes as well as for different exposures to physical workload factors. In line with our results, other studies have reported disability retirement as an important reason for WYL (14-16, 21, 22). Perhaps a counterintuitive conclusion based on the presented figures was that self-employed persons had the highest WLE, despite high levels of physical workload. Self-employed persons may be among men eg, freelance construction workers or farmers and among women service workers. A previous study from Finland reported that entrepreneurs (or freelancers) had a slightly lower WLE at age 50 compared to the upper non-manual class (15). Another Finnish study on pensions and pensions earnings found that self-employed workers have the longest working careers in Finland when taking into account their total working life (31). Reasons for a high WLE among self-employed seem to be twofold. Part of the self-employed enjoy working and continue until an older age, whereas another part have not contributed sufficiently to their pension insurance and need to continue working to be able to receive sufficient pension (32). Studies in The Netherlands showed that financial stimulants and autonomy at work played a role in prolonging working lives (33).

Strengths and limitations

Firstly, one of the main strengths of our study is the use of longitudinal data from a representative national sample of 70% of the population and data on episodes of employment and benefit receipt derived from complete national registers. Secondly, the national registers were used to distinguish between multiple detailed labor market states, while other WLE studies have had to rely on more limited data such as main source of income (14) or self-reported employment state (18), which limits the amount and the precision of distinguishable labor market states. Thirdly, information on physical workload factors has been derived from JEM by linking to job titles. However, using the JEM with the national representative sample did mean we lost some observations due to missing job codes. Fourthly, with the use of a multistate Cox regression model the possibility to re-enter into the labor market was taken into account.

The study also has some limitations. Firstly, the division into labor market states is somewhat arbitrary since, in the model, persons cannot be in multiple labor market states at one time - although in practice this can be the case. Priority was given to non-working states in order to minimize underestimation of WYL. For example, work done during unemployment or full retirement is often very minimal. As an exception, work done during partial work disability was categorized as work, since it was expected to involve a larger amount of working time. Part-time sickness beneficiaries are always required to work 40-60% of normal working time and partial disability pensioners can receive up to 60% of the previous earning level without losing the benefit. Secondly, occupational titles were only measured at the end of 2004, and workers could have changed jobs in the following years. However, since the study population was aged 50-63 years in 2005, it can be hypothesized that major job changes were not likely. Thirdly, although we consider the JEM to define the exposure to physical workload factors as a strength, the JEM is developed in a broader age group (18-64 years) compared to our study sample (50-63 years). It might be that the true exposure in this older age group differs from the exposure to physical workload factors in the broader age group that was used to develop the JEM. In addition, the group-based assessment of physical workload factors in the JEM may differ from individual-based assessment of physical workload factors, but we lack information to hypothesize whether this would result in an underestimation or overestimation of differences in WLE between exposed and non-exposed. Fourthly, during the follow-up period, there were several changes in the economic situation and in sickness absence legislation. Differences over time, as a result of economic and legal changes in WLE and WYL due to physical workload factors, were not part of the current study and would be of interest for future research. Lastly, the absolute values of our study are not easily generalized to other populations. While WYL due to high physical load and lower WLE in lower occupational classes have been reported before, their exact magnitude may vary across populations with different arrangements for disability and retirement benefits.

Concluding remarks

This study shows differences in WLE by occupational class and number of physical workload factors in later working life among both men and women. Both manual workers and workers with exposure to multiple physical workload factors have a reduced WLE. The difference in WLE between occupational classes can be primarily explained by WYL due to unemployment and, to a smaller extent, ill-health. The difference between the exposure groups is primarily attributable to WYL due to ill-health-related reasons, including disability retirement and time-restricted work disability.

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Sidebar

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Office design as a risk factor for disability retirement: A prospective registry study of Norwegian

employees

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ABSTRACT (ENGLISH)

Objectives This aim of this study was to (i) examine differences in risk of subsequent disability retirement between employees working in cellular, shared, and open-plan offices and (ii) determine the contribution of gender, skill-level, work ability, medically certified sickness absence, leadership position, and personality traits (extroversion, agreeableness, conscientiousness, neuroticism, and openness) as confounders. **Methods** Survey data on predictor variables combined with official objective registry data on disability retirement and sickness absence were extracted from a large Norwegian occupational cohort of office workers (N=6779, 53.5% women). Questionnaire data included the respondents office designs, comparing cellular, shared, and open-plan offices, demographic characteristics, workability, and personality factors. Objective data on disability retirement and medically certified sickness absence were extracted from the sickness and disability benefit register of the Norwegian Labor and Welfare Administration. **Results** In the final fully adjusted model, employees working in shared [hazard ratio (HR) 1.52, 95% confidence interval (CI) 1.08-2.16] and open-plan (HR 1.95, 95% CI 1.31-2.90) offices had significantly higher risk of subsequent disability retirement compared to employees in cellular offices. Gender, work ability, medically certified sickness absence, and conscientiousness had independent direct effects on risk of disability retirement. **Conclusion** This study shows that open and shared workspace designs have detrimental effects by increasing risk of disability retirement among office workers, even when taking other known predictive factors into account.

FULL TEXT

Headnote

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Methods Survey data on predictor variables combined with official objective registry data on disability retirement and sickness absence were extracted from a large Norwegian occupational cohort of office workers (N=6779, 53.5% women). Questionnaire data included the respondents office designs, comparing cellular, shared, and open-plan offices, demographic characteristics, workability, and personality factors. Objective data on disability retirement and medically certified sickness absence were extracted from the sickness and disability benefit register of the Norwegian Labor and Welfare Administration.

Results In the final fully adjusted model, employees working in shared [hazard ratio (HR) 1.52, 95% confidence interval (CI) 1.08-2.16] and open-plan (HR 1.95, 95% CI 1.31-2.90) offices had significantly higher risk of subsequent disability retirement compared to employees in cellular offices. Gender, work ability, medically certified sickness absence, and conscientiousness had independent direct effects on risk of disability retirement.

Conclusion This study shows that open and shared workspace designs have detrimental effects by increasing risk of disability retirement among office workers, even when taking other known predictive factors into account.

Key terms cellular office; cost; health; open office; open-plan office; shared office; sickness absence; work ability; workplace architecture.

The move of office workers from cellular offices to shared or open-plan workspaces is a predominant trend in contemporary working life. Reducing space per employee - and thereby the costs of office space - is an obvious motivator for this change. It is also commonly assumed that open-plan office layouts will facilitate social interactions and communication, enhancing innovation and productivity (1). On the other hand, contrasting such assumptions about the potential benefits of open-plan workspaces, emerging evidence from both primary studies and systematic reviews indicate that open and shared office design layouts also have significant costs as manifested through increased health problems (2-4) and sickness absence rates (5-7) among employees. However, research on outcomes of office designs has been criticized. A recent scoping review of the literature argued that most previous studies were based on inadequate study designs (8). With a few notable exceptions (7, 9), previous studies of office design layouts have reported subjective evaluations of outcomes such as distractions, satisfaction, well-being, productivity, and sickness absence. Self-report measures may be influenced by extraneous factors like the design and context of the measurements and susceptible to method bias (10). Consequently, one may argue that cost estimates of subjective factors are prone to error and/or that costs of the subjective effects recorded so far are negligible. Hence, there is a need for studies of objectively measured outcomes of office designs.

In addition to the limitations in study designs, few studies have investigated potential confounding factors that can explain the associations between office designs and outcomes (8). For instance, as previous research has shown that levels of work ability and sickness absence are related both to office design (5, 6) and subsequent disability retirement (11-13), work ability and sickness absence are likely to confound associations between office design and risk of disability retirement. Furthermore, office design encompasses a plethora of different layouts and principles. Open-plan offices may be based on fixed seating positions or shared activity-based seating positions, the space or area per employee may vary, and the availability of sound-attenuated cubicles or meeting rooms may differ, and so on. Such variations in office design layouts determine the nature and frequency of exposure to sounds, noise, and visual stimuli from other employees. An important aspect in this regard is that individual differences in perceptions and appraisals of such exposures may vary (14). Accordingly, previous findings suggest that age, gender, job status and role in the organization could influence individual satisfaction with, and reactions to, workspace design and layouts (15, 16).

The personality characteristics of employees may play an especially important role with regard to outcomes of office design but have received limited attention in past research. Drawing upon the five-factor model of personality (FFM) (17, 18) it seems reasonable to assume that certain individual traits may be particularly relevant with regard to how office designs affect the individual worker. In particular, due to the extrovert's preference for activities that involve social interactions and group work, high levels of extroversion could be associated with a more positive appraisal of sharing space with other people. Neuroticism is another personality trait of the FFM that is likely to influence the outcomes of office designs. As neuroticism is associated with negativity, maladjustment, and problems handling stressors (19), high levels of neuroticism may be associated with lower tolerance for stimuli that are likely to be present in open workspaces.

Effects of the FFM personality traits in combinations with type of office design (cell, shared room, open-plan, and flex) on self-reported distractions, job satisfaction, and job performance were examined in 1205 Swedish employees (20). The findings showed that low levels of neuroticism were associated with lower levels of distraction, particularly among those working in flex offices, whereas both agreeableness and openness to experience were associated with higher levels of distraction among participants in open-plan compared to cellular offices (20). No interactions were found between extroversion and office type in relation to distraction, nor did the personality traits influence the impact of office designs on job satisfaction and performance.

Addressing the limitations of previous research, the present study will add to knowledge of the effects of workspace design by including objectively measured outcome data, ie, officially registered disability retirement, and examining the role of appropriate confounding variables. Disability retirement incurs large costs and knowledge about the causes is therefore a highly relevant and important outcome. In Norway, a country with a population of approximately 5.3 million people, about 369 500 persons received disability retirement compensations in 2018. The

national cost for disability benefits was 86.3 billion kroner (about UK£8 billion; see www.regjeringen.no/no/aktuelt/folketrygdens-utgifter/id2613905). This is equivalent to about 2.4% of Norway's gross domestic product (GDP) of 3536 billion kroner for 2018. Several previous studies have reported that psychosocial work factors contribute to early retirement due to disability (21). Considering that office design contributes to functioning, productivity, and health among employees (22), it seems reasonable to expect that office design is also a predictor for disability retirement. The two main objectives of the present study were to determine (i) associations between cellular, shared, and open-plan office designs and risk of subsequent disability retirement and (ii) whether the associations between office designs and risk of disability retirement among employees are influenced by gender, work ability, levels of medically certified registry based sickness absence, skill level, leadership position, and personality traits as reflected through the FFM of personality.

Methods

Study design

This study is a part of the research project: "The new workplace II: work factors, sickness absence, and exit from working life among Norwegian employees". The study protocol provides a full description of the research project, procedures, and data material, including demographic information (23). The data material encompasses survey responses (questionnaire) linked with official registry data on medically certified sickness absence and disability benefits. Survey responses were collected from a large sample of adults employed in a full- or part-time position. Subjects were recruited from organizations in Norway that were contacted and offered to participate in the study. At the organizational level, this sampling procedure was based on a convenience approach with no pre-defined criteria for participation. All employees, excluding those on long-term sick leave, were mailed a letter with information about the survey, which explained the aims of the project and assured that responses would be treated confidentially in strict accordance with the general guidelines and specific license from the Norwegian Data Protection Authority. The survey was mainly web-based although about 15% of the participants completed a paper version due to limited access to computers at work. Type of survey response method (web versus paper) was not related to subsequent risk of disability retirement.

The organizations from which employees were recruited provided data on employees' departmental affiliation, home address, and occupational title according to the Norwegian standard classification of the occupations (STYRK) - a system developed by Statistics Norway based on the International Classification of Occupation (ISCO-88). In return for participation in the project, the organizations received written reports and oral presentations of results to support management and personnel in the process of monitoring their work conditions.

Ethical approval

The Regional Committees for Medical and Health Research Ethics (REC) in Norway approved this study, which has permission from the Norwegian Data Protection Authority and was conducted in accordance with the World Medical Association Declaration of Helsinki. All study participants provided their informed consent. When accessing the web-based questionnaire by a personal login code, informed consent had to be confirmed before responding to the questionnaire. The Norwegian Data Protection Authority and REC approved this consent procedure. Respondents were treated anonymously in the data analyses. Only respondents who actively (by response) permitted the linking of their answers to official registries were included in this study. For the respondents consenting to registry linkage, we had access to information on disability retirement compensation recorded in the Norwegian Labor and Welfare Administration (NAV) registry up to 1 January 2015.

Respondents

From November 2004 to March 2014, organizations encompassing a total of 30 585 employees were invited to participate in the survey for the first time. At the time of invitation 28 883 subjects were aged 18-62 and eligible for disability retirement. Employees aged 62-66 may also receive disability pension but are additionally entitled to early statutory pension. Consequently, and as we did not have access to the statutory pension registry, subjects >62 years of age were excluded from the present study. Of the subjects eligible for disability pension only, 16 651 responded to any of the exposure measures in the questionnaire relevant to this study (response rate: 57.6%).

Altogether 14 501 permitted linking their responses to official registry data on sickness absence and disability retirement from the Norwegian Labor and Welfare Service (acceptance rate: 87.1%). As the aim of this study was to examine the impact of office design on risk of disability retirement, only respondents that reported working in a cellular, shared, or openplan office were retained for analyses. After removing respondents that did not work in an office, the final sample for this study comprised 6779 respondents.

Questionnaire instruments

Office design was assessed with a single item question phrased: "Do you work...." (i) "alone in your own office", (ii) "In a shared office with one or more colleagues", (iii) "In an open-plan workspace", (iv) "In a shop/service station, etc.", (v) "Treatment institution", or (vi) "Outdoors". Respondents who reported alternatives iv-vi were not included in this study as they do not work in an office.

Self-reported work ability was assessed with a previously validated single item from the work ability index (WAI; 24). This item is phrased: "We assume that your work ability can be valued with 10 points at its best. How many points will you give your current work ability (0 means that you are unable to work at the moment)?" Responses were given on an 11-point scale ranging from 0 ("without ability to work") to 10 ("work ability at its best").

Information about gender and leadership position was assessed with single item questions. Response categories for leadership position were "no" and "yes".

The big-5 personality factors were measured with a 15-item abbreviated version of the International Personality Item Pool (IPIP; 25) developed by Nielsen & Knardahl (26). The questionnaire measures extroversion, agreeableness, conscientiousness, neuroticism, and openness with three items for each subscale. Each item is rated on a 7-point Likert scale (from "very inaccurate" to "very accurate"). Due to limitations in other indicators such as Cronbach's alpha, mean inter-item correlation between items has been suggested as the most adequate indicator of internal consistency in short personality markers (see 27-29). Briggs & Cheek (28) recommend an optimal range for the mean inter-item correlation of 0.2-0.4. In this study, all scales had internal consistency within the recommended range at both measurement points, thus indicating high reliability: Extroversion (0.40), agreeableness (0.35), conscientiousness (0.30), neuroticism (0.34), and openness (0.23).

Registry data on skill-level, disability retirement and sickness absence

Information about employee skill-level were extracted from the employee registries of the participating organizations. Skill levels were determined by classification of occupation according to the International Standard for Classification of Education (ISCED). The skill level classification reflects the differences in education or the level of working experience required for the respective occupations. The levels were: 1=occupations that normally require education equivalent to a first or postgraduate university degree, or college exams based on a similar length of study (>16 years); 2=occupations that normally require 1-3 years of education at university or college (but not equivalent to the first university-level) (13-15 years); 3=occupations that normally require 1-3 years of secondary education (10-12 years); 4=occupations that require <9 years of primary education; and 5=unspecified (occupations in which the level of education may vary substantially). In cases where no information on occupational group (ISCO-88) had been provided by the subjects' respective companies, missing values were substituted with self-reported skill level information (N=102).

Based on informed consent from participants, survey data were linked to the sickness and disability benefit NAV register by the unique 11-digit national identity number. The registers provide complete records of disability retirement that are compensated by the national insurance sickness benefit (30). All residents of Norway are members of the National Insurance Scheme. Residents aged 18-66 who have been a member of the National Insurance Scheme for at least three consecutive years before the onset of disease, illness, or injury are eligible for the disability pension scheme (31). A disability retirement is only granted to those with a physician-certified permanent reduction in the ability to work of minimum 50%. Time on sick-leave is not a criteria for disability retirement. Information about specific diagnoses were not available. Hence, the present study investigated all-cause disability retirement.

Information on official register-based medically certified sickness absence included complete registrations of all

medically certified sickness absence 12 months prior to and 12 months after the survey. The current study focuses on absence prior to the survey, although findings on absence succeeding the survey also are presented. The current study had access to data on total number of days with medically certified absence but not the number of absence spells, duration of spells, or medical diagnosis.

Statistical analysis

Data analysis was conducted with SPSS 23.0 (IBM, Armonk, NY, USA) and R version 3.2.2 (survival package). Scale variables (ie, personality indicators) were treated as continuous variables in the analyses. Hazard ratios (HR) and 95% confidence intervals (CI) were calculated with Cox regression analysis to determine the influence of office design on post-response risk of disability retirement. Cox regression (or proportional hazards regression) is a method for investigating the effect of several variables upon the time at which a specified event takes place. As recommended for studies in healthy populations (32), attained age (at censoring/ event) was the underlying time scale in these analyses rather than "time-on-study" (ie, years since baseline response). However, to address the impact of time on study, the length of the follow-up period was included as a covariate in the final fully adjusted regression model. The use of age as the time scale variable made age adjustment redundant in the Cox regressions. Missing data were excluded with listwise deletion. Gender, days with medically certified sickness absence 12 months prior to the survey, having a leadership position, workability, and skill level were included as covariates in all adjusted analyses. Because the last category of the skill-level variable was unspecified, reflecting varying degrees of educational attainment, the variable was treated as nominal in all analyses.

The analyses were performed in four steps. In step one, disability retirement was regressed on office design without taking into account confounding variables. In step 2, gender, medically certified sickness absence, self-reported work ability, skill-level, and leadership position were included as control variables. Step 3 included all of the aforementioned variables and added the personality markers extroversion, conscientiousness, agreeableness, openness, and neuroticism. Medically certified sickness absence and self-reported work ability were included as potential confounding variables since employees with low levels of work ability and/or high levels of absence may have been provided with separate cellular offices as a measure to prevent premature working life exit. Since the respondents participated at different time-points, the analyses were adjusted for the length of the follow-up period (before linkage to the registry data) in step 4.

Subjects were censored at the end of follow-up (1 January 2015) or earlier in case of death, emigration, or reaching the eligible age for early statutory pension (62 years). Mean follow-up time for the respondents was 6.5 (SD 2.7; range 1.0-10.1) years. We examined the proportional hazards assumption by the testing of nonzero slopes and plotting scaled Schoenfeld residuals. No violation of the assumption was detected ($P>0.05$).

Results

Prevalence rates and descriptive findings

The majority of the sample conducted their work in a cellular office (56.5%), while 26.2% worked in a shared office, and 17.3% worked in an open-plan office. A total of 226 persons (3.3%) became recipients of disability retirement in the course of the study period. Demographic characteristics for the sample and bivariate associations between demographic characteristics and disability retirement are presented in table 1. Mean age in the sample was 47.77 (SD 9.68; range: 20-62) years. Mean self-reported work ability (range 0-10) was 8.70 (SD 1.49). Female respondents were significantly more likely to receive disability retirement compared to male respondents. Risk of disability retirement was highest among respondents in occupations normally requiring 13-15 years of education whereas the lowest risk was found among respondents in occupations normally requiring >16 years of education and in occupations in which the level of required education varies substantially. Non-leaders had significantly higher risk of disability retirement than respondents in leadership positions.

Differences in the study variables between the office design categories are displayed in tables 2 and 3. Although statistical differences were found between the office designs with regard to age of the respondents, length of follow-up period, and work ability, the effect sizes show that that the actual differences were very small. There were significant, but small, differences in the prevalence of subsequent disability retirement between the three office

designs ($\chi^2=6.17$; $df=6779/2$; $P<0.05$) as respondents in shared offices (4.1%) and open-plan offices (3.7%) had higher rates than respondents in cellular offices (2.9%). As for personality traits, a one-way ANOVA indicated significant differences between the respondents in the different office designs concerning scores on openness ($F=5.32$; $df=6415/2$; $P<0.01$) and neuroticism ($F=4.68$; $df=6415/2$; $P<0.01$), but not for scores on extroversion, agreeableness, or conscientiousness. A Bonferroni post hoc test showed that respondents in cellular offices exhibited higher scores on openness compared to respondents in shared offices, and lower scores on neuroticism compared to respondents in shared and open-plan offices. However, estimates of effect sizes indicated that the actual differences in both neuroticism (partial η^2 0.001) and openness (partial η^2 0.002) between the office designs were very small.

Office design impact on risk of disability retirement

Findings from the Cox regression analysis with attained age (at censoring/event) as the underlying time scale are presented in table 4. Analyses were conducted in four steps with additional confounding variables at each subsequent step. Office design had a significant main effect on disability retirement in step 1 of the regression. Respondents working in shared offices (HR 1.86, 95% CI 1.38-2.50) and open-plan offices (HR 1.87, 95% CI 1.31-2.67) had a significantly higher risk of disability retirement when compared to respondents in cellular offices. The association between office design and disability retirement remained significant after adjusting for gender, self-reported work ability, days with sickness absence during the 12 months before the survey, skilllevel, and leadership position in the second step. High work ability reduced the risk of disability retirement (HR 0.79, 95% CI 0.75-0.84), whereas female gender (HR 2.49, 95% CI 1.79-3.46) and having >28 days of sickness absence during the year prior to the survey (HR 2.41, 95% CI 1.73-3.36) increased the risk of disability retirement.

The five personality markers were added to the regression in the third step. Conscientiousness was the only personality variable that had a significant relation with risk of disability retirement (HR 0.85, 95% CI 0.73-0.98). The coefficient shows that higher scores on the conscientiousness variable were associated with lower risk of disability retirement.

In the fourth and final step, the analyses were adjusted for the length of the follow-up period between survey response and linking to registry data. Length of follow-up period was not associated with risk of disability retirement (HR 1.06; 95% CI 0.99-1.12). In this final model, the established associations between office designs and risk disability retirement remained significant as employees in shared offices (HR 1.58, 95% CI 1.12-2.22) and open-plan offices (HR 1.93, 95% CI 1.30-2.87) exhibited higher risk of disability retirement compared to employees in cellular offices. Work ability, sickness absence, gender, and low level of conscientiousness remained significant predictors of disability retirement. A graphical presentation of the associations between office design and disability retirement from the fully adjusted model are shown in figure 1.

Step 2-4 of the Cox-regression was reanalyzed using days of absence 12 months succeeding the survey, instead of prior to the survey, as an indicator of medically certified sickness absence. The findings were consistent with the main analysis. In the fully adjusted model (step 4), respondents working in shared (HR 1.47, 95% CI 1.04-2.06) and open-plan offices (HR 1.73, 95% CI 1.16-2.56) had significantly higher risk of disability retirement when compared to respondents in cellular offices. Having >28 days of sickness absence during the 12 months succeeding the survey (HR 3.76, 95% CI 2.71-5.21) increased the risk of disability retirement.

Discussion

Based on official registry data on disability retirement from a large Norwegian occupational cohort of office workers, the present prospective study showed that working in a shared or open-plan office is associated with an increased risk of early retirement from work due to disability when compared to employees working in cellular offices. Findings from adjusted analyses showed that the risk of disability retirement was independent of the respondents' gender, skill-level, number of days with medically certified sickness absence, leadership position, self-reported work ability, personality traits, and length of follow-up period between survey response and linking to registry data. Secondary findings from this study indicate that work ability, female gender, >28 days with sickness absence during a 12 month period, and lower levels of conscientiousness have independent main effects on subsequent risk of disability

retirement.

Having established office design as a risk factor for disability retirement, it is important to provide mechanisms that can explain this association. Previous research on the effects of office design on health outcomes has pointed to an increased risk of infectious diseases as a possible explanation for why employees in shared and open-plan offices report more health problems and higher sickness absence rates (7). However, it is unlikely that transmission of viruses should lead to permanent disability and early retirement. Hence, alternative explanations for how and why type of office design may lead to disability retirement seem warranted. In the following, we will highlight two plausible and potentially interconnected explanations that may be a topic for upcoming research. First, sharing office workspace implies coping with distractions from noise and behavior of other persons (33-35). Humans tend to pay attention to speech and sharing an office may pose added demands for concentration and tax the tolerance for distractions. Indeed, based on questionnaires and room acoustic measurements in 21 offices, it has been found that distracting background speech largely explains the overall perception of noise in that the less the speech intelligibility, the lower the share of employees disturbed by noise (34). Constant noise can make you tired and lead to a sense of sensory overload, even a three-hour exposure to simulated office noise can lead to increased urinary adrenaline levels (35). Finally, self-reported frequent exposure to disturbing noise at work is associated with increased risk of long-term sickness absence among office workers (33). Consequently, effects of noise in open offices spaces may result in more tiredness, fatigue, and health complaints including headache and mental distress (36, 37). The combination of these health problems may eventually facilitate exit from working life. In support of this hypothesis, frequent self-reported exposure to disturbing noise at work has been found to be associated with increased risk of long-term sickness absence among office workers (33).

A second explanation why open workspaces may increase the disability risk is that such office architecture may compromise the need for privacy, ie, not being constantly observed or listened to by others (9). Privacy is a fundamental human need (9, 38) and diminished privacy may inflict dissonance and distress. Reduced opportunities for privacy may substantially affect perceptions of "control" ie, the possibilities for a person to influence what happens in their work environment. Notably, a recent systematic review concluded that job control was the most consistent work-related predictor of disability retirement (21).

Both the above explanations highlight health problems as the mechanism that explains how office design may influence risk of disability retirement. Hence, a limitation of our study is that we did not have access to the specific diagnoses for the disability pension grant. The current study is therefore unable to inform whether the higher risk of disability retirement when working in shared or open workspaces mainly are due to somatic or mental health issues. Such information would have strengthened the study and should therefore be included in upcoming replications. The magnitude of the association between office design and disability retirement remained significant after accounting for the effects of gender, self-reported work ability, medically certified sickness absence, skill-level, leadership position, personality, and length of follow-up period. Both female gender, medically certified sickness absence, and work ability contributed independently to the disability retirement-risk rate - indicating that future research of the impacts of office design on the disability risk should account for these factors. The substantive effect of gender corroborates findings of past disability retirement studies (39, 40). The impact of self-reported work ability also confirms previous findings indicating that individuals' negative evaluation of their work ability predict subsequent exit from working life due to disability (11). Hypothetically, work ability could confound the association between office layout and disability retirement since employees with lower levels of work ability may be given a cell office as a measure of workplace accommodation or adaptation. However, it should also be noted that work ability, as well as sickness absence, may be operating as a mediators; type of office design should arguably have the potential of affecting level of work ability, which in turn, affects the risk of premature retirement. Thus, the adjustment of work ability and sickness absence in our analyses may have partialled out some proportion of the substantive effect of office design on the disability retirement-risk.

