Report Information from ProQuest

17 October 2023 02:17

TABLE OF CONTENTS

SEARCH STRATEGY

Set No.	Searched for	Databases	Results
S1	Scandinavian Journal of Work, Environment & Health	Ebook Central, Public Health Database, Publicly Available Content Database	22325*

* Duplicates are removed from your search, but included in your result count.

Educational differences in duration of working life and loss of paid employment: working life expectancy in The Netherlands

Robroek, Suzan JW, PhD [1] ; Nieboer, Daan, MSc [1] ; Järvholm, Bengt, MD PhD [2] ; Burdorf, Alex, PhD [1]
[1] Erasmus University Medical Center Rotterdam, Department of Public Health, PO Box 2040, 3000 CA Rotterdam, The Netherlands [2] Umeå University, Department of Public Health and Clinical Medicine, Umeå, Sweden

ABSTRACT (ENGLISH)

Objectives This study aims to provide insight into educational differences in duration of working life by working life expectancy (WLE) and working years lost (WYL) through disability benefits and other non-employment states in the Netherlands. Methods Monthly information on employment status of the Dutch population (N=4 999 947) between 16 and 66 years from 2001-2015 was used to estimate working life courses and loss of working years for specific non-employment states. Across educational groups, bi-directional transitions between paid employment and nonemployment states were calculated. Using a multistate model, the WLE and WYL at age 16, 30, 50 and up to 66 years as statutory retirement age were estimated for each educational group, stratified by gender. Results Low-educated men and women had a 7.3 (men) and 9.9 (women) years lower WLE at age 30 than high-educated men and women. Among low-educated men, 3.4 working years were lost due to disability benefit compared to 0.8 among high-educated men. Low-educated women lost 3.0 working years due to disability benefit compared to 1.4 among high-educated women. Conclusions There are large educational inequalities over the course of working life. Among low-educated workers, more working years are lost due to unemployment, no income, and especially disability benefits. The latter reflects large educational inequalities in health and working conditions. The metrics of WLE and WYL provide useful insights into the life-course perspective on working careers.

FULL TEXT

Headnote

Objectives This study aims to provide insight into educational differences in duration of working life by working life expectancy (WLE) and working years lost (WYL) through disability benefits and other non-employment states in the Netherlands.

Methods Monthly information on employment status of the Dutch population (N=4 999 947) between 16 and 66 years from 2001-2015 was used to estimate working life courses and loss of working years for specific non-employment states. Across educational groups, bi-directional transitions between paid employment and nonemployment states were calculated. Using a multistate model, the WLE and WYL at age 16, 30, 50 and up to 66 years as statutory retirement age were estimated for each educational group, stratified by gender.

Results Low-educated men and women had a 7.3 (men) and 9.9 (women) years lower WLE at age 30 than high-educated men and women. Among low-educated men, 3.4 working years were lost due to disability benefit compared to 0.8 among high-educated men. Low-educated women lost 3.0 working years due to disability benefit compared to 1.4 among high-educated women.

Conclusions There are large educational inequalities over the course of working life. Among low-educated workers, more working years are lost due to unemployment, no income, and especially disability benefits. The latter reflects

large educational inequalities in health and working conditions. The metrics of WLE and WYL provide useful insights into the life-course perspective on working careers.

Key terms education; educational inequality; ill health; inequalities; working life course; working years lost.

With increasing life expectancy and a rapidly ageing population, there is a need to increase the labor force participation until age 65 and beyond. The proportion of older workers in the workforce is growing and, hence, an increasing proportion of the workforce will face health problems during working life. A meta-analysis has illustrated that individuals with poor health are at increased risk for premature labor force exit due to disability benefits [risk ratio (RR) 3.61], unemployment (RR 1.44), and early retirement (RR 1.27) (1). Particularly workers with a low educational level are at risk for labor force exit and health-related labor force exit (2, 3). Educational inequalities in health-related exit from paid employment are substantial in all European countries (4), and it may be hypothesized that, with increasing retirement age, these disparities will increase, especially in the last years of working life (5). Although educational inequalities in labor force exit and re-employment are well-established, studies on the influence of socioeconomic position and poor health on displacement from the labor market do not present a clear insight into the cumulative loss of work capacity during working life. A life-course perspective is needed.

The metric of working life expectancy (WLE) as a measure of duration of working careers was first introduced in 1977 by Hoem (6), and revitalized by Nurminen and colleagues (7) and others (8). WLE expresses, in analogy to the concept of life expectancy, the number of years that a person is expected to spend in paid employment until he or she finally leaves the labor force for statutory retirement (7). It is important to note that WLE is a population measure, ie, it presents an estimate of duration of working careers based on the cumulative labor force attachment of all persons in a particular study population. With the increasing statutory retirement age in many countries, WLE has been acknowledge as an interesting measure to capture working life course (9). The gap measure working years lost (WYL) reflects the working time lost due to premature exit from paid employment (10). This life-course perspective of the workforce, captured in WLE and health-related WYL, can be used to evaluate long-term consequences of policy changes in labor legislation, and provides insight into socioeconomic inequalities during the working life course.

In the past decade several studies have estimated the expected duration of working life. In Finland, Nurminen et al (7) have estimated a WLE at age 16-64 years of 29.7 years for women and 31.4 years for men (7). They also reported that 50-year old Finnish persons with poor health may lose 13-16 months of their remaining working life. Recently, Pedersen &Bjorner (11) found that Danish workers with a poor self-perceived health have a 1.4 year lower WLE at age 55 than workers in good selfperceived health (11). In particular occupations, healthrelated WYL may be substantially higher, for example in the construction industry (10). Studies in specific populations of chronically diseased persons have shown that persons with mental disorders may lose up to 15 years of their total working life due to disability benefits (12) and workers with arthritis three (women) or four (men) years (13). Focusing on WYL at age 50, Dudel &Myrskylä (14) have shown an educational gradient with an 8-year difference in WLE between workers with higher education and those with less than high school diploma (14). Leinonen et al (15) reported that in Finland manual workers were expected to spend 3.6-3.7 years less in work than upper non-manual employees (15). These studies have illustrated that a substantial part of working careers is lost due to poor health and strenuous working conditions. However, existing studies on WLE and WYL have some disadvantages that hamper interpretation and comparability. First, some studies have addressed only disability benefits as an exit route (12, 13) without taking into account the competing risks of other exit routes (16). Second, other studies have ignored that exit from paid employment may be temporary, even after receiving a disability benefit (12, 13, 17). Third, some studies have relied on small study populations (14) or cross-sectional data (18), which are sensitive to selection bias. Fourth, most studies have focused on WLE at age >50 (16, 19), while many working years might be lost earlier in working life.

This study aims to estimate the working life expectancy in different educational groups in The Netherlands, and to study the working years lost in these educational groups through disability benefits and other states of non-employment. The study is based on a large proportion of the workforce in the Netherlands over a period of 15 years.

It uses a multistate model that takes into account all dynamic patterns of entering and quitting paid employment to get insight into educational inequalities in labor force participation with a longitudinal perspective over the working life course.

Methods

Data

For this study, Statistics Netherlands enriched the social statistical database with register information on gender, age, educational level, and vital status, in order to calculate transition probabilities for entering and exiting the labor force. In total, complete information was available for 4 999 947 Dutch individuals aged 16-66 years at January 2001, of which N=2 761 301 were between 30-66 years. A starting age of 16 was chosen since in The Netherlands it is obligatory to go to school until that age. Individuals of this cohort were followed-up for 15 years (until December 2014). The age of 66 years was chosen to capture the recent increase in retirement age. We focus the current presentation on individuals aged 30-66 years because at age 30 most individuals will have finished their education and entered the labor force.

(Non)employment states

The social statistical database stores monthly information on the main income components, ie, gross wages, social benefits, and pensions, derived from Dutch tax registers (20). This information distinguishes seven mutually exclusive states (i): paid employment, (ii) disability benefits, (iii) unemployment, (iv) no income through paid employment, (v) (early) retirement, (vi) being a student, and (vii) emigration. Death is based on mortality statistics. Employed persons had their main source of income through paid employment or having their own business, defined by a monthly transaction on income.

Disability benefit is defined as receiving these benefits for >50% of the personal income. In The Netherlands, individuals may be granted a disability benefit when they are partially or fully incapable of working after two years of sickness absence. The degree of the disability is determined by the loss of earnings due to illness relative to the earnings before. Only when there is a reduction in income of >35% will disability benefits be granted (21).

In The Netherlands, individuals receive unemployment benefits in case of loss of paid employment, with a maximum of 38 months in the study period - depending on length of contract of past paid employment. After this period, the corresponding household may receive a social security benefit in case the disposable (household) income is below the legislative threshold (21). The state "unemployment" contains both those with unemployment and social security benefits.

Individuals with no income did not have a personal income or receive any benefits. These individuals may have left paid employment voluntarily or may belong to a household whose disposable income is above the critical threshold for social security benefits. This category could also include persons who are unemployed but do not yet receive an unemployment benefit, and individuals not in education, employment, or training (NEET). Therefore, individuals who had <3 months with "no income" and received unemployment afterwards were considered to be in unemployment also in those first months with no income.

The state pension (AOW) is a base pension. Until 2013, the state pension age was 65 years, and it increased for both men and women with one month to 65 years and 3 months in 2015 (still increasing to 67 years and 3 months in 2023). In addition, pension benefits could be available in case of a pension agreement with the employer. During the study period (2001-2015), it was also possible to retire early. In 2005, arrangements for early retirement pensions became more stringent, which for most employees became effective from 2006 onwards. We defined an individual as (early-)retired when his or her main source of income was a retirement benefit. Since retirement before the age of 45 years is highly unlikely, individuals who were registered as having retired before the age of 45 were assigned their most recent non-employment state before the "retirement" state. Younger individuals may have retirement as most important income source due to, for example, survivor pension.

Students are individuals who are registered at an educational institution. Emigration concerns those individuals outside the population, and might therefore also include those individuals lost in the registrations.

Sociodemographics

Individual characteristics included gender, age, and educational level. Age at baseline was calculated based on month and year of birth. The highest level of education was coded according to the 1997 International Standard Classification of Education (ISCED-97) and categorized into low (pre-primary, primary, and lower secondary), intermediate (upper secondary) and high (post-secondary) education. The highest level of education, certified by officially acquired degrees and diplomas, in the period 2001-2014 was used.

Statistical analyses

Multistate model. The information on monthly transitions between states of (non-)employment was used to assess the transitions rates (intensities) between states of (non-) employment in order to calculate the WLE and WYL. Individuals may move between stages of (non-)employment over time. The multi-state model is composed of the previously mentioned seven states of (non-)employment and death as the absorbing state - since no further transitions are possible after death. All other transitions between states are possible (total 49 transition possibilities). A transition matrix was constructed to define the possible transitions between these states and with death. The calculations were censored at age of 66 years, and the estimated WLE is thus based on the transitions from ages 16, 30, and 50 until 66 years.

The R package mstate (version 0.2.11, in R studio version 1.0.153), developed by Putter et al (22-24), was used to estimate cumulative transition rates and transition probabilities and to fit the multistate models. Analyses were stratified by gender and educational level. Within each stratum, a semi-parametric cox proportional hazard model was fitted to estimate the transition rates between (non)employment states, using age as a time variable. Within each stratified analysis, a Markov assumption was made, meaning that the transition rates are only dependent on the current state. For each of the possible transitions in the multistate model, the baseline transition hazards were used to obtain transition probabilities.

WLE and WYL. Using the estimated transition probabilities in the multi-state model, we were able to calculate the expected length of stay (ELOS) in a state, given the current state (ELOS function in the mstate R package). This is estimated by integrating the transition probabilities from the starting time until a give horizon age, in this study set at age 66 years (25). WLE is defined as the number of years in the "employed" state, conditional on being in paid employment at the starting ages of respectively 16, 30, and 50 years. In addition, the weighted WLE is also calculated across all persons in the population, thus including those in paid employment as well as those in all possible non-employment states at the starting age of 30. Uncertainty around the expected length of stay was calculated using bootstrapping. Bootstrapping consists of resampling from the study population with replacement. On the bootstrapped population, the ELOS is calculated, and this is repeated 1000 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 the specific exit pathways were calculated as the difference between the age of 66 years and the WLE at ages 16, 30, and 50 respectively. In this publication, the key findings are presented for WYL at age 30, as at this age most individuals will have entered the labor force. Results for ages 16 and 50 can be found in the appendix (www.sjweh.fi/show_abstract. php?abstract_id=3843), supplementary files 3 and 5. The scripts are included in supplementary file 1.

Results

In the 2001 Dutch workforce, disability benefits among men (5.0 times) and women (2.2 times) were more prevalent among individuals with a low compared to high educational level (table 1). Men (4.3 times) and women (4.6 times) with a low educational level were also more likely to be unemployed. Participation in (self-)employment between 30-66 years is the highest (men 90.5%, women 81.5%) among high-educated individuals. The mean age among men and women decreased by educational level, reflecting the increased educational level over time. The figure in supplementary file 2 graphically presents the proportion of individuals in the different states by age, stratified by education and gender.

Educational differences in working life expectancy

Table 2 shows the WLE at different ages, stratified by educational level and gender. At age 30, the WLE for men was 20.9 years among low-educated and 28.2 years among high-educated individuals with a gap of 7.3 years. For

women, this gap was 9.9 years, primarily due to the low WLE of 16.86 years among low-educated women. For those working at age 50, there were still educational differences in WLE (men: 2.5 years, women: 3.4 years). At all ages, the educational inequalities were larger for men than women. The gap in WLE is relatively small between the intermediate and high educational levels and is particularly apparent for the low education level. Table 2 shows the WLE conditional of being in paid employment at ages 30 and 50 (age 16 in supplementary files 3). When other starting non-employment states are taken into account, the weighted WLE at age 30 was up to 1 year lower compared to WLE based on paid employment as starting state (supplementary table S5).

Educational differences in working years lost

Low-educated men at age 30 lost in total 15.1 years of paid employment during their working life of which 41.5% due to unemployment, 22.5% to disability, 10.5% to no income, and 13.1% to (early) retirement (see table 3, for working years lost at age 16 and 50 years, supplementary files S3 and S5). The other non-employment states (time spent in education: 0.2%, emigration: 5.9%, and mortality: 6.4%) accounted for 12.5% of the WYL. Absolute educational inequalities in WYL were largest for unemployment and disability benefits. Low-educated men lost 4.3 (unemployment) and 2.6 (disability benefits) working years more than high-educated individuals.

Low-educated women lost in total 19.1 years of paid employment during their working life of which 36.3% due to unemployment, 31.3% to no income, 15.7% to disability, and 10.7% to early retirement. The other non-employment states (time spent in education: 0.3%, emigration: 2.5%, and mortality: 3.2%) contributed 6.0% to the WYL. Absolute educational inequalities in WYL among women were largest for unemployment (5.2 years), followed by no income (3.6 years), and disability benefits (1.7 years).

From age 30 onwards, educational inequalities were lowest for emigration, (early) retirement, death, and being a student. High-educated workers had slightly higher emigration and also spent slightly more years in (early) retirement than low-educated workers. Mortality was substantially higher among men than women and also showed the expected educational gradient. WYL at age 16 (supplementary file 3) shows that high educated workers spent >7 years (men: 7.8 years, women: 7.4 years) in education, whereas low educated workers lose a similar amount of working years due to unemployment. Educational inequalities concerning WYL at age 50 are largest for unemployment and disability benefits (men) and for unemployment and no income (women) (supplementary file 5)

Discussion

This study showed large educational inequalities in working life expectancy in the workforce in The Netherlands. At age 30, high-educated men are expected to work 7.3 years longer during their life course than low-educated men. Among women, this difference is 9.9 years. A considerable amount of the lost working time, up to 4.4 years among low-educated men, is health-related due to disability benefits and premature death. Educational inequalities in health-related working years lost were much larger among men than women. Both among men and women, absolute inequalities were largest for unemployment.

The WLE and WYL metrics provide information regarding labor force participation and premature loss of paid employment during the life course. As mentioned in the introduction, several models have been developed to estimate WLE and WYL. Our model improves these models by using bi-directionality of entering and quitting paid employment and different exit routes to non-participation. Our model also encompasses a broad age range instead of older workers only, and presents detailed estimates for gender and educational level. A previous study has shown a substantial return to paid employment after a period of non-employment, including non-employment due to disability (26). The presented model takes into account that individuals can re-enter paid employment after non-employment and disability benefit.

Recently, two studies estimating WLE in The Netherlands were published - both focusing on WLE of older workers. Van der Noordt et al (17) reported WLE at age 58 years varying from 4.1-5.1 among lower educated individuals to 5.0-5.9 among higher educated individuals (17). De Wind et al (19) reported, based on the same data, a WLE at age 55 years of 5.7-6.8 years. Our study adds to these publications a life-course perspective on labor force participation from young age onwards. Our results show an WLE at age 30 of 21-28 years among men and 17-27 years among women. Assuming the age of 66 as an absorbing state, men lose 8-15 working years over the working life course

and women 9-19 years. Especially among lower educated workers, a substantial number of working years are already lost before the age of 50 years.
The WLE at age 16 among Dutch men (32.7 years) is higher than the WLE in Finland projected for 2006 (31.4 years), as reported by Nurminen et al (7). Among Dutch women, the WLE at age 16 (29.3 years) was marginally lower compared to the WLE of 29.7 years among Finnish women. Our model takes into account the main source of income, regardless the number of working hours that may differ between Finnish and Dutch women. This comparison of WLE between Finland and The Netherlands also captures other differences. Our study presents WLE to the age of 66, compared to an age of 64 in the Finnish study, which will result in higher estimates in The Netherlands. In contrast, the higher labor force participation in Finland, especially among women, will have increased WLE compared to The Netherlands. In the more recent study period, in The Netherlands national policies to postpone early retirement have been enacted, which will have increased WLE in The Netherlands compared to Finland. It is of interest to note that in an international comparison of WLE across 26 European countries in 2009, the WLE at age 50 in the Netherlands was among the highest quartile for men, but only around the mean value for women (27).
The contribution of the different exit pathways to the number of working years lost is a unique feature of this study and shows large differences between sociodemographic groups. At age 30, when the majority of the individuals have finished their school or study, low-educated individuals have a 7 (men) to 10 (women) years lower WLE than high educated individuals. While individuals with a low educational level enter paid employment much earlier than individuals with a high educational level, our model indicates that over the total life course high-educated persons spent substantially more years in paid employment than low-educated persons. Among women, the educational inequalities are larger than among men, and this can particularly be attributed to lost WYL due to "no income".
Poor health is a prerequisite for receiving disability benefits and the educational differences in years with disability benefits reflect educational inequalities in health (28), as well as in strenuous working conditions and unhealthy behaviors. Our results concerning educational inequalities in working years lost due to disability benefits are in line with a recent Finnish study showing that the highest educated men lost 0.6 years due to disability retirement compared to 2.7 years among the lowest educated group. For women this was 0.7 and 2.6 years (29). The working years lost due to premature death also reflect the well-known educational inequalities in mortality. The health-related WYL are underestimated, since in The Netherlands a disability benefit is usually granted after a period of two years of (partial) sickness absence paid by the employer. In our study, these years in sickness absence are counted as paid employment, since information is lacking on time spent in full sickness absence or partial return to work. Two mechanisms might play a role in the educational inequalities in disability benefit. First, poor health is more prevalent among individuals with a low educational level (30) leading to a higher prevalence of disability benefits in this educational group. Second, individuals with a low educational level are more likely to carry out more strenuous work. With similar health problems, workers with strenuous work demands might be more likely to become work disabled (3). More insight is needed to disentangle these two mechanisms.
Health problems are also related to unemployment (1), which is also more common among low- compared to high-educated individuals. New old-age retirement regulations might further influence socioeconomic health inequalities, since particularly lower educated workers will have more problems to stay healthy at work until the increased statutory retirement age. An uniform retirement age completely disregards the large educational inequalities in life expectancy and, in particular, healthy life expectancy. It would be relevant to get insight into the influence of WYL on (healthy) life expectancy after retirement.
It is of interest to note that 2-2.5 working years are lost due to (early) retirement, and higher educated workers spent more time in retirement than lower educated workers. Workers with a low educational level might need to work longer because they lack financial resources. In The Netherlands, collective agreements to retire early have been abolished from 2006 onwards, leading to a steep rise in the actual retirement age in The Netherlands. At the same time eligibility criteria for disability benefits have become more stringent. In Finland, a decrease has been shown in the time spent on disability pension over time. Since 2013, the statutory retirement age has also risen to 67 years

and 3 months for future generations. It is of interest to get insight on how this rising retirement age has influenced loss of paid employment through other exit pathways out of paid employment.

If we disregard WYL due to education, the results show that workers with a high educational level in particular lose working years after the age of 50. For those with a low educational level, a substantial number of working years is already lost between 16-50 years. This indicates that in order to increase participation in paid employment among individuals with a low educational level, it is important to target also those in the younger age groups, while for high-educated workers measures targeting those aged >50 years might be more effective.

The model presented can be expanded to evaluate the impact of policy changes on participation in paid employment and working years lost due to specific exit pathways. Therefore, the concepts of WLE and WYL could therefore also be highly relevant for policy-makers.

A strength of the study is the use of a large national dataset representing Dutch individuals with 15 years of follow-up with monthly information on tax registries to define the states of employment and non-employment, which provides a robust estimate of WLE. The large time span includes diverse economic situations, which makes the estimation less vulnerable to specific situations in a certain year. There are also limitations to be mentioned. First, in the Dutch system, the states of unemployment and no income cannot be distinguished optimally. Unemployed persons may receive unemployment or social security benefits, but the latter benefit depends on the household income. Therefore, individuals with no income may have lost their job, and, therefore, the WYL due to unemployment may have been underestimated. Second, although the register contains a large number of individuals, for 6 725 061 individuals no information on educational level was present. The linkage of school diplomas with education level was implemented in the early 1970s, and, thus, for many older workers educational level is not available. However, the current study population still contains a large number of older workers and the measures of WLE and WYL are not sensitive to the age distribution. Furthermore, there is also missing information on education as a consequence of immigration and emigration. Third, the model is based on the Markov assumption that a future state only depends on the current state, and not on the events that occurred before. This might not always be the case. For example, Schuring et al (26) have shown that a transition from disability benefits to paid employment is more likely during the first two years of disability than after a longer period of disability. A linked limitation is that changes in transition rates over calendar time are disregarded. In our model, the estimated transitional probabilities reflect the mean transition in a given year, based on the underlying distribution of years in and out of paid employment, which will largely account for time-dependent events.

The study shows that there are large educational differences in WLE, both among men and women. A considerable amount of the lost working time is healthrelated due to disability benefits and premature mortality. In comparison to high-educated workers, those with a low educational level lose a much larger part of their working life due to disability benefit, unemployment, and no income. The metrics of WLE and WYL provide unique insights into the life-course perspective of how health will influence duration of working careers.

Acknowledgements

We thank Coos H Arts and Ferdy WJ Otten from Statistics Netherlands for discussing our work, providing the data, and answering many questions. This work was conceived with financial support from the Joint Programming Initiative More Years Better Lives (WORKLONG project). Suzan Robroek was funded by a fellowship from the Erasmus University Rotterdam.

Sidebar

Robroek SJW, Nieboer D, Järvholm B, Burdorf A. Educational differences in duration of working life and loss of paid employment: working life expectancy in The Netherlands. Scand J Work Environ Health. 2020;76(1):77-84. doi:10.5271/ sjweh.3843

Correspondence to: Suzan JW Robroek, Erasmus University Medical Center Rotterdam, Department of Public Health, PO Box 2040, 3000 CA Rotterdam, the Netherlands. [E-mail: s.robroek@erasmusmc.nl]

References

References

1. van Rijn RM, Robroek SJ, Brouwer S, Burdorf A. Influence of poor health on exit from paid employment: a systematic review. Occup Environ Med 2014 Apr;71(4):295-301. https://doi.org/10.1136/oemed-2013-101591.
2. Carr E, Fleischmann M, Goldberg M, Kuh D, Murray ET, Stafford M et al. Occupational and educational inequalities in exit from employment at older ages: evidence from seven prospective cohorts. Occup Environ Med 2018 May;75(5):369-77. https://doi.org/10.1136/ oemed-2017-104619.
3. Robroek SJ, Rongen A, Arts CH, Otten FW, Burdorf A, Schuring M. Educational inequalities in exit from paid employment among Dutch workers: the influence of health, lifestyle and work. PLoS One 2015 Aug;10(8):e0134867. https://doi.org/10.1371/journal.pone.0134867.
4. Schuring M, Schram J, Robroek SJ, Burdorf A. The contribution of health to educational inequalities in exit from paid employment in five European regions. Scand J Work Environ Health 2019;45(4):346-355. https://doi. org/10.5271/sjweh.3796.
5. Kadefors R, Nilsson K, Östergren PO, Rylander L, Albin M. Social inequality in working life expectancy in Sweden. Z Gerontol Geriatr 2019 Feb;52 Suppl 1:52-61. https://doi. org/10.1007/s00391-018-01474-3.
6. Hoem JM. A Markov chain model of working life tables. Scand Actuar J 1977; 1(1):1-20. https://doi.org/10.1080/03461238.1977.10405621.
7. Nurminen M, Nurminen T. Multistate worklife expectancies. Scand J Work Environ Health 2005 Jun;31(3):169-78. https://doi.org/10.5271/sjweh.866.
8. Lievre A, Jusot F, Barnay T, Sermet C, Brouard N, Robine JM et al. Healthy working life expectancies at age 50 in Europe: a new indicator. J Nutr Health Aging 2007 NovDec;11(6):508-14.
9. Eurostat [Internet]. Duration of working life - statistics. Luxembourg, 2017. Available from: http://ec.europa.eu/eurostat/statistics-explained/index.php/Duration_of_ working_life_statistics
10. Järvholm B, Stattin M, Robroek SJ, Janlert U, Karlsson B, Burdorf A. Work disability and consequences for working life in Swedish construction workers during long term follow-up. Scand J Work Environ Health 2014;40:335-42. https://doi.org/10.5271/sjweh.3413.
11. Pedersen J, Bjorner JB. Worklife expectancy in a cohort of Danish employees aged 55-65 years - comparing a multi-state Cox proportional hazard approach with conventional multistate life tables. BMC Public Health 2017 Nov;17(1):879. https://doi.org/10.1186/s12889-017-4890-7.
12. Knudsen AK, Øverland S, Hotopf M, Mykletun A. Lost working years due to mental disorders: an analysis of the Norwegian disability pension registry. PLoS One 2012;7(8):e42567. https://doi.org/10.1371/journal. pone.0042567.
13. Lacaille D, Hogg RS. The effect of arthritis on working life expectancy. J Rheumatol 2001 Oct;28(10):2315-9.
14. Dudel C, Myrskylä M. Working Life Expectancy at Age 50 in the United States and the Impact of the Great Recession. Demography 2017 Dec;54(6):2101-23. https:// doi.org/10.1007/s13524-017-0619-6.
15. Leinonen T, Martikainen P, Myrskylä M. Working Life and Retirement Expectancies at Age 50 by Social Class: Period and Cohort Trends and Projections for Finland. J Gerontol B Psychol Sci Soc Sci 2018 Jan;73(2):302-13. https://doi. org/10.1093/geronb/gbv104.
16. Reeuwijk KG, van Klaveren D, van Rijn RM, Burdorf A, Robroek SJ. The influence of poor health on competing exit routes from paid employment among older workers in 11 European countries. Scand J Work Environ Health 2017 Jan;43(1):24-33. https://doi.org/10.5271/sjweh.3601.
17. van der Noordt M, van der Pas S, van Tilburg TG, van den Hout A, Jh Deeg D. Changes in working life expectancy with disability in the Netherlands, 1992-2016. Scand J Work Environ Health. 2019;45(1):73-81. https://doi.org/10.5271/ sjweh.3765.
18. Hytti H. Nio I [Internet]. Monitoring the employment strategy and the duration of active working life. Finland: Ministry of Labour, Kela, the Social Insurance Institution, 2004. Available from: https://ec.europa.eu/eurostat/cache/metadata/Annexes/lfsi_dwl_a_esms_an1.pdf.
19. de Wind A, van der Noordt M, Deeg DJ, Boot CR. Working life expectancy in good and poor self-perceived health among Dutch workers aged 55-65 years with a chronic disease over the period 1992-2016. Occup Environ Med 2018 Nov;75(11):792-7. https://doi.org/10.1136/ oemed-2018-105243.

20) Bakker BFM, Van Rooijen J, Van Toor L. The system of social statistical datasets of Statistics Netherlands: an integral approach to the production of register-based social statistics. Statistical journal of the United Nations ECE. 2014;30:411424.
21.Ministry of social affairs and employment. A short survey of social security. Government [Internet]. The Netherlands, the Hague, 30 June 2011. https://www.government.nl/ documents/leaflets/2011/06/30/short-survey-of-social-security-in-the-netherlands-1-july-2011.
22. Putter H [Internet]. Tutorial in biostatistics: Competing risks and multi-state models. Analyses using the mstate package. Available from: https://cran.r-project.org/web/packages/ mstate/vignettes/Tutorial.pdf
23. Putter H, Fiocco M, Geskus RB. Tutorial in biostatistics: competing risks and multi-state models. Stat Med 2007 May;26(11):2389-430. https://doi.org/10.1002/sim.2712.
24. De Wreede LC, Fiocco M, Putter H. An R package for the Analysis of Competing Risks and Multi-State Models. J Stat Softw 2011 ;38(11).
25. Beyersmann J, Putter H. A note on computing average state occupation times. Demogr Res 2014;30:1681-96. https:// doi.org/10.4054/DemRes.2014.30.62.
26. Schuring M, Robroek SJ, Otten FW, Arts CH, Burdorf A. The effect of ill health and socioeconomic status on labor force exit and re-employment: a prospective study with ten years follow-up in the Netherlands. Scand J Work Environ Health 2013 Mar;39(2):134-43. https://doi.org/10.5271/ sjweh.3321.
27. Loichinger E, Weber D. Trends in working life expectancy in Europe. J Aging Health 2016 Oct;28(7):1194-213. https://doi.org/10.1177/0898264316656509.
28. Dieker AC, IJzelenberg W, Proper KI, Burdorf A, Ket JC, van der Beek AJ et al. The contribution of work and lifestyle factors to socioeconomic inequalities in self-rated health - a systematic review. Scand J Work Environ Health 2019 Mar;45(2):114-25. https://doi.org/10.5271/sjweh.3772.
29. Laaksonen M, Rantala J, Järnefelt N, Kannisto J. Educational differences in years of working life lost due to disability retirement. Eur J Public Health 2018 Apr;28(2):264-8. https://doi.org/10.1093/eurpub/ckx221.
30. Mackenbach JP, Stirbu I, Roskam AJ, Schaap MM, Menvielle G, Leinsalu M et al.; European Union Working Group on Socioeconomic Inequalities in Health. Socioeconomic inequalities in health in 22 European countries. N Engl J Med 2008 Jun;358(23):2468-81. https:// doi.org/10.1056/NEJMsa0707519.
Received for publication: 5 April 2019

DETAILS

Subject:	Population; Socioeconomic factors; Employment; Working conditions; Life span; Age; Inequalities; Life expectancy; Retirement; Studies; Education; Premature labor; Women; Careers; Social security; Labor force; Workforce; Personal income
Business indexing term:	Subject: Careers Social security Employment Labor force Working conditions Workforce Personal income
Location:	Netherlands; Finland
Publication title:	Scandinavian Journal of Work, Environment &Health; Stockholm
Volume:	46
Issue:	1
Pages:	77-84

Publication year:	2020
Publication date:	2020
Section:	Original article
Publisher:	Scandinavian Journal of Work, Environment &Health
Place of publication:	Stockholm
Country of publication:	Finland, Stockholm
Publication subject:	Occupational Health And Safety
ISSN:	03553140
e-ISSN:	1795990X
Source type:	Scholarly Journal
Language of publication:	English
Document type:	Journal Article
DOI:	https://doi.org/10.5271/sjweh.3843
ProQuest document ID:	2344259883
Document URL:	https://www.proquest.com/scholarly-journals/educational-differences-duration-working-life/docview/2344259883/se-2?accountid=211160
Copyright:	Copyright Scandinavian Journal of Work, Environment &Health 2020
Last updated:	2023-08-22
Database:	Pub lic Health Database

Heme oxygenase 1 polymorphism, occupational vapor, gas, dust, and fume exposure and chronic obstructive pulmonary disease in a Danish population-based study

Würtz, Else Toft, PhD [1] ; Brasch-Andersen, Charlotte, PhD [2] ; Steffensen, Rudi, PhD [3] ; Hansen, Jens Georg, DMSc [4] ; Malling, Tine Halsen, PhD [1] ; Schlünssen, Vivi, PhD; Omland, Øyvind, PhD [1]
Department of Occupational and Environmental Medicine, Danish Ramazzini Centre, Aalborg University Hospital, Aalborg, Denmark. [2] Department of Clinical Genetics, Odense University Hospital, Odense C,

Denmark. [3] Department of Clinical Immunology, Aalborg University Hospital, Aalborg, Denmark. [4] Department of Clinical Epidemiology, Aarhus University Hospital, Aarhus N, Denmark.

ABSTRACT (ENGLISH)

Objectives The number of dinucleotide repeats (GT)n modulate expression of heme oxygenase 1 (HMOX1), a stress response gene. Multiple repeats might affect chronic obstructive pulmonary disease (COPD) susceptibility. We aimed to investigate the association of this polymorphism with COPD and its interaction with occupational exposures (vapor, gas, dust, or fumes). Methods This population-based cross-sectional study included 4703 Danes, aged 45-84 years. HMOX1 $(GT)_n$ was genotyped and grouped as short: <26, medium: 27-32 and long: >33 alleles. COPD was defined by the lower limit of normal (2.5th FEV/FVC and FEV_1 centiles). Occupational exposure was defined as ever exposed to vapor, gas, dust, or fume in expert-selected jobs. Associations were analyzed by adjusted mixed logistic regression. Results The population included 6% with COPD, 48% who had smoked >10 pack-years, and 46% with occupational exposure. HMOX1 was genotyped in 4423 participants. The adjusted odds ratio (OR) for the association between HMOX1 long allele and COPD was 1.75 [95% confidence interval (CI) 1.18-2.60]. An interaction was evident between HMOX1 long allele and occupational exposure, OR 2.38 (95% CI 1.04-5.46), versus HMOX1 short/medium without exposure. Analyses were replicated in another cohort, aged 20-44 years, N=1168, including 3% with COPD, 25% who had smoked >10 pack-years and 20% with occupational exposure. No associations were seen between COPD and HMOX1 long allele here. Conclusions Long alleles in HMOX1 alone and in interaction with occupational exposure seem to be associated with COPD. Failure to replicate data may be due to premature age for COPD development and low occupational exposure prevalence. We propose this long allele may be a genetic contributor to the COPD pathogenesis.

FULL TEXT

Headnote

Würtz ET, Brasch-Andersen C, Steffensen R, Hansen JG, Malling TH, Schlünssen V, Omland Ø. Heme oxygenase 1 polymorphism, occupational vapor, gas, dust, and fume exposure and chronic obstructive pulmonary disease in a Danish population-based study. Scand J Work Environ Health. 2020;76(1):96-104. doi:10.5271/sjweh.3846

Objectives The number of dinucleotide repeats (GT)n modulate expression of heme oxygenase 1 (HMOX1), a stress response gene. Multiple repeats might affect chronic obstructive pulmonary disease (COPD) susceptibility. We aimed to investigate the association of this polymorphism with COPD and its interaction with occupational exposures (vapor, gas, dust, or fumes).

Methods This population-based cross-sectional study included 4703 Danes, aged 45-84 years. HMOX1 $(GT)_n$ was genotyped and grouped as short: <26, medium: 27-32 and long: >33 alleles. COPD was defined by the lower limit of normal (2.5th FEV/FVC and FEV_1 centiles). Occupational exposure was defined as ever exposed to vapor, gas, dust, or fume in expert-selected jobs. Associations were analyzed by adjusted mixed logistic regression.

Results The population included 6% with COPD, 48% who had smoked >10 pack-years, and 46% with occupational exposure. HMOX1 was genotyped in 4423 participants. The adjusted odds ratio (OR) for the association between HMOX1 long allele and COPD was 1.75 [95% confidence interval (CI) 1.18-2.60]. An interaction was evident between HMOX1 long allele and occupational exposure, OR 2.38 (95% CI 1.04-5.46), versus HMOX1 short/medium without exposure. Analyses were replicated in another cohort, aged 20-44 years, N=1168, including 3% with COPD, 25% who had smoked >10 pack-years and 20% with occupational exposure. No associations were seen between COPD and HMOX1 long allele here.

Conclusions Long alleles in HMOX1 alone and in interaction with occupational exposure seem to be associated with COPD. Failure to replicate data may be due to premature age for COPD development and low occupational

exposure prevalence. We propose this long allele may be a genetic contributor to the COPD pathogenesis.

Key terms COPD; Denmark; dust exposure; gas exposure; gene-by-occupational interaction; genetic effect; HMOX1; lung function; occupational exposure; rs3074372; vapor exposure.

Chronic obstructive pulmonary disease (COPD) is a common and complex disease with a genetic contribution (1). The most well-established risk polymorphisms are single-nucleotide polymorphisms (SNP) in the SERPINA gene causing alpha-1-antitrypsin deficiencies (2, 3). However, only a few percent of COPD cases can be explained by the presently identified genetic variants. Further genetic studies in COPD are therefore needed to identify new genetic variants in order to establish new molecular targets for primary prevention, diagnosis, and treatment (4, 5).

Heme oxygenase 1 (HMOX1) is an anti-oxidant and anti-inflammatory heme-degrading enzyme and the gene is known as a cytoprotective stress response gene (6-8). A dinucleotide repeat (GT)n sequence in the 5' of the promoter region of the HMOX1 gene (rs3074372) modulates gene expression. A long allele (many repeats) has been shown to reduce enzyme activity and associate with various diseases (8, 9). Several studies have previously discussed whether this polymorphism affects COPD and impairs lung function yet with divergent outcomes and conclusions (4).

The main risk factor for COPD is smoking, but several occupational exposures are causally related to COPD (10). Furthermore, a genome-wide interaction study of gene-by-occupational exposure has recently identified new genetic variants associated with the level of forced expiratory volume in the first second of expiration (FEV1), where seven single nucleotide polymorphisms interacted with one of the occupational exposures (11).

In a Danish population-based cohort of 45-84-yearold participants, we previously suggested occupational exposure to vapor, gas, dust, or fume (VGDF) is associated with COPD (12). In this paper, we hypothesise that the effect of a genetic variant may be different in occupationally exposed compared to smoking subjects. This is due to a lower inflammatory effect on lungs by occupational exposure than by individual smoking. Thus, the genetic effect may be more pronounced in unexposed subjects or less occupational exposed subjects.

The aim of this cross-sectional study was first to investigate the association of HMOX1 promoter polymorphism of (GT)n repeats with COPD and second to investigate the presence of a possible gene-by-environment interaction with VGDF and smoking.

Methods

Population

The study population is based on the Danish North Jutland COPD Prevention Study (NCPS), the primary aims of which were to estimate the prevalence of COPD in the Danish population aged 45-84 years and to determine the prevalence of cases without appropriate medical treatment (13). General practitioners (GP) from two former counties in northern Jutland enrolled participants in the period October 2004 - September 2006. Patients listed with participating GP were selected randomly from the Danish Civil Registration System based on the expected prevalence of COPD in sex-specific 10-year age groups. Thus, the sample a priori had an overweight of elderly participants and men. Data were gathered from selfadministered questionnaires (on education, work, family history of lung disease, medical information, smoking and alcohol habits, asthma, and allergy) and medical examinations including spirometry and blood samples. The response rate in the study was 36% (13). We studied occupational VGDF exposure in this cohort and included 4717 participants (12). All participants of non-Scandinavian descent were identified through their names and excluded in the genetic part of the study (N=14).

Lung function and COPD definition

The GPs obtained measures of FEVj and forced vital capacity (FVC) by spirometry. All healthcare staff performing spirometry participated in a one-day training module before entering the study, and all spirometers were calibrated twice every year. A bronchodilator was not administered to all participants; hence, pre-bronchodilator spirometry was used consistently throughout the study. The lower limit of normal (LLN) approach was used to define COPD (14) in a screening setting based on the FEVļ/FVC 2.5th centile (z-score = -1.96) (15). COPD severity was assessed using a detailed grading system based on LLN according to FEVļ. To distinguish subjects with at least moderate airway obstruction, we added the recommended criterion of LLN for FEVj of a z-score = -2.0 (rounded 2.5th centile) (16). As

reference population, we used the Global Lung Function 2012 Equations (15) in the "GLI-2012 Desktop Software for Large Data Sets version 1.3.4 build 3" (17).

Occupational exposure

The duration of occupational exposure (years in occupations with exposure) was used as a proxy for cumulative occupational exposure and assessed based on a self-administered questionnaire of past and present occupations. The lifetime occupational VGDF exposure was divided into: organic dust, inorganic dust, vapor, and gas/fume. To improve the validity of the self-reported exposure information, we restricted such information as to a priori expert-selected jobs with known occupational exposures to VGDF using the Danish adapted version of the International Standard Classification of Occupations, revision 1988 (DISCO-88) (18) (supplementary material www.sjweh.fi/show_abstract.php?abstract_id=3846, table S1). The expert-selected jobs with occupational exposure included 72 of 372 DISCO-88 codes. VGDF exposure was originally assessed in four levels: never, low (<5 years), medium (5-14 years), and high (>15 years) occupational lifetime exposure. VGDF was used as a dichotomized never versus ever (low/medium/high) exposure variable due to power issues when the genetic variant was included.

Genotyping

The repeat polymorphism in the promoter region in HMOX1 (rs3074372, GRCh38:22:35,381,06635,394,213) was amplified by polymerase chain reaction (PCR) using a fluorescent-labelled sense primer (5'-AGAGCCTGCAGCTTCTCAGA-3') and an unlabeled antisense primer (5'-ACAAAGTCTGGCCATAGGAC-3') covering the (GT)n repeats (19-21). The PCR products were subsequently genotyped according to size using an ABI 3730XL DNA Analyzer (Thermo Fischer Scientific, Waltham, MA, USA) using GeneMarker® software (SoftGenetics, State College, PA, USA). The output of each allele GT repeats was blinded and calculated in respect to an internal size standard where 128 base pairs equals 30 GT repeats. Of the blood samples, 31 were missing, 48 were insufficient (eg, serum) and 201 failed in the HMOX1 analysis, which resulted in 4423 participants with a valid HMOX1 genotype. The cut-off of the GT repeats was defined as short (S): <26; medium (M): 27-32; and long (L): >33 GT repeats (21-23). The individual S/M/L genotype was grouped according to an L-dominant genetic model as HMOX1 L- (S/S, S/M, M/M) and HMOX1 L+ (S/L, M/L, L/L) groups.

Smoking

Cumulated smoking estimated as smoked pack-years was categorized into three levels, namely, <10, 10-20, and >20 pack-years. Different types of smoking were converted into number of smoked cigarettes as follows: one cheroot=three cigarettes; one cigar=four cigarettes; one pipe bowl=three cigarettes; and a package of pipe tobacco (50 gram)=17 pipe bowls.

Statistics

Statistical analyses were conducted in Stata 14.2 (StataCorp LP, College Station, TX, USA). The significance level was set at 5%. The 95% confidence interval (CI) was calculated using a normal approximation. The chisquare test for categorical variables was used to assess differences between sub-groups of the study population. Status of Hardy-Weinberg Equilibrium (HWE) was performed among non-COPD participants according to their HMOX1 S/M/L genotype. Associations of the HMOX1 polymorphism with COPD were analyzed in univariate and mixed random effect logistic regression models (24) with GP practice as a random variable. Likelihood-ratio tests were performed for possible gene-by-environment interactions of occupational exposure and smoking, respectively. The odds ratio (OR) from the mixed regression model was adjusted for pack-year, sex, occupational exposure, and age as fixed effects. Additionally, analyses were presented in a separate table as recommended by Knol et al (25), including post-estimation of any additive interaction. We used five regression models to compare no COPD with each level of COPD severity. Sensitivity analyses were performed by restriction according to (i) never smokers; (ii) no prior self-reported asthma; (iii) different dichotomization of occupational VGDF exposure: never/low versus medium/high and never/low/ medium versus high occupational exposure; and (iv) different HMOX1 L± cut-offs according to (GT)n promoter repeats (N=31, 32, 34 and 35). The arguments for these analyses were: (a) to emphasize the a priori assumption of a diverse effect of HMOX1 polymorphism between a large smoking exposure and a low occupational exposure, by excluding the major risk factor of COPD, (b) to avoid the predisposing effect of asthma to COPD in the

analysis (26, 27), (c) to investigate the effect of different levels of occupational exposures in the model, and (d) to analyze the effect of different cut-offs of the HMOX1 repeat polymorphism due to no clear argument for the used HMOX1 cut-offs in the literature.

