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Advancing mediation analysis in occupational health research

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ABSTRACT (ENGLISH)

What has been largely overlooked, however, is the fact that these approaches are only valid in linear models and rely on the assumption that there is no interaction between exposure and mediator on the outcome (6). [...]because the importance of controlling for mediator-outcome confounders was never mentioned in Baron &Kenny, many studies have neglected to account for potential confounding factors of the mediator-outcome relationship. [...]whereas a total effect can always be decomposed into a natural direct and indirect effect, controlled direct effects are estimated for every level of the mediator (which may differ substantially depending on the magnitude of the interaction effect between exposure and mediator). An alternative approach in mediation analysis is to quantify controlled direct effects that only rely on assumptions (i) and (iii): no uncontrolled exposure-outcome confounding and no uncontrolled mediator-outcome confounding. [...]some have argued that controlled direct effects are much more policy-relevant because they estimate the proportion of the total effect of the exposure on the outcome that could be eliminated by a specific intervention on the mediator (13, 14). [...]sensitivity analysis is helpful to assess the robustness of the results to potential violations of the underlying assumptions.

FULL TEXT

Headnote

Key terms: editorial; exposure; mediation analysis; mediator; methodology; occupational health research; outcome; research; research framework; study design

In recent years, mediation analysis has become a popular means to identify and quantify pathways linking an exposure to an outcome, thereby elucidating how a particular exposure contributes to the occurrence of a specific outcome. When a mediator is a modifiable risk factor, this opens up new opportunities for interventions to block (part) of the exposure's effect on the outcome. Recent examples in *Scandinavian Journal of Work Environment Health* have addressed the mediating effect of wellbeing on the association between type of office and job satisfaction (1) and examined whether workplace social capital contributes to the association between organizational changes and employee exit from work (2).

Mediation analysis requires a specific study design ensuring that the temporal sequence of exposure, mediator, and outcome supports the argument for causation. A good illustration presented by Halonen and colleagues (3) used the Swedish Longitudinal Occupational Survey of Health (SLOSH) with biannual waves to investigate whether depressive symptoms mediated the association between effort-reward imbalance and subsequent neck-shoulder pain. The longitudinal design allowed for a mediation analysis whereby exposure was measured two years before the mediator, and the mediator was assessed two years before the outcome of interest. When exposure and mediator are self-reported, without assurance that the mediator occurred after the exposure (eg, years of education in school preceding exposure to working conditions), mediation analysis is prone to reversed causality (ie, not the exposure causing the mediator but the mediator causing the exposure) and has little to offer in terms of a better understanding of the mechanism how exposure is linked to the outcome. A linked issue is the stability of the mediator over time. Some authors have argued that mediation analysis is bound to fail in studies with a time window

of measurements that does not sufficiently capture the fluctuations of the potential mediator over time (4). Recent debates on mediation analysis have specifically addressed the methodology and assumptions that allow for a causal interpretation. The traditional approach to mediation analysis in health research has largely relied on the influential 1986 paper of Baron & Kenny (5). In this approach, mediation is assessed by estimating the effect of the exposure on the mediator and the effect of the mediator on the outcome (adjusting for the exposure), and multiplying the two estimates to derive the indirect or mediated effect (the "product-of-coefficients" approach). Alternatively, the effect of the exposure on the outcome is estimated with and without adjustment for the mediator, and the difference between the two estimates is used to quantify the mediated effect (the "difference-of-coefficients" approach). What has been largely overlooked, however, is the fact that these approaches are only valid in linear models and rely on the assumption that there is no interaction between exposure and mediator on the outcome (6). Moreover, because the importance of controlling for mediator-outcome confounders was never mentioned in Baron & Kenny, many studies have neglected to account for potential confounding factors of the mediator-outcome relationship. An eloquent illustration of the problems of the classical mediation method and the risk of severe bias in the mediated effect is presented by Pearce & Vandenberg (7).

In response to the limitations of traditional mediation methods, a new mediation methodology is rapidly developing and often referred to as "causal mediation analysis" (6, 8). This methodology has derived counterfactual definitions of direct and indirect effects, which are independent of any model, and - under explicitly stated assumptions - allow for a causal interpretation of the estimated effects (9). These definitions enable greater flexibility and provide researchers with the tools to scrutinize the assumptions underlying mediation analysis better. The causal inference approach to mediation has given rise to two different types of effects: (i) natural direct and indirect effects, and (ii) controlled direct effects. Natural direct and indirect effects by definition always sum up to the total effect, even in the presence of exposure-mediator interaction. Intuitively, the natural direct effect captures the effect of the exposure on the outcome that is not due to its effect on the mediator, whereas the natural indirect effect captures the effect of the exposure on the outcome that is due to its effect on the mediator (8). Controlled direct effects, on the other hand, quantify the effect of the exposure on the outcome if the mediator was fixed at a specific value uniformly in the population. Consequently, whereas a total effect can always be decomposed into a natural direct and indirect effect, controlled direct effects are estimated for every level of the mediator (which may differ substantially depending on the magnitude of the interaction effect between exposure and mediator).

Decomposition of a total effect of an exposure on an outcome into natural direct and indirect effects requires that there is no unmeasured confounding of the (i) exposure-outcome, (ii) exposure-mediator, and (iii) mediator-outcome relationships. Furthermore, a critical assumption is (iv) that there are no measured or unmeasured mediator-outcome confounders that are themselves affected by the exposure (6). The first three assumptions are depicted in Figure 1: if C_1 , C_2 and C_3 include all relevant confounders of the three pathways under study ($A \rightarrow Y$, $A \rightarrow M$, and $M \rightarrow Y$), the first three assumptions are met.

The critical fourth assumption that the mediator-outcome association is not confounded by any variable that is itself affected by the exposure is depicted in figure 2. Here (L) is both a confounder of the $M \rightarrow Y$ path and a mediator on the $A \rightarrow Y$ path. An example would be the association between shift work (A) and diabetes mellitus (Y), as reported by Tucker and colleagues (10). Lack of leisure-time physical activity may be considered a mediator (M). Whereas controlling for confounders (C) (eg, age and sex) is straightforward, controlling for overweight (L) may be problematic. The issue here is that overweight may be a confounder of the association between leisure-time physical activity and diabetes mellitus (individuals with overweight might find it difficult to be active in their leisure), and overweight may also be on the causal pathway from shift work to diabetes mellitus (eg, by an effect of shift work on dietary patterns or physiological processes). In the presence of such exposure-induced mediator-outcome confounders, the researcher is stuck between bad choices: not adjusting for (L) will bias the estimated effect of the mediator; adjusting for (L) will bias the estimated effect of the exposure. Hence, researchers must convince themselves that such confounding is not present. When potential confounding is a serious possibility, natural direct and indirect effects cannot be identified, regardless of whether (L) is measured or not. In such a situation, new

methods are required that allow for effect decomposition in the presence of exposure-induced mediator-outcome confounders by using so-called interventional (in)direct effects, which consider potential interventions on a population level (11, 12).

An alternative approach in mediation analysis is to quantify controlled direct effects that only rely on assumptions (i) and (iii): no uncontrolled exposure-outcome confounding and no uncontrolled mediator-outcome confounding.

Moreover, some have argued that controlled direct effects are much more policy-relevant because they estimate the proportion of the total effect of the exposure on the outcome that could be eliminated by a specific intervention on the mediator (13, 14). Although controlled direct effects can still be estimated in the presence of exposure-induced mediator-outcome confounders, this does require more sophisticated methods, such as marginal structural models (15, 16) or the g-formula (17). Albeit still infrequently used, these approaches offer an important new toolbox for health research and are often easily implemented in standard statistical software (18).

To conclude, mediation analysis has gained a lot of attention in recent years and is rapidly developing with regard to approach and methods. We invite researchers to move away from traditional mediation analysis and apply the newer mediation methods in their studies. First, a critical stance is required to evaluate whether the study design and data collected permit a meaningful mediation analysis. Second, studies should explicitly address the crucial assumptions that are fundamental for a causal interpretation of mediation. Third, sensitivity analysis is helpful to assess the robustness of the results to potential violations of the underlying assumptions.