Although it has been argued that the outcomes of office design vary due to individual differences among employees (14), our findings showed that the magnitude of the association between office design and disability retirement was

not influenced by personality traits (41, 42). Based on common sense, one might presume that extroversion, which includes preferences for social settings and a tendency to be outgoing, would be beneficial in shared or open-plan offices. At the other end of the extroversion-introversion spectrum, one might presume that introversion, which includes preferences for solitary experiences, would be negative in open workspaces. However, in line with a previous study on the role of personality in outcomes of office design (20), our findings did not suggest any impact of level of extroversion on the association between office design layout and risk disability retirement.

Although the examined personality traits had no impact on the association between office designs and disability retirement, we found an important direct relation between the conscientiousness trait and disability retirement as respondents with high scores on the trait had lower risk of disability retirement. Conscientiousness is defined as the relatively stable pattern of individual differences in the tendencies to follow socially prescribed norms for impulse control, be goal-directed, planful, delay gratification, and follow norms and rules (41). Evidence indicate that people with higher scores on the conscientiousness trait are healthier and live longer lives (42), and it is therefore not surprising that higher scores on conscientiousness were associated with lower risk of disability retirement in this study. It should also be noted that the neuroticism trait had a close to significant relation with risk of disability retirement. Neuroticism is a trait that predisposes to health problems and is therefore also likely to be a risk factor for disability (43, 44). Due to the uncertainty of estimates in a single sample study, the role of neuroticism, in addition to conscientiousness, with regard to disability should therefore be further examined in upcoming studies.

Strengths and limitations

The prospective study design, large sample size, and use of official registry data to assess disability retirement are strengths of this study. The fact that the average work ability scores in the sample were high and that employees on long-term sick-leave were not invited to the survey suggest that the baseline population was healthy. There were no major changes in national regulations of disability benefits in the survey period that could have influenced our findings. The general economy of Norway was excellent throughout the follow-up period with low levels of unemployment compared to most other countries. It is likely that the financial situation of a country influences the health and work ability of workers, as well as the national welfare benefits such as disability retirement schemes. As Norway is a relatively wealthy country where the welfare programs are highly prioritized by the government, direct comparisons with countries that have other types of welfare arrangements should therefore be done with caution. Although the survey had a response rate in line with the estimated average for organizational surveys (45), altogether 52% of invited respondents did not participate in the questionnaire survey. While the sample was large, the non-random recruitment of participating organizations limits the external validity of the findings. However, it should be noted that probability sampling at the individual level was conducted as all employees in the participating organizations were invited to survey participation (46).

The survey data of this study were collected between 2004 and 2014. Hence, at the individual level, the follow-up period varies between the respondents. Compared to respondents with a shorter follow-up period, it is likely that respondents with a longer follow-up may have experienced changes in the design of the workplace or in their perceptions of the workplace. The followup period was therefore considered in the analyses by including a time-scale variable and adjusting for the length of the period. The associations between office design and disability retirement remained significant even after this adjustment.

The question about office design had only three response categories. Employees may have access to several kind of office solutions for their work (eg, flexoffices) and thereby select the working place according to the task at hand. A more refined indicator could have provided more detailed information about the actual office design and whether respondents used more than one type of office solution during their workday. On the other hand, due to the relatively low incidence of disability retirement cases during the follow-up period, a more fine-grained measure with several response categories would require a larger sample size in order to detect differences. Still, future research could extend our result by adding further information about office design and the physical work environment, such as distraction due to noise (33, 34). With regard to the indicator of office design, the phrasing of the response categories for "shared office" and "openplan" offices may have led to some overlap as respondents who work in

small open-plan offices may have considered this as a shared cellular office.

The respondents' skill-level was used as an indicator of work task. This is a relatively coarse way of categorizing work tasks and a more fine-grained categorization with more specific information about the tasks may have led to other results. The exposure data on office type should be valid since the subject reported his or her present office type at baseline. Work ability was assessed with a previously validated single item from the work ability index. The employed FFM personality instrument has been psychometrically tested in a previous study (26). However, it should be noted that this condensed version of the original inventory has its limitations by not providing information about the sub-facets of each trait. Nevertheless, the complete 240-item Revised Neuroticism-Extroversion-Openness Personality Inventory (NEO-PI) (47), may not be suitable for incorporation in investigations primarily addressing work environment aspects.

Comparison with other studies

To our knowledge, this is the first study of the impact of office design layout on risk of disability retirement. Previous studies have reported that working in shared offices or open-plan offices increases the risk of sickness absence compared to individual cellular-type offices (5-7). However, only the study by Nielsen & Knardahl (7), which utilized an overlapping sample to the current study, was based on registry data. Hence, the findings of the present study extend previous research by showing that working in an open space design is a risk factor for subsequent disability retirement.

While a previous study found that personality characteristics influence the association between office designs and outcomes (14), we found no confounding effects of personality traits in the current study. However, the association between office design and disability retirement was somewhat attenuated when adjusting for gender, medically certified sickness absence, and work ability, thus pointing to these variables as important confounders. The finding that high levels of sickness absence are associated with increased risk of disability retirement is in line with previous research (12, 13).

Concluding remarks

Early exit from working life due to disability retirement may lead to a poorer quality of life, loss of social identity, and mental complaint (48). Knowledge about predictors of retirement due to disability is therefore important. Our findings from a Norwegian setting indicate that open and shared workspace designs could have negative effects in the form of increased risk of employee disability retirement, even when taking other risk factors for disability retirement into account. To reduce the risk of disability retirement, organizations and employers may benefit from addressing well-known challenges inherent in open workspaces such as auditory and visual noise (49), reduced privacy (1), and reduced communication and interaction (9). Providing employees with the opportunity to use cellular offices may be one way of dealing with these challenges. Future research should determine the mechanism that can explain how office design increase the risk of disability retirement and also investigate the generalizability of our findings to other countries and settings. In order to extend this study, future research should apply a more refined measure of office design that allows for investigating different kinds of open-plan offices, such as flex offices and activity-based working.

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Sidebar

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DETAILS

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Respiratory health effects of the fiberglass-reinforced plastic lamination process in the yacht-building industry

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ABSTRACT (ENGLISH)

Objectives Fiberglass-reinforced plastics (FRP) manufacturing has been related to cases of severe airway obstruction and elevated risk of respiratory mortality. But the specific job content risk is not clear. This study evaluated the respiratory health effects of the FRP lamination process. Methods A questionnaire was used to evaluate respiratory symptoms of workers in two yacht-building plants. Pre-shift (07:30-08:30 hours) and post-shift (17:00-18:00 hours) lung function was measured, while post-shift induced sputum was collected on the first day of the week. The participants were grouped into FRP laminators and non-laminators. Linear and logistic regression was used to investigate the effects of the lamination process on lung function. Results Laminators had a higher prevalence of chronic cough, lower pre-shift forced expiratory volume in first second (FEV1) and FEV1/force vital capacity (FVC) (-3.3% and -1.5%), lower post-shift FVC and FEV1 (-3.6% and -4.9%), and larger post-shift reduction of FVC (-2.1%) compared to non-laminators. The laminators also had higher risk of early obstructive and overall (obstructive plus restrictive) lung function impairment, and post-shift reduction of FVC >10% [odds ratio (OR) 5.98, 4.98, and 3.87, respectively). They also had higher percentages of neutrophils and lymphocytes in the induced sputum. Conclusion Laminators should undergo regular check-ups of respiratory symptoms and lung function. Further toxicologic studies are warranted to identify the specific causal agent in the FRP lamination process.

FULL TEXT

Headnote

Chen C-H, Tsai P-J, Wang Y-F, Pan C-H, Hung P-C, Ho J-J, Perng D-W, Nemery B, Guo YL. Respiratory health effects of the fiberglass-reinforced plastic lamination process in the yacht-building industry. *Scand J Work Environ Health*. 2021;47(1):6269. doi:10.5271/sjweh.3924

Objectives Fiberglass-reinforced plastics (FRP) manufacturing has been related to cases of severe airway obstruction and elevated risk of respiratory mortality. But the specific job content risk is not clear. This study evaluated the respiratory health effects of the FRP lamination process.

Methods A questionnaire was used to evaluate respiratory symptoms of workers in two yacht-building plants. Pre-shift (07:30-08:30 hours) and post-shift (17:00-18:00 hours) lung function was measured, while post-shift induced sputum was collected on the first day of the week. The participants were grouped into FRP laminators and non-laminators. Linear and logistic regression was used to investigate the effects of the lamination process on lung function.

Results Laminators had a higher prevalence of chronic cough, lower pre-shift forced expiratory volume in first second (FEV1) and FEV1/force vital capacity (FVC) (-3.3% and -1.5%), lower post-shift FVC and FEV1 (-3.6% and -4.9%), and larger post-shift reduction of FVC (-2.1%) compared to non-laminators. The laminators also had higher risk of early obstructive and overall (obstructive plus restrictive) lung function impairment, and post-shift reduction of FVC >10% [odds ratio (OR) 5.98, 4.98, and 3.87, respectively). They also had higher percentages of neutrophils and lymphocytes in the induced sputum.

Conclusion Laminators should undergo regular check-ups of respiratory symptoms and lung function. Further toxicologic studies are warranted to identify the specific causal agent in the FRP lamination process.

Key terms induced sputum; laminating process; laminator; lung function; respiratory symptom; styrene.

In 2013, eight workers involved in laying up fiberglass woven roving with polyester resins were reported to have obliterative bronchiolitis, a severe irreversible airway obstructive disease involving the small bronchioles (1, 2). Two of them received lung transplantation and one died while waiting for an organ donor. These cases echoed findings of past cohort studies. Two studies that followed up a large cohort of workers in 30 reinforced plastics manufacturing plants in the United States found elevated mortality risk due to non-malignant respiratory diseases, particularly obstructive airway diseases (3, 4). Another cohort study reported elevated mortality risk due to the code Pneumoconiosis and other respiratory diseases from the US reinforced plastic boat-building industry (5). However, a Danish cohort did not show the same risk (6).

Aside from case reports and death registry analysis, epidemiologic surveys using lung function tests and other biomarkers can provide pathophysiologic information for non-diagnosed and subclinical cases. Epidemiologic studies on the respiratory health of workers in fiberglass reinforced plastics (FRP) manufacturing remain limited.

Because styrene is one of the most abundant volatile compounds used in FRP and is the active diluent of polyester resin (36-45% of weight concentration), it is a major concern (7). Previous evidence on the effects of styrene exposure on lung function are mixed. Helal et al (8) and McCague et al (9) both report an association of styrene exposure and obstructive lung function impairment among workers in FRP manufacturing plants. However, Lorimer et al (10) do not report either obstructive or restrictive lung function impairment among workers involved in styrene monomer or polymer fabrication. Whether the observed lung function effects are related to styrene or the additives used in FRP is unknown. Another study reports on increased lung inflammation among workers exposed to FRP dusts related to cutting, grinding, and finishing processes (11). What kind of work process is most hazardous to the lungs is still not clear.

Identifying the health risk of a specific group with similar exposure is an important step in occupational health. In the light of previous case reports, all of which involve manually wiping the glue and laying up the FRP, we conducted this study to evaluate the respiratory effects associated with the lamination process.

Methods

Design and study population

A cross-sectional study on two yacht-building plants in Taiwan was conducted in 2011 (plant A) and 2015 (plant B). All the employees (68 in the plant A and 54 in the plant B), including administrative personnel, were invited to participate. The Institutional Review Board of the National Taiwan University Hospital approved the study protocol (201110017RC), and each participant provided informed consent. Pre-shift (07:30-08:30 hours) and post-shift (17:00-18:00 hours) lung function was measured, and post-shift induced sputum was collected on Mondays - the first workday of the workweek. Each participant received two measurements of lung function and one collection of sputum. All of the participants answered a questionnaire that provided demographic information, respiratory symptoms, cigarette smoking habits, and medical diagnoses.

Measurements of styrene concentrations

Aerial concentrations of styrene were measured during the study. In plant A, first, we performed stationary monitoring with the use of photo-ionized detector (PID) to measure concentrations of total volatile organic compounds near the lamination process paired with air sampling by canisters for 40 minutes. Canister-sampled air was further analyzed for concentrations of various chemicals, including styrene, by GC-MS. Eight repeats of PID-canister-paired monitoring were done, and the styrene estimation formula by PID values was obtained. Next, we measured total volatile organic compounds by PID for 10 minutes near the breathing zone of laminators who were doing lamination. A total of 36 person-times PID monitoring was done among 13 laminators. Their styrene exposures were then estimated by PID values. In plant B, styrene was sampled by personal active samplers with active carbon tubes for seven hours during work and analyzed by GC-FID method. We took 47 measurements, including 9 for lamination work, 12 for administration, 9 for woodwork, 6 for grinding work, and 11 for maintenance. Concentrations of styrene were expressed as parts per million (ppm) (1 ppm=4.26 mg/m³).

The processes of lamination, grinding, and woodwork were similar in the two plants, and employees involved in these three processes worked in the same building structure of each plant. Plant A and plant B were both semi-open. The employees involved in the lamination (laminators) usually stood inside the wooden yacht mold and repeatedly used rollers to impregnate the resin and rolled it onto the glass fiber roving layer-by-layer. Sometimes the laminators needed to enter more restricted compartments for lamination. Employees engaged in grinding work used a hand-held grinder to polish the surface of the hull. Woodworkers were responsible for the manufacture of wood-related furniture and facilities inside the hull. Woodworkers were usually exposed to wood dust and sometimes paint. The administrative staff's office in plant A was located in a building separate from the yacht construction factory, while, in plant B, it was located in the same building structure. Maintenance workers were responsible for the maintenance of water, electricity, and various machinery and equipment in the factory, and their working place was not fixed inside the building of lamination work. Regarding personal protective equipment, plant A provided a half-face mask with a cartridge for the laminators, but plant B only used general cotton or activated carbon masks. During the surveys, due to the hot weather, many workers did not use the respirator correctly.

Pulmonary function measurement

Spirometry was measured based on the guidelines of the American Thoracic Society (12). Each participant underwent lung function assessment in a sitting position. At least three forced expiratory maneuvers with smooth flow-volume loops without artifacts and <5% or 150 ml difference in lung volume between the best two blows were required. Forced vital capacity (FVC), forced expiratory volume in one second (FEV₁), and the ratio of FEV₁ to FVC (FEV₁/FVC) were used for data analyses. Spirometer (Chest-graph HI-101; CHEST MI, Tokyo, Japan) was calibrated before each survey using a 3L flow-volume syringe. Lung function results were defined as obstructive if either pre- or post-shift FEV₁/FVC was less than the lower limit of normal (LLN), and defined as restrictive if maximum FVC was less than LLN with normal FEV₁/FVC. The predicted values of FVC and FEV₁ and the LLN values of FEV₁/FVC and FVC were calculated from the Global Lung Initiative 2012 equation, with ethnic adjustments for South East Asians (13).

Sputum induction and processing

Sputum was induced through increasing concentrations of saline (eg, 3%, 4%, and 5%), as described by Perng et al (14). The procedure was performed after the lung function assessment. Only the opaque and dense portions of the induced sputum (mucus plugs) were selected and collected to minimize contamination by oropharyngeal secretion. The sputum was processed within four hours after collection. Due to the shortage of laboratory support, the preparation of a stained cytospin slide with the cell suspension of induced sputum and the assessment of its differential cell count were only performed in the survey of plant A. A sample was considered appropriate if squamous cells were <20% of the total cell count. If oral squamous cell contamination is <20%, the percentage of differential cell counts in induced sputum cell count is a widely used marker for phenotyping airway inflammation with good reproducibility (15). Since the selection and filtration process of sputum may cause deviations in the total cell number, resulting in unreliable absolute cell number (16), we select the percentages of differential cell counts for analysis in this study. The proportion of differential cell counts was calculated as a percentage of total inflammatory cell count.

Statistical analysis

The participants were grouped into laminators and nonlaminators (ie, administrative and maintenance staff, carpenters, and grinding workers). Between-group differences in demographic information and respiratory symptoms were analyzed by Chi-square, Fisher exact test, or Student's t-test. Between-group differences in differential count in the induced sputum were analyzed by Wilcoxon rank sum test.

Linear and logistic regressions were used to evaluate the relationship between the FRP lamination process (laminators/non-laminators), tenure of lamination work (in years), lung function parameters, and patterns of ventilatory defects, with adjustments for age, sex, educational attainment, tenure, current smoking, past smoking, and cumulative smoking amount. To examine whether sputum differential cell counts could be an intermediate biomarker for functional phenotyping of the respiratory system, we used linear regression to assess the association between the percentage of each cell type with lung function parameters. Statistical significance was set at $P < 0.05$.

Results

Overall, the study participants consisted of 113 employees, 63 from plant A and 50 from plant B. The proportions of female workers and educational attainment <13 years were higher among the laminators than among the non-laminators (table 1). There were no significant differences in age, tenure, and smoking habits between the two groups. The proportion of current and past smokers was much higher among male (19.7%) than female (4.7%) workers.

Geometric mean concentrations of styrene measured for laminating work amounted to 7.5 ppm in plant A and 16.5 ppm in plant B, ie, approximately 30-66 times higher than the geometric mean of 0.2-0.3 ppm measured (in plant B only) for the other jobs (table 2). In general, laminating in an enclosed space or over larger surfaces exposed workers to higher styrene concentrations, thus explaining the broad range of measured concentrations of 1.5-46 ppm in plant A and 2.7-71 ppm in plant B.

Laminators had a statistically higher prevalence of chronic cough than non-laminators (table 1). Laminators more

commonly complained of cough during work at daytime and before sleep at night. There was a borderline significance in the difference of cough and wheeze relieved during holidays between the two groups, but there was no significant difference in phlegm production and nasal symptoms.

The pre-, post-, and between-shift changes of lung function revealed that after adjustments for confounding factors, laminators had significantly lower pre-shift FEV1 and FEV1/FVC, lower post-shift FVC and FEV1, and larger post-shift reduction of FVC compared to nonlaminators (table 3). In terms of patterns of lung function impairment (table 4), laminators had higher prevalences of obstructive and overall (obstructive plus restrictive) impairments. The prevalence of post-shift reduction of FVC >10% was also higher among laminators. The tenure for lamination work was negatively associated with pre- and post-shift FVC or FEV1 (supplementary material www.sjweh.fi/show_abstract.php?abstract_id=3924, table S2). We further stratified all participants in to three groups, non-laminators (never) and those with lamination tenure <or >6.14 years (the median among laminators), and found that only those with lamination tenure <6.14 years had significantly higher risk of obstructive and overall (obstructive plus restrictive) impairments (table S3).

Sputum was collected from 51 out of 63 participants in plant A: 12 could not produce sputum after hypertonic saline inhalation, while 2 were excluded due to inadequate sputum quality (squamous cell >20% of total cells). Laminators had higher percentages of neutrophils and lymphocytes, and lower percentage of macrophages than non-laminators (table 5). The percentage of neutrophils in the induced sputum was associated with the cross-shift reduction in FEV1 and FEV1/FVC, while the percentage of lymphocytes was negatively associated with post-shift FVC and FEV1 (table S1). The percentage of macrophages was positively associated with post-shift FEV1/FVC and cross-shift changes in FEV1 and FEV1/FVC (table S1).

Discussion

In this cross-sectional study in two FRP manufacturing plants, we found that laminators chronically exposed to moderately high styrene levels exhibited an excess of respiratory complaints (mainly cough), impaired spirometry and signs of pulmonary inflammation when compared to non-laminators.

The prevalence of chronic cough (generally nonproductive) was higher among laminators than nonlaminators, even though the former had fewer smokers. Cough was a more common complaint during work at daytime and before sleep at night, but with recovery the next morning. Airway symptoms (cough or wheeze) also improved during holidays or days-off. These respiratory symptoms are suggestive of asthma and may explain why such affected workers were likely to be treated as asthmatic patients, thereby ending up with irreversible fixed airway obstructive disease, as noted in published reports (1, 2). Progressive dry cough, dyspnea, and occasional wheeze are the main symptoms of bronchiolitis obliterans (17, 18). In patients with flavoring-related bronchiolitis obliterans cough improved after leaving employment, but dyspnea did not disappear (18). Thus, regular check-up of respiratory symptoms, including persistent cough or cough with wheeze that are related to work, may provide useful information for identifying workers with significant pulmonary problems caused by exposure to the FRP lamination process. The laminators had an elevated risk of obstructive lung function impairment. This is consistent with previous case reports and epidemiologic studies (1, 2, 8, 9). An epidemiologic study that used styrene as an indicator of exposure to FRP-related resins also demonstrated a higher risk of obstructive lung function impairment in the high exposure group (8, 9). However, styrene effect was not a consistent factor in other studies. A cohort study with analysis of mortality data revealed that increased risk of non-malignant respiratory death was not positively correlated to the cumulative dosage of styrene exposure (3). An epidemiologic study in a styrene producing industry also did not show a risk of obstructive or restrictive impairment due to styrene exposure (10). Although the present study does not tell us whether styrene or other chemicals is the causal agent, our findings point to laminating as the critical exposure. Consequently, laminators are the group requiring active preventive interventions.

Workers involved in the FRP lamination process using the open-molding method are usually exposed to the highest levels of evaporated chemicals from polyester resins (7). Aside from styrene, several chemicals are added to the resins. Peroxides like methylethylketone peroxide (1-1.5%) or benzoyl peroxide are used as initiators or catalysts to initiate the curing process. Peroxide catalysts require dimethyl aniline (0.1-0.3%) to be effectively activated at room

temperature. Promoters such as cobalt naphthenate (0.3-1%) are also added to resins to increase the cure rate. However, no toxicologic information is available for these aforementioned additives in terms of respiratory toxicity or bronchiolitis obliterans. Regarding the filaments, the diameter of the fibers in the woven roving or mat used for the hand lay-up lamination of yacht construction is >10 micrometers, which makes it less likely to be directly inhaled into deep airways. Sometimes, the laminators need to eliminate air bubbles in the composite by hand-holding grinders, which break down glass fiber and resins into inhalable particles. But their overall dust exposure is not as high as that in grinding workers. Therefore, despite that we cannot completely exclude the possibility of filament-related respiratory effect, it is more likely other causal agents play more important roles. Although the causal agent remains unclear, applying closed molding, such as vacuum-assisted resin transfer molding, as well as adequately wearing respirators with organic vapor cartridges have been reported to be effective for reducing personal exposure to FRP-related chemicals (7).

Increased cross-shift reduction in FVC suggests restrictive lung function effects of acute exposure to FRP lamination-related substances. However, the pathophysiology is not identified or described in this study because of the lack of information on total lung capacity and post-bronchodilator lung function. It can only be speculated that the change may be related to processes in the small rather than large airways (mainly FEV1/FVC). Small airway diseases can present as a reduction in FVC due to occlusion or dynamic collapse of small bronchioles (19, 20). Some cases of bronchiolitis obliterans have restrictive or mixed restrictive and obstructive lung function impairment (18, 21). In the light of previous research on flavoring-related bronchiolitis obliterans, a survey using pre-bronchodilator spirometry has demonstrated a high prevalence of restrictive lung function impairment among flavoring workers (22). A spectrum ranging from obstructive to restrictive lung diseases is suggested for such toxic chemical inhalation (23). Therefore, FRP workers with either an obstructive or restrictive ventilatory defect on pre-bronchodilator spirometry need more detailed lung function assessments.

Susceptibility to bronchiolitis obliterans related to FRP chemicals is unknown, although some relevant clues have been provided in previous literature. First, only a small number of cases are reported to have severe obstructive lung disease and the symptoms often manifest shortly after employment (6-12 months), whereas other co-workers do not have the same symptoms or illness even under similar working conditions (1, 2). Second, there is a high risk of non-malignant respiratory mortality among FRP workers with less than one year of employment (5), and this risk is not related to cumulative exposure (3). Our research found that only workers with <6.14 years of employment in lamination have a higher risk of obstructive ventilatory disorder, which is consistent with previous research. Our study showed that a small percentage of workers experienced a cross-shift drop in lung function, suggesting an acute response. These "responders" may be the susceptible subgroup. Further longitudinal studies are needed to assess longterm respiratory outcomes among them.

The present study revealed an elevated percentage of sputum neutrophils rather than eosinophils among laminators. This is consistent with results by McCague et al (9) who showed suppressed exhaled nitric oxide levels, an indicator of eosinophilic airway inflammation. The association of neutrophils and cross-shift FEV1 and FEV1/FVC reduction also suggests a neutrophil-mediated response to airway injury and inflammation. In other words, sputum neutrophils might be used as an intermediate biomarker for the respiratory toxicity of FRP-lamination-related exposure. This finding is in line with previous literature showing that neutrophilic airway inflammation has been associated with toxic inhalation and chronic airway diseases, including bronchiolitis obliterans and chronic obstructive pulmonary diseases (24-26).

The elevated percentage of induced sputum lymphocytes among laminators, and its association with postshift lung capacity, suggests that lymphocytes associated inflammation also play a role in the laminating related respiratory effect. A previous study has demonstrated an increased lymphocyte percentage in induced sputum in several interstitial lung diseases (27) in contrast to airway diseases like asthma or chronic bronchitis (28). Further animal studies or lymphocyte subset analysis may advance knowledge as to the pathophysiologic response to inhalational exposure in the lamination process.

The percentage of sputum macrophages in laminators was lower than that in non-laminators. Alveolar macrophages

usually play a defensive role in respiratory exposure to pathogens and particulate matters (29). A previous study has shown an increase in the number of macrophages in bronchoalveolar lavage among workers exposed to FRP grinding dust (11). An animal study showed that wood dust could increase alveolar macrophages (30). Therefore, the observed reduction in its percentage in laminators may be related to lower dust exposure compared to employees involved in grinding and woodwork, and a relative increase in numbers of neutrophils and lymphocytes. The positive association between macrophage and cross-shift lung function change in this study also suggests a protective role of macrophages in respiratory physiology.