Ethics

The NCPS study was performed in accordance with the Helsinki Declaration and approved by the Danish Scientific Ethics Committee (VN2003/62) and the Danish Data Protection Agency (2007-41-1576). Written informed consent was obtained from all participants. The Danish Scientific Ethics Committee also approved blood usage in the genetic analyses (N-20130038).

Replication study

The analyses were replicated in the Danish RAV (risk factors for asthma among adults) cohort (28), which is based on the European Community Respiratory Health Survey (ECHRS) protocol (29). Briefly, the RAV cohort, which was designed primarily to identify risk factors for asthma, comprised 20-44-year-old subjects (N=1191) of whom 44% were males, 54% were never smokers, and 30% had ever self-reported asthma. Thirty-four COPD cases were present (3%). In addition, data on lung function, occupational history of the latest ten jobs and blood samples were available. Participants were excluded if they were born outside Scandinavia (N=23); 86 blood samples failed in the HMOX1 analysis. Hence, 1082 participants with a valid HMOX1 genotype were available for analysis.

Results

The study population is characterized in table 1 according to genotype and stratified by presence of the long allele (L± GT33 repeats). The population included 6% with COPD, 48% who had smoked >10 pack-years, and 46% with occupational VGDF exposure. Only the prevalence of asthma and COPD differed between the L- and the L+ genotypes. The (GT)n allelic distribution of the longest allele is shown in figure 1. An HMOX1 L+ genotype was present in 10.6%. HMOX1 L+ in non-COPD participants fulfilled the criteria of being in HWE, P=0.24. The crude association between COPD and a long (GT)n allele (HMOX1 L+) was OR 1.66 (95% CI 1.17-2.34) while the adjusted OR slightly increased OR 1.75 (95% CI 1.18-2.60) (table 2). Additionally increased OR of COPD was observed when having HMOX1 L+ and occupational VGDF exposure together in a gene-by-environment interaction, OR 2.38 (95% CI 1.04-5.46), versus HMOX1 S+M and no exposure. There seemed to be a positive additive interaction as well as a positive interaction on the multiplicative scale between HMOX1 L+ and VGDF exposure (table 3). As the estimated OR exceeded the expected OR, we additionally analyzed the data without any adjustments (supplementary table S2.A) and without the pack-year adjustment (supplementary table S2.B); these estimated OR were 2.75 (95% CI 1.30-5.80) and 2.62 (95% CI 1.15-5.95), respectively.

No significant interaction was seen between the HMOX1 L+ and smoking: HMOX1 and >20 packyears OR 1.13 (95% CI 0.38-3.35), likelihood-ratio test P=0.98 (supplementary table S3).

Sensitivity analyses: (i) Restricted to never smokers, the crude association between COPD and HMOX1 L+ was increased. Excluding sex and age variables in the model among never smokers barely changed the association between COPD and HMOX1 L+, OR 2.39 (95% CI 0.76-7.55); however, the impact of VGDF exposure seemed to decrease, OR 3.35 (95% CI 1.24-9.05). (ii) Among non-asthmatics, the crude association between COPD and HMOX1 L+ was similar to that of all participants, OR 1.69 (95% CI 1.07-2.28). (iii) Changing the occupational exposure to never/low versus medium/high slightly increased the effect of the VGDF and HMOX1 interaction. Comparing with the high exposure the estimate decreased into insignificance. (iv) Different genetic HMOX1 L cut-offs were analyzed. The main cut-off was 33 GT repeats, as shown in figure 1 by the dotted line. Of all the different cut-off models, only the lowest cutoff L+31 was insignificant according to HMOX1. All other models were similar to the used model with 33 GT repeats (L+).

Analysis according to COPD severity and HMOX1 L+ revealed no associations or indication of a trend (data not shown).

Replication study

In the RAV cohort, 19% had occupational VGDF exposure. The median age was 35 (standard deviation 7.0) years and 3% (N=32) had COPD. The (GT)n allelic distribution in the RAV cohort across genotypes (L-: S/S 15%, S/M

47%, M/M 38% and L+: S/L 34%, M/L 63%, L/L 4%) was similar to the NCPS distribution shown in table 1. HMOX1 L+ in non-COPD participants fulfilled the criteria of being in HWE, P=0.74. The estimates are included in table 2, showing no replication of the genetic effect and no replication of the HMOX1-VGDF interaction associated with COPD. Later, we additionally used asthma as outcome in the analysis of the younger RAV cohort since asthma predisposes to COPD. We found an insignificant, positive association with HMOX1 L+, OR 1.15 (95% CI 0.76-1.74).

Discussion

We found an increased risk of COPD in subjects carrying >1 long GT allele in the HMOX1 alone and in a gene-environmental interaction with occupational VGDF exposure. The combined COPD effect exceeded the effect of occupational VGDF exposure alone, suggesting that the association of the long allele of HMOX1 with occupational VGDF exposure is stronger than the association of HMOX1 with smoking between which no significant interaction was observed. The results among never smokers tend to support the association between COPD and HMOX1 L+ (similar OR) and VGDF (increased OR) compared to the main model without gene-environmental interaction (table 2). As asthma predisposes to COPD development (26, 27), analyses performed among non-asthmatics might underestimate the true association. On the other hand, due to the same reason, inclusion of asthmatics might also have overestimated the association. Thus, the best epidemiological estimate probably lies somewhere between the estimates obtained with models including and excluding asthmatics. The insignificance occurred when changing the occupational exposure to never/low/medium versus high exposure could be explained by low power and/or a healthy worker effect (supplementary table S4).

We applied the commonly used cut-off of L+ >33 GT repeats for the HMOX1 promotor polymorphism. However, the model was slightly sensitive for change in HMOX1 L cut-offs between L32 and L35.

Comparable studies in European populations regarding COPD and the (GT)n repeats have been studied. Matokanovic et al (30) found no association between COPD and the length of the GT repeat polymorphism in a small (N=225) Croatian population. In that study, COPD was defined by the GOLD criteria, and the study used cut-offs in GT repeats (S<25, M 26-31, L>32) that were slightly different from ours. Although, Hersh et al (20) found no association between COPD and the previously used S, M, and L groups of GT repeats in HMOX1, they found associations with the two most common single-number of repeats (GT repeats 30 and 31) in two different study populations (case-control and pedigree family-based). These populations included <1000 participants each. Guenegou et al (21) studied associations of GT repeats in HMOX1 and 8-year lung function decline in 749 French participants in the European Community Respiratory Health Survey. L+ allele carriers had a more rapid decline in FEV1/FVC, and this decline was significantly steeper among heavy smokers. Siedlinski et al (22) later replicated these results in a Dutch general population (N=1390). The FEV1 decline was significantly increased in the M/L+L/L genotype, and the decline remained significant in restricted analyses in ever and heavy smokers (22).

In table 3, VGDF+ exposure was stratified within the HMOX1 L± strata, and the estimated OR was 3.30 (95% CI 1.33-8.19) in the HMOX1 L+ exposure group. As smoked pack-years were equally distributed between HMOX1 L± (table 1) and the expected OR according to table 3 would be OR 2.90 (= 3.07/1.06) and lower than the estimated OR, we interpret this stratified estimate as an indication of some interaction between HMOX1 L+ and smoking. To validate this interpretation, we analyzed the data without any adjustments (supplementary table S2.A) and without the pack-year adjustment (supplementary table S2.B); the calculated estimated OR were 2.75 (95% CI 1.30-5.80) and 2.62 (95% CI 1.15-5.95), respectively. Since these OR were more in line with the expected values, the data suggest that HMOX1 L+ interacts to a smaller extent with smoking than with VGDF in a gene-by-environmental pathway with COPD, see supplementary table S3; interaction between HMOX1 and >20 pack-years OR 1.13 (95% CI 0.38-3.35). We interpret this as the intense smoking exposure is less modified by the presence of HMOX1 L+, than the low-dose environmental exposures, eg, occupational exposure. Both additive and multiplicative statistical interactions of VGDF and HMOX1 were present (table 3). The additive estimate of interaction suggests the presence of a mechanistic interaction as a sufficient cause interaction, equally the relative excess risk due to interaction (RERI)>1. Although, RERI is not significant as the lower 95% CI are <1. Nevertheless, the biological role of HMOX1 appears rather well documented (31, 32), suggesting that our finding does represent a biological effect.

Two studies combined the promoter GT repeats in HMOX1 and lung function with other exposures of ozone (33) and PM10 (particulate matter <10 pm) (23). These studies point in the same direction as our study despite different L cut-offs, exposures and outcomes. Thus indicative of, a HMOX1 promoter polymorphism association with exogenous exposure.

Strengths and limitations

The strengths of the present study are its size, the expertvalidated occupational exposures, and that genotyping was validated in a blinded setting. Ethnic variability was restricted although non-differential misclassification might occur. Another limitation is that we did not include other genetic risk factors that might affect the association with the VGDF exposure and HMOX1 interaction.

Of the samples in the HMOX1 analysis, 201 (NCPS) and 86 (RAV) failed, however, we deem the analytical success rate (95%) to be acceptable. The failed HMOX1 data not included in the analysis were equally distributed among plates. Among the study participants, there were more young women and fewer participants in the oldest group than among non-responders. This might introduce an age-dependent healthier study population, which would tend to underestimate the associations. The use of a spirometrically defined outcome of COPD implies that some COPD patients with compliance difficulties might have been excluded from the analysis, resulting in biased associations. Possible information bias of occupational VGDF exposure was reduced by using independent, specialist-assessed exposure based on job titles. The external study validity is considered good in a Western world setting with a similar occupational distribution and a Northern European genetic structure.

Replication

Although the distribution of HMOX1 genotypes was similar in RAV and NCPS, no associations were seen in the RAV cohort. We attribute this to the smaller study size and lower VGDF exposure in RAV and the short time period for development of COPD in this cohort. A priori, we assumed that the HMOX1 repeat polymorphism would be associated with COPD and not interact with occupational exposure. However, in the younger RAV cohort with less occupational exposure, HMOX1 L+ was inversely associated with COPD, and our data regrettably lacked power to analyze for the combined exposure. Although insignificant, the finding according to asthma might suggest that in this young cohort, an association could be relevant between HMOX1 L+ and obstructive lung disease.

To our knowledge, this is the largest populationbased study analyzing promoter repeats in HMOX1. However, our findings would benefit from other replication studies with more VGDF exposure in an older cohort than the present study.

The intension of social threshold values as a tool for primary prevention is that workers doing their job will not be at increased risk of disease from occupational exposure, not even if they are genetically susceptible. The data may suggest that the actual threshold values ought to be lowered to meet the intension of the current labor market regulations. Moreover, the genetic marker may inform secondary prevention measures in workers with lung symptoms exposed to VGDF. Subjects with long GT alleles in HMOX1 may be more susceptible and would benefit from shifting to other work tasks with less VGDF exposure.

Concluding remarks

The present data support an association between subjects with a long GT allele in HMOX1 and COPD. A long GT allele in HMOX1 seems furthermore to interact with occupational VGDF exposure in a gene-by-occupational setting. We propose that the positive association with a long GT allele in HMOX1 may be a new genetic contributor to the pathogenesis of COPD. Additionally, the HMOX1 interaction with occupational VGDF exposure provide an argument for VGDF exposure level regulation in respect of primary and secondary prevention.

Acknowledgements

The authors wish to acknowledge collaborators who participated in the study, the general practitioners who collected data, biostatistical assistance from the Unit of Epidemiology and Biostatistics, Aalborg University Hospital, and the effort of additional members of the RAV study group for making the RAV cohort available for analysis.

Sidebar

Correspondence to: Else Toft Würtz, Department of Occupational and Environmental Medicine, Danish Ramazzini

Centre, Aalborg University Hospital, Havrevangen 1,4, 9000 Aalborg, Denmark. [E-mail: etw@rn.dk]

References

References

1. Eisner MD, Anthonisen N, Coultas D, Kuenzli N, PerezPadilla R, Postma D et al.; Committee on Nonsmoking COPD, Environmental and Occupational Health Assembly. An official American Thoracic Society public policy statement: novel risk factors and the global burden of chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2010 Sep;182(5):693-718. https://doi. org/10.n64/rccm.200811-1757ST.
2. Lieberman J, Winter B, Sastre A. Alpha 1-antitrypsin Pitypes in 965 COPD patients. Chest 1986 Mar;89(3):370-3. https://doi.org/10.1378/chest.89.3 370.
3. Dahl M, Tybjaerg-Hansen A, Lange P, Vestbo J, Nordestgaard BG. Change in lung function and morbidity from chronic obstructive pulmonary disease in alpha1antitrypsin MZ heterozygotes: A longitudinal study of the general population. Ann Intern Med 2002 Feb;136(4):270-9. https://doi.org/10.7326/0003-4819-136-4-20020219000006.
4. Bossé Y. Updates on the COPD gene list. Int J Chron Obstruct Pulmon Dis 2012;7:607-31. https://doi. org/10.2147/COPD.S35294.
5. Agustí A, Celli B. Natural history of COPD: gaps and opportunities. ERJ Open Res 2017 Dec;3(4):00117-02017. https://doi.org/10.n83/23120541.00117-2017.
6. Raval CM, Lee PJ. Heme oxygenase-1 in lung disease. Curr Drug Targets 2010 Dec;11(12):1532-40. https://doi.org/10. 2174/1389450111009011532.
7. Wegiel B, Hauser CJ, Otterbein LE. Heme as a danger molecule in pathogen recognition. Free Radic Biol Med 2015 Dec;89:651-61. https://doi.org/10.1016/j. freeradbiomed.2015.08.020.
8. Riquelme SA, Carreño LJ, Espinoza JA, Mackern-Oberti JP, Alvarez-Lobos MM, Riedel CA et al. Modulation of antigen processing by haem-oxygenase 1. Implications on inflammation and tolerance. Immunology 2016 Sep;149(1):1-12. https://doi.org/10.1111/imm.12605.
9. Exner M, Minar E, Wagner O, Schillinger M. The role of heme oxygenase-1 promoter polymorphisms in human disease. Free Radic Biol Med 2004 Oct;37(8): 1097-104. https://doi.org/10.1016/j.freeradbiomed.2004.07.008.
10. Omland O, Würtz ET, Aasen TB, Blanc P, Brisman JB, Miller MR et al. Occupational chronic obstructive pulmonary disease: a systematic literature review. Scand J Work Environ Health 2014 Jan;40(1):19-35. https://doi. org/10.5271/sjweh.3400.
11. de Jong K, Vonk JM, Timens W, Bosse Y, Sin DD, Hao K, et al. Genome-wide interaction study of gene-by-occupational exposure and effects on FEV1 levels. J Allergy Clin Immunol. 2015;136(6):1664-72.
12. Würtz ET, Schlünssen V, Malling TH, Hansen JG, Omland Ø. Occupational chronic obstructive pulmonary disease in a danish population-based study. COPD 2015 Aug;12(4):43543. https://doi.org/10.3109/15412555.2014.974739.
13. Hansen JG, Pedersen L, Overvad K, Omland Ø, Jensen HK, Sørensen HT. The Prevalence of chronic obstructive pulmonary disease among Danes aged 45-84 years: population-based study. COPD 2008 Dec;5(6):347-52. https://doi.org/10.1080/15412550802522635.
14. Pellegrino R, Viegi G, Brusasco V, Crapo RO, Burgos F, Casaburi R et al. Interpretative strategies for lung function tests. Eur Respir J 2005 Nov;26(5):948-68. https://doi.org/1 0.1183/09031936.05.00035205.
15. Quanjer PH, Stanojevic S, Cole TJ, Baur X, Hall GL, Culver BH et al.; ERS Global Lung Function Initiative. Multi-ethnic reference values for spirometry for the 3-95yr age range: the global lung function 2012 equations. Eur Respir J 2012 Dec;40(6):1324-43. https://doi. org/10.1183/09031936.00080312.
16. Quanjer PH, Pretto JJ, Brazzale DJ, Boros PW. Grading the severity of airways obstruction: new wine in new bottles. Eur Respir J 2014 Feb;43(2):505-12. https://doi. org/10.1183/09031936.00086313.
17. The Global Lung Function Initiative. [cited 2014 April 28]. Available from: http://www.lungfunction.org/.
18. Statistics Denmark. The Danish version of the International Standard of Occupations, version-88 (DISCO-88). [cited 2014 November 26]. Available from: http://www.dst.dk/da/ Statistik/dokumentation/Nomenklaturer/DISCO-88.aspx.

19. Yamada N, Yamaya M, Okinaga S, Nakayama K, Sekizawa K, Shibahara S et al. Microsatellite polymorphism in the heme oxygenase-1 gene promoter is associated with susceptibility to emphysema. Am J Hum Genet 2000 Jan;66(1):187-95. https://doi.org/10.1086/302729.
20. Hersh CP, Demeo DL, Lange C, Litonjua AA, Reilly JJ, Kwiatkowski D et al. Attempted replication of reported chronic obstructive pulmonary disease candidate gene associations. Am J Respir Cell Mol Biol 2005 Jul;33(1):718. https://doi.org/10.1165/rcmb.2005-0073OC.
21 . Guénégou A, Leynaert B, Bénessiano J, Pin I, Demoly P, Neukirch F et al. Association of lung function decline with the heme oxygenase-1 gene promoter microsatellite polymorphism in a general population sample. Results from the European Community Respiratory Health Survey (ECRHS), France. J Med Genet 2006 Aug;43(8):e43. https:// doi.org/10.1136/jmg.2005.039743.
22. Siedlinski M, van Diemen CC, Postma DS, Boezen HM. Heme oxygenase 1 variations and lung function decline in smokers: proof of replication. J Med Genet 2008 Jun;45(6):400. https://doi.org/10.1136/jmg.2008.058123.
23. Curjuric I, Imboden M, Schindler C, Downs SH, Hersberger M, Liu SL et al.; SAPALDIA team. HMOX1 and GST variants modify attenuation of FEF25-75% decline due to PM10 reduction. Eur Respir J 2010 Mar;35(3):505-14. https://doi.org/10.1183/09031936.000443-2009.
24. Rabe-Hesketh S, Skrondal A. Multilevel and Longitudinal Modeling Using Stata. 3rd ed. College Station, Texas: Stata Press; 2012.
25. Knol MJ, VanderWeele TJ. Recommendations for presenting analyses of effect modification and interaction. Int J Epidemiol 2012 Apr;41(2):514-20. https://doi.org/10.1093/ ije/dyr218.
26. Rasmussen F, Taylor DR, Flannery EM, Cowan JO, Greene JM, Herbison GP et al. Risk factors for airway remodeling in asthma manifested by a low postbronchodilator FEV1/ vital capacity ratio: a longitudinal population study from childhood to adulthood. Am J Respir Crit Care Med 2002 Jun;165(11):1480-8. https://doi.org/10.1164/rccm.2108009.
27. von Mutius E. Childhood experiences take away your breath as a young adult. Am J Respir Crit Care Med 2002 Jun;165(11):1467-8. https://doi.org/10.1164/rccm.2204011.
28. Malling TH, Sigsgaard T, Andersen HR, Frischknecht L, Deguchi Y, Skadhauge L et al. Sex determines the influence of smoking and gene polymorphism on glutathione peroxidase activity in erythrocytes. Scand J Clin Lab Invest 2009;69(2):295-302. https://doi. org/10.1080/00365510802632155.
29. Burney PG, Luczynska C, Chinn S, Jarvis D. The european community respiratory health survey. Eur Respir J 1994 May;7(5):954-60. https://doi.org/10.1183/09031936.94.07 050954.
30. Matokanović M, Rumora L, Popović-Grle S, Čepelak I, Čulić O, Barišić K. Association of hsp70-2 (+1267A/G), hsp70-hom (+2437T/C), HMOX-1 (number of GT repeats) and TNF-alpha (+489G/A) polymorphisms with COPD in Croatian population. Clin Biochem 2012 Jul;45(10-11):7704. https://doi.org/10.1016/j.clinbiochem.2012.04.003.
31. Fredenburgh LE, Perrella MA, Mitsialis SA. The role of heme oxygenase-1 in pulmonary disease. Am J Respir Cell Mol Biol 2007 Feb;36(2):158-65. https://doi.org/10.1165/ rcmb.2006-0331TR.
32. Haines DD, Lekli I, Teissier P, Bak I, Tosaki A. Role of haeme oxygenase-1 in resolution of oxidative stress-related pathologies: focus on cardiovascular, lung, neurological and kidney disorders. Acta Physiol (Oxf) 2012 Apr;204(4):487501. https://doi.org/10.1111/j.1748-1716.2011.02387.x.
33.Alexeeff SE, Litonjua AA, Wright RO, Baccarelli A, Suh H, Sparrow D et al. Ozone exposure, antioxidant genes, and lung function in an elderly cohort: VA normative aging study. Occup Environ Med 2008 Nov;65(11):736-42. https://doi.org/10.1136/oem.2007.035253.
Received for publication: 9 April 2019

DETAILS

Subject:	Obstructive lung disease; Population; Airway management; Software; Dust; Random variables; Fumes; Disease; Stress response; Alleles; Chronic obstructive pulmonary disease; Confidence intervals; Genotype &phenotype; Statistical analysis; Employment; Polymorphism; Gene expression; Cigarettes; Smoking; Occupational exposure; Vapors; Exposure; Health risk assessment; Lung diseases; Occupational health; Heme; Pathogenesis; Regression analysis; Occupations; Enzymes; Population studies; Oxygenase
Location:	Jutland; United States--US
Publication title:	Scandinavian Journal of Work, Environment &Health; Stockholm
Volume:	46
Issue:	1
Pages:	96-104
Publication year:	2020
Publication date:	2020
Section:	Original article
Publisher:	Scandinavian Journal of Work, Environment &Health
Place of publication:	Stockholm
Country of publication:	Finland, Stockholm
Publication subject:	Occupational Health And Safety
ISSN:	03553140
e-ISSN:	1795990X
Source type:	Scholarly Journ al
Language of publication:	English
Document type:	Journal Article
DOI:	https://doi.org/10.5271/sjweh.3846
ProQuest document ID:	2344259877
Document URL:	https://www.proquest.com/scholarly-journals/heme-oxygenase-1-polymorphism-occupational-vapor/docview/2344259877/se-2?accountid=211160
Copyright:	Copyright Scandinavian Journal of Work, Environment &Health 2020

Last updated:	2020-01-24
Database:	Public Health Database

Sedentary work and risk of venous thromboembolism

Johannesen, Camilla Ditlev Lindhardt, MSc [1] ; Flachs, Esben Meulengracht, PhD [1] ; Ebbehøj, Niels E, DMSc [1] ; Marott, Jacob Louis, MSc [2] ; Jensen, Gorm Boje, DMSc [2] ; Nordestgaard, Børge G, DMSc; Schnohr, Peter, DMSc; Bonde, Jens Peter E, PhD [1] Department of Occupational and Environmental Medicine, Bispebjerg and Frederiksberg Hospital, Denmark [2] Copenhagen City Heart Study, Frederiksberg University Hospital, Denmark

ABSTRACT (ENGLISH)

Objective Prolonged seated immobility during long-distance flights is related to an increased risk of venous thromboembolism (VTE), but little, if anything, is known about the risk related to sedentary work. The objective of this paper was to examine the risk of VTE according to sitting posture at work. Methods This prospective study includes a total of 78 936 participants from the Copenhagen City Heart Study and the Copenhagen General Population Study, all without previous thromboembolic events and aged <65 years. An assessment of the number of hours spent in sitting position at work was assigned each participant at baseline using a job exposure matrix. VTE was identified through national patient registries. Survival analyses were performed to determine the risk of VTE according to sedentary position at work with adjustment for a range of known determinants including lifestyle and coagulation factors. Results During the follow-up period of 582 411 person years (mean follow-up, 7.4 years) 911 participants experienced their first VTE event. Multivariable adjusted analyses showed no difference in risk of VTE between occupational sitting >6.5 hours/day and occupational sitting <3.5 hours/day (hazard ratio 1.11, 95% confidence interval 0.92-1.34). Conclusion This study does not support the hypothesis that sedentary work is a risk factor for VTE in the general population. Whether certain occupations with particularly high exposure to immobilized sitting positions are associated with thromboembolic events is not addressed.

FULL TEXT

Headnote

Johannesen CDL, Flachs EM, Ebbehøj NE, Marott JL, Jensen GB, Nordestgaard BG, Schnohr P, Bonde JPE. Sedentary work and risk of venous thromboembolism. Scand J Work Environ Health. 2019;46(1): 69-76. doi:10.5271/sjweh.3841

Objective Prolonged seated immobility during long-distance flights is related to an increased risk of venous thromboembolism (VTE), but little, if anything, is known about the risk related to sedentary work. The objective of this paper was to examine the risk of VTE according to sitting posture at work.
Methods This prospective study includes a total of 78 936 participants from the Copenhagen City Heart Study and the Copenhagen General Population Study, all without previous thromboembolic events and aged <65 years. An assessment of the number of hours spent in sitting position at work was assigned each participant at baseline using

a job exposure matrix. VTE was identified through national patient registries. Survival analyses were performed to determine the risk of VTE according to sedentary position at work with adjustment for a range of known determinants including lifestyle and coagulation factors.

Results During the follow-up period of 582 411 person years (mean follow-up, 7.4 years) 911 participants experienced their first VTE event. Multivariable adjusted analyses showed no difference in risk of VTE between occupational sitting >6.5 hours/day and occupational sitting <3.5 hours/day (hazard ratio 1.11, 95% confidence interval 0.92-1.34).

Conclusion This study does not support the hypothesis that sedentary work is a risk factor for VTE in the general population. Whether certain occupations with particularly high exposure to immobilized sitting positions are associated with thromboembolic events is not addressed.

Key terms occupational exposure; thrombosis; VTE.

Venous thrombosis is the formation of a blood clot in one of the deep veins, usually in the lower limbs. If detached an embolus is transported in the veins and may become lodged in the lungs. Venous thromboembolism (VTE), comprising deep vein thrombosis and pulmonary embolism, is reported with an incidence of about 1.5 per 1000 individuals per year in high-income countries (1).

VTE has a multifactorial pathogenesis encompassing both inherited and acquired conditions, eg, prolonged immobility, including surgery and hospitalization, malignancy, obesity, hormone therapy, oral contraception and Factor V Leiden gene mutation (2-8). Virchow's triad describes three main causes of deep vein thrombosis: changes in blood flow, alterations in blood viscosity, and abnormalities in the vessel wall (9, 10). Prolonged standing is thought to increase risk of venous insufficiency, which can cause leg oedema, heaviness, and dermatitis. Prolonged sitting may cause vein compression, which reduces blood flow and thereby increases the risk of VTE.

Seated immobility thromboembolism is a term used for all occurrences of VTE related to prolonged seated immobility during travel, work and recreation. A wellknown risk factor to seated immobility thromboembolism is long-distance air travel (10-12), while a possible association to prolonged immobility related to work and computer use has been studied to a lesser extent. Initially an association was recognized in a number of case reports and a case series (13-18). Since, three New Zealand case-control studies have reported one significant multivariate odds ratio (OR) for VTE of 2.8 [95% confidence interval (CI) 1.2-6.1], but insignificant multivariate OR for VTE in both the first and the latest study (19-21). All three studies reported an increased risk of VTE by 8-10% per hour longer sitting. The two latest of these studies considered occupational groups as well and found no association in the multivariate analyses (20, 21). A Polish study has found computer use to be a predictor of seated immobility thromboembolism and an American study has found a positive association between TV viewing and VTE risk (22, 23). A Danish register-based cohort study found that sedentary workers, defined by different driver occupations, have a higher risk of VTE than workers with dynamic exertion at work, with a relative risk of 1.13 (95% CI 0.99-1.29) (24).

Considering these findings and the overall frequency of sedentary occupations, the objective of this paper is to examine if sedentary occupational activity increases the risk of VTE compared to non-sedentary occupational activity while taking advantage of the strengths of this study compared to earlier studies. These strengths comprise the study size, the long follow-up time and the large range of potential confounding factors including individual risk factors.

Methods

The study population

The present study used data from two Danish prospective cohort studies: the Copenhagen City Heart Study and the Copenhagen General Population Study. Participants invited to the studies were aged >20 years and randomly selected from the national Danish Civil Registration System (7, 25). The Copenhagen City Heart Study was initiated in 1976-1978, with follow-up examinations in 1981-1983, 1991-1994, and 2001-2003, each of which invited new participants to further supplement the cohort. The Copenhagen General Population study was initiated in 2003 with ongoing enrolment. Both studies obtained data from self-administered questionnaires, reviewed by an examiner, physical examinations, and blood samples.

Participants with a VTE diagnose prior to examination date were excluded together with participants aged >65 years as this is the standard retirement age in Denmark (figure 1). Eligible participants were followed from 1 January 1977 or the date of entry into the study, whichever came latest, until one of the following occurred: first VTE event, death, emigration, age 65 or end of follow-up (31 December 2015).

Venous thromboembolic events

Information on deep vein thrombosis and pulmonary embolism diagnoses were obtained from the National Patient Registry, containing information on all in and out patient contacts in Denmark from 1 January 1977 until 9 March 2017, and the Danish Register of Causes of Death, containing information on all deaths in Denmark from 1 January 1977 until 31 December 2015. International Classification of Disease (ICD) codes were used to identify events, ICD-8 codes classifying diagnoses in the time period 1977-1993 and ICD-10 codes from of 1 January 1994 (ICD-8 codes 451.00, 451.08-09, 451.90, 451.92, 671.01-03 and 671.08-09 for deep vein thrombosis and 450.99 and 673.99 for pulmonary embolism; ICD-10 codes I80.1-3, O22.3 and O87.1 for deep vein thrombosis and I26.0, I26.9 and O88.2 for pulmonary embolism).

Occupational sitting

We constructed a job exposure matrix (JEM) linking occupational sitting hours to the Danish version of Standard Classification of Occupations (DISCO) using data from the Danish Work Environmental Cohort Study (26). The Danish Work Environmental Cohort Study systematically maps health and working conditions among Danish employees and takes place every fifth year (since 1990) and comprising information on >10 000 adults in Denmark. Through questionnaires occupational sitting was measured by the question "Does your job involve sitting?" and the following six response categories: almost all the time, approximately ¾of the time, approximately ½of the time, approximately ¼of the time, rarely, and never. As a standard Danish working day is 8 hours, this was converted into the corresponding values: 8, 6, 4, 2, and 0 hours. The JEM was defined as the mean of self-reported occupational sitting hours within every DISCO code and linked to the study population. A categorical variable was then created dividing occupational sitting hours in three with the following cut-offs: >6.5, 3.5-6.5, and <3.5 hours, the first category representing sedentary work.

Covariates

Information on age and sex was obtained from the social security number. The self-registered questionnaire provided baseline information on smoking status (divided into never, former, and current smokers), alcohol intake (daily, weekly, monthly, or never), leisure time activity level per week (<2 hours exercise, 2-4 hours light exercise, 2-4 hours demanding exercise or >4 hours exercise), education (<9 years for elementary, 10-12 years for high school, or >12 years for academic), use of hormones (oral contraception and oestrogens) and menopause (yes/no). At the physical examinations height (m), weight (kg) and systolic/diastolic blood pressure (mmHg) was measured (25). Body mass index (BMI) was calculated as weight (in kg) divided by height (in meters) squared. Biochemical analysis of blood samples provided data on blood concentrations of the following constituents considered of interest for this study: total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides, glucose, C-reactive protein, erythrocyte volume fraction, thrombocytes, coagulation factors II+VII+X, fibrinogen, complement C3, and Factor V Leiden (8, 27, 28). Information on cancer, cardiovascular disease, major surgery, and births was collected from the National Patient Registry.

Statistical analyses

Throughout analyses, data from the first examination the participants attended was used and the continuous variables systolic and diastolic blood pressures, BMI and blood concentrations were divided into tertiles (table 1 and supplementary tables S1-2, www.sjweh.fi/ show_abstract.php?abstract_id=3841). Time-dependent risk factors include three binary (0/1) variables; one taking the value 1 within one year before or after the onset of any cancer, another takes the value 1 within three months before any major surgery and the third takes the value 1 nine months before or 3 months after giving birth (table 1). A categorical variable, divided into decades, was created on basis of examination date to adjust for calendar time.

Cox proportional hazards models were fitted, allowing for time varying covariates, with age as time scale. Results

were reported as hazard ratios (HR) with 95% CIs and throughout analyses the group of less occupational sitting (<3.5 hours) was used as reference. Some of the well-established risk factors for VTE were selected a priori to an initial multivariate model including age, sex, smoking status, education, use of hormones, BMI, cancer, cardiovascular disease, births, and major surgery. With respect to the initial model remaining covariates, except Factor V Leiden, were tested stepwise, including only those with a statistical significance level <0.01 in the final model. A priori defined interaction terms were added to the final model to test for interactions between occupational sitting and leisure time activity level, BMI, sex, and age, respectively.

To ensure correct assumptions to the final model several sensitivity analyses were carried out, including Factor V Leiden, genotyped in 55% of the population, analysis on imputed data and starting the risk time at the age of 50 years as it is expected that most events will occur at older ages.

Imputation on missing values was performed by Markov chain Monte Carlo method with all variables of the final models as predictors.

All statistical analyses were performed in SAS 9.4 statistical software (SAS Institute, Cary, NC, USA).

Results

A total of 78 936 eligible participants were included in the study. Of these, 897 (1%) were drivers, 24 577 (31%) were sitting >6.0 hours equaling ¾of the workday, and 9090 (11%) were categorized in occupational sitting >6.5 hours (table 1). The follow-up period was 582 411 person years in total (mean follow-up, 7.4 years) and 79% of the participants had <10 years of follow-up. During this time, 911 participants experienced their first venous thromboembolic event with an average age of 48.3 years (table 2). Complete case data consists of 60 120 (76%) participants, blood samples account for 80% of the missing data and smoking status 14%. Wellestablished risk factors were found to be associated to increased risk of thromboembolic events (figure 2).

Venous thromboembolism and occupational sitting (complete case analyses)

Univariate analyses showed a decreased risk of thromboembolic events in employees with sedentary work, but when adjusting for covariates no association was found (table 3). Multivariate analyses showed insignificant HR of 1.11 (95% CI 0.92-1.34) for occupational sitting >6.5 hours/day and 0.94 (0.83-1.07) for occupational sitting 3.5-6.5 hours/day.

Within the group of high occupational sitting (>6.5 hours), the three most frequent DISCO classifications are accounting, sales, and financing which represents 33%.

Interactions

No significant interactions between occupational sitting and the covariates sex, age, BMI, and activity level in leisure time, respectively, were found.

Sensitivity analyses

When further adjusting for Factor V Leiden or changing retirement age from 65 to either 60 or 70 years results were consistent. Imputation of the missing data yielded a borderline insignificant HR of 1.16 (95% CI 1.00-1.36) for occupational sitting >6.5 hours (table 3), resembling primary results.

At least two examinations are available for 12% of the study population (N=9 766), and, of these, 10% changed category of occupational activity to less active, 9% changed to more active, and 81% remained in the same category of occupational activity. Inclusion of data from repeated examinations, thereby allowing participants to change level of occupational sitting and covariate status during the follow up period, resulted in a HR of 1.21 (95% JI 0.75-1.95) for occupstionsl sitting >6.5 hours, similar to the primary results.

Participants aged >50 ynsrs account for 657 nvnnts (72%) and 332 296 (57%) years of follow-up. Results from analyses on this subgroup yielded a HR of 1.07 (95% JI 0.87-1.33) for occupational sitting >6.5 hours, consistent with primary results.

Discussion

This study does not support the hypothesis that sedentary work is a risk factor for VTE in the general population. This study found that 31% of the population sits more than ¾of their workday, which is in line with previous findings (29). Several studies have indicated that prolonged immobility related to work and computer use is a risk factor for

VTE, considering a minimum of 8 hours sitting during a day, whereas the present study has a cut-off at 6.5 hours sitting in the group of high occupational sitting and moreover did not account for immobilized sitting (19-22). It is possible that it is the quantity of prolonged sitting within a sedentary occupation, which increases the risk of VTE; as suggested by Healy et al (20) who found an increased risk of VTE for every hour longer sitting and for those who ate lunch at their desk (20).

When considering occupational groups Healy et al and Braithwaite et al found no association between occupations classified as sedentary and VTE (19-22). However, their classification put drivers into the less sedentary category, which is inconsistent with Suadicani et al (24) who found an increased risk of VTE in a sedentary occupational group based on drivers of various vehicles. This shows that the definition of a sedentary occupation might vary somewhat across studies. In the present study, no sub analyses on drivers were carried out as they represent 1% only of the study population. The three most frequent occupations in the high sedentary work group represent one third and are high-skilled white-collar workers, thus sedentary work represents a wide-range category of primarily office work, which might involve frequent interruptions, resulting in an attenuation of a possible association.

Blood samples representing the majority of missing data were added in the latest examination round, and thus not examined in participants only attending the first rounds of examination. Furthermore, the vast majority in these rounds are newly invited participants. Therefore, analyses of blood samples for fibrinogen, coagulation factors II+VII+X, thrombocytes, C-reactive protein, blood complement C3, and Factor V Leiden are presumed to be missing at random (supplementary table S2). As results on imputed analysis resembles results from primary complete case analyses this presumption is validated.

The highest age group has a comparatively low HR (figure 2). Participants are invited to the examinations regardless of labor market participation, but those of the invited who participate might represent the healthier part, thus suggesting a healthy participant effect.

Information on traumas and long-term hospitalizations, representing possible confounders, is not available in the present study. By including major surgery, though, a part of these cases might be addressed.

Strengths

The size of the cohort is a major strength of the study. So is the prospective design in which data on occupational sitting was collected before onset of a VTE diagnosis, excluding participants with a VTE episode prior to start of follow-up. Contrary to earlier studies, it was possible to adjust for a large number of confounders. Significant increased risk of VTE found in covariates that are wellestablished risk factors for VTE supports the validity of the present study.

Limitations

Although the category of highest occupational sitting (>6.5 hours/day) only constitutes 11% of the study population, it might represent a too wide-range group of occupations, thereby reducing the feasibility to identify potential associations between some highly sedentary occupational groups, eg, drivers, and VTE

Using self-reported occupational sitting hours may potentially lead to misclassification bias, but when used in large population-based studies, an acceptable validity to this measure has been reported (30, 31).

VTE diagnoses in the National Danish Patient Registry have reported a positive predictive value of 0.59 (32). If random, this would not affect the results. However, the positive predictive value was found to be lower among women compared to men. This introduces a potential for misclassification bias as there is an uneven distribution of sex across categories of occupational sitting hours. For example, women representing a smaller part in the highest occupational sitting category (>6.5 hours/day) than the less occupational sitting category (<3.5 hours/day), causing the positive predictive value to be lower for physically active work than sedentary work, may bias effect estimates towards the null.

The analyses were based on data from the first examination as follow-up examinations are only available for 12% of the participants and, therefore, do not consider any changes in occupational sitting over time. However, 81% in the subset of participants with at least two consecutive examinations remained in the same category of occupational sitting. Furthermore, as there are about ten years between consecutive examinations and 79% of the participants

had a follow-up period of ten years or less, considering baseline data only most likely does not change the data for analyses in the greater part of the study population. In addition, results from the sensitivity analyses including activity level data from repeated examinations are similar to those for the primary results.

The study includes mainly Caucasians of European descent, recruited from the Metropolitan region in Denmark. All categories of occupational sitting are represented, and we are not to believe that risk profiles should change across the country. There is no data suggesting different outcomes in other populations.

Concluding remarks

The findings of this study indicate that there is no link between sedentary work and the risk of VTE when sedentary work is defined as occupational sitting >6.5 hours/day. More studies should address the risk of VTE in selected highly immobilized occupations such as drivers.

Ethics

All participants in the Copenhagen City Heart Study and the Copenhagen General Population Study gave informed consent.

This study complies with the Declaration of Helsinki and was approved by Frederiksberg, Herlev and Gentofte Hospital and Danish ethics committees (ID of approval: H-KF-01-144/01).

Acknowledgement

We thank staff and participants of the Copenhagen City Heart Study and the Copenhagen General Population Study for their contributions.

The study was funded by a scientific scholarship from Bispebjerg and Frederiksberg University Hospital. The Copenhagen City Heart Study is supported by the Danish Heart Association and The Metropolitan Region of Denmark.

Sidebar

Correspondence to: Camilla Ditlev Lindhardt Johannesen, Department of Occupational and Environmental Medicine, Frederiksberg and Bispebjerg Hospital, Bispebjerg Bakke 23, DK-2400 Copenhagen NV, Denmark. [E-mail: cjoh0108@regionh.dk]

References

References

1. Raskob GE, Angchaisuksiri P, Blanco AN, Buller H, Gallus A, Hunt BJ et al.; ISTH Steering Committee for World Thrombosis Day. Thrombosis: a major contributor to global disease burden. Arterioscler Thromb Vasc Biol 2014 Nov;34(11):2363-71. https://doi.org/10.1161/ ATVBAHA.114.304488.

2. Heit JA, Silverstein MD, Mohr DN, Petterson TM, O'Fallon WM, Melton LJ 3rd. Risk factors for deep vein thrombosis and pulmonary embolism: a population-based case-control study. Arch Intern Med 2000 Mar;160(6):809-15. https:// doi.org/10.1001/archinte.160.6.809.

3. Holst AG, Jensen G, Prescott E. Risk factors for venous thromboembolism: results from the Copenhagen City Heart Study. Circulation 2010 May;121(17):1896-903. https://doi. org/10.1161/CIRCULATIONAHA.109.921460.

4. Scarabin PY. Hormones and venous thromboembolism among postmenopausal women. Climacteric 2014 Dec;17 Suppl 2:34-7. https://doi.org/10.3109/13697137.2014.9567 17.

5. van Hylckama Vlieg A, Helmerhorst FM, Vandenbroucke JP, Doggen CJ, Rosendaal FR. The venous thrombotic risk of oral contraceptives, effects of oestrogen dose and progestogen type: results of the MEGA case-control study. BMJ 2009 Aug;339:b2921. https://doi.org/10.1136/bmj. b2921

6. Folsom AR, Cushman M, Tsai MY, Aleksic N, Heckbert SR, Boland LL et al. A prospective study of venous thromboembolism in relation to factor V Leiden and related factors. Blood 2002 Apr;99(8):2720-5. https://doi. org/10.1182/blood.V99.8.2720.