Sidebar

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Does occupational lifting affect the risk of hypertension? Cross-sectional and prospective associations in the Copenhagen City Heart Study

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ABSTRACT (ENGLISH)

Objective The aim of this study was to investigate cross-sectional and prospective associations between heavy occupational lifting and hypertension. **Methods** Data from the third, fourth and fifth examinations of the Copenhagen City Heart Study were included. Multivariable logistic regression models were applied to adjust for sex, age, body mass index (BMI), smoking, education, self-rated cardiorespiratory fitness, vital exhaustion and baseline blood pressure, and were used to estimate (i) the cross-sectional association between heavy occupational lifting and hypertension, defined as using anti-hypertensives or having a systolic blood pressure (SBP) >140 mmHg or diastolic blood pressure (DBP) >90 mmHg, and (ii) the prospective association between heavy occupational lifting and risk of becoming a systolic blood pressure case, defined as an above median change (from baseline to follow-up) and/or a shift from no use of anti-hypertensives at baseline to use of anti-hypertensives at a ten-year follow-up. **Results** Both cross-sectional [odds ratio (OR) 1.06, 95% confidence interval (CI) 0.94-1.20] and prospective (OR 1.10, 95% CI 0.92-1.31) analysis indicated no relations. Explorative prospective analyses suggested linear associations between heavy occupational lifting and systolic blood pressure among participants using antihypertensives. Exposure to heavy occupational lifting tended to increase the incidence of hypertension (OR 1.30, 95% CI 0.97-1.73) among participants >50 years. **Conclusions** No associations were seen among the general population. Positive associations were seen among users of anti-hypertensives and participants >50 years, indicating these groups as vulnerable to increases in blood pressure when exposed to occupational lifting.

FULL TEXT

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Methods Data from the third, fourth and fifth examinations of the Copenhagen City Heart Study were included. Multivariable logistic regression models were applied to adjust for sex, age, body mass index (BMI), smoking, education, self-rated cardiorespiratory fitness, vital exhaustion and baseline blood pressure, and were used to estimate (i) the cross-sectional association between heavy occupational lifting and hypertension, defined as using anti-hypertensives or having a systolic blood pressure (SBP) >140 mmHg or diastolic blood pressure (DBP) >90 mmHg, and (ii) the prospective association between heavy occupational lifting and risk of becoming a systolic blood pressure case, defined as an above median change (from baseline to follow-up) and/or a shift from no use of anti-hypertensives at baseline to use of anti-hypertensives at a ten-year follow-up.

Results Both cross-sectional [odds ratio (OR) 1.06, 95% confidence interval (CI) 0.94-1.20] and prospective (OR 1.10, 95% CI 0.92-1.31) analysis indicated no relations. Explorative prospective analyses suggested linear associations between heavy occupational lifting and systolic blood pressure among participants using antihypertensives. Exposure to heavy occupational lifting tended to increase the incidence of hypertension (OR 1.30, 95% CI 0.97-1.73) among participants >50 years.

Conclusions No associations were seen among the general population. Positive associations were seen among users of anti-hypertensives and participants >50 years, indicating these groups as vulnerable to increases in blood pressure when exposed to occupational lifting.

Key terms blood pressure; blue collar; cardiovascular disease; cohort study; heavy lifting; manual handling; occupational epidemiology; occupational physical activity.

Recent surveys have concluded that heavy occupational lifting is described as a risk for low-back pain (1), however heavy lifting also affects the cardiovascular system through acute increases in blood pressure (BP) (2). Some workers perform occupational lifting for several hours per day, many days per week, and therefore may be at risk for developing hypertension due to the frequency and duration of acutely increased BP (3). Thus heavy occupational lifting may act as an occupational risk factor for hypertension (4, 5). The prevalence of hypertension varies across occupational groups, supporting the impact by the working environment (6). Hypertension is a major preventable cardiovascular risk factor (7-9) and is estimated to cause 14% of all annual deaths globally (10). However, only few studies (4, 5, 11) have investigated the relation between heavy occupational lifting and hypertension, showing

conflicting results. Thus, investigating these associations could reveal a potential for prevention of hypertension, especially among the 22% of the Danish workforce and 32% of European workers estimated to be exposed to heavy occupational lifting on a regular basis (12) (6th survey in Eurofound).

This study's objective was to explore associations between heavy occupational lifting and hypertension in the Copenhagen City Heart Study, with the hypothesis that heavy occupational lifting is associated with a higher prevalence of hypertension and an increased incidence of new-onset hypertension in normotensives.

Methods

A detailed protocol for this study has been reported elsewhere (13). Briefly, randomly selected Copenhagen citizens, aged >20 years, were examined in the Copenhagen City Heart Study, containing person-based information on health as well as a large variety of biological, environmental and lifestyle-related factors (14). Data from the third (1991-94, response rate 61.2%), fourth (2001-03, response rate 49.5%) and fifth (2011-15, response rate 46.6%) examination were included in this study. Thus, the cross-sectional analysis had a possibility of three observations per participant, and the prospective analysis had possibility of two observations per participant.

Inclusion criteria

All participants with data on BP, level of occupational physical activity (OPA) (including heavy lifting) and use of anti-hypertensives were included in the cross-sectional analysis.

All normotensive participants with data on level of OPA at the third and/or fourth examination (n) and data on BP and use of anti-hypertensives in examination (n and n+1) were included in the prospective analysis.

Assessment of heavy lifting

Self-reported level of OPA was obtained by use of the same question in all three examinations: "Please describe your level of occupational physical activity within the past year" with the following response categories: (i) predominantly sedentary; (ii) sitting or standing, some walking; (iii) walking, some handling of material; (iv) heavy manual work". If answering iii or iv, an additional question regarding heavy occupational lifting was applied: "Do you lift heavy burdens?" with the response categories: yes or no. In the analysis, the participants were classified as exposed to heavy occupational lifting by answering "yes" to the question concerning heavy burdens, and those participants answering i, ii and iii or iv in combination with not lifting heavy burdens were set as the reference group. No information was collected in between examinations. In the prospective analysis, the stability of exposure was accounted for by cross-tabulating the self-reported exposure at examination three by exposure at examination four, and also the self-reported exposure at examination four by exposure at examination five. An evaluation of the agreement (Cohen's kappa) between exposures to heavy occupational lifting across the examinations showed fair agreement (13), and thus the baseline exposure were regarded as valid and used throughout.

Definition of hypertension

Hypertension, the primary outcome measure, was defined as reported use of anti-hypertensives or a measured systolic blood pressure (SBP) >140 mmHg or diastolic blood pressure (DBP) >90 mmHg (15) in the cross-sectional analysis. In the prospective analysis, hypertension was defined as the shift from from no use of anti-hypertensives in examination (n) to use of antihypertensives in examination (n+1) or an above median delta value of SBP [SBP in examination (n+1) - SBP in examination (n)]. Additionally, pulse pressure (PP) ($PP = SBP - DBP$), mean arterial pressure (MAP) ($MAP = (2 \times DBP + SBP) / 3$) and mid BP ($\frac{1}{2} SBP + \frac{1}{2} DBP$) were investigated as secondary outcomes.

BP was measured according to the WHO guidelines recommended by Rose & Blackburn (16). Using a London School of Hygiene sphygmomanometer (17), BP was measured one time on the non-dominant arm after 5-minute sitting rest. The fall of the mercury column was set to 2 mm/s. The specially trained technicians were instructed in the same way, and all conditions during the measurements were identical at all examinations.

Assessment of covariates

A number of factors have previously been shown to be associated both with exposure to OPA, such as occupational lifting, and BP. Thus, the following factors were included as covariates: sex (male/female) (18); age (<40, 40-49, 50-59, 60-69, 70-79, >80 years) (19); body mass index (BMI) (<18.5, 18.5-24.9, 25.0-29.9, >30 kg/m²) (20) calculated

from measured body height and weight; smoking (non-smoking; currently smoking) (21); length of education (no formal education; low educated up to 3 years; vocationally educated 1-3 years; higher educated; academically educated) (22); and, for the prospective analysis only, additional adjustment for vital exhaustion, split in four categories defined elsewhere (0, 1-4, 5-9, 10-17) (23); self-rated cardiorespiratory fitness (lower, similar, higher cardiorespiratory fitness compared to peers of same sex and age) (24); SBP at baseline (80-89, 90-99, 100-109, 110-119, 120-129, 130-139, >140 mmHg) (25), and DBP at baseline (40-49, 50-59, 60-69, 70-79, 80-89, >90 mmHg).

Statistical analyses

The primary null-hypothesis for the cross-sectional analysis was that heavy occupational lifting is not associated to hypertension, defined as using anti-hypertensives or having a measured SBP >140 mmHg or DBP >90 mmHg. In the prospective analysis, the primary null-hypothesis was that heavy occupational lifting at baseline does not increase the incidence of new-onset hypertension in normotensives.

The overall significance level was set at 0.05. However, Bonferroni corrections were applied meaning that the two primary hypotheses were tested at a significance level of 0.025 (13). The exploratory secondary analyses were not tested for statistical significance but reported by 95% confidence interval (CI).