This study has some strengths. First, we conducted field research before and after work on Monday, which minimized the effect of exposures on the previous days. Therefore, the impact on pre-shift lung function is likely to be related to chronic exposures and the effect on cross-shift lung function changes linked to acute exposures. Second, the laminators who participated in this study usually remained in hand lay-up work in FRP manufacturing rather than moving around different kind of processes, which minimized the interference from other exposures, such as wood dust, painting, and FRP grinding dust. Third, this study included exposed and non-exposed groups in the same plant, which minimized bias related to environmental exposure (eg, ambient air pollution).

Some limitations are noteworthy. First, the study's cross-sectional design may have caused an underestimation of the health hazards due to the healthy worker or healthy worker survival effect. Airway symptoms, such as cough or dyspnea, may alert workers to leave work. Since we have already observed the effects on lung function, the healthy worker effect may have prevented us from observing more severe cases of impaired respiratory function. Second, grouping laminators into a single exposure group may underestimate the health effects in the extremely high exposure groups, such as those more commonly working in an enclosed structure or with large surface lamination processes. The incomplete and differential measurement of styrene in the two plants prevented us from assessing the exposure-response relationship for the entire data set. Finally, as this is a simple cross-sectional study without long-term followup, reversed causality should be cautiously considered.

Concluding remarks

Workers using the hand lay-up method for FRP lamination have higher risk of chronic cough, obstructive lung function impairment, cross-shift drop in lung function, and elevated neutrophilic and lymphocytic inflammation of the airways. Until the true causal agent used in the lamination process is identified and replaced, laminators should undergo regular health examinations with focus on respiratory symptoms and lung function. Workers should also use adequate personal protective equipment.

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Conflict of interest

The authors declare no conflicts of interest.

Sidebar

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Effect of welding fumes on the cardiovascular system: a six-year longitudinal study

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ABSTRACT (ENGLISH)

Objective This study investigated whether low-to-moderate exposure to welding fumes is associated with adverse effects on the cardiovascular system. **Methods** To test this, we performed a longitudinal analysis of 78 mild steel welders and 96 controls; these subjects were examined twice, six years apart (ie, timepoints 1 and 2). All subjects (male and non-smoking at recruitment) completed questionnaires describing their health, work history, and lifestyle. We measured their blood pressure, endothelial function (by EndoPAT), and risk markers for cardiovascular disease [low-density lipoprotein (LDL), homocysteine, C-reactive protein]. Exposure to welding fumes was assessed from the responses to questionnaires and measurements of respirable dust in their breathing zones adjusted for use of respiratory protection equipment. Linear mixed-effect regression models were used for the longitudinal analysis. **Results** Median respirable dust concentrations, adjusted for respirable protection, of the welders were 0.7 (5-95 percentile range 0.2-4.2) and 0.5 (0.1-1.9) mg/m³ at timepoints 1 and 2, respectively. Over the six-year period, welders showed a statistically significant increase in systolic [5.11 mm Hg, 95% confidence interval (CI) 1.92-8.31] and diastolic (3.12 mm Hg, 95% CI 0.74-5.5) blood pressure compared with controls (multi-variable adjusted mixed effect models). Diastolic blood pressure increased non-significantly by 0.22 mm Hg (95% CI -0.02-0.45) with every additional year of welding work. No consistent significant associations were found between exposure and endothelial function, LDL, homocysteine, or C-reactive protein. **Conclusion** Exposure to welding fumes at low-to-moderate levels is associated with increased blood pressure, suggesting that reducing the occupational exposure limit (2.5 mg/m³ for inorganic respirable dust in Sweden) is needed to protect cardiovascular health of workers.

FULL TEXT

Headnote

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Objective This study investigated whether low-to-moderate exposure to welding fumes is associated with adverse effects on the cardiovascular system.

Methods To test this, we performed a longitudinal analysis of 78 mild steel welders and 96 controls; these subjects were examined twice, six years apart (ie, timepoints 1 and 2). All subjects (male and non-smoking at recruitment) completed questionnaires describing their health, work history, and lifestyle. We measured their blood pressure, endothelial function (by EndoPAT), and risk markers for cardiovascular disease [low-density lipoprotein (LDL), homocysteine, C-reactive protein]. Exposure to welding fumes was assessed from the responses to questionnaires and measurements of respirable dust in their breathing zones adjusted for use of respiratory protection equipment. Linear mixed-effect regression models were used for the longitudinal analysis.

Results Median respirable dust concentrations, adjusted for respirable protection, of the welders were 0.7 (5-95 percentile range 0.2-4.2) and 0.5 (0.1-1.9) mg/m³ at timepoints 1 and 2, respectively. Over the six-year period, welders showed a statistically significant increase in systolic [5.11 mm Hg, 95% confidence interval (CI) 1.92-8.31] and diastolic (3.12 mm Hg, 95% CI 0.74-5.5) blood pressure compared with controls (multi-variable adjusted mixed effect models). Diastolic blood pressure increased non-significantly by 0.22 mm Hg (95% CI -0.02-0.45) with every additional year of welding work. No consistent significant associations were found between exposure and endothelial function, LDL, homocysteine, or C-reactive protein.

Conclusion Exposure to welding fumes at low-to-moderate levels is associated with increased blood pressure, suggesting that reducing the occupational exposure limit (2.5 mg/m³ for inorganic respirable dust in Sweden) is needed to protect cardiovascular health of workers.

Key terms biomarker; blood pressure; cardiovascular disease; C-reactive protein; CVD; endothelial function; homocysteine; LDL; metal; occupational medicine; particle.

Worldwide, over 11 million welders and additional 110 million workers are exposed to welding fumes (1). In Sweden,

there are 13 000 registered full-time welders (2, 3), while an additional 250 000 workers perform some welding in their jobs (3). Welding generates respirable particles and gases. Welders are mainly exposed to small particles of iron and manganese but also to particles of other metals (eg, nickel and chromium) and particles of non-metal origin (4) due to the material being welded but also the technique. The majority of primary particles in different welding aerosols have diameters ranging from 5-40 nm but they have a tendency to form chainlike agglomerates (5). By mass, welding aerosols have a broad size distribution from coarse [particulate matter (PM) 2.5-10] to fine (PM 0.1-2.5) and ultrafine (PM 0.1), with the fine and ultrafine particles generating higher levels of reactive oxygen species (6).

In the general population, acute and chronic exposure to fine particles has been associated with increased risk of morbidity and mortality from cardiovascular diseases (CVD) (7). Furthermore, recent evidence suggests that long-term exposure to PM₁ and PM_{2.5} increases blood pressure (8, 9). Although welders are exposed to particle levels many times higher than experienced by the general public, we still lack compelling epidemiological evidence from longitudinal studies of whether welding causes CVD. However, cross-sectional and case studies have associated exposure to welding fumes with higher blood pressure (BP) (10), impaired cardiac autonomic function (11), decreased heart rate variability and ectopic heartbeats (12), as well as damage to human coronary artery epithelial cells (13).

In this study, we aimed to investigate risk markers of CVD among currently working welders and controls, in a longitudinal cohort, by combining detailed exposure assessment data with measurements of BP, endothelial function, and plasma biomarkers.

Methods

Study participants

During 2010-2011 (timepoint 1), a total of 101 mild steel welders and 127 controls (with low occupational exposure to particles) in southern Sweden were enrolled in the study; all of them were male and non-smoking (figure 1). These welders worked in small- and medium-sized welding companies (N=10) involved in the manufacturing of forklift trucks, hydraulic lifting tables, dump trucks, asphalt rollers, heating boilers, and stoves. The controls worked mainly in warehouses with food storage and in municipalities as gardeners or janitors. Full details of the recruitment process at timepoint 1 were reported in two prior studies (10, 14).

Approximately six years later (2016-2017), a follow-up study of the welders and controls was performed [timepoint 2; see Gliga et al (15) for full description of the recruitment (15)]. At timepoint 2, welders from 9 of the 10 welding companies were included (one of the companies had closed). Of the 101 welders that participated at timepoint 1, 78 (77%) also participated at timepoint 2. Similarly, of the 127 controls that participated at timepoint 1, 96 (76%) also participated at timepoint 2. The welders and controls that did not participate at timepoint 2 either declined participation without giving any particular reason, were sick on the medical examination day, or had died since timepoint 1. Apart from welding years, which was significantly higher among those who participated at both timepoints, the baseline health and exposure characteristics did not differ between participants at timepoint 1 only (N=23) and timepoints 1 and 2 (N=78). Among the 78 welders participating in both cycles, 7 had retired or quit working due to illness since timepoint 1, and another 12 were employed at the same company as before but were no longer actively involved in welding. Those 7 who had quit working were invited to visit either their old company or the clinic for the follow-up examination. For those individuals, no respirable dust measurements or cumulative exposure data (see below) were available at timepoint 2.

Questionnaire-based data

We used essentially the same questionnaires at timepoints 1 and 2 (with minor differences in phrasing). These were distributed to all participants one week before their medical examination and sampling. On each visit, a trained nurse checked each questionnaire for completeness and consistency of the responses. The questionnaires were used to obtain detailed job history, information about use of safety equipment (ie, personal protective equipment) and other precautions taken to avoid exposure to dust and fumes in the workplace as well as any hobbies which could entail exposure to particles (eg, from welding fumes outside of work, or diesel exhaust). The questionnaires also asked the

participants about their dietary habits, physical activity, alcohol and tobacco use, education, current and past known illnesses, medication usage (prescribed by doctors or non-prescribed), and family history of CVD and other chronic diseases.

Respirable dust measurement

Personal exposure measurement of respirable dust was performed for the active welders, and stationary area-monitoring of respirable dust monitoring was conducted for the controls. For personal sampling, a cyclone (BGI4L, BGI, Mesa Labs, USA; cut-off = 4 µm) was used for collecting respirable dust. The cyclone was fitted with a filter cassette, containing 37-mm mixed cellulose ester filters with an 0.8-µm pore size (pre-weighed) and was placed within the breathing zone of each welder. The airflow through the sampler was set to 2.2 L/min and regularly checked before, during, and after sampling with a flow meter (TSI Model 4100 Series, TSI Incorporated, USA). This personal sampling was coordinated with each company's shift working hours and the average sampling duration was approximately 7 hours for both timepoints. Measured dust concentrations were corrected if respiratory protection was used: the measured concentration (outside respiratory protection) was divided by three as a correction factor to reflect the actual exposure level (10, 16). At timepoint 2, one welder used a half-mask, for which a correction factor of 2 was used instead (17), and another four welders used newer versions of powered air-purifying respirators with double visors, for which a factor of 50 was used [personal communication with Karlsson J-E, occupational hygienist, Clinic of Occupational and Environmental Medicine, Lund University Hospital, Sweden]. The filter samples were analyzed gravimetrically according to a validated method for determination of respirable dust. The limit of detection was set to 0.05 mg/sample.

For those welders with incomplete exposure data, their respective exposure level was estimated individually using geometric mean exposure data obtained from welders working at the same work station, engaged in similar tasks or in the same company. The use of protection devices was then corrected for as described above. For two welders, to complete missing data for the exposure assessment, exposure data previously collected at the welding companies (10, 16) were also used. Only active welders (ie, not retired or welders with nonwelding work tasks) had either measured or assessed respirable dust data. In the end, there were 56 welders who had respirable dust data at both timepoints (timepoint 1: measured N=28, estimated N=28; timepoint 2: measured N=46, and estimated N = 10). For the controls at timepoint 1, full-shift personal breathing zone samples of respirable dust were collected from two companies for 19 control subjects. From four companies, area-level air pollution monitoring of respirable dust was performed using a direct reading monitor, SidePak Model AM510 (TSI Incorporated, Shoreview, MN, USA) with a Dorr-Oliver cyclone (10). At timepoint 2, stationary area monitoring of respirable dust fractions was performed using a DustTrak DRX monitor (TSI Incorporated). At both timepoints, these monitors were placed at breathing zone height in the area where workers spent the most time during their work shifts. On average, the monitoring of each control lasted approximately 4 hours at each company's work site. In companies where workers spent time at two different workstations, measurements were taken in both areas, and a time-weighted average of the two sites was calculated.

Calculation of cumulative exposure

For each welder, the cumulative exposure was calculated by taking the respirable dust measurement adjusted for respiratory protection and multiplying it by years of welding reported, as follows:

Cumulative exposure₁ = respirable dust timepoint₁ x years welding timepoint₁

Cumulative exposure timepoint₂ = cumulative exposure timepoint₁ + (respirable dust timepoint₂ x [years welding timepoint₂ - years welding timepoint₁])

We only calculated the cumulative exposure for active welders, ie, welders with measured or assessed respirable dust.

Analysis of metals on filters from respirable dust sampling

Filters from timepoint 2 (total N=104, out of which N=46 individuals are included in this longitudinal study) were analyzed for element concentrations of Mg, Al, K, V, Cr, Mn, Fe, Co, Ni, Cu, Zn, Cd, Tl, Th, and Pb. After weighing, the filters were digested in 1 mL of concentrated nitric acid at 70 °C for 16 hours. After dilution with Milli-Q water, the

metal concentrations were determined by inductively coupled plasma-mass spectrometry (ICP-MS; iCAP Q, Thermo Scientific GmbH, Dreieich, Germany) in collision cell mode, with kinetic energy discrimination, using helium as the collision gas. The detection limits were calculated as three times the standard deviation (SD) of blank filters and are as follows: 0.005 pg (Co, Cd, Tl, Pb, Th), 0.007 pg (V, Ni), 0.01 pg (Cu), 0.02 pg (Mn), 0.05 pg (Cr, Zn), 0.08 pg (Mg), 0.15 pg (Al), 0.89 pg (Fe), and 7.4 pg (K). Analytical accuracy was verified using certified reference filters in the analysis of samples, N=20 (Trace Metal on Filter Media D, Part nr. QC-TMFM-D, Lot 1530803; HighPurity Standards, North Charleston, SC, USA). The obtained versus certified mean values were 2.46 (SD 0.03), 2.45 (SD 0.04), 2.51 (SD 0.04), 2.49 (SD 0.03), and 2.51 (SD 0.03) pg versus 2.50 (SD 0.03) pg for V, Cr, Co, Ni, and Cu, respectively; 2.47 (SD 0.04) and 2.45 (SD 0.03) pg versus 2.50 (SD 0.05) pg for Tl and Pb, respectively; 1.04 (SD 0.02) and 0.98 (SD 0.01) pg versus 1.00 (SD 0.01) pg for Mn and Cd, respectively; 2.70 (SD 0.21) versus 2.50 (SD 0.1) pg for Fe; 2.39 (SD 0.07) pg versus 2.50 (SD 0.2) pg for Zn; and 49.0 (SD 0.86) pg versus 50.0 (SD 0.5) pg for Al. No reference values were available for Mg, K, or Th.

Workload

There are indications that workload and occupational heavy lifting are important risk factors for CVD (18, 19). An occupational hygienist therefore roughly estimated the ergonomic workload and lifting by watching short videos (minutes) collected on the sampling days for most participants (welders and controls) at all work sites at timepoint 2. At the warehouses (controls), the workload varied greatly among work tasks, which ranged from manually moving food packaging between pallets and driving trucks from storage points to reloading points. The workload differed among the welders, but at all sites any heavy lifting was done using lifting aids. The individual workload over time was difficult to estimate reliably because the videos were too short and the tasks varied too much. An overall difference in workload between welders and controls could not be discerned; hence, workload was presumed to span a similar range at all the welders' and controls' companies, and it was not used as a covariate in the statistical analysis.

Medical examination and blood sampling

A trained occupational nurse conducted the physical examinations of welders and controls, which included measurements of height, weight, BP, pulse rate, and peripheral arterial tonometry as a measure of endothelial function. At the end of each examination, blood samples were taken to assess biomarkers of risk of CVD [C-reactive protein (CRP), LDL, homocysteine]. Blood samples were left to clot at room temperature for exactly 10 minutes and then centrifuged at 2200 x g for 10 minutes. It should be noted that homocysteine values increase with time before separation (20) and slightly elevated values can be expected due to the 10 minutes of clotting before separation. Nevertheless, all samples were treated in the same way. After separation, plasma samples were aliquoted and kept on dry ice while they were moved to the laboratory in the Division of Occupational and Environmental Medicine at Lund University, where they were stored at -80 °C until analysis.

Blood pressure measurement

A skilled occupational nurse measured the BP of welders and controls using a digital monitor (Boso Medicus, Bosch & Sohn GMBH, Ingelheim am Rhein, Germany) with an adjustable cuff to accommodate different arm circumferences. All measurements were performed in dim light in a silent room with comfortable seating and subjects in the supine position. For timepoint 1, one BP reading was taken from each participant; for timepoint 2, two reliable measurements were taken at 2-minute intervals and their average per participant used in later analyses.

Peripheral arterial tonometry measurement of endothelial function

Peripheral arterial tonometry was performed during the daytime working shift. The participants' height, weight, age, and blood pressure were first entered into an EndoPAT instrument (Itamar Medical, Caesarea, Israel). The participants were lying in a comfortable bed with both arms resting on an armrest to limit their muscle activity. The finger probes were placed on both index fingers to record the digital pulse wave amplitude (PWA) and a digital blood pressure monitor cuff was positioned on the left arm. The PWA was measured for 6 minutes until it was stable. A baseline measurement was taken for 5 minutes, after which the cuff was inflated over 200 mm Hg or to at least 60 mm Hg above the subject's recorded systolic BP. Following the baseline recording, the cuff was deflated and a post-

occlusion reactive hyperemia (RHI) signal recorded for 5 minutes. The EndoPAT software computed values for endothelial function (reactive hyperemia index, RHI), arterial stiffness (augmentation index, AI), and normalized AI at 75 beats per min (AI@75). An RHI score <1.67 indicates impaired coronary endothelial function (21).

Statistical analysis

For the analysis of examined participants present at both timepoints 1 and 2, we used linear mixed-effects models to evaluate the influence of being a welder (versus being a control) upon the cardiovascular outcomes of systolic and diastolic BP, EndoPAT measurements (RHI, AI@75), and cardiovascular risk biomarkers (LDL, homocysteine, CRP). Exposure-response relationships of respirable dust, welding years, and cumulative exposure were analyzed among welders' only in separate linear mixed-effects models analyses against the same outcomes. The mixed models included the participants as a random factor (random intercept) because they were measured twice and thus lacked independence over time, and all other predictor variables as fixed factors. Covariates included in the models were participants' age (continuous), body mass index (BMI) (continuous), education status (from secondary school to university studies in five ordinal categories), residence (from large cities to countryside in four ordinal categories), physical activity (sedentary to intense physical in four ordinal categories), smoking (current smoker, party smoker, non-smoker), use of snus (a moist powdered form of tobacco packaged in pouches that is placed under the upper lip; yes, no), frequency of alcohol consumption (times/day/week), and frequency of vegetable consumption (times/day/week) and fish intake (>1-0/day in seven ordinal categories). Familial history of CVD (yes, no) and use of drugs potentially affecting EndoPAT (yes, no) were added for analyzing the EndoPAT outcomes only. Pearson standardized residuals were visually inspected for evaluating model assumptions of normal distributions and equal variance (homogenous). We conducted a sensitivity analysis where we used BMI from timepoint 1 to adjust for at both timepoint 1 and timepoint 2, to test whether BMI at timepoint 2 could be an intermediate between exposure at timepoint 1 and outcomes at timepoint 2. There was no major difference in the estimates or significance levels, which indicates that the main analysis was only adjusted for potential confounders and not intermediates. All statistical analyses were carried out in the R platform, version 3.4.3, with the lme package used to fit the linear mixed models. The variance explained by fixed factors (Rm²) was calculated using the RsqGLM function in the Bioconductor package MuMin.

Results

Characteristics of the study participants

Table 1 summarizes the demographic data, lifestyle factors, and health conditions of the study participants in the longitudinal cohort of welders (N=78) and controls (N=96). The median years of welding was ten years at timepoint 1 and 14.5 years at timepoint 2. It should be noted that some controls had done some welding work in the past (N=21 at timepoint 1 and N=22 at timepoint 2). For the welders, their respirable dust concentrations in the working environment decreased with approximately 20% from timepoints 1 to 2 while the exposure to respirable dust (adjusted for respiratory protection equipment) decreased by approximately 30% between timepoints 1 and 2 (table 1). For timepoint 2, the main metals found in the respirable dust were Fe (median=0.41 mg/m³, max=5.37 mg/m³) and Mn (median=0.06 mg/m³, max=1.54 mg/m³) (metal concentrations on the filters were not adjusted for personal breathing protection, N=46). For the controls, the stationary area-level of respirable dust concentrations was 0.09 (min-max: 0.02-0.2) mg/m³ at timepoint 1 and 0.03 (0.02-0.06) mg/m³ at timepoint 2.

The welders and controls were similar in age, BMI, education, alcohol consumption, snus use, and smoking history. However, the welders were to a larger extent born outside Sweden and lived in small towns when compared with the controls (P<0.005, paired analysis). The median systolic BP decreased from timepoints 1 to 2 in the welders, whereas the diastolic BP increased in the controls from timepoints 1 to 2.

Supplementary table S1 (www.sjweh.fi/show_abstract.php?abstract_id=3908) shows the self-reported and doctor-diagnosed prevalence of CVD and use of doctors' prescribed medication, as well as familial history of CVD.

Between timepoints 1 and 2, welders reported an increased prevalence of hypertension (welders: 26% at timepoint 1 to 41% at timepoint 2; controls: 15% at timepoint 1 and 26% at timepoint 2) and use of prescribed medication (beta blocker and angiotensin-converting enzyme - ACE - inhibitor) to treat hypertension (welders 12% at timepoint 1 to

21% at timepoint 2; controls: 4% at timepoint 1 and 7% at timepoint 2). There were, however, no significant differences between welders and controls as regards changes in doctor's diagnosis and medication between timepoints 1 and timepoint 2.

Cardiovascular disease markers among welders and controls

Table 2 reports the differences between welders and controls for BP, heart rate, endothelial function, and cardiovascular risk biomarkers in plasma (dependent variables) in the study cohort. Over the six-year followup period, the systolic BP among welders significantly exceeded that of controls by 5.11 mmHg and the diastolic BP by 3.12 mmHg (model 2). The effect estimates for BP, variance explained by fixed factors, and levels of significance were similar between model 1 only adjusted for age and BMI and the fully adjusted model 2. No significant changes in the markers of endothelial function or risk biomarkers measured in plasma were detected among welders compared with controls over time. In addition, we performed a sensitivity analysis where we excluded the controls who previously welded, and the effect estimates as well as the level of significance were similar to the main analysis.

Exposure-response relationships

The effects of respirable dust, years of welding, and cumulative exposure on cardiovascular outcomes are presented in table 3. The fully adjusted model 2 had in general a higher percentage of variance explained in comparison to models only adjusted for age and BMI. Diastolic BP increased non-significantly by 0.22 mm Hg ($P=0.063$) with each additional year of welding. Associations between welding years and BP became even stronger when including both welders and controls in the analysis: systolic BP increased 0.25 mmHg with each additional year of welding (95% CI 0.07 - 0.44, $P=0.006$) and diastolic BP with 0.15 mmHg (95% CI 0.01-0.29, $P=0.029$). The CRP concentrations increased by 0.86 mg/L with each increment of 1 mg/m³ of respirable dust; however, CRP decreased by 0.08 mg/L with each welding year during the follow-up. Homocysteine concentrations in welders decreased by 1.71 pmol/L with every 1 mg/m³ increase of respirable dust, whereas cumulative exposure was not associated with any outcome. In order to evaluate non-linear associations, linear mixed models using splines were performed for systolic and diastolic BP (and the same variables as in the main analysis). When comparing the models with and without splines (by ANOVA), there was no significant difference ($P=0.169$ for systolic BP and $P=0.285$ for diastolic BP).

Discussion

In this study, we found evidence that low-to-moderate exposure to welding fumes increases BP. Although the exposure-response relationship was weak, the diastolic BP seemed to increase with years spent welding. Importantly, this was observed among welders with an average exposure below half the current Swedish occupational exposure limit (OEL) of 2.5 mg/m³ for inorganic respirable dust (22). We also uncovered associations between exposure to welding fumes and CRP.

In a previous cross-sectional study of the same welders and controls recruited for cycle 1, we showed that welders have an approximately 5 mm Hg higher systolic and diastolic BP compared with controls (10). In the current study, we validated that putative link between welding and increased BP through a longitudinal experiment design, in which the same welders and controls were revisited six years later. Admittedly, the differences of 5.11 and 3.12 mm Hg respectively for systolic and diastolic BP between the welders and controls in the longitudinal study are rather subtle in relation to known risks of CVD (10, 23). Compared to the previous cross-sectional study on the same cohort (10), in this longitudinal study we observe a similar effect estimate for the BP outcome despite the welders having performed an average four and a half additional years of welding. This could, in part, be related to the BP measurement at timepoint 2 that was more reliable as it included more measurements. In addition, we cannot completely exclude a potential effect of healthy worker selection. Nonetheless, our findings emphasize that the current OEL of 2.5 mg/m³ is too high to protect against risk factors for CVD.

For diastolic BP, a weak positive exposure-response relationship with number of years working as a welder (long-term exposure) was revealed, yet no association was found between BP and respirable dust (short-term exposure). It should be noted that respirable dust was evaluated during one day of working and can be considered a measure of acute exposure, which is dynamic but likely a crude proxy for overall level of exposure. This could potentially result in a misclassification of exposure to respirable dust. Instead, respirable dust was associated with CVD-related

serum markers CRP and homocysteine in our study, for which higher levels in all have been linked to greater CVD risk (24-26), though Mendelian randomization studies have questioned the role of CRP (27). Increased CRP was positively associated with respirable dust in this longitudinal study suggesting an increased risk of CVD, whereas homocysteine was negatively associated with respirable dust. CRP is an acute phase protein involved in systemic inflammation, and its range of values that define different risk categories are quite narrow (low risk <1.0 mg/L, intermediate risk=1.0-3.0 mg/L, and high risk >3.0 mg/L (28);). Moreover, CRP has also been associated with PM_{2.5} exposure in several recent studies (29-31), pointing to systemic inflammation as the underlying mechanism between PM exposure and CVD. Yet, since respirable dust was not measured on the same day as blood sampling, its presented associations with plasma markers should be interpreted cautiously as the levels of exposure can vary highly between working days.