7. Klovaite J, Benn M, Nordestgaard BG. Obesity as a causal risk factor for deep venous thrombosis: a Mendelian randomization study. J Intern Med 2015 May;277(5):57384. https://doi.org/10.1111/joim.12299

8. Juul K, Tybjaerg-Hansen A, Schnohr P, Nordestgaard BG. Factor V Leiden and the risk for venous thromboembolism in the adult Danish population. Ann Intern Med 2004 Mar;140(5):330-7.

https://doi.org/10.7326/0003-4819-1405-200403020-00008.
9. Rosendaal FR. Venous thrombosis: a multicausal disease. Lancet 1999 Apr;353(9159):1167-73. https://doi.org/10.1016/S0140-6736(98)10266-0.
10. Johnston RV, Hudson MF; Aerospace Medical Association Air Transport Medicine Committe. Travelers' thrombosis. Aviat Space Environ Med 2014 Feb;85(2):191-4. https://doi. org/10.3357/ASEM.3822.2014.
11. Cannegieter SC, Doggen CJ, van Houwelingen HC, Rosendaal FR. Travel-related venous thrombosis: results from a large population-based case control study (MEGA study). PLoS Med 2006 Aug;3(8):e307. https://doi.org/10.1371/journal.pmed.0030307.
12. Chandra D, Parisini E, Mozaffarian D. Meta-analysis: travel and risk for venous thromboembolism. Ann Intern Med 2009 Aug;151(3):180-90. https://doi.org/10.7326/00034819-151-3-200908040-00129.
13. Aldington S, Pritchard A, Perrin K, James K, Wijesinghe M, Beasley R. Prolonged seated immobility at work is a common risk factor for venous thromboembolism leading to hospital admission. Intern Med J 2008 Feb;38(2): 133-5. https://doi.org/10.1111/j.1445-5994.2007.01597.x.
14. Beasley R, Heuser P, Raymond N. SIT (seated immobility thromboembolism) syndrome: a 21st century lifestyle hazard. N Z Med J 2005 Apr;118(1212):U1376.
15. Beasley R, Raymond N, Hill S, Nowitz M, Hughes R. eThrombosis: the 21st century variant of venous thromboembolism associated with immobility. Eur Respir J 2003 Feb;21(2):374-6. https://doi.org/10.1183/09031936.03.00039403.
16. Lee H. A new case of fatal pulmonary thromboembolism associated with prolonged sitting at computer in Korea. Yonsei Med J 2004 Apr;45(2):349-51. https://doi. org/10.3349/ymj.2004.45.2.349.
17. Ng SM, Khurana RM, Yeang HW, Hughes UM, Manning DJ. Is prolonged use of computer games a risk factor for deep venous thrombosis in children? Case study. Clin Med (Lond) 2003 Nov-Dec;3(6):593-4. https://doi.org/10.7861/ clinmedicine.3-6-593.
18. Braithwaite I, Shirtcliffe P, Jurevics R, Beasley R. Gaming: a 21st century variant of seated immobility thromboembolism. N Z Med J 2018 Feb;131(1469):66-8.
19. West J, Perrin K, Aldington S, Weatherall M, Beasley R. A case-control study of seated immobility at work as a risk factor for venous thromboembolism. J R Soc Med 2008 May;101(5):237-43. https://doi.org/10.1258/jrsm.2008.070366.
20. Healy B, Levin E, Perrin K, Weatherall M, Beasley R. Prolonged work- and computer-related seated immobility and risk of venous thromboembolism. J R Soc Med 2010 Nov;103(11):447-54. https://doi.org/10.1258/jrsm.2010.100155.
21. Braithwaite I, Healy B, Cameron L, Weatherall M, Beasley R. Venous thromboembolism risk associated with protracted work- and computer-related seated immobility: A case-control study. JRSM Open 2016 Aug;7(8):2054270416632670. https://doi.org/10.1177/2054270416632670.
22. Siniarski A, Wypasek E, Fijorek K, Gajos G, Undas A. Association between thrombophilia and seated immobility venous thromboembolism. Blood Coagul Fibrinolysis 2014 Mar;25(2): 135-41. https://doi.org/10.1097/MBC.0b013e3283648163.
23. Kubota Y, Cushman M, Zakai N, Rosamond WD, Folsom AR. TV viewing and incident venous thromboembolism: the Atherosclerotic Risk in Communities Study. J Thromb Thrombolysis 2018 Apr;45(3):353-9. https://doi. org/10.1007/s11239-018-1620-7.
24. Suadicani P, Hannerz H, Bach E, Gyntelberg F. Jobs encompassing prolonged sitting in cramped positions and risk of venous thromboembolism: cohort study. JRSM Short Rep 2012 Feb;3(2):8. https://doi.org/10.1258/shorts.2011.011121.
25. Schnohr P, Jensen G, Lange P, Scharling H, Appleyard M. The Copenhagen City Heart Study: Østerbroundersøgelsen: tables with data from the third examination 1991-1994. Eur Heart J 2001;3(Suppl H):H1-H83.
26. Environment NRCftW [Internet]. Copenhagen: National Research Centre for the Working Environment; [Updated

December 12th, 2010; Accessed September 3rd, 2018]. Available from: http://olddata.arbejdsmiljoforskning.dk/Nationale%20Data/NAK2005.aspx.
27. Nørgaard I, Nielsen SF, Nordestgaard BG. Complement C3 and High Risk of Venous Thromboembolism: 80517 Individuals from the Copenhagen General Population Study. Clin Chem 2016 Mar;62(3):525-34. https://doi.org/10.1373/ clinchem.2015.251314.
28. Klovaite J, Nordestgaard BG, Tybjæ rg-Hansen A, Benn M. Elevated fibrinogen levels are associated with risk of pulmonary embolism, but not with deep venous thrombosis. Am J Respir Crit Care Med 2013 Feb;187(3):286-93. https://doi.org/10.1164/rccm.201207-1232OC.
29. van der Ploeg HP, Møller SV, Hannerz H, van der Beek AJ, Holtermann A. Temporal changes in occupational sitting time in the Danish workforce and associations with all-cause mortality: results from the Danish work environment cohort study. Int J Behav Nutr Phys Act 2015 Jun;12:71. https://doi. org/10.1186/s12966-015-0233-1.
30. Clark BK, Thorp AA, Winkler EA, Gardiner PA, Healy GN, Owen N et al. Validity of self-reported measures of workplace sitting time and breaks in sitting time. Med Sci Sports Exer 2011 Oct;43(10):1907-12.
31. Reis JP, Dubose KD, Ainsworth BE, Macera CA, Yore MM. Reliability and validity of the occupational physical activity questionnaire. Med Sci Sports Exerc 2005 Dec;37(12):207583. https://doi.org/10.1249/01.mss.0000179103.20821.00.
32. Severinsen MT, Kristensen SR, Overvad K, Dethlefsen C, Tjønneland A, Johnsen SP. Venous thromboembolism discharge diagnoses in the Danish National Patient Registry should be used with caution. J Clin Epidemiol 2010 Feb;63(2):223-8. https://doi.org/10.1016/j. jclinepi.2009.03.018.
Received for publication: 29 October 2018

DETAILS

Subject:	Population; Sitting position; Posture; Cholesterol; Questionnaires; Thromboembolism; Codes; Exposure; Confidence intervals; Coagulation; Birth control; Risk analysis; Embolisms; Thrombosis; Age; Surgery; Health risk assessment; Risk factors; Veins &arteries; Population studies
Location:	Denmark
Publication title:	Scandinavian Journal of Work, Environment &Health; Stockholm
Volume:	46
Issue:	1
Pages:	69-76
Publication year:	2020
Publication date:	2020
Section:	Original article
Publisher:	Scandinavian Journal of Work, Environment &Health
Place of publication:	Stockholm

Country of publication:	Finland, Stockholm
Publication subject:	Occupational Health And Safety
ISSN:	03553140
e-ISSN:	1795990X
Source type:	Scholarly Journal
Language of publication:	English
Document type:	Journal Article
DOI:	https://doi.org/10.5271/sjweh.3841
ProQuest document ID:	2344259774
Document URL:	https://www.proquest.com/scholarly-journals/sedentary-work-risk-venous-thromboembolism/docview/2344259774/se-2?accountid=211160
Copyright:	Copyright Scandinavian Journal of Work, Environment &Health 2020
Last updated:	2022-04-26
Database:	Public Health Database

Individual placement and support for young adults at risk of early work disability (the SEED trial). A randomized controlled trial

Sveinsdottir, Vigdis, MSc [1] ; Lie, Stein Atle, PhD [2] ; Bond, Gary R, PhD [3] ; Eriksen, Hege R, PhD [4] ; Tveito, Torill H, PhD [1] ; Grasdal, Astrid L, DrPol; Reme, Silje E, PhD [1] NORCE Norwegian Research Centre, Bergen, Norway [2] Department of Clinical Dentistry, Faculty of Medicine, University of Bergen, Bergen, Norway [3] Westat, Lebanon, NH, USA [4] Department of Sport, Food and Natural Sciences, Western Norway University of Applied Sciences, Bergen, Norway

ABSTRACT (ENGLISH)

Objectives Individual placement and support (IPS) is an effective approach for helping people with severe mental illness gain employment. This study aimed to investigate if IPS can be effectively repurposed to support young adults at risk of early work disability due to various social and health related problems. Methods A randomized controlled trial including 96 young adults (18–29 years; 68% men) was conducted in Norway. Participants were not

in employment, education, or training, received temporary benefits due to social or health-related problems, and were eligible for traditional vocational rehabilitation (TVR). Participants were randomized to IPS (N=50) or TVR (N=46). Self-reported data were collected at baseline and at 6- and 12-months follow-up. The primary outcome was obtaining any paid employment in the competitive labor market during followup. Secondary outcomes were physical and mental health, well-being, coping, alcohol consumption, and drug use. Results Significantly more IPS participants obtained competitive employment compared to TVR participants during 12-months follow-up (48% versus 8%; odds ratio 10.39, 95% confidence interval 2.79–38.68). The IPS group reported significantly better outcomes than the TVR group in subjective health complaints, helplessness, and hopelessness. In post hoc analyses adjusted for baseline and missing data, the IPS group reported significantly better outcomes on these measures in addition to level of disability, optimism about future well-being, and drug use. Conclusions IPS is effective for young adults at risk of early work disability. IPS was superior to TVR in increasing competitive employment and promoted improvements in some non-vocational outcomes. IPS services should be offered to improve employment rates in this vulnerable group.

FULL TEXT

Headnote

Objectives Individual placement and support (IPS) is an effective approach for helping people with severe mental illness gain employment. This study aimed to investigate if IPS can be effectively repurposed to support young adults at risk of early work disability due to various social and health related problems.
Methods A randomized controlled trial including 96 young adults (18-29 years; 68% men) was conducted in Norway. Participants were not in employment, education, or training, received temporary benefits due to social or health-related problems, and were eligible for traditional vocational rehabilitation (TVR). Participants were randomized to IPS (N=50) or TVR (N=46). Self-reported data were collected at baseline and at 6- and 12-months follow-up. The primary outcome was obtaining any paid employment in the competitive labor market during follow-up. Secondary outcomes were physical and mental health, well-being, coping, alcohol consumption, and drug use.
Results Significantly more IPS participants obtained competitive employment compared to TVR participants during 12-months follow-up (48% versus 8%; odds ratio 10.39, 95% confidence interval 2.79-38.68). The IPS group reported significantly better outcomes than the TVR group in subjective health complaints, helplessness, and hopelessness. In post hoc analyses adjusted for baseline and missing data, the IPS group reported significantly better outcomes on these measures in addition to level of disability, optimism about future well-being, and drug use.
Conclusions IPS is effective for young adults at risk of early work disability. IPS was superior to TVR in increasing competitive employment and promoted improvements in some non-vocational outcomes. IPS services should be offered to improve employment rates in this vulnerable group.

Key terms health; intervention; NEET; RCT; supported employment; vocational rehabilitation; work.

High rates of young people who are not in employment, education, or training (NEET) represent an important international challenge (1). The NEET population is diverse, and includes individuals who are short-term unemployed or in temporary transition-phases, as well as other more vulnerable groups at higher risk of lifelong disengagement (2).

Exclusion from the labor market is associated with adverse health effects (3, 4) and leads to considerable societal costs (1). In Norway, disability benefits are offered as income compensation for individuals with permanently reduced earning capacity. During the last decade, there has been a shift in disability benefits toward younger recipients, and the share of young adults aged 18-29 has increased considerably (5). This group differs from the older beneficiaries as the majority (56%) of young recipients are male compared to 42% across all age groups. In addition, 63% of the disability determinations in the 18-29-year-old age group are attributed to mental and behavioral disorders compared to 35% across all age groups. The dominant role of mental and behavioral disorders is not unique in a Norwegian context but is among the leading causes for years lost due to disability among youth in most high-income countries (6).

Given the heterogeneity of the NEET population, efforts to integrate young people into employment should target

specific subgroups. Existing policies bear the risk of being more appropriate for those who are work-ready while failing to reach more disadvantaged groups (1). A recent systematic review found limited evidence for effective re-engagement interventions for NEET, and emphasized that existing knowledge is insufficient to guide policy-makers in the planning and implementation of new programs (7).

The individual placement and support (IPS) model of supported employment is an evidence-based intervention that is effective in improving competitive employment outcomes for patients with severe mental illness (8). While IPS generally does not directly improve non-vocational outcomes (9), competitive employment has beneficial effects, including reduced symptoms and increased self-esteem (10). The IPS model is based on eight principles emphasizing focus on competitive employment, rapid job search, no exclusion due to evaluation of work readiness or other reasons, attention to client preferences, long-term individualized support, integrated services, systematic job development, and benefits counseling (11). While the model was originally developed for patients with severe mental illness, recent studies suggest that it may be effective for other disability groups (12). No previous studies have however investigated the effectiveness of IPS for young adults at risk of early work disability due to various social and health-related problems, that may or may not involve mental illness.

The project "Supported Employment and preventing Early Disability" (SEED) aimed to investigate whether IPS can be repurposed to serve NEET at risk of early work disability in Norway. The SEED trial also aimed to evaluate the effectiveness of IPS compared to traditional vocational rehabilitation (TVR) on outcomes of competitive employment as well as physical and mental health and well-being.

Methods

Trial design

SEED was a two-armed randomized controlled trial (RCT) comparing IPS to TVR. The trial was investigator-initiated and funded by the Research Council of Norway. The Norwegian Regional Committees for Medical and Health Research Ethics exempted the project as it did not fall under the Health Research Act (13) and referred it to the Data Protection Services at the Norwegian Centre for Research Data, which approved the project (project #38271). All participants gave written informed consent before study inclusion, and the ethical principles of the Helsinki declaration were followed. The project was registered in ClinicalTrials.gov (registration #NCT02375074), and the study protocol is available online (14).

Eligibility criteria

The eligibility criteria for SEED included: (i) age 18-29 at year of inclusion; (ii) not in employment or education; (iii) receiving temporary benefits from the Norwegian Labor and Welfare Service (NAV), and thereby required to keep up to an activity plan involving treatment and/ or vocational rehabilitation while work ability is being assessed; (iv) considered eligible for and expected to participate in the TVR intervention "traineeship in a sheltered business" by the individual's caseworker at NAV. Eligibility applies to individuals with impaired work capability that require close and broad supervision and assistance (15).

Exclusion criteria were not expressing interest in getting help to obtain competitive work upon inclusion and insufficient language skills to answer questionnaires in Norwegian. There were no exclusion criteria based on diagnosis, and individuals with any type of social or health-related problem were invited to participate.

Recruitment, randomization, and blinding

The recruitment period lasted from June 2014 through December 2016. Eligible participants were referred to information meetings by staff at one central and nine local labor and welfare offices in and around the city of Bergen, or at a secondary care district psychiatric center with subsequent follow-up at the local labor and welfare office. Eligible participants were given verbal and written information by the project coordinator and invited to participate. After participants agreed to participate and completed the baseline questionnaire, they were randomly assigned to one of two conditions using a computergenerated randomization sequence with a block size of 8 and a 1:1 randomization ratio to the two groups. The ratio was temporarily changed for a period of three months to 2:1 (with two participants assigned to IPS for every one assigned to TVR), in order to enable sufficient caseloads for the job specialists. Staff at Uni Research Health carried out the randomization and communicated the results to the

individual's caseworker at NAV by email. Created by a statistician who had no contact with the participants, the randomization sequence was concealed from participants, service providers, and the researcher responsible for controlling the data analyses. The researcher responsible for quality control of the data analyses was blinded for intervention assignment.

Interventions

Both IPS and TVR were offered by vocational rehabilitation organizations overseen by the NAV, which provides employment services to temporary benefit recipients in Norway.

Individual placement and support (IPS). IPS participants were referred to an organization with two trained job specialists. The specialists sought to follow the IPS principles (11) and find a good job match while avoiding the use of prevocational training or subsidized or unpaid work. Unlike traditional vocational approaches, IPS focuses exclusively on competitive employment, clients are not screened for job readiness, client preferences guide choices and decisions, and job specialists continue to provide ongoing support after clients attain employment. An IPS team leader supervised the job specialists, and an external IPS trainer advised the team. Because the study population had various social and healthrelated challenges that did not necessarily involve mental illness, the IPS principle of integrating services with mental health treatment was not implemented, although job specialists contacted health personnel involved in the treatment of individual participants in cases where this was applicable and accepted by the participant. The intervention was offered for up to three years, and the duration and intensity depended on individual needs and preferences.

Traditional vocational rehabilitation (TVR). The TVR group was referred to an organization offering a traditional employment scheme called "traineeship in a sheltered business", aiming to improve the opportunities for finding a job (15). This intervention represented treatment as usual and served as an active control condition. The traineeships involved testing work capability and providing preparatory work training adapted to the individual's challenges and skill level, in a sheltered setting with close follow-up. According to usual practice, participants were allocated to various sheltered businesses in the area providing different types of work settings, including food and catering, child care, mechanic services, transportation services, and warehouse handling, based on individual interests and goals as well as availability. The intervention was offered for up to two years, and the duration was customized to the individual's options on the labor market. The usual intensity of the intervention is full-time, with a requirement of >50% of full-time (15).

Data collection

Data were collected using questionnaires distributed at baseline, and 6 and 12 months after enrollment. For more information about data collection and management, see the study protocol (14). In order to increase the response rate to the primary outcome, non-respondents were contacted by telephone, text message, and e-mail. Participants who provided ambiguous responses to the primary outcome in the questionnaire were also contacted by telephone for clarification. In cases where contact was not obtained, log-books from the job specialists were used to provide information on the primary outcome for IPS participants (N=7).

Outcomes

Primary outcome: competitive employment (12-months follow-up). The primary outcome was any competitive employment during the 12-months follow-up. Competitive employment was defined as paid employment in the competitive labor market, and thus did not include subsidized or unpaid work. It was measured by self-report using a single item asking the participants to indicate the number of weeks, days, or hours worked in competitive employment during the first 12 months after enrollment. A dichotomous variable indicating any competitive work versus no competitive work was created.

Secondary employment-related outcomes (12-months and long-term follow-up). Additional standardized indicators of successful employment (16) during 12-months followup included percentage of participants ever working >20 hours per week, total number of hours worked, weeks from enrollment to first job, and weeks worked at longestheld job, were also included in the questionnaires.

Register data on benefit recipiency and income from NAV, and financial assistance and educational activity from

Statistics Norway, will also be collected during long-term follow-up for up to five years after enrollment.
Secondary health-related outcomes (6- and 12-months follow-up). Secondary outcomes were level of disability, using the World Health Organization Disability Assessment Schedule (WHODAS) 2.0 (17); psychological distress, using the Hopkins Symptom Checklist (HSCL-25) (18, 19); severity of subjective health complaints, using the Subjective Health Complaints Inventory (SHC) (20); fatigue, using the Chalder Fatigue Questionnaire (CFQ) (21); coping, helplessness and hopelessness, using the Theoretically Originated Measure of the Cognitive Activation Theory of Stress (TOMCATS) (22); alcohol consumption, using the Alcohol Use Disorders Identification Test consumption questions (AUDIT-C) (23); and drug use, using the Drug Use Disorders Identification Test consumption questions (DUDIT-C) (24, 25). Global wellbeing was measured using a 10-point Cantril Ladder Scale (26) ranging from 1 (worst life possible) to 10 (best life possible) asking about the current situation, the situation one year ago, and one year in the future. This measure replaced the EQ-5D measuring quality of life described in the study protocol (14), in order to shorten the questionnaire. Higher scores on each scale indicated higher levels of the respective outcome. Measures of social support and illness perceptions, which were also included in the study protocol (14), will be investigated in a future paper examining moderators of treatment effects.
Fidelity and process measures for the IPS intervention. To assess the adherence to the evidence-based IPS Supported Employment Fidelity Scale (27), the external IPS trainer regularly conducted fidelity reviews throughout the project period. Each review was conducted over two consecutive days and involved document and calendar review, observations, and interviews of the different stakeholders. The scale consists of 25 items rated on a 5-item behaviorally anchored scale with total scores ranging from 25-125; scores <73 do not fulfill the minimal criteria for IPS.
IPS participants received additional questions at follow-up related to adherence to and satisfaction with the intervention. At 6- and 12-months follow-up, participants were asked to indicate on 5-point scales how satisfied they were with the intervention in general; how satisfied they were with their job specialist; and how useful it had been to participate in the intervention. In addition, IPS participants were asked at 6-months follow-up whether or not they had initiated at least one of the goals they had set with their job specialist during their first meetings (eg, finding references, drafting their CV), and to indicate barriers and helpful factors for participation.
Sample size
A required sample size of 124 participants was estimated based on input data from previous IPS studies with a mean competitive employment rate of 61% for IPS and 23% for control groups (28). Calculations were performed using the Hmisc library in the statistical package R (29), based on a 5% significance level and a power of 90%, accounting for stratified analyses to investigate treatment effects for two sub-groups (eg, gender).
Statistical analysis
Descriptive statistics on demographic and health-related characteristics were calculated for the total sample and each intervention group at baseline. Baseline differences between the groups, and between respondents and non-respondents at follow-up, were analyzed using chi square tests for dichotomous variables and independent t-tests for continuous variables.
Analysis on the primary outcome was conducted using chi square test comparing crude employment rates of participants in each group. The odds ratio (OR) was also calculated. Rates of working >20 hours per week were compared with the same method, and number of hours worked were compared using t-tests. In order for effect sizes to be comparable across dichotomous and continuous outcomes, the effect size for differences between proportions was calculated using the arcsine formula (30).
For the secondary health-related outcomes, unadjusted differences between groups at each follow-up point were compared using t-tests. However, due to multiple observations for participants, at baseline and 6 and 12 months, and to adjust for missing observations and baseline ratings on each outcome, post hoc analyses with mixed effects regression models were also applied. In the mixed effect model, maximum likelihood estimation (MLE) will robustly adjust for missing observations. Using this approach accounts for complex structures of missing data (31).
All analyses followed the intention-to-treat (ITT) principle according to the randomized groups, regardless of

compliance per protocol. The significance level was a=0.05. Analyses were performed using IBM SPSS Statistics version 25.0 (IBM Corp, Armonk, NY, USA) and StataIC version 15 (StataCorp. College Station, TX, USA).

Results

Participant flow

A total of 98 participants were included and randomized (50 to IPS and 46 to TVR). Two participants were excluded before intervention and follow-up due to ineligibility according to the inclusion criteria (figure 1). The final sample consisted of 96 participants [68% male, mean age 24 (SD 3.25) years].

The response rate for the primary outcome (main analysis) was N=83 (86%), and there was no significant difference in response rate between the groups (P=0.098). The response rate on questionnaires with secondary outcomes was 72% at 6-months follow-up, dropping to 64% at 12-months follow-up. There was a significant difference in response rate between IPS and TVR groups at 6-months follow-up (x2(1)=7.59, P=0.006, Cohen's d=0.57) but no significant difference at 12-months follow-up (P=0.602).

Baseline characteristics

There were no significant differences between the groups on demographic or health-related variables at baseline (table 1). For more information on baseline characteristics, see Sveinsdottir et al. (32).

There were no significant baseline differences between respondents and non-respondents at 6-months follow-up. Respondents at 12-months follow-up were, however, more likely than non-respondents to be female (X2(1)=5.78, P=0.016, Cohen's d=0.54) and to have more than a high school education (x2(1)=7.10, P=0.008, Cohen's d=0.55), but did not differ significantly on health-related variables.

When comparing baseline differences between the reduced samples of respondents in the IPS and TVR groups, respondents to 6-months follow-up in the TVR group reported higher baseline global well-being (mean 5.73, SD=1.96, N=22) than respondents in the IPS group (mean 4.71, SD=1.69, N=35), t(55)=2.07, P=0.043, Cohen's d=0.55. There were no significant baseline differences between respondents to 12-months follow-up in the IPS and TVR groups.

Primary and secondary employment-related outcomes

Compared to the TVR group, a significantly higher proportion of the IPS group obtained competitive employment at any time during the 12-months follow-up period (table 2). A significantly higher proportion of the IPS group had also ever worked >20 hours per week, and participants in the IPS group worked more hours on average, compared to the TVR group (table 2).

Due to problems in the data collection of weeks from enrollment to first job, and weeks worked at longest-held job, data on these outcomes were insufficient and are not reported.

The register data with long-term follow-up have a time lag, and will be reported after they are available.

Secondary health-related outcomes

Unadjusted analyses. Groups did generally not differ in secondary outcomes in the unadjusted analyses, with some exceptions in favor of the IPS group in severity of subjective health complaints and helplessness at 6-months follow-up, and in hopelessness at 12-months follow-up (table 3).

Adjusted post hoc analyses. In the adjusted post hoc analyses, participants in the IPS group reported significantly more positive effects on secondary outcomes of anxiety (P=0.045), subjective health complaints (P=0.001), pseudoneurology (P=0.033), helplessness (P=0.002), hopelessness (P=0.029), and drug use (P=0.043) compared to the TVR group at 6-months follow-up. With the exception of anxiety and pseudoneurology, effects were maintained at 12 months, for subjective health complaints (P=0.017), helplessness (P=0.017), hopelessness (P=0.006), and drug use (P=0.036). Participants in the IPS group also showed significantly lower levels of disability (P=0.038) and more optimism about future well-being (P=0.038) at 12 months compared to the TVR group.

Fidelity to the IPS model and participants' experiences with the intervention. Five fidelity reviews were conducted in June and December of 2015 and 2016 and in July 2017, coinciding with the time period of recruitment and 12-months follow-up. Due to the adaptions made to the IPS intervention noted above, fidelity items concerning integration with mental health treatment were rated as 1 (lowest score). The total score for the first review started at

a low point of 47, and there was a general increase up to a score of 77 at the last review. Three of five reviews were above the cut-off for "fair" fidelity (29).

At 6-months follow-up, most participants in the IPS group (N=36, 95%) reported having initiated at least one of the goals they had set with their job specialist. At 6-months follow-up, N=30 (77%) were quite or very satisfied with their job specialist, N=28 (72%) were quite or very satisfied with the intervention, and N=26 (68%) reported that participation had been quite or very useful. At 12-months follow-up, N=20 (63%) were quite or very satisfied with their job specialist, N=19 (59%) were quite or very satisfied with the intervention, and N=16 (50%) reported that participation had been quite or very useful. Challenges with illness was the most common barrier for participating in the intervention (N=18, 53%) followed by the content of the intervention not meeting expectations (N=7, 21%) and transportation challenges (eg, meeting the job specialist or potential employers) (N=7, 21%). The most commonly reported helpful factors were the availability of the job specialist (N=30, 83%), having the choice of whether or not to disclose their illness to employers or others (N=29, 83%), regular follow-up from the job specialist (N=25, 81%), and having specific steps in the individualized job search plan during the process (N=25, 76%).

Discussion

The SEED trial compared two contrasting vocational rehabilitation approaches for young adults assessed as having impaired work capability and who were not in education, employment, or training. IPS was superior to TVR in increasing participation in competitive employment among this group.

Participants who received IPS were more likely to be competitively employed during one year follow-up compared to participants receiving treatment as usual in TVR. Additionally, IPS participants worked more hours, and more often worked >20 hours per week. These results, together with the fidelity and process measures, show that the IPS methodology can be applied to young adults at risk of early disability due to social or healthrelated problems that do not necessarily involve mental illness. The findings are in line with previous literature of IPS for patients with severe mental illness, showing that IPS is more effective than control conditions in promoting competitive employment (33). The employment rates of 48% versus 8% are similar to findings from a recent Swedish IPS study (34).

Only 8% of TVR participants obtained any competitive employment during follow-up. Although the TVR intervention involves prevocational training with close follow-up aimed at finding a job (15), the sheltered nature of the approach may preclude competitive employment by placing participants in a training situation outside the labor market and in an environment with others who are in the same situation. Although the current study does not have data on the duration and intensity of the intervention for the individual participants, the results indicate that participation in TVR may have left little time for efforts aimed toward attaining competitive employment. The results strongly suggest that providing direct support to finding and keeping competitive jobs rather than preparing clients in sheltered training settings is a more effective way to reintegrate vulnerable NEET into the competitive labor market.

Although participants were generally satisfied with the IPS intervention, the program scored low on fidelity. The quality of the implementation was thus below fidelity benchmarks attained in many prior IPS studies. One continuing weakness in IPS implementation was the lack of integration between employment and health care services. Other issues were low scores on providing follow-up after employment, assertive engagement and outreach for clients who missed appointments, agency focus on competitive employment, and job specialists spending too much time on non-vocational services. Previous studies have shown that higher fidelity is associated with better employment outcomes (35, 36), which may also be true for this population, but this cannot be demonstrated until a high fidelity IPS program has been evaluated. These issues should therefore be considered in future efforts to provide IPS to non-psychiatric populations and may, for example, require the establishment of more structured routines to integrate any relevant health services in the intervention.

Participants mainly reported psychological problems as a reason for unemployment at baseline, which mirrors the statistics of youth in high-income countries (6) as well as young disability benefit recipients in Norway (37). Other health or non-health related reasons were however also common, which illustrates the sample's diversity in terms of type of social and health-related problems compared to previous IPS trials. Baseline characteristics among the participants are discussed in more detail in a previous paper (32), showing that the prevalence of adverse social

experiences (ie, bullying and violence) was highly prevalent, while more than half of participants also reported scores above predefined cut-offs for psychological distress as well as alcohol use, and about one third reported severe disability. Findings on secondary health-related outcomes at follow-up were inconsistent, but indicated that IPS also had more favorable effects on some non-vocational outcomes. Unadjusted analyses showed few significant findings, but the loss to follow-up resulted in reduced power and possibly increased risk of type-II error. In the adjusted analyses, participants in the IPS group had significantly less disability, subjective health complaints, drug use, helplessness and hopelessness, and a more optimistic view on future well-being, compared to the TVR group. The findings provide an interesting addition to the existing IPS literature, which has generally not found effects on non-vocational outcomes (9). The finding that participants felt more helpless and hopeless after receiving TVR compared to IPS, indicates that traditional sheltered interventions may preclude individual's feelings of control and promote the belief that the actions they take may not have any effect on their situation, or even make it worse (38). The current study is also the first to demonstrate positive outcomes of IPS on drug use and optimism about future well-being. Findings on disability and subjective health complaints are however in line with a recent Norwegian trial of patients with moderate and severe mental illness (39) but appear weaker and more inconsistent on outcomes related to mental health. This may be partly explained by characteristics of the sample in the current study, who generally had less severe psychiatric symptoms than IPS participants in previous trials. It is however also important to note that participation in IPS was not associated with any negative impact on health, even though participants represented a vulnerable group qualified for sheltered work training. This aligns with the previous research on IPS (40) and suggests that concerns for potential detrimental health effects of non-sheltered approaches for this group may be unsubstantiated.

Strengths and limitations

The main strengths of the current study include the rigorous RCT design and the investigation of IPS for a new and important target group. The study addresses an established need in the literature for effective interventions to help NEET enter the labor market (1) and indicates that IPS may have the potential to forestall entry into the disability system for this group.

The study also has several limitations. The relatively small sample size precluded subgroup analyzes and may reduce generalizability. Although findings on the main outcome were strong, the confidence interval was large, indicating that there is need for larger replication studies to confirm the results. The power calculation was only performed for the primary outcome, and the small sample size reduces the chance of reaching statistical significance, in particular for secondary outcomes with missing data at follow-up. Differential attrition at 6-months is a threat to internal validity. This was mitigated by applying mixed effects models (with MLE), which is a recommended approach to handle complex structures of missing data (31). Due to the considerable number of secondary outcome measures included in the study, alpha inflation is a concern, suggesting caution in interpreting these findings.

The dichotomous primary outcome is a simplistic measure, which may be too crude to capture the many aspects of employment (16). It is however the most commonly used outcome in previous IPS studies and serves as a useful general-purpose measure (16), which was supplemented with data on ever working >20 hours per week and the continuous measure of hours worked. Due to problems in the data collection we were however unable to collect sufficient data on further indicators of successful employment, which represents a limitation to the study. The use of self-report data for competitive employment may also increase the risk of bias, and it is also uncertain whether the effects will hold up in the long-term. This will be followed up in a subsequent paper with objective register data from the NAV, which will provide a more conservative, yet reliable and complete measure of labor market participation for up to five years after enrollment. These data will also form the basis for a cost-benefit analysis.

Data on potential harms was not collected in the study. There were routines for reporting and handling any harms/adverse effects reported directly to the project group or to the job specialists, but there were no such reports.

Concluding remarks

The results showed that IPS can be successfully applied to NEET with impaired work capability due to various social or health-related problems. IPS was superior to TVR in increasing participation in competitive employment among

this group, and also promoted improvements in level of disability, subjective health, feelings of helplessness and hopelessness, and drug use, when adjusted for missing observations. Based on the results from the current study, we recommend that IPS services should be offered to improve labor market participation among young adults at risk of early work disability.

Acknowledgements

We would like to thank all the participants who took part in the project, and the staff at Fretex Western Norway, NAV, and IPS Norge for their collaboration. We also thank Line Solberg, Adrian Løken, and Nina Konglevoll for their efforts as research assistants. The Research Council of Norway funded the SEED trial (project #227002/H20) but did not have any role in the study design, data collection or analysis, or decisions to publish. The authors declare no conflicts of interest.

Sidebar

Sveinsdottir V, Lie SA, Bond GR, Eriksen HR, Tveito TH, Grasdal AL, Reme SE. Individual placement and support for young adults at risk of early work disability (the SEED trial). A randomized controlled trial. Scand J Work Environ Health. 2020;46(1):50-59. doi:10.5271/sjweh.3837

Correspondence to: Vigdis Sveinsdottir, NORCE Norwegian Research Centre, POB 7810, 5020 Bergen, Norway. [E-mail: visv@norceresearch.no]

References

References

1. Eurofound. NEETs - Young people not in employment, education or training: Characteristics, costs and policy responses in Europe. Luxembourg: Publications Office of the European Union; 2012.

2. Eurofound. Exploring the diversity of NEETs. Luxembourg: Publications Office of the European Union; 2016.

3. Paul KI, Moser K. Unemployment impairs mental health: Meta-analyses. J Vocat Behav. 2009;74(3):264-82. https://doi. org/10.1016/j.jvb.2009.01.001

4. McKee-Ryan F, Song Z, Wanberg CR, Kinicki AJ. Psychological and physical well-being during unemployment: a meta-analytic study. J Appl Psychol. 2005;90(1):53-76. https://doi.org/10.1037/0021-9010.90.1.53

5. Norwegian Labor and Welfare Administration. Utviklingen i uføretrygd per 30. september 2018 [The development of disability benefits, by September 30th 2018]. Oslo: NAV; 2018.

6. Gore FM, Bloem PJN, Patton GC, Ferguson J, Joseph V, Coffey C, et al. Global burden of disease in young people aged 10-24 years: a systematic analysis. Lancet. 2011;377(9783):2093102.https://doi.org/10.1016/S0140-6736(11)60512-6

7. Mawn L, Oliver EJ, Akhter N, Bambra CL, Torgerson C, Bridle C, et al. Are we failing young people not in employment, education or training (NEETs)? A systematic review and metaanalysis of re-engagement interventions. Systematic reviews. 2017;6(1):16. https://doi.org/10.1186/s13643-016-0394-2

8. Drake RE, Bond GR, Goldman HH, Hogan MF, Karakus M. Individual Placement And Support Services Boost Employment For People With Serious Mental Illnesses, But Funding Is Lacking. Health affairs (Project Hope). 2016;35(6):1098-105. https://doi.org/10.1377/hlthaff.2016.0001

9. Kukla M, Bond GR. A randomized controlled trial of evidencebased supported employment: Nonvocational outcomes. J Vocat Rehabil. 2013;38:91-8.

10. Luciano A, Bond GR, Drake RE. Does employment alter the course and outcome of schizophrenia and other severe mental illnesses? A systematic review of longitudinal research. Schizophrenia research. 2014;159(2-3):312-21. https://doi. org/10.1016/j.schres.2014.09.010

11. Drake RE, Bond GR, Becker DR. Individual Placement and Support: An Evidence-Based Approach to Supported Employment. New York: Oxford University Press, USA; 2012. https://doi.org/10.1093/acprofoso/9780199734016.001.0001

12. Bond GR, Drake RE, Pogue JA. Expanding Individual Placement and Support to Populations With Conditions and Disorders Other Than Serious Mental Illness. Psychiatric services (Washington, DC). 2019. https://doi.org/10.1176/ appi.ps.201800464

13. LOV-2008-06-20-44 §4a. The Act on Medical and Health Research (the Health Research Act). http://app.uio.no/ub/ ujur/oversatte-lover/data/lov-20080620-044-eng.pdf.
14. Sveinsdottir V, Tveito TH, Bond GR, Grasdal AL, Lie SA, Reme SE. Protocol for the SEED-trial: Supported Employment and preventing Early Disability. BMC Public Health. 2016;16:579.https://doi.org/10.1186/s12889-016-3280-x
15. Norwegian Labor and Welfare Administration. Kravspesifikasjon for tiltak i skjermede virksomheter [Requirement Specification for Services in Sheltered Businesses]. Oslo: NAV; 2011 [cited 2017 May 5th]. Available from: https://www.nav.no/_attachment/87667.
16. Bond GR, Campbell K, Drake RE. Standardizing measures in four domains of employment outcomes for individual placement and support. Psychiatric services (Washington, DC). 2012;63(8):751-7. https://doi.org/10.1176/appi. ps.201100270
17. Üstün TB, Kostanjsek N, Chatterji S, Rehm J. Measuring health and disability: manual for WHO Disability Assessment Schedule (WHODAS 2.0). Geneva: World Health Organization; 2010.
18. Derogatis LR, Lipman RS, Rickels K, Uhlenhuth EH, Covi L. The Hopkins Symptom Checklist (HSCL): a selfreport symptom inventory. Behav Sci. 1974;19(1):1-15. https://doi.org/10.1002/bs.3830190102
19. Winokur A, Winokur DF, Rickels K, Cox DS. Symptoms of emotional distress in a family planning service: stability over a four-week period. Br J Psychiatry. 1984;144:395-9. https://doi.org/10.1192/bjp.144.4395
20. Eriksen HR, Ihlebaek C, Ursin H. A scoring system for subjective health complaints (SHC). Scandinavian journal of public health. 1999;27(1):63-72. https://doi.org/10.1177/140 34948990270010401
21. Chalder T, Berelowitz G, Pawlikowska T, Watts L, Wessely S, Wright D, et al. Development of a fatigue scale. Journal of psychosomatic research. 1993;37(2): 147-53. https://doi. org/10.1016/0022-3999(93)90081-P
22. Odeen M, Westerlund H, Theorell T, Leineweber C, Eriksen HR, Ursin H. Expectancies, Socioeconomic Status, and SelfRated Health: Use of the Simplified TOMCATS Questionnaire. International journal of behavioral medicine. 2013;20(2):24251.https://doi.org/10.1007/s12529-012-9221-x
23. Bush K, Kivlahan DR, McDonell MB, Fihn SD, Bradley KA. The AUDIT alcohol consumption questions (AUDIT-C): an effective brief screening test for problem drinking. Ambulatory Care Quality Improvement Project (ACQUIP). Alcohol Use Disorders Identification Test. Arch Intern Med. 1998;158(16):1789-95. https://doi.org/10.1001/ archinte.158.16.1789
24. Berman AH, Bergman H, Palmstierna T, Schlyter F. DUDIT (Drug Use Disorders Identification Test) Manual. Stockholm: Karolínska Institutet; 2003. https://doi.org/10.1037/t02890000
25. Sinadinovic K, Wennberg P, Berman AH. Targeting problematic users of illicit drugs with Internet-based screening and brief intervention: a randomized controlled trial. Drug Alc Dep. 2012;126(1-2):42-50.https://doi.org/10.1016/j. drugalcdep.2012.04.016
26. Cantril H. The pattern of human concerns. New Brunswick, NJ: Rutgers University Press; 1965.
27. Becker DR, Swanson S, Reese SL, Bond GR, McLeman BM. Supported Employment Fidelity Review Manual 3ed. Lebanon, NH: Dartmouth Psychiatric Research Center; 2015.
28. Bond GR, Drake RE, Becker DR. An update on randomized controlled trials of evidence-based supported employment. Psychiatr Rehabil J. 2008;31(4):280-90. https://doi. org/10.2975/31.4.2008.280.290
29. R Core Team. R: A language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing; 2013.
30. Lipsey MW. Design Sensitivity: Statistical Power for Experimental Research. Newbury Park, CA: SAGE; 1990.
31. Rabe-Hesketh S, Skrondal A. Multilevel and Longitudinal Modeling Using Stata: Continuous Responses, Third Edition. College Station, TX: Stata Press; 2012.
32. Sveinsdottir V, Eriksen HR, Baste V, Hetland J, Reme SE. Young Adults at Risk of Early Work Disability: Who are they? BMC Public Health. 2018;18:1176.https://doi.org/10.1186/ s12889-018-6095-0
33. Modini M, Tan L, Brinchmann B, Wang MJ, Killackey E, Glozier N, et al. Supported employment for people with severe mental illness: systematic review and meta-analysis of the international evidence. Bri J Psych.

2016;209(1):14-22. https://doi.org/10.1192/bjp.bp.115.165092
34. Bejerholm U, Areberg C, Hofgren C, Sandlund M, Rinaldi M. Individual Placement and Support in Sweden-A randomized controlled trial. Nord J Psychiatry. 2014;1:1-10. https://doi.org/10.3109/08039488.2014.929739
35. Bond GR, Becker DR, Drake RE. Measurement of Fidelity of Implementation of Evidence-Based Practices: Case Example of the IPS Fidelity Scale. Clin Psychol-Sci Pr. 2011;18(2):12641. https://doi.org/10.1111/j.1468-2850.2011.01244.x
36. Bond GR, Peterson AE, Becker DR, Drake RE. Validation of the Revised Individual Placement and Support Fidelity Scale (IPS-25). Psych Ser (Washington, DC). 2012;63(8):758-63. https://doi.org/10.1176/appi.ps.201100476
37. Norwegian Labor and Welfare Administration. Utviklingen i uførediagnoser per 30. juni 2015 [The development of disability benefit diagnoses, by June 30th 2015]. Oslo: NAV; 2018.
38. Ursin H, Eriksen HR. The cognitive activation theory of stress. Psychoneuroendocrinology. 2004;29(5):567-92. https://doi. org/10.1016/S0306-4530(03)00091-X
39. Reme SE, Monstad K, Fyhn T, Sveinsdottir V, Lovvik C, Lie SA, et al. A randomized controlled multicenter trial of individual placement and support for patients with moderateto-severe mental illness. Scand J Work Environ Health. 2019;45(1):33-41. https://doi.org/10.5271/sjweh.3753
40. Luciano A, Drake RE, Bond GR, Becker DR, Carpenter-Song E, Lord S, et al. Evidence-based supported employment for people with severe mental illness: Past, current, and future research. J Vocat Rehabil. 2014;40(1):1-13.
Received for publication: 27 December 2018

DETAILS

Subject:	Principles; Mental health; Mental health care; Intervention; Mental disorders; Young adults; Researchers; Risk; Placement; Missing data; Age; Confidence intervals; Rehabilitation; Drug use; Medical research; Clinical trials; Adults; Randomization; Occupational health; Control methods; Training; Employment; Vocational rehabilitation; Labor market; Unemployment
Business indexing term:	Subject: Training Employment Vocational rehabilitation Labor market Unemployment
Location:	Norway
Publication title:	Scandinavian Journal of Work, Environment &Health; Stockholm
Volume:	46
Issue:	1
Pages:	50-59
Publication year:	2020
Publication date:	2020
Section:	Original article
Publisher:	Scandinavian Journal of Work, Environment &Health

Place of publication:	Stockholm
Country of publication:	Finland, Stockholm
Publication subject:	Occupational Health And Safety
ISSN:	03553140
e-ISSN:	1795990X
Source type:	Scholarly Journal
Language of publication:	English
Document type:	Evidence Based Healthcare, Journal Article
DOI:	https://doi.org/10.5271/sjweh.3837
ProQuest document ID:	2344259455
Document URL:	https://www.proquest.com/scholarly-journals/individual-placement-support-young-adults-at-risk/docview/2344259455/se-2?accountid=211160
Copyright:	Copyright Scandinavian Journal of Work, Environment &Health 2020
Last updated:	2021-03-22
Database:	Public Health Database

The influence of multiple occupational exposures on absence from work in pregnancy: a prospective cohort study

Sejbaek, Camilla Sandal, PhD [1] ; Pedersen, Jacob, PhD [1] ; Schlünssen, Vivi, PhD [1] ; Begtrup, Luise Mølenberg, PhD [2] ; Juhl, Mette, PhD [3] ; Bonde, Jens Peter, PhD; Kristensen, Petter, PhD; Bay, Hans; Ramlau-Hansen, Cecilia Høst, PhD; Hougaard, Karin Sørig, PhD [1] National Research Centre for the Working Environment, Copenhagen, Denmark [2] Department of Occupational and Environmental Medicine, Bispebjerg University Hospital, Copenhagen, Denmark [3] Faculty of Health, Department of Midwifery and Therapeutic Sciences, University College Copenhagen, Copenhagen, Denmark

ABSTRACT (ENGLISH)

Objectives Many women experience absence periods from work during pregnancy. Several single risk factors for absence are identified, whereas the impact of multiple concurrent exposures has been sparsely studied. We hypothesized that the presence of multiple occupational exposures would be associated with an increased risk of absence from work during pregnancy. Methods We included women from the Danish National Birth Cohort (1996-2002), pregnant with one child and working >30 hours/week at interview (mean gestational week 17 (standard deviation 4.0); N=50 142). Information about five occupational exposures (job demands, job control, work posture, work shift, lifting) were retrieved from the interview, each assigned values of 0/1, and summed into an index (0-5). The woman's first absence from work (both regular and related to pregnancy) after the interview was available from a nationwide administrative register. We analyzed data with Cox regression using gestational age as the underlying time-variable. Results Few women experienced none of the occupational exposures (3.6%) and most experienced two exposures (34.7%). Only 24.3% of the women were absent from work before gestational week 31. The number of occupational exposures was associated with an increasing risk of absence. The adjusted hazard ratio for absence increased from 1.3 [95% confidence interval (CI) 1.1-1.5] for one exposure to 2.9 (95% CI 2.5-3.3) for four to five exposures compared to no occupational exposure. Conclusion The higher the number of potentially adverse occupational exposures pregnant women experienced, the higher the risk for absence from work during pregnancy.