Primary analyses

In the cross-sectional and prospective analyses, as a function of heavy occupational lifting, the odds of being hypertensive and becoming a SBP case, respectively, were estimated using logistic regression in a generalized estimating equation (GEE) model, with no exposure to heavy occupational lifting as reference. Observations from the same person were treated as repeated measurements. A first order autoregressive correlation structure was assumed. The cross-sectional analysis was controlled for sex, age, BMI, smoking and education. In addition, the prospective analysis was controlled for self-rated cardiorespiratory fitness, vital exhaustion, and BP at baseline.

Secondary analyses

Linear regressions. The associations between heavy occupational lifting and SBP, DBP, PP and MAP (mmHg) were investigated, first cross-sectionally and then prospectively (change in mmHg from examination n to examination $n + 1$), by use of linear regression models. These linear regressions were applied to both the entire included population as well as a population excluding those participants who reported to use anti-hypertensives.

Sensitivity to choice of comparison group. To investigate how sensitive the adjusted primary analyses were to the choice of comparison group, we performed an additional linear regression with SBP as outcome only. Here the comparison group was split into three different subgroups according to the self-reported categories of OPA, thus an exposure variable with four instead of two categories was created.

Sensitivity to the definition of hypertension. Due to the variety in cut-points for defining hypertension [SBP >160 mmHg or DBP >100 mmHg (14); SBP >180 mmHg or DBP >110 mmHg (15, 26) or SBP >130 mmHg or DBP >80 mmHg (25)], we investigated whether the OR for hypertension as a function of heavy occupational lifting was sensitive to the cut-point for defining hypertension. Thus, two additional cross-sectional logistic regression analyses were conducted using alternative cut-points: SBP >160 mmHg or DBP >100 mmHg and SBP >130 mmHg or DBP >80 mmHg.

Stratification by age. Due to the lack of occupational exposures as a result of old age pension (65 years) and/ or early retirement (60 years) at the follow-up examination, analysis similar to the primary analysis stratified by age at baseline (> versus <50 years) were performed.

Results

From examination three, 5106 observations were excluded: 2717 from examination four and 1689 from examination five. Hence, 7052 and 4014 participants were included in the cross-sectional and prospective analyses, respectively (figure 1 and table 1).

Primary analysis

The crude primary cross-sectional analysis showed that those performing heavy occupational lifting had Table 3. Adjusted associations between self-reported heavy occupational lifting and systolic blood pressure (BP) (mmHg),

diastolic BP (mmHg), pulse pressure (mmHg) and mean arterial pressure (mmHg), stratified on use of anti-hypertensive. Occupational physical activity groups are clustered by answering "yes" or "no" to exposure to heavy occupational lifting; "yes" are in the heavy lifting category and "no" are divided in the other categories set by their self-reported level of occupational physical activity where the categories of walking, some handling of material AND heavy manual work, but no heavy lifting are collapsed. [CI=confidence interval.] a 12% higher prevalence for hypertension than the non-exposed. However, when adjusting for relevant confounders, heavy occupational lifting did not affect the prevalence of hypertension (table 2). The prospective models did not show significantly increased risks for becoming a SBP or DBP case when exposed to heavy occupational lifting (table 2).

Secondary analyses

Linear regressions. Secondary analyses were performed by linear regressions to investigate the differences in SBP, DBP, PP, and MAP between participants exposed, or not, to heavy occupational lifting (13). The linear regressions relating heavy occupational lifting to BP showed no significant associations with any of the BP outcomes either in the cross-sectional or in the prospective analyses (supplementary material, www.sjweh.fi/show_abstract.php?abstract_id=3850, table S1). The linear regressions relating heavy occupational lifting to BP, stratified on use of anti-hypertensives, showed that, among participants not using anti-hypertensives, no significant associations between heavy occupational lifting and any of the BP outcomes neither cross-sectionally nor prospectively were seen (table 3). Also among users of anti-hypertensives no significant associations were seen cross-sectionally (table 3). However, positive associations between heavy occupational lifting and SBP and MAP were seen prospectively among users of antihypertensives (table 3).

Sensitivity to choice of comparison group

By stratifying the participants by their self-reported level of OPA the sensitivity to choice of comparison group of the secondary linear regression was tested. However, this analysis did not show any significant associations neither in the cross-sectional nor the prospective analysis (supplementary file, table S2).

Sensitivity to definition of hypertension

The sensitivity analyses applying cut-points for the definition of hypertension being higher (SBP >160 mmHg or DBP >100 mmHg) and lower (SBP >130 mmHg or DBP >80 mmHg) than the cut-point used in the primary analysis (SBP >140 mmHg or DBP >90 mmHg), showed that the OR for being hypertensive as a function of heavy occupational lifting was sensitive to the cut-points for definition of hypertension. By application of the higher cut-points, no relation between risk for hypertension and heavy occupational lifting was seen (OR 0.96, 95% CI 0.82-1.11), whereas the lower cut-points showed a tendency towards an increased OR for being hypertensive when exposed to heavy occupational lifting (OR 1.13, 95% CI 0.99-1.28).

Age stratified analysis

The cross-sectional and prospective analyses among both participants <50 and >50 years old showed that heavy occupational lifting did not affect the odds for being hypertensive or becoming a SBP or DBP case (table 4). However, a tendency of an increased risk for becoming a DBP case was seen among participants >50 years old.

Discussion

This study aimed to investigate cross-sectional and prospective relations between heavy occupational lifting and hypertension. Neither the cross-sectional nor the prospective analysis could reject the primary null hypothesis of no effect of heavy occupational lifting on the prevalence nor incidence of hypertension since non-significant increases in the prevalence and incidence of hypertension by 6% and 10%, were seen (table 2). The secondary analyses showed large rises in BP (ASBP 16 mmHg, 95% CI 5-27 mmHg, and ΔMAP 7 mmHg, 95% CI 1-14 mmHg, table 3) among participants using anti-hypertensives when exposed to heavy occupational lifting. Another sensitivity analysis indicated that participants aged >50 years were at 30% increased risk (OR 1.30, 95% CI 0.97-1.73) for becoming a DBP case when exposed to heavy occupational lifting. Further investigations of these associations are therefore warranted for prevention of hypertension, particularly across older workers and workers using anti-hypertensives. These indications of increases in BP can be explained by the acutely increasing effect on BP from lifting, due to the acute increases in total peripheral resistance from the occlusion of vessels by the static muscle activity (2, 28).

However, longitudinal studies show that leisure time resistance training lowers BP (29, 30), which may be explained by the physiologic adaptations in the cardiorespiratory system, taking place during restitution, leading to beneficial effects as increased cardiorespiratory fitness (28). Yet, the lack of these beneficial effects from OPA could be explained by the insufficient recovery due to the high frequency (5 days a week) and long duration (7-9 hours per day) (31, 32). Across some occupations, heavy occupational lifting is a part of OPA, and could therefore prospectively raise BP due to the high frequency and duration of lifting combined with an insufficient recovery (3). However, studies investigating the relation between heavy occupational lifting and BP are few and conflicting (4, 5, 33).

One major challenge in this research field is the healthy worker selection, described as workers migrating away from occupations with high OPA into more sedentary occupations (34). This selection could be based on symptoms of deteriorated health, eg, angina pectoris. Hypertension could be seen as non-symptomatic, however high SBP are thought to impact risk for angina (35). Future analysis should therefore investigate relations between heavy occupational lifting and risk factors for cardiovascular disease (CVD) by use of nonsymptomatic outcomes or precursors of hypertension to bypass the healthy worker selection.

The secondary analyses revealed two sub-groups: users of anti-hypertensives and participants aged >50 years as being particularly vulnerable for exposure to heavy occupational lifting.

The prospective linear associations relating heavy occupational lifting to BP, stratified on use of antihypertensives, showed large rises in BP Δ SBP 16 mmHg, 95% CI 5-27 mmHg, and Δ MAP 7 mmHg, 95% CI 1-14 mmHg, table 3) among users of these medications. Additionally, the 95% CI for the prospective linear relations between heavy occupational lifting and Δ DBP and Δ PP likewise indicated clinically relevant hazardous increases (25). These increases in BP may be explained by these participants being more susceptible to having a low compliance in the arteries due to decreased elasticity caused by the endothelia damage from the increased level of mean arterial pressure (36) initially causing the use of anti-hypertensives. Low arterial compliance decreases the ability of the arteries to dilate sufficiently when the blood are being pumped from the heart, this combined with occlusion of the vessels during static activities, such as lifting, will lead to major increases of the BP (28).