In both timepoints 1 and 2 of this study, the median respirable dust levels (both in the working environment and after correction for personal respiratory protective equipment) fell below the Swedish OEL of 2.5 mg/ m³ established in 2018 (22). Still, we found relationships between welding and BP and between respirable dust and CVD risk markers in plasma. Together, these results indicate that Sweden's OEL remains too high to protect welders from CVD-related health effects from occupational exposure, particularly for those individuals working long-term in welding. It should be noted that the levels of respirable dust were lower in timepoint 2 compared with timepoint 1. We speculate that this may be due to the recommendations for improvement of the work environment that we gave along with the results for respirable dust to each company after timepoint 1. Each company participating in the study received a report about their respirable dust level (welding companies) or stationary particle measurements (control companies) where the levels were related to the Swedish OEL and suggestions of actions were given to reduce the exposure levels (if above the OEL). Apart from that, we also sent out a short report to each worker that participated at the first timepoint about the results of that study (cross-sectional analyses of the cohort).

Although the median respirable dust in the air was below the OEL, the median levels of respirable Mn were above the OEL for Mn [0.05 mg/m³ (22)] at timepoint 2, and concentrations nearly 30 times the OEL were detected (the Mn concentrations on the filters were not adjusted for personal breathing protection). The mild steel used by the welders in this study was the most commonly used type in terms of its Fe and Mn contents, and our results suggest that many welders in Sweden are exposed to excess levels of respirable Mn. However, since Mn exposure from welding fumes is known to cause neurological effects (32, 33), but is not suspected to be a risk factor for CVD, Mn exposure was not evaluated in relation to CVD-related outcomes in this study.

We must note that median systolic BP among welders in the longitudinal study group was lower at timepoint 2 than timepoint 1, which is an unexpected result given the higher age - and longer working history in welding - of participants at timepoint 2. However, the reported hypertension increased among welders increasing from timepoints 1 to 2 and some of the reduction in systolic BP may be due to increased use of medicine against hypertension. Another explanation for the lower median BP at timepoint 2 is that measurements were taken differently between cycles; at timepoint 1 one measurement was used whereas at timepoint 2 an average of two measurements were used. Thus, the latter data should more accurately convey resting BP. Nevertheless, since these measurements were identical between welders and controls within each cycle, they should be valid for comparison between groups over time.

There are both strengths and limitations to this study. Its strengths include the longitudinal study design wherein the same repeated measurements were performed on the same individuals six years apart. Moreover, many influential factors were considered in this study, and we have excluded two important confounders of CVD by recruiting only non-smoking welders and controls at baseline and assessing workloads of welders and controls (found to be similar). However, we cannot completely exclude unmeasured differences between the welders and controls, which may explain discrepancies between results obtained in welders and controls and the exposure-response associations in welders only. Furthermore, the exposure to welding fumes was robustly characterized through individual respirable dust measurements performed for many welders. However, it should be noted that respirable dust is performed during one day of working and can be considered a measure of acute exposure and a crude

measure of level of exposure. This could potentially result in a misclassification of exposure to respirable dust. Additional limitations include that recommended conditions for EndoPAT measurements [ie, fasting (a minimum of 4-8 hours), avoiding smoking, snus, or consuming caffeine for >8 hours before measurements, as well as not taking CVD-related medication on the testing day] were not feasible at workplaces during the daytime. Moreover, follow-up measurements of participants at the same time of the day could not be ensured, and, as mentioned already, the conditions for BP measurements were not identical between timepoints.

In conclusion, this study has supported previously documented associations between welding and increased BP and thereby strengthens the link between welding and CVD. Furthermore, the results suggest the occupational exposure of Swedish welders persists at levels that can cause biological effects and the current OEL for respirable dust of 2.5 mg/m³ is too high to adequately protect welders from work-related CVD.

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Sidebar

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Footnote

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DETAILS

Subject:	Dust; Welding; Welding machines; Regression analysis; Cardiovascular diseases; Questionnaires; Aerosols; Fumes; Blood pressure; C-reactive protein; Cardiovascular system; Proteins; Welding fumes; Occupational exposure; Occupational health; Health risks; Metal workers; Regression models; Outdoor air quality; Statistical analysis; Longitudinal studies; Pressure effects; Exposure limits; Confidence intervals; Low carbon steels; Cardiovascular disease; Biomarkers; Homocysteine; Correlation analysis; Low density lipoprotein
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Increasing labor force participation in older age requires investments in work ability

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ABSTRACT (ENGLISH)

The increasing number of older people relative to the working-age population will exert pressures on economic growth, increase age-related social costs and endanger the sustainability of government finances. A large proportion of these differences can be explained by physical work demands, work time control, and self-rated work ability (18). [...]it seems that the factors affecting working beyond the statutory retirement age are, at least in part, similar to factors that relate to early exit. Even though hard physical labor has become less common during recent decades, many jobs still involve physical work demands. [...]efforts to reduce physical work exposures are needed to prevent early labor market exit among older workers. [...]efforts to promote mental health and well-being are increasingly important for maintaining a high labor market participation.

FULL TEXT

For well over 100 years, life expectancy in developed societies has increased by 2.5 years per decade (1). At first, most of the increase was due to decreased death rates at younger ages, but since the 1950s, the main reason has been better survival after age 65. Factors contributing to our increasing lifespan include better living conditions, healthier lifestyles, advances in healthcare and a shift from heavy jobs to non-manual occupations.

Coupled with a long-term fall in fertility rates, the consequence of this increasing length of life has been a growing number and share of the elderly population. Currently, almost one fifth of the population in the European Union (EU) has reached the age of 65, and this share is projected to increase during the next decades. While the increase in life expectancy is a great accomplishment, the growing share of older people also poses a range of economic and social challenges. By 2050, nearly 30% of the EU population will be older than 65, and the old-age dependency ratio will exceed 50% (2). The increasing number of older people relative to the working-age population will exert pressures on economic growth, increase age-related social costs and endanger the sustainability of government finances.

This development has raised the topic of extending working lives high on the political agenda. To counter the economic costs of the growing elderly population, reforms to increase the statutory retirement age, cut the routes to early retirement and increase labor force participation among older workers have been put forward in most European countries (3). This has also led to positive developments, as the average age of transition into retirement has increased in many countries, and the employment rate in older ages has improved (4).

However, a large proportion of people are unable to continue in paid employment until the increasing statutory retirement age. Poor health and work ability are major reasons for early exit from the labor market. Disability retirement is one of the most common pathways for premature exit from working life, but poor health is also associated with exit from work through unemployment (5). Unemployment and poor health are interrelated in complex ways: poor health may increase the risk of unemployment and unemployment, in turn, may increase health problems. Long term, they may form a self-reinforcing cyclical relationship. Unemployment is also associated with an increased risk of disability retirement (6, 7).

Working life expectancy is a measure that summarizes the effect of various, often competing, exit routes on the length of working lives (8). This measure indicates how much of the remaining lifetime will be spent in employment or in labor market activity. It also takes into account the timing of labor market exit so that earlier withdrawal gets more weight. Studies have shown that working life expectancy is shorter in the lower socioeconomic groups (9, 10) and in occupations with high physical demands (11).

In this issue of *The Scandinavian Journal of Work, Environment and Health*, Schram et al (12) analyse the influence of occupational class and physical workload on working life expectancy and lost working years using multistate Cox regression models. In the age range 50-63 years, working life expectancy among manual workers was one year lower than that among upper non-manual employees. Nearly two thirds of this difference was explained by unemployment and one third by disability retirement. Physically demanding work was also related to lost working years, mostly due to ill-health-based exit routes. The effect of physical work on lowered working life expectancy could not be reduced back to occupational class, as it was consistently observed within occupational classes. Manual workers with physically demanding work had the lowest working life expectancy.

Another element in extending working lives is continuing to work after reaching the statutory retirement age. So far, most people have stopped working at that stage and relatively few have continued. However, the proportion of people working beyond the retirement age has been increasing (13). Evidence on factors that affect working beyond the retirement age is more limited than information on premature retirement.

For many, extending working beyond the retirement age is voluntary, but others may be forced to continue working for financial reasons if their retirement income is low. It is known that men, the better educated and those who have recently reached their retirement age are typically more likely to participate in paid work after reaching their retirement age. Own motivation and job satisfaction, as well as many aspects of personal life, such as the partner's labor market position, are important factors affecting the retirement decision. Many older employees prefer part-time

work, and they appreciate possibilities for worktime arrangements and other flexibility (14).

Being in good health is an important precondition for working beyond the retirement age (15, 16). Working conditions also play an important role, and they are obviously related to the previously mentioned motivation, job satisfaction and work ability. Also in this issue, the study by Andersen et al (17) shows that higher physical work demands are associated with a lower likelihood and a good psychosocial work environment with a higher likelihood of working beyond the state retirement age. A good psychosocial work environment is important for both employees in sedentary and physically active work. It has also been shown that employees with higher occupational classes are much more likely to continue working beyond the retirement age compared to those with lower occupational classes. A large proportion of these differences can be explained by physical work demands, work time control, and self-rated work ability (18). Thus, it seems that the factors affecting working beyond the statutory retirement age are, at least in part, similar to factors that relate to early exit.

Despite the generally favorable development in population health, the increasing statutory retirement age means that people approaching the end of their working careers will inevitably encounter chronic conditions (19). Increasing attention is needed to ensure that people are able to continue their working lives despite such conditions. In this respect, work accommodation and vocational rehabilitation activities are of high value. Even though hard physical labor has become less common during recent decades, many jobs still involve physical work demands. Thus, efforts to reduce physical work exposures are needed to prevent early labor market exit among older workers. Such efforts and a continuous development of skills need to be started well in advance. Working lives must also become more flexible for different working abilities and life situations.

An increasing level of education and changes in the occupational structure from physically heavy jobs to service sector occupations may have been partly responsible for the increase in working life expectancy. At the same time, increasing cognitive demands, work-related stress and fast changes in technology pose new challenges. Such psychosocial working conditions may particularly relate to mental work ability (20). If mental health problems are involved, continuing in work may be challenging, regardless of whether the health problems initially originate from the workplace or not. As mental health problems often emerge in young adulthood, they may result in a large number of lost working years and continue to affect one's life throughout the whole life course (21-23). Therefore, efforts to promote mental health and well-being are increasingly important for maintaining a high labor market participation.

Socioeconomic position is one of the key determinants of extending working lives. So far, those who are better educated and work in higher non-manual occupations seem to be in a better position to continue their working lives. Extending working lives further implies that special attention needs to be paid to occupations where the physical and psychosocial risk factors are common. If all work environments do not allow continued employment, the increase in the length of working lives may be uneven and lead to increasing economic inequalities in older age. Reducing work-related risks and ensuring a healthy and safe work environment for everyone until retirement is also a primary target in tackling health inequalities.

Sidebar

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DETAILS

Subject:	Population; Market exit; Socioeconomic factors; Mental health; Older workers; Work environment; Physical work; Market positioning; Employment; Economic growth; Sustainability; Age; Older people; Manual workers; Labor market; Job satisfaction; Life expectancy; Retirement; Labor; Labor force; Participation; Employees; Working conditions; Disability pensions; Economic development
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Comments on a recent case-control study of malignant mesothelioma of the pericardium and the tunica vaginalis testis/Authors' response

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ABSTRACT (ENGLISH)

Among females, the distributions of cases of pericardial mesothelioma and controls by birth year are less dissimilar ($P < 0.05$). [...]the female cases of pericardial mesothelioma are better matched to controls on year of birth than are male cases of either mTVT or pericardial mesothelioma. In the Marinaccio et al (1) sensitivity analysis restricted to subjects born before 1950, the distributions of cases and controls by period of birth remain significantly different. [...]based on the reported evidence, cases and controls were not matched on birth cohort, thereby possibly biasing the results. The fact that few, if any, cases of mTVT and pericardial mesothelioma occurred in industries traditionally associated with high asbestos exposure raises the possibility that the results of Marinaccio et al (1) are attributable to deficiencies in study design, very possibly bias in the selection of controls, and deficiencies in exposure assessment and classification as described above, leading to a spurious association of occupational exposure with

mTVT and male pericardial mesothelioma. All authors have worked as both consulting and testifying experts in litigation matters related to asbestos exposure and asbestos-related disease.

FULL TEXT

As the first case-control study of malignant mesothelioma of the pericardium and the tunica vaginalis testis (mTVT), the paper by Marinaccio et al (1) is potentially an important epidemiologic contribution. A careful review of the paper, however, raises a number of methodological issues.

Any case-control study can be viewed as being nested within a conceptual cohort, with controls being sampled from the at-risk cohort as cases arise over time. This view of case-control studies leads to the concept of incidence-density sampling of controls (eg, 2, 3). For Marinaccio et al (1) this would mean that, as cases were registered over the study period, each would be matched to an individual control or set of controls of the same gender, age, and region of the country (since asbestos exposure varies by time and region [4]). For example, if a case were 50 years old in 1995, then any matched control should be close to age 50 in 1995 and of the same gender and from the same region as the case. Matching for age in this fashion automatically results in matching for year of birth, which is essential in this context because birth-cohort effects are determinants of asbestos exposure and mesothelioma incidence (eg, 5-8). If Marinaccio et al (1) used this scheme for age-matching, one would expect to see similar distributions of cases (table 1) and controls (table S3 in the supplemental material) by period of birth. Among males, however, the distributions of mesothelioma cases (whether pericardial or mTVT) and controls by period of birth are clearly different ($P < 0.001$). Among females, the distributions of cases of pericardial mesothelioma and controls by birth year are less dissimilar ($P = 0.05$). Thus, the female cases of pericardial mesothelioma are better matched to controls on year of birth than are male cases of either mTVT or pericardial mesothelioma. We note also that the distributions of male and female controls by year of birth are distinctly different ($P < 0.002$), whereas the birth-year distributions of cases of mesothelioma by site and gender are not ($P = 0.8$).

In the Marinaccio et al (1) sensitivity analysis restricted to subjects born before 1950, the distributions of cases and controls by period of birth remain significantly different. Therefore, based on the reported evidence, cases and controls were not matched on birth cohort, thereby possibly biasing the results. Similarly, bias may result from the lack of matching on geographic region; while cases were registered from across Italy, controls were selected from only six regions. Although a sensitivity analysis restricted cases and controls to those from only the six regions, a comparison of tables S1 and S3 indicates that the regional distribution of controls is different from that of person-time observed; that is, the controls do not appear to be representative of the underlying population at risk by region. The second major issue of concern has to do with ascertainment of asbestos exposure. Information on exposure for the cases was presumably obtained at the time of registration. The two sets of controls, obtained from previously unpublished case-control studies, were interviewed during 2014-2015 and 2014-2016; that is, many years after the exposure for most cases was ascertained (1993-2015). Few other details of the control groups are provided, except that participation by one set of controls was $< 50\%$, raising additional concerns about selection bias. For details on the second set of controls, Marinaccio et al (1) reference a paper by Brandi et al (9). On review of that paper, however, we found no description of the control group, only references to three earlier papers. Marinaccio et al (1) present analyses only with both sets of controls combined; to evaluate potential sources of bias from the use of different sets of controls, they should also report results using each set of controls separately.

The authors also did not detail their methods of exposure classification. For example, what does probable or possible exposure mean? The authors should at least present separate analyses of definite occupational exposure. Eighty cases of mTVT were registered, but only 68 were included in the analyses. Information on the 12 omitted cases (eg, age, year of birth, and region) would be helpful. Marinaccio et al (1) did not provide clear information on what occupations and/or industries they considered as exposed to asbestos. In an earlier study, Marinaccio et al (10) remarked on the absence of pericardial mesothelioma and mTVT in industries with the highest exposures to asbestos, saying, "[t]he absence of exposures in the shipbuilding, railway and asbestos-cement industries ... for all the 67 pericardial and testicular cases is noteworthy but not easy to interpret." By contrast, Marinaccio et al (1)

stated, "[t]he economic sectors more frequently associated with asbestos exposure were construction, steel mills, metal-working industry, textile industry and agriculture." The possibility of exposure in the "agriculture economic sector" was not mentioned in Marinaccio et al (10) and appears not to have been considered in previous epidemiologic studies in Italy. In general, epidemiologic studies indicate that farmers and agricultural workers are not at increased risk of developing mesothelioma (eg, 11-17). The fact that few, if any, cases of mTVT and pericardial mesothelioma occurred in industries traditionally associated with high asbestos exposure raises the possibility that the results of Marinaccio et al (1) are attributable to deficiencies in study design, very possibly bias in the selection of controls, and deficiencies in exposure assessment and classification as described above, leading to a spurious association of occupational exposure with mTVT and male pericardial mesothelioma.

Conflict of interest

This research has received no outside funding. All authors are employees of Exponent, Inc., an international scientific and engineering consulting company. All authors have worked as both consulting and testifying experts in litigation matters related to asbestos exposure and asbestos-related disease.

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Authors' response: Mezei et al's "Comments on a recent case-control study of malignant mesothelioma of the pericardium and the tunica vaginalis testis"

Mezei et al's letter (1) is an opportunity to provide more details about our study on pericardial and tunica vaginalis testis (TVT) mesothelioma (2), which is based on the Italian national mesothelioma registry (ReNaM): a surveillance system on mesothelioma, with individual asbestos exposure assessment.

Incidence of pericardial mesothelioma has been estimated around 0.5 and 0.2 cases per 10 million person-years in men and women, respectively, and around 1 case for TVT mesothelioma. ReNaM collected 138 cases thanks to its long period of observation (1993-2015) and national coverage. Conducting a population-based case-control study with incidence-density sampling of controls across Italy and over a 23 year time-span should have been planned in 1993 and would have been beyond feasibility and ReNaM scope. We rather exploited two existing series of controls (3).

The resulting incomplete time- and spatial matching of cases and controls is a limitation of our study and has been acknowledged in our article. The analysis of case-control studies can nevertheless be accomplished in logistic models accounting for the variables of interest, in both individually and frequency matched studies (4). Furthermore, analyses restricted to (i) regions with enrolled controls, (ii) cases with definite diagnosis, (iii) incidence period 2000-2015, and (iv) subjects born before 1950 have been provided in the manuscript, confirming the strength of the association with asbestos exposure (supplemental material tables S4-7).

Following Mezei et al's suggestion, we performed further sensitivity analyses by restriction to regions with controls and fitting conditional regression models using risk-sets made of combinations of age and year of birth categories (5-year classes for both). We confirmed positive associations with occupational exposure to asbestos of pericardial mesothelioma, with odds ratios (OR) (adjusted for region) of 9.16 among women [95% confidence interval (CI) 0.56-150] and 5.63 (95% CI 1.02-31.0) among men; for TVT mesothelioma the OR was 7.70 (95% CI 2.89-20.5). Using risk sets of age categories and introducing year of birth (5-year categories) as a covariate (dummy variables) the OR were similar: OR (adjusted for region) of 9.17 among women (95% CI 0.56-150) and 5.76 (95% CI 1.07-31.0) among men; for TVT the OR was 9.86 (95% CI 3.46-28.1).

Possible bias from incomplete geographical overlap between cases and controls has been addressed in the paper (table S4) and above. In spatially restricted analyses, OR were larger than in those including cases from the whole country, indicating that bias was towards the null. Mezei et al further noted that "the regional distribution of controls is different from that of person-time observed". This objection is not relevant because the above analyses were adjusted by region.

Our controls were provided by a population-based study on pleural mesothelioma (called MISEM) and a hospital-based study on cholangiocarcinoma (called CARA). In MISEM, the response rate was 48.4%, a low but not

unexpected rate as participation among population controls is usually lower and has been declining over time (5). It is important to underline that ReNaM applied the same questionnaire that was used for interviews and carried out the same exposure assessment as both MISEM and CARA.

As repeatedly stated in ReNaM papers (6-7), each regional operating center assesses asbestos exposure based on the individual questionnaire, other available information, and knowledge of local industries. Occupational exposure to asbestos is classified as definite, probable or possible. Occupational exposure is (i) definite when the subject's work was reported or otherwise known to have involved the use of asbestos or asbestos-containing materials (MCA); (ii) probable when subjects worked in factories where asbestos or MCA were used, but their personal exposure could not be documented; and (iii) possible when they were employed in industrial activities known to entail the use of asbestos or MCA. Hence, the definite and probable categories are closer to one another and were combined in our analyses. In any case, restricting analyses to subjects with definite occupational exposure and using each set of controls separately, as suggested by Mezei et al, yielded elevated OR for TVT and pericardial mesothelioma among men using both the above described modelling strategies; the OR could not be calculated for women.

There were 70 (25 pericardial and 45 TVT) occupationally exposed mesothelioma cases. In population-based studies, analyses by occupation are limited by the low prevalence of most specific jobs. As briefly reported in our paper, for purely descriptive purposes, the industrial activity of exposure (cases may have multiple exposures), were construction (22 exposures, 7 and 15 for pericardial and TVT mesotheliomas, respectively), steel mills and other metal working industries (4 and 11), textile industries (2 and 3), and agriculture (2 and 5); other sectors had lower exposure frequencies. The absence of industries like asbestos-cement production, shipbuilding and railway carriages production/repair should not be surprising and had already been observed (7). In the Italian multicenter cohort study of asbestos workers (8), given the personyears of observation accrued by workers employed in these industries and gender- and site-specific crude incidence rates, approximately 0.1 case of pericardial and 0.2 of TVT mesothelioma would have been expected from 1970 to 2010. Even increasing ten-fold such figures to account for higher occupational risks among these workers would not change much.

Asbestos exposure in agriculture has been repeatedly discussed in ReNaM reports (9: pages 70, 73, 128, 164 and 205). Exposure opportunities included the presence of asbestos in wine production, reuse of hessian bags previously containing asbestos, or construction and maintenance of rural buildings. Similarly, mesothelioma cases and agricultural workers exposed to asbestos have been noted in France (10).

In conclusion, the additional analyses we performed according to Mezei et al's suggestions confirm the association between asbestos exposure and pericardial and TVT mesothelioma, supporting the causal role of asbestos for all mesotheliomas. ReNaM's continuing surveillance system with national coverage is a precious platform for launching analytical studies on pleural and extra pleural mesothelioma.

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DETAILS

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Work factors facilitating working beyond state pension age: Prospective cohort study with register follow-up

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ABSTRACT (ENGLISH)

Objectives The demographic changes in Europe underline the need for an extension of working lives. This study investigates the importance of physical work demands and psychosocial work factors for working beyond the state pension age (65 years). **Methods** We combined data from three cohorts of the general working population in Denmark (DWECS 2005 and 2010, and DANES 2008), where actively employed workers aged 55-59 years replied to questionnaires about work environment and were followed until the age of 66 years in the Danish AMRun register of paid employment. Using logistic regression analyses, we calculated prevalence ratios (PR) and 95% confidence intervals (CI) for the association between physical and psychosocial work factors and working beyond state pension age, adjusted for age, sex, cohort, cohabiting, sector, income, vocational education, working hours, lifestyle, and previous sickness absence. **Results** Of the 2884 workers aged 55-59 years, 1023 (35.5%) worked beyond the state pension age. Higher physical work demands was associated with a lower likelihood (PR 0.69, 95% CI 0.58-0.82) and a good psychosocial work environment was associated with higher likelihood (average of 7 items: PR 1.81, 95% CI 1.49-2.20) of working beyond state pension age. Stratified analyses did not change the overall pattern, ie, a good overall psychosocial work environment - as well as several specific psychosocial factors - increased the likelihood of working beyond state pension age, both for those with physically active and seated work. **Conclusion** While high physical work demands was a barrier, a good psychosocial work environment seems to facilitate working beyond state pension age, also for those with physically active work.

FULL TEXT

Headnote

Objectives The demographic changes in Europe underline the need for an extension of working lives. This study investigates the importance of physical work demands and psychosocial work factors for working beyond the state pension age (65 years).

Methods We combined data from three cohorts of the general working population in Denmark (DWECS 2005 and

2010, and DANES 2008), where actively employed workers aged 55-59 years replied to questionnaires about work environment and were followed until the age of 66 years in the Danish AMRun register of paid employment. Using logistic regression analyses, we calculated prevalence ratios (PR) and 95% confidence intervals (CI) for the association between physical and psychosocial work factors and working beyond state pension age, adjusted for age, sex, cohort, cohabiting, sector, income, vocational education, working hours, lifestyle, and previous sickness absence.

Results Of the 2884 workers aged 55-59 years, 1023 (35.5%) worked beyond the state pension age. Higher physical work demands was associated with a lower likelihood (PR 0.69, 95% CI 0.58-0.82) and a good psychosocial work environment was associated with higher likelihood (average of 7 items: PR 1.81, 95% CI 1.49-2.20) of working beyond state pension age. Stratified analyses did not change the overall pattern, ie, a good overall psychosocial work environment - as well as several specific psychosocial factors - increased the likelihood of working beyond state pension age, both for those with physically active and seated work.

Conclusion While high physical work demands was a barrier, a good psychosocial work environment seems to facilitate working beyond state pension age, also for those with physically active work.

Key terms health; older worker; physical work demand; physical workload; psychosocial; retirement; statutory retirement age.

In many Western societies, labor force participation rates have increased among individuals >60 years since the mid- or late-1990s (1). Increasing labor force participation rates are important in the light of the need in many countries of adapting to the increasing share of the population being 65 and older until the middle of this century. The main increase in older workers' labor market participation has taken place before the state pension age, but working lives are also increasingly extended beyond this age (2). Extending work life beyond the state pension age can be a choice due to, eg, finding one's job fulfilling, a necessity arising from lack of income as a retiree, or something in between (3, 4).

The state pension age is around 65 years in most EU countries (5). The propensity to work beyond this age differs to a large extent within the EU. The average employment rate in 2018 for the age group 65-74 years was 10.1%. However, this rate ranged from 2.7% in Luxembourg to 37.5% in Iceland (6). Working after the state pension age is less pronounced in Denmark (where the state pension age was 65 until the end of 2018) than in the other Scandinavian countries. Hence, the employment rate in 2018 for the 65-74-year-olds was 14.1% in Denmark compared to 16.8% in Sweden and 18.7% in Norway (7).