FULL TEXT

Headnote

Objectives Many women experience absence periods from work during pregnancy. Several single risk factors for absence are identified, whereas the impact of multiple concurrent exposures has been sparsely studied. We hypothesized that the presence of multiple occupational exposures would be associated with an increased risk of absence from work during pregnancy.

Methods We included women from the Danish National Birth Cohort (1996-2002), pregnant with one child and working >30 hours/week at interview (mean gestational week 17 (standard deviation 4.0); N=50 142). Information about five occupational exposures (job demands, job control, work posture, work shift, lifting) were retrieved from the interview, each assigned values of 0/1, and summed into an index (0-5). The woman's first absence from work (both regular and related to pregnancy) after the interview was available from a nationwide administrative register. We analyzed data with Cox regression using gestational age as the underlying time-variable.

Results Few women experienced none of the occupational exposures (3.6%) and most experienced two exposures (34.7%). Only 24.3% of the women were absent from work before gestational week 31. The number of occupational exposures was associated with an increasing risk of absence. The adjusted hazard ratio for absence increased from 1.3 [95% confidence interval (CI) 1.1-1.5] for one exposure to 2.9 (95% CI 2.5-3.3) for four to five exposures compared to no occupational exposure.

Conclusion The higher the number of potentially adverse occupational exposures pregnant women experienced, the higher the risk for absence from work during pregnancy.

Key terms epidemiology; pregnancy-related absence; job control; job demand; lifting; work posture; work shift.

A large proportion of women experience absence from work during pregnancy. In Denmark, two thirds of all pregnant women were absent from work at some point during pregnancy, and almost one third of the pregnant women were absent for >8 weeks during pregnancy. Furthermore, absence from work in pregnancy seems to increase (1). In 2016, the employment rate was 72% for Danish women in the reproductive age (18-44 years) (2), and each year around 60 000 children are born in Denmark. The societal costs due to absence from work are therefore high due to payment of benefits and reduction of manpower. Absence from work is also problematic for pregnant women because work is perceived as an important part of life. Reduction of absence from work during pregnancy therefore encompasses economic as well as individual advantages. It is therefore important to study how occupational exposures may be associated with absence from work during pregnancy to enable formulation of efficient preventive measures.

A number of occupational factors have been described as risk factors for absence from work during pregnancy. Previous studies have investigated occupational exposures such as job strain [defined by the combination of job

demands and job control (3)], work posture, lifting, and work shift. These were each associated with the first episode of absence during gestational week (GW) 10-29 of pregnancy in a previous Danish study (4); while another study found similar exposures to be associated to absence for >10% of the scheduled work time during pregnancy among hospital employees (5). The relationship between occupational exposures and absence from work during pregnancy has mostly been assessed for individual factors, one at a time, rather than for combinations of exposures. However, one crosssectional study investigated an index of occupational exposures and showed that, with an increasing number of exposures, the risk of self-reported sickness absence during pregnancy increased (6). Findings described in a Danish report indicated that pregnant women concurrently exposed to several occupational exposures had more absences from work than pregnant women with fewer or no exposures at work (7). This study was crosssectional, sickness absence was self-reported, and details of the analyses were not available. Hence, in research of associations between occupational exposures and absence from work during pregnancy, there is a need to use prospective study designs and register rather than self-reported data on the outcome.

We hypothesized that exposure to multiple concurrent occupational exposures would increase the risk of absence from work. We constructed an index of several occupational exposures (4) with the hypothesis that exposures, which have been indicated to relate to absence from work during pregnancy, will also increase the risk of absence when they are present concurrently and that the risk will increase for additional exposures, ie, the higher the number of exposures the higher the risk of absence.

Methods

Study population

We used data from the Danish National Birth Cohort (DNBC) with 100 418 pregnancies (1996-2002) (8). During the first antenatal visit, the general practitioner invited the pregnant women to participate in the cohort if they planned to complete the pregnancy, lived in Denmark, and could carry out a comprehensive telephone interview in Danish. For more details, see elsewhere (8).

We included women if they (i) completed DNBC's first pregnancy interview between the first day in GW 11 and the last day in GW 30 [mean 16.7 (SD 4.0) GW], (ii) were pregnant with their first singleton pregnancy registered in the DNBC, (iii) worked >30 hours per week, and (iv) had full information on all exposures of interest, covariables and outcome (figure 1, N=50 142).

The DNBC and the Danish Data Protection Agency permitted use and storage of data at Statistics Denmark where the available data were fully anonymized. According to the Danish legislation, approval from the Ethical Committee was not needed.

Occupational exposures

An index variable constructed, as described by Miranda and colleagues (9), was generated from the five selected occupational exposures: work posture, work shift, lifting, job demands, and job control (table 1). These factors were included in the analyses as they had previously been found to be associated with absence from work during pregnancy, albeit job demands and job control was associated to absence from work as the combined exposure job strain (4). Lifting was constructed from four questions, while the rest of the exposures were based on one question each (table 1). Each heavy and medium lift were assigned values of 22.5 and 15 kg/lift, respectively, and the cumulative burden of lifting was calculated (10). The scoring of lifting, work posture and work shift (0 or 1 point; table 1) was based on the findings in Hansen et al (4). Job demands and job control were included as separate measures, dichotomized and scored (0 or 1 point; table 1) based on Larsen et al (11) and Juhl et al (12). These two questions were dichotomized in order to obtain as much contrast as possible. For the index variable, the points were summarized across the five occupational exposures for each woman. The final index variable ranged from 0-5, where 4 and 5 were combined into one category due to an assumption that few women would experience a high amount of occupational exposures.

Outcome

Information on doctor-certified absence from work was obtained from the Danish Register for Evaluation of Marginalization (DREAM). This register contains data for all types of social payments with unique codes for each

benefit, eg, sickness and maternity benefit, educational funds, and retirement pension. The data has a hierarchical structure and is assessed on a weekly basis with one code registered in DREAM per week. Absence from work during pregnancy was registered as either regular or pregnancy-related. Regular sickness absence was registered if the women were absent from work for >15 days and subsequently backdated to day 1. Pregnancy-related absence from work relates to absence due to pregnancy factors, eg, pelvic pain or harmful working condition(s) for mother or child and was registered from the first day of absence. In order for the absence period, no matter the type, to be entered into DREAM it had to be doctor-certified. For the two types of absence, the employers were reimbursed for the sickness benefit from day 15 and 1, respectively. Pregnancy-related absence constituted 88.0% and regular sickness absence 12.0% of the total absences from work during pregnancy. These two were in the statistical analyses combined into a single outcome (yes/no) and the term "absence from work" is used for the outcome measure in the following.

Potential confounders

We investigated the previous literature and incorporated the identified potential confounders in a directed acyclic graph (DAG). This served as partial basis for selection of confounders together with the availability of information in the interview and the DREAM register. We included sickness absence during the year prior to pregnancy and during early pregnancy (until the first interview), which were combined into the variable previous sickness absence. The other confounders included were maternal age at conception, parity, fertility treatment, socio-economic status (SES), pre-pregnancy body mass index, during pregnancy smoking and leisure time exercise. SES was based on self-reported job titles converted into the Danish International Standard Classification of Occupations (DISCO-88). The confounders are presented in table 2.

Statistical analysis

In the analyses, we investigated the association between the index variable and absence from work. We analyzed data in Cox proportional hazard regression models with adjustment for covariates with gestational age (days) as the underlying time variable. Calculation of gestational age was based on the self-reported first day of the last menstrual period from the interview. Entry time was the date of the interview, and end time was the date of receiving the first episode of absence from work after the interview. Observations were censored if the women terminated pregnancy, gave birth (stillbirth or preterm birth), emigrated, went on leave other than maternity leave, received other social benefits, or the end of the study period was reached at 30 completed GW, whichever came first.

All variables were tested relative to the proportional hazard assumption by investigating the cumulative proportional hazards and reclassified when needed (see footnotes to table 2).

The results are presented as hazard ratios (HR) with 95% confidence intervals (CI) from the crude and two adjusted models; one model including all potential confounders except SES, and one model also including SES. A third model was included because inclusion of SES might result in over-adjustment.

Previous sickness absence could indicate an inherent propensity for later sickness absence (13). In the subgroup analyses, we therefore conducted the analyses with the women stratified into four groups based on their absence from work prior to pregnancy (0, 1-2, 3-5, and >6 weeks absence) and on their absence from work both prior to and during early pregnancy (see categorization in table 2). As a sensitivity analysis, we investigated the index variable with six categories instead of five in relation to absence from work.

The statistical analyses were conducted in SAS 9.4 (SAS Institute Inc, Cary, NC, USA).

Results

In this study, 24.3% of the women had their first spell of absence from work before GW 31, on average at GW 24.0 (SD 4.7). About 80% of the women experienced between 1-3 occupational exposures, while <4% experienced 0 exposure at work of interest for this study. Women in the youngest age group or with lower educational level, more children, more smoking, or higher BMI experienced more exposures at work. Previous sickness absence was also associated with more exposures at work. Women who had received fertility treatment experienced less exposures compared to women without fertility treatment (table 2).

The women were on average followed for 11.6 weeks; women registered with absence from work were followed for

7.6 weeks (mean), while women with no absence from work were followed for 12.9 weeks (mean). Both the crude and adjusted analyses showed that with an increasing number of occupational exposures the risk of absence from work increased (figure 2), albeit adjustment attenuated the findings both from model 1 to 2 and from model 2 to 3. In the fully adjusted analysis, the HR increased from 1.25 (95% CI 1.08-1.45) for one occupational exposure to 2.87 (95% CI 2.49-3.30) for 4-5 compared with 0 occupational exposures (figure 2).

In a sensitivity analysis, we investigated the index as a 6-category variable, ie, without combining 4 and 5 occupational exposures. Being exposed to 4 occupational exposures resulted in the fully adjusted analysis in a HR of 2.77 (95% CI 2.40-3.19) for absence from work, exposure to 5 occupational exposures gave a HR of 3.23 (95% CI 2.77-3.77) for absence from work. Hence, the risk of absence from work further increased when the number of occupational exposures increased from 4 to 5.

We conducted subgroup analyses to test for effect modification by previous sickness absence in two different analyses. First, a test of effect modification by sickness absence prior to pregnancy (0, 1-2, 3-5 and >6 weeks) was investigated for the index variable. In each of the subgroups in this variable, we found a pattern with increasing number of occupational exposures the risk of absence from work also increased. For women with no sickness absence prior to pregnancy, the risk of absence from work increased compared to the main analysis, ie, for 4-5 occupational exposures, the fully adjusted HR was 3.26 (95% CI 2.79-3.81) compared to HR 2.87 (95% CI 2.49-3.30) in the main analysis. In the test including sickness absence prior to and during early pregnancy (no, before, early, and both before and during early pregnancy), we saw a similar pattern, except for the group of women absent from work both before and during pregnancy, where we found no association.

Discussion

Approximately 25% of the pregnant women in the study had >1 spell of absence from work during the followup until the end of GW 30. We found an increasing risk of absence with an increasing number of occupational exposures when analyzed by use of an index variable including exposures that were earlier shown to be associated with the risk of absence (4). The results supported our hypothesis that more exposures at work led to a higher risk of absence from work.

Our findings were in line with two previous studies; a cross-sectional study showed a dose-response relationship between an cumulated index of occupational exposures and absence from work (6). However, information about both exposures and absence was collected after the women gave birth. A previous Danish report (7) also found that pregnant women exposed to several occupational exposures had an increased risk of absence from work. Our study on the other hand is, as far as we know, the first prospective study to use register information for the outcome investigating the association between combinations of occupational exposures.

Each variable included in the index was dichoto- mized into yes/no and job demands and control was included as separate exposures and not as job strain (3). Albeit the index variable does not distinguish between the included occupational exposures, the results yield information on the consequences of concomitant multiple occupational exposures for absence.

We had decided, a priori, to collapse exposure to four and five occupational exposures into one category as we did not think that many would experience all five at the same time, but subsequently performed the analyses with four and five occupational exposures as separate groups. Both the main and the sensitivity analysis showed a clear dose-response relationship between the index variable and absence from work with the highest risk of absence in the group experiencing five occupational exposures.

One point for discussion is whether the absence we investigate is related to work or pregnancy. The employers were reimbursed for the pregnancy-related absence from day 1 but first from day 15 for general sickness absence. The employer would therefore have had an economical incentive to report absence as pregnancy-related which might explain that regular sickness absence constituted only 12.0% of the total number of absences from work. The lack of information on the reason(s) for the absence from work in DREAM precluded distinction between regular and pregnancy-related absence. Unfortunately, the data did not provide the possibility to investigate this issue further.

In this study, SES was based on the women's selfreported job titles. SES would be expected to be highly correlated

to the investigated occupational exposures; perhaps mainly the physical exposures as the types of jobs held by skilled and un-skilled workers would be depicted by more physically straining work (14, 15). In the analyses, we adjusted for SES only in the final statistical models to avoid potential over-adjustment. Sickness absence generally increases with lower SES, in pregnant as well as non-pregnant populations (1, 16-18). An explanation of the influence of SES could be the presence of differential exposure and vulnerability. Differential exposure refers to the number of differential exposures either as type, duration, or amount that varies between the social positions and thereby the health risks (19). The lower the SES, the higher the risk of being exposed to risk factors and not only in the professional life. This might entail that the impact of a single (occupational) exposure could be stronger in groups of lower compared to groups of higher SES, ie, differential vulnerability (19). However, adjustment for SES only discretely attenuated estimates. Another explanation could also be different attitudes towards working during pregnancy and personality, which we could not control for due to lack of data.

The women from the DNBC were probably healthier than the general population. Previously, Jacobsen and colleagues (20) showed that women with low socioeconomic resources were underrepresented in this cohort, and furthermore, we only included women with >30 weekly work hours and excluded women receiving sickness benefit due to special circumstances. Less than 25% of the pregnant women were absent from work. Other studies or reports found levels of absence from work in pregnancy of 43-68%, irrespective of weekly working hours and time of absence from work in pregnancy (1, 4, 21, 22). We, on the other hand, investigated the risk of absence from work in a rather healthy cohort and showed that even here the risk of absence increases with an increasing number of occupational exposures.

The study was conducted within the DNBC, which was established between 1996 and 2002, ie, around 20 years ago. The recommendations issued by the Danish Work Environment Authorities on working conditions for pregnant women have not changed much since 2002 (23-25). Only one major change regarding lifting has been introduced over the years, as the recommendation has been eased since 2009: the maximum lifting restriction of 1000 kg per day has been removed (23-26). Psychosocial working conditions were first mentioned in 2002, solely to be considered together in combinations with other factors such as lifting (24).

The findings from the subgroup analyses partly confirmed our main findings for women with no prior absence due to sickness. However, for women with previous sickness absence, the subgroup analyses did not show the same results as the main findings. This might be due to the small numbers, or perhaps women with previous sickness absence become absent during pregnancy earlier than pregnant women without previous sickness absence, and therefore no association was shown in these subgroups.

Our study suggests that absence from work among pregnant women may potentially be reduced by lowering the number of occupational exposures. Studies on absence from work show that women are most often absent due to general pregnancy-related discomfort, which can be exacerbated when doing strenuous work. Hence, job adjustment can help pregnant women to continue working. This is indicated by previous studies, showing that absence can be reduced if job adjustment is considered relevant and implemented (27, 28). At Akershus University Hospital in Oslo, a new approach was implemented where all newly pregnant employees were offered an interview with their leader and a midwife early in pregnancy to explore the need for and implement job adjustment. The hospital subsequently experienced a large reduction in absence among their pregnant employees (29).

A priori, we wished to investigate the combined effect of two specific occupational exposures - lifting and job strain - in relation to absence from work. However, due to power issues when including a 16-category variable of combined lifting (10) and job strain (3) and the two main effects (lifting and job strain) in the same analyses, we did not include these (data not shown).

The major strengths of this study include the large cohort with prospective data collection combined with national register data on the outcome. In addition, we only included women working >30 hours/week because fewer weekly work hours could increase recuperation from work-related strain and thereby reduce the need for reduction of work by absence. This is supported by findings of reduced absence from work among pregnant women working <30 hours/week (22). In contrast, a previous study on absence during pregnancy based on the DNBC showed that

pregnant women working <37 hours/week had an increased risk of absence, while women working >37 hours/week had a decreased the risk of absence, both compared to women working 37 hours/week (4). However, women working >37 hours/ week might be a selected group and more robust, hence, their risk of absence during pregnancy is lower.

One limitation relates to the choice of the five occupational exposures included in the index. Other exposures such as social relationships, including quality of leadership and social support, or workplace violence, including physical violence and bullying, could have been included. However, work posture, work shift, and lifting, were previously investigated in relation to absence in pregnancy in DNBC (4). Job strain was also previously studied for this outcome, albeit not with job demands and job control as separate measures (4). Of note, we have not taken the potential correlation of the variables into account. However, the correlations of the variables were tested after the index variable was created. The results showed that only lifting and work posture were moderately to strongly correlated, while the other variables were less correlated. The results for each increment in the index may therefore not be completely independent of each other, but the normal distribution of the index variable as a variable ranging from 0 to 5 is reassuring. The questions used to generate the index were not validated, which could have led to bias. The most likely scenario would be non-differential misclassification and potential bias toward the null.

Notwithstanding these limitations, a cautious recommendation based on the presented findings would be to raise awareness of the number of occupational exposures that pregnant women experience. The novelty with the present study is that the number of exposures could possibly be a way to assess the risk of absence in pregnancy. This knowledge may be used to guide the employers on how to reduce absence from work among pregnant employees through an exposure reduction when several concomitant exposures are present at a time. This recom- mendation aligns well with the guidelines from the Danish Working Environment Authority (23) that the work conditions of pregnant women ought to be assessed as a whole in cases with exposure to high physical strain. Furthermore, initiatives of job adjustment addressing the straining occupational exposure might be one way to decrease absence from work in this group of workers.

Concluding remarks

We found the number of occupational exposures including job demands, job control, work posture, work shift and lifting, associated with an increased risk of absence from work during pregnancy. It may be useful to develop an index of work exposures with suggested adverse effects on absence from work during pregnancy. Thereby, it would be possible to identify pregnant women needing exposure reduction at work or to identify workplaces with a general need for preventive interventions to reduce absence among pregnant employees. Future studies should investigate job adjustment by addressing the number, type, and quality of occupational exposures among pregnant women that might reduce absence from work during pregnancy to reduce discomfort, absence, and societal and personal costs.

Acknowledgments

The Danish National Research Foundation established the Danish Epidemiology Science Centre that initiated and created the DNBC. The cohort is furthermore funded by major grant from this foundation. Additional support for the DNBC is obtained from the Pharmacy Foundation, the Egmont Foundation, the March of Dimes Birth Defects Foundation, the Augustinus Foundation and the Health Foundation. The present study was supported by grants from the Danish Work Environment Research Foundation (grant 20150018124/3).

The authors declare no conflicts of interest.

Sidebar

Sejbaek CS, Pedersen J, Schlünssen V, Begtrup LM, Juhl M, Bonde JP, Kristensen P, Bay H, Ramlau-Hansen CH, Hougaard KS. The influence of multiple occupational exposures on absence from work in pregnancy: a prospective cohort study. Scand J Work Environ Health. 2020;46(1):60-68. doi:10.5271/sjweh.3840

Correspondence to: Camilla Sandal Sejbaek, PhD, National Research Centre for the Working Environment, Lersø Parkalle 105, DK-2100 Copenhagen, Denmark. [E-mail: css@nfa.dk].

References

References

1. Danish Ministry of Employment. Analyse af graviditetsbetinget fravæ r [Analysis of pregnancy-related absence]. Copenhagen (DK): Danish Ministry of Employment, 2010 May.
2. Statistics Denmark. Erhvervs- og beskæ ftigelsesfrekvenser (ultimo november) efter område, herkomst, alder (16-64 år), køn og frekvens (2008-2016) [Profession- and employment frequences (ultimo November) by area, ancestry, age (16-64 years), sex and frequence (2008-2016)]. 2018. Available from http://www.statistikbanken.dk/statbank5a/default. asp?w=1680.
3. Karasek RA. Job Demands, Job decision latitude and mental strain: Implications for job redesign. Adm Sci Q 1979;24:285-308. https://doi.org/10.2307/2392498.
4. Hansen ML, Thulstrup AM, Juhl M, Kristensen JK, RamlauHansen CH. Occupational exposures and sick leave during pregnancy: results from a Danish cohort study. Scand J Work Environ Health 2015 Jul;41(4):397-406. https://doi. org/10.5271/sjweh.3507.
5. Kaerlev L, Jacobsen LB, Olsen J, Bonde JP. Long-term sick leave and its risk factors during pregnancy among Danish hospital employees. Scand J Public Health 2004;32(2):1117. https://doi.org/10.1080/14034940310017517.
6. Henrotin JB, Vaissière M, Etaix M, Dziurla M, Malard S, Lafon D. Exposure to occupational hazards for pregnancy and sick leave in pregnant workers: a cross-sectional study. Ann Occup Environ Med 2017 May;29:12. https://doi. org/10.1186/s40557-017-0170-3.
7. Bach H, Henriksen A. Gravides sygefravæ r [Sickness absence among pregnant]. Copenhagen: SFI - The Danish National Centre for Social Reserach, 2010.
8. Olsen J, Melbye M, Olsen SF, Sørensen TI, Aaby P, Andersen AM et al. The Danish National Birth Cohort-its background, structure and aim. Scand J Public Health 2001 Dec;29(4):300-7. https://doi.org/10.1177/14034948010290 040201.
9. Miranda H, Gore RJ, Boyer J, Nobrega S, Punnett L. Health behaviors and overweight in nursing home employees: contribution of workplace stressors and implications for worksite health promotion. Sci World J 2015;2015:915359. https://doi.org/10.1155/2015/915359.
10. Juhl M, Strandberg-Larsen K, Larsen PS, Andersen PK, Svendsen SW, Bonde JP et al. Occupational lifting during pregnancy and risk of fetal death in a large national cohort study. Scand J Work Environ Health 2013 Jul;39(4):335-42. https://doi.org/10.5271/sjweh.3335.
11. Larsen AD, Hannerz H, Juhl M, Obel C, Thulstrup AM, Bonde JP et al. Psychosocial job strain and risk of adverse birth outcomes: a study within the Danish national birth cohort. Occup Environ Med 2013 Dec;70(12):845-51. https://doi.org/10.1136/oemed-2013-101453.
12. Juhl M, Andersen PK, Olsen J, Andersen AM. Psychosocial and physical work environment, and risk of pelvic pain in pregnancy. A study within the Danish national birth cohort. J Epidemiol Community Health 2005 Jul;59(7):580-5. https:// doi.org/10.1136/jech.2004.029520.
13. Christensen KB, Andersen PK, Smith-Hansen L, Nielsen ML, Kristensen TS. Analyzing sickness absence with statistical models for survival data. Scand J Work Environ Health 2007 Jun;33(3):233-9. https://doi.org/10.5271/ sjweh.1132.
14. Schrijvers CT, van de Mheen HD, Stronks K, Mackenbach JP. Socioeconomic inequalities in health in the working population: the contribution of working conditions. Int J Epidemiol 1998 Dec;27(6):1011-8. https://doi.org/10.1093/ ije/27.6.1011.
15. Sejbaek CS, Bay H, Larsen AD, Kristensen P, Schlünssen V, Andersen AN et al. Combined exposure to lifting and psychosocial strain at work and adverse pregnancy outcomes-A study in the Danish National Birth Cohort. PLoS One 2018 Sep; 13(9):e0201842. https://doi.org/10.1371/ journal.pone.0201842.
16. Kaikkonen R, Härkänen T, Rahkonen O, Gould R, Koskinen S. Explaining educational differences in sickness absence: a population-based follow-up study. Scand J Work Environ Health 2015 Jul;41(4):338-46. https://doi.org/10.5271/ sjweh.3499.
17. Niedhammer I, Lesuffleur T, Memmi S, Chastang JF. Working conditions in the explanation of occupational inequalities in sickness absence in the French SUMER study. Eur J Public Health 2017 Dec;27(6):1061-8. https://

doi.org/10.1093/eurpub/ckx052.
18. Sydsjö A, Claesson IM, Ekholm Selling K, Josefsson A, Brynhildsen J, Sydsjö G. Influence of obesity on the use of sickness absence and social benefits among pregnant working women. Public Health 2007 Sep;121(9):656-62. https://doi.org/10.1016/j.puhe.2006.11.010.
19. Diderichsen F, Evans T, Whitehead M. The Social Basis of Disparities in Health. In: Evans T, Whitehead M, Diderichsen F, Bhuiya A, Wirth M, editors. Challenging Inequities in Health. 1st ed. New York: Oxford University Press; 2001.
20. Jacobsen TN, Nohr EA, Frydenberg M. Selection by socioeconomic factors into the Danish National Birth Cohort. Eur J Epidemiol 2010 May;25(5):349-55. https:// doi.org/10.1007/s10654-010-9448-2.
21. Sydsjö G, Sydsjö A. Newly delivered women's evaluation of personal health status and attitudes towards sickness absence and social benefits. Acta Obstet Gynecol Scand 2002 Feb;81(2):104-11. https://doi.org/10.1034/j.16000412.2002.810203.x.
22. Melsom AM. Long-term sickness absence during pregnancy and the gender balance of workplaces. Scand J Public Health 2014 Nov;42(7):627-34. https://doi. org/10.1177/1403494814541596.
23. Danish Working Environment Authority. Gravides og ammendes arbejdsmiljø [The working environment of pregnant and breast feeding]. Copenhagen (DK): Danish Working Environment Authority, 2015 October. Report No.: At-vejledning A.1.8-5.
24. Danish Working Environment Authority. Gravides og ammendes arbejdsmiljø. [The working environment of pregnant and breast feeding]. Copenhagen (DK): Danish Working Environment Authority, 2002 February Report No.: At-vejledning A1.8.
25. Danish Working Environment Authority. Gravides og ammendes arbejdsmiljø [The working environment of pregnant and breast feeding]. Copenhagen (DK): Danish Working Environment Authority, 2009 January. Report No.: At-vejledning, A.1.8.
26. Danish Working Environment Authority. Gravides og ammendes arbejdsmiljø [The working environment of pregnant and breast feeding]. At-anvisning. Copenhagen (DK): Danish Working Environment Authority, 1998 Marts. Report No.: At-anvisning, Nr. 4.0.0.2.
27. Kristensen P, Nordhagen R, Wergeland E, Bjerkedal T. Job adjustment and absence from work in mid-pregnancy in the Norwegian Mother and Child Cohort Study (MoBa). Occup Environ Med 2008 Aug;65(8):560-6. https://doi. org/10.1136/oem.2007.035626.
28. Strand K, Wergeland E, Bjerkedal T. Job adjustment as a means to reduce sickness absence during pregnancy. Scand J Work Environ Health 1997 Oct;23(5):378-84. https://doi. org/10.5271/sjweh.235.
29. Jenssen IK, Berger MA. Pregnant at work [Gravid i jobb]. Ramazzini. 2017;24(4):9-12.
30. Ramlau-Hansen CH, Thulstrup AM, Nohr EA, Bonde JP, Sørensen TI, Olsen J. Subfecundity in overweight and obese couples. Hum Reprod 2007 Jun;22(6):1634-7. https://doi. org/10.1093/humrep/dem035.
Received for publication: 25 October 2018

DETAILS

Subject:	Pregnancy; Posture; Age; Confidence intervals; Studies; Occupational exposure; Exposure; Gestational age; Risk factors; Occupational health; Regression analysis; Women; Statistical analysis; Risk analysis; Occupational stress; Maternity benefits; Cohort analysis
Business indexing term:	Subject: Occupational stress Maternity benefits
Location:	Denmark

Publication title:	Scandinavian Journal of Work, Environment &Health; Stockholm
Volume:	46
Issue:	1
Pages:	60-68
Publication year:	2020
Publication date:	2020
Section:	Original article
Publisher:	Scandinavian Journal of Work, Environment &Health
Place of publication:	Stockholm
Country of publication:	Finland, Stockholm
Publication subject:	Occupational Health And Safety
ISSN:	03553140
e-ISSN:	1795990X
Source type:	Scholarly Journal
Language of publication:	English
Document type:	Journal Article
DOI:	https://doi.org/10.5271/sjweh.3840
ProQuest document ID:	2344259039
Document URL:	https://www.proquest.com/scholarly-journals/influence-multiple-occupational-exposures-on/docview/2344259039/se-2?accountid=211160
Copyright:	Copyright Scandinavian Journal of Work, Environment &Health 2020
Last updated:	2023-03-06
Database:	Public Health Database

A silent epidemic: occupational exposure limits are insufficiently protecting individual worker health

Albin, Maria, MD; Gustavsson, Per, MD

ABSTRACT (ENGLISH)

In an editorial in an earlier issue of this journal, Johanson &Tinnerberg (1) expressed serious and well-founded concern over the large number of future occupational cancer cases that will result if exposures for a number of substances are not reduced below the so-called "binding occupational exposure limit values" (BOELV) issued by the EU (2). While the EU's Scientific Committee on Occupational Exposure Limits (SCOEL) recommended an OEL <0.05 (5) in order to protect workers reasonably well against negative health effects, the EU decided on a BOELV of 0.1 mg/m3 for RCS (2). The report estimates the future number of lung cancer cases attributable to occupational exposure to RCS in the EU up to 2069. The US OSHA estimated that exposing 1000 workers for 45 years at 0.1 mg/m3 would result in 33 extra lung cancer deaths as life-time risk, corresponding to an individual risk of 3.3% (6), exceeding the maximum tolerable risk nearly 10-fold. Since the EU Directive concerns cancer, the report did not consider other health effects, which is necessary for a general risk assessment.

FULL TEXT

In an editorial in an earlier issue of this journal, Johanson &Tinnerberg (1) expressed serious and well-founded concern over the large number of future occupational cancer cases that will result if exposures for a number of substances are not reduced below the so-called "binding occupational exposure limit values" (BOELV) issued by the EU (2). The balance between what is perceived as possible to comply with and the foreseeable health gain when setting BOELV is further discussed in a letter to the Editor by Cherrie (3). This debate raises several important aspects of how to protect workers from cancer as well as other potentially lethal diseases. Herewith, we discuss some of these aspects.

One problem in setting OEL is that levels that are considered safe may not be seen as feasible when accounting for technological and societal aspects. The EU has recognized this problem by distinguishing between so-called "indicative" (health-based) and legally binding OEL (4). However, a BOELV that does not protect from a high risk for severe health effects is not adequate. Both Johanson &Tinnerberg and Cherrie point to respirable crystalline silica (RCS) as an example: While the EU's Scientific Committee on Occupational Exposure Limits (SCOEL) recommended an OEL <0.05 (5) in order to protect workers reasonably well against negative health effects, the EU decided on a BOELV of 0.1 mg/m3 for RCS (2). The US Occupational Health and Safety administration (OSHA) has come to a different conclusion and decided on an OEL of 0.05 mg/m3 (6).

The EU has presented an extensive risk assessment for RCS developed within the SHEcan project (7). We argue that a BOELV at 0.1 is insufficient and partly may be due to misinterpretations of the SHEcan report. The report estimates the future number of lung cancer cases attributable to occupational exposure to RCS in the EU up to 2069. Four scenarios are discussed: (i) a baseline scenario, essentially predicting future numbers of cases without further regulatory action, (ii) a BOELV of 0.2 mg/m3 with 99% compliance, (iii) a BOELV of 0.1 mg/ m3 with 99% compliance, and (iv) a BOELV of 0.05 mg/ m3 with 99% compliance.

The estimations are based on an assumption of a latency period of 10-50 years from reduction of exposure until cancer risk drops. This assumption, in itself reasonable from present evidence, has the consequence that there is virtually no difference in projected annual future cases between the four scenarios for >40 years. The reduction in exposure in scenarios ii-iv comes into effect first only in the year 2050 (see figure 4.1 on p49 in ec.europa.eu/social/BlobServlet?docId=10161&la ngId=en). An assumption of 99% compliance with the BOELV in scenarios ii-iv has a dramatically stronger effect on the projected number of cases than the OEL itself: Even if the OEL was doubled to 0.2 mg/m3 the number of attributable cancer registrations in 2060 would be reduced by 70% just from the assumption of almost full compliance. The additional number of attributable cancer registrations that

are prevented when an OEL of 0.1 (scenario iii) is compared to an OEL of 0.05 (scenario iv) under an assumption of almost full compliance is comparatively small (7, p123). The reason for this strong effect of a 99% compliance is that exposure often will exceed the OEL. The report may lead to the misconception that an OEL of 0.05 mg/m3 has little benefit over an OEL of 0.1 mg/m3, especially if the cases saved are expressed as lives saved per year over the entire 60-year period. For Sweden and other countries where OEL already have legal status, the introduction of BOELV would have no legal implications.

The SHEcan report shows that occupational exposure to silica will cause in all 440 000 cancer cases between 2010 and 2069 in the EU if nothing further is done (scenario i). This number must be reduced even if it will take time until preventive measures have full effect. An analogy with asbestos is obvious: it is well known that reductions in the mesothelioma rate were seen first only many decades after asbestos was banned - yet no one would argue that it was not worth reducing asbestos exposure for this reason.

The report assumes an annual 7% decrease in silica exposure levels until the period 2020-2029 even if no further regulatory action is taken. This is a very questionable assumption that went unconfirmed in a recent French report (8) that gave no evidence for reduced exposure to RCS in the French construction sector during the last decade. This indicates that even the very high number of 440 000 attributable cancer registrations is underestimated by the report, to which, in addition, should be added the number of chronic obstructive pulmonary disease and kidney disease cases, for which a much shorter latency period until risk drops is likely.

The concepts "maximum tolerable risk" and "acceptable risk" have been developed for exposure to genotoxic carcinogens, for which no exposure level could be considered safe. A life-time extra number of four cases per 1000 exposed workers over a 40-year working life has been suggested as a maximum tolerable risk, and four cases per 100 000 exposed workers as an acceptable risk, both in Germany and in the Netherlands (9, 10). These figures can be transformed to the individual life-time risk of contracting cancer from the exposure as 4/1000, corresponding to 0.4% individual risk. While these limits are not absolute and can be discussed, it is of interest to apply them to the case of RCS.

The risk associated with an OEL of 0.1 mg/m3 for RCS is associated with risks far higher than "maximum tolerable", ie, 0,4%. The US OSHA estimated that exposing 1000 workers for 45 years at 0.1 mg/m3 would result in 33 extra lung cancer deaths as life-time risk, corresponding to an individual risk of 3.3% (6), exceeding the maximum tolerable risk nearly 10-fold. Since the EU Directive concerns cancer, the report did not consider other health effects, which is necessary for a general risk assessment. The US OSHA estimated there would be another 85 deaths from non-malignant lung disease (8.5%) and, roughly estimated, 39 deaths from renal disease (3.9%) that should be added to this toll. This adds up to an individual excess death risk of 15%, which by far clearly exceeds what is generally seen as the maximum tolerable risk of 0.4%! Still, this is a conservative estimate, which includes neither excess deaths from myocardial infarction that occur from 0.025 mg/m3 and up (11) nor excess autoimmune disease, eg, rheumatoid arthritis and other autoimmune diseases (12, 13). In support of Johanson &Tinnerberg (1), we argue that the lifetime excess death risk for silica-exposed workers is totally incompatible with fundamental workers' rights of health and safety.

This aspect, which must be safeguarded by the OSH society, will be even more important when working life is prolonged and when exposure conditions may be more diverse, ie, workers with high exposure and excessive risk may be too few to impact the disease burden in society but in that group the burden may still be extreme. In our view, the assumption of 99% compliance is unrealistic and it is necessary to lower the OEL. In addition, leaving the BOELV at 0.1 mg/m3 means this will continue for the future, a silent epidemic that is deeply unethical to ignore.

Sidebar

Maria Albin, Professor, MD,1 2 Per Gustavsson, Senior professor, MD12

1 The Unit of Occupational Medicine, Institute of Environmental Medicine, Karolinska Institutet, Sweden.

2 Centre for Occupational and Environmental Medicine, Region Stockholm, Sweden.

Correspondence to: Per Gustavsson, Centre for Occupational and Environmental Medicine, Torsplan 4, 113 65, Stockholm, Sweden. [E-mail: per.gustavsson@ki.se]

References

References

1.Johanson G, Tinnerberg H. Binding occupational exposure limits for carcinogens in the EU - good or bad? Scand J Work Environ Health 2019 May;45(3):213-4. https://doi. org/10.5271/sjweh.3825.

2. Directive EU. (EU) 2019/130 of the European parliament and of the council of 16 January 2019. Available from: https://eur-lex.europa.eu/legal-content/EN/TXT/ PDF/?uri=CELEX:32019L0130.

3. Cherrie JW. Binding occupational exposure limits for carcinogens in the EU - necessary but not sufficient to reduce risk. Scand J Work Environ Health 2019 Jul;45(4):423-4. https://doi.org/10.5271/sjweh.3836.

4. SCOEL. SCOEL's involvement in setting Occupational Exposure Limits: Webpage accessed 2019-10-23. Available from: http://ec.europa.eu/social/BlobServlet?docId=3879& langId=en.

5. SCOEL. Recommendation from the Scientific Committee on Occupational Exposure Limits for Silica, Crystalline (respirable dust). SCOEL/SUM/94. November 2003. Available from: http://ec.europa.eu/social/BlobServlet?doc Id=3803&langId=en.

6. OSHA. Occupational Exposure to Respriable Crystalline Silica. Federal Register/vol 81, no 58/Friday, March 25, 2016/ Rules and Regulations. Occupational Safety and Health, Department of Labour, Administration (Docket No. OSHA2010-0034) RIN 1218/AB70. OSHA 2016. Available from: https://www.govinfo.gov/content/pkg/FR-2016-03-25/ pdf/2016-04800.pdf.

7. Cherrie JW, Gorman Ng M, Searl A, Shafrir A, van Tongeren M et al. Health, socio-economic and environmental aspects of possible amendments to the EU Directive on the protection of workers from the risks related to exposure to carcinogens and mutagens at work. Respirable crystalline silica. IOM Research Project: P937/8, May 2011. Available from: https://ec.europa. eu/social/BlobServlet?docId=10161&langId=en).

8. ANSES. Agence nationale de sécurité sanitaire alimentation, environnement, et du travail (ANSES). Dangers, expositions et risques relatifs a la silice cristalline. Avis de l'Anses Raports d'expertise collective (Saisine no 2015-SA-0236). Avril 2019. Edition scientifique. ANSES English summary: Available from: https://www.anses.fr/en/content/exposure-crystallinesilica-poses-high-risks-worker-health

9. Federal Institute for Occupational safety and Health. The riskbased concept for carcinogenic substances developed by the Committee for Hazardous Substances. Federal Institute for Occupational safety and Health (BAuA), Dortmund, Germany, 2013. Available from: www.baua.de/dok/3581564

10. Health Council of the Netherlands. Guidelines for the calculation of occupational cancer risk values. Health Council of the Netherlands, 2012. Available from: www. healthcouncil.nl/documents/advisory-reports/2012/10/26/ guideline-for-the-calculation-of-occupational-cancer-riskvalues.

11. Liu Y, Zhou Y, Hnizdo E, Shi T, Steenland K, He X et al. Total and Cause-Specific Mortality Risk Associated With Low-Level Exposure to Crystalline Silica: A 44-Year Cohort Study From China. Am J Epidemiol 2017 Aug;186(4):48190. https://doi.org/10.1093/aje/kwx124.

12. Stolt P, Källberg H, Lundberg I, Sjögren B, Klareskog L, Alfredsson L; EIRA study group. Silica exposure is associated with increased risk of developing rheumatoid arthritis: results from the Swedish EIRA study. Ann Rheum Dis 2005 Apr;64(4):582-6. https://doi.org/10.1136/ ard.2004.022053.

13. Parks CG, Conrad K, Cooper GS. Occupational exposure to crystalline silica and autoimmune disease. Environ Health Perspect 1999 Oct;107 Suppl 5:793-802.

DETAILS

Subject:	Epidemics; Compliance; Disease; Workers; Disease control; Lung cancer; Environmental health; Disease prevention; Risk assessment; Medicine; Exposure limits; Occupational exposure; Health risk assessment; Occupational health; Occupational safety; Asbestos; Health risks

Location:	Sweden; United States--US
Company / organization:	Name: Occupational Safety &Health Administration--OSHA; NAICS: 926150
Publication title:	Scandinavian Journal of Work, Environment &Health; Stockholm
Volume:	46
Issue:	1
Pages:	110-112
Publication year:	2020
Publication date:	2020
Section:	Letter to the Editor
Publisher:	Scandinavian Journal of Work, Environment &Health
Place of publication:	Stockholm
Country of publication:	Finland, Stockholm
Publication subject:	Occupational Health And Safety
ISSN:	03553140
e-ISSN:	1795990X
Source type:	Scholarly Journal
Language of publication:	English
Document type:	Journal Article
DOI:	https://doi.org/10.5271/sjweh.3864
ProQuest document ID:	2344258895
Document URL:	https://www.proquest.com/scholarly-journals/silent-epidemic-occupational-exposure-limits-are/docview/2344258895/se-2?accountid=211160
Copyright:	Copyright Scandinavian Journal of Work, Environment &Health 2020
Last updated:	2021-01-13
Database:	Public Health Database

Trends and success stories in research on occupational and environmental health

Härmä, Mikko, MD PhD

ABSTRACT (ENGLISH)

[...]the Journal's transformation over more than four decades can be used as a good example of how occupational research and publishing policy has adapted to the new trends in scientific knowledge and information technology. During the same period, the number of submitted papers has doubled allowing us to be more selective and publish only the best research, which is depicted in the current acceptance rate of 15%. Since the beginning of 2012, the non-profit Nordic Association of Occupational Safety and Health (NOROSH) has published the Journal. Papers published on epidemiology, especially those associated with psychosocial factors (18-21), long working hours and shift work (22-26), as well as papers on musculoskeletal disorders, physical activity, work careers and return-to-work (27-31) performed better than average with respect to citations. Starting in 2020, open access will be by opt-out only and in 2022, we will publish 100% unlocked content. [...]the Scandinavian Journal of Work, Environment &Health will remain a relevant, high-quality, non-profit scientific journal that is unique in many ways.

FULL TEXT

The headline in a main Finnish newspaper on 16 November announced: "Trust and interest for published science has increased in Finland". I would have hypothesized that evidence-based knowledge was losing the game against the rush of non-scientific and commercial information - but I was wrong. A 3-year follow-up survey among the Finland population was clear on this. Could the growth in electronic and social media information actually be causing people to search for knowledge based on scientific facts?

Forty-five years have passed since the publication of the first issue of the Scandinavian Journal of Work, Environment &Health (SJWEH) in January 1975. The Journal is unique due to its non-profit profile in a sea of large, commercial publishing house journals. With a current impact factor of 3.491, SJWEH is recognized for its high quality and interesting content. The main aim of the Journal has always been to promote good and impactful research in the field of occupational and environmental health and safety. The Journal makes a difference by providing its readership with innovative topics, systematic reviews on existing knowledge, and papers using advanced research methods. Over the years, the scientific focus areas of occupational research, research methods, and academic publishing have undergone major changes. In fact, the Journal's transformation over more than four decades can be used as a good example of how occupational research and publishing policy has adapted to the new trends in scientific knowledge and information technology.