The estimated OR from the analysis stratified by age (</>50 years) showed tendencies of stronger associations between heavy lifting and hypertension among participants aged >50 years (OR of becoming a SBP case of 1.22 and a DBP case of 1.30) compared to among participants aged <50 years (1.03 and 0.94) (table 4). This can be explained by the age and health-dependent decreases in aerobic capacity, leading to increased cardiorespiratory load from performing heavy occupational lifting (37). Also, the age-dependent loss of compliance in the arteries contributes to increases in BP due to the increased total peripheral resistance (28, 38).

The literature proposes differences in cut-points for being classified as hypertensive (15, 26, 27), and therefore two additional cut-points of hypertension [SBP >160 mmHg or DBP >100 mmHg (15, 26) and SBP >130 mmHg or DBP >80 mmHg (27)] were applied to the cross-sectional analyses. These sensitivity analyses showed that the OR for being hypertensive as a function of heavy occupational lifting seemed to be sensitive to the choice of cut-point; the cut-point of SBP >130 mmHg or DBP >80 mmHg yielded an OR of 1.13, whereas the cut-point of SBP >160 mmHg or DBP >100 mmHg yielded an OR of 0.96, and the cut-point of SBP >140 mmHg or DBP >90 mmHg yielded an OR of 1.06.

Taken together, this paper contributes to the knowledge of risk for hypertension from heavy occupational lifting and sheds light on the need for specific attention among those performing heavy occupational lifting while using anti-hypertensives (25). These results could therefore feed into prevention initiatives of hypertension specifically targeted workers exposed to heavy occupational lifting.

Methodological challenges

These analyses should be interpreted in light of the present limitations: the self-reported exposure to heavy occupational lifting and level of cardiorespiratory fitness might be affected by recall bias (39, 40); self-reported data are only collected from participants at the examinations, which could add a selection bias to the collected data. To collect exposures of heavy lifting independently of participation, future studies could consider receiving the exposure

data from job exposure matrices, additionally could the recall bias be bypassed by use of technical measures of exposure to heavy occupational lifting. The collection of BP only in consultation during rest gives a lower prognostic value than obtained by monitoring of 24 hours BP or BP during sleep (41, 42); and the lowered odds for having prolonged working hours when exposed to heavy occupational lifting (33), which was not possible to adjust for in the present analysis due to the lacking information of amount of weekly working hours. Future studies investigating these relations could consider collecting the exposure information by use of a job exposure matrix or technical measures, not holding the limitations of being self-reported.

However, the analysis also holds some strengths; the follow-up time of 8-10 years and the determination of hypertension based both on use of prescription medicine and the resting BP in mmHg, limiting the risk of classifying participant as false negative. Also the randomly selected study population is a strength as well as the inclusion criteria of no use of anti-hypertensives, as these medications potentially may conceal, reverse or otherwise distort effects of heavy occupational lifting on BP. In line with this, participants diagnosed with hypertension at baseline were excluded from the prospective analysis because they were likely to receive anti-hypertensive medication in the in the time period between examinations. On the other hand, exclusion of those participants being diagnosed as hypertensive and/ or using anti-hypertensives decreases variability of the analyzed population towards a more healthy population and thereby lacks the potential of investigating the effects of heavy occupational lifting among a population proposedly at higher risk for cardiovascular endpoints (31).

Implications of the results

Heavy lifting acutely increases BP (2). Approximately 22% of Danish workers and 32% of European workers are regularly exposed to heavy occupational lifting (12) (6th survey in Eurofound), and due to the frequency and duration of the occupational lifting, it is likely that increases in BP and hypertension will occur (3). Hypertension is a major risk factor for CVD and mortality (7, 8, 10). In spite of this, the Danish Working Environment Authority guideline for occupational lifting from 2005 (arbejdstilsynet.dk/da/regler/at-vejledninger//d-31-loft-traek-og-skub) only concerns risk factors for musculoskeletal disorders. Therefore we conducted this study to feed into the discussion on cardiovascular risk factors from heavy occupational lifting. This study finds that the prevalence and incidence of hypertension, to some extent, may increase by exposure to heavy occupational lifting. Although these OR are uncertain, the indications of rises in risk for hypertension up to 10% might still be of preventive importance for the general working population.

Secondly, the results showed that workers using anti-hypertensives would be expected to experience rises in SBP - from exposure to heavy occupational lifting - by 16 mmHg, which indicates a major increase in CVD risk (7, 9, 25). Also older workers (aged >50 years old at baseline) seemed to be more vulnerable to developing hypertension from exposure to heavy occupational lifting than younger workers (aged <50 years old at baseline). Hence, exposure to heavy occupational lifting could impact the workability as well as employability among workers aged >50 years old or those who use anti-hypertensives due to the fact that high SBP are thought to impact risk for angina (35), and thereby migration from occupations exposed to heavy occupational lifting to occupations with more light physical activity levels. Thus, it could be considered that tailoring the exposure to heavy occupational lifting to the age and general health of the worker would impact risk for hypertension and work sustainability beneficially.

These results suggest that the risk for hypertension might be lowered by reducing the exposure to heavy occupational lifting, especially among workers using anti-hypertensives and aged >50 years. These results are drawn among participants who showed up at examinations in a randomly selected adult Danish population and since the work environmental laws and regulations of occupational lifting are the same in the entire nation, we believe that the result of the study to some extent may be generalized to the entire Danish workforce. Yet, these conclusions are solely based on those who participated in examinations and, thus, a future investigation of this association might benefit from a study design not dependent on participation, such as a job exposure matrix. Nonetheless, knowledge is still needed to verify these findings and also to investigate the effect of accumulation of exposure from heavy occupational lifting on hypertension. Future studies investigating these relations could consider collecting the exposure information by use of job exposure matrices or technical measures, without the limitations of

being self-reported.

Concluding remarks

No associations between heavy occupational lifting and prevalence and incidence of hypertension were seen among the general population. The secondary analyses showed positive associations between heavy occupational lifting and risk of hypertension among two vulnerable sub-groups, ie, (i) users of anti-hypertensives, and (ii) workers aged >50 years. Yet, these conclusions should be interpreted with the methodological limitations of this study in mind, and therefore further research is needed to confirm these associations.

Conflicts of interest

None declared.

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Sidebar

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DETAILS

Subject:

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Health economic evaluations of interventions to increase physical activity and decrease sedentary

behavior at the workplace: a systematic review

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ABSTRACT (ENGLISH)

Objective The workplace is an ideal setting to implement public health strategies, but economic justification for such interventions is needed. Therefore, we performed a critical appraisal and synthesis of health economic evaluations (HEE) of workplace interventions aiming to increase physical activity (PA) and/or decrease sedentary behavior (SB).
Methods A comprehensive search filter was developed using appropriate guidelines, such as the Peer Review of Electronic Search Strategies (PRESS) checklist, and published search algorithms. Six databases and hand searches were used to identify eligible studies. Full HEE of workplace interventions targeting PA/SB were included. Methodological quality was assessed using the Consensus Health Economic Criteria (CHEC) list. Two researchers independently performed all procedures. Hedges' g was calculated to compare intervention effects. Outcomes from HEE were recalculated in 2017 euros and benefit-standardized. Results Eighteen HEE were identified that fulfilled on average 68% of the CHEC list criteria. Most studies showed improvements in PA/SB, but effects were small and thus, their relevance is questionable. Interventions were heterogeneous, no particular intervention type was found to be more effective. HEE were heterogeneous regarding methodological approaches and the selection of cost categories was inconsistent. Indirect costs were the main cost driver. In all studies, effects on costs were subject to substantial uncertainty. **Conclusions** Due to small effects and uncertain impact on costs, the economic evidence of worksite PA/SB interventions remains unclear. Future studies are needed to determine effective strategies. The HEE of such interventions should be developed using guidelines and validated measures for productivity costs. Additionally, studies should model the long-term costs and effects because of the long pay-back time of PA/SB interventions.

FULL TEXT

Headnote

Objective The workplace is an ideal setting to implement public health strategies, but economic justification for such interventions is needed. Therefore, we performed a critical appraisal and synthesis of health economic evaluations (HEE) of workplace interventions aiming to increase physical activity (PA) and/or decrease sedentary behavior (SB).
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interventions should be developed using guidelines and validated measures for productivity costs. Additionally, studies should model the long-term costs and effects because of the long pay-back time of PA/SB interventions. Key terms cost-benefit; cost-effectiveness; public health; worksite health promotion (ProQuest: ... denotes formulae omitted.)