Working after the state pension age in Denmark is, presumably, to a lesser extent the result of necessity compared to many other countries, since the at-risk-of-poverty rate among individuals >65 years is fairly low in Denmark (8) - a result applying across gender and educational level due to fairly high replacement rates (ie, percentage of an individual's annual employment income that is replaced by retirement income when they retire) for low income groups (9). In Denmark, only approximately 20% of working retirees - ie, those having paid work while also receiving pension - work in high-strain jobs. This is less than in many other European countries, eg, 30% in Sweden and between 40-50% in Estonia and Italy (4). Dingemans & Henkens (4) characterize high-strain jobs as unfavorable working conditions for older workers, namely full-time work, high physical and mental job demands, and low levels of job control. Their findings for working retirees suggest that participation in high-strain jobs is driven by necessity to a higher degree than participation in low-strain jobs, which is more likely to be a choice.

The present study considers the importance of good working conditions for working beyond the state retirement age when working is assumed to be mainly a choice. Therefore, the aim was first to investigate the role of physical and psychosocial work factors for working beyond the state pension age of 65 years. Further, distinguishing between two sub-groups, namely physically active jobs and seated jobs, the second aim was to explore whether the association between psychosocial work factors and working beyond the state retirement age differed by physical work characteristics. These analyses are critical for guiding employers in directing efforts towards retaining workers beyond the state pension age, in particular workers with physically active jobs, when work after this age is mainly a choice.

Most previous studies on working conditions and retirement have focused on retirement behavior in general or early retirement, while existing knowledge about working conditions that facilitate staying beyond the state pension age is more scarce and mainly based on cross-sectional or retrospective data (10). The results of these studies suggest that working conditions and psychological work environment are important determinants of working beyond the state pension age. Retrospective data (11) show that job control and work autonomy are associated with working after age 65 in Sweden, while having a physically or psychologically demanding job reduces the likelihood of working beyond this age. Similarly, using cross-sectional data from 16 European countries, the SHARE study reported that psychosocial working conditions were generally better among those working beyond retirement compared to previous conditions among those retired. In a review article distinguishing between work-related 'facilitators' and 'barriers' for a prolonged work life after pensionable age, working conditions tailored to individuals' desire to contribute, flexible working hours, the possibility to upgrade existing and acquire new skills, and being offered financial gains are highlighted as facilitators, while barriers include stress, a lack of support, negative attitudes, physical and cognitive demands, and an overemphasis on lack of qualifications (12). Along the same line, a Finnish cohort study suggested that good mental health combined with the opportunity to control work time is a key factor in this respect (13). Finally, another Finnish cohort study showed that a higher likelihood of prolonging working life after state pension age among employees with higher occupational classes compared to lower occupational classes was explained by having physically light job, better work time control, and better self-rated work ability (14). Altogether, evidence from prospective studies are scarce.

The aim of this prospective cohort study with register follow-up was to investigate the role of physical and psychosocial work factors for working beyond the state pension age of 65 years. We hypothesized that physical work demands would act as a barrier and that positive psychosocial work factors would facilitate working beyond state pension age. As a secondary aim, we also explored whether the importance of psychosocial work factors were different for workers with physically active versus seated work.

This paper adds to the scarce literature using prospective data to examine the role of physical and psychosocial work factors on working beyond the state pension age. The novelty of the paper is that separate but symmetric analyses are conducted on samples of older workers with physically active and seated work, respectively, providing for the first time, comparable estimates of the relative importance of a number of psychosocial work measures on working beyond the state pension age for these two groups of workers.

Methods

Study population

This study combines data of workers aged 55-59 years from three cohorts in Denmark (DWECS 2005 and 2010 and DANES 2008) (15-17), where actively employed workers replied to questionnaires about work environment and health. DWECS 2005 (N=19 855) and 2010 (N=31 210) were performed in the general working population and DANES 2008 (N=9913) in the general working population with an oversampling of those aged >50 years (N=4477, the sub-sample is called DANES 2008-senior). The response percentages of DWECS 2005 and 2010 and DANES 2008 were 63%, 53%, and 76%, respectively. Using the following five inclusion criteria, where each step adds to the previous criteria, the flow of participants was: (i) age 55-59 years and responding to the questionnaire (N=6079), (ii) actively employed at the time of the questionnaire response (N=5253), (iii) 66 years or older in 2018, i.e. we had access to AMRun register data (Danish: Arbejdsmarkedsregnskab uden timenormering) up until 2018 (N=3724), (iv) alive and not emigrated at the age of 66 years (N=3598), and (v) no missing covariates (N=2884). Thus, the final population for the present study consisted of 2884 workers aged 55-59 years at baseline.

Predictors

Physical work demands was assessed with the single-item question "How would you describe your physical activity at your main job?" with four response categories (i) mostly sedentary work that does not require strenuous physical activity; (ii) mostly work while standing or walking but does not require strenuous physical activity; (iii) work while standing or walking with some lifting and carrying; and (iv) heavy or fast moving work that is physically strenuous (18).

For the psychosocial work factors, seven questions that were available in all three cohorts were included. All questions were originally developed to the Copenhagen Psychosocial Questionnaire (COPSOQ) (19, 20) and included (i) influence at work ("Do you have a large degree of influence concerning your work?"), (ii) workplace ("Do you have to work very fast?"), (iii) time to tasks ("How often do you not have time to complete all your work tasks?"), (iv) information about decisions ("At your place at work, are you informed well in advance concerning for example important decisions, changes, or plans for the future?"), (v) information to do well ("Do you receive all the information you need in order to do your work well?"), (vi) recognition from management ("Is your work recognized and appreciated by the management?"), and (vii) possibilities for development ("Do you have the possibility of learning new things through your work?"). The specific questions with response categories are provided in the supplementary material (www.sjweh.fi/show_abstract.php?abstract_id=3904), table S1.

Normalization of predictor variables

For the predictor variables, physical work demands was linearly normalized on a scale of 0-1, ie, 0=seated work, 1/3=standing and walking at work, 2/3=lifting and carrying, and 1=heavy and fast. Response categories of the psychosocial variables were linearly normalized on a scale of 0-1, where 0 is worst and 1 is best.

Outcome

The outcome variable was "working after state pension age" (yes/no), which was 65 years in Denmark until 2018. The AMRun register contains individual day-to-day information about labor market participation, unemployment, education, granted social benefits etc. of all citizens in Denmark (21). We defined working after state pension age as having any paid employment in the period from 65 years and 3 months to 66 years and 0 months. The reason for leaving out the first three months after turning 65 years is that there may be a short time lag from being eligible for state pension until actually leaving the labor market. With this definition, 35% of the participants in our study worked after the eligible state pension age.

Control variables

The analyses were controlled for a number of factors that may influence the decision to work beyond state pension age; sex (man, woman), age at baseline (continuous variable 55-59 years), cohort (DWECS 2005, DWECS 2010, DANES 2008), cohabiting (married, cohabiting, single), sector (public sector, private sector), body mass index (BMI: underweight <18.5, normal weight 18.5-24.9, overweight 25-29.9 and obese >30 kg/m²), smoking status (never, former, current smoker), household disposable income (after tax, rent, and other fixed expenses) (0-15, 15-50, 50-85, 85-100 percentile; the 15th, 50th and 85th percentile are respectively 180 785, 263 031, and 367 067 Dkr, where 7.5 Dkr ~ 1 euro), weekly working hours (<35, 35-40, >40 hours), vocational education [unskilled, skilled, and higher education (higher education includes short cycle higher educations, vocational bachelor educations, bachelor programs, masters programs, and PhD programs)], and long-term sickness absence within two years before baseline (yes, no). Information about sex, age, cohabiting, sector, family available income, vocational education, and previous long-term sickness absence were obtained at each respective baseline (2005, 2008 and 2010) based on registers from Statistic Denmark. Body weight and height (to subsequently calculate BMI), as well as smoking status and work hours were self-reported in the questionnaires.

Statistics

Using log-binomial regression analysis (Proc Genmod, SAS version 9.4, SAS Institute, Cary NC, USA), we modelled the prevalence ratio (PR) for working after the state pension age as a function of each respective psychosocial work factor and physical work demands. Estimating the PR from log-binomial regression - rather than the odds ratio from logistic regression - is recommended when the outcome is common (ie, >10%) (22). As most of the psychosocial factors were correlated with each other, we performed separate analysis for each factor to avoid multicollinearity. In model 1 (minimally adjusted), we adjusted for sex, baseline age, and cohort. In model 2 (fully adjusted), we adjusted for all the control variables mentioned before. As a next step, we analyzed in model 2 whether each of the psychosocial factors interacted with physical work demands, by including both the psychosocial factor and the physical activity at work factor in the same fully adjusted analysis, plus an interaction term between the particular psychosocial factor and the physical work demands (multiplicative interaction). For this purpose, the question about

physical work demands was dichotomized, with 'physically active work' defined as the last three response categories (N=1595), and 'seated work' defined as the first response category (N=1248). We also performed an analysis with an overall measure of the psychosocial work environment, by first dichotomizing the 7 items to 0 or 1, then adding them together, and finally averaging by 7 (ie, normalized scale 0-1). Finally, we performed the analyses of each psychosocial factor as well as the overall measure of the psychosocial work environment stratified for physical work demands. In the fully adjusted model, we also tested for any interactions between the control variables 'cohort', 'sex' and 'vocational education' with each of the psychosocial work factors, the overall psychosocial work environment, and physical work demands. None of the interactions were statistically significant; hence we did not include the interaction terms in the final statistical models. Results are reported as PR and 95% CI. PR express the difference between 0 and 1 on the normalized scale.

Results

Of the 2884 workers aged 55-59 years, 1023 (35.5%) worked beyond the state pension age of 65 years.

Table 1 shows the baseline characteristics of the 2884 workers. There were relative uniform distributions of men/women, DWECS/DANES cohort participants, normal weight/overweight participants, and public/private sector employees. Table 1 also illustrates baseline characteristics of those who retired at or before 65 years and those who continued to work beyond 65 years.

Table 2 shows in the fully adjusted model that having higher physical work demands was associated with lower probability of working beyond retirement age (PR 0.69, 95% CI 0.58-0.82). In the fully adjusted model, all of the psychosocial work factors were associated with working beyond retirement age, with a PR range of 1.23-1.55. When combining the seven psychosocial factors ('overall psychosocial work environment'), the PR was 1.81 (95% CI 1.49-2.20). Sex-stratified analyses showed largely similar results, although women tended to be more affected by high physical work demands than men (interaction: sex by physical work demands, $P=0.07$, sex-stratified PR in supplementary table S2).

The interaction term between physical activity at work and psychosocial work environment was not statistically significant for any of the psychosocial variables. However, we still performed exploratory analyses to see if there were any marked numerical differences between the estimates. Table 3 shows the exploratory analysis with stratification for physical work demands. Four of the seven psychosocial work factors were significant for both for those with seated and physically active work. Thus, the stratified analyses did not change the overall picture.

Discussion

In this prospective cohort study with register followup, we investigated the importance of physical work demands and psychosocial work factors for working beyond the state pension age. Higher physical work demands decreased the likelihood for continued work and can thus be considered a push factor. Higher influence, lower workpace, more time to complete tasks, more information about decisions, more information to do well, higher level of recognition from management and better possibilities for development increased the likelihood for working beyond retirement age. These psychosocial factors can thus be considered as stay factors. Subgroup analyses of those with seated and physically active work did not change the overall picture.

Previous studies have documented that high physical work demands act as a push factor (23-25). Thus, it was not surprising to find in the present study that those with a physically active work were only half as likely to work beyond the state pension age as those with seated work, even when adjusting for possible confounders. Poor health - eg, musculoskeletal pain - combined with high physical work demands likely plays an important role (26). Even at the same level of poor physical health, people with physically active work - eg, lifting, bending and twisting the back - are much more likely to be affected negatively in relation to being able to do their work (27). To break this barrier, workplaces may need to adapt the physical demands for those with physically active work who are still willing to work beyond the state pension age. The SeniorWorkingLife study showed that, among workers still active in the labor market, 25% of the men and 36% of the women with mainly physically active work would choose to stay longer in the labor market if the work was less physically strenuous (28).

As the most important finding, our results indicate that a good psychosocial work environment is associated with

higher likelihood of work participation beyond the state pension age, even for those with physically active work. Previous studies on Dutch workers have shown mixed findings about the role of the psychosocial work environment; two studies on the same population of Dutch older workers showed significant associations between appreciation and interesting work and working beyond retirement (29, 30), although these associations were no longer present when health and work engagement were included in the analyses (29). A study on a prediction model for working beyond retirement showed that more procedural justice was associated with working beyond retirement, but again, the predictive power of health and sector of work was stronger in the final model (31).

Strengths and limitations

A strength of the present study is its prospective design with reporting of the work environment several years before state pension age and follow-up in a high-quality Danish register until after the state pension age. By contrast, the majority of previous studies assessing important factors for working beyond retirement age has been cross-sectional questionnaire or qualitative interview studies. Another strength is that we controlled for a number of possible confounders that may influence the decision to work beyond the state pension age. Table 1 shows some clear differences at baseline between the groups, which highlights the need to control for possible confounders. However, there is a risk of over-adjustment when including income and vocational education in the analyses, as there may be some collinearity with the psychosocial factors and physical work demands. For this reason, we provided both a minimally and fully adjusted model, although the estimates of the fully adjusted model may be more conservative. A limitation is that we used single-item questions rather than full scales. However, these few and simple questions were associated with working beyond state pension age. The sample size is a limitation as it is difficult to detect possible statistical interactions with a relatively small sample of about 3000 participants. Thus, none of the interaction analyses were statistically significant, either because no relevant interaction exists or because the study was underpowered to detect such interactions. We provided exploratory stratified analyses of those with seated and physically active work, but these analyses should be interpreted with caution due to the sample size. While it would also be relevant to test associations for different levels of physical activity at work, the sample size in the present study is not large enough to allow for further stratification. Nevertheless, the overall picture is that the results hold true, also for those with physically active work. Another limitation is that we did not have information about the type of work that the participants did after the age of 65 years, ie, they may have changed to a less demanding job. A strength is that we controlled the analyses for previous sickness absence, as poor health is a strong predictor of early labor market exit. Nevertheless, we cannot exclude that the healthy worker effect influenced the findings. Furthermore, because the participants were of different ages, ie, 55-59 years, the follow-up time until the age of 66 years differed. However, controlling for age of the participants inherently accounts for this difference. Some of the control variables may be confounders whereas others may be effect modifiers. We tested for interactions of each of the psychosocial factors, the overall psychosocial work environment, and physical work demands with cohort, sex and vocational education. None of these showed significant interactions. To avoid the chance of mass significance, and because we did not have any specific hypotheses for doing so, we did not test for interactions with the remaining control variables.

Concluding remarks

The present study investigated the importance of physical and psychosocial work factors for working beyond the state pension age. Higher physical work demands were a barrier for continued work and can thus be considered a push factor. By contrast, our result indicates that positive psychosocial work factors, such as high level of influence, recognition from the management, and possibilities for development can extend working life beyond state pension age, both among those with seated and physically active work. These can thus be considered stay factors.

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The authors declare no conflict of interest.

Sidebar

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Occupational exposure to organic dust and risk of lymphoma subtypes in the EPILYMPH case-control study

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ABSTRACT (ENGLISH)

Objectives This study aimed to estimate the risk of lymphoma and its major subtypes in relation to occupational exposure to specific organic dusts. **Methods** We explored the association in 1853 cases and 1997 controls who participated in the EpiLymph case-control study, conducted in six European countries in 1998-2004. Based on expert assessment of lifetime occupational exposures, we calculated the risk of the major lymphoma subtypes associated with exposure to six specific organic dusts, namely, flour, hardwood, softwood, natural textile, synthetic textile, and leather, and two generic (any types) groups: wood and textile dusts. Risk was predicted with unconditional regression modeling, adjusted by age, gender, study center, and education. **Results** We observed a 2.1-fold increase in risk of follicular lymphoma associated with ever exposure to leather dust [95% confidence interval (CI) 1.01-4.20]. After excluding subjects who ever worked in a farm or had ever been exposed to solvents, risk of B-cell lymphoma was elevated in relation to ever exposure to leather dust [odds ratio (OR) 2.2, 95% CI 1.00-4.78], but it was not supported by increasing trends with the exposure metrics. Risk of Hodgkin lymphoma was elevated (OR 2.0, 95% CI 0.95-4.30) for exposure to textile dust, with consistent upward trends by cumulative exposure and three independent exposure metrics combined (P=0.023, and P=0.0068, respectively). **Conclusions** Future, larger studies might provide further insights into the nature of the association we observed between exposure to textile dust and risk of Hodgkin lymphoma.

FULL TEXT

Headnote

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Objectives This study aimed to estimate the risk of lymphoma and its major subtypes in relation to occupational exposure to specific organic dusts.

Methods We explored the association in 1853 cases and 1997 controls who participated in the EpiLymph case-control study, conducted in six European countries in 1998-2004. Based on expert assessment of lifetime occupational exposures, we calculated the risk of the major lymphoma subtypes associated with exposure to six specific organic dusts, namely, flour, hardwood, softwood, natural textile, synthetic textile, and leather, and two generic (any types) groups: wood and textile dusts. Risk was predicted with unconditional regression modeling, adjusted by age, gender, study center, and education.

Results We observed a 2.1-fold increase in risk of follicular lymphoma associated with ever exposure to leather dust

[95% confidence interval (CI) 1.01-4.20]. After excluding subjects who ever worked in a farm or had ever been exposed to solvents, risk of B-cell lymphoma was elevated in relation to ever exposure to leather dust [odds ratio (OR) 2.2, 95% CI 1.00-4.78], but it was not supported by increasing trends with the exposure metrics. Risk of Hodgkin lymphoma was elevated (OR 2.0, 95% CI 0.95-4.30) for exposure to textile dust, with consistent upward trends by cumulative exposure and three independent exposure metrics combined ($P=0.023$, and $P=0.0068$, respectively).

Conclusions Future, larger studies might provide further insights into the nature of the association we observed between exposure to textile dust and risk of Hodgkin lymphoma.

Key terms B cell lymphoma; epidemiology; flour dust; Hodgkin lymphoma; leather dust; textile dust; wood dust.

Lymphoma includes a heterogeneous group of hematological malignancies. The overall combination of lymphoma subtypes ranks fifth of the most common cancer in the developed regions of the world (1). Several epidemiological studies have provided evidence of a link with occupational exposures, such as solvents and pesticides (2, 3), but results on the association with exposure to organic dust are inconsistent (4-10).

Workplace exposure to organic dust is a well-established cause of respiratory disorders. This includes allergic conditions, such as asthma, hypersensitivity pneumonitis, and organic dust toxic syndrome (11), which have shown a moderate inverse association with risk of malignant lymphomas in several case-control studies (12-14). However, a large registry-based cohort study in Sweden reported an increase in risk of nonHodgkin lymphoma (NHL) and Hodgkin lymphoma (HL) in prick-test positive patients affected by a range of atopy-related diseases (15); also, incident cases of lymphoma did not exceed the expectation in another cohort of patients who tested positive for allergy (16). On the other hand, occupational exposure to seven high molecular weight sensitizing agents, some of which related to organic dust, identified with the aid of a job-exposure matrix (17), was inversely associated with NHL risk (18, 19). Although the mechanism remains elusive, the well-known role of immunological factors in lymphoma development lends credibility to the hypothesis that chronic stimulation of the immune system by endogenous and exogenous exposures, including high molecular weight allergens related to some organic dusts, might protect against risk of developing NHL (18).

In this paper, we investigated the association between exposure to specific organic dusts, selected at the early stage of planning the study based on an extensive literature search on occupational risk factors, namely wood dust (any), hardwood, softwood, textile dust (any), natural textile, synthetic textile, flour dust, and leather dust, and risk of lymphoma overall, B-cell lymphoma, and five major lymphoma subtypes.

Methods

Study design and participants

The EPILYMPH study is a multicenter case-control study on the etiology of lymphoma, which was conducted in six European countries, namely the Czech Republic, France, Germany, Ireland, Italy, and Spain, in 1998-2004. A detailed description of the study can be found elsewhere (20). Briefly, eligible cases were consecutive adult patients first diagnosed with any lymphoma subtype during the study period and resident in the referral area of the participating centers. The diagnosis was classified according to the 2001 WHO classification of lymphoma (21), and an international team of pathologists, coordinated by Marc Maynadié, reviewed the slides of about 20% of cases from each center. Controls from Germany and Italy were randomly selected by sampling from registers of the resident population. In the other countries, hospital controls were recruited, with eligibility criteria restricted to diagnoses other than cancer, infectious diseases and immunodeficiency. Both population and hospital controls were frequency matched to the cases by gender, 5-year age group and residence area. Approval from the relevant ethics committees was obtained in all centers. A signed informed consent was obtained directly from the 2348 lymphoma cases and 2462 controls who participated in the study prior to interview and blood withdrawal. Overall, the participation rate was 88% in cases, 81% in hospital controls, and 52% in population controls.

Questionnaire and occupational history

Trained interviewers gathered information directly from all the cases and controls, using the same standardized questionnaire translated into the language of each country, on socio-demographic factors, lifestyle habits, and

lifetime work history. Study subjects who reported having worked in jobs of prior interest, including bakers, woodworkers, and workers in the leather and the textile industry, were administered a job-specific module inquiring in more detail into the exposures of interest. Questions in the job-specific modules referred to work procedures, tasks accomplished, tools used, as well as chemicals, such as glues, paints, dyes, wood preservatives, insecticides, or fungicides, indoor/outdoor work, presence and functioning of ventilation systems if indoor, and use of personal protective equipment.

Occupational exposure assessment

In each participating center, industrial hygienists, blinded to the case/control status of study subjects, reviewed the questionnaire information for each job in their work history to assess exposure to 43 agents, of prior interest for study, including any wood dust, hardwood dust, softwood dust, any textile dust, natural textile dust, synthetic textile dust, flour dust, and leather dust, using the following exposure metrics:

- confidence about the exposure assessment, representing the industrial hygienist's degree of certainty that the worker had been truly exposed to the agent, based upon two criteria: (i) the probability of the agent occurring while performing the tasks implying exposure (unexposed; exposure possible, but not probable; probable; certain); and (ii) the proportion of workers exposed among those in the same job (1=<40%; 2=40-90%; 3=>90%);
- intensity of exposure, expressed on a four-point scale (unexposed; low; medium; high). Agent-specific cut-off points of intensity categories were set based on the respective most recent threshold limit value, or benchmark occupations when no threshold limit value existed. When grouping individual agents, such as any wood dust, or any textile dust, the group intensity level was that of the contributing agent attaining the highest intensity level;
- frequency of exposure, representing the proportion of working time involving contact with the agent (unexposed; 1-5% ; 5-30%; >30% work time).

A cumulative exposure score was calculated for each agent as follows (22):

$$C_j = \sum_i (y_i \cdot x_i \cdot f_i)$$

where C_j is the cumulative exposure score; i is the study subject; j is the j th job in the work history of the i th study subject; y_i is the duration of exposure (in years) of the j th job of the i th study subject; x_i is the exposure intensity level the j th job of the i th study subject; and f_i is the exposure frequency level in the j th job of the i th study subject.

For the purposes of the analysis, cumulative exposure scores were then categorized into quartiles among the exposed cases and controls, corresponding to increasing level of lifetime cumulative exposure. Due to sparse data within each exposure category, in the analysis of lymphoma subtypes, the score of cumulative exposure was categorized as either below or above the median value.

Statistical methods

We used unconditional logistic regression models to assess risk of lymphoma (all subtypes), B-cell lymphoma, and its major subtypes, including diffuse large B cell lymphoma (DLBCL), chronic lymphocytic leukemia (CLL), follicular lymphoma (FL), and multiple myeloma (MM), as well as HL associated with exposure to each of the specific organic dusts of prior interest. The following covariates were included in the regression models: age (continuous), gender, study center, education (categorized as <8, 9-12, >13 years), ever worked in a farm, ever exposed to solvents, and ever suffering from atopy, including any previous diagnosis of asthma, eczema, hay fever, or other allergies excluding drug allergies. We also ran regression models with ever occupational exposure to pesticides as a covariate instead of farm work. Consistently with previous papers, we included age, gender, the two variables used for frequency matching controls to cases, and study center as covariates in the regression models to account for the varying proportion of refusals in the participating centers (22), and the varying distribution by age and gender of the specific lymphoma subtypes. In the analyses for this study, we considered farm work, and solvents as possible confounders, being occupational risk factors for several lymphoma subtypes (22, 23), and possibly associated with exposure to one or more of the six organic dusts object of this report. Occupational experts supported by agronomists assessed exposure to pesticides in the same dataset. We extracted the information from previous work (24), and used it as a covariate instead of farm work, to better characterize agricultural confounders.

To maximize the potential for detecting what are presumably weak associations, we excluded all subjects who had

ever been exposed to any organic dust from the unexposed cases and controls, so as to have the same unexposed reference when investigating each specific organic dust. After excluding 871 subjects exposed to unspecified organic dust and 89 subjects who did not have any job entry in the work history, 1853 cases and 1997 controls remained available for inclusion in the analysis. We therefore retained as exposed 1112 subjects (551 cases and 561 controls) who had ever been exposed to one or more of the specific organic dusts we considered, and 2738 subjects (1302 cases and 1436 controls) who had never been exposed to the specific organic dusts of interest or any unspecified organic dust. We conducted further analyses by excluding study subjects who had ever been exposed to solvents and subjects who ever worked in a farm or had ever been exposed to pesticides, alternatively, and by type of controls, whether hospital controls or population controls.

We calculated the Wald test for trend with four exposure metrics - intensity, frequency, duration of exposure, and cumulative exposure - after linear transformation of all the covariates in the regression model, and we set the two-sided statistical threshold to reject the null hypothesis at $P < 0.05$. In the analysis, we did not use the confidence metric, as the large majority of study subjects were in the high confidence category (table 1), and the proportion of those classified with medium or high confidence ranged 95.1-100% across the specific organic dusts. The reciprocal independence between the categorical metrics of frequency, intensity and duration of exposure was previously assessed (25), which provided the conditions to apply the Fisher method for combined probability testing to calculate the chance probability associated with a positive trend observed with these three independent tests bearing upon the same overall hypothesis (26). We used the Cochran's Q test to detect heterogeneity in risk across study centers and across subtypes (26). All the analyses were conducted using SPSS® version 16.0 (IBM, Armonk, NY, USA).