Well-known professor of epidemiology and specialist in occupational medicine, Sven Hernberg was the first Editor-in-Chief (EC) of the Journal. SJWEH was based on earlier ancestor journals (1), but in practice Sven had to start from scratch both scientifically and economically. Together with Sven, Markku Nurminen, epidemiologist and biostatistician, and native English-speaking copy editor Georgianna Oja belonged to the first editing team. SJWEH was launched as the joint activity of the Swedish, Danish, Norwegian and Finnish national research institutes. Even though the Journal's main focus in the beginning was on occupational medicine, toxicology and epidemiology, Sven wanted to support some developing fields of research at the time such as research of musculoskeletal disorders and biological monitoring. He was interested in preventive actions and the initialization of long follow-up studies in occupational medicine (2). The very first SJWEH paper was a review on neurophysiological methods (3). The first

paper on psychosocial factors, published by Theorell in 1977, was on the association of psychosocial factors in concrete work with myocardial infarction (4).

Based on the 20 "citation classics" (defined as publications with >100 citations) of the five most distinguished occupational medicine journals (5), citation classics dealing with toxicology were published in each decade during those times. However, well-cited papers on solvents appeared only during the 1970s and 1980s and were instrumental in the phasing out of organic solvents-based paints. Citations classics on work-related musculoskeletal disorders emerged in the 1980s and gained in popularity in the later decades (5). Compared to other occupational health journals, SJWEH had the second highest number of citation classics during the early decades of its existence. With >900 citations in Scopus, a 1993 paper on the association of psychosocial factors with musculoskeletal diseases by Bongers (6) was among one of the most cited.

I took up the position of Assistant EC after Markku in 1994. During the next few years, Sven and I updated our editing processes. A new electronic publishing system was created in 1998, making it possible to shift to a joint co-editor model. Several new Associate Editors (AE) were brought on board, increasing the expertise of the Journal significantly and making the editing process more interactive. Eira Viikari-Juntura, Petter Kristensen, Per Malmberg, Thomas Schneider, Lars Hagmar, Michiel Kompier, Kjell Larson, and Gunnar Aronson joined the Journal in the first wave starting 1999-2000. When Sven retired at the end of 1999, I became the EC sharing, however, the key management and decision-making together with Eira, who took on the role of Assistant EC in 2000. As a supplement to the paper version, an electronic version of the Journal was launched in 2001.

In his last editorial before retiring (7), Sven emphasized the significance of the need to shift the focus to new areas of research. While traditional occupational diseases were - and still are - a burden in many countries, he highlighted that the main roadblock in their remedy is not additional research but implementation of already existing knowledge (7). Taking the lead, we started to focus on new areas where existing knowledge was not great, especially psychosocial issues and musculoskeletal disorders, while maintaining a strong presence in epidemiological and clinical research on occupational epidemiology.

During the 1990s, we had already started to publish editorials and reviews in all issues of the Journal. Several of the latter became citation classics, for example those on exposure assessment and musculoskeletal issues by Burdorf (8) and Burdorf &Sorock (9) and a review on shift work and cardiovascular diseases by Bøggild &Knutsson (10). We also published consensus reports on key issues like the new Helsinki criteria for diagnosis and attribution on asbestos, asbestosis and cancer (11), extensively cited later, up to its update a few years ago (12), and special issues on growing research areas like work-related stress: health-risks, mechanisms and countermeasures (13) and shift work and health (14). These special issues included several reviews that also became citation classics. The review on psychosocial factors and mental health by Stansfeld &Candy (15), in particular, has been cited >900 times based on Scopus, as well as a review on work stress and coronary heart disease by Kivimäki and colleagues (16) (>500 times).

During the 2000s, in addition to relevance, emphasis was placed on shortening article processing time and improving accessibility of the Journal (17). Some new AE were brought onto the team to improve the Journal's expertise in new key research areas. Being among the key scientists publishing and actively reviewing for the Journal, Alex Burdorf, Bengt Järvholm, Göran Kecklund, Jos Verbeek, Hannu Norppa, Antero Aitio, and Jens Peter Bonde all started as new AE. To speed up the flow of manuscripts and improve accessibility, we shifted to a full electronic submission and review process and launched the "online first" policy, making all papers open access until their publication in the print version. These efforts, along with higher quality submissions increased citations and raised the impact factor. When Georgianna retired in 2009, Lisa O'Donoqhue-Lindy started as the new Managing Editor. In addition to being responsible for copy editing, Lisa promoted the electronic and open access services of the Journal and has always been very active in its development and benchmarking against other journals.

From 2008 to today, the impact factor of the Journal has doubled, and currently we hold a close second among all journals in the field of occupational and environmental health. During the same period, the number of submitted papers has doubled allowing us to be more selective and publish only the best research, which is depicted in the

current acceptance rate of 15%. Since the beginning of 2012, the non-profit Nordic Association of Occupational Safety and Health (NOROSH) has published the Journal. As earlier, the Nordic research institutes play a key role as founding members of NOROSH.

Papers published on epidemiology, especially those associated with psychosocial factors (18-21), long working hours and shift work (22-26), as well as papers on musculoskeletal disorders, physical activity, work careers and return-to-work (27-31) performed better than average with respect to citations. However, papers introducing or using new methodologies (32-34) have gained much attention, too.

The last two years have been historical for the Journal for several reasons. Sven sadly passed away (2). When Eira retired as Assistant EC in 2018, Alex Burdorf, Head of the Department of Public Health at Erasmus University Medical Centre joined me as co-EC. And when I decided to step down at end of 2019, Reiner Rugulies, Professor of Psychosocial Issues and Mental Health at the Danish National Research Centre for the Working Environment became EC alongside Lex, after earlier having been an AE. I will continue as an AE for the topics of shift work and working hours. In the meantime, several new AE have joined the team: Karin Broberg, Håkan Wallin, David Lombardi, Karl-Christian Nordby, Carel Hulshof, Susanne Svendsen, Hermann Burr and Vivi Schlünssen several years ago, and, more recently, Annina Ropponen, Henrik Kolstad, Cécile Boot, and Paul Kuijer.

In the future, as the editorial team has pointed out, the Journal will place greater emphasis on scientific quality and innovative research topics and methods (35). Staying ahead of the Open Science Movement, we recently decided to take the important step towards becoming a fully fledged open access journal. Starting in 2020, open access will be by opt-out only and in 2022, we will publish 100% unlocked content. Thus the Scandinavian Journal of Work, Environment &Health will remain a relevant, high-quality, non-profit scientific journal that is unique in many ways.

Sidebar

Mikko Härmä, MD, PhD
Research Professor
Finnish Institute for Occupational Health
Helsinki
Finland
[Email: mikko.harma@ttl.fi]

References

References

1. Smith DR. A history of the Scandinavian Journal of Work, Environment &Health. Scand J Work Environ Health. 2016;42(3):177-80. https://www.sjweh.fi/show_abstract.php?abstract_id=3558
2. Rantanen J. Professor Sven Hemberg, 1934-. Scand J Work Environ Health. ;45(3):527-8. https://doi.org/10.5271/sjweh.3849
3. Seppäläinen AM. Applications of neurophysiological methods in occupational medicine. A review. Scand J Work Environ Health. 1975;1(1):1-14. https://doi.org/10.5271/sjweh.2865
4. Theorell T, Olsson A, Engholm G. Concrete work and myocardial infarction. Scand J Work Environ Health. 1977;3(3):144-53. https:// doi.org/10.5271/sjweh.2779
5. Gehanno JF, Takahashi K, Darmoni S, Weber J. Citation classics in occupational medicine journals. Scand J Work Environ Health. 2007;33(4):245-51. https://doi.org/10.5271/sjweh.1139
6. Bongers PM, de Winter CR, Kompier MA, Hildebrandt VH. Psychosocial factors at work and musculoskeletal disease. Scand J Work Environ Health. 1993;19(5):297-312. https://doi.org/10.5271/sjweh.1470
7. Hernberg S. Towards a new millennium. Scand J Work Environ Health. 1999;25(6):465-9. https://doi.org/10.5271/sjweh.468
8. Burdorf A. Exposure assessment of risk factors for disorders of the back in occupational epidemiology. Scand J Work Environ Health. 1992;18(1):1-9. https://doi.org/10.5271/sjweh.1615
9. Burdorf A, Sorock G. Positive and negative evidence of risk factors for back disorders. Scand J Work Environ Health. 1997;23(4):24356. https://doi.org/10.5271/sjweh.217

10. Boggild H, Knutsson A. Shift work, risk factors and cardiovascular disease. Scand J Work Environ Health. 1999;25(2):85-99. https:// doi.org/10.5271/sjweh.410
11. Tossavainen K. Asbestos, asbestosis, and cancer: the Helsinki criteria for diagnosis and attribution. Scand J Work Environ Health. 1997;23(4):311-6. https://doi.org/10.5271/sjweh.226
12. Wolff H, Vehmas T, Oksa P, Rantanen J, Vainio H. Asbestos, asbestosis, and cancer, the Helsinki criteria for diagnosis and attribution 2014: recommendations. Scand J Work Environ Health. 2015;41(1):5-15. https://doi.org/10.5271/sjweh.3462
13. Härmä M, Kompier MA, Vahtera J. Work-related stress and health-risks, mechanisms and countermeasures. Scand J Work Environ Health. 2006;32(6):413-9. https://doi.org/10.5271/sjweh.1047
14. Härmä M, Kecklund G. Shift work and health - how to proceed? Scand J Work Environ Health. 2010;36(2):81-4. https://doi. org/10.5271/sjweh.2902
15. Stansfeld S, Candy B. Psychosocial work environment and mental health-a meta-analytic review. Scand J Work Environ Health. 2006;32(6):443-62. https://doi.org/10.5271/sjweh.1050
16. Kivimäki M, Virtanen M, Elovainio M, Kouvonen A, Väänänen A, Vahtera J. Work stress in the etiology of coronary heart disease-a meta-analysis. Scand J Work Environ Health. 2006;32(6):431-42. https://doi.org/10.5271/sjweh.1049
17. Härmä M, Viikari-Juntura E. Development of the Scandinavian Journal of Work, Environment &Health-the challenge of relevance, speed and accessibility. Scand J Work Environ Health. 2007;33(1):1-3. https://www.sjweh.fi/show_abstract.php?abstract_id=1058
18. Gilbert-Ouimet M, Trudel X, Brisson C, Milot A, Vezina M. Adverse effects of psychosocial work factors on blood pressure: systematic review of studies on demand-control-support and effort-reward imbalance models. Scand J Work Environ Health. 2014;40(2):109-32. https://doi.org/10.5271/sjweh.3390
19. Nielsen MB, Indregard AM, Overland S. Workplace bullying and sickness absence: a systematic review and meta-analysis of the research literature. Scand J Work Environ Health. 2016;42(5):359-70. https://doi.org/10.5271/sjweh.3579
20. Rugulies R, Aust B, Madsen IE. Effort-reward imbalance at work and risk of depressive disorders. A systematic review and meta-analysis of prospective cohort studies. Scand J Work Environ Health. 2017;43(4):294-306. https://doi.org/10.5271/sjweh.3632
21. Klingelschmidt J, Milner A, Khireddine-Medouni I, Witt K, Alexopoulos EC, Toivanen S, et al. Suicide among agricultural, forestry, and fishery workers: a systematic literature review and meta-analysis. Scand J Work Environ Health. 2018;44(1):3-15. https://doi. org/10.5271/sjweh.3682
22. Oakman J, Neupane S, Proper KI, Kinsman N, Nygard CH. Workplace interventions to improve work ability: A systematic review and meta-analysis of their effectiveness. Scand J Work Environ Health. 2018;44(2):134-46. https://doi.org/10.5271/sjweh.3685
23. Bannai A, Tamakoshi A. The association between long working hours and health: a systematic review of epidemiological evidence. Scand J Work Environ Health. 2014;40(1):5-18. https://doi.org/10.5271/sjweh.3388
24. Jørgersen JT, Karlsen S, Stayner L, Andersen J, Andersen ZJ. Shift work and overall and cause-specific mortality in the Danish nurse cohort. Scand J Work Environ Health. 2017;43(2):117-26. https://doi.org/10.5271/sjweh.3612
25. Vistisen HT, Garde AH, Frydenberg M, Christiansen P, Hansen AM, Andersen J, et al. Short-term effects of night shift work on breast cancer risk: a cohort study of payroll data. Scand J Work Environ Health. 2017;43(1):59-67. https://doi.org/10.5271/sjweh.3603
26. Torquati L, Mielke GI, Brown WJ, Kolbe-Alexander T. Shift work and the risk of cardiovascular disease. A systematic review and meta-analysis including dose-response relationship. Scand J Work Environ Health. 2017. https://doi.org/10.5271/sjweh.3700
27. Virtanen M, Jokela M, Madsen IE, Magnusson Hanson LL, Lallukka T, Nyberg ST, et al. Long working hours and depressive symptoms: systematic review and meta-analysis of published studies and unpublished individual

participant data. Scand J Work Environ Health. 2018;44(3):239-50. https://doi.org/10.5271/sjweh.3712
28. Arends I, van der Klink JJ, van Rhenen W, de Boer MR, Bültmann U. Predictors of recurrent sickness absence among workers having returned to work after sickness absence due to common mental disorders. Scand J Work Environ Health. 2014;40(2):195-202. https:// doi.org/10.5271/sjweh.3384
29. Jakobsen MD, Sundstrup E, Brandt M, Jay K, Aagaard P, Andersen LL. Effect of workplace- versus home-based physical exercise on musculoskeletal pain among healthcare workers: a cluster randomized controlled trial. Scand J Work Environ Health. 2015;41(2):15363. https://doi.org/10.5271/sjweh.3479
30. Commissaris DA, Huysmans MA, Mathiassen SE, Srinivasan D, Koppes L, Hendriksen IJ. Interventions to reduce sedentary behavior and increase physical activity during productive work: a systematic review. Scand J Work Environ Health. 2016;42(3):181-91. https:// doi.org/10.5271/sjweh.3544
31. Reeuwijk KG, van Klaveren D, van Rijn RM, Burdorf A, Robroek SJ. The influence of poor health on competing exit routes from paid employment among older workers in 11 European countries. Scand J Work Environ Health. 2017;43(1):24-33. https://doi.org/10.5271/ sjweh.3601
32. van der Beek AJ, Dennerlein JT, Huysmans MA, Mathiassen SE, Burdorf A, van Mechelen W, et al. A research framework for the development and implementation of interventions preventing work-related musculoskeletal disorders. Scand J Work Environ Health. 2017;43(6):526-39. https://doi.org/10.5271/sjweh.3671
33. Schelvis RM, Oude Hengel KM, Burdorf A, Blatter BM, Strijk JE, van der Beek AJ. Evaluation of occupational health interventions using a randomized controlled trial: challenges and alternative research designs. Scand J Work Environ Health. 2015;41(5):491-503. https://doi.org/10.5271/sjweh.3505
34. Thiart H, Lehr D, Ebert DD, Berking M, Riper H. Log in and breathe out: internet-based recovery training for sleepless employees with work-related strain - results of a randomized controlled trial. Scand J Work Environ Health. 2015;41(2):164-74. https://doi.org/10.5271/ sjweh.3478
35. McInnes JA, Akram M, MacFarlane EM, Keegel T, Sim MR, Smith P. Association between high ambient temperature and acute workrelated injury: a case-crossover analysis using workers' compensation claims data. Scand J Work Environ Health. 2017;43(1):86-94. https://doi.org/10.5271/sjweh.3602
36. Burdorf A, Härmä M. The future of Scandinavian Journal of Work, Environment &Health in the era of open science. Scand J Work Environ Health ;45(3):(213-4. https://doi.org/10.5271/sjweh.3826

DETAILS

Subject:	Information technology; Physical activity; Health; Epidemiology; Trends; Working conditions; Environmental health; Scholarly publishing; Toxicology; Editing; Research methodology; Medicine; Journals; Research centers; Occupational safety; Editors; Knowledge; Open access publishing; Cardiovascular disease; Shift work; Impact factors; Mental health; Working hours; Nonprofit organizations; Occupational health; Musculoskeletal diseases
Business indexing term:	Subject: Shift work Occupational health Working hours
Location:	Finland
Publication title:	Scandinavian Journal of Work, Environment &Health; Stockholm
Volume:	46
Issue:	1

Pages:	1-4
Publication year:	2020
Publication date:	2020
Section:	Editorial
Publisher:	Scandinavian Journal of Work, Environment &Health
Place of publication:	Stockholm
Country of publication:	Finland, Stockholm
Publication subject:	Occupational Health And Safety
ISSN:	03553140
e-ISSN:	1795990X
Source type:	Scholarly Journal
Language of publication:	English
Document type:	Editorial
DOI:	https://doi.org/10.5271/sjweh.3870
ProQuest document ID:	2344258747
Document URL:	https://www.proquest.com/scholarly-journals/trends-success-stories-research-on-occupational/docview/2344258747/se-2?accountid=211160
Copyright:	Copyright Scandinavian Journal of Work, Environment &Health 2020
Last updated:	2023-02-28
Database:	Public Health Database

Public health and evidence-informed policy-making: The case of a commonly used herbicide

Vainio, Harri, MD PhD

ABSTRACT (ENGLISH)

"Despite substantial evidence that Roundup weed killer is safe and non-carcinogenic if used properly, a federal judge last week appointed attorney Kenneth Feinberg to oversee court-mandated settlement talks between Bayer AG (the company that owns Roundup S producer, Monsanto) and plaintiff's who claim that the product caused their non-Hodgkin 's lymphoma." The Monographs apply rigorous procedures for the scientific review and evaluation of carcinogenic hazards by independent experts, free from conflict of interest. Since publishing Monograph conclusions on some pesticides (3), the IARC has been subject to intense efforts to undermine its evaluation and the whole organization. [...]of the widespread usage, glyphosate is present at low levels in a wide range food items (10). [...]scientists, toxicologists, epidemiologists, other health professionals, patients and populations have a collective responsibility not simply to be originators of scientific data but to be scrutinizers of their use, thereby protecting the interests of the many rather than the few.

FULL TEXT

Headnote

"Despite substantial evidence that Roundup weed killer is safe and non-carcinogenic if used properly, a federal judge last week appointed attorney Kenneth Feinberg to oversee court-mandated settlement talks between Bayer AG (the company that owns Roundup S producer, Monsanto) and plaintiff's who claim that the product caused their non-Hodgkin 's lymphoma." (1).

For almost half a century, the International Agency for Research on Cancer (IARC) has run a Monographs programme, which has been the premier global resource for the identification of agents that cause cancer (2). The Monographs apply rigorous procedures for the scientific review and evaluation of carcinogenic hazards by independent experts, free from conflict of interest. Since publishing Monograph conclusions on some pesticides (3), the IARC has been subject to intense efforts to undermine its evaluation and the whole organization. The conclusion in March 2015 that glyphosate is "probably carcinogenic to humans" in addition to being genotoxic and carcinogenic in animals led to unprecedented lobbying by the herbicide producer Monsanto, and resulted in high profile court cases in the USA (4).

Monsanto's tactic has been to discredit the glyphosate evaluation, the scientists involved, the Monograph programme and the IARC in general (see the Monsanto papers, 5-7). This has manifested in an orchestrated exercise of damage-generation played out through a coordinated and repetitive misrepresentation of facts, planned already before the March 2015 meeting took place (5). The once-confidential Monsanto papers have exposed the "cozy connections" between the company leadership, some regulatory agencies, and the media to undermine and discredit the actions and evaluation report of the IARC. They have revealed company scientists casually discussing "ghost-writing" scientific papers and suppressing science that conflicts with corporate assertions of Roundup's safety. The Monsanto documents demonstrate the company's manipulation of science and regulators, which may have reflected on the conclusions around the safety of the herbicide (6-8).

Evaluations of pesticides

IARC has evaluated more than 60 of the 100s of active ingredients in pesticide formulations, less than 12 of which have been formally evaluated as either group 1 (human carcinogens) or 2A (probable human carcinogens) (2). Some of these, such as dichlorodiphenyltrichloromethane (DDT) and lindane, have now been banned in most countries.

The evaluation of pesticides typifies the problems associated with research and regulation of commonly used consumer and agricultural products. IARC's evaluation of "probably carcinogenic to humans" (group 2A) is the second strongest category of evidence in a fourtier scale. The industry reaction to the evaluation of glyphosate was not foreseen. The two other chemicals evaluated in the same meeting as probably carcinogenic to humans (group 2A), diazinon and malathion, engendered no public debate.

If a widely used herbicide turns out to be a putative cancer-causing chemical, the consequences for the producer

can be potentially devastating. In May 2019, a court in California ordered Bayer AG to pay US$2 billion to a couple who claimed their cancers were caused by years of using Roundup. This was the third legal loss since August 2018 for Bayer AG, which has seen its market value plummet to $52 billion, cut nearly in half since it acquired Monsanto a year ago (9). More than 13 000 similar claims have been lodged (1).

How is the herbicide used 'properly'?

Ever since Monsanto introduced its line of Roundup weed-killers in 1974, the products have been touted as extremely safe. The company's statement that glyphosate is "safe and non-carcinogenic if used properly" is difficult to interpret in practice: even if you were dealing with a putative carcinogen, the cancer risk is not realized if you are not exposed to the agent, ie, the product is "safe if used properly".

So what is the "proper use" of a herbicide? One would assume it is use that is according to instructions on the label and guidance given by the producer. But when spreading the weed killer, it may be difficult to avoid human exposure. The occupational exposure in agriculture is likely to carry the most significant risk, followed by environmental exposures and risks to the consumers. Occupational exposure of glyphosate may occur via inhalation, dermal contact, and/or ocular contact during manufacture, transport, use and disposal. The absorption through skin is a real possibility. The general population may be exposed to glyphosate through dermal contact with consumer products, crops, foliage, or soils containing residues of this chemical. As a result of the widespread usage, glyphosate is present at low levels in a wide range food items (10).

The health risk is dependent on the level of exposure - it is the dose which makes the poison. The more intensively you are exposed, the longer the exposure period, and the higher the risk. The IARC evaluation does not take a position on the quantity or acceptability of the risk. This is not the task of the Agency but rather that of national decision-makers. The IARC evaluation constitutes a 'hazard evaluation' step in the risk assessment and management process - it is followed by an exposure analysis, quantitative risk assessment and risk-benefit analysis done in the policy-making process usually at the national regulatory level.

What is evidence-informed policy-making?

Simply put, evidence-informed policy is when decision-makers use the best available evidence to guide policy and regulations. Policy-makers in contemporary societies want to use evidence to make well-informed decisions, and scientists and scientific organizations are expected to provide the best evidence for their attention. A good supply of quality evidence and a healthy independent research community that is producing robust policy-relevant research is thus needed.

A common issue is how to synthesize evidence that is more often than not sparse, full of gaps, and difficult to manage, to do it in a transparent fashion and to transfer the conclusions into reasonable policy decisions. Evidence-informed policy-making can be undermined by the manipulation or selective use of data, which is often driven by vested interests (11, 12). The point is well-taken in public health, with tobacco a prime example (13). Analysis of millions of internal tobacco industry documents has revealed the multiple strategies via which the tobacco industry has sought to, and often successfully, undermine public health policies (14). Tobacco is clearly an exceptional product; no other consumer product kills two in three users when used exactly as intended (15). But there is little to suggest that, as a corporate actor, "Big Tobacco" differs fundamentally from, eg., "Big Booze" or "Big Food" (16, 17). Disruptions of the scientific process and creation of doubt may lead to delays in translating evidence into policy, with the potential to cost lives (11). Consequently, scientists, toxicologists, epidemiologists, other health professionals, patients and populations have a collective responsibility not simply to be originators of scientific data but to be scrutinizers of their use, thereby protecting the interests of the many rather than the few.

Some national regulatory bodies have asserted that glyphosate poses no public risk

The regulatory European Food Safety Authority (EFSA) and the US Environmental Protection Agency (EPA) have asserted that glyphosate poses no public risk. But the US Agency for Toxic Substances &Disease Registry (ATSDR) has joined IARC in concluding that there is a potential cancer hazard with glyphosate and its formulations (3, 18). Several of the national health agencies in Europe, the USA, and elsewhere have sided with the interpretation of the producer - that the herbicide is safe when used properly. Campaigns against glyphosate are the strongest in the

European Union, where member nations in 2017 only narrowly reapproved a 5-year authorization of the compound. Why this discrepancy?

As stated by Alfredo Morabia in a recent American Journal of Public Health editorial, "to defend what they perceive as in their best interests, some corporations not only pressure governmental agencies, they fight them." (19) In the same journal, Jonathan Samet (20) describes how Monsanto has moved extremely aggressively against the science, the unpaid expert volunteers, and institutions such as the IARC. The independent assessment of risk by "unpaid expert volunteers cannot be replaced by reviews from scientists paid by the industry." (20) The risk management may go beyond scientific evidence and imply the contribution of social values and social theory, in contrast to independent risk assessment (21).

Through the Monsanto papers, it has become clear that while the company was not willing to conduct the proposed long-term product safety studies (eg, a longterm carcinogenicity bioassay on the formulated product), the company spent millions of dollars on secretive PR campaigns - including $17 million in one year after the IARC evaluation had been published - to finance "ghost-written" studies and editorials aimed at discrediting independent scientists whose work had found dangers with Monsanto's pesticides. These controversial "ghost-written" papers have been available as evidence for non-carcinogenicity in the regulatory processes.

The EFSA has had apparent links with the pesticides industry, eg, through organizations such as International Life Sciences Institute (ILSI). A recent analysis of ILSI's activities concluded that the organisation "should be regarded as an industry group - a private body - and regulated as such, not as a body acting for the greater good" (22). While ILSI purports to be working for health and wellbeing of populations internationally, the authors of the analysis "identified overt attempts by ILSI to influence individuals, positions, and policy, both at national and international levels, alongside clear statements that ILSI's corporate members deploy it as a tool to thwart policies or leaders who are hostile to their interests." (22)

It is noteworthy that the chair of ILSI's Board of Trustees chaired the UN's joint Food and Agriculture Organization (FAO)/World Health Organization (WHO) meeting on glyphosate that found the herbicide to be "probably not carcinogenic to humans" (23). This was of great interest to ILSI major donors Monsanto and its industry representative CropLife International. The final meeting report included no conflict of interest statement, even though ILSI Europe had received donations worth more than US$1 million (from Monsanto and Croplife International) (23).

The EU hazard-based approach

Individuals connected to ILSI continue to play a role in the EU's advisory mechanisms. These activities have contributed to recommendations such as a slew of industry positions on pesticides (23). Their report recommended inter alia that the EU's precautionary hazard -based approach should be re-examined to determine whether it is delivering the intended levels of protection. The report recommended replacing current rules that outlaw any product that could harm with a US-style concept of "acceptable risk" (24). Unique to Europe, "the hazards approach" means that any pesticide found to be carcinogenic, mutagenic, reprotoxic, persistent or bioaccumulative, occurring even at low levels, can be regulated or even banned.

Monsanto has been careful to ensure that the US EPA is on board (25). Ominously, EPA staff has been accused of collusion with Monsanto to downgrade the health hazards of glyphosate (26). Jess Rowland, formerly a manager in the EPA's pesticide division, is said to have boasted in an April 2015 conversation with a Monsanto regulatory affairs manager that "If I can kill this, I should get a medal" (27). In October 2015, the EPA's Cancer Assessment Review Committee (CARC), chaired by Rowland, produced an internal report claiming that glyphosate, contrary to the IARC findings, was "not likely to be carcinogenic to humans" (28).

The US EPA has recently reconfirmed its position of "no risks to public health when glyphosate is used in accordance with the its current label" and "glyphosate is not a carcinogen" (29).

Health risks are not the only concern with glyphosate. The vast increase in its use has also caused a substantial increase in glyphosate-tolerant weeds, dubbed "superweeds" by some (30).

Conflict of interests

As the proverb states: "Who pays the piper, calls the tune", most of us understand what is meant by "conflict of

interest". The professional ethics codes have paid attention to conflicts of interest since 1970s, with better or worse consequences. Connected with conflict of interest, "duty of loyalty" is a term used in corporate law to describe a fiduciary's "conflict of interest". Accordingly, fiduciaries must put the corporation's interests ahead of their own (31). Indeed, the fiduciary responsibilities of all corporations require them to maximize their profits regardless of consequences to health, society, or the environment and thus to oppose policies that could reduce their profits (32). This obviously causes problems in evaluating evidence if the topic of evaluation - such as a particular pesticide - falls under the interest of the corporation.

Corporations defend their rights and their primary interests, which most often are financial ones. In the case of public health, the health of the population is the primary interest. In some situations, corporations have meddled in public policy-making on chemicals and topics where they have vested interests in terms of financial profits, trade and market shares. This all means a strong conflict of interest situation: the primary interests in public health are displaced by the interests of the corporations (21).

Corporations cannot be expected to assess impartially the potential toxicity of their own products. The independent creation of evidence requires specific procedures and skills necessary to draw conclusions based on the review and summary of a large body of evidence in order for it to be transparent and useful for policy decisions. As Morabia puts it: "IARC Monographs are an ingenious way to do exactly that" (19).

Discussion

Drawing conclusions on the causation of adverse health effects by environmental chemicals can have important societal consequences, leading to policy-making which can control, limit or even prevent the exposure to the pollutant through regulation and litigation. There are critical lessons to be learned from the Monsanto saga. The whole process of evidence-informed policy-making is under threat. The case of glyphosate is by no means over; further research is needed to cover the knowledge gaps, but this should be done independently and with full transparency.

The IARC Monographs provide the scientific evaluation of the evidence based on comprehensive review of the scientific literature, but it remains the responsibility of individual governments and other international organizations to recommend, if any, regulations, legislation and other public health interventions. The IARC Monographs evaluate the hazard, but the societal decisions take also other factors into account while making the risk management decisions. The risk management philosophies for pesticides in various countries are different - in the EU, for example, the hazards (inherent properties) are emphasized while, in the US, the utilitarian acceptable risk approach prevails.

The active ingredients for pesticide formulations are under constant development. Sometimes the dominant role of one ingredient may have a damping effect in the innovation paths. This seems to have been the case with the weed-killing chemical glyphosate. The company which produces glyphosate has a central role in the weed-killer and the associated genetically modified tolerant crops market. Glyphosate dominates the field of weed killers worldwide: no compound with a new way of attacking weeds, or mode of action, has been commercialized for more than 30 years (9).

Glyphosate is at the center of a public herbicide debate. Cropping systems are currently very reliant on herbicides. If glyphosate is pulled out of the market, what are the alternatives? It is clear that companies need to ramp up their R&D efforts to develop new candidate chemicals - or nonchemical alternatives - and new technologies for sustainable weed control, such as targeted spraying of herbicides directly into weeds, use of lasers, blades or electricity to kill weeds, are needed.

Evidence based on independent research provides the best tools to protect humans from harmful products, behaviors, and policies. Many responsible companies that market products that may have wide-spread exposure (such as pesticides) or potentially pose a risk to humans are collaborating internationally to gather the evidence. Instead of attacking the science, scientists, and science organizations and manipulating the media, such companies are working with the science community to secure human health and protect the environment.

Disclosure statement

In my past career, I served on the IARC Monographs program as a staff member from 1983 to the early 1990s. I

have not been involved in the evaluation of glyphosate at any level. I currently have no employment links to the IARC or any financial interests in writing this commentary. While my spouse serves currently as the Director of IARC, she is in no way responsible for any part of the text. All the responsibility lies with me and me only.

Sidebar

Harri Vainio, MD, PhD 1

1 Department of Environmental and Occupational Health, Faculty of Public Health, Kuwait University, Kuwait. Correspondence to: Prof. Harri Vainio, Faculty of Public Health, Kuwait University, P.O. Box 24923, Safat, 13110 Kuwait. [Email: Harri.Vainio@hsc.edu.kw]

References

References

1. Braceras JC. Rounding Up the Science Behind the Roundup Nuisance Litigation. Independent Women's Forum, May 28, 2019.

2. International Agency for Research on Cancer (IARC). Agents Classified by the IARC Monographs, Volumes 1-124. Available from: https://Monographs.iarc.fr/agents-classifiedby-the-iarc/ [Accessed May 30, 2019.]

3. Guyton KZ, Loomis D, Grosse Y, El Ghissassi F, BenbrahimTallaa L, Guha N et al. Carcinogenicity of tetrachlorvinphos, parathion, malathion, diazinon, and glyphosate. Lancet Oncol. 2015;16(5):490-1. https://doi.org/10.1016/S14702045(15)70134-8

4. Reuters. Monsanto ordered to pay $289 million in Roundup cancer trial. The New York Times; 10 August 2018. Available from: https://www.nytimes.com/2018/08/10/business/ monsanto-roundup-cancer-trial.html. [Accessed May 30, 2019].

5. Monsanto. Exhibit 42 - IARC carcinogen rating of glyphosate preparedness and engagement plan. UCSF Library, Chemical Industry Documents. Available from: https://www.industrydocumentslibrary.ucsf.edu/chemical/ docs/#id=xhmn0226. 2015. [Accessed May 31, 2019].

6. Horel S, Foucart S. The Monsanto Papers, Part 1 - Operation: Intoxication. Environmental Health News. Available from: https://www.ehn.org/monsanto-glyphosate-cancer-smearcampaign-250910888.html. 2017. [Accessed May 30, 2019].

7. Horel S, Foucart S. The Monsanto Papers, Part 2 - Reaping a bitter harvest. Environmental health News. Available from: https://www.ehn.org/monsanto-takes-on-world-healthorganization-2509721283.html. 2017. [Accessed May 30, 2019].

8. McHenry LB. The Monsanto Papers: poisoning the scientific well. Int J Risk Saf Med 2018;29(3-4):193-205. https://doi.org/10.3233/JRS-180028.

9. Stokstad E. Costly cancer lawsuits may spur search to replace world's most common weed killer. Science 2019;(May):22. Available from: https://www.sciencemag. org/news/2019/05/costly-cancer-lawsuits-may-spur-searchreplace-worlds-most-common-weed-killer

10. Food and Agriculture Organization (FAO) and World Health Organization. (WHO). Pesticides residues in food 2016. Special session of the joint FAO/WHO meeting on pesticide residues. FAO plant production and protection paper. Geneva: FAO and WHO; 2017;25(April). Available from: http://www.fao.org/3/a-i5693e.pdf

11. Michaels D. Doubt is their Product, How Industry's Assault on Science Threatens Your Health. 1st edition ed., New York: Oxford University Press; 2008.

12. Pearce N. Corporate influences on epidemiology. Int J Epidemiol 2008 Feb;37(1):46-53. https://doi.org/10.1093/ije/dym270.

13. Bero L. Implications of the tobacco industry documents for public health and policy. Annu Rev Public Health 2003;24:267-88. https://doi.org/10.1146/annurev. publhealth.24.100901.140813.

14. World Health Organization. Tobacco Industry Interference with Tobacco Control. Geneva: WHO; 2008. Available from: http://www.who.int/tobacco/resources/publications/ Tobacco0/o20Interference-FINAJ.

15. Roberts M. Tobacco 'kills two in three smokers'. BBC News, 24 February 2015. Available from https://www.bbc.com/ news/health-31600118

16. Bond L, Daube M, Chikritzhs T. Selling addictions: Similarities in approaches between Big Tobacco and Big Booze. AMJ 2010;3(6):325-32. https://doi.org/10.4066/ AMJ.2010.363.
17. Petticrew M, Maani Hessari N, Knai C, Weiderpass E. How alcohol industry organisations mislead the public about alcohol and cancer. Drug Alcohol Rev 2018 Mar;37(3):293303. https://doi.org/10.nn/dar.12596.
18. Agency for Toxic Substances &Disease Registry (ATSDR). Toxicological Profile for Glyphosate. (Draft for Public Comment). Atlanta, GA: U.S. Department of Health and Human Service; 2019.
19. Morabia A. Fighting independent risk assessment of talc and glyphosate: whose benefit is it anyway? [editorial]. Am J Public Health 2019 Jul;109(7):955-6. https://doi. org/10.2105/AJPH.2019.305144.
20. Samet JM. Expert review under attack: glyphosate, talc, and cancer [editorial]. Am J Public Health 2019 Jul;109(7):9768. https://doi.org/10.2105/AJPH.2019.305131.
21. Vineis P. Public health and independent risk assessment. Am J Public Health 2019 Jul;109(7):978-80. https://doi. org/10.2105/AJPH.2019.305142.
22. Steele S, Ruskin G, Sarcevic L, McKee M, Stuckler D. Are industry-funded charities promoting "advocacy-led studies" or "evidence-based science"?: a case study of the International Life Sciences Institute. Globalization and Health 2019; 15: 36-44. https://globalizationandhealth.biomedcentral.com/ track/pdf/10.1186/s12992-019-0478-6
23. Neslen A. UN/WHO panel in conflict of interest row over glyphosate cancer risk. The Guardian. 2016. Available from: https://www.theguardian.com/environment/2016/may/17/ unwho-panel-in-conflict-of-interest-row-over-glyphosatescancer-risk. [Accessed June 2, 2019].
24. The EC's Group of Chief Scientific Advisors: EU authorisation processes of plant protection products. Scientific Opinion 5/2018. Brussels: European Commission Unit RTD, Scientific Advice Mechanism.
25. Infante PF, Melnick R, Vainio H, Huff J. Commentary: IARC Monographs Program and public health under siege by corporate interests. Am J Ind Med 2018 Apr;61(4):27781. https://doi.org/10.1002/ajim.22811.
26. Rosenblatt J, Mulvany L, Waldman P. EPA Official Accused of Helping Monsanto "kill" Cancer Study. Bloomberg. 2017: March 14. Available from: https://www.bloomberg.com/ news/articles/2017-03-14/monsanto-accused-of-ghostwriting-papers-on-roundup-herbicide-cancer-allegations/.
27. Monsanto lawsuit document 189, case 3-16-md-02741. Filed 3/14/17.
28. US EPA. Glyphosate issue Paper: Evaluation of Carcinogenic Potential.EPA's Office of Pesticide Programs. 2016; Sept 12. Available from: https://www.epa.gov/sites/production/ files/2016-09/documents_issue_paper_evaluation_of_ carcinogenic_potential.pdf.
29. US EPA. Proposed Interim Registration Review Decision and Responses to Public Comments for Glyphosate. 2019. Available from: https://www.epa.gov/ingredients-usedpesticide-products/glyphosate.
30. Sass J. Regulatory failures = Superweeds and Glyphosate Cancers. Expert blog. April 11, 2019. Available from: https:// www.nrdc.org/experts/jennifer-sass/regulatory-failuressuperweeds-and-glyphosate-cancers.
31. Wikipedia. 2019. Duty of Loyalty. Corporations. Fifth Edition. Examples and Explanations. Alan R. Palmiter. ASPEN. Retrieved 2009-03-17.
32. Gilmore AB, Savell E, Collin J. Public health, corporations and the new responsibility deal: promoting partnerships with vectors of disease? [editorial]. J Public Health (Oxf) 2011 Mar;33(1):2-4. https://doi.org/10.1093/pubmed/fdr008.
Received for publication: 6 June 2019

DETAILS

Subject:	Cancer; Conflicts of interest; Pesticides; Scientists; Public health; Herbicides; Carcinogens; Glyphosate; Lymphoma; Monographs; Epidemiology; Health risk assessment; Regulatory agencies; Medical personnel; Tobacco industry

Business indexing term:	Subject: Tobacco industry
Location:	United States--US
Company / organization:	Name: Environmental Protection Agency--EPA; NAICS: 924110; Name: Bayer AG; NAICS: 325180, 325412; Name: Monsanto Co; NAICS: 325180, 325199
Publication title:	Scandinavian Journal of Work, Environment &Health; Stockholm
Volume:	46
Issue:	1
Pages:	105-109
Publication year:	2020
Publication date:	2020
Section:	Commentary
Publisher:	Scandinavian Journal of Work, Environment &Health
Place of publication:	Stockholm
Country of publication:	Finland, Stockholm
Publication subject:	Occupational Health And Safety
ISSN:	03553140
e-ISSN:	1795990X
Source type:	Scholarly Journal
Language of publication:	English
Document type:	Journal Article
DOI:	https://doi.org/10.5271/sjweh.3851
ProQuest document ID:	2344258615
Document URL:	https://www.proquest.com/scholarly-journals/public-health-evidence-informed-policy-making/docview/2344258615/se-2?accountid=211160
Copyright:	Copyright Scandinavian Journal of Work, Environment &Health 2020
Last updated:	2022-04-18
Database:	Public Health Database

Risk factors of hospitalization for carpal tunnel syndrome among the general working population

Hulkkonen, Sina, MD [1] ; Shiri, Rahman, MD PhD [2] ; Auvinen, Juha, MD PhD [3] ; Miettunen, Jouko, PhD [3] ; Karppinen, Jaro, MD PhD [4] ; Ryhänen, Jorma, MD PhD [1] Department of Hand Surgery, Helsinki University Hospital and University of Helsinki, Finland [2] Finnish Institute of Occupational Health, Helsinki, Finland [3] Center for Life Course Health Research, University of Oulu, Oulu, Finland [4] Medical Research Center Oulu, Oulu University Hospital and University of Oulu, Oulu, Finland

ABSTRACT (ENGLISH)

Objectives Carpal tunnel syndrome (CTS) causes a considerable amount of sick leave and healthcare costs. The etiology of CTS is multifactorial, involving both personal and occupational risk factors. To date, few prospective cohort studies on occupational risk factors of CTS have examined the general working population. Methods The study population consisted of participants from the Northern Finland Birth Cohort of 1966 who attended the 31-year follow-up in 1997 and were working >3 days a week in a paid job (N=6326). Information on socio-economic status, weight and height, smoking, exposure to occupational physical factors, and long-term illnesses was collected at baseline in 1997. Data on hospitalizations due to CTS came from the Care Register for Health Care, 1997-2016. Results Between 1997 and 2016, 3.4% of the participants had been hospitalized (attended secondary care) for CTS. After adjusting for confounders, women [hazard ratio (HR) 3.77, 95% confidence interval (CI) 2.70-5.25], overweight/obese participants (HR 1.69, 95% CI 1.29-2.22), smokers (HR 1.48, 95% CI 1.12-1.96), farmers and manual workers (HR 3.02, 95% CI 1.85-4.92 compared with upper clerical workers), lower clerical workers (HR 1.74, 95% CI=1.08-2.80), workers exposed to hand vibration (HR 2.29, 95% CI 1.48-3.54) and participants with physically demanding jobs (HR 1.71, CI 1.06-2.76) were at increased risk of hospitalization for CTS. Physically demanding work increased the risk of hospitalization for CTS for overweight/obese participants at baseline, but not for participants of normal weight. Conclusions Excess body mass and occupational physical factors increase the risk of hospitalization for CTS. Excess body mass potentiates the adverse effects of strenuous work on CTS.

FULL TEXT

Headnote

Objectives Carpal tunnel syndrome (CTS) causes a considerable amount of sick leave and healthcare costs. The etiology of CTS is multifactorial, involving both personal and occupational risk factors. To date, few prospective cohort studies on occupational risk factors of CTS have examined the general working population.

Methods The study population consisted of participants from the Northern Finland Birth Cohort of 1966 who attended the 31-year follow-up in 1997 and were working ≥3 days a week in a paid job (N=6326). Information on socio-economic status, weight and height, smoking, exposure to occupational physical factors, and long-term illnesses was collected at baseline in 1997. Data on hospitalizations due to CTS came from the Care Register for Health Care, 1997-2016.