The positive health effects of physical activity (PA) are undisputed. PA is well known to improve muscular and cardiorespiratory fitness and therefore decreases the risk for many non-communicable diseases such as hypertension, stroke, diabetes, coronary heart disease and various cancers (1). The World Health Organization (WHO) recommends >150 minutes of moderate-intensity aerobic PA, 75 minutes of vigorous-intensity aerobic PA or an equivalent combination of both, per week (2). About 31.1% of adults worldwide do not meet these criteria and are thus physically inactive (3). At the same time, sedentary behavior (SB) in today's society is increasing (4, 5). SB is defined as "any waking behavior characterized by an energy expenditure < 1.5 metabolic equivalent of task (MET) while in a sitting, reclining or lying posture" (6). Physical inactivity (PIA) and SB are not synonymous. For example, one can meet the recommendations for PA (and thus be sufficient physically active) while being too sedentary. Furthermore, causes for SB and PIA as well as biological mechanisms affecting health may be different for SB and PIA (7). However, there is evidence of an interaction between PIA and SB in relation to health. A large-scale meta-analysis showed that PA can attenuate or even eliminate the detrimental influence of SB on health (8). Therefore, increasing PA or reducing SB are both beneficial for health and interventions should focus on both. The consequences of PIA and SB are substantial. Insufficient PA is a major cause of >35 chronic diseases (9) and represents the fourth leading risk factor for mortality (10). PIA is responsible for 13.4 million disability-adjusted life years (DALY) and >5 million deaths every year (11, 12). Likewise, excessive SB is clearly correlated with major chronic diseases and all-cause mortality (13, 14).

PIA and SB result in an important economic burden to societies. Worldwide, in 2013, the economic burden related to PIA was estimated at INT\$53.8 billion (direct medical costs) and INT\$13.7 billion (indirect costs due to productivity loss) (11). As epidemiologist Jerry Morris pointed out as early as 1994, PA to treat PIA is a "best buy" intervention (15). "Best buy" interventions are highly cost-effective and have substantial public health impact. Decreasing the prevalence of PIA will thus not only positively impact health but also have a high probability of counteracting the rising health care costs. As an example, a Canadian health impact analysis showed that a 10% reduction in the prevalence of PIA would save the society CAN\$150 million each year (16).

The reduction of PIA by 10% by 2025 is one of the WHO's nine global non-communicable-disease targets (1). However, societal trends like urbanization, motorized transportation, electronic entertainment and internet-based communication devices, may hamper the attempts to decrease prevalence of PIA and SB. Global and national policy developments as well as intervention strategies to increase PA among populations at risk, thus far, have not worked satisfactorily (17). The 2016 Lancet series on PA pointed out that the WHO target will not be reached without an immediate increase in action (18).

A promising way to tackle PIA and SB through activities of daily living is to offer interventions at the workplace (19-21). Adults spend most of their waking time at work and many occupations are typically related to SB (22). Furthermore, productivity of employees is known to be positively influenced by higher activity levels (23-26). Thus, employers may also benefit from reduced PIA and SB through decreased absenteeism and presenteeism. While there is evidence to support effectiveness of interventions at the workplace to counteract PIA and SB (19, 27-29), consequences on costs and health effects (ie, the "efficiency") should also be considered. Making an economic case for reducing PIA and SB at the workplace may sensitize employers, the public health sector, as well as political decision-makers, to support, develop, fund and implement such interventions at the workplace (8, 18, 30).

To our knowledge, only one review on the costeffectiveness (31) and one review on the cost-benefit (32) of PA and nutrition interventions at the workplace have been performed. Regarding cost-benefit analyses, the results were ambivalent as the authors found a positive return-on-investment (ROI) in non-randomized trials but a negative ROI among randomized trials. No conclusion could be made in terms of cost-effectiveness of workplace PA interventions because the methodological quality of the included studies was low and the results uncertain. Compared to these

two reviews by van Dongen et al (31, 32), there are three novel parts in the current study. First, PA and SB seem to have an interactive relationship with health (8). Therefore, the current study focused on both PA and SB interventions. Second, some of the interventions reviewed by van Dongen et al did not directly measure the impact on PA. To better understand the impact of the interventions, only studies which reported effects on PA/SB were included in the current review. Third, since the van Dongen et al reviews were published in 2011 and 2012, it is very likely that more recent evidence exists. As no review on the present research question is available, the goal of the present study is to perform a critical appraisal and synthesis of health economic evaluations of interventions aiming to increase PA and/or decrease SB at the workplace.

Methods

This systematic review was carried out following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (PRISMA) (33) and the five-step approach for systematic reviews of economic evaluations (34). The protocol was registered in the PROSPERO database (CRD42019122063).

Eligibility criteria

Studies performing a full health economic evaluation (HEE), ie, simultaneously analyzing costs as well as health effects of an intervention to increase PA and/or decrease SB in the context of worksite health promotion (WHP) compared with one or more alternatives (ie, the comparator) were included. This includes cost-effectiveness analyses (CEA), cost-utility analyses (CUA) or cost-benefit analyses (CBA). In such analyses, costs are always expressed in monetary units, while effect sizes can be expressed in terms of natural units (CEA), quality-of-life proxies (CUA) or in monetary units (CBA). Single-study based HEE (ie, alongside an RCT/ cohort study) and model-based HEE (ie, modelled costs and effects with data derived from different sources such as the literature or databases) were eligible for inclusion.

No limits were set for gender, country or type of industry in which the WHP program took place. Interventions could include education, counselling, online interventions, any form of PA (eg, lunch walks, fitness centers, exercise groups) or ergonomic interventions (eg, standing desks). Multicomponent interventions which focused on different health outcomes were included if the intervention for PA/SB constituted a main component of the WHP program. Studies were included if they reported effects on PA and/or SB. Effects could be reported in "natural units" (eg, MET minutes, energy expenditure, time of moderate/vigorous PA, sitting/standing time etc.) or as proportions (eg, number meeting the PA guidelines, prevalence of PIA etc.). Table 1 summarizes the PICO (problem/ patient/population, intervention/indicator, comparison, outcome) elements of this review.

No language limitations were set. The time horizon was set to the previous 20 years (1998-August 2019), as since then, computers and the internet have had a revolutionary impact on culture, communication and working conditions.

Information sources

A comprehensive literature search was performed in Medline (PubMed), Embase, EconLit, Web of Science, Scopus and NHS Economic Evaluation Database. Additionally, a keyword search in Google Scholar was carried out. In order to increase the sensitivity of the search, references of relevant reviews and from included articles were checked (backward tracking). Furthermore, screening of "cited by" articles (forward tracking) as well as expert interviews were performed. Update notifications from database searches were set and relevant studies were added throughout the process.

Search strategy and study selection

The database search strategy was established using the Peer Review of Electronic Search Strategies (PRESS) checklist (35), CADTH's Database Search Filters (36) and published recommendations to identify economic evaluations (37).

Sensitive search filters according to PICO were built. The C-element (comparison) was not further defined for the search strategy and was therefore omitted to maintain sensitivity of the search filter (see supplementary material, www.sjweh.fi/show_abstract.php?abstract_id=3871, table S1). Search results were stored in reference manager software (Zotero, version 5.0.59). After removing duplicates, titles and abstracts were screened. Fulltexts of relevant studies were consulted for definitive inclusion and reasons for exclusion were noted. Two independent researchers

performed the search, the screening process and inclusion of studies. A consensus discussion between the researchers took place after title and abstract screening, as well as after fulltext consultation.

Data collection

Two independent researchers extracted data on study characteristics and outcomes of the economic evaluations and captured these in prepared digital forms. A consensus discussion took place at the end of the data extraction process. The research team was consulted in case of discrepancies and ambiguities.

Data items

The following data were extracted from the included studies: study details (publication year, country, design, perspective, time horizon), characteristics of study participants, details of the intervention and the comparator, measurement and valuation of effects and costs, incremental costs, incremental effects and economic metrics (incremental cost-effectiveness ratios (ICER), incremental costs-utility ratios (ICUR), net monetary benefit (NMB), benefit-cost-ratio (BCR) and return-oninvestment (ROI)). Where applicable, 95% confidence intervals (95% CI) were reported. Study authors were contacted in case of missing data.

Data synthesis

To the best of our knowledge, no general accepted method to pool estimates from HEE (ie, ICER) is available. Standard deviations (SD) or CI for cost data are often lacking, which makes pooling of costs impossible (32). It is difficult to compare WHP interventions because they need to match individual and local situations in companies as well as national (health) policy regulations. Consequently, reviewers concluded that interventions, time horizons and outcome measures differ substantially among studies (38, 39). Taking this heterogeneity into account, plausibility to pool effects was not present and hence, pooling was not deemed possible. Thus, our analysis remains purely descriptive and studies were analyzed qualitatively. However, several approaches were performed to enhance comparability of included studies. To quantify the effects, standardized effect sizes (Hedges' g) were calculated following the instructions in the Cochrane handbook (40).