Results

Table 1 shows the distribution of selected variables in the study population. There were no substantial differences by case-control status in the core variables. Also, the proportion of ever exposed to the organic dusts did not vary by case-control status. Among the exposed, subjects in the top level of confidence of exposure were the large majority, ranging 67-94% by type of dust and case-control status. When considering only subjects with high confidence of exposure, being ever exposed to synthetic textile dust, were more prevalent among the cases ($P=0.055$). There was no difference between cases and controls by having ever been working in a farm, or exposed to pesticides or solvents, known risk factors for lymphoma ($P=0.729$, $P=0.431$, $P=0.450$, respectively). History of atopy did not vary by case-control status (table 1). There was no substantial overlap between exposure to organic dust and exposure to the other known occupational risk factors for lymphoma, namely solvents, and pesticides (data not shown). Risk of DLBCL was elevated in relation to ever exposure to textile dust [odds ratio (OR) 1.4, 95% confidence interval (CI) 1.00-1.98], and risk of FL was elevated in relation to ever exposure to leather dust (OR=2.1, 95% CI 1.01-4.20) (table 2). However, we did not detect an upward trend in risk of either subtype by increasing cumulative exposure level ($P=0.097$ and $P=0.267$, respectively) (table 2).

With regard to the individual metrics of exposure to textile dust, DLBCL risk did not show an upward trend by intensity, frequency, or duration of exposure (supplementary material, www.sjweh.fi/show_abstract.php?abstract_id=3925, table S2d), nor did risk vary by type of textile dust, whether from natural or synthetic textiles (supplementary tables S2e-2f). There was no association between textile dust exposure and risk of lymphoma overall, B-cell lymphoma, nor any of the other major lymphoma subtypes we could analyze. FL risk did not increase by intensity ($P=0.187$), frequency ($P=0.063$), or duration of exposure (Wald test for trend: $P=0.210$) (supplementary table S2h) to leather dust. The Fisher method for combined probability testing resulted in a chance probability of an upward trend in FL risk with these three metrics of $P=0.062$.

Neither lymphoma (any subtype), nor B cell lymphoma, nor any of the other lymphoma subtypes showed increased risks suggestive of an association with exposure to leather dust or wood dust. Risks were all consistently inverse for ever exposure and cumulative exposure to flour dust, although for none it was possible to exclude chance as an explanation (supplementary tables S2a-c and 2g). Results did not change when replacing farm work with ever exposure to pesticides in the regression model (data not shown).

When excluding subjects ever exposed to solvents and subjects who had ever been working in a farm (table 3), risk

of lymphoma (any subtype), and particularly B-cell lymphoma (accounting for 77% of all lymphoma in this analysis) was increased in association with ever exposure to leather dust (B-cell lymphoma: OR 2.2, 95% CI 1.00-4.78). However, we did not observe an upward trend with increasing level of cumulative exposure ($P=0.096$), nor by frequency, intensity or duration of exposure, although the Fisher test for combined probabilities was of borderline significance ($P=0.050$). B-cell lymphoma subtypes contributing to the association included FL (OR 2.8, 95% CI 0.73-10.9; P for trend=0.429), and multiple myeloma (OR 2.4, 95% CI 0.61-9.71; P for trend=0.079), both represented by a number of cases too small for a profitable more in depth investigation of the association. Also, risk of HL showed a two-fold increase in risk (OR 2.0, 95% CI 0.95-4.30) and an upward trend with cumulative exposure to textile dust (Wald test for trend: $P=0.023$). Results were similar for exposure to natural (OR 2.0, 95% CI 0.90-4.44, Wald test for trend: $P=0.045$) and to synthetic textile dust (OR 1.6, 95% CI 0.63-4.02, Wald test for trend: $P=0.197$). A sensitivity analysis conducted by excluding one study center at a time confirmed the excess risk ranging 1.8-3.0 (supplementary table S3). We did not detect heterogeneity in risk across study centers (Cochran's $Q=3.23$, $DF=5$, $P=0.665$), nor across lymphoma subtypes (Cochran's $Q=6.01$, $DF=4$, $P=0.074$). Risk of HL increased consistently by duration ($P=0.092$), intensity ($P=0.047$), and frequency ($P=0.032$) of exposure to textile dust (table 4). The Fisher method for combined probability testing provided some evidence that all null hypotheses associated with the individual tests of an upward trend in risk of HL could be reasonably rejected ($P=0.0068$) (table 4). Notably, such excess risk was observed among subjects aged <31 years, the median age of HL cases, but not among subjects aged >31 . This finding was consistent over the whole study population (age <30 , OR 3.2, 95% CI 0.62-16.1; age >31 , OR 0.5, 95% CI 0.25-0.96), and in the subgroup of the unexposed to solvents and/or farm work (age <30 , OR 4.3, 95% CI 0.56-32.9; age >31 , OR 0.7, 95% CI 0.38-1.27) (data not shown).

Excluding from the analysis subjects ever exposed to solvents and subjects who had ever been working in a farm did not support the association between exposure to textile dust and risk of DLBCL. Results after the exclusions did not change in respect to the fully adjusted regression models for any of the lymphoma groups and subtypes we analyzed in relation to exposure to wood dust and flour dust (table 3)

Again, results did not change when excluding subjects ever exposed to pesticides instead of farm work (data not shown).

Discussion

Our results provide tentative evidence of an increased risk of some lymphoma subtypes associated with exposure to specific organic dusts. There was an increase in risk of FL among subjects ever exposed to leather dust but no exposure-response trend. The association between exposure to textile dust and risk of DLBCL was only observed with hospital controls (supplementary table S1); it was similar, though weakened because of smaller numbers, after excluding subjects exposed to solvents and those who ever worked in a farm. In addition, it did not increase with any of exposure metrics either before (Fisher test: $P=0.101$) (supplementary table S2d) or after (data not shown) exclusions.

After excluding farm workers and subjects exposed to solvents from the analysis, results were inconclusive for an association between risk of B-cell lymphoma and exposure to leather dust, while the number of cases was too small to allow further analysis on FL risk and MM risk. Risk of HL emerged in relation to exposure to textile dust (OR 2.0, 95% CI 0.90-4.44), with consistently significant upward trends by the four exposure metrics we used in this study. Several previous studies reported an excess risk of non-Hodgkin lymphoma among leather workers (27-29) and specifically FL (30); leather dust was among the suspected agents. However, a large multicenter study did not confirm the association (31). Our results support the only previous report of an association between risk of Hodgkin lymphoma and fabric dust in a large Canadian case-control study (32). On the other hand, our results are not consistent with previous publications (6, 9) suggesting that exposure to wood dust might contribute to increasing risk of some mature B-cell lymphoma subtypes, such as CLL and MM.

The International Agency for Research on Cancer (IARC) Monograph N. 100C confirmed the classification of wood dust and leather dust as group 1 human carcinogens, based mainly on the evidence for nasal cavity and nasopharyngeal cancer (33, 34). According to the IARC evaluation, the overall epidemiological findings would not

provide evidence of an association of wood dust and leather dust with cancer of other sites. Exposures in the textile industry, including cotton, wool, flax and hemp dust, were considered in the IARC Monograph N. 48 (35), which concluded for limited evidence of an increase in risk of cancer of the nasal cavity among weavers (group 2B). Epidemiological findings were inconsistent for cancers other than the nasal cavity, including HL and NHL (35). Enzymes, proteins and additives in flour dust can cause non-allergic and allergic reactions, such as baker's asthma, among exposed workers (36). On the other hand, an excess risk of head and neck cancer was described among male, but not female, workers exposed to flour dust (37); also, exposure to flour dust was included among the high molecular weight allergens that were inversely related to risk of lymphoma (16, 17). We considered atopy as a possible confounder; however, in our multivariate analysis, having ever suffered from an atopic condition did not affect risk of lymphoma; and - for none of the inverse associations between exposure to flour dust and risk of lymphoma and its subtypes - was it possible to rule out chance as the determinant.

The organic dust definition includes a vast array of different agents, of diverse origin, with different physiochemical properties. Therefore, as we had a more precise definition of organic dust exposure, we refrained from using the generic category as the exposure variable. However, exposures in workplaces where organic dusts occur can be quite diverse: various types of dust may mix up with a range of different chemicals in wood preserving, in synthetic and natural textile fabricating from vegetal or animal fibers, and in leather curing and tanning. Besides, fungal and bacterial contaminants would develop in conditions of elevated moisture and temperature; and exposure to endotoxin, a component of the outer membrane of gram-negative bacteria, can also occur (38). Therefore, the question is whether the responsible agent would be a component of the organic dusts themselves, or other associated exposures. For instance, exposure to endotoxin originates a strong inflammatory response in atopic subjects accompanied by secretion of proinflammatory cytokines, including tumor necrosis factor alpha (TNF- α) (38). The hypothesis of a role of endotoxin exposure in the etiology of some lymphoma arises from the observation that TNF- α polymorphisms, resulting in TNF- α over-expression, are associated with an increase in DLBCL risk (39). However, household exposure to endotoxin did not show an association with NHL risk (40).

We adjusted our analysis for concurrent exposure to other known occupational causes of lymphoma, such as solvents, farm work, and pesticides, and we designed the unexposed reference by excluding subjects ever exposed to undefined organic dust, which would have allowed the effect of the specific organic dusts we focused on to emerge, if any existed. Also, we conducted analyses by excluding farm workers and subjects exposed to solvents, known to be at risk for lymphoma; and by excluding one study center at the time. Positive findings emerged after excluding from the analysis farm workers and subjects exposed to solvents; overlapping was marginal between both farm work and solvents on one side, and textile and leather dust on the other side, respectively, with the proportion of concurrent exposures ranging 6-14%, and it was highest for solvents and textiles, among DLBCL cases (17%) in respect to the controls (14%). We therefore consider that the apparent association between DLBCL risk and exposure to textile dust was due to bias from the imbalance in the distribution of coexposure to solvents and textile dust by case-control status, not completely adjusted for in the multivariate regression analysis. On the other hand, the opposite might have happened in the distribution of co-exposure to solvents and textile dust between HL cases (8%) and the controls (14%), suggesting a bias in the opposite direction, again not completely adjusted for with the multivariate regression analysis. However, we cannot exclude chance as the explanation.

Limitations in interpreting our results include the small size of the study population in the analysis by lymphoma subtypes, which contributed to instability of the risk estimates associated with the categorical exposure metrics we used. Also, we made multiple comparisons; as a consequence, the few positive associations we observed might have arisen simply by chance. As expected, the response rate was lower among the population controls. We have no evidence of selection bias, as there was no significant difference between the two types of controls for the selected confounding variables. However, positive findings appeared mostly in the analyses with hospital controls (supplementary table S1).

Our study has also some strengths as the diagnosis was histologically verified for all the cases, and - instead of relying on self-reported exposures - expert industrial hygienists conducted the exposure assessment blinded to the

case/control status of study subjects. The residual misclassification was likely to have been non-differential, and therefore likely to have impaired our ability to detect significant associations and exposure-response trends. In conclusion, our analysis of a large European data set tentatively suggests that exposure to textile dust might contribute to increase risk of HL. Although difficult to interpret because of the small number of cases, our findings seem to suggest that subjects exposed to textile dust at younger age might be at higher risk of HL. Further research is warranted to clear up the interpretative doubts raised by the limitations in our study and to disentangle the effects of presumably protective conditions, such as atopy, and the possible carcinogenic action of specific organic dusts with due consideration of the confounding role of several other known occupational carcinogens in the etiology of lymphoma subtypes.

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The authors declare no financial relationships, affiliation with, or involvement in an organization with a direct financial interest in the matters discussed in this paper.

Protection of research participants

Following the Helsinki protocol for studies involving human subjects, all study subjects provided written consent before participation, in which they acknowledged that their identity could not be identified via the papers and that samples would have been fully anonymized.

Local Ethics Committees approved the study in each of the six study centers.

Sidebar

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DETAILS

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The impact of a meal, snack, or not eating during the night shift on simulated driving performance post-shift

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ABSTRACT (ENGLISH)

Objective The commute home following a night shift is associated with an increased risk for accidents. This study investigated the relationship between food intake during the night shift and simulated driving performance post-shift. **Methods** Healthy non-shift working males (N=23) and females (N=16), aged 18-39 years (mean 24.5, standard deviation 5.0, years) participated in a seven-day laboratory study and underwent four simulated night shifts. Participants were randomly allocated to one of three conditions: meal at night (N=12; 7 males), snack at night (N=13; 7 males) or no eating at night (N=14; 9 males). During the night shift at 00:30 hours, participants either ate a large meal (meal at night condition), a snack (snack at night condition), or did not eat during the night shift (no eating at night condition). During the second simulated night shift, participants performed a 40-minute York driving simulation at 20:00, 22:30, 01:30, 04:00, and 07:30 hours (similar time to a commute from work). **Results** The effects of eating condition, drive time, and time-on-task, on driving performance were examined using mixed model analyses. Significant condition[^]time interactions were found, where at 07:30 hours, those in the meal at night condition displayed significant increases in time spent outside of the safe zone (percentage of time spent outside 10 km/hour of the speed limit and 0.8 meters of the lane center; P<0.05), and greater lane and speed variability (both P<0.01) compared to the snack and no eating conditions. There were no differences between the snack and no eating conditions. **Conclusion** Driver safety during the simulated commute home is greater following the night shift if a snack, rather than a meal, is consumed during the shift.

FULL TEXT

Headnote

Objective The commute home following a night shift is associated with an increased risk for accidents. This study investigated the relationship between food intake during the night shift and simulated driving performance post-shift.

Methods Healthy non-shift working males (N=23) and females (N=16), aged 18-39 years (mean 24.5, standard deviation 5.0, years) participated in a seven-day laboratory study and underwent four simulated night shifts.

Participants were randomly allocated to one of three conditions: meal at night (N=12; 7 males), snack at night (N=13; 7 males) or no eating at night (N=14; 9 males). During the night shift at 00:30 hours, participants either ate a large meal (meal at night condition), a snack (snack at night condition), or did not eat during the night shift (no eating at night condition). During the second simulated night shift, participants performed a 40-minute York driving simulation at 20:00, 22:30, 01:30, 04:00, and 07:30 hours (similar time to a commute from work).

Results The effects of eating condition, drive time, and time-on-task, on driving performance were examined using mixed model analyses. Significant condition[^]time interactions were found, where at 07:30 hours, those in the meal at night condition displayed significant increases in time spent outside of the safe zone (percentage of time spent outside 10 km/hour of the speed limit and 0.8 meters of the lane center; $P < 0.05$), and greater lane and speed variability (both $P < 0.01$) compared to the snack and no eating conditions. There were no differences between the snack and no eating conditions.

Conclusion Driver safety during the simulated commute home is greater following the night shift if a snack, rather than a meal, is consumed during the shift.

Key terms cognition; meal pattern; meal timing; nocturnal eating; shift work.

The commute home following a night shift is a time of great risk for driver safety (1, 2), with shift workers frequently reporting falling asleep at the wheel and experiencing near-misses (3, 4). For shift workers, this may be due to the increase in homeostatic sleep pressure after being awake for a long period of time overnight (5), which may be exacerbated by the length of the commute (6) and an increase in morning road users at the time of the post-shift commute (7).

Several strategies are commonly utilized to improve alertness for the commute home, including caffeine, playing loud music, napping, bright light, and stopping for breaks (7-11). While these strategies may subjectively improve alertness, empirical evidence does not support the use of all of these countermeasures for improving driving performance (9, 12). As the need for shiftwork increases, so too does the need to identify new countermeasures and strategies to reduce the impacts of fatigue on the commute home (8, 13). One way of identifying new countermeasures is to consult the strategies and behaviors that shift workers already report on-shift. Altered eating behaviors during the night compared to day shift is one such behavior that that is common amongst shift workers (14) and could have implications for performance on-shift.

Our research has previously shown that restricting the amount of food consumed during a simulated night shift improved driving performance during the night and reduced subjective sleepiness (15). It is unknown if this impairment would extend to 07:30 hours when workers are typically driving home and whether reducing or limiting food during the night could improve driving performance. This study investigated the impact of eating a meal, snack, or not eating during the night shift on driving performance during a simulated post-night shift commute home.

Methods

Study design

The study was a seven-day experimental, three-condition, between-group design conducted in the windowless, sound attenuated, and time-isolated Sleep and Chronobiology Laboratory at the University of South Australia (UniSA). All participants gave written informed consent and the UniSA Research Ethics Committee approved the study (#0000033621), which was registered with the Australian New Zealand Clinical Trials Registry (ANZCTR12615001107516). This manuscript reports secondary outcome data from a larger study and additional measures have been published elsewhere (15, 16).

Participants

Healthy, non-shift working participants were recruited from the general population via flyers and website postings. All participants were 18-45 years, within a body mass index (BMI) range of 18.5-27kg/m², non-smokers, had no chronic medical illnesses, were not shift workers, and had habitual sleep patterns that included going to bed between 21:00-00:00 hours and waking between 06:00-09:00 hours [for specific exclusion criteria, please see (15, 16)].

Protocol design

Ambient temperature was controlled [mean 22, standard deviation (SD) 1 °C] and light intensity was <100 lux at eye-level during wake and <0.03 lux during sleep. The protocol of the seven-day simulated shift work study has been described in detail elsewhere (16), and this study describes results from night shift 2 of the larger study. Figure 1 shows the protocol for night shift 2 (day 3). This was the only morning that a 07:30 hour simulated drive was included as an exploratory measure of driving performance during the commute home, without increased sleep pressure.

During the previous night shift (night shift 1), participants experienced 28 hours of extended wake by the end of the night shift to simulate the conditions commonly reported by shift workers (17). Participants completed simulated night shifts from 20:00-06:00 hours, with seven-hour daytime sleep opportunities from 10:00-17:00 hours. During night shift 2, participants in all groups underwent driving performance assessments at 20:00, 22:30, 01:30, 04:00, and 07:30 hours. During the night shift, participants also had free time to read, watch movies, play board games, and interact with other participants and laboratory staff, however no vigorous activity was allowed.

To ensure there were no differences between conditions for sleep quality and quantity, sleep was objectively recorded using polysomnography for the baseline sleep, daytime sleep after night shift 3, and the recovery sleep. Recording used Compumedics Graef EEG amplifier and acquisition software (Compumedics Ltd. Melbourne, Australia). Standard polysomnography (PSG) electrode placements were used (F3, F4, C3, C4, O1 and O2 sites), referenced to a contralateral mastoid (M1, M2). Polysomnography (PSG) data were analyzed using Rechtschaffen & Kales sleep stage scoring criteria (18). Additionally, participants wore activity monitors (Actiwatch 2, Philips Respironics Inc, Bend, OR, USA) during each sleep period.

Eating conditions

Participants were randomized at the run-level (in groups of 3-4) to one of three eating conditions: meal at night (MN), snack at night (SN), no eating at night (NE) (table 1). Estimated energy requirement (EER) was calculated for each participant and daily 24-hour macronutrient content was consistent with the average Australian diet and standardized to approximately 40% carbohydrate, 33% fat, 17% protein, and 23g of fibre per 24 hours (Australian Bureau of Statistics 1997). For an example meal plan, see Gupta et al (16).

During each night shift of the simulated shiftwork protocol, participants in the MN condition consumed meals at 19:00 (dinner), 00:30 (lunch-type meal) and 06:15-07:00 (breakfast) hours. These were 40%, 30% and 30% of 24-hour energy intake, respectively. The time of breakfast ranged from 06:15-07:00 hours because of metabolic testing as part of the larger study. The SN condition consumed meals and snacks at 19:00 (dinner), 00:30 (snack), 06:15-07:00 (breakfast) and 17:00 (snack) hours. These were 40%, 10%, 30% and 20% of 24-hour energy intake respectively. The NE condition consumed meals and snacks at 19:00 (dinner), 06:15-07:00 (breakfast), 09:30 (snack) and 17:00 (snack) hours. These were 40%, 30%, 10% and 20% of 24-hour energy intake respectively. Participants had 45 minutes to consume dinner, 30 minutes to consume the lunch-type meal and snacks, and 15 minutes to consume breakfast. At 00:30 hours, the NE condition were able to continue with free time activities such as watching tv, and no vigorous activity was allowed.

Driving performance

Driving performance was assessed using a 40-minute York highway driving simulator task (York Computer Technologies, Kingston, ON, for further details please see Gupta et al (15)). Variables used for analysis were time spent in the safe zone (SZ) (percentage of time spent within 10 km/h of the speed limit and within 0.8 m of the lane center), speed variability (SV, km/h), and lane variability (LV, m).

Statistical analyses

Analyses were conducted with the researchers blinded to condition. Analyses were conducted using SPSS 22.00 (IBM Corp, Armonk, NY, USA). Statistical significance was defined as $P < 0.05$. A final sample of $N = 39$ (MN: $N = 12$;

SN: N=13; and NE: N=14) was analyzed, with five participants excluded due to a failure to comply with driving simulator instructions. Analyses of time spent outside of the SZ, SV, and LV were conducted using mixed-effects ANOVA with fixed effects of condition (MN, SN or NE), time of drive (20:00, 22:30, 01:30, 04:00, and 07:30 hours), time-on-task (40-minute drive split into eight 5-minute bins), all 2- and 3-way interaction effects involving condition, and a random effect of participant ID.

Results

The sample had a mean age of 24.5 (SD 5.0) years, mean BMI of 23.4 (SD 2.3) kg/m², and a mean 24-hour energy requirement of 9406.2 (SD 927.1) kJ. There were no significant differences between conditions for age, BMI, or average 24-hour energy intake (16). As previously published, there were no differences between groups for sleep quality or quantity (15, 16).

The two-way interaction between eating condition and performance time was significant for SZ [F(8, 934.01)=17.91, P<0.001], SF [F(8, 934.01)=8.72, P<0.001], and LV [F(8, 934.00)=13.58, P<0.001]. Post hoc analyses revealed no differences between the 20:00 and 22:30-hour drives, however driving performance worsened across the simulated night shift, with greater impairments seen at 01:30, 04:00, and 07:30 hours in the meal compared to the snack and no eating conditions (figure 2). No differences were found between the snack and the no eating condition at 07:30 hours.

The two-way interaction between condition and time-on-task was not significant for SZ [F(8, 934.01)=17.91, P=0.988], SV [F(8, 934.01)=8.72, P<0.001], or LV [F(8, 934.00)=13.58, P<0.001]. The three-way interaction between condition, performance time and time-on-task was not significant for SZ [F(56, 934.00)=0.45, P=1.00], SV [F(56, 934.00)=0.38, P=1.00], or LV [F(56, 934.00)=0.35, P=1.00].

The main effect of drive was significant for SZ [F(4, 934.01)=151.43, P<0.001], SV [F(4, 934.01)=95.51, P<0.001], and LV [F(4, 934.00)=177.80, P<0.001], and the main effect of time-on-task was significant for SZ [F(7, 934.00)=13.45, P<0.001], SV [F(7, 934.00)=2.55, P=0.01], and LV [F(7, 934.01)=12.03, P<0.001]. The main effect of condition was significant for SZ [F(2, 24.00)=3.62, P=0.04], but not significant for SV [F(2, 24.00)=3.11, P=0.06] or LV [F(2, 24.00)=3.26, P=0.06].

Discussion

This study investigated the post-prandial impact on driving performance at the end of a simulated night shift, following consumption of a meal. Driving performance followed the expected pattern of impairment, worsening across the night from 01:30-07:30 hours and with increasing time-on-task, regardless of eating condition (1, 19). This was exacerbated for those who consumed the meal compared to the snack or ate no food during the night. Those who consumed the meal were still significantly more impaired during the commute home than those who consumed a snack and those who did not eat during the night. This provides preliminary evidence that reducing the amount of food consumed during the night shift may be a modifiable factor to improve safety on the commute home. Additionally, we have previously found that while those who consumed a snack during the night shift did not report feeling full across the night shift, they did not report a greater desire to eat than those who consumed the meal (16). This suggests that the recommendation to consume a snack during the night shift may be a feasible option as workers may be satisfied with this amount of food.

The difference in driving performance between conditions may be influenced by subjective sleepiness. Previously published findings from this study have shown increased subjective sleepiness across the night shift, with greater sleepiness at 04:00 compared to 20:00 hours (15). Further, the greatest increase in subjective sleepiness was reported by those who had consumed the meal during the night shift compared to the snack (15). While subjective sleepiness was not recorded immediately prior to the commute home, a reason for the driving impairment during the commute among those who consumed the meal may be greater subjective sleepiness as a result of the meal at 00:30 hours. In addition to increased sleepiness, there are several suggested mechanisms for the post-prandial impairment found after eating a large meal during the biological night. Reduced glucose tolerance (20) and reduced rates of gastric emptying (21) at night may cause the meal to be a greater challenge to the digestive system compared to snacking or not eating. Further, performing cognitive tasks at night requires a redistribution of blood

flow (22), and, given that brain resources are also required to digest the meal, these competing demands may lead to cognitive impairment.

In contrast to eating during the night, the breakfast meal did not further impact performance beyond the increasing pattern of impairment in which the data were already trending. This study is limited in that we do not have a 'no breakfast' comparison in order to specifically quantify the impact of the breakfast, and that the between-subjects nature of the experimental groups (despite random assignment) leaves an open question as to the potential contribution of individual differences to the observed patterns. Given that the breakfast was the same size as the meal at night, the minimal impact of the breakfast on driving performance may further reinforce the importance of considering the timing of meals. That is, it could be (very tentatively) argued from these data that eating a meal of the same size during the biological night (at 00:30 hour) may have a larger impact on the post-shift commute than eating in the morning before the drive (06:15-07:00 hours).

Overall, results support the value of researching the possibility of changing meal size and timing as a countermeasure for night shift workers, however there are limitations to these results that must be considered. While the controlled laboratory environment was a necessary first step to investigate post-prandial effects on performance, the controlled lighting, temperature, time cues, and sound may have increased sleep quality and quantity in comparison to real-world shift workers who must contend with external factors such as environmental noise and outside light (17). This reduced sleep may worsen cognitive performance during the commute home, due to increasing sleep pressure (17) and may influence the post-prandial response (23). A further limitation to consider is that the participants in the study were young, healthy, and had no shift working experience. This does limit generalizability to shiftwork populations, which may include those with a higher risk of conditions that may worsen the post-prandial response, such as health issues such as obesity and metabolic disorders (23, 24). Further, this exploratory analysis used a low fidelity driving simulator, with minimal traffic and a speed limit of 100 km/hour. While this was chosen as a measure of sustained attention in monotonous conditions, shift workers in the real-world may be faced with factors such as reduced visibility and increased traffic during the commute home (25). Additionally, potential between-group differences in uncontrolled variables could potentially help to explain some of the findings. However, given randomized group allocation and no evidence of any relevant differences between groups (15), this appears unlikely.