Results Between 1997 and 2016, 3.4% of the participants had been hospitalized (attended secondary care) for CTS. After adjusting for confounders, women [hazard ratio (HR) 3.77, 95% confidence interval (CI) 2.70-5.25], overweight/obese participants (HR 1.69, 95% CI 1.29-2.22), smokers (HR 1.48, 95% CI 1.12-1.96), farmers and manual workers (HR 3.02, 95% CI 1.85-4.92 compared with upper clerical workers), lower clerical workers (HR 1.74, 95% CI=1.08-2.80), workers exposed to hand vibration (HR 2.29, 95% CI 1.48-3.54) and participants with physically

demanding jobs (HR 1.71, CI 1.06-2.76) were at increased risk of hospitalization for CTS. Physically demanding work increased the risk of hospitalization for CTS for overweight/obese participants at baseline, but not for participants of normal weight.
Conclusions Excess body mass and occupational physical factors increase the risk of hospitalization for CTS. Excess body mass potentiates the adverse effects of strenuous work on CTS.
Key terms cohort study; median nerve; musculoskeletal disorder; occupational exposure; overweight.
Carpal tunnel syndrome (CTS) is the most common entrapment neuropathy of the upper extremities, with an incidence rate of 3.3-3.5 per 1000 person-years and a prevalence of 1-5% in the general population (1-4). CTS can cause pain, numbness and loss of hand function in the affected hand. Of all musculoskeletal problems occurring in the working population, CTS causes a considerable amount of sick leave and healthcare costs (5-8).
The etiology of CTS is considered multifactorial, and involves both personal and occupational risk factors. Female gender, obesity (9), diabetes (10) rheumatoid arthritis (11), hypothyroidism (12), and smoking (13) have previously been recognized as risk factors. The prevalence of CTS varies from 0.6-61% in different working populations (14). In studies conducted in specific occupational groups, high force gripping (15), lifting heavy objects, exposure to vibration to hands, and repetitive wrist movements (16-19) were associated with increased risk for CTS. To date, only a limited number of prospective cohort studies of occupational risk factors of CTS have been conducted among the general working population (3, 20).
Knowledge of CTS risk factors is essential for preventing the condition. The aim of the current study was to determine the effects of personal factors and exposure to occupational physical workload factors on hospitalization for CTS in the general population.
Methods
Study population
The study population consisted of the Northern Finland Birth Cohort of 1966 (NFBC1966). Originally, 12 231 participants with an expected date of birth in 1966 were born in the cohort in the Oulu and Lapland provinces (21). A total of 8719 individuals participated in the 31-year follow-up study in 1997 and signed their informed consent to voluntarily participate in the study. Of these, 16 participants were diagnosed with CTS before the 31-year follow-up and were excluded from the analyses. Of the remaining 8703 participants, we only included those who were working >3 days a week in a paid job and answered the postal questionnaire on work-related factors (N=6326). The subsample consisted of 3824 participants who answered additional workrelated questions in a questionnaire conducted during the clinical examination. In both the total sample and the subsample, we only included participants with no missing data (figure 1).
The participants' personal identification numbers were replaced with study identification codes. The Ethics Committee of the Northern Ostrobothnia Hospital District approved the study (ETTMK: 107/2017), which followed the principles of the Declaration of Helsinki (as revised in 2008) of the World Medical Association.
Hospitalizations for carpal tunnel syndrome
The data on hospitalizations due to CTS were obtained from the Care Register for Health Care. This is a national register that covers both public and private hospitals in Finland (22). It contains information on patients' demographic features, diagnoses, surgical procedures, and dates of admission and discharge. The diagnoses are coded according to the International Classification of Diagnoses (ICD). CTS diagnosis was coded 357.2 according to the eighth revision of ICD, 1981-1986, 354.0 according to the ninth revision of ICD, 1987-1995, and G56.0 according to the tenth revision of ICD, 1996-2016. The diagnoses were obtained from hospital data, including both out- and inpatientbased services and specialist care, with CTS as the primary diagnosis.
Study population at baseline
The cohort population was examined at 31 years in 1997. Data at 31 years was collected via postal questionnaire and during a clinical examination. In all, 6326 participants answered the questions on occupational risk factors in the postal questionnaire: "Are you exposed to the following in your work?" The exposures were defined as: heat, cold, temperature changes, and vibration to hands. The participants who answered the additional occupational questions

in the clinical examination formed the subsample (N=3824). The additional occupational questions were: "Do you encounter the following in your work?" with the definitions: heavy physical work, repetitive movements, lifting 1-15 kg objects, lifting >15 kg objects, and working with arms elevated above shoulder level. The answers to the postal questionnaire and additional questions on occupational exposure were divided into two categories: none/light, and moderate/heavy exposure.

According to Statistics Finland, socioeconomic status was defined by occupation and activity in working life with nine categories: farmers, entrepreneurs, clerical workers (lower and upper), manual workers, students, pensioners, the unemployed, and unknown (23). As we only included participants active in working life, the variable was divided into four categories: upper clerical workers, lower clerical workers, entrepreneurs, and farmers/manual workers (categories combined). Body mass index (BMI, kg/m2) was calculated from height and weight measurements in the clinical examination or, if missing, from the height and weight information in the postal questionnaire. The variable was given two categories: normal (18.5<BMI<25) and overweight/ obese (BMI>25). A small number of individuals had BMI <18.5 and were excluded from the analysis (N=54). We collected information on smoking history by the postal questionnaire. The participants were divided into two categories: never-smokers and smokers (including both previous and present regular smokers). Information on diabetes, rheumatoid arthritis, hypothyroidism and other illnesses were self-reported at 31-year follow-up (no/yes).

Statistical analysis

First, the associations of the background characteristics and occupational physical factors with hospitalization for CTS were assessed using the univariable Cox proportional hazards regression model. Second, all the variables that remained significant in the sex-specific analyses or in the both sexes combined analyses, and were controlled for sex were included in the multivariable Cox proportional hazards regression models. The five variables made up of additional occupational questions were analyzed in the subsample (N=3824). We ran the final models for the variables that remained statistically significant in the multivariable models. Moreover, we performed stratified analyses to determine whether overweight/obesity modifies the associations between occupational physical workload factors and hospitalization for CTS. A variable was considered significant if its 95% CI did not include 1. We also tested multiplicative interactions between gender and personal or occupational variables by adding gender X to the variable of interest in the multivariate models. Every variable of interest was tested separately. For the statistical analysis we used R version 3.4.4.

Results

At baseline, 23% of the study population were upper clerical workers, 35% lower clerical workers, 8% entrepreneurs and 34% farmers or manual workers; 40% were overweight or obese; and 49% were past or current smokers. Of the 6326 study participants, 77 had diabetes, 105 had thyroid disease and 53 had rheumatoid arthritis. The follow-up started in 1997 and ended in 2016 and the mean follow-up time was 18.3 [standard deviation (SD) 4.1] years. During the follow-up period, 215 participants (3.4%) were hospitalized due to CTS. The incidence of hospitalization for CTS was higher among women than men (figure 2). The incidence of hospitalization for CTS was 2.6 per 1000 person-years among women and 1.2 per 1000 person-years among men. The demographic features of the whole study sample and the study subsample were similar.

Socioeconomic status, smoking, a BMI of >25, exposure to heat, temperature changes, and exposure to vibration to hands were associated with CTS in the analyses controlled for sex. Diabetes, thyroid diseases and rheumatoid arthritis were not statistically significantly associated with hospitalization for CTS (table 1). In sex-specific analyses, socioeconomic status, smok- ing, a BMI of >25, self-reported exposure to heat, and temperature changes were associated with CTS among women. Among men, socio-economic status, and selfreported exposure to heat, cold, temperature changes and vibration to hands were associated with CTS, whereas the associations of smoking and a BMI of >25 with CTS were not statistically significant (table 1).

In the multivariate Cox's proportional hazards regression models, the association of socioeconomic status and CTS remained statistically significant among both men and women and also when both sexes were combined in the analyses. Smoking and obesity were associated with CTS among women and when both sexes were combined. Of

the occupational risk factors, only self-reported exposure to vibration to hands was associated with CTS, only among men and when both sexes were combined (table 2).

In the subsample of 3824 participants, physically demanding work at baseline increased the risk of hospitalization for CTS during the follow-up period, whereas lifting <15 kg, lifting >15 kg, work requiring arm elevation, and work demanding repetitive movements were not statistically significantly associated with the incidence of hospitalization for CTS (table 3). In stratified analyses, physically demanding work increased the risk of hospitalization for CTS among overweight or obese participants at baseline, but not among participants of normal weight (supplementary material www.sjweh.fi/show_abstract. php?abstract_id=3835, tables S1 and S2). There were no statistically significant interactions between gender and any personal and occupational variables.

Discussion

In the current study, female gender, overweight or obesity, smoking, and certain socioeconomic classes (lower clerical workers, farmers and manual workers) were risk factors for hospitalization due to CTS. The most important occupational risk factors were exposure to vibration to hands and physically demanding work.

The NFBC1966 is a representative sample of a single-age cohort. The participants are the same age and come from all backgrounds and socioeconomic classes. Their participation in follow-ups has been high. The Care Register of Heath Care data are highly reliable and comprehensive, and basically cover the whole healthcare system in Finland. The follow-up time in the presented study is long (mean 18.3 years, SD 4.1 years), and comparable to other published longitudinal studies on CTS (16, 17, 24, 25). During such a long period, it is questionable whether all the exposures remain stable throughout the whole follow-up period.

In this study, the occupational exposures were selfreported and not measured at the workplace. In addition, we had no information on the precise duration of the daily exposure or the number of years exposed. This may have caused misclassification of the exposures. However, CTS has been diagnosed during the follow-up period and its assessment was independent of exposure assessment at baseline.

The socioeconomic status classification includes both occupation and activity in working life (23). In our study, vibration to hands revealed the most significant occupational exposure, especially among men. Previous prospective studies (17, 26, 27) have reported similar findings. Among women, none of the occupational exposures were associated with CTS in the adjusted analysis, whereas female farmers and manual workers, overweight/obese participants and smokers were at an increased risk. Men and women were divided into socioeconomical classes differently; men more often worked as farmers and manual workers and less often as lower clerical workers than women. The occupational exposures differ among men and women; men might encounter more physical risk factors compared to women. The risk factors for CTS may also differ between men and women; occupational exposures being more important among men and personal risk factors among women. However, the current study had low statistical power for sex-specific results. Further larger prospective cohort studies are needed to determine the differences between risk factors for CTS among men and women.

In the subsample analysis, physically demanding work increased the risk of hospitalization for CTS among overweight or obese participants at baseline, but not among normal weight. Obesity may cause CTS through the accumulation of adipose tissue in the carpal tunnel (28). Exposure to physical workload factors may potentiate the adverse effect of obesity through local ischemia-induced reperfusion injury (29).

Although the sample size of the cohort was large (N=6326), the number of participants diagnosed with CTS in the follow-up was quite small (N=215). This might be due to the relatively young age of the cohort, and the registry data we used. As the incidence of CTS has two peaks: 50-59 and 70-79 years (1), the fact that follow-up ended just after the cohort had turned 50 might partially explain the small number of cases. In Finland, public healthcare is divided into primary care (health centers) and hospitals. CTS and suspicion of CTS are coded under the same diagnosis code in the Care Register for Health Care. We only used hospital data because health center data might not be sufficiently reliable. This excludes cases with only mild symptoms and those not willing to consider operations or visiting the hospital polyclinic. All the CTS cases in our cohort were doctor-diagnosed.

To conclude, overweight and exposure to physical workload factors increase the risk of hospitalization for CTS.

Being overweight potentiates the adverse effects of strenuous work on CTS. Workplace interventions aimed at reducing excessive workload factors among overweight workers might prevent CTS, but more evidence is needed on this.

Acknowledgements

We thank all the cohort members and researchers who participated in the 31-year study. We also wish to acknowledge the work of the NFBC1966 project center.

Conflict of interest

The authors declare no conflicts of interest.

Funding

The studies presented in this article were supported by personal research grant from the Lapland Regional Fund of Finnish Cultural Foundation to Sina Hulkkonen.

Sidebar

Hulkkonen S, Shiri R, Auvinen J, Miettunen J, Karppinen J, Ryhänen J. Risk factors of hospitalization for carpal tunnel syndrome among the general working population. Scand J Work Environ Health - online first. doi:10.5271/sjweh.3835

Correspondence to: Sina Hulkkonen, Department of Hand Surgery, Helsinki University Hospital and University of Helsinki, PO Box 266, FI-00029 HUS, Finland. [E-mail: sina.hulkkonen@gmail.com]

References

References

1. Mondelli M, Giannini F, Giacchi M. Carpal tunnel syndrome incidence in a general population. Neurology 2002 Jan;58(2):289-94. https://doi.org/10.1212/WNL.58.2.289.

2. Nordstrom DL, DeStefano F, Vierkant RA, Layde PM. Incidence of diagnosed carpal tunnel syndrome in a general population. Epidemiology 1998 May;9(3):342-5. https://doi. org/10.1097/00001648-199805000-00021.

3. Latinovic R, Gulliford MC, Hughes RA. Incidence of common compressive neuropathies in primary care. J Neurol Neurosurg Psychiatry 2006 Feb;77(2):263-5. https://doi.org/10.n36/jnnp.2005.066696.

4. Atroshi I, Gummesson C, Johnsson R, Ornstein E, Ranstam J, Rosén I. Prevalence of carpal tunnel syndrome in a general population. JAMA 1999 Jul;282(2): 153-8. https://doi. org/10.1001/jama.282.2.153.

5. Foley M, Silverstein B. The long-term burden of workrelated carpal tunnel syndrome relative to upper-extremity fractures and dermatitis in Washington State. Am J Ind Med 2015 Dec;58(12): 1255-69. https://doi.org/10.1002/ ajim.22540.

6. Daniell WE, Fulton-Kehoe D, Franklin GM. Work-related carpal tunnel syndrome in Washington State workers' compensation: utilization of surgery and the duration of lost work. Am J Ind Med 2009 Dec;52(12):931-42. https://doi. org/10.1002/ajim.20765.

7. Silverstein B, Welp E, Nelson N, Kalat J. Claims incidence of work-related disorders of the upper extremities: washington state, 1987 through 1995. Am J Public Health 1998 Dec;88(12): 1827-33. https://doi.org/10.2105/ AJPH.88.12.1827.

8. Feuerstein M, Miller VL, Burrell LM, Berger R. Occupational upper extremity disorders in the federal workforce. Prevalence, health care expenditures, and patterns of work disability. J Occup Environ Med 1998 Jun;40(6):546-55. https://doi.org/10.1097/00043764- 199806000-00007.

9. Shiri R, Pourmemari MH, Falah-Hassani K, Viikari-Juntura E. The effect of excess body mass on the risk of carpal tunnel syndrome: a meta-analysis of 58 studies. Obes Rev 2015 Dec;16(12): 1094-104. https://doi.org/10.1111/obr.12324.

10. Pourmemari MH, Shiri R. Diabetes as a risk factor for carpal tunnel syndrome: a systematic review and meta-analysis. Diabet Med 2016 Jan;33(1):10-6. https://doi.org/10.1111/ dme.12855.

11. Shiri R. Arthritis as a risk factor for carpal tunnel syndrome: a meta-analysis. Scand J Rheumatol 2016 Oct;45(5):339-46. https://doi.org/10.3109/03009742.2015.1114141.

12. Shiri R. Hypothyroidism and carpal tunnel syndrome: a meta-analysis. Muscle Nerve 2014 Dec;50(6):879-83.

https://doi.org/10.1002/mus.24453.
13. Pourmemari MH, Viikari-Juntura E, Shiri R. Smoking and carpal tunnel syndrome: a meta-analysis. Muscle Nerve 2014 Mar;49(3):345-50. https://doi.org/10.1002/mus.23922.
14. Hagberg M, Morgenstern H, Kelsh M. Impact of occupations and job tasks on the prevalence of carpal tunnel syndrome. Scand J Work Environ Health 1992 Dec;18(6):337-45. https://doi.org/10.5271/sjweh.1564.
15. Abbas MF, Faris RH, Harber PI, Mishriky AM, ElShahaly HA, Waheeb YH et al. Worksite and personal factors associated with carpal tunnel syndrome in an Egyptian electronics assembly factory. Int J Occup Environ Health 2001 Jan-Mar;7(1):31-6. https://doi.org/10.1179/ oeh.2001.7.1.31.
16. Nathan PA, Istvan JA, Meadows KD. A longitudinal study of predictors of research-defined carpal tunnel syndrome in industrial workers: findings at 17 years. J Hand Surg [Br] 2005 Dec;30(6):593-8. https://doi.org/10.1016/J. JHSB.2005.06.019.
17. Nathan PA, Meadows KD, Istvan JA. Predictors of carpal tunnel syndrome: an 11-year study of industrial workers. J Hand Surg Am 2002 Jul;27(4):644-51. https://doi. org/10.1053/jhsu.2002.34003.
18. Violante FS, Farioli A, Graziosi F, Marinelli F, Curti S, Armstrong TJ et al. Carpal tunnel syndrome and manual work: the OCTOPUS cohort, results of a ten-year longitudinal study. Scand J Work Environ Health 2016 Jul;42(4):280-90. https://doi.org/10.5271/sjweh.3566.
19. Kapellusch JM, Gerr FE, Malloy EJ, Garg A, HarrisAdamson C, Bao SS et al. Exposure-response relationships for the ACGIH threshold limit value for hand-activity level: results from a pooled data study of carpal tunnel syndrome. Scand J Work Environ Health 2014 Nov;40(6):610-20. https://doi.org/10.5271/sjweh.3456.
20. Lam N, Thurston A. Association of obesity, gender, age and occupation with carpal tunnel syndrome. Aust N Z J Surg 1998 Mar;68(3):190-3. https://doi. org/10.1111/j.1445-2197.1998.tb04743.x.
21. Haapea M, Miettunen J, Läärä E, Joukamaa MI, Järvelin MR, Isohanni MK et al. Non-participation in a field survey with respect to psychiatric disorders. Scand J Public Health 2008 Sep;36(7):728-36. https://doi. org/10.1177/1403494808092250.
22. Sund R. Quality of the Finnish Hospital Discharge Register: a systematic review. Scand J Public Health 2012 Aug;40(6):505-15. https://doi. org/10.1177/1403494812456637.
23. http://www.tilastokeskus.fi [Internet]. Statistics Finland [cited 2018 Dec 01]. Available from: http://www.tilastokeskus.fi.
24. Gell N, Werner RA, Franzblau A, Ulin SS, Armstrong TJ. A longitudinal study of industrial and clerical workers: incidence of carpal tunnel syndrome and assessment of risk factors. J Occup Rehabil 2005 Mar;15(1):47-55. https://doi. org/10.1007/s10926-005-0873-0.
25. Harris-Adamson C, Eisen EA, Kapellusch J, Garg A, Hegmann KT, Thiese MS et al. Biomechanical risk factors for carpal tunnel syndrome: a pooled study of2474 workers. Occup Environ Med 2015 Jan;72(1):33-41. https://doi. org/10.1136/oemed-2014-102378.
26. Roquelaure Y, Mariel J, Dano C, Fanello S, PenneauFontbonne D. Prevalence, incidence and risk factors of carpal tunnel syndrome in a large footwear factory. Int J Occup Med Environ Health 2001;14(4):357-67.
27. Wieslander G, Norbäck D, Göthe CJ, Juhlin L. Carpal tunnel syndrome (CTS) and exposure to vibration, repetitive wrist movements, and heavy manual work: a case-referent study. Br J Ind Med 1989 Jan;46(1):43-7.
28. Bland JD. Carpal tunnel syndrome. Curr Opin Neurol 2005 Oct; 18(5):581-5. https://doi.org/10.1097/01. wco.0000173142.58068.5a.
29. Sud V, Freeland AE. Biochemistry of carpal tunnel syndrome. Microsurgery 2005;25(1):44-6. https://doi. org/10.1002/micr.20071.
Received for publication: 1 February 2019

DETAILS

Subject:	Physical factors; Population; Smoking; Diabetes; Socioeconomic factors; Womens health; Etiology; Hypothyroidism; Body mass index; Rheumatoid arthritis; Health care; Gender; Hands; Heat; Thyroid gland; Overuse injuries; Risk analysis; Body weight; Hospitalization; Statistical analysis; Employee benefits; Body mass; Vibration; Agricultural economics; Confidence intervals; Occupational exposure; Carpal tunnel syndrome; Illnesses; Obesity; Risk factors; Variables; Occupational health; Population studies; Manual workers; Workloads; Clerical personnel; Sick leave; Overweight
Business indexing term:	Subject: Manual workers Workloads Clerical personnel Sick leave
Location:	Finland
Publication title:	Scandinavian Journal of Work, Environment &Health; Stockholm
Volume:	46
Issue:	1
Pages:	43-49
Publication year:	2020
Publication date:	2020
Section:	Original article
Publisher:	Scandinavian Journal of Work, Environment &Health
Place of publication:	Stockholm
Country of publication:	Finland, Stockholm
Publication subject:	Occupational Health And Safety
ISSN:	03553140
e-ISSN:	1795990X
Source type:	Scholarly Journal
Language of publication:	English
Document type:	Journal Article
DOI:	https://doi.org/10.5271/sjweh.3835
ProQuest document ID:	2344258449
Document URL:	https://www.proquest.com/scholarly-journals/risk-factors-hospitalization-carpal-tunnel/docview/2344258449/se-2?accountid=211160

Psychosocial work stressors and risk of all-cause and coronary heart disease mortality: A systematic review and meta-analysis

Taouk, Yamna, MPH [1] ; Spittal, Matthew J, PhD [1] ; LaMontagne, Anthony D, ScD [2] ; Milner, Allison J, PhD [1] 1 Melbourne School of Population and Global Health, The University of Melbourne, Parkville, Victoria Australia 2 Centre for Population Health Research, Deakin University, Burwood, Victoria Australia

ABSTRACT (ENGLISH)

Objectives Psychosocial work stressors are common exposures affecting the working population, and there is good evidence that they have adverse health consequences. There is some evidence that they may impact on mortality, but this has not been systematically examined. We performed a systematic review, including risk of bias, and meta-analyses of observational studies to examine the association between psychosocial work stressors and all-cause mortality and death due to coronary heart disease (CHD). Methods Electronic databases were searched to identify studies and information on study characteristics and outcomes extracted in accordance with PRISMA guidelines. Risk estimates of outcomes associated with psychosocial work stressors: specifically, all-cause mortality, and death due to CHD were pooled using inverse variance weighted random effects meta-analysis. Results We identified 45 eligible cohort studies, of which 32 were included in the quantitative analyses of psychosocial work stressors and mortality. Low job control was associated with an increased risk of all-cause mortality [hazard ratio (HR) 1.21, 95% confidence interval (CI) 1.07-1.37, minimally-adjusted; HR 1.05, 95% CI 1.01-1.10, multivariable-adjusted; HR 1.03, 95% CI 1.00-1.06 exclusion of low quality studies and multivariable-adjusted] and CHD mortality [HR 1.50, 95% CI 1.42-1.58, minimally-adjusted; HR 1.23, 95% CI 1.17-1.30, multivariable-adjusted; HR 1.19, 95% CI 1.01-1.40, exclusion of low quality studies and multivariable-adjusted]. Conclusions Workers with low job control are at increased risk of all-cause and CHD mortality compared to workers with high job control. Policy and practice interventions to improve job control could contribute to reductions in all-cause and CHD mortality.

FULL TEXT

Headnote

Objectives Psychosocial work stressors are common exposures affecting the working population, and there is good evidence that they have adverse health consequences. There is some evidence that they may impact on mortality, but this has not been systematically examined. We performed a systematic review, including risk of bias, and meta-analyses of observational studies to examine the association between psychosocial work stressors and all-cause mortality and death due to coronary heart disease (CHD).

Methods Electronic databases were searched to identify studies and information on study characteristics and outcomes extracted in accordance with PRISMA guidelines. Risk estimates of outcomes associated with psychosocial work stressors: specifically, all-cause mortality, and death due to CHD were pooled using inverse variance weighted random effects meta-analysis.
Results We identified 45 eligible cohort studies, of which 32 were included in the quantitative analyses of psychosocial work stressors and mortality. Low job control was associated with an increased risk of all-cause mortality [hazard ratio (HR) 1.21, 95% confidence interval (CI) 1.07-1.37, minimally-adjusted; HR 1.05, 95% CI 1.01-1.10, multivariable-adjusted; HR 1.03, 95% CI 1.00-1.06 exclusion of low quality studies and multivariable-adjusted] and CHD mortality [HR 1.50, 95% CI 1.42-1.58, minimally-adjusted; HR 1.23, 95% CI 1.17-1.30, multivariable-adjusted; HR 1.19, 95% CI 1.01-1.40, exclusion of low quality studies and multivariable- adjusted].
Conclusions Workers with low job control are at increased risk of all-cause and CHD mortality compared to workers with high job control. Policy and practice interventions to improve job control could contribute to reductions in all-cause and CHD mortality.
Key terms all-cause mortality; cardiovascular disease mortality; CHD; death; job control; occupational stress; psychological stress; stress; work stress.
Psychosocial work stressors represent the objective characteristics of the work environment, including design, organization and context of work, which may elicit stress response in workers and cause physiological or psychological harm (1). Exposure to psychosocial work stressors have been associated with coronary heart disease (CHD), diabetes, clinical depression, as well as a range of other physical and mental health outcomes (2-18). Work stressors have also been associated with poor organizational outcomes, including sickness absence and presenteeism (19-21).
Research into the effect of psychosocial work stressors on mortality is sparse and has produced inconsistent results. Most studies thus far have examined components of the Karasek's job-demand-control model, which is composed of the psychosocial factors job demands which refer to the pace and intensity of work, and job control comprising decision authority and skill discretion (22, 23). The model posits that job strain which results from the combined effects of low job control and high job demands may cause stress-related illhealth (23). The model was further extended to include an additional component representing social support in the workplace (24). Work stressors conceptualized and measured according to the job-demand-control-support model has been found to increase the risk of mortality in some studies (25-31), but not in others (32-43).
The concept of work stressors was broadened beyond proximal job task characteristics to include organizational factors in the effort-reward imbalance (ERI) model which recognizes both the effort and the reward structure of work (44). The model is based upon the premise that work-related benefits depend upon a reciprocal relationship between efforts and rewards at work and that lack of reciprocity due to an imbalance between high effort and low rewards is stressful to workers and may result in adverse health outcomes (44). Cohort studies examining the effect of high ERI on mortality have had mixed findings (28, 34, 39). A further work stressor model, the organizational justice model, which measures employees' degree of perceived fairness of treatment in the workplace proposes that increased perceived unfairness may lead to increased stress responses, resulting in physiological and behavioral reactions adversely impacting on workers' health and well-being (45, 46). The effect of increased perceived unfairness on mortality is not clear (47, 48). More recently, broader constructs of work stressors encompassing labor market arrangements including long working hours, shift work and job insecurity have been examined as risk factors for mortality with mixed results (11, 26, 36, 49-55).
Given these mixed findings and the fact that there have been no previous reviews of evidence about psychosocial work stressors and mortality, a comprehensive systematic review and meta analyses is needed to clarify the relationship. The objective of this study was to evaluate the evidence for the association between (i) psychosocial work stressors and all-cause mortality and (ii) psychosocial work stressors and mortality due to CHD. We included CHD mortality as a secondary outcome because the association with job stressors is biologically plausible, and it is one of the most frequently studied mortality outcomes (56).

Methods

A comprehensive systematic review of the available literature until the end of 2017 for studies providing information on the risk of mortality in relation to psychosocial work stressors was conducted as per the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines (57). A search strategy was formulated to identify studies systematically that answer the research question "What is the effect of psychosocial work stressors on mortality?". The question was specified by defining the "PICOS' modules as follows: Population (P) = workers; Intervention or exposure (I) = exposed to the psychosocial work stressors: low job control, high job demands, high job strain, low support at work, job insecurity, organization injustice, ERI, long working hours, shift work; Outcome (O) = total mortality, mortality due to cardiovascular heart disease; and Study type (S) = longitudinal studies.

Search strategy

A search of seven electronic databases covering a range of disciplines - including Medline, PubMed, EMBASE, Web of Science (medical science database), Scopus (social science database), PsycINFO (psychology database), and Global Health (public health database) - for eligible literature published from their respective commencement date to present was undertaken. A three-tier search strategy was used to identify eligible studies (see table 1 and supplementary material www.sjweh.fi/show_abstract.php7abstract_ id=3854, table S1). The first and the second stages were combined with an "or" operator and matched with the third using the "and" operator. No restrictions were placed on the date, status, or language of publications. A secondary search included examination of the reference list of all studies identified for potential inclusion in the systematic review. The first author conducted the initial data searches and, together with the last author, independently screened all potentially relevant titles and abstracts to retrieve relevant articles to minimize the possibility of selective selection.

Eligibility criteria

Original articles that had the key search terms in the title or abstract and mortality as an outcome variable were considered for inclusion in the systematic review. We excluded reviews, letters, editorials, case reports, book chapters, studies with no English translation, and conference abstracts. Studies investigating physical exposure to work-related factors including physical, chemical, ergonomic, and biological factors were excluded as the focus of the review is exposure to psychosocial work stressors in association with mortality. Studies examining deaths from karoshi, the Japenese term for death by overwork, were excluded from the review as karoshi conflates the exposure and outcome making it difficult to assign a common cause of death. Prospective population-level studies (cohort studies) and case control studies that contained quantitative estimates and 95% confidence intervals (CI) of the relative risk, rate ratio (RR), odds ratio (OR, or hazard ratio (HR) for mortality associated with psychosocial work stressors were included in the systematic review.

Studies were screened for eligibility using a twostage process. Titles and abstracts of studies with the key search terms in the title or abstract, retrieved using the search strategy, were screened independently by the two review authors to identify studies that potentially met the inclusion criteria. Following review of the full text, studies that met the eligibility criteria were retained and any disagreements were resolved by consensus or through discussion with an independent researcher.

Data extraction

Methodological details and data including study description, author, cohort, year, country, population (sample size, gender, age), exposure assessment and exposure level, description of mortality (method of assessment and incidence), study design, duration of follow-up, number of events, confounders adjusted for in the analyses, effect size for mortality, and CI were extracted from each included study.

Quality assessment

The quality of studies was assessed by the same two independent researchers using the Scottish Intercollegiate Guidelines Network (SIGN) methodological checklist for cohort and case-control studies version 3 (58) (supplementart table S2). Studies with little or no risk of bias were rated as high quality. Studies that mostly agreed with the guidelines but containing some flaws with an associated risk of bias were rated as acceptable. Studies that did not agree with the criteria or contained significant flaws with respect to study design were rated as low quality.

Disagreements over quality assessment were resolved by discussion, with involvement of a third independent researcher where necessary.

Data analysis

There was limited scope for quantitative synthesis because of the heterogeneity in exposures measured across a small number of studies. But where possible, we conducted quantitative analyses of studies with sufficiently similar exposures, outcomes and study populations. For multiple studies reporting on the same study data, only the most recent study with longer follow up period was included in the quantitative analysis. Multiple studies with the same author/s were included in the meta-analysis insofar as the study sample, exposures, or outcomes differed. Studies were included if age-adjusted effect estimates were available, otherwise we excluded studies with unadjusted crude measurements because age is such a strong predictor of mortality. OR, RR, and HR were combined to estimate pooled effect sizes (59).

We conducted inverse variance random-effects metaanalyses to assess the association between each psychosocial work stressor and the primary outcome: all-cause mortality; and the secondary outcome: deaths due to CHD, in minimally- and multivariable-adjusted analyses. Our analyses were restricted to combining estimates when more than two studies were available for pooling. For studies reporting multiple levels of an exposure (eg, job strain quartiles), the referent group was only included once in the meta-analyses. Hence highest job demands level was compared to lowest job demands level, job strain was compared to no job strain, and lowest job control level was compared to highest job control level. For studies reporting multiple categories of shift work (eg, evening shift work, night shift work, rotating shift work), the category with the highest frequency was compared to the referent category, no shift work.

In addition to the pooled effect size for individual psychosocial work stressors, we undertook separate subgroup random-effects meta-analyses for studies where effect estimates were stratified by gender. The I2 statistic was used to measure the heterogeneity between studies. Funnel plots were used to assess the precision of estimates and publication bias (60) and a modified Egger's test was performed to test for small study effects by regressing effect estimates on their standard errors weighted by the reciprocal of the variance of intervention effect estimates (61).

Two sensitivity analyses were conducted. The first sensitivity analysis tested differences between studies without low quality assessment compared with the inclusion of all studies irrespective of quality assessment. The second sensitivity analysis tested differences between studies that assessed relatively healthy study samples (participants with pre-existing diseases and/ or cancer other than melanoma were excluded from the study analysis or the study controlled for health status) compared with studies that did not exclude participants due to ill health from their analysis or control for health status.

All analyses were conducted using Stata 14.2 (Stata Corp, College Station, TX).

Results

A total of 13 237 studies were initially identified (figure 1). After removing duplicates, 6778 records were screened by the title and abstract and 146 were further screened by full text for eligibility assessment and the reference lists were examined. 102 studies were excluded (supplementary table S3) resulting in 45 eligible studies for inclusion in the systematic review (11, 25-43, 47, 49-55, 62-78). Too few studies examined the risk of mortality and low social support at work, high ERI, or long working hours hence 32 studies were included in the quantitative analyses for low job control, high job demands, high job strain, shift work or job insecurity and mortality (11, 25-42, 50-54, 65, 66, 71-74, 76, 77).

Quality assessment

Twenty-seven studies were assessed to be of acceptable quality and eighteen studies were assessed as low quality (supplementary table S4). No study was judged to be of high quality.

Characteristics and results of reviewed studies

Twenty-seven studies were from Finland, Sweden and Denmark (11, 25, 28-30, 35, 37-39, 42, 43, 47, 50, 51, 53, 63, 64, 67-74, 76, 78). A further nine studies came from the USA (26, 27, 31, 32, 36, 41, 62, 65, 75), two studies from UK (54, 66) and Japan (40, 77), and one study each in Poland (34), Israel (33), France (49), Ireland (55), and

Russia (52). The earliest study was published in 1981 (30) and the most recent published in 2017 (62, 74). The 45 articles included in the review used data from thirty-seven different studies. Four studies used data from the Valmet study (28, 39, 43, 47); and the Nurses' Health Study (41, 75), Copenhagen Male Study (69, 70), Stockholm Heart Epidemiology Program (67, 68), Statistics Finland Quality of Work Life Surveys (50, 51), and UK industrial cohort (54, 66) data were used in two studies each (supplementary table S5).

The effect of psychosocial work stressors on mortality was based on males in thirteen studies (11, 25, 30, 42, 54, 64-66, 69, 70, 73, 76, 77), and females in five studies (27, 36, 41, 74, 75). Twenty-six studies examined psychosocial work stressors and mortality in all persons (26, 28, 29, 31-35, 37-40, 43, 47, 49-51, 53, 55, 62, 63, 67, 68, 71, 72, 78). Components of the main job-strain model used to measure work stress (22-24), including job demands, job control, job strain, support at work and/or iso-strain and the risk of mortality were investigated in twenty-seven studies (25-43, 49, 51, 62, 64, 65, 67, 71, 72). Eleven studies examined shift work and mortality (11, 50, 53, 54, 63, 66, 73-77), six studies looked at job insecurity and mortality (26, 36, 51, 52, 68, 78), three studies explored ERI and mortality (28, 34, 39), two studies included working hours and mortality (55, 69), one study inspected organizational justice and mortality (47), and another psychological pressure and mortality (70). Most studies used self-reported exposure measures, however five studies used a psychosocial job exposure matrix to assign job demands and job control values for each occupation (26, 27, 29, 42, 65), one study used both self-reported and occupation-based measures of work-related stress (38), four studies assessed shift work exposure from company records (54, 66, 73, 76), and one study used company records to assess employment status (78). Median follow up in these studies ranged from 4-30 years. The outcome, all-cause mortality, was identified independently of the exposure from official national or regional death registers in almost all studies. One study did not report on outcome ascertainment (32), and three others relied on outcome status information provided from relatives and friends (26, 52, 62). Deaths due to CHD were ascertained from International Classifications of Diseases codes assigned for cardiovascular disease, ischemic heart disease, myocardial infarction and/or strokes on death certificates. Seventeen studies reported on specific working populations (industrial workers (28, 39, 43, 47, 54, 65, 66, 71, 73, 76), health professionals (36, 41, 74, 75), municipal and/or hospital employees (35, 72, 78)), two studies used non-fatal acute myocardial infarction cases (67, 68), and one study examined graduates from Wisconsin high schools in 1957 (62). The other twenty-five studies used a random working population sample drawn from the general population.

Various effect sizes were reported across studies. Thirty studies used HR (27, 28, 31, 33-39, 43, 47, 49-53, 55, 63, 67-75, 77, 78), nine studies used RR (11, 25, 29, 32, 40-42, 64, 65), four studies used OR (30, 54, 62, 66), and one study used standardized relative rates (76). The referent group for components of the job-strain model, job demands, job control and job strain differed across studies due to variation in exposure measurements and classifications between studies. Some studies reported results as continuous measures (31-33, 43, 62, 65) and various categorical measures were derived across studies. Different referent groups were used among studies with shift work exposure (supplementary table S6).

Quantitative analysis

Individual meta-analysis results for each of the five exposures, and risk of all-cause mortality and risk of CHD mortality are shown in supplementary figures S1-S17, and pooled results are depicted in figures 2-5. Pooled results for psychosocial work stressors and mortality in minimally adjusted analysis showed that employees in low control jobs had a significantly higher mortality risk than those in high control jobs (all-cause mortality: HR 1.21, 95% CI 1.07-1.37, k=3; CHD mortality: HR 1.50, 95% CI 1.42-1.58, k=5). The increased risk for low job control and mortality persisted in multivariable-adjusted analysis (all-cause mortality: HR 1.05, 95% CI 1.01-1.10, k=10; CHD mortality: HR 1.23, 95% CI 1.17-1.30, k=6), although risk estimates were attenuated.

Pooled results for high job demands, job strain, and shift work were not associated with risk of all-cause mortality (HR 0.93, 95% CI 0.81-1.08, k=3; HR 1.07, 95% CI 0.82-1.39, k=3; and HR 1.01, 95% CI 0.961.07, k=5 respectively) or CHD mortality (HR 0.89, 95% CI 0.61-1.29, k=4; HR 1.31, 95% CI 0.91-1.88, k=7; and HR 1.08, 95% CI 0.94-1.25, k=7 respectively) in minimally adjusted analysis.

The pooled result for high job demands was not found to be associated with all-cause mortality in multivariable-adjusted analysis (HR 0.96, 95% CI 0.90-1.02, k=8) and differed little from pooled results for job demands and mortality in minimally adjusted analysis. Pooled results for job strain and risk of all-cause mortality (HR 1.04, 95% CI 0.92-1.18, k=7) and risk of CHD mortality (HR 1.26, 95% CI 0.82-1.94, k=4) included the null. An effect of shift work on all-cause mortality (HR 0.97, 95% CI 0.82-1.14, k=5) and CHD mortality (HR 1.06, 95% CI 0.87-1.29, k=6) was not observed, though the risk estimates were in opposite directions. Results for high job demands and CHD mortality were not able to be pooled due to insufficient number of studies available for analysis.

The pooled results for job insecurity and all-cause mortality were inconclusive (minimally adjusted analysis HR 1.33, 95% CI 0.94-1.88, k=3 and multivariableadjusted analysis HR 1.26, 95% CI 0.92-1.73, k=3). Pooled estimates for job insecurity and CHD mortality were not able to be calculated due to insufficient number of individual studies.

Some heterogeneity was observed in studies pooled for examination of low job control and all-cause mortal- ity (/2=59.0%, P=0.045), high job demands and mortality (all-cause mortality /2=68.6%, P=0.013; CHD mortality /2=69.4%, P=0.011), job strain and mortality (all-cause mortality /2=77.0%, p=0.002; CHD mortality P=55.2%, P=0.029), shift work and CHD mortality (/2=58.0%, P=0.020), and job insecurity and all-cause mortality (/2=66.9%, P=0.017) in minimally adjusted analysis. Heterogeneity was also seen in studies pooled for analysis of shift work and mortality (all-cause mortality 72=73.8%, P=0.002; CHD mortality/2=60.2%, P=0.020), low job control and all-cause mortality (72=46.2%, P=0.030), and job insecurity and all-cause mortality (/2=59.0%, P=0.045) in multivariable-adjusted analysis.

No heterogeneity was observed in studies pooled for analysis of low job control and CHD mortality (/2=0.0%, P=0.543) or shift work and all-cause mortality (/2=0.0%, P=0.707) in minimally adjusted analyses, or in studies pooled for analysis of low job control and mortality (CHD mortality /2=0.0%, P=0.983), high job demands and all-cause mortality (/2=21.3%, P=0.234), or job strain and mortality (all-cause mortality /2=11.2%, P=0.337; CHD mortality /2=35.0%, P=0.202) in multivariable-adjusted analysis.

Investigation of funnel plots (supplementary figures S18-S21) suggested some degree of asymmetry. Almost all studies had small standard errors and risk estimates ranging from under one to approximately two. The few studies with larger risk estimates approximating four had larger standard errors estimates possibly due to small study effects or methodological limitations. Due to the small number of studies included in the meta-analyses, it is difficult to reliably assess publication bias solely based on the funnel plots (79), hence formal testing for asymmetry was performed using Egger's test (61). Formal statistical testing did not detect strong evidence of small study effects and risk of publication bias in the studies included in quantitative analyses, however there was some suggestion of small study effects for job insecurity and mortality (minimally adjusted analysis P=0.09 and multivariable-adjusted analysis P=0.08).

Sensitivity analyses excluding studies with low quality assessment resulted in attenuated pooled estimates and wider confidence intervals, probably due to validity issues with low quality studies. However, the association between exposure to low job control and mortality remained the same (minimally adjusted analysis: all-cause mortality HR 1.16, 95% CI 1.06-1.26, k=2; CHD mortality HR 1.36, 95% CI 1.19-1.56, k=4 and multivariable-adjusted analysis: all-cause mortality HR 1.03, 95% CI 1.00-1.06, k=5; and CHD mortality HR 1.19, 95% CI 1.01-1.40, k=4). As to be expected there was almost perfect overlap between studies with low quality assessment and studies that did not exclude or adjust for unhealthy participants at baseline, hence results of the sensitivity analyses examining differ- ences between studies that assessed relatively healthy participants and studies that did not exclude unhealthy participants or control for health status were very similar to the aforementioned results.

Discussion

Main findings

This systematic review and meta-analysis examined the association between mortality and psychosocial work stressor exposures. Our findings show that workers with low job control have a 21% increased risk of all-cause mortality, and 50% increased risk of CHD mortality, compared with workers with high job control. Even after adjustment for relevant confounders in the multivariable-adjusted analysis, the increased risk of low job control and

CHD mortality persisted as did the risk of all-cause mortality remain elevated, albeit attenuated, for workers with low job control. Excluding studies with low quality assessment attenuated the risk estimates but the association between low job control and mortality persisted. Low job control increased the risk of all-cause mortality by 3% and the risk of CHD mortality by 19% in the multivariable-adjusted analyses. A decreased risk of mortality for workers with exposure to high job demands was persistent across all subgroup analyses but was not statistically significant. Similarly, an elevated, but not significant, risk of mortality was observed for job strain and job insecurity. There did not appear to be any evidence supporting an association between exposure to shift work, and CHD mortality or all-cause mortality.

Comparison with other studies

This is the first review to synthesize systematically and quantitatively the respective epidemiological evidence for psychosocial work stressor exposures and CHD mortality or all-cause mortality. The observed association between low job control and increased all-cause mortality, in addition to CHD mortality, in minimally adjusted and multivariable-adjusted analyses strengthens the argument that job control is predictive of mortality. Many individual studies observe an elevated risk of mortality and low job control, but the association was not supported following adjustments for relevant covariates (28, 32, 35, 42, 65, 71, 72). However, these studies were generally small and underpowered to detect associations between mortality and job control, with most reporting less than several hundred deaths (28, 32, 42, 65, 71, 72), thus combining studies in a meta-analysis greatly increased the power to detect an association. A few studies detected decreased or no risk of mortality and low job control (31, 33, 38, 40). Variations in the underlying methodological design across studies, including differences in the measurement of the exposure and referent group, and assessment of potential confounders, may have contributed to inconsistent results.

Results for high job demands and mortality are consistent with results of individual studies. Most studies observed a reduced but non-significant risk of mortality and high job demands (26, 27, 33, 40, 51, 65), in contrast to Karasek (30) who found that high job demands increased the risk of CHD mortality. Self-reported assessments of job demands may not be a homogeneous measure across different occupations as job demands are experienced and interpreted differently across various occupational groups. There is a such a diversity of demands that responses might represent a range of job demands, such as psychological, physical, emotional, social, or organizational. It may also be that perceptions of job demands have changed over time. This along with inconsistent harmonization of scales across studies may explain the inconsistency in the literature.

Analyses of job strain and mortality were suggestive of a relationship between job strain and CHD mortality, but results were not conclusive. There is growing evidence that job strain and increased risk of mortality may be more pertinent in workers with existing cardiometabolic disease than for healthy workers. A study of patients with CHD based on three small prospective studies (67, 80, 81) reported a 60% increased risk of recurrent CHD events associated with job strain (82), and a more recent multicohort study examining work stress and mortality in workers with and without cardiometabolic disease reported a 70% increased risk of mortality in men with prevalent cardiometabolic disease (83). Analyses of job strain and CHD mortality were for healthy participants in all individual studies included in this review.

Results of the effects of shift work are consistent with the limited epidemiologic evidence that is available (12). Studies investigating shift work exposure can be prone to healthy shift work hire worker and healthy shift worker survivor selection bias due to unhealthy workers being less likely to take up shift work and healthier workers being more likely to remain in shift work employment compared to less healthy workers. This may explain the variation in mortality rates across studies. The evidence for job insecurity and mortality was inconclusive due to the small number of published studies available for inclusion in this review.