All costs were converted to 2017 euros. In step 1, original costs were adjusted using the gross domestic product (GDP) deflator index provided by the International Monetary Fund (IMF) World Economic Outlook Database (41). As published GDP deflator indices by the IMF are only available till 2017, all prices were adjusted to the price year 2017. If the reference year for costs was not reported in the studies, the year of publication was used in conversion. In step 2, original currencies were converted into euros (Belgium), accounting for purchasing power parities (PPP) between countries (42). Costs in the target currency and the target price year were calculated according to the following formula (43):

Cost...

Where:

GDP1 is the GDP deflator index for the original currency in the original price year;

GDP2 is the GDP deflator index for the original currency in the price year 2017;

PPP1 is the PPP conversion rate for the original currency in the price year 2017;

PPP2 is the PPP conversion rate for the target currency in the price year 2017; and

Costoriginal is the original cost in the original currency.

All economic metrics were recalculated using 2017 Euros. Economic metrics are often calculated using different methods (44). The following formulas were applied in this study:

ICER or ICUR...

ROI...

NMB = benefits - costs

BCR...

Whether an intervention is cost-effective or costbeneficial depends on the perspective and thus on which costs were considered in the HEE. To provide a more comprehensive synthesis, benefit-standardized ROI/ ICER were calculated (32). If, for example, productivity costs and health care costs were considered, three ROI/ ICER were calculated: one considering only productivity costs, one considering only health care costs and one considering both.

Costs and CBA metrics were calculated for each study and descriptively summarized by means, SD, and medians (32).

Methodological quality appraisal

The Consensus Health Economic Criteria (CHEC) list was used to assess the methodological quality of the HEE (45). The CHEC list is a generally accepted criteria list consisting of 19 items, which should be regarded as a minimum standard for HEE. Items can be rated as positive, negative (inadequate methodology or insufficient information) or not applicable (NA). Two independent researchers applied the CHEC list and agreement among raters was evaluated using Inter Class Correlation (ICC) statistics. Discrepancies were discussed in a consensus meeting.

Results

Literature search

Database searches yielded 3124 results of which 624 were duplicates. Additionally, 32 articles were identified through reference screening of 52 reviews in the field of WHP. After screening 2530 records, 198 fulltexts were assessed for eligibility and 17 studies (45-62) were included. One additional study (63) was included in the course of the work progress due to notifications from saved searches in databases (figure 1). Searches in databases other than PubMed did not yield additional studies.

General study characteristics

Eleven studies were randomized controlled trials (RCT), of which seven used a cluster-randomization. All cluster-RCT randomized the clusters at once and all but one took clustering into account for the statistical analysis. One study only randomly allocated a proportion of the participants. Non-randomized controlled trials (N-RCT) were cohort studies (N=6) of which three were partially modelled (eg, the impact of health benefits on health care costs). One study was completely modelbased. Sample sizes ranged from 60-1260 in RCT and 25-63 646 in N-RCT. Studies were carried out in The Netherlands (N=6), United States (N=6), United Kingdom (N=4), and Australia (N=2). Time horizons ranged from 6 months to 5 years, whereby ten studies used time horizons between 9-18 months. The model-based study used a lifetime Markov simulation. Studies were published between 2004-April 2019, of which 14 were published in 2011 or later.

In most studies, participants were employees with no specific health condition (N=12). These studies used general exclusion criteria such as pregnancy, inability to perform PA, long-term sick leave or no regular employment contract. Three studies focused on overweight employees and one study each on older employees (45 years), employees with an unhealthy life-style and employees with the diagnosis of diabetes, hyperlipidemia or hypertension. See table 2 for more details.

Interventions

Five studies focused on PA, six on PA and nutrition, and one on SB. Effectiveness data of the latter study were used in the model-based study. Five studies focused on a number of different health risks (eg, PIA, smoking, high alcohol consumption, high cholesterol, blood pressure or poor nutrition) which were identified through a health risk appraisal. All but one study used some form of education/ counseling, but the techniques differed between studies. Studies used one or a combination of the following elements: written information, websites, e-mails, face-to-face coaching, group sessions, phone calls, videos or posters. Most studies reminded employees on a regular basis to implement the suggestions from the counseling sessions. Five trials also distributed pedometers and two studies provided financial incentives for performing PA. Two studies described environmental interventions such as the introduction of table tennis and exercise balls or a scan of environmental factors which may inhibit PA (eg, no shower facilities). Fourteen studies described that the intervention included techniques of behavior change. However, it was difficult to evaluate to what extent these techniques were put into practice. Often, it was not clear to what extent employees had access to facilities to perform PA (eg, exercise groups, swimming pools, fitness centers, walking paths), which was explicitly reported in five studies. In one study, the intervention was actually a PA intervention consisting of one weekly yoga session, one weekly fitness workout and one weekly unsupervised training session.

The studies on SB used counseling techniques together with the implementation/installation of standing desks.

Effects

Five studies used PA and two studies SB as primary outcome. Other studies reported general health risks, body weight, vitality or quality of life as primary outcome and thus, PA/SB as secondary outcome. As this review focuses on PA/SB interventions, only effects on PA/SB are reported here. For six studies, effects on PA/SB were reported in a separate publication and thus retrieved from there.

Selected outcome measures for PA across studies were heterogeneous, including steps per day, prevalence of meeting PA recommendations, MET minutes, minutes of moderate or vigorous PA per week, minutes of sport per week, or energy expenditure. SB was measured in terms of sitting-time per day or standing-time per day.

To enhance comparability of effects across studies, standardized effect sizes (Hedges' *g*) were computed (figure 2). For two studies, the standardized effect size could not be calculated due to insufficient data. Four effect sizes for PA were negative (-0.25- -0.01), eleven were 0-0.3 and five were >0.3. The median effect size was found to be 0.1 (interquartile range 0.02-0.24). There was no clear pattern for different intervention contents or type of outcome measure related to the effect size. However, the only study which applied a PA intervention (weekly yoga and fitness sessions) yielded the biggest effect size ($g=1.3$). From all 20 PA-related effect sizes, six were significantly larger than zero. Three of eleven RCT and three of four N-RCT reported significant effects.

The three effect sizes regarding SB ranged from 0.06-0.29, with one being significantly larger than zero.

Costs

Costs reported in the studies could be divided into three subgroups: intervention, direct medical (health care, out-of-pocket) and indirect (due to absenteeism and presenteeism) costs. All but two studies reported intervention costs. One of the latter studies did not report any of the costs separately. Descriptive analysis of the intervention costs among 16 studies yielded an arithmetic mean of €174 (SD €147, median €128) per person. Ten studies included direct medical costs of which seven found them to be lower in the intervention group during follow-up. However, these differences were uncertain due to large SD and thus, not statistically significant. Twelve studies included indirect cost in terms of presenteeism (N=1), absenteeism (N=3), or both (N=8). In ten of the twelve studies considering indirect costs, they were found to be lower in the intervention group during follow-up. Again, these differences were not significant. Indirect costs were the main cost-driver. In studies providing sufficient information on indirect costs (N=6), these represented 87.9% of the total costs. In four studies reporting absenteeism costs and presenteeism costs separately, presenteeism accounted for 82.4% of indirect costs.

The mean difference in total costs between intervention and control group was calculated for each study. Descriptive summary of these differences among studies yielded a mean difference of €0.45 (SD €752, median €31.4) per person in favor of the control group. A complete overview on costs can be found in table S3.

Methodological quality of economic evaluations

Agreement between the two raters for total scores of the CHEC list was high (ICC 0.98, 95% CI 0.94- 0.99). On average, studies fulfilled 68% of the minimum-standard criteria of the CHEC list. Most studies described the study population (N=17), posed a clear research question (N=18), chose an appropriate time horizon (N=17) and identified all relevant outcomes (N=16). Less than half of the studies identified all relevant costs (N=8), measured costs in physical units (N=8), valued costs appropriately (N=7) and performed sensitivity analyses (N=7). Of eight studies with a time horizon over one year, three discounted costs. See table S2 for more detail.

Health Economic Evaluations

The perspective of the HEE was reported in thirteen studies. For the remaining five, the perspective was anticipated based on the available information. HEE of included studies used the employer's perspective (N=9), the societal perspective (N=4), the societal and the employer's perspective (N=3), the healthcare payer perspective (N=1) as well as the healthcare payer perspective and the employer's perspective (N=1). Studies consisted of CBA (N=7), CEA (N=3), CUA (N=3), CBA and CEA (N=3), CEA and CUA (N=1) and all three types (N=1). Studies reporting multiple perspectives typically performed a CEA or a CUA from the societal perspective and a CBA from the employer's perspective.