The next steps include systematic investigation of different eating patterns to quantify the potential impacts of all pre-commute eating occasions (especially breakfast), varying macronutrient content, combinations of other countermeasures (eg, snack plus caffeine), and objective measures of alertness and sleepiness before and during the drive, as well as moving to field trials in shift working populations with different health profiles to our laboratory participants (24). A further suggestion for future investigation is the cumulative impact of food intake on post-prandial performance during the commute home across multiple night shifts. Although we did not find an impact on driving performance during the night shift after four consecutive night shifts (15), perhaps after an increased number of consecutive shifts with reduced sleep intake between shifts commonly reported for shift workers (17), we would see a cumulative effect.

The present study showed that under simulated conditions, a snack during the night shift is a better option for post-shift driving performance compared to larger amounts of food. Future research should continue to explore food intake during shift work as a potential fatigue countermeasure in real-life settings among shift working populations.

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Sidebar

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DETAILS

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Exposure to psychosocial work strain and changes in smoking behavior during pregnancy - a longitudinal study within the Danish National Birth Cohort

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[ProQuest document link](#)

ABSTRACT (ENGLISH)

Conclusions Psychosocial strain influenced the women's smoking behavior during pregnancy, especially in job types with low control.

ABSTRACT (ENGLISH)

Objective Knowledge of the relationship between psychosocial strain in the work environment and smoking during pregnancy is scarce. This study aimed to examine the association between psychosocial job strain and change in smoking behavior during pregnancy. Methods The cohort included 65 645 pregnancies from the Danish National Birth Cohort (1996-2002), where pregnant women were interviewed on job factors and lifestyle during the first and third trimesters. Smoking was categorized into non-, non-daily, and daily smoking at each interview. Psychosocial job strain was categorized into four groups based on the concept of Karasek's demand-control model: low strain (reference), passive, active and high strain. Associations between psychosocial strain and change in smoking status between the first and second interviews were analyzed by multinomial logistic regression, separately for each smoking category at first interview. Results Non-smoking women exposed to high strain work were more likely to become daily smokers [adjusted odds ratio (OR_{adj}) 1.41, (95% confidence interval (CI) 1.08-1.83)] compared to non-smoking women exposed to low strain work. Non-smoking women exposed to passive work were more likely to become both non-daily and daily smokers [OR_{adj} 1.59 (95% CI 1.21-2.08) and OR_{adj} 1.32 (95% CI 1.03-1.70), respectively]. Daily smoking women exposed to high strain work were less likely to decrease their smoking [OR[^] 0.57 (95% CI 0.32-0.99)] compared to daily smoking women exposed to low strain work.

FULL TEXT

Headnote

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Objective Knowledge of the relationship between psychosocial strain in the work environment and smoking during pregnancy is scarce. This study aimed to examine the association between psychosocial job strain and change in smoking behavior during pregnancy.

Methods The cohort included 65 645 pregnancies from the Danish National Birth Cohort (1996-2002), where pregnant women were interviewed on job factors and lifestyle during the first and third trimesters. Smoking was categorized into non-, non-daily, and daily smoking at each interview. Psychosocial job strain was categorized into four groups based on the concept of Karasek's demand-control model: low strain (reference), passive, active and high strain. Associations between psychosocial strain and change in smoking status between the first and second interviews were analyzed by multinomial logistic regression, separately for each smoking category at first interview. Results Non-smoking women exposed to high strain work were more likely to become daily smokers [adjusted odds ratio (OR_{adj}) 1.41, (95% confidence interval (CI) 1.08-1.83)] compared to non-smoking women exposed to low strain work. Non-smoking women exposed to passive work were more likely to become both non-daily and daily smokers [OR_{adj} 1.59 (95% CI 1.21-2.08) and OR_{adj} 1.32 (95% CI 1.03-1.70), respectively]. Daily smoking women exposed to high strain work were less likely to decrease their smoking [OR_{adj} 0.57 (95% CI 0.32-0.99)] compared to daily smoking women exposed to low strain work.

Conclusions Psychosocial strain influenced the women's smoking behavior during pregnancy, especially in job types with low control.

Key terms Denmark; job strain; pregnant population; psychosocial stress; smoking cessation.

It is well established that smoking during pregnancy is detrimental for perinatal health; yet smoking is still common among pregnant women in several countries (1). In Denmark, around 9% of all pregnant women smoke during early pregnancy and almost 7% continue throughout the pregnancy (2). To help women quit smoking during pregnancy it is important to understand which factors influence smoking behavior during pregnancy.

Studies among male and non-pregnant female smokers indicate that work conditions, such as stress, are associated with smoking intensity, probability of cessation and the risk of relapse (3-5). High psychosocial strain at work could contribute to continuous smoking in several ways. Smoking itself might represent a way of coping with high demands in the work situation; its stress-relieving properties are often stated as a reason for continued smoking (6, 7). Further, experience of high strain at work might leave little psychological room for undertaking another challenge such a smoking cessation (7).

A majority of women of reproductive age are occupationally active (76%, Denmark, 2015) (8) and spend a large part of their time at work, also during pregnancy (9). Earlier results from a non-pregnant population on the influence of psychosocial work strain might not be generalizable to a pregnant population. Pregnant women conceivably differ in their motivation to quit smoking compared to their non-pregnant counterparts (10, 11). At the same time they might face a different setting of stressors, and thus, pregnancy might not be seen as a possible time to cope with smoking cessation (7). Additionally, the societal pressure and focus on the need to quit smoking could actually make it harder to do so (11).

Earlier research examining work-related psychosocial strain has reported that high strain is associated with continued smoking during pregnancy, however, the studies are few (12-15), were done in small populations (13, 14), used a cross-sectional design (12), or did not distinguish work-related strain from other stressful life events (12-15). Lastly, none of the studies examined associations between work strain and smaller changes in smoking intensity, such as a reduction in the number of cigarettes smoked. The only two studies that explicitly investigated psychosocial job strain focused on the timeframe between conception and up until the end of the first trimester (14, 15). No studies have investigated potential associations after the first trimester. Studying maternal smoking behavior for this period of gestation is important as women who quit smoking before the third trimester show the same risk of low birth weight and preterm birth as women who never smoked during pregnancy (16-20).

In the present study, using a large, previously established pregnancy cohort - the Danish National Birth Cohort (DNBC), we aimed to investigate if psychosocial strain at work influenced smoking status between the first and the third trimester. We also investigated if the likelihood of change depended on the women being a non-, non-daily, or daily smoker in the first trimester. We hypothesized that women experiencing high psychosocial strain at work were more likely to continue smoking or to increase their level of smoking in comparison to women experiencing low strain at work.

Methods

Study population

The study population was the DNBC, a nation-wide, population-based cohort consisting of 101 042 pregnancies, enrolled in 1996-2002 (21). The pregnant women were recruited by their general practitioner at their first antenatal visit. In Denmark, this normally takes place during gestational weeks 6-12, and almost all pregnant women undergo maternal healthcare (22). Approximately 50% of the general practitioners participated, and about 60% of the invited pregnant women participated in the DNBC (21). To become a part of this cohort, the women should be pregnant, intend to carry the pregnancy to term, live in Denmark, and be able to participate in a telephone interview in Danish. Two interviews were conducted during pregnancy - at early (12-14 weeks) and late (30-32 weeks) pregnancy. The first interview included topics such as maternal health habits, medical problems, and medication as well as physical and psychosocial working environment. The second interview followed up many of these topics.

This study included data from both interviews in which a total of 82 646 women participated. For this study, the women should be pregnant at both interviews, be working, and have valid data on smoking behavior and psychosocial job strain exposure (N=67 408). Unemployed women were not included as the questionnaire only addressed demands and control at work. Women with missing data on any of the covariates included in the subsequent analyses were excluded. The final study population included 65 646 pregnancies, with complete information on all relevant variables.

Data was pseudo-anonymized before they were accessed via Statistics Denmark. Permissions to use and store data were obtained from the DNBC and the Danish Data Protection Agency. Danish legislation requires approval from the Ethical Committee only for use of human tissue; hence, no ethical approval was needed.

Outcome - change in smoking behavior during pregnancy

The main outcome of interest was change in smoking behavior between the first and the second interview. We additionally investigated change in smoking prior to the first interview. There were three questions on smoking behavior in the first interview: "Did you smoke at any time during your pregnancy?", "Are you smoking right now?", and "Have you smoked at any time during pregnancy, including very first time after conception?". In the second

interview, the questions were: "Have you been smoking since the last interview?" and "Are you smoking right now?". An affirmative answer to these questions led to a follow-up question where the participant was asked to quantify the number of cigarettes smoked and if the smoking was daily or non-daily. The information on number of cigarettes was not usable for this study due to the low quality of the data. Smoking during pregnancy was therefore categorized at both the first and second interviews as follows: (i) non-smoking, (ii) non-daily smoking, and (iii) daily smoking. For each of these smoking strata at the first interview, the women could either maintain their smoking level, decrease or increase their levels until the second interview.

Exposure - Psychosocial strain at work

The women's psychosocial working environment was estimated according to the concept of Karasek's demand-control model (23). Information on the demand and control dimensions of the model was extrapolated from the first interview in the DNBC based on the questions: "Do you have too many tasks at your work?" (denoting the demand dimension) and "Do you have the possibility to influence your work tasks and working conditions?" (denoting the control dimension). The questions could be answered with seldom, sometimes, and often. The questions were combined according to these responses into four categories of psychosocial strain: (i) low (low demands, high control), which served as the reference category, (ii) passive (low demands, low control), (iii) active (high demands, high control) and lastly (iv) high (high demands, low control) strain (23). Figure 1 depicts how the categorization was done according to the answers listed above.

Covariates

The following covariates were decided a priori and retrieved from the first DNBC interview: maternal age at conception (categorized in the models: <25, 25-29, 30-34, and >35 years), maternal body mass index (BMI) before pregnancy (<18.5, 18.5-<25, 25-<30, and >30 kg/m²), parity/number of previous children (0, 1 and >2), socio-economic position derived from self-reported job titles (high educational level, medium educational level, skilled work, unskilled work, student), exposure to second-hand smoke/partner smoking (no exposure, nondaily exposure, daily exposure), and exposure to passive smoking (in this case partner's smoking). We chose to include partner's smoking rather than cohabiting status as this was considered to have a larger influence on smoking habits.

Statistical analyses

The associations between psychosocial job strain and smoking behavior between the first and the second interview were explored using multinomial logistic regressions generating odds ratios (OR) and 95% confidence intervals (CI), to account for the three possible outcomes (no change, decrease or increase in smoking level). The three strata of smoking status at the first interview (nonsmoking, non-daily smoking and daily smoking) were analyzed separately, with no change in smoking habit considered the reference category. In all analyses, the different categories of psychosocial strain were compared to low strain. All analyses, including the crude estimates, were analyzed with a cluster term to account for dependency, since some of the women contributed with more than one pregnancy in the cohort (N=3483).

Initial models investigated job strain separately, after which we included the covariates described above.

To investigate the robustness of the results, we also performed the following subgroup analyses to investigate if patterns in change in smoking behavior differed between the following groups: (i) stratifying primiparous from multiparous women and (ii) stratifying socio-economic position into high/medium education and skilled/unskilled work (excluding students). Lastly, we also investigated the odds of quitting smoking at any time before the second interview, among the women having smoked at any time during pregnancy (including both the period prior to the first interview and between the first and second interviews). Conventional logistic regression analyses were used for these analyses as the women were only asked whether or not they had been smoking, without specification of the amount smoked. All analyses were carried out in Stata version 13.1 (StataCorp, College Station, TX, USA).

Results

There were 15 900 women (24.2%) stating that they had smoked during pregnancy prior to the first interview. The daily smoking prevalence was 13.6% and 13.9% at the first and second interview, respectively. Fewer women stated that they were non-daily smokers (1.5% and 1.4%, respectively). Thus, the rate of any pregnancy smoking (both

daily and non-daily) was reduced from 24.2% to 15.1% by the time of the first interview. Table 1 shows the baseline characteristics among the included women, stratified on smoking status at the first interview. Daily smokers were younger, had lower educational levels and were more often exposed to daily secondhand smoke by their partner, compared to non-smokers (table 1).

Table 2 shows changes in smoking status between the first and second interview. The percentage of women who changed their smoking behavior was highest among the non-daily smokers, where 76.2% changed their smoking behavior until the second interview compared to 2.0% and 9.2% among non-smokers and daily smokers, respectively.

For women reporting any smoking during pregnancy (also before the first interview), the crude and adjusted OR (ORadj) of quitting at any time before the second interview are shown in table 3. Compared to the reference category (low strain), women experiencing high strain were less likely to quit smoking [ORadj 0.87 (95% CI 0.78-0.98)].

Table 4 shows the crude and ORadj following multinomial logistic regression analyses performed separately for each of the three smoking strata at interview 1. Non-smoking women experiencing high strain were more likely to become daily smokers [ORadj 1.41 (95% CI 1.08-1.83)] compared to non-smoking women experiencing low strain; and non-smoking women in the passive group were more likely to become both non-daily and daily smokers [ORadj 1.59 (95% CI 1.21-2.08) and ORadj 1.32 (95% CI 1.03-1.70), respectively].

Among non-daily smoking women, there was no statistically significant association between psychosocial strain and change in smoking behavior, but there was a trend toward a lower OR for quitting smoking among women exposed to high strain work [ORadj 0.53 (95% CI 0.27-1.03)] compared to non-daily smoking women exposed to low strain. Women smoking daily at the first interview were less likely to decrease their smoking to non-daily smoking, if they were exposed to high psychosocial strain [ORadj 0.57 (95% CI 0.43-0.99)], compared to women in the low strain group. There were no associations between psychosocial strain and their likelihood to stop completely [ORadj 0.99 (95% CI 0.74-1.29)].

All estimates remained more or less unchanged after adjustment for potential confounders, except for non-smoking women experiencing passive work or high psychosocial strain, respectively, where point estimates were somewhat lower in the adjusted analyses (table 4).

The subgroup analyses did not reveal notable changes to the overall patterns described above, apart from widening of some of the confidence intervals due to smaller numbers of women (data not shown).

Discussion

In this large national birth cohort, the overall findings indicated that psychosocial strain at the workplace influenced smoking behavior during pregnancy, particularly among the women who experienced low levels of control at work (the passive and high strain categories). Women who did not smoke at the first interview were more likely to increase their level of smoking if they belonged to these two categories of psychosocial strain. High strain at work was furthermore linked to a lower propensity to reduce smoking if the women were daily smokers at the first interview. Our study additionally showed that most women who stopped smoking did so in the early part of pregnancy (the prevalence of any pregnancy smoking reduced from 24.2% to 15.1% before the first interview took place), which is in line with earlier findings (24).

The finding that many women increased their smoking during pregnancy was somewhat unexpected, although there are qualitative findings that support this pattern (7). Compared to the other smoking strata, nondaily smoking women had the largest proportions of change in smoking behavior in either direction (32.9% decreased and 43.4% increased their smoking). This was, however, not statistically significantly related to psychosocial job strain in our analyses, possibly due to the small numbers in this group. It could be speculated that non-daily smoking women are more prone to changing of smoking behavior before pregnancy, and therefore are more likely to change behavior also during pregnancy. The non-daily smokers could also reflect women who smoked before pregnancy who did not manage to quit completely and, thus, resumed smoking during pregnancy. From a clinical perspective, this group, even though it is small, might be an important target group for additional support during pregnancy. Indeed,

increasing worry about the upcoming birth has been reported as a cause of increased smoking in the later stages of pregnancy (7). Also, low levels of support during pregnancy has been shown to be linked with a higher risk for continued smoking, where a Swedish study found instrumental support (ie, access to advice, information and practical service) to be the most important for smoking cessation (14). Similarly, the importance of adequate maternal healthcare for smoking cessation has also been highlighted in a recent review (25). Interestingly, job support was not related to the risk of persistent smoking in the Swedish study cited above (14).

Among the women who reported not smoking at the first interview, 2% increased their level of smoking. This proportion was on par with the proportion of daily smokers who managed to quit (1.9%) from the first to the second interview. Unfortunately, we did not have information on smoking before pregnancy in the DNBC. We hypothesize that the non-smoking women who increased their smoking levels during pregnancy are likely women who had stopped smoking before or very early in pregnancy and then resumed smoking, rather than never-smokers beginning to smoke during pregnancy, even though the latter scenario is a possibility: an American study found that 3.3% of women who had never smoked started smoking when they were pregnant (26). The study, however, was performed in a specific population of low-income urban women with low educational attainment. We could not find any reports on incident pregnancy smoking in a more representative sample or a Nordic population.

Pregnancy is often viewed as a window of opportunity for smoking cessation. Nonetheless, quitting rates vary considerably. The majority of the published studies show that more than half of the women who smoked during pregnancy failed to quit (as reviewed by Schneider et al) (27). Generally, the scientific discussion considers complete quitting and potential smoking relapse postpartum (28), but the present study suggests that the potential risk for increased smoking or relapse during pregnancy should be addressed further.

One explanation for this pattern might be that smoking is used as a coping strategy in the handling of increased demands (6, 7). The burden to quit then becomes two-fold: not only does the woman lose a way of coping with stress, but quitting would then add another demand to an already strained situation. Paradoxically, the pressure to stop smoking could then actually reinforce that same habit as smoking is used to cope also with this demand (11, 12).

The finding in our study, that women exposed to high strain are less likely to quit or decrease their smoking, confirms prior research but in a much larger population (14, 15). Previous studies of job strain in relation to smoking during pregnancy are few and most were performed in small populations (12-15). Additionally, these studies only considered major changes in smoking behavior such as odds of persistent smoking (14) quitters vs non-quitters (15) and abstinence fraction, i.e. the percentage of non-smokers among pre-pregnancy smokers (12). No previous studies have considered nondaily smoking in their analyses. Exposure classifications varied between studies: two studies used the psychosocial strain model according to Karasek with multi-item measurements denoting the two dimensions (14, 15). A Norwegian study evaluated psychosocial exposure based on several independent questions regarding workload and opportunities to limit it (12). Lastly, an American study applied a composite measure of any type of stress (emotional, financial, work-related) (13).

The present study adds new information on the influence of psychosocial job strain on smoking behavior during pregnancy. We had information on smoking behavior during the third trimester, which is important in order to investigate whether any cessation or reduction in smoking was maintained. We were, furthermore, able to investigate if the likelihood of change depended on the women's smoking level early in pregnancy. Other strengths of the present study include the longitudinal design of the study, the large population and good generalizability of the results as the women worked in an array of different trades, had different educational levels and demographic characteristics.

The present study also has several limitations. First, all data are based on self-report. Concerns have been risen regarding the validity of self-reported data on smoking during pregnancy, considering that there is a stigma surrounding smoking in this period. This might lead women to underreport their true smoking status. Nonetheless, a study from Sweden comparing self-reported smoking to a biomarker of nicotine exposure indicated that women tend to report their smoking behavior truthfully (29). Thus, we believe that using self-reported data on smoking status is

justified.

The job strain model could constitute a weakness of the study, as only one question was used to reflect each of the demand and control dimensions, respectively. We are not aware of any studies that have validated the specific two questions used in our study to capture psychosocial job strain. Potentially, use of different questions might have categorized the women differently, which could have changed the results. On the other hand, a study validating the use of two single-item measures of stress concluded that it had similar validity as the use of multi-item measures (30). We also assumed that job exposure remained constant throughout pregnancy, since data on working conditions were only present in the first interview. These conditions could have changed, particularly among those exposed to high strain, if preventive measures or work adjustments were implemented.

The complex interplay between work-related strain and psychosocial strain in private life also ought to be considered. There were no questions in the first DNBC interview specifically related to stressors in private life; hence, this could not be accounted for. However, an Australian study investigating the contribution of stress at work and outside work relative to development of common mental disorders found that the effect of work-stressors could not be explained by co-exposure to stressors outside work (31). Also, according to the Danish national questionnaire survey 'The Danish Work Environment Cohort Study', among people who report suffering from stress, a much higher frequency report that the stress is work-related rather than related to private life (32).

Another potential limitation is that the data was collected more than 20 years ago. The rate of pregnancy smoking has since decreased from around 23% in 2000 to 9% in 2017 (2). It is more difficult to evaluate changes in the psychosocial work environment. Overall, including stress both at and outside of work, stress seems to have increased (33, 34). However, according to 'the Danish Work Environment Cohort Study', indicators of neither demand nor control has changed between 2010 to 2018, indicating that job strain have been relatively constant (32). In summary, since pregnancy smoking is still prevalent, and psychosocial work strain at best levels with the period of data collection, we believe the findings from the present study are still likely to have bearings on today's working population, especially since there are signs of a rise in smoking in younger age groups (35).

The benefits of smoking cessation during pregnancy have been established multiple times (16-19). Generally, women who quit smoking during the first trimester have the same risk of giving birth pre-term or to a child with low birth weight as a non-smoking woman (16, 20). They also reduce their risk of placenta previa/ablatio, stillbirth and neonatal mortality otherwise associated with smoking during pregnancy (24).

In conclusion, this study indicates that exposure to psychosocial strain at work is associated with a decreased likelihood of reducing smoking during pregnancy, in particular for work types with low control. Further studies with more detailed classification of smoking habits and work task exposures during pregnancy are needed to elucidate the findings. Intervention studies would further contribute to determine if there are benefits, in terms of change in smoking habits, to be gained by an adjustment of the psychosocial work environment for pregnant women.

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Competing interests

The authors declare that they have no competing interests to disclose. All authors have had full access to the data

presented in the study and take responsibility for the integrity of the data and accuracy of the data analysis.

Sidebar

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DETAILS

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Occupational exposure to noise in relation to pregnancy-related hypertensive disorders and diabetes

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ABSTRACT (ENGLISH)

Objectives Exposure to environmental noise has been associated with an increased risk of cardiovascular diseases and diabetes, but evidence for occupational noise is limited and conflicting, especially related to pregnancy outcomes. This study aimed to evaluate the association of occupational noise exposure with hypertensive disorders of pregnancy (HDP) and gestational diabetes. **Methods** Our population-based cohort study utilized data on 1 109 516 singletons born to working mothers in Sweden between 1994-2014 from the Medical Birth Register and the Longitudinal Integration Database for Health Insurance and Labor Market Studies. Noise exposure came from a job exposure matrix (JEM) in five categories <70, 70-74, 75-80, 80-85, >85 dB(A). Relative risks (RR), adjusted for confounders and other job exposures, were calculated by modified Poisson regressions for the full sample and a subsample of first-time mothers reporting full-time work. **Results** Exposure to 80-85 dB(A) of noise was associated with an increased risk of all HDP [RR 1.12, 95% confidence interval (CI) 1.05-1.18] and preeclampsia alone (RR 1.14, 95% CI 1.07-1.22) in the full sample. Results were similar for first-pregnancy, full-time workers. Exposure to >85 dB(A) of noise was also associated with an increased risk of gestational diabetes (RR 1.57, 95% CI 1.10-2.24) in the analysis restricted to first-time mothers working full-time. **Conclusion** In this study, exposure to noise was associated with an increased risk for HDP and gestational diabetes, particularly in first-time mothers who work full-time. Further research is needed to confirm findings and identify the role of hearing protection on this association so prevention policies can be implemented.

FULL TEXT

Headnote

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Objectives Exposure to environmental noise has been associated with an increased risk of cardiovascular diseases and diabetes, but evidence for occupational noise is limited and conflicting, especially related to pregnancy outcomes. This study aimed to evaluate the association of occupational noise exposure with hypertensive disorders of pregnancy (HDP) and gestational diabetes.

Methods Our population-based cohort study utilized data on 1 109 516 singletons born to working mothers in Sweden between 1994-2014 from the Medical Birth Register and the Longitudinal Integration Database for Health Insurance and Labor Market Studies. Noise exposure came from a job exposure matrix (JEM) in five categories <70, 70-74, 75-80, 80-85, >85 dB(A). Relative risks (RR), adjusted for confounders and other job exposures, were calculated by modified Poisson regressions for the full sample and a subsample of first-time mothers reporting full-time work.

Results Exposure to 80-85 dB(A) of noise was associated with an increased risk of all HDP [RR 1.12, 95% confidence interval (CI) 1.05-1.18] and preeclampsia alone (RR 1.14, 95% CI 1.07-1.22) in the full sample. Results were similar for first-pregnancy, full-time workers. Exposure to >85 dB(A) of noise was also associated with an increased risk of gestational diabetes (RR 1.57, 95% CI 1.10-2.24) in the analysis restricted to first-time mothers working full-time.

Conclusion In this study, exposure to noise was associated with an increased risk for HDP and gestational diabetes, particularly in first-time mothers who work full-time. Further research is needed to confirm findings and identify the role of hearing protection on this association so prevention policies can be implemented.

Key terms employment; gestational hypertension; gestational diabetes; hypertension; JEM; job exposure matrix; noise exposure; occupational health; preeclampsia; work-related factor.

Hypertensive disorders of pregnancy (HDP) - which include gestational hypertension, preeclampsia, and eclampsia - and gestational diabetes mellitus, are some of the most common conditions during pregnancy, affecting between 1-15% of pregnancies throughout the world (1, 2). HDP can lead to adverse birth outcomes, such as preterm placenta separation, preterm birth, and small for gestational age (3). Preeclampsia and eclampsia, in particular, are leading causes of maternal mortality, accounting for approximately 13% of maternal deaths in developed countries (4). Among those who survive, women who were diagnosed with HDP are more likely to develop a cardiovascular disease in the future (5). Likewise, gestational diabetes can lead to adverse outcomes both during and after pregnancy. For instance, pregnancies in women with gestational diabetes are more likely to include complications such as large-for-gestational age and neonatal hypoglycemia. Both women and their offspring are then later at an increased risk for type 2 diabetes (2).

Approximately one quarter of all hypertension cases during pregnancy will progress to preeclampsia; however, predicting who progresses has proven difficult (6). The causes of HDP in general are not well understood. Similarly, the etiology of gestational diabetes mellitus, has not been fully elucidated. Both disorders resolve after birth, share many of the same risk factors - such as increased age, obesity, and insulin resistance (3, 7) - and are associated with an increased risk for cardiovascular comorbidities in the long-term. These characteristics give rise to the theory that perhaps these disorders, and in particular preeclampsia, are a result of one of two patterns: (i) women without predisposing conditions who suffer from stresses additional to the normal adaptation to pregnancy, or (ii) women with weaker vasculature and/or predisposing condition in which the adaptation to pregnancy pushes them into the disordered state (8). These patterns, of course, could happen in a continuum, in which both external stressors and predisposing conditions interact and potentially lead to HDP or gestational diabetes.