Biological plausibility

The observed associations are biologically plausible. Changes in brain stress-responsive neurocircuitry stimulate peripheral physiological responses in the sympa- thetic autonomic nervous system and hypothalamuspituitary-adrenal (HPA) through the release and control of adrenaline and stress hormone cortisol throughout the body, and

increase inflammatory protein levels despite the absence of pathogens (56). To cope with stress, the body's systems adjust psychological and physiological processes, resulting in chronic over-activity or underactivity of allostatic systems, fixing new baselines levels for psychological and physiological performances, causing deterioration of body systems from repeated and unresolved stressors (84). The cardiovascular system is particularly affected by stress. Combined effects of dysfunction of both the autonomic nervous system and HPA-axis responses over time can result in increases in platelet activation, blood fibrinogen levels and blood pressure levels, accelerating the atherosclerotic process and increasing the likelihood of fatal and non-fatal cardiovascular or cerebrovascular events (56, 84).

Strengths and limitations of the study

The review has several strengths, including thorough systematic review conducted according to PRISMA guidelines (57) of 45 studies and the inclusion of 32 studies from Europe, United States, Israel, and Japan, most of which were assessed as acceptable quality. Sensitivity analyses attenuated results, but still excluded the null, with estimates remaining consistent even when omitting studies with low quality assessment or studies that did not exclude or adjust for unhealthy participants at baseline. Assessment of study quality was conducted using a rigorously validated scoring tool recognized as a useful assessment tool for assessing quality and susceptibility to bias in observational studies (58, 85).

There was some heterogeneity in pooled study results, ranging from 0-77% across the analyses, likely due to the variation in composition and classification of psychosocial work stressor exposures and referent groups between studies, and variation in composition of study sample (eg, general working population, specific industries, gender-specific), as well as due to variations in study period and geography. Furthermore, participants with previous history of CHD and/or cancer were excluded in some studies but not by others.

There is a concern about insufficient variance for psychosocial work stressor exposures when using generic work strain instruments in single occupation studies that may have biased our results towards the null. These generic measures although well-validated may not have measured psychosocial work stressors pertinent to some occupations, eg, healthcare workers' exposure to violence. It should be also mentioned that the design of the review precluded assessment of the relation between single stressful occupations and mortality.

Nearly all studies measured exposure to psychosocial work stressors along with occupational, behavioral and/or biological risk factors at baseline and estimated their association with mortality during lengthy follow-up periods. Studies with single assessment of job characteristics and long follow-up periods without repeated assessment of exposure status over time measuring cumulative exposure, may bias results to null due to assessment of exposure to work stressors temporally distant from the outcome (86). Measurements of psychosocial work stressor exposures were self-reported in most individual studies and may have been subjected to reporting bias, however external measurements of work stress, like organizational downsizing, have been found to be associated with an increased risk of cardiovascular mortality (87). A few of the studies included in the review used occupation-based measures of psychosocial work stressors based on a job exposure matrix and may be susceptible to nondifferential exposure misclassification bias, biasing toward the null. In particular, job demands, a subjective measurement, may not be suitable for use in an exposure imputation system designed to measure environmental differences (30, 42, 65).

The individual studies had some degree of potential selection bias, including selective attrition due to cessation of employment as a result of job stressor exposure during the follow up period, and survivor bias (healthy worker effect) due to healthier participants being more willing to participate in health surveys, and less likely to be in low status jobs with high stress, that may have attenuated results. Of concern in shift work studies, the composition of the reference category may have influenced mortality risk estimates as healthier workers are more likely to take up shift work than less healthy workers and remain in shift work employment compared to those who develop debilitating conditions and depart shift work or retire from work altogether.

The lack of high-quality studies for inclusion in the meta-analyses is a limitation that may have potentially biased the results of our study towards the null. However, our analyses represent a summary of the existing knowledge. The fact that no high-quality study has been conducted is significant. More recent epidemiological methods including

marginal structural methods and causal mediation analysis should be considered in future studies examining mortality outcomes in longitudinal studies with long periods of follow-up. It must be noted that this review's narrow focus on psychosocial work stressors conceptualized from well-studied and validated work stress models is a limitation. Other conceptualizations of psychosocial work stressors for example burnout due to chronic exhaustion in combination with a negative attitude and diminished efficacy at work as a result of imbalance between job demands and resources (88, 89), and cognitive ergonomics such as the mental burden of specific tasks (90) and extra burdens created by time pressure and barriers hindering performance (91), were not included in this review. However, research into these work stressors and mortality is limited and their broad psychosocial framework may not be consistent with assumptions of homogeneity and variability between studies required for meta-analyses (92). The outcomes, all-cause mortality and mortality due to CHD, were ascertained through record linkage and ICD codes for most studies included in the review following the assessment of exposure to psychosocial work stressors. Potential reverse causation due to confounding was considered by study authors, and controlled for in the analysis, or at the design stage of the study by the exclusion of participants at baseline based on health status. Despite the evidence for psychosocial work stressors and mental health disorders (10), suiciderelated mortality was not included as a third outcome in this study, as several of the authors involved in this review had previously undertaken a comprehensive systematic review and meta-analysis of psychosocial job stressors and suicidality (93). The association between psychosocial work stressors and mortality may have been modified by gender, but we were unable to assess this effect moderation due to an insufficient number of studies presenting gender-stratified results. Nonetheless, we did provide pooled results by gender in supplementary figures S1-S17.

Concluding remarks

In conclusion, the results of the systematic review and meta-analyses suggest that workers with low job control are at increased risk of all-cause and CHD mortality compared to workers with high job control. Given the observed association between low job control and mortality along with the inconclusive findings for the other work stressors, further research is recommended to examine mechanisms underlying the observed effect between low job control and mortality and to elucidate the relationship between psychosocial work stressors and mortality. The strongest effect observed was that of deaths due to CHD and low job control, even after controlling for relevant confounders and the exclusion of low-quality studies. If the observed association is causal, then policy and practice interventions to improve job control could contribute to reductions in all-cause and CHD mortality.

Acknowledgement

We would like to pay our gratitude and our respects to our co-author and beloved colleague, Associate Professor Allison Milner who was tragically killed in August of 2019. She was Deputy Director of the Disability and Health Unit at the Centre for Health Equity, Melbourne School of Population and Global Health, at the University of Melbourne, with a passion for research pertaining to mental health and the workplace. Allison Milner was a tireless and prolific researcher and had made significant progress in broadening our understanding of psychological health at work and suicides and our understanding of the work stressors affecting workers health. She is remembered as an outstanding scholar, an exceptional mentor, and a loving and generous person with great affection by all who knew her. She certainly was in our thoughts whilst preparing this paper for publication.

Ethical approval

The Melbourne School of Population and Global Health Human Ethics Advisory Group approved this study (ethics application ID: 1750707.1).

Conflicts of Interest

The authors declare no conflicts of interest.

Sources of funding

This study was supported in part by an Australian Government Research Training Program Scholarship provided by the Australian Commonwealth Government. AM was funded by a Victorian Health and Medical Research Fellowship. MS is a recipient of an Australian Research Council Future Fellowship (project number FT180100075) funded by the Australian Government. The funding sources had no role in the design or conduct of the study;

collection, management, analysis, and interpretation of the data; or preparation, review, or approval of the manuscript including the decision to submit for publication.

Sidebar

Taouk Y, Spittal MJ, LaMontagne AD, Milner AJ. Psychosocial work stressors and risk of all-cause and coronary heart disease mortality: A systematic review and meta-analysis. Scand J Work Environ Health. 2020;46(1):19-31. doi:10.5271/sjweh.3854

Correspondence to: Yamna Taouk, MPH, Melbourne School of Population and Global Health, Level 4, 207 Bouverie Street, The University of Melbourne, Parkville, Victoria 3010 Australia. [E-mail: taouk.y@unimelb.edu.au]

References

References

1. Rohmert W. An International Symposium on Objective Assessment of Work Load in Air Traffic Control Tasks held at the Institute of Arbeitswissenschaft, the University of Technology, Darmstadt, German Federal Republic. Ergonomics 1971 Sep;14(5):545-7. https://doi. org/10.1080/00140137108931273.

2. Kivimäki M, Nyberg ST, Batty GD, Fransson EI, Heikkilä K, Alfredsson L et al.; IPD-Work Consortium. Job strain as a risk factor for coronary heart disease: a collaborative meta-analysis of individual participant data. Lancet 2012 Oct;380(9852):1491-7. https://doi.org/10.1016/S01406736(12)60994-5.

3. Goh J, Pfeffer J, Zenios S. Workplace stressors and health outcomes: health policy for the workplace. Behavioral Science &Policy. 2015;1(1):43-52. https://doi.org/10.1353/ bsp.2015.0001.

4. Van der Doef M, Maes S. The job demand-control(-support) model and physical health outcomes: A review of the strain and buffer hypotheses. Psychol Health 1998;13(5):909-36. https://doi.org/10.1080/08870449808407440.

5. Belkic KL, Landsbergis PA, Schnall PL, Baker D. Is job strain a major source of cardiovascular disease risk? Scand J Work Environ Health 2004 Apr;30(2):85-128. https://doi. org/10.5271/sjweh.769.

6. Huang Y, Xu S, Hua J, Zhu D, Liu C, Hu Y et al. Association between job strain and risk of incident stroke: A metaanalysis. Neurology 2015 Nov;85(19):1648-54. https://doi. org/10.1212/WNL.0000000000002098.

7. Fishta A, Backé EM. Psychosocial stress at work and cardiovascular diseases: an overview of systematic reviews. Int Arch Occup Environ Health 2015 Nov;88(8):997-1014. https://doi.org/10.1007/s00420-015-1019-0.

8. Nyberg ST, Fransson EI, Heikkilä K, Ahola K, Alfredsson L, Bjorner JB et al.; IPD-Work Consortium. Job strain as a risk factor for type 2 diabetes: a pooled analysis of 124,808 men and women. Diabetes Care 2014 Aug;37(8):2268-75. https://doi.org/10.2337/dc13-2936.

9. Fransson EI, Nyberg ST, Heikkilä K, Alfredsson L, Bjorner JB, Borritz M et al. Job strain and the risk of stroke: an individual-participant data meta-analysis. Stroke 2015 Feb;46(2):557-9. https://doi.org/10.1161/ STROKEAHA.114.008019.

10. Madsen IE, Nyberg ST, Magnusson Hanson LL, Ferrie JE, Ahola K, Alfredsson L et al.; IPD-Work Consortium. Job strain as a risk factor for clinical depression: systematic review and meta-analysis with additional individual participant data. Psychol Med 2017 Jun;47(8):1342-56. https://doi.org/10.1017/S003329171600355X.

11. Bøggild H, Knutsson A. Shift work, risk factors and cardiovascular disease. Scand J Work Environ Health 1999 Apr;25(2):85-99. https://doi.org/10.5271/sjweh.410.

12. Frost P, Kolstad HA, Bonde JP. Shift work and the risk of ischemic heart disease - a systematic review of the epidemiologic evidence. Scand J Work Environ Health 2009 May;35(3):163-79. https://doi.org/10.5271/sjweh.1319.

13. Bannai A, Tamakoshi A. The association between long working hours and health: a systematic review of epidemiological evidence. Scand J Work Environ Health 2014 Jan;40(1):5-18. https://doi.org/10.5271/sjweh.3388.

14. Virtanen M, Jokela M, Madsen IE, Magnusson Hanson LL, Lallukka T, Nyberg ST et al. Long working hours and depressive symptoms: systematic review and meta-analysis of published studies and unpublished individual participant data. Scand J Work Environ Health. 2018;44(3):239-50. https://doi. org/10.5271/sjweh.3712.

15. Virtanen M, Nyberg ST, Batty GD, Jokela M, Heikkilä K, Fransson EI, et al. Perceived job insecurity as a risk factor for incident coronary heart disease: systematic review and metaanalysis. BMJ: 2013;347:f4746. https://doi.org/10.1136/bmj. f4746.

16. Sverke M, Hellgren J, Näswall K. No security: a metaanalysis and review of job insecurity and its consequences. J Occup Health Psychol 2002 Jul;7(3):242-64. https://doi. org/10.1037/1076-8998.7.3.242.
17. Ferrie JE, Virtanen M, Jokela M, Madsen IE, Heikkilä K, Alfredsson L et al.; IPD-Work Consortium. Job insecurity and risk of diabetes: a meta-analysis of individual participant data. CMAJ 2016 Dec;188(17-18):E447-55. https://doi.org/10.1503/cmaj.150942.
18. Stansfeld S, Candy B. Psychosocial work environment and mental health-a meta-analytic review. Scand J Work Environ Health 2006 Dec;32(6):443-62. https://doi. org/10.5271/sjweh.1050.
19. Parent-Thirion A, Biletta I, Cabrita J, Vargas O, Vermeylen G, Wilczynska A et al. Eurofound (2017), Sixth European Working Conditions Survey - Overview report (2017 update). Publications Office of the European Union, Luxembourg.
20. Landsbergis PA, Dobson M, LaMontagne AD, Choi B, Schnall P, Baker DB. Occupational Stress. In: Levy BS, Wegman DH, Baron SL, Sokas RK, editors. Occupational and Environmental Health. 7th ed: Oxford University Press; 2017.
21. Milner A, Butterworth P, Bentley R, Kavanagh AM, LaMontagne AD. Sickness absence and psychosocial job quality: an analysis from a longitudinal survey of working Australians, 2005-2012. Am J Epidemiol 2015 May;181(10):781-8. https://doi.org/10.1093/aje/kwu355.
22. Karasek RA. Job Demands, Job Decision Latitude, and Mental Strain: Implications for Job Redesign. Adm Sci Q 1979;24(2):285-308. https://doi.org/10.2307/2392498.
23. Karasek R, Theorell T. Healthy work: Stress, productivity, and the reconstruction of working life. New York: Basic Books; 1990.
24. Johnson JV, Hall EM. Job strain, work place social support, and cardiovascular disease: a cross-sectional study of a random sample of the Swedish working population. Am J Public Health 1988 Oct;78(10):1336-42. https://doi. org/10.2105/AJPH.78.10.1336.
25. Falk A, Hanson BS, Isacsson SO, Ostergren PO. Job strain and mortality in elderly men: social network, support, and influence as buffers. Am J Public Health 1992 Aug;82(8):1136-9. https://doi.org/10.2105/AJPH.82.8.1136.
26. Amick BC 3rd, McDonough P, Chang H, Rogers WH, Pieper CF, Duncan G. Relationship between all-cause mortality and cumulative working life course psychosocial and physical exposures in the United States labor market from 1968 to 1992. Psychosom Med 2002 May-Jun;64(3):370-81. https:// doi.org/10.1097/00006842-200205000-00002.
27. Sabbath EL, Mejía-Guevara I, Noelke C, Berkman LF. The long-term mortality impact of combined job strain and family circumstances: A life course analysis of working American mothers. Soc Sci Med 2015 Dec;146:111-9. https://doi.org/10.1016/j.socscimed.2015.10.024.
28. Kivimäki M, Leino-Arjas P, Luukkonen R, Riihimäki H, Vahtera J, Kirjonen J. Work stress and risk of cardiovascular mortality: prospective cohort study of industrial employees. BMJ 2002 Oct;325(7369):857. https://doi.org/10.1136/ bmj.325.7369.857.
29. Toivanen S, Hemström O. Income differences in cardiovascular disease: is the contribution from work similar in prevalence versus mortality outcomes? Int J Behav Med 2006;13(1):89-100. https://doi.org/10.1207/ s15327558ijbm1301_11.
30. Karasek R, Baker D, Marxer F, Ahlbom A, Theorell T. Job decision latitude, job demands, and cardiovascular disease: a prospective study of Swedish men. Am J Public Health 1981 Jul;71(7):694-705. https://doi.org/10.2m5/AJPH.7U.694.
31. Hibbard JH, Pope CR. The quality of social roles as predictors of morbidity and mortality. Soc Sci Med 1993 Feb;36(3):217-25. https://doi.org/10.1016/02779536(93)90005-0.
32. Eaker ED, Sullivan LM, Kelly-Hayes M, D'Agostino RB Sr, Benjamin EJ. Does job strain increase the risk for coronary heart disease or death in men and women? The Framingham Offspring Study. Am J Epidemiol 2004 May;159(10):950-8. https://doi.org/10.1093/aje/kwh127.
33. Shirom A, Toker S, Alkaly Y, Jacobson O, Balicer R. Workbased predictors of mortality: a 20-year follow-up of

healthy employees. Health psychology: official journal of the Division of Health Psychology, American Psychological Association. 2011 ;30(3):268-75.
34. Tobiasz-Adamczyk B, Brzyski P, Florek M, Brzyska M. Job stress and mortality in older age. Int J Occup Med Environ Health 2013 Jun;26(3):349-62. https://doi.org/10.2478/ s13382-013-0114-2.
35. von Bonsdorff MB, Seitsamo J, von Bonsdorff ME, Ilmarinen J, Nygård CH, Rantanen T. Job strain among blue-collar and white-collar employees as a determinant of total mortality: a 28-year population-based follow-up. BMJ Open 2012 Mar;2(2):e000860. https://doi.org/10.1136/ bmjopen-2012-000860.
36. Slopen N, Glynn RJ, Buring JE, Lewis TT, Williams DR, Albert MA. Job strain, job insecurity, and incident cardiovascular disease in the Women's Health Study: results from a 10-year prospective study. PLoS One 2012;7(7):e40512. https://doi.org/10.1371/journal. pone.0040512.
37. Padyab M, Blomstedt Y, Norberg M. No association found between cardiovascular mortality, and job demands and decision latitude: experience from the Västerbotten Intervention Programme in Sweden. Soc Sci Med 2014 Sep;(117):58-66. https://doi.org/10.1016/j. socscimed.2014.07.033.
38. Nilsen C, Andel R, Fritzell J, Kåreholt I. Work-related stress in midlife and all-cause mortality: can sense of coherence modify this association? Eur J Public Health 2016 Dec;26(6): 1055-61. https://doi.org/10.1093/eurpub/ ckw086.
39. Brunner EJ, Kivimäki M, Siegrist J, Theorell T, Luukkonen R, Riihimäki H et al. Is the effect of work stress on cardiovascular mortality confounded by socioeconomic factors in the Valmet study? J Epidemiol Community Health 2004 Dec;58(12):1019-20. https://doi.org/10.1136/ jech.2003.016881.
40. Tsutsumi A, Kayaba K, Hirokawa K, Ishikawa S, Jichi Medical School Cohort Study G. Psychosocial job characteristics and risk of mortality in a Japanese community-based working population: the Jichi Medical School Cohort Study. Soc Sci Med. 2006 Sep;63(5):1276-88..
41. Lee S, Colditz G, Berkman L, Kawachi I. A prospective study of job strain and coronary heart disease in US women. Int J Epidemiol 2002 Dec;31(6):1147-53. https://doi. org/10.1093/ije/31.6.1147.
42. Johnson JV, Stewart W, Hall EM, Fredlund P, Theorell T. Long-term psychosocial work environment and cardiovascular mortality among Swedish men. Am J Public Health 1996 Mar;86(3):324-31. https://doi.org/10.2105/ AJPH.86.3.324.
43. Kivimäki M, Leino-Arjas P, Kaila-Kangas L, Luukkonen R, Vahtera J, Elovainio M et al. Is incomplete recovery from work a risk marker of cardiovascular death? Prospective evidence from industrial employees. Psychosom Med 2006 May-Jun;68(3):402-7. https://doi.org/10.1097/01. psy.0000221285.50314.d3.
44. Siegrist J. Adverse health effects of high-effort/low-reward conditions. J Occup Health Psychol 1996 Jan;1(1):27-41. https://doi.org/10.1037/1076-8998.1.1.27.
45. Elovainio M, Heponiemi T, Sinervo T, Magnavita N. Organizational justice and health; review of evidence. G Ital Med Lav Ergon 2010 Jul-Sep;32(3 Suppl B):B5-9.
46. Virtanen M, Elovainio M. Justice at the Workplace: A Review. Camb Q Healthc Ethics 2018 Apr;27(2):306-15. https://doi.org/10.1017/S0963180117000639.
47. Elovainio M, Leino-Arjas P, Vahtera J, Kivimäki M. Justice at work and cardiovascular mortality: a prospective cohort study. J Psychosom Res 2006 Aug;61(2):271-4. https://doi. org/10.1016/j.jpsychores.2006.02.018.
48. Kivimäki M, Ferrie JE, Brunner E, Head J, Shipley MJ, Vahtera J et al. Justice at work and reduced risk of coronary heart disease among employees: the Whitehall II Study. Arch Intern Med 2005 Oct;165(19):2245-51. https://doi. org/10.1001/archinte.165.19.2245.
49. Niedhammer I, Bourgkard E, Chau N; Lorhandicap Study Group. Occupational and behavioural factors in the explanation of social inequalities in premature and total mortality: a 12.5-year follow-up in the Lorhandicap study. Eur J Epidemiol 2011 Jan;26(1):1-12. https://doi. org/10.1007/s10654-010-9506-9.
50. Nätti J, Anttila T, Oinas T, Mustosmäki A. Night work and mortality: prospective study among Finnish employees over the time span 1984 to 2008. Chronobiol Int 2012 Jun;29(5):601-9. https://doi.org/10.3109/07420528.2012.675262.

51. Nätti J, Kinnunen U, Mäkikangas A, Mauno S. Type of employment relationship and mortality: prospective study among Finnish employees in 1984-2000. Eur J Public Health 2009 Apr;19(2):150-6. https://doi.org/10.1093/ eurpub/ckp002.
52. Perlman F, Bobak M. Assessing the contribution of unstable employment to mortality in posttransition Russia: prospective individual-level analyses from the Russian longitudinal monitoring survey. Am J Public Health 2009 Oct;99(10):1818-25. https://doi.org/10.2105/ AJPH.2008.154815.
53. Hublin C, Partinen M, Koskenvuo K, Silventoinen K, Koskenvuo M, Kaprio J. Shift-work and cardiovascular disease: a population-based 22-year follow-up study. Eur J Epidemiol 2010 May;25(5):315-23. https://doi.org/10.1007/ s10654-010-9439-3.
54. Yadegarfar G, McNamee R. Shift work, confounding and death from ischaemic heart disease. Occup Environ Med 2008 Mar;65(3):158-63. https://doi.org/10.1136/ oem.2006.030627.
55. O'Reilly D, Rosato M. Worked to death? A census-based longitudinal study of the relationship between the numbers of hours spent working and mortality risk. Int J Epidemiol 2013 Dec;42(6): 1820-30. https://doi.org/10.1093/ije/ dyt211.
56. Kivimäki M, Steptoe A. Effects of stress on the development and progression of cardiovascular disease. Nat Rev Cardiol 2018 Apr;15(4):215-29. https://doi.org/10.1038/ nrcardio.2017.189.
57. Moher D, Liberati A, Tetzlaff J, Altman DG, Group P; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. J Clin Epidemiol 2009 Oct;62(10):1006-12. https://doi. org/10.1016/jjclinepi.2009.06.005.
58. Scottish Intercollegiate Guidelines Network (SIGN). SIGN 50: a guideline developer's handbook. Edinburgh: SIGN, Available from: http://www.sign.ac.uk. SpnNAfU; 2015.
59. Borenstein M, Hedges LV, Higgins JP, Rothstein HR. Introduction to meta-analysis. UK: John Wiley &Sons; 2011.
60. Sterne JA, Harbord RM. Funnel plots in metaanalysis. Stata J 2004;4: 127-41. https://doi. org/10.1177/1536867X0400400204
61. Harbord RM, Harris RJ, Sterne JA. Updated tests for smallstudy effects in meta-analyses. Stata J 2009;9(2):197. https:// doi.org/10.1177/1536867X0900900202.
62. Gonzalez-Mule E, Cockburn B. Worked to death: the relationships of job demands and job control with mortality. Person Psychol 2017;70(1):73-112. https://doi.org/10.1111/ peps.12206.
63. Akerstedt T, Kecklund G, Johansson SE. Shift work and mortality. Chronobiol Int 2004;21(6):1055-61. https://doi. org/10.1081/CBI-200038520.
64. Johnson JV, Hall EM, Theorell T. Combined effects of job strain and social isolation on cardiovascular disease morbidity and mortality in a random sample of the Swedish male working population. Scand J Work Environ Health 1989 Aug;15(4):271-9. https://doi.org/10.5271/sjweh.1852.
65. Alterman T, Shekelle RB, Vernon SW, Burau KD. Decision latitude, psychologic demand, job strain, and coronary heart disease in the Western Electric Study. Am J Epidemiol 1994 Mar;139(6):620-7. https://doi.org/10.1093/oxfordjournals. aje.a117051.
66. McNamee R, Binks K, Jones S, Faulkner D, Slovak A, Cherry NM. Shiftwork and mortality from ischaemic heart disease. Occup Environ Med 1996 Jun;53(6):367-73. https:// doi.org/10.1136/oem.53.6.367.
67. László KD, Ahnve S, Hallqvist J, Ahlbom A, Janszky I. Job strain predicts recurrent events after a first acute myocardial infarction: the Stockholm Heart Epidemiology Program. J Intern Med 2010 Jun;267(6):599-611. https://doi. org/10.1111/j.1365-2796.2009.02196.x.
68. László KD, Engström K, Hallqvist J, Ahlbom A, Janszky I. Job insecurity and prognosis after myocardial infarction: the SHEEP Study. Int J Cardiol 2013 Sep;167(6):2824-30. https://doi.org/10.1016/j.ijcard.2012.07.005.
69. Holtermann A, Mortensen OS, Burr H, Søgaard K, Gyntelberg F, Suadicani P. Long work hours and physical fitness: 30-year risk of ischaemic heart disease and allcause mortality among middle-aged Caucasian men. Heart 2010 Oct;96(20):1638-44. https://doi.org/10.1136/ hrt.2010.197145.

70. Holtermann A, Mortensen OS, Burr H, Søgaard K, Gyntelberg F, Suadicani P. Physical fitness and perceived psychological pressure at work: 30-year ischemic heart disease and all-cause mortality in the Copenhagen Male Study. J Occup Environ Med 2011 Jul;53(7):743-50. https:// doi.org/10.1097/JOM.0b013e318223d47e.
71. Joensuu M, Kivimäki M, Koskinen A, Kouvonen A, PulkkiRåback L, Vahtera J et al. Differential associations of job control components with mortality: a cohort study, 19862005. Am J Epidemiol 2012 Apr;175(7):609-19. https://doi. org/10.1093/aje/kws028.
72. Joensuu M, Kivimäki M, Pentti J, Virtanen M, Väänänen A, Vahtera J. Components of job control and mortality: the Finnish Public Sector Study. Occup Environ Med 2014 Aug;71(8):536-42. https://doi.org/10.1136/ oemed-2014-102111.
73. Yong M, Nasterlack M, Messerer P, Oberlinner C, Lang S. A retrospective cohort study of shift work and risk of cancerspecific mortality in German male chemical workers. Int Arch Occup Environ Health 2014 Feb;87(2):175-83. https:// doi.org/10.1007/s00420-013-0843-3.
74. Jørgensen JT, Karlsen S, Stayner L, Andersen J, Andersen ZJ. Shift work and overall and cause-specific mortality in the Danish nurse cohort. Scand J Work Environ Health 2017 Mar;43(2):117-26. https://doi.org/10.5271/sjweh.3612.
75. Gu F, Han J, Laden F, Pan A, Caporaso NE, Stampfer MJ et al. Total and cause-specific mortality of U.S. nurses working rotating night shifts. Am J Prev Med 2015 Mar;48(3):24152. https://doi.org/10.1016/j.amepre.2014.10.018.
76. Karlsson B, Alfredsson L, Knutsson A, Andersson E, Torén K. Total mortality and cause-specific mortality of Swedish shift- and dayworkers in the pulp and paper industry in 1952-2001. Scand J Work Environ Health 2005 Feb;31(1):30-5. https://doi.org/10.5271/sjweh.845.
77. Fujino Y, Iso H, Tamakoshi A, Inaba Y, Koizumi A, Kubo T et al.; Japanese Collaborative Cohort Study Group. A prospective cohort study of shift work and risk of ischemic heart disease in Japanese male workers. Am J Epidemiol 2006 Jul;164(2):128-35. https://doi.org/10.1093/aje/ kwj185.
78. Kivimäki M, Vahtera J, Virtanen M, Elovainio M, Pentti J, Ferrie JE. Temporary employment and risk of overall and cause-specific mortality. Am J Epidemiol 2003 Oct;158(7):663-8. https://doi.org/10.1093/aje/kwg185.
79. Sterne JA, Sutton AJ, Ioannidis JP, Terrin N, Jones DR, Lau J et al. Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials. BMJ 2011 Jul;343:d4002. https://doi. org/10.1136/bmj.d4002.
80. Orth-Gomér K, Wamala SP, Horsten M, SchenckGustafsson K, Schneiderman N, Mittleman MA. Marital stress worsens prognosis in women with coronary heart disease: The Stockholm Female Coronary Risk Study. JAMA 2000 Dec;284(23):3008-14. https://doi.org/10.1001/ jama.284.23.3008.
81. Aboa-Eboulé C, Brisson C, Maunsell E, Mâsse B, Bourbonnais R, Vézina M et al. Job strain and risk of acute recurrent coronary heart disease events. JAMA 2007 Oct;298(14):1652-60. https://doi.org/10.1001/ jama.298.14.1652.
82. Li J, Zhang M, Loerbroks A, Angerer P, Siegrist J. Work stress and the risk of recurrent coronary heart disease events: A systematic review and meta-analysis. Int J Occup Med Environ Health 2015;28(1):8-19.
83. Kivimäki M, Pentti J, Ferrie JE, Batty GD, Nyberg ST, Jokela M et al.; IPD-Work consortium. Work stress and risk of death in men and women with and without cardiometabolic disease: a multicohort study. Lancet Diabetes Endocrinol 2018 Sep;6(9):705-13. https://doi. org/10.1016/S2213-8587(18)30140-2.
84. McEwen BS. Protective and damaging effects of stress mediators. N Engl J Med 1998 Jan;338(3):171-9. https://doi. org/10.1056/NEJM199801153380307.
85. Sanderson S, Tatt ID, Higgins JP. Tools for assessing quality and susceptibility to bias in observational studies in epidemiology: a systematic review and annotated bibliography. Int J Epidemiol 2007 Jun;36(3):666-76. https://doi.org/10.1093/ije/dym018.
86. Chandola T, Britton A, Brunner E, Hemingway H, Malik M, Kumari M et al. Work stress and coronary heart disease: what are the mechanisms? Eur Heart J 2008 Mar;29(5):6408. https://doi.org/10.1093/eurheartj/ehm584.
87. Vahtera J, Kivimäki M, Pentti J, Linna A, Virtanen M, Virtanen P et al. Organisational downsizing, sickness

absence, and mortality: 10-town prospective cohort study. BMJ 2004 Mar;328(7439):555. https://doi.org/10.1136/bmj.37972.496262.0D.
88. Maslach C, Schaufeli WB, Leiter MP. Job burnout. Annu Rev Psychol 2001;52:397-422. https://doi.org/10.1146/annurev.psych.52.1.397.
89. Schaufeli WB, Bakker AB. Job demands, job resources, and their relationship with burnout and engagement: a multisample study. J Organ Behav 2004;25(3):293-315. https:// doi.org/10.1002/job.248.
90. Singleton WT. A. T. Welford-a commemorative review. Ergonomics 1997 Feb;40(2):125-40. https://doi.org/10.1080/001401397188251.
91. Greiner B, Leitner K. Assessment of job stress: The RHIAInstrument. Recent developments in job analysis. Philadelphia, PA, US: Taylor &Francis; 1989. p. 53-66.
92. Rothman KJ, Greenland S, Lash TL. Modern epidemiology. 3rd ed. Philadelphia: Wolters Kluwer Health/Lippincott Williams &Wilkins; 2008.
93. Milner A, Witt K, LaMontagne AD, Niedhammer I. Psychosocial job stressors and suicidality: a metaanalysis and systematic review. Occup Environ Med 2018 Apr;75(4):245-53. https://doi.org/10.1136/ oemed-2017-104531.
Received for publication: 29 April 2019

DETAILS

Subject:	Physiology; Population; Risk management; Identification methods; Mortality; Heart diseases; Cardiovascular diseases; Researchers; Quality; Bias; Stress; Confidence intervals; Cardiovascular disease; Multivariable control; Heart; Systematic review; Coronary artery disease; Databases; Occupational stress; Shift work; Working hours
Business indexing term:	Subject: Occupational stress Shift work Working hours
Publication title:	Scandinavian Journal of Work, Environment &Health; Stockholm
Volume:	46
Issue:	1
Pages:	19-31
Publication year:	2020
Publication date:	2020
Section:	Original article
Publisher:	Scandinavian Journal of Work, Environment &Health
Place of publication:	Stockholm
Country of publication:	Finland, Stockholm
Publication subject:	Occupational Health And Safety
ISSN:	03553140

e-ISSN:	1795990X
Source type:	Scholarly Journal
Language of publication:	English
Document type:	Evidence Based Healthcare, Journal Article
DOI:	https://doi.org/10.5271/sjweh.3854
ProQuest document ID:	2344258413
Document URL:	https://www.proquest.com/scholarly-journals/psychosocial-work-stressors-risk-all-cause/docview/2344258413/se-2?accountid=211160
Copyright:	Copyright Scandinavian Journal of Work, Environment &Health 2020
Last updated:	2023-05-26
Database:	Public Health Database

Smoking and sickness absence: a systematic review and meta-analysis

Troelstra, Sigrid A, MSc [1] ; Coenen, Pieter, PhD [1] ; Boot, Cécile R L, PhD [1] ; Harting, Janneke, PhD [2] ; Kunst, Anton E, PhD [2] ; van der Beek, Allard J, PhD [1] Department of Public and Occupational Health, Amsterdam UMC, VU University Amsterdam, Amsterdam Public Health Research Institute, Amsterdam, The Netherlands [2] Department of Public Health, Amsterdam UMC, University of Amsterdam, Amsterdam Public Health Research Institute, Amsterdam, The Netherlands

ProQuest document link

ABSTRACT (ENGLISH)

Objectives Evidence on the effect of smoking on sickness absence could guide workplace smoking cessation interventions and encourage employers to promote smoking cessation among their employees. This systematic review and meta-analysis aimed to summarize evidence on the association between smoking and sickness absence and determine whether there are differences in this association for study design, methodology, and sample characteristics. Methods We searched for studies that reported on smoking status and sickness absence, used empirical data, were published in a peer-reviewed journal in the last 25 years, and written in English. We conducted pooled analyses in which uni- and multivariate generalized linear regression models were applied. Results After screening 2551 unique records, 46 articles from 43 studies were included, of which 33 studies (with 1 240 723 participants) could be included in the pooled analyses. Smoking was associated with an 31% increase in risk of sickness absence compared to non-smoking (95% confidence interval (CI) 1.24-39). We did not find statistically significant different effect sizes for study location, gender, age, occupational class, study design, assessment of

sickness absence, short- versus long-term sickness absence, and adjustment for relevant confounders. Furthermore, smoking was associated with 2.89 more sickness absence days per year compared to non-smoking (95% CI 2.08-3.70). Conclusions We found robust evidence showing that smoking increases both the risk and number of sickness absence days in working populations, regardless of study location, gender, age, and occupational class. Encouraging smoking cessation at the workplace could therefore be beneficial for employers and employees.

FULL TEXT

Headnote

Objectives Evidence on the effect of smoking on sickness absence could guide workplace smoking cessation interventions and encourage employers to promote smoking cessation among their employees. This systematic review and meta-analysis aimed to summarize evidence on the association between smoking and sickness absence and determine whether there are differences in this association for study design, methodology, and sample characteristics.

Methods We searched for studies that reported on smoking status and sickness absence, used empirical data, were published in a peer-reviewed journal in the last 25 years, and written in English. We conducted pooled analyses in which uni- and multivariate generalized linear regression models were applied.

Results After screening 2551 unique records, 46 articles from 43 studies were included, of which 33 studies (with 1 240 723 participants) could be included in the pooled analyses. Smoking was associated with an 31% increase in risk of sickness absence compared to non-smoking (95% confidence interval (CI) 1.24-39). We did not find statistically significant different effect sizes for study location, gender, age, occupational class, study design, assessment of sickness absence, short- versus long-term sickness absence, and adjustment for relevant confounders. Furthermore, smoking was associated with 2.89 more sickness absence days per year compared to non-smoking (95% CI 2.08-3.70).

Conclusions We found robust evidence showing that smoking increases both the risk and number of sickness absence days in working populations, regardless of study location, gender, age, and occupational class. Encouraging smoking cessation at the workplace could therefore be beneficial for employers and employees.

Key terms absenteeism; meta-regression analysis; smoker; sick leave; tobacco.

Smoking is one of the biggest public health threats; worldwide it kills more than seven million people yearly (1). First-hand smoking causes many different types of cancer, including lung, mouth and throat, stomach, liver, kidney and colorectal cancer, and leukemia. Furthermore, smoking can cause stroke, coronary heart disease, chronic obstructive pulmonary disease (COPD), diabetes, blindness, asthma, rheumatoid arthritis, and reduced fertility (2). Finally, smokers are more likely to experience a mental illness compared non-smokers (3). Therefore, smoking poses a significant societal burden, which can be expressed in terms of both healthcare costs and lost work productivity (4). Productivity loss could be caused by sickness absence, presenteeism, work disability, or death.

A wide range of studies have been performed to study the association between smoking and productivity (5). In 2013, a systematic review on the association between smoking and sickness absence was published. From this review, it was concluded that smoking increased the risk of sickness absence and number of sickness absence days (5). However, the generalizability of this systematic review to a general working population was limited since the authors included studies with specific samples of participants who were already predisposed to high levels of sickness absence, such as workers with severe pain (6) or diabetes mellitus (7), and studies that only examined sickness absence due to specific conditions, such as airway infections (8) and back pain (9-11). Furthermore, an updated review on this topic could be of added value, since several new studies have been published in the meantime (12-15).

Clear evidence on the impact of smoking on sickness absence, especially evidence that can be translated to a wide variety of populations and workplace settings, could encourage employers to promote smoking cessation among their employees. Promoting smoking cessation at the workplace can be highly effective from a public and

occupational health perspective since the occupational setting has the potential to reach large groups of people, have higher intervention participation rates compared to other settings, and encourage peersupport and positive peer pressure (12). Furthermore, several effective workplace smoking cessation interventions have been proven effective, such as group behavior therapy, individual counselling, nicotine replacement therapy (NTR) provision, comprehensive programs (12), and financial incentives (13). Therefore, it is important to review systematically the available evidence regarding the association of smoking and sickness absence from a general working population perspective.

We aimed to (i) summarize the evidence on the extent to which smoking influences sickness absence in the working population by performing a systematic review and meta-analysis on this topic and (ii) determine whether effect sizes are different across sources of variation in study design, methodology, and population characteristics.

Methods

Search strategy and study selection

This systematic review has been a-priori registered and was executed according to PRISMA statement guidelines (14). In February 2018, a systematic literature search was conducted in PubMed, Embase, and the Cochrane library. Search terms were related to: (i) exposure, ie, smoking, (ii) outcome, ie, some measure of work-related productivity1, and (iii) setting, ie, the workplace. Furthermore, in order to restrict our reference screening to a more manageable number of references (from 9812 to 1291), we added an additional part that consisted of search terms related to costs, long-term implications or effects, and economic, social or occupation burden. In order to ensure that we did not miss any relevant studies, we preselected 20 studies that we definitely wanted to include in our review. Of these, 19 were retrieved by using the current search strategy. The one study that was not retrieved did not have a term related to smoking in either title, abstract or keywords, and was therefore also not retrieved by the wider search. The search terms used for each of the databases can be found in the supplementary data (www.sjweh.fi/show_abstract.php?abstract_id=3848, table S1). Records retrieved from the different databases were combined and duplicates were removed.

Two reviewers independently screened 20% of the retrieved records on title and abstract using the Rayyan online tool (rayyan.qcri.org). Articles had to fulfill all of the following inclusion criteria in order to be included. First, an article was eligible if the sample consisted of adults with a paid job in any occupation. Second, articles had to report on smoking status, based on self-reports, employee records or biomarkers, and to include both current smokers and current non-smokers in order to compare these groups. Articles only reporting information on passive smoking were excluded. Third, an article had to report on sickness absence. Fourth, we included all types of study designs, as long as the article reported on empirical data. Fifth, articles were included only if they had been published in the last 25 years, since there have been substantial changes in employment relations and social benefit systems, and thereby in determinants of sickness absence. Sixth, only articles written in English and published in peer-reviewed journals were included.

In total, the two reviewers had 17 conflicts while screening 500 titles and abstracts. Discrepancies regarding in- and/or exclusion were discussed and the criteria were adjusted accordingly. To the second criterion, we added that articles using proxies of smoking status, such as having a smoking associated disease (eg, COPD or pulmonary cancer), should be excluded. To the fourth criterion, we added that simulation studies that made assumptions regarding smoking prevalence or the impact of smoking on work-related productivity should be excluded. Finally, we added as a seventh criterion, that articles only reporting on specific subsamples of employees with certain diseases or disabilities should be excluded.

After reaching agreement, the first author screened the remaining 80% of the retrieved records only on title and abstract. Fulltext articles were retrieved for the selected records, which two reviewers screened. Discrepancies between reviewers were discussed until consensus was reached. Finally, references of relevant systematic reviews and the included articles were checked for additional articles and screened by two reviewers for eligibility.

Data extraction and quality assessment

A data extraction sheet was developed, pilot tested on ten randomly selected included articles and then refined.

After finalizing the data extraction sheet, one reviewer performed the initial data extraction for all included articles and a second reviewer checked all proceedings. Per study, the following data were extracted: author, publication year and country, study sample (including dataset/cohort/register, number, gender, age), design (type and follow-up period), statistical method, assessment of smoking status, smoking prevalence, assessment of sickness absence, and the relation between smoking and sickness absence [eg, risk ratio (RR), odds ratio (OR), hazard ratio (HR)]. Corresponding authors were asked for additional information in cases where data provided in the published articles were insufficient. Two reviewers independently performed the quality assessment using a pilot tested set of ten predefined criteria (supplementary table S2). A quality assessment tool for observational cohort and cross-sectional studies (15) and a review on the quality of prognosis studies (16) were used to formulate the criteria for the quality assessment.

Data analysis

Included studies were described based on the extracted data and methodological quality. In cases where multiple articles reported on results from the same study, only complementary information from the various articles was used for further analysis. In our statistical pooling, we differentiated between studies that reported on a dichotomous outcome measure where effect sizes were expressed in a measure of relative risk (eg, OR, RR, HR), and a continuous outcome measure, which were standardized into mean difference in sickness absence days per year (assuming 8 working hours per day and 40 working hours per week). We assumed that for measures of relative risk, several effect estimates (eg, OR, RR and HR) could be interpreted equally, even though OR overstate the effect size if interpreted as a relative risk, especially if prevalence is high (17). For some studies only an excess of missed workdays for smokers compared to non-smokers was reported. For these studies, to calculate the standardized mean difference, we counted the excess number of missed workdays as the total number of missed workdays for smokers, and thereby assumed that the number of missed workdays for non-smokers was 0 with a standard deviation of 1. If multiple outcomes were reported on in one study, but participants were not mutually exclusive, for example when short-and long-term absence were reported separately while participants could be included in both categories, then a weighted average effect size was calculated. If an article reported on outcomes separately for ex- and non-smokers, we only used the latter effect size. If an article distinguished between different categories of smoking exposure (eg, heavy, light, or incidental smokers), we calculated a weighted average effect size. If it was not possible to convert the study outcome to either a relative risk of sickness absence or a number of sickness absence days per year, then the study findings were only described narratively.

Exposure-outcome associations of individual studies, expressed in relative risk and mean difference were pooled using Review Manager (RevMan) version 5.3. Pooled exposure-outcome associations, derived from a random effects model, were presented in a forest plot. In a meta-regression, the results expressed in relative risk of sickness absence were stratified based on eight characteristics, which were defined a-priori based on theoretical plausibility: (i) study location: western versus non-western countries, (ii) gender: mixed versus mostly male (>75% male) versus mostly female (>75% female), (iii) mean age: <40 versus 40-48 versus >48 years (cut-offs were defined based on the number of studies within each age group), (iv) occupational class: mixed versus blue- versus pink- versus white-collar workers, (v) study design: longitudinal versus cross-sectional, (vi) assessment of sickness absence: self-reported absence versus company records, (vii) duration of sickness absence: undefined versus short-term (<4 consecutive weeks) versus long-term (>4 consecutive weeks), and (viii) whether associations were adjusted for gender, age and socioeconomic position (not adjusted for all three confounders versus adjusted for all three confounders).