Cost-effectiveness analyses

ICER for fifteen studies could be benefit-standardized, ie, they were calculated considering different combinations of cost categories. The most generalizable perspective for an HEE is the societal perspective as it includes all costs (34). ICER from the societal perspective were calculated for eight studies and were found to be heterogeneous. In three studies, the ICER was dominant, ie, the intervention was more effective and less expensive than the comparison. For example, the ICER in the study by van Wier et al (61) was -€3.11/minute PA, meaning that €3.11 were saved per one additional minute of PA per week. In three studies, the intervention was more effective but also more costly as compared to the comparison. For example, the ICER in van Dongen et al's study (59) was €18.63/minute of sport, meaning that the increase in participation in sport of one minute per week costs society €18.63. In one study, the intervention was less costly but also less effective. One study yielded conflicting results as there was a negative and a positive effect among the two PA-related outcome measures. In two studies, the sample size for costs and effects differed; in two other studies, the follow-up time for costs and effects differed and in one study, both differed.

None of the studies yielded significant differences in costs and effects. This indicates that ICER are subject to substantial uncertainty and should therefore be interpreted with caution. For more detail on benefit-standardized ICER, see table 3.

Cost-benefit analyses

In line with ICER, the ROI were also recalculated and benefit-standardized for each study providing sufficient data. As with ICER, ROI across studies presented a heterogeneous picture. When considering the societal perspective and thus, including all the costs, ROI ranged from -450.47-864%. There was one outlier (12 246.18%) which was due to a very small investment (difference in intervention costs between the groups was only €13.21) rather than very high benefits. The median ROI was close to zero, regardless of whether direct costs (-30.09%), indirect costs (44.64%) or all costs (31.09%) were included (supplementary figure S1). Only one study reported 95% CI of ROI estimates.

The ROI was found to be related to study design: the median ROI was -39.0% in RCT and 292.37% in N-RCT ($P=0.03$, figure S2). Spearman's rank correlation between CHEC list rating and ROI was -0.63 ($P=0.03$, figure S3). See table 3 for more detail.

Discussion

This systematic review aimed to evaluate and synthesize the health economic evidence of workplace interventions designed to increase PA and/or decrease SB. Eighteen HEE were included and analyzed.

Effects

Most interventions improved PA across all outcome measures, but effects on PA were variable and generally small. Although most studies used some form of counseling, interventions were heterogeneous. We were unable to link particular intervention elements to higher effects. These findings are in line with the findings of previous reviews which investigated effectiveness of worksite PA interventions (19, 64). However, two studies with large effects have been identified. White et al's study (62) reported that exercise, expressed as time/ week, had increased by 106 minutes (Hedges' $g=1.04$). In this small ($N=25$) study, participants received comprehensive and individual health coaching from an interprofessional intervention team, led by a pharmacist. Compared to the other included studies, this intervention corresponds more to a clinical setting rather than a typical workplace setting and was clearly higher dosed. Furthermore, this study used a pre-post design, included volunteer employees and may therefore be subject to selection bias. Finally, it should be mentioned that despite the large effect, variation among participants was large. The van Dongen et al study (59) found that employees in the intervention group increased their sport time/week by 33 minutes compared to the controls (Hedges' $g=1.3$). This was the only intervention which consisted of a physical activity program (ie, exercise classes) rather than counseling only. Offering concrete situations to perform PA may therefore be more effective. Interestingly, the reported intervention costs in this study were €162 and thus not different from mean intervention costs from all studies (€174). However, it is worth mentioning that the large effect size was mainly achieved by a very small SD rather than a large effect.

Three studies measured SB and all found positive effects. The only study which set SB as primary outcome, found

significant and relevant effects.

Although PA may attenuate or even eliminate the detrimental influence of SB on health (8), SB and PA are different behaviors requiring individual management and thus, should both be addressed. Reducing SB while increasing PA may boost effectiveness of interventions meaning that such interventions may be more likely to be cost-effective in the long-term. The present review identified only two studies in which both SB and PA were targeted. However, effects of these outcomes were not considered for the HEE and thus, no conclusion for combined interventions can be drawn. A large trial among 69 219 employees found that besides significant improvement in PA and SB, significant changes in health outcomes were also found (65). HEE of such PA and SB interventions are needed to provide decision makers with the evidence to make informed decisions about allocation of scarce resources (18). Six studies implemented interventions for employees with specific health conditions (eg, overweight). We found no relevant difference for effects between studies which focused on such groups (median Hedges' $g=0.09$) and studies which focused on healthy employees (median Hedges' $g=0.15$). This is somewhat surprising, as previous research showed larger effects of worksite PA-intervention when focusing on employees with specific health conditions (21). Furthermore, focusing on specific groups may also reduce intervention costs because the intervention is not directed at employees who are already physically active and thus, the intervention is likelier to be cost-effective.

Health economic evaluations

The included HEE differed in several ways. In CBA, the effect on the outcome is expressed in monetary terms. This was typical for HEE from the employer's perspective because the employer will only implement an intervention if the benefits are at least as high as the investment. HEE from the societal perspective, however, typically performed CEAs which results in an ICER. Most ICERs indicated that the intervention was more effective and more costly. It is difficult to determine if such interventions are cost-effective because costeffectiveness depends on the willingness-to-pay. To our knowledge, this willingness-to-pay threshold for PA/ SB has not been established as yet and would be an important subject for future studies.

We found that, even when using the same perspective and the same analytical approach, HEE included different cost categories, which hinder between-study comparisons. As in most HEE (66), our data showed that indirect costs (productivity) were the main cost-drivers. For example, in the study by Goetzel et al (50), the ROI was -42% excluding indirect costs but 103% including indirect costs. A systematic review found that PA was related to increased psychosocial health in employees (27) and there is also evidence that such health outcomes reduce presenteeism (67). Furthermore, low PA was found to be related to increased absenteeism (68). These are reasonable arguments why productivity should be considered in HEE of WHP. However, six studies did not include indirect costs. One reason may be that the methods for valuing productivity are controversial (66). However, in the last years, efforts were undertaken to provide practical guidance on how to estimate health-related productivity costs (66). Future studies should use such guides.

Between 6-10% of major non-communicable-disease can be avoided with the elimination of PIA (12). However, the pay-back time of PA/SB is long, which represents a challenge for controlled trials. A common approach in HEE is to model effects and costs over the long-term. We only found one study which modelled long-term costs and effects (63). There is thus a need for model-based HEE to better understand the economic value of worksite PA/SB-interventions in the long-term.

It was found that N-RCT delivered more favorable ROI compared to RCT. Furthermore, we found an inverse relationship between CHEC scores and ROI. This is in line with previous research in this field and often referred to selection bias (32, 44).

Strengths and limitations

The literature search yielded only eighteen studies, two of which focused on SB. This small number of studies may limit the significance of this review, especially regarding SB. The number of retrieved references from database searches was 2530, which may seem to be small. However, this can be explained by the search filters targeting the setting (workplace) and the HEE which made the search strategy more specific.

With the use of published guidelines and search algorithms, we aimed to maximize the comprehensiveness of our

search strategy. Furthermore, intensive reference tracking as well as search notifications from databases were applied in order to reduce the risk of missing studies. Nevertheless, restriction of some keywords to title or abstract may have limited the search, possibly resulting in missing some relevant studies.

The identified HEE were heterogeneous which limits comparison and thus drawing conclusions. As a consequence of this heterogeneity, it was inappropriate to carry out a meta-analysis, although initially planned. Descriptive analyses of the costs were performed. However, as interventions were heterogeneous, the mean costs should be interpreted with caution. Regarding external validity, we tried to provide a best possible comparison of studies by reporting all costs in 2017 euros and by calculating benefit-standardized economic outcomes. However, even if a uniform methodology was to be developed and used, comparisons across studies would be complicated because outcomes from HEE also depend on other factors like local regulations or national health policies.

Before applying the CHEC list, the two authors discussed the items thoroughly, which may explain the high reliability for rating the HEE. Nevertheless, some items were difficult to rate. For example, we did not define a threshold for "Is the chosen time horizon appropriate?" but decided individually, depending on the intervention and the outcome measures. Seventeen studies fulfilled this item which is contradictory with the fact that PA/ SB interventions have a long pay-back time. Likewise, there are no clear criteria for "Do the conclusions follow from the data reported?", where most disagreements were found (N=5).

Concluding remarks

Although most studies showed improvements in PA/ SB, effects were small and their relevance is questionable. No particular intervention type was found to be more effective. HEE were heterogeneous regarding methodological approaches and the selection of cost categories was inconsistent. Furthermore, effects on costs were subject to substantial uncertainty. Therefore, the economic evidence for worksite PA/SB interventions remains unclear.

Future studies are needed to determine which strategies work best for whom and under what circumstances. HEE of such interventions should be established using guidelines and validated, consistent measures of productivity costs as they were the main cost driver in included HEE. Additionally, studies should model the long-term costs and effects because of the long pay-back time of PA/SB interventions.

Sidebar

Health economic evaluations of interventions to increase physical activity and decrease sedentary behavior at the workplace: a systematic review

This systematic review identified 18 economic evaluations of worksite physical activity and sedentary behaviour interventions. Effects were small and the impact on costs was uncertain. Therefore, the economic evidence of these interventions remains unclear. Future studies are needed to determine which strategies work best. Economic evaluations of such interventions should be established using sound methodology and model the long-term cost-effectiveness.

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Key terms: cost-benefit; cost-effectiveness; economic evaluation; health economic evaluation; intervention; physical activity; public health; review; sedentary behavior; systematic review; worksite health promotion

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Additional material

Please note that there is additional material available belonging to this article on the Scandinavian Journal of Work, Environment & Health -website.

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DETAILS

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Status incongruence in human service occupations and implications for mild-to-severe depressive symptoms and register-based sickness absence: A prospective cohort study

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ABSTRACT (ENGLISH)

Objective This study aimed to investigate the hypothesis that negative status incongruence may contribute to explain higher risk of mental ill-health and sickness absence in human service occupations (HSO). **Methods** Participants from the Swedish Longitudinal Occupational Survey of Health who responded to questionnaires in both 2014 and 2016 (N=11 814; 42% men, 58% women) were included. Status incongruence between register-based educational level and subjective social status was assessed. The association between employment in a HSO and status incongruence was estimated in linear regression analyses adjusted for age, income, work hours, sickness absence, childcare, and job qualification match. The prospective associations between status incongruence and mild-to-severe depressive symptoms and register-based sickness absence ≥ 31 days respectively were estimated with logistic regression analyses in models adjusted for age and outcomes at baseline. All analyses were stratified by gender. **Results** Employment in a HSO was associated with more negative status incongruence in both genders [standardized coefficient men 0.04, 95% confidence interval (CI) 0.02-0.07; women 0.06, 95% CI 0.04-0.09]. More negative status incongruence was furthermore associated with higher odds of mild-to-severe depressive symptoms (men OR 1.18, 95% CI 1.08-1.29; women OR 1.17, 95% CI 1.09-1.26) and sickness absence ≥ 31 days (men OR 1.40, 95% CI 1.23-1.59; women OR 1.17, 95% CI 1.07-1.28) two years later. **Conclusion** Status incongruence is somewhat higher among HSO than other occupations and associated with increased odds of depressive symptoms and sickness absence.

FULL TEXT

Headnote

The study contributes with a completely novel hypothesis, namely that negative status incongruence between educational attainment and subjective social status may partly explain the excess risk of mental ill-health and sickness absence among employees in human service occupations. The results support this hypothesis with possible implications for associations between established work stressors and health.

Key terms: cohort study; depression; depressive symptom; gender; gender theory; human service occupation; mental health; mild-to-severe depressive symptom; prospective cohort study; register; register-based sickness absence; sick leave; sickness absence; status incongruence; status inconsistency

Objective This study aimed to investigate the hypothesis that negative status incongruence may contribute to explain

higher risk of mental ill-health and sickness absence in human service occupations (HSO).

Methods Participants from the Swedish Longitudinal Occupational Survey of Health who responded to questionnaires in both 2014 and 2016 (N=11 814; 42% men, 58% women) were included. Status incongruence between register-based educational level and subjective social status was assessed. The association between employment in a HSO and status incongruence was estimated in linear regression analyses adjusted for age, income, work hours, sickness absence, childcare, and job qualification match. The prospective associations between status incongruence and mild-to-severe depressive symptoms and register-based sickness absence >31 days respectively were estimated with logistic regression analyses in models adjusted for age and outcomes at baseline. All analyses were stratified by gender.

Results Employment in a HSO was associated with more negative status incongruence in both genders [standardized coefficient men 0.04, 95% confidence interval (CI) 0.02-0.07; women 0.06, 95% CI 0.04-0.09]. More negative status incongruence was furthermore associated with higher odds of mild-to-severe depressive symptoms (men OR 1.18, 95% CI 1.08-1.29; women OR 1.17, 95% CI 1.09-1.26) and sickness absence >31 days (men OR 1.40, 95% CI 1.23-1.59; women OR 1.17, 95% CI 1.07-1.28) two years later.

Conclusion Status incongruence is somewhat higher among HSO than other occupations and associated with increased odds of depressive symptoms and sickness absence.

Key terms depression; gender; gender theory; mental health; sick leave; status inconsistency.

A large number of the Swedish workforce, particularly women, are employed in occupations in which contact with children, students, sick, or older people is part of the everyday work tasks (1). It has in recent years been acknowledged that employees in these so-called "human service occupations" (HSO) have increased risks of mental ill-health and sickness absence compared with other occupations on the Swedish labor market (1, 2). Several possible reasons for this increase have been suggested, such as poorer working conditions in these professions (2) and a higher total burden of emotionally demanding work from paid and unpaid work together (3). However, the increased risks may also be due to a negative incongruence between the high education required for many of these professions and the perceived social status associated with them. According to gender theory (4, 5), different job tasks are assigned gendered symbolic meanings and status. Technical work tasks are typically considered male-gendered and associated with characteristics such as rationality and high skill requirements while work tasks such as caring for and developing other people are classified as female-gendered with skills typically considered to be inherent in the female nature. The former work tasks are often associated with higher status than the latter (6). A mismatch between an individual's different status positions is often referred to as status inconsistency or incongruence (7, 8). A negative status incongruence indicates for example high educational attainment but low occupational position and a positive status incongruence the contrary. Theories on status inconsistency or incongruence were developed in the 1940s (9), and sociologists and epidemiologists have been studying the health effects of various forms of status incongruence since the 1950s (10). In the early 1970s, the extent to which congruence measure adds anything beyond that of main effects of traditional measures of socioeconomic status was disputed (11), but researchers revisited the concept again in the 1990s, some proposing a measure that summarizes several of the indicators of socioeconomic status (10). In sum, the research field is diverse, with little consensus around definitions and measures of status incongruence. Status incongruence has in later years been measured in several different ways in relation to health outcomes, and the general finding is that negative status incongruence is associated with an increased risk of adverse health outcomes (12-17).

Several theories have been developed to explain the stress that could be associated with a negative status incongruence (8, 15). The theory of relative deprivation (18) argues that individuals may experience stress if they, when comparing themselves with peers with corresponding educational attainment, perceive that they are less successful in terms of, for example, income or occupational position. However, not only socioeconomic position, but also cultural dimensions such as social status (eg, esteem, respect, and prestige) associated with for example different genders, ethnicities, or occupations have been suggested as important for durable inequalities (5, 19). Both individuals' objective socioeconomic positions and their perceptions of their social status have also been found to be

associated with various mental and physical health outcomes, the latter over and above the former (20-22). For many HSO, the skill requirements are high and the work tasks are complex. For example, teaching and nursing professions require several years of university education. These professionals may experience an inconsistency between the education they invested in and the esteem, respect or prestige that society attributes these occupations. In the present study, we investigate if employment in a HSO is associated with negative status incongruence between educational level and subjective social status over and beyond that of factors commonly measured in the status incongruence literature, such as income (16, 23, 24) and qualification match with job demands (15, 24). If so, experienced lower status in relation to educational attainment could, as suggested by gender theory, be due to the fact that these female-gendered occupations are associated with lower status in society. Lower status associated with female-gendered occupations may not only have a direct effect on health but could also affect relationships between established psychosocial work factors and health outcomes (25-29). HSO include a wide variety of occupations, and the professions with higher educational requirements are more often held by men than by women (1). Furthermore, men more often than women advance to higher organizational levels, occupy managerial positions, and receive better salaries (1, 30) suggesting that the association between employment in a HSO and status incongruence may differ by gender.

The overall aim of the present study was to investigate the hypothesis that status incongruence between educational attainment and subjective social status may partly explain the excess risk of mental ill-health and sickness absence among women and men in HSO. The specific research objectives are to estimate if, among men and women (i) employment in a HSO is