Several studies have linked environmental noise exposure to cardiovascular disease (9-11) and diabetes (12) in the general population. However, a recent review by the World Health Organization concluded that there is not enough evidence of sufficient quality to make firm conclusions regarding the effects of noise on pregnancy (13). The

workplace is an important and understudied source of noise exposure outside of the home and, significantly, offers the potential for prevention strategies. In fact, in Sweden, approximately 20% of women report being exposed for at least one quarter of their working day to noise so loud they cannot carry a conversation in a normal tone of voice (14). Globally this burden is even higher as developing countries move to more industrial economies (15). Despite the widespread nature of occupational sources of noise, little research has been done to investigate its impact on pregnancy outcomes. Studies focusing on gestational hypertension report mixed results, with only a small number of cases, and often relying on self-reported data (16-20). To our knowledge, no current study has investigated the impact of occupational noise on gestational diabetes.

The aim of this study is to explore whether noise exposure during pregnancy is associated with HDP, looking specifically at women who develop preeclampsia alone, as well as gestational diabetes, using a large, register-based, prospective dataset, adjusting for other occupational exposures and potential cofounders.

Methods

Data collection

A prospective cohort was formed based on information on each pregnancy from the Swedish Medical Birth Register for all births between 1994-2014. In this register, covering approximately 99% of all pregnancies (21), data are recorded from prenatal care unit visits occurring around week 10 of pregnancy until the birth of the child. Data include background characteristics collected in early pregnancy (such as date of birth, occupation, smoking status, weight, height, and nationality) as well as information on previous pregnancies, parity, and any diagnoses received during pregnancy. For this study, we only included women whose pregnancies resulted in single births and who reported working full- or parttime at the time of the first appointment at the prenatal care unit occurring on or around gestational week 10. Additionally, women who did not report an occupation were not included.

This register was merged with the Longitudinal Integration Database for Health Insurance and Labor Market Studies (Swedish acronym LISA) utilizing the unique personal identification number assigned to all individuals living in Sweden in order to obtain information on socioeconomic characteristics, such as mother's highest education at the time of delivery and marital status. LISA has complete coverage of all individuals aged 16 and older residing in Sweden.

Noise exposure

To examine noise exposure, we used a job exposure matrix (JEM) linked to the cohort data using occupational codes. Occupational information provided at the prenatal care unit was recorded as free text, which was then coded into the ISCO-88-based standard for Swedish occupational classification 96 (SSYK96) coding system by an occupational hygienist. The coding details are presented elsewhere (22). SSYK96 is provided in a fourdigit level, with each digit, from left to right, providing greater detail regarding the occupation.

The noise exposure job matrix includes information on annual average 8-hour occupational noise level in decibel [dB(A)] in five-year intervals from 1970-2014 for 321 occupations. Noise levels were derived from measurement reports from occupational health services and clinics as well as large companies throughout Sweden and were specified in five categories: <70, 70-74, 75-80, 80-85, >85 dB(A) (23). A previous version of this matrix has been shown to be valid (23). We linked these levels to the maternal data based on the occupational code and birth year. Some occupations did not have enough detail to be given a 4-digit SSYK96 code and were given a 2- or 3digit code; thus, they could not be matched directly with the JEM job groups. For these cases, imputation was done in one of two ways. First, if all occupations within this 2- or 3-digit job groups had the same noise category, that category was imputed for the missing observations. For instance, all occupations within the 'manager of small companies and entities' job group had the lowest noise level; therefore, women who were coded as belonging to this overall job group were also given the same level. Second, if the noise levels varied within the 2- or 3-digit job group, an occupational hygienist with expertise on noise exposure and blinded to the diagnoses of individuals within each group was consulted, and he then assigned the most likely noise level for those observations.

Outcome

For each mother-child pair included in our study, we extracted diagnoses coded at the end of each pregnancy

reported in the Medical Birth Register. These were coded using the International Classification of Diseases, ninth and tenth revisions (ICD-9 and ICD-10). For HDP, ICD-9 codes 642, 642D, 642E, 642F, 642G, and 642H and ICD-10 codes O11, O13, O14.0, O14.1, O14.2, O14.9, O15.0, O15.1, O15.2, and O15.9 were used. For preeclampsia, ICD-9 codes 642E, 642F, and 642H and ICD-10 codes O11.9, O14.0, O14.1, O14.2, O14.9, O15.0, O15.1, O15.2, and O15.9 were used. Finally, for gestational diabetes, ICD-9 codes 648A and 648W and ICD-10 codes O24.4 and O24.9 were used.

Potential confounders

Several potential confounders were considered. From the Medical Birth Register we obtained maternal age at delivery (<25, 25-30, 30-35, or >35 years), smoking status at week 10 (non-smokers, smokers), educational level (some high school or less, high school graduate, some university or higher), marital status (not in a registered partnership or living alone, married or in a registered partnership), family situation (living with the father, living alone or another arrangement), body mass index (BMI) calculated using height and weight [underweight (<18.5 kg/m²), normal weight (18.5-25 kg/m²), overweight (25-30 kg/m²), obese (>30 kg/m²)], country of birth (Sweden, Europe excluding Sweden, and rest of the world), parity (first pregnancy, >1 pregnancy), and employment status (full-time, part-time). Occupational exposures considered were whole body vibrations, any particle exposure, physically strenuous work, job strain, and exposure to low temperatures, which were obtained from various JEM and matched to each woman based on occupational code and year, if applicable.

Whole body vibration was categorized as 0-0.1, 0.1-0.3, 0.3-0.5, and >0.5 m/s². The occupations that did not have enough detail (coded on a 2- or 3-digit SSSYK96) were those in which all sub-groups (coded on a 4-digit SSSYK96) were not exposed to vibrations; therefore, all were assigned a value of 0. We also considered occupational exposure to particles by including a JEM based on the Finnish Information System on Occupational Exposure JEM (24) and adapted to Swedish conditions, which included estimates for 24 agents: asbestos, silica, lead, iron, nickel, chromium, concrete/stone, other inorganic dust, wood, animal, paper, textile, flour, oil mist, cooking fumes, other organic dust, asphalt, diesel, benzo(a)pyrene, polycyclic aromatic hydrocarbons, other combustion fumes, and welding fumes. An occupation that was exposed to any of these agents was classified as exposed to particles. The physical workload, psychosocial stress, and temperature JEM have continuous measures based on questionnaires. For these JEM, when SSSYK96 codes did not have enough detail, we calculated an average weighted according to the population distribution of Swedish women working in the sub-groups each occupational group. In other words, if a sub-group had a greater proportion of women compared to other sub-groups, their exposure was given more weight in the average calculation. A total of 15 894 (1.4%) women were given imputed values. Physical load was used as an average of several physical exposures (bending, heavy lifting, stooping, working in a twisted position, rapid breathing, working with hands above shoulder level, physically strenuous work, and repetitive work), divided into quartiles. We used the decision authority and demand domains of the psychosocial stress JEM to create the job strain variable. A job exposed to above the mean value of either domain was considered to be exposed to high levels, and below the mean to low levels. Values for cold temperatures were divided into tertiles.

Data analyses

For all analyses, we included women who had a single birth and reported being employed (full-time or part-time). Covariate adjustment followed a two-step procedure. First, we selected separate sets of confounders for each analytical model based on known risk factors for HDP and gestational diabetes (3, 7), placement on a causal diagram (25-27), and impact on the association between exposure and each outcome using a 5% cutoff. Then, in a second step, to ensure consistency and ease of interpretation between outcomes, if a variable was selected into one model, it was entered into the final model for all other outcomes. All covariates previously mentioned were considered for inclusion, and ultimately, confounders added to the final model were: maternal age at delivery, smoking status, educational level, country of birth, parity, employment status, any particle exposure, physical load, job strain, and exposure to low temperatures.

To explore multicollinearity between the exposure and confounders, we included them into a linear regression model and calculated the variance inflation index (VIF). VIF values were well <5 for all categories of all covariates,

indicating that, statistically, there were no major issues with multicollinearity.

Because different births from the same mother could not be assumed to be independent, relative risks (RR) were estimated using a modified Poisson regression for correlated binary data (28). Crude and adjusted models were created for each outcome (HDP, preeclampsia, gestational diabetes), with the adjusted model including complete cases only. We repeated the analysis with a subsample of women with a first-time pregnancy who reported full-time employment to investigate the association for those who are most likely exposed to the category of noise assigned to their job code. Women, with previous pregnancy complications may work less or change their work tasks during a subsequent pregnancy and those who work part-time will be exposed to less noise than those who work full-time. The same modified Poisson regression was utilized to estimate RR; however, no correlation adjustment was necessary as each woman only contributed with one observation. Further sensitivity analyses were done on the full sample by investigating age interactions. All statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA).

This study was conducted with approval from the regional ethical review board in Stockholm, Sweden.

Results

A total of 1 109 516 mother-child pairs were included in the study. The characteristics of the cohort are described in table 1. The majority (63%) of women were exposed to the <70 dBA in their workplace; 19% were exposed to 70-75 dBA, 5% to 75-79 dBA, 12% to 80-84 dBA, and <1% were exposed to levels >85 dBA. Compared to those who were exposed to the lowest noise category, women who were exposed to the highest category of noise (>85 dBA) were younger, more often smokers, more often had lower levels of education, and were born in European countries other than Sweden. These women were also more often employed full-time, and were concomitantly more often exposed to particles, high physical load, job strain, and cold temperatures. Table 2 lists the ten most common occupations within each exposure category.

Results from the regression analyses for the full sample, which includes both full- and part-time workers, as well as first and subsequent pregnancies, are found in table 3. After adjusting for all confounders, exposure to the second highest category of noise (80-85 dBA) was associated with an increased risk of HDP of pregnancy (RR 1.10, 95% CI 1.06-1.14) and preeclampsia (RR 1.11, 95% CI 1.07-1.16). No associations were observed for gestational diabetes. We conducted a separate analysis restricting to women who were in their first pregnancy and working full-time, the part of the full sample who were more likely to be present at work and thus more likely to be exposed to the levels within the assigned noise category. This resulted in a subsample of 349 300 pregnancies; results are presented in table 4. The same patterns were seen as in table 3, but with slightly stronger associations. The second highest noise category showed a statistically significant increased association of 1.12 (95% CI 1.05-1.18) for HDP and 1.14 (95% CI 1.07-1.22) for preeclampsia. For the highest noise category, the RR were increased, but not statistically significant (RR 1.06, 95% CI 0.92-1.22 for HDP and RR 1.09, 95% CI 0.93-1.28 for preeclampsia). Results for gestational diabetes did not follow the same patterns as table 3. For this sample, we observed that both 80-85 dB(A) (RR 1.23, 95% CI 1.04-1.46) and the >85 dB(A) (RR 1.57, 95% CI 1.10-2.24) categories were associated with increased risks when compared to those unexposed to noise. Analyses investigating an interaction between noise and age did not show evidence of any multiplicative interaction (data not shown).

Discussion

In this nationwide cohort study, exposure to noise at the workplace was associated with an increase in HDP and preeclampsia, notably for first-time pregnant women who worked full-time, the subsample of the full cohort we believe are more likely to be truly exposed. These associations were present beginning at 80 dB(A); however, were not statistically significant at levels >85 dB(A). Occupational noise exposure was further associated with an increase in gestational diabetes among first-time pregnant women working full-time who were exposed to noise levels >80 dB(A).

Previous studies have found conflicting results regarding noise exposure and pregnancy outcomes. One environmental study reported an increased risk for severe and early onset preeclampsia but not for mild and late onset (29). Three occupational studies find some increased, but nonsignificant, risk of gestational hypertension

and/or preeclampsia associated with noise exposure in the workplace (16, 17, 19), while two studies (18, 20) find no associations. Even among studies reporting an increased risk, results are inconsistent. One of these, found a significantly increased association only among women who are also exposed to shift work (16), while another found a nonsignificant increase among parous women only (17). Risks obtained from this study fall somewhere between those reported previously. All these studies, however, are small and adjust for a limited number of pregnancy, lifestyle, and demographic confounders. Additionally, the few that adjust for other working conditions only adjust for shift work or physical load. To our knowledge, this is the first study to account for several job exposures, which lessens the likelihood that our results are due to other job exposures. There are no previous studies that investigate occupational noise and gestational diabetes. However, one study investigating environmental noise report odds ratios in the highest quartile of nighttime noise that are similar to our findings (30).

Our results for the 80-85 dB(A) category were largely driven by the childcare workers, which make up the majority of this group. Because data for this study come from a birth register with routine data collection, we do not believe that women who work in childcare and have a pregnancy outcome are disproportionately represented in the dataset. Restricting the sample and removing child care workers gives the similar results as in the full sample, except for the sub-group of restaurant and kitchen workers, whose inclusion did not show an increased risk (data not shown). Further studies should be conducted to elucidate these findings.

The subsample analysis of women who were in their first pregnancy and working full-time showed a similar effect for both HDP and preeclampsia. Preeclampsia is generally considered to be a disorder of the first pregnancy (3). In our sample, even though women who were in first pregnancies and worked full-time accounted for approximately one third of the full sample, almost half of the HDP and preeclampsia cases were in this group. Therefore, it is unsurprising that we see similar results in the general cohort.

While we observed no increased risk of gestational diabetes in association with noise exposure in the full cohort, we observed strong risks among the subsample of first pregnancies. Gestational diabetes recurrence is known to be high among those who had it during their first pregnancy, and, therefore, it might seem counterintuitive that risks are not seen in the full cohort including both first and successive pregnancies (31). We speculate that there is a lower likelihood of misclassification in the subsample of first pregnancies who work full-time, since it is possible that women who had a previous complication may change their tasks, go on leave, work less than full-time, or request to be reassigned. These women may be more absent or working less due to childcare responsibilities. Thus, even though results have lower precision due to the reduced sample size, estimates are more likely to be accurate because this subsample is more likely to be exposed to the assigned noise levels.

To date, the mechanism through which a woman develops HDP and gestational diabetes is unclear. For cardiovascular and metabolic diseases in general, noise is thought to induce a stress response, activating the sympathetic nervous and endocrine systems, leading to increased blood pressure, vascular damage, and metabolic disorders through oxidative stress and increased inflammation (10). Because pregnancy itself is characterized by increased hypothalamus-pituitary-adrenal axis function and concentration of stress hormones (13), the same pathway via which noise can lead to cardiovascular and metabolic disease. Therefore, it is plausible that the added stress response due to noise exposure can influence a woman's likelihood of developing these pregnancy disorders. With this mechanism in mind, one would expect to find the greatest risk at levels >85 dB(A), in other words, increasing levels of noise leading to an increased stress response; however, in our data this was not the case. One explanation could be that at these levels, workers are required to use hearing protection, which would protect mothers from the any adverse effects of noise. At the 80-85 dB(A) levels, workers are required to have access to, but do not necessarily have to use, hearing protection. One study, however, found no decrease in the risk of gestational hypertension among women who self-reported use of hearing protection (16). Regardless, the effect of hearing protection on this association is an area that warrants further exploration, not in the least because it may offer effective mitigation strategies. Another explanation is that perhaps women who are exposed to these high levels of noise are more likely to have jobs that would require them to be reassigned or go on leave, and in this case, women in the highest categories would not be exposed for the entirety of the pregnancy. Lastly, occupations

with the highest noise level are also exposed to many other factors, and though we have checked for multicollinearity, it is possible that the inclusion of a combination of occupational factors attenuated the results. This study has some limitations. Regarding exposure ascertainment, the noise levels provided by the JEM are not measured on an individual level, and thus misclassification can occur. The JEM were developed for general use based on measurements on both male and female workers and expert knowledge, without consideration for any particular outcome. Therefore, any misclassification is most likely non-differential and, as such, would only attenuate the risk reported. We did not have information on use of hearing protection. As mentioned, it is possible that the lower risk and lack of significant findings in the highest exposure category is due to use of hearing protection, but we could not test this hypothesis. Similarly, we did not have information on task reassignment. We did have information on pregnancy leave; however, because diagnoses were only given at the end of the pregnancy, we had no way to ascertain that the leave preceded any issues arising from HDP or gestational diabetes. Thus, we could not account for duration of exposure in our analyses. Due to local regulations, task reassignment and leave would most often be associated with physically strenuous work, for which our results are adjusted. Finally, we did not have information on the percentage of time part-time employees work, which can also affect the extent of exposure.

On the other hand, this study benefitted from a large sample and a prospective design. Even though HDP and gestational diabetes are the most common conditions of pregnancy, they are still relatively rare in the population. At the same time, the multifactorial nature of these disorders indicates there is likely no one major causative factor. Therefore, only a nationwide register this large can capture the number of exposed cases needed to detect the magnitude of differences expected. Additionally, because the data covers approximately 99% of all births in Sweden, results are generalizable to all pregnant women in Sweden. Another advantage is that data from this national, well-established register were collected as part of routine maternal care by healthcare professionals with nearly complete coverage of all pregnancies; therefore, data are more likely to be accurate and consistent for the entire sample. In this study, we were also able to control for several other exposures that confound the association between noise and pregnancy disorders via other JEM. These JEM were developed by experts in their respective fields and are based on the Swedish workforce, which should reduce misclassification at the occupational groups level.

In conclusion, this study indicates that there is an increased risk in HDP associated with exposure to noise at levels >80 dB(A). There is also an increased risk for gestational diabetes associated with these levels for firsttime pregnant women who work full-time. Additional studies are needed to confirm this association, as well as investigate whether hearing protection can mitigate these risks.

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Conflicts of interest

The authors declare no conflicts of interest. The source of funding has played no role in the study design, collection, analyses, interpretation of the data, drafting of the manuscript, and decision to submit for publication.

Sidebar

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DETAILS

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Schram, J. L. D., M.Sc, Solovieva, S., PhD., Leinonen, T., PhD., Viikari-Juntura, E., Burdorf, A., PhD., & Robroek, S. J. W., PhD. (2021). The influence of occupational class and physical workload on working life expectancy among older employees. *Scandinavian Journal of Work, Environment & Health*, 47(1), 5-14.
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Objective This study investigates the impact of physical workload factors and occupational class on working life expectancy (WLE) and working years lost (WYL) in a sample of older Finnish workers. **Methods** A 70% random sample of Finns in 2004 was linked to a job exposure matrix for physical workload factors and register information on occupational class and labor market status until 2014. Transitions between being at work, time-restricted work disability, unemployment, economic inactivity, disability retirement, retirement and death were estimated. A multistate Cox regression model with transition-specific covariates was used to estimate the WLE and WYL at age 50 up to 63 years for each occupational class and physical workload factor for men and women (N=415 105). **Results** At age 50, male and female manual workers had a WLE of 10.13 and 10.14 years, respectively. Among both genders, manual workers had one year shorter WLE at age 50 than upper non-manual employees. This difference was largely attributable to unemployment (men: 0.60, women: 0.66 years) and disability retirement (men: 0.28, women: 0.29 years). Self-employed persons had the highest WLE (11.08 years). Men and women exposed to four or five physical workload factors had about one year lower WLE than non-exposed workers. The difference was primarily attributable to ill-health-related reasons, including disability retirement (men: 0.45 years, women: 0.53 years) and time-restricted work disability (men: 0.23, women: 0.33 years). **Conclusions** Manual workers and those exposed to physical workload factors had the lowest WLE. The differences in WYL between exposure groups can primarily be explained by ill-health-based exit routes.

Nielsen, M. B., PhD., Emberland, J. S., PhD., & Knardahl, S., PhD. (2021). Office design as a risk factor for disability retirement: A prospective registry study of norwegian employees. *Scandinavian Journal of Work, Environment & Health*, 47(1), 22-32. doi:<https://doi.org/10.5271/sjweh.3907>

Objectives This aim of this study was to (i) examine differences in risk of subsequent disability retirement between employees working in cellular, shared, and open-plan offices and (ii) determine the contribution of gender, skill-level, work ability, medically certified sickness absence, leadership position, and personality traits (extroversion, agreeableness, conscientiousness, neuroticism, and openness) as confounders. **Methods** Survey data on predictor variables combined with official objective registry data on disability retirement and sickness absence were extracted from a large Norwegian occupational cohort of office workers (N=6779, 53.5% women). Questionnaire data included the respondents office designs, comparing cellular, shared, and open-plan offices, demographic characteristics, workability, and personality factors. Objective data on disability retirement and medically certified sickness absence were extracted from the sickness and disability benefit register of the Norwegian Labor and Welfare Administration. **Results** In the final fully adjusted model, employees working in shared hazard ratio (HR) 1.52, 95% confidence interval (CI) 1.08-2.16] and open-plan (HR 1.95, 95% CI 1.31-2.90) offices had significantly higher risk of subsequent disability retirement compared to employees in cellular offices. Gender, work ability, medically certified sickness absence, and conscientiousness had independent direct effects on risk of disability retirement. **Conclusion** This study shows that open and shared workspace designs have detrimental effects by increasing risk of disability retirement among office workers, even when taking other known predictive factors into account.

Chen, Chi-Hsien, M.D., PhD., Tsai, P., PhD., Wang, Y., PhD., Pan, C., PhD., Hung, P., PhD., Ho, J., PhD., . . . Guo, Yue Leon, M.D., PhD. (2021). Respiratory health effects of the fiberglass-reinforced plastic lamination process in the yacht-building industry. *Scandinavian Journal of Work, Environment & Health*, 47(1), 62-69.
doi:<https://doi.org/10.5271/sjweh.3924>

Objectives Fiberglass-reinforced plastics (FRP) manufacturing has been related to cases of severe airway obstruction and elevated risk of respiratory mortality. But the specific job content risk is not clear. This study evaluated the respiratory health effects of the FRP lamination process. **Methods** A questionnaire was used to

evaluate respiratory symptoms of workers in two yacht-building plants. Pre-shift (07:30-08:30 hours) and post-shift (17:00-18:00 hours) lung function was measured, while post-shift induced sputum was collected on the first day of the week. The participants were grouped into FRP laminators and non-laminators. Linear and logistic regression was used to investigate the effects of the lamination process on lung function. Results Laminators had a higher prevalence of chronic cough, lower pre-shift forced expiratory volume in first second (FEV1) and FEV1/force vital capacity (FVC) (-3.3% and -1.5%), lower post-shift FVC and FEV1 (-3.6% and -4.9%), and larger post-shift reduction of FVC (-2.1%) compared to non-laminators. The laminators also had higher risk of early obstructive and overall (obstructive plus restrictive) lung function impairment, and post-shift reduction of FVC >10% odds ratio (OR) 5.98, 4.98, and 3.87, respectively). They also had higher percentages of neutrophils and lymphocytes in the induced sputum. Conclusion Laminators should undergo regular check-ups of respiratory symptoms and lung function. Further toxicologic studies are warranted to identify the specific causal agent in the FRP lamination process.

Taj, T., PhD., Gliga, A. R., PhD., Hedmer, M., PhD., Wahlberg, K., PhD., Assarsson, E., R.N., Lundh, T., PhD., . . . Broberg, K., PhD. (2021). Effect of welding fumes on the cardiovascular system: A six-year longitudinal study. *Scandinavian Journal of Work, Environment & Health*, 47(1), 52-61. doi:<https://doi.org/10.5271/sjweh.3908>

Objective This study investigated whether low-to-moderate exposure to welding fumes is associated with adverse effects on the cardiovascular system. **Methods** To test this, we performed a longitudinal analysis of 78 mild steel welders and 96 controls; these subjects were examined twice, six years apart (ie, timepoints 1 and 2). All subjects (male and non-smoking at recruitment) completed questionnaires describing their health, work history, and lifestyle. We measured their blood pressure, endothelial function (by EndoPAT), and risk markers for cardiovascular disease [low-density lipoprotein (LDL), homocysteine, C-reactive protein]. Exposure to welding fumes was assessed from the responses to questionnaires and measurements of respirable dust in their breathing zones adjusted for use of respiratory protection equipment. Linear mixed-effect regression models were used for the longitudinal analysis. **Results** Median respirable dust concentrations, adjusted for respirable protection, of the welders were 0.7 (5-95 percentile range 0.2-4.2) and 0.5 (0.1-1.9) mg/m³ at timepoints 1 and 2, respectively. Over the six-year period, welders showed a statistically significant increase in systolic 5.11 mm Hg, 95% confidence interval (CI) 1.92-8.31] and diastolic (3.12 mm Hg, 95% CI 0.74-5.5) blood pressure compared with controls (multi-variable adjusted mixed effect models). Diastolic blood pressure increased non-significantly by 0.22 mm Hg (95% CI -0.02-0.45) with every additional year of welding work. No consistent significant associations were found between exposure and endothelial function, LDL, homocysteine, or C-reactive protein. **Conclusion** Exposure to welding fumes at low-to-moderate levels is associated with increased blood pressure, suggesting that reducing the occupational exposure limit (2.5 mg/m³ for inorganic respirable dust in Sweden) is needed to protect cardiovascular health of workers.

Laaksonen, M., PhD. (2021). Increasing labor force participation in older age requires investments in work ability. *Scandinavian Journal of Work, Environment & Health*, 47(1), 1-3. doi:<https://doi.org/10.5271/sjweh.3941>

The increasing number of older people relative to the working-age population will exert pressures on economic growth, increase age-related social costs and endanger the sustainability of government finances. A large proportion of these differences can be explained by physical work demands, work time control, and self-rated work ability (18). ...]it seems that the factors affecting working beyond the statutory retirement age are, at least in part, similar to factors that relate to early exit. Even though hard physical labor has become less common during recent decades, many jobs still involve physical work demands. ...]efforts to reduce physical work exposures are needed to prevent early labor market exit among older workers. ...]efforts to promote mental health and well-being are increasingly important for maintaining a high labor market participation.

Mezei, G.,M.D.PhD., Chang, E. T., ScD., Mowat, F. S., PhD., Moolgavkar, S. H., M.B.B.S., Consonni, D., PhD., Marinaccio, A., M.Sc., . . . Iavicoli, S., PhD. (2021). Comments on a recent case-control study of malignant mesothelioma of the pericardium and the tunica vaginalis testis/Authors' response. *Scandinavian Journal of Work, Environment & Health*, 47(1), 85-89. doi:<https://doi.org/10.5271/sjweh.3909>

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