We composed a dataset including the effect estimates and the study characteristics. Univariate and multivariate meta-regression models were applied to determine the effect of the eight aforementioned study characteristics (independent variables) on the association between smoking and risk of sickness absence (dependent variable). Since a mean difference in sickness absence days per year could only be estimated for a limited number of studies, we did not conduct a meta-regression analysis for these studies.

Results

Study selection

The study selection process is presented in figure 1. The literature search yielded a total of 3753 records. After removal of duplicates, 2551 unique records were screened on title and abstract. Subsequently, 87 articles were assessed for eligibility based on the fulltext, while including 28 articles (see figure 1). After screening reference lists of these studies and earlier systematic reviews, an additional 18 articles were included. In total, 46 articles reporting on 43 studies were included (6, 11, 18-62).

Study descriptives

The characteristics of the 43 included studies are summarized in table 1. In total, these studies included more than 1 354 126 participants (one study did not report numbers). The number of participants per study varied from 292 (33) up to 383 778 (55). The majority of studies reported on absence from workers in Western countries (N=39) (eg, Europe, USA, Australia, NewZealand), while six studies were from a non-Western country, such as Uganda (26), Brazil (48), China (19), and Japan (21, 38, 44). Two studies reported on workers in both Western and non-Western countries (19, 44). About half of the studies had a longitudinal study design, varying in duration of follow-up from a few months (33) up to several years (44). Most studies reported on populations including both males and females, while some studies reported separate outcomes for both genders (31, 46, 47, 52, 58) or included only male employees (23, 44). Studies took place in a wide range of occupational settings, including a military base (26), schools (24), the construction industry (23), municipal government (18, 37, 44, 52) and an airline reservation office (33).

Sickness absence was assessed by self-report (25 studies), company record information (17 studies), or both self-report and company record information (1 study) and defined in several ways. The most frequently used measures were any absence (yes/no) and the total number of sickness absence days during a certain time period. Less frequently used were change in number of sickness absence days (32), sickness absence percentage (19, 28), workers' compensation costs (34, 45, 54), number of sickness absence episodes (41, 59), and sickness absence hours (61).

The risk of bias according to the ten methodological quality criteria is presented in figure 2. None of the articles scored low risk on all ten items. The majority of articles scored high risk of bias on the item regarding study confounding; they only reported univariate associations between smoking and sickness absence. Furthermore, the majority of studies scored high or uncertain risk of bias on the item of study participation, as they did not report sufficient information to gain insight into the participation rate of eligible persons.

Risk of sickness absence

For 25 studies (with a total of 765 088 participants), reporting on a total of 30 associations, the outcome measures could be pooled into an estimate of relative risk of sickness absence (figure 3). These studies were used for the meta-regression analyses, assessing the associations between study characteristics, study design, and outcomes. Smoking was significantly associated with an increase in sickness absence, showing a total RR of 1.31 (95% CI 1.24-1.39) (table 2). Although not impacting on our conclusions, there are small differences in pooled effect size between table 2 and figure 3 due to differences in the estimation of the effect size. For the meta-analyses (figure 3), a random-effects model was applied, and for the meta-regression analyses (table 2), a fixed-effects model was used.

We did not find statistically significant differences in association between smoking and sickness absence for study location, gender, age, occupational class, study design, type of assessment of sickness absence, short- versus long-term sickness absence, and adjustment for gender, age and socioeconomic position (table 2). However, we found potentially relevant differences in effect size for age and duration of sickness absence. For studies with a mean sample age <40, 40-48, and >48 years, we found a relative risk of sickness absence for smokers compared to non-smokers of 1.42 (95% CI 1.17-1.73), 1.28 (95% CI 1.19-1.39), and 1.27 (95% CI 1.20-1.35) respectively. For studies measuring shortterm (<4 weeks) and long-term (>4 weeks) sickness absence, the RR was 1.22 (95% CI 0.88-1.70) and 1.46 (95% CI 1.13-1.89), respectively. The stratified study findings are tabulated in supplementary figures S3-S10.

Sickness absence days

For eight studies (with a total of 475 635 participants) (19, 24-26, 33, 36, 42, 61), reporting on 11 associations in total, we were able to calculate a weighted mean difference in sickness absence days per year (table 1). The pooled weighted mean difference of sickness absence days per year for smokers compared to non-smokers was 2.89 days (95% CI 2.08-3.70) (figure 4).

Studies not included in pooled analyses

In total, ten studies were not included in the statistical pooling. For five studies (27, 29, 41, 56, 58), we did not have sufficient information to estimate either relative risk of sickness absence or number of sickness absence days. This was due to a lack of reporting of standard errors and CI of the outcome measure (27, 29, 41, 58) or no information on number or proportion of smokers in the research population (56). The corresponding authors of these studies were contacted but either did not respond or were unable to provide the required information. Other studies reported on different outcome measures, such as change in sickness absence over time (32), workers compensation costs (34, 45, 54), and sickness absence rate per 100 person years (59).

The studies not included in the statistical pooling all reported more absence for smokers compared to nonsmokers, such as 34 more sickness absence days when comparing absences >5 consecutive days (27), 2.3 more sickness absence days per year (29), one less workday missed, two years after quitting smoking (32), 50% more sickness absence episodes (P<0.01) and 12.5 more sickness absence hours per 1000 working hours (P<0.05) (41). Furthermore, these studies reported higher total lost productivity time (2.85 for heavy smokers versus 1.45 for never smokers) (56), higher sickness absence frequency rates (smoking 33.0 versus non-smoking 22.4 (P<0.05) men; smoking 42.4 versus non-smoking 17.7 (P<0.05) women (58), and a higher sickness absence rate per 100 persons (smokers 20.9 versus non-smokers 12.2) (59). Additionally, studies reporting workers compensation costs found that these were higher for smokers compared to non-smokers (US$1010 for smokers versus US$767 for non-smokers (34); US$2189 for smokers versus US$176 for non-smokers (45); US$2697 for smokers versus US$2023 for non-smokers (54).

Additional analyses

As an additional analysis, we compared outcomes from studies that scored relatively low on risk of bias (low risk of bias on >8 items) with studies that scored relatively high on risk of bias (low risk of bias on <8 items). We did not find statistically significant differences in outcomes (RR 1.23, 95% CI 1.20-1.26 versus RR 1.21, 95% CI 1.18-1.23) between these two groups of studies (supplementary figure S11).

To determine whether the year of publication was of influence on study outcome, we conducted an additional meta-analysis to test for differences in risk of sickness absence for studies conducted before and after 2008. The studies published before 2008 generally scored higher on risk of sickness absence compared to studies published after 2008 (RR 1.38, 95% CI 1.23-1.53 versus RR 1.21, 95% CI 1.16-1.27, respectively) (supplementary figure S12). This suggests that the effect of smoking on sickness absence might decrease over time, which could indicate that the effect sizes reported in our study might have been larger if we would have included papers published longer than 25 years ago.

Discussion

Summary of findings

In this study, we aimed to review and summarize evidence on the association between smoking and sickness absence and determine whether there are differences in associations for studies with differences in study design, methodology and sample characteristics. Overall, we found evidence that smoking increased both the risk of sickness absence and the number of sickness absence days. Smoking was associated with a 31% higher risk of sickness absence compared to non-smoking and 2.89 more sickness absence days per year compared to nonsmoking. We did not find statistically significant different effect sizes with varying study location, gender, age, occupational class, longitudinal versus cross-sectional design, assessment of sickness absence, duration of sickness absence, and whether outcomes were adjusted for gender, age, and socioeconomic status.

Strengths and limitations

A strength of our systematic review is that we were able to include a sufficient number of studies to perform a meta-regression analysis. In this way, we were able to take into account the influence of variations in sample characteristics such as study location, gender, age, and occupational class, which enables us to draw more generalizable conclusions. Another strength of the present systematic review is its generalizability to a general working population. By excluding studies that reported on specific sub-populations with disabilities or chronic diseases that are associated with more sickness absence, such as diabetes mellitus (7) or chronic obstructive pulmonary disease (63), our study is of high relevance to employers aiming to improve workers' health and increase the organizations' productivity.

The present review has some limitations. First, some subgroups in the meta-regression analysis had only a small number of studies, as a result of which we might have been unable to detect important differences. For example, only a few studies had samples from non-western countries (19, 21, 26, 38, 44, 48), from a specific occupational class (11, 18, 23, 37, 44, 52) or consisted of mainly female participants (31, 37, 46, 47, 52). Furthermore, only a limited number of studies specified the duration of sickness absence, of which two associations (47) were classified as short-term absence and four associations (18, 20, 31) were classified as long-term absence.

Second, of the 46 articles we included, 18 articles we identified through screening references of included stud- ies and previous reviews. A study from Greenhalgh and colleagues concluded that by relying solely on protocoldriven search strategies, important evidence might be missed and that "snowball" methods can identify high quality evidence that would not have been detected otherwise (64). A potential explanation for the high number of relevant studies identified through reference screening in the present review is that in studies researching the association between health and work productivity, smoking is often treated as a covariate and only reported in tables, figures or in the fulltext (but not in study title and abstract). By screening references of included studies and previous reviews, we were able to include several studies that we would otherwise have missed.

Third, we assumed that OR and HR could be interpreted as relative risks. However, OR can overstate the actual effect size when they are interpreted as relative risks (17). Since smoking increases sickness absence, the OR could be an overestimation of the RR. This may have caused some inaccuracy in the pooled estimation of the effect sizes (65). Furthermore, for five studies we assumed that the number of missed workdays for nonsmokers was 0, with a standard deviation of 1, since only the excess number of missed workdays for smokers compared to non-smokers was reported, and not the actual number of missed workdays for smokers and nonsmokers. We conducted sensitivity analyses with larger standard deviations but did not find large differences in the number of sickness absence days.

Fourth, smoking status was determined based on self-reports in all included studies and sickness absence was based on self-reports in about half of the included studies. Self-reported smoking status has been shown to be reliable (66, 67) and has shown to somewhat underestimate smoking status obtained by saliva or urine cotinine levels (68). A study comparing self-reported sickness absence days with employer registered sickness absence concluded that agreement between these two types of assessment of sickness absence is relatively good (69). In line with these findings, we did not find statistically significant differences in study outcomes for self-reported versus sickness absence versus objective assessment of sickness absence in our meta-regression analysis. Therefore, we expect the potential for bias due to self-reported sickness absence to be very small.

Interpretation of findings

Overall, we found evidence that smoking increased both the risk of sickness absence and the number of sickness absence days. Smoking can influence sickness absence through several pathways. First, smoking can lower an employee's health status, due to, amongst other reasons, a decreased immune status, respiratory problems, cardiovascular problems, and cancer (2). Second, smokers might be more prone to accidents and injuries due to personality characteristics, smoking-associated disabilities, or being distracted while smoking a cigarette or while experiencing nicotine withdrawal (70, 71). Third, since smoking is associated with mental illness and substance abuse, the relation between smoking and sickness absence might partially be explained by mental illness and substance abuse as causes for absenteeism (72).

Our findings that smoking is associated with 31% higher risk of sickness absence and 2.89 more sickness absence days compared to non-smoking are consistent with a former systematic review on this topic by Weng and colleagues (5), who found a 33% higher risk of work absence and 2.74 more sickness absence days per year among smokers compared to non-smokers. We checked all the studies included in Weng et al's review for eligibility but could only include 13 of the 29 studies in the present systematic review. Of the 16 studies not included 9 studies were excluded because they were not published in the past 25 years and 7 because they reported on specific subsamples of people with a disability that were not representative of the general working population. Therefore, the results of the present review are a more accurate reflection of the current working environment and the general employee population.

We did not find evidence that gender, age, study location and occupation class influenced the risk of smoking on sickness absence. This strengthens our conclusion and suggests that all employers and employees, irrespective of these characteristics, could equally benefit from smoking cessation, and therefore that all employee populations should equally be offered the opportunity to participate in smoking cessation interventions. However, for some covariates we found substantial differences in effect size, for example with regard to age and duration of sickness absence (73). This might indicate that some subgroups, such as younger workers (12), could benefit more from smoking cessation interventions and that potential effects might be more pronounced for longer periods of sickness absence. Therefore, more research should be conducted on the association between smoking and sickness absence in these sub-populations.

Several studies have estimated the costs of smoking at the workplace, based on empirical research of the association between smoking and work productivity (58, 74-79). These studies all conclude that smoking places a large economic burden on society. Halpern and colleagues found that for workers who quit smoking, productivity levels decreased in the first year compared to for those who continue smoking, but eventually exceeded productivity levels of continuous smokers in the following years (33). Potentially, productivity among former smokers can increase towards productivity levels of never smokers in the long term (80). Therefore, encouraging smoking cessation at the workplace could be highly cost-effective for employers and employees.

Multiple effective workplace-based smoking cessation interventions are already available, such as group behavior theory, individual counselling, NTR provision, and comprehensive programs (12). According to a qualitative evidence synthesis on employees views on workplace smoking cessation interventions, workplace smoking cessation inventions should have multiple components in order to facilitate employees in various phases of the cessation process, since needs and preferences can vary considerably between workers (81). A study simulating the effect of a worksite smoking cessation program found that potential savings from reduced sickness absence by far exceeded the program costs (80).

Concluding remarks

We found robust evidence that smoking increases both the risk and number of sickness absence days in the working population, regardless of differences in gender, age and occupational class. Encouraging smoking cessation at the workplace could be beneficial for employers and employees.

Acknowledgements

The authors would like to thank Ralph de Vries for developing the systematic literature search strategy and Marianne de Maaker-Berkhof for assisting with reviewing titles and abstracts.

Sidebar

Troelstra SA. Coenen P, Boot CRL, Harting J, Kunst AE, van der Beek AJ. Smoking and sickness absence: a systematic review and meta-analysis. Scand J Work Environ Health. 2020;46(1):5-18. doi:10.5271/sjweh.3848

Correspondence to: Cécile R. L. Boot, Department of Public and Occupational Health, Amsterdam UMC, VU University Amsterdam, Amsterdam Public Health research institute, Amsterdam, The Netherlands. [E-mail: crl.boot@vumc.nl]

Footnote

1 This article is part of a larger review on the relation between smoking and multiple work productivity measures. In

this article we only included studies that reported on the relation between smoking and sickness absence.

References

References

1. World Health Organization. Tobacco. Key facts. 2018 [cited 2018 March 19]. Available from: http://www.who.int/en/ news-room/fact-sheets/detail/tobacco.
2. U.S. Department of Health and Human Services. The Health Consequences of Smoking-50 Years of Progress: A Report of the Surgeon General. Atlanta: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2014.
3. Lasser K, Boyd JW, Woolhandler S, Himmelstein DU, McCormick D, Bor DH. Smoking and mental illness: A population-based prevalence study. JAMA 2000 Nov;284(20):2606-10. https://doi.org/10.1001/ jama.284.20.2606.
4. Goodchild M, Nargis N, Tursan d'Espaignet E. Global economic cost of smoking-attributable diseases. Tob Control 2018 Jan;27(1):58-64. https://doi.org/10.1136/ tobaccocontrol-2016-053305.
5. Weng SF, Ali S, Leonardi-Bee J. Smoking and absence from work: systematic review and meta-analysis of occupational studies. Addiction 2013 Feb;108(2):307-19. https://doi. org/10.1111/add.12015.
6. Andersen LL, Mortensen OS, Hansen JV, Burr H. A prospective cohort study on severe pain as a risk factor for long-term sickness absence in blue- and white-collar workers. Occup Environ Med 2011 Aug;68(8):590-2. https://doi.org/10.1136/oem.2010.056259.
7. De Backer G, Leynen F, De Bacquer D, Clays E, Moreau M, Kornitzer M. Diabetes mellitus in middle-aged people is associated with increased sick leave: the BELSTRESS study. Int J Occup Environ Health 2006 Jan-Mar;12(1):28-34. https://doi.org/10.1179/oeh.2006.12.1.28.
8. Eriksen W, Bruusgaard D, Knardahl S. Work factors as predictors of sickness absence attributed to airway infections; a three month prospective study of nurses' aides. Occup Environ Med 2004 Jan;61(1):45-51.
9. Holmberg SA, Thelin AG. Predictors of sick leave owing to neck or low back pain: a 12-year longitudinal cohort study in a rural male population. Ann Agric Environ Med 2010;17(2):251-7.
10. Skillgate E, Vingård E, Josephson M, Holm LW, Alfredsson L. Is smoking and alcohol consumption associated with long-term sick leave due to unspecific back or neck pain among employees in the public sector? Results of a three-year follow-up cohort study. J Rehabil Med 2009 Jun;41(7):550-6. https://doi.org/10.2340/16501977-0370.
11. Tsai SP, Bhojani FA, Wendt JK. Risk factors for illness absence due to musculoskeletal disorders in a 4-year prospective study of a petroleum-manufacturing population. J Occup Environ Med 2011 Apr;53(4):434-40. https://doi. org/10.1097/JOM.0b013e3182128b12.
12. Cahill K, Lancaster T. Workplace interventions for smoking cessation. Cochrane Database Syst Rev. 2014(2).
13. van den Brand FA, Nagelhout GE, Winkens B, Chavannes NH, van Schayck OC. Effect of a workplace-based group training programme combined with financial incentives on smoking cessation: a cluster-randomised controlled trial. Lancet Public Health 2018 Nov;3(11):e536-44. https://doi. org/10.1016/S2468-2667(18)30185-3.
14. Troelstra SA, Coenen P, Boot CRL, Harting J, Kunst AE, van der Beek AJ. Smoking and sickness absenteeism: a systematic review and meta-regression analysis. PROSPERO. 2018;CRD42018104624.
15. National Institutes of Health. Quality Assessment Tool for Observational Cohort and Cross-sectional Studies. 2014.
16. Hayden JA, Côté P, Bombardier C. Evaluation of the quality of prognosis studies in systematic reviews. Ann Intern Med 2006 Mar;144(6):427-37. https://doi.org/10.7326/00034819-144-6-200603210-00010.
17. Davies HT, Crombie IK, Tavakoli M. When can odds ratios mislead? BMJ 1998 Mar;316(7136):989-91. https://doi. org/10.1136/bmj.316.7136.989.
18. Airaksinen J, Jokela M, Virtanen M, Oksanen T, Koskenvuo M, Pentti J et al. Prediction of long-term absence due to sickness in employees: development and validation of a multifactorial risk score in two cohort studies. Scand J Work Environ Health 2018 May;44(3):274-82. https://doi. org/10.5271/sjweh.3713.
19. Baker CL, Flores NM, Zou KH, Bruno M, Harrison VJ. Benefits of quitting smoking on work productivity and

activity impairment in the United States, the European Union and China. Int J Clin Pract 2017 Jan;71(1). https://doi.org/10.nn/ijcp.12900.
20. Roelen C, Thorsen S, Heymans M, Twisk J, Bültmann U, Bjørner J. Development and validation of a prediction model for long-term sickness absence based on occupational health survey variables. Disabil Rehabil 2018 Jan;40(2):168-75. https://doi.org/10.1080/09638288.2016.1247471.
21. Suwa K, Flores NM, Yoshikawa R, Goto R, Vietri J, Igarashi A. Examining the association of smoking with work productivity and associated costs in Japan. J Med Econ 2017 Sep;20(9):938-44. https://doi.org/10.1080/13696998.2017.1 352507.
22. Aaviksoo E, Baburin A, Kiivet RA. Risk factors for sickness absence among Estonian employees. Occup Med (Lond) 2013 Mar;63(2):156-9. https://doi.org/10.1093/occmed/ kqs222.
23. Alavinia SM, van den Berg TI, van Duivenbooden C, Elders LA, Burdorf A. Impact of work-related factors, lifestyle, and work ability on sickness absence among Dutch construction workers. Scand J Work Environ Health 2009 Oct;35(5):32533. https://doi.org/10.5271/sjweh.1340.
24. Alker HJ, Wang ML, Pbert L, Thorsen N, Lemon SC. Impact of school staff health on work productivity in secondary schools in Massachusetts. J Sch Health 2015 Jun;85(6):398404. https://doi.org/10.1111/josh.12266.
25. Asay GR, Roy K, Lang JE, Payne RL, Howard DH. Absenteeism and Employer Costs Associated With Chronic Diseases and Health Risk Factors in the US Workforce. Prev Chronic Dis 2016 Oct;13:E141. https://doi.org/10.5888/pcd13.150503.
26. Basaza R, Otieno E, Musinguzi A, Mugyenyi P, Haddock CK. Factors influencing cigarette smoking among soldiers and costs of soldier smoking in the work place at Kakiri Barracks, Uganda. Tob Control 2017 May;26(3):330-3. https://doi.org/10.1136/tobaccocontrol-2015-052878
27. Bhojani FA, Tsai SP, Wendt JK, Koller KL. Simulating the impact of changing trends in smoking and obesity on productivity of an industrial population: an observational study. BMJ Open 2014 Apr;4(4):e004788. https://doi.org/10.1136/bmjopen-2014-004788.
28. Boles M, Pelletier B, Lynch W. The relationship between health risks and work productivity. J Occup Environ Med 2004 Jul;46(7):737-45. https://doi.org/10.1097/01. jom.0000131830.45744.97.
29. Bunn WB 3rd, Stave GM, Downs KE, Alvir JM, Dirani R. Effect of smoking status on productivity loss. J Occup Environ Med 2006 Oct;48(10):1099-108. https://doi. org/10.1097/01.jom.0000243406.08419.74.
30. Bush R, Wooden M. Smoking and absence from work: australian evidence. Soc Sci Med 1995 Aug;41(3):437-46. https://doi.org/10.1016/0277-9536(94)00350-3.
31. Christensen KB, Lund T, Labriola M, Bültmann U, Villadsen E. The impact of health behaviour on long term sickness absence: results from DWECS/DREAM. Ind Health 2007 Apr;45(2):348-51. https://doi.org/10.2486/indhealth.45.348.
32. Gifford B. Modifiable health risks and illness absence from work: evidence from the panel study of income dynamics. J Occup Environ Med 2013 Mar;55(3):245-51. https://doi. org/10.1097/JOM.0b013e31828349e7.
33. Halpern MT, Shikiar R, Rentz AM, Khan ZM. Impact of smoking status on workplace absenteeism and productivity. Tob Control 2001 Sep;10(3):233-8. https://doi.org/10.1136/ tc.10.3.233.
34. Henke RM, Carls GS, Short ME, Pei X, Wang S, Moley S et al.; The Relationship Between Health Risks and Health and Productivity Costs Among Employees at Pepsi Bottling Group. The relationship between health risks and health and productivity costs among employees at Pepsi Bottling Group. J Occup Environ Med 2010 May;52(5):519-27. https://doi.org/10.1097/JOM.0b013e3181dce655.
35. Karlsson N, Skargren E, Kristenson M. Emotional support predicts more sickness absence and poorer self assessed work ability: a two-year prospective cohort study. BMC Public Health 2010 Oct;10:648. https://doi.org/10.1186/1471-2458-10-648.
36. Kirkham HS, Clark BL, Bolas CA, Lewis GH, Jackson AS, Fisher D et al. Which modifiable health risks are associated with changes in productivity costs? Popul Health Manag 2015 Feb;18(1):30-8. https://doi.org/10.1089/pop.2014.0033.

37. Kivimäki M, Vahtera J, Thomson L, Griffiths A, Cox T, Pentti J. Psychosocial factors predicting employee sickness absence during economic decline. J Appl Psychol 1997 Dec;82(6):858-72. https://doi.org/10.1037/00219010.82.6.858.
38. Kondo K, Kobayashi Y, Hirokawa K, Tsutsumi A, Kobayashi F, Haratani T et al. Job strain and sick leave among Japanese employees: a longitudinal study. Int Arch Occup Environ Health 2006 Mar;79(3):213-9. https://doi.org/10.1007/s00420-005-0027-x.
39. Kowlessar NM, Goetzel RZ, Carls GS, Tabrizi MJ, Guindon A. The relationship between 11 health risks and medical and productivity costs for a large employer. J Occup Environ Med 2011 May;53(5):468-77. https://doi.org/10.1097/ JOM.0b013e31821586b8.
40. Laaksonen M, Piha K, Martikainen P, Rahkonen O, Lahelma E. Health-related behaviours and sickness absence from work. Occup Environ Med 2009 Dec;66(12):840-7. https:// doi.org/10.1136/oem.2008.039248.
41. Lucey SP. Can pre-placement health assessments predict subsequent sickness absence? Occup Med (Lond) 2008 Aug;58(5):355-60. https://doi.org/10.1093/occmed/kqn029.
42. Lundborg P. Does smoking increase sick leave? Evidence using register data on Swedish workers. Tob Control 2007 Apr;16(2):114-8. https://doi.org/10.n36/tc.2006.017798.
43. Merrill RM, Aldana SG, Pope JE, Anderson DR, Coberley CR, Grossmeier JJ et al.; HERO Research Study Subcommittee. Self-rated job performance and absenteeism according to employee engagement, health behaviors, and physical health. J Occup Environ Med 2013 Jan;55(1):10-8. https://doi.org/10.1097/JOM.0b013e31827b73af.
44. Morikawa Y, Martikainen P, Head J, Marmot M, Ishizaki M, Nakagawa H. A comparison of socio-economic differences in long-term sickness absence in a Japanese cohort and a British cohort of employed men. Eur J Public Health 2004 Dec;14(4):413-6. https://doi.org/10.1093/eurpub/14.4.413.
45. Musich S, Napier D, Edington DW. The association of health risks with workers' compensation costs. J Occup Environ Med 2001 Jun;43(6):534-41. https://doi. org/10.1097/00043764-200106000-00005.
46. Niedhammer I, Bugel I, Goldberg M, Leclerc A, Guéguen A. Psychosocial factors at work and sickness absence in the Gazel cohort: a prospective study. Occup Environ Med 1998 Nov;55(11):735-41. https://doi.org/10.1136/oem.55.11.735
47. Pai CW, Mullin J, Payne GM, Love J, O'Connell G, Edington DW. Factors associated with incidental sickness absence among employees in one health care system. Am J Health Promot 2009 Sep-Oct;24(1):37-48. https://doi.org/10.4278/ajhp.081117-QUAN-286.
48. Rabacow FM, Levy RB, Menezes PR, do Carmo Luiz O, Malik AM, Burdorf A. The influence of lifestyle and gender on sickness absence in Brazilian workers. BMC Public Health 2014 Apr;14:317. https://doi.org/10.1186/14712458-14-317.
49. Rabacow FM, Luiz OC, Malik AM, Burdorf A. Lifestyle factors, direct and indirect costs for a Brazilian airline company. Rev Saude Publica 2014 Dec;48(6):949-57. https://doi.org/10.1590/S0034-8910.2014048005227.
50. Robroek SJ, van den Berg TI, Plat JF, Burdorf A. The role of obesity and lifestyle behaviours in a productive workforce. Occup Environ Med 2011 Feb;68(2):134-9. https://doi. org/10.1136/oem.2010.055962.
51. Robroek SJ, van Lenthe FJ, Burdorf A. The role of lifestyle, health, and work in educational inequalities in sick leave and productivity loss at work. Int Arch Occup Environ Health 2013 Aug;86(6):619-27. https://doi.org/10.1007/s00420012-0793-1.
52. Roos E, Lallukka T, Lahelma E, Rahkonen O. The joint associations of smoking and obesity with subsequent short and long sickness absence: a five year follow-up study with register-linkage. BMC Public Health 2017 Dec;17(1):978. https://doi.org/10.1186/s12889-017-4997-x.
53. Serxner SA, Gold DB, Bultman KK. The impact of behavioral health risks on worker absenteeism. J Occup Environ Med 2001 Apr;43(4):347-54. https://doi. org/10.1097/00043764-200104000-00010.
54. Sherman BW, Lynch WD. The relationship between smoking and health care, workers' compensation, and productivity costs for a large employer. J Occup Environ Med 2013 Aug;55(8):879-84. https://doi.org/10.1097/JOM.0b013e31829f3129.

55. Sindelar JL, Duchovny N, Falba TA, Busch SH. If smoking increases absences, does quitting reduce them? Tob Control 2005 Apr;14(2):99-105. https://doi.org/10.1136/ tc.2003.005884.
56. Stewart WF, Ricci JA, Chee E, Morganstein D. Lost productive work time costs from health conditions in the United States: results from the American Productivity Audit. J Occup Environ Med 2003 Dec;45(12):1234-46. https://doi. org/10.1097/01.jom.0000099999.27348.78.
57. Torres Lana A, Cabrera de León A, Marco García MT, Aguirre Jaime A. Smoking and sickness absence among public health workers. Public Health 2005 Feb;119(2):1449. https://doi.org/10.1016/j.puhe.2004.06.010.
58. Tsai SP, Wendt JK, Ahmed FS, Donnelly RP, Strawmyer TR. Illness absence patterns among employees in a petrochemical facility: impact of selected health risk factors. J Occup Environ Med 2005 Aug;47(8):838-46. https://doi. org/10.1097/01.jom.0000169091.28589.8a.
59. Tsai SP, Wendt JK, Cardarelli KM, Fraser AE. A mortality and morbidity study of refinery and petrochemical employees in Louisiana. Occup Environ Med 2003 Sep;60(9):627-33. https://doi.org/10.1136/oem.60.9.627.
60. Wacker M, Holle R, Heinrich J, Ladwig KH, Peters A, Leidl R et al. The association of smoking status with healthcare utilisation, productivity loss and resulting costs: results from the population-based KORA F4 study. BMC Health Serv Res 2013 Jul; 13:278. https://doi.org/10.1186/1472-6963-13278.
61. Williden M, Schofield G, Duncan S. Establishing links between health and productivity in the New Zealand workforce. J Occup Environ Med 2012 May;54(5):545-50. https://doi.org/10.1097/JOM.0b013e31824fe0c8.
62. Suárez-Bonel MP, Villaverde-Royo MV, Nerín I, SanzAndrés C, Mezquida-Arno J, Córdoba-García R. Health care costs and work absenteeism in smokers: study in an urban community. Arch Bronconeumol 2015 Dec;51(12):615-20. https://doi.org/10.1016/j.arbr.2015.10.010.
63. Rai KK, Adab P, Ayres JG, Siebert WS, Sadhra SS, Sitch AJ et al.; BLISS research team·. Factors associated with work productivity among people with COPD: birmingham COPD Cohort. Occup Environ Med 2017 Dec;74(12):859-67. https://doi.org/10.1136/oemed-2016-104014.
64. Greenhalgh T, Peacock R. Effectiveness and efficiency of search methods in systematic reviews of complex evidence: audit of primary sources. BMJ 2005 Nov;331(7524):1064-5. https://doi.org/10.1136/bmj.38636.593461.68.
65. Higgins JP, editor. GS. Cochrane Handbook for Systematic Reviews of Interventions. The Cochrane Collaboration; 2011.
66. Morabia A, Bernstein MS, Curtin F, Berode M. Validation of self-reported smoking status by simultaneous measurement of carbon monoxide and salivary thiocyanate. Prev Med 2001 Jan;32(1):82-8. https://doi.org/10.1006/ pmed.2000.0779.
67. Wong SL, Shields M, Leatherdale S, Malaison E, Hammond D. Assessment of validity of self-reported smoking status. Health Rep 2012 Mar;23(1):47-53.
68. Connor Gorber S, Schofield-Hurwitz S, Hardt J, Levasseur G, Tremblay M. The accuracy of self-reported smoking: a systematic review of the relationship between self-reported and cotinine-assessed smoking status. Nicotine Tob Res 2009 Jan;11(1):12-24. https://doi.org/10.1093/ntr/ntn010.
69. Ferrie JE, Kivimäki M, Head J, Shipley MJ, Vahtera J, Marmot MG. A comparison of self-reported sickness absence with absences recorded in employers' registers: evidence from the Whitehall II study. Occup Environ Med 2005 Feb;62(2):74-9. https://doi.org/10.1136/ oem.2004.013896.
70. Ryan J, Zwerling C, Orav EJ. Occupational risks associated with cigarette smoking: a prospective study. Am J Public Health 1992 Jan;82(1):29-32. https://doi.org/10.2105/ AJPH.82.1.29.
71. Sacks JJ, Nelson DE. Smoking and injuries: an overview. Prev Med 1994 Jul;23(4):515-20. https://doi.org/10.1006/ pmed.1994.1070.
72. Bonnie RJ, Stratton K, Kwan LY. The Effects of Tobacco Use on Health. Public Health Implications of Raising the Minimum Age of Legal Access to Tobacco Products: National Academies Press (US); 2015.
73. Baker WL, White CM, Cappelleri JC, Kluger J, Coleman CI; Health Outcomes, Policy, and Economics (HOPE) Collaborative Group. Understanding heterogeneity in meta-analysis: the role of meta-regression. Int J Clin Pract 2009 Oct;63(10):1426-34. https://doi.org/10.1111/j.17421241.2009.02168.x.

74. Parrott S, Godfrey C, Raw M. Costs of employee smoking in the workplace in Scotland. Tob Control 2000 Jun;9(2):18792. https://doi.org/10.1136/tc.9.2.187.
75. Chen J, McGhee S, Lam TH. Economic costs attributable to smoking in Hong Kong in 2011: a possible increase from 1998. Nicotine Tob Res 2019 Mar;21(4):505-12. https://doi. org/10.1093/ntr/ntx254.
76. Hoang Anh PT, Thu T, Ross H, Quynh Anh N, Linh BN, Minh NT. Direct and indirect costs of smoking in Vietnam. Tob Control 2016 Jan;25(1):96-100.
77. Lasocka J, Jakubczyk M, Siekmeier R. Costs of smokingattributable productivity losses in Poland. Adv Exp Med Biol 2013;755:179-87. https://doi.org/10.1007/978-94-0074546-9_23.
78. Neubauer S, Welte R, Beiche A, Koenig HH, Buesch K, Leidl R. Mortality, morbidity and costs attributable to smoking in Germany: update and a 10-year comparison. Tob Control 2006 Dec;15(6):464-71. https://doi.org/10.1136/ tc.2006.016030.
79. Rasmussen SR, Prescott E, Sørensen TI, Søgaard J. The total lifetime health cost savings of smoking cessation to society. Eur J Public Health 2005 Dec;15(6):601-6. https:// doi.org/10.1093/eurpub/cki024.
80. Warner K. J. Smith R, Smith D, E. Fries B. Health and Economic Implications of a Worksite Smoking-Cessation Program: A Simulation Analysis. J Occup Environ Med 1996;38:981-92. https://doi.org/10.1097/00043764199610000-00008.
81. Carroll C, Rick J, Leaviss J, Fishwick D, Booth A. A qualitative evidence synthesis of employees' views of workplace smoking reduction or cessation interventions. BMC Public Health 2013 Nov;13:1095. https://doi. org/10.1186/1471-2458-13-1095.
Received for publication: 27 March 2019

DETAILS

Subject:	Cancer; Population; Smoking cessation; Smoking; Diabetes; Regression analysis; Regression models; Gender; Drug addiction; Empirical analysis; Statistical analysis; Chronic obstructive pulmonary disease; Quality; Sampling methods; Confidence intervals; Cardiovascular disease; Cigarette smoking; Population studies; Systematic review; Productivity; Employers; Working hours; Employees; Meta-analysis; Sick leave
Business indexing term:	Subject: Productivity Employers Working hours Employees Sick leave
Publication title:	Scandinavian Journal of Work, Environment &Health; Stockholm
Volume:	46
Issue:	1
Pages:	5-18
Publication year:	2020
Publication date:	2020
Section:	Review
Publisher:	Scandinavian Journal of Work, Environment &Health

Place of publication:	Stockholm
Country of publication:	Finland, Stockholm
Publication subject:	Occupational Health And Safety
ISSN:	03553140
e-ISSN:	1795990X
Source type:	Scholarly Journal
Language of publication:	English
Document type:	Evidence Based Healthcare, Journal Article
DOI:	https://doi.org/10.5271/sjweh.3848
ProQuest document ID:	2344258360
Document URL:	https://www.proquest.com/scholarly-journals/smoking-sickness-absence-systematic-review-meta/docview/2344258360/se-2?accountid=211160
Copyright:	Copyright Scandinavian Journal of Work, Environment &Health 2020
Last updated:	2023-08-22
Database:	Public Health Database

Bibliography

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

Robroek, S. J. W., PhD., Nieboer, D., M.Sc, Järvholm, B., MD PhD, & Burdorf, A., PhD. (2020). Educational differences in duration of working life and loss of paid employment: Working life expectancy in the netherlands. Scandinavian Journal of Work, Environment & Health, 46(1), 77-84. doi:https://doi.org/10.5271/sjweh.3843

Objectives This study aims to provide insight into educational differences in duration of working life by working life expectancy (WLE) and working years lost (WYL) through disability benefits and other non-employment states in the Netherlands. Methods Monthly information on employment status of the Dutch population (N=4 999 947) between 16 and 66 years from 2001-2015 was used to estimate working life courses and loss of working years for specific non-employment states. Across educational groups, bi-directional transitions between paid employment and nonemployment states were calculated. Using a multistate model, the WLE and WYL at age 16, 30, 50 and up to 66 years as statutory retirement age were estimated for each educational group, stratified by gender. Results Low-educated men and women had a 7.3 (men) and 9.9 (women) years lower WLE at age 30 than high-educated men and women. Among low-educated men, 3.4 working years were lost due to disability benefit compared to 0.8 among high-educated men. Low-educated women lost 3.0 working years due to disability benefit compared to 1.4 among high-educated women. Conclusions There are large educational inequalities over the course of working life. Among low-educated workers, more working years are lost due to unemployment, no income, and especially disability benefits. The latter reflects large educational inequalities in health and working conditions. The metrics of WLE and WYL provide useful insights into the life-course perspective on working careers.

Würtz, E. T., PhD, Brasch-Andersen, C., Steffensen, R., PhD., Hansen, J. G., D.M.Sc, Malling, T. H., PhD., Schlünssen, V., PhD, & Omland, Ø., PhD. (2020). Heme oxygenase 1 polymorphism, occupational vapor, gas, dust, and fume exposure and chronic obstructive pulmonary disease in a danish population-based study. Scandinavian Journal of Work, Environment & Health, 46(1), 96-104. doi:https://doi.org/10.5271/sjweh.3846

Objectives The number of dinucleotide repeats (GT)n modulate expression of heme oxygenase 1 (HMOX1), a stress response gene. Multiple repeats might affect chronic obstructive pulmonary disease (COPD) susceptibility. We aimed to investigate the association of this polymorphism with COPD and its interaction with occupational exposures (vapor, gas, dust, or fumes). Methods This population-based cross-sectional study included 4703 Danes, aged 45-84 years. HMOX1 (GT)n was genotyped and grouped as short: 33 alleles. COPD was defined by the lower limit of normal (2.5th FEV/FVC and FEV1 centiles). Occupational exposure was defined as ever exposed to vapor, gas, dust, or fume in expert-selected jobs. Associations were analyzed by adjusted mixed logistic regression. Results The population included 6% with COPD, 48% who had smoked >10 pack-years, and 46% with occupational exposure. HMOX1 was genotyped in 4423 participants. The adjusted odds ratio (OR) for the association between HMOX1 long allele and COPD was 1.75 95% confidence interval (CI) 1.18-2.60]. An interaction was evident between HMOX1 long allele and occupational exposure, OR 2.38 (95% CI 1.04-5.46), versus HMOX1 short/medium without exposure. Analyses were replicated in another cohort, aged 20-44 years, N=1168, including 3% with COPD, 25% who had smoked >10 pack-years and 20% with occupational exposure. No associations were seen between COPD and HMOX1 long allele here. Conclusions Long alleles in HMOX1 alone and in interaction with occupational exposure seem to be associated with COPD. Failure to replicate data may be due to premature age for COPD development and low occupational exposure prevalence. We propose this long allele may be a genetic contributor to the COPD pathogenesis.

Johannesen, C. D. L., M.Sc, Flachs, E. M., PhD., Ebbehøj, N. E., DMSc, Marott, J. L., M.Sc, Jensen, G. B., D.M.Sc, Nordestgaard, B., . . . Bonde, J. P. E., PhD. (2020). Sedentary work and risk of venous thromboembolism. Scandinavian Journal of Work, Environment & Health, 46(1), 69-76. doi:https://doi.org/10.5271/sjweh.3841

Objective Prolonged seated immobility during long-distance flights is related to an increased risk of venous thromboembolism (VTE), but little, if anything, is known about the risk related to sedentary work. The objective of this paper was to examine the risk of VTE according to sitting posture at work. Methods This prospective study includes a total of 78 936 participants from the Copenhagen City Heart Study and the Copenhagen General

Population Study, all without previous thromboembolic events and aged 6.5 hours/day and occupational sitting <3.5 hours/day (hazard ratio 1.11, 95% confidence interval 0.92-1.34). Conclusion This study does not support the hypothesis that sedentary work is a risk factor for VTE in the general population. Whether certain occupations with particularly high exposure to immobilized sitting positions are associated with thromboembolic events is not addressed.

Sveinsdottir, V., M.Sc, Lie, S. A., PhD., Bond, G. R., PhD., Eriksen, H. R., PhD., Tveito, T. H., PhD., Grasdal, A. L., DrPol, & Reme, S. E., PhD. (2020). Individual placement and support for young adults at risk of early work disability (the SEED trial). A randomized controlled trial. Scandinavian Journal of Work, Environment & Health, 46(1), 50-59. doi:https://doi.org/10.5271/sjweh.3837

Objectives Individual placement and support (IPS) is an effective approach for helping people with severe mental illness gain employment. This study aimed to investigate if IPS can be effectively repurposed to support young adults at risk of early work disability due to various social and health related problems. Methods A randomized controlled trial including 96 young adults (18–29 years; 68% men) was conducted in Norway. Participants were not in employment, education, or training, received temporary benefits due to social or health-related problems, and were eligible for traditional vocational rehabilitation (TVR). Participants were randomized to IPS (N=50) or TVR (N=46). Self-reported data were collected at baseline and at 6- and 12-months follow-up. The primary outcome was obtaining any paid employment in the competitive labor market during followup. Secondary outcomes were physical and mental health, well-being, coping, alcohol consumption, and drug use. Results Significantly more IPS participants obtained competitive employment compared to TVR participants during 12-months follow-up (48% versus 8%; odds ratio 10.39, 95% confidence interval 2.79–38.68). The IPS group reported significantly better outcomes than the TVR group in subjective health complaints, helplessness, and hopelessness. In post hoc analyses adjusted for baseline and missing data, the IPS group reported significantly better outcomes on these measures in addition to level of disability, optimism about future well-being, and drug use. Conclusions IPS is effective for young adults at risk of early work disability. IPS was superior to TVR in increasing competitive employment and promoted improvements in some non-vocational outcomes. IPS services should be offered to improve employment rates in this vulnerable group.

Sejbaek, C. S., PhD., Pedersen, J., PhD., Schlünssen, V., PhD, Begtrup, L. M., PhD., Juhl, M., PhD., Bonde, J. P., PhD., . . . Hougaard, K. S., PhD. (2020). The influence of multiple occupational exposures on absence from work in pregnancy: A prospective cohort study. Scandinavian Journal of Work, Environment & Health, 46(1), 60-68. doi:https://doi.org/10.5271/sjweh.3840

Objectives Many women experience absence periods from work during pregnancy. Several single risk factors for absence are identified, whereas the impact of multiple concurrent exposures has been sparsely studied. We hypothesized that the presence of multiple occupational exposures would be associated with an increased risk of absence from work during pregnancy. Methods We included women from the Danish National Birth Cohort (1996-2002), pregnant with one child and working >30 hours/week at interview (mean gestational week 17 (standard deviation 4.0); N=50 142). Information about five occupational exposures (job demands, job control, work posture, work shift, lifting) were retrieved from the interview, each assigned values of 0/1, and summed into an index (0-5). The woman's first absence from work (both regular and related to pregnancy) after the interview was available from a nationwide administrative register. We analyzed data with Cox regression using gestational age as the underlying time-variable. Results Few women experienced none of the occupational exposures (3.6%) and most experienced two exposures (34.7%). Only 24.3% of the women were absent from work before gestational week 31. The number of occupational exposures was associated with an increasing risk of absence. The adjusted hazard ratio for absence increased from 1.3 95% confidence interval (CI) 1.1-1.5] for one exposure to 2.9 (95% CI 2.5-3.3) for four to five exposures compared to no occupational exposure. Conclusion The higher the number of potentially adverse occupational exposures pregnant women experienced, the higher the risk for absence from work during pregnancy.

Albin, M., M.D., & Gustavsson, P., M.D. (2020). A silent epidemic: Occupational exposure limits are insufficiently protecting individual worker health. Scandinavian Journal of Work, Environment & Health, 46(1), 110-112.

doi:https://doi.org/10.5271/sjweh.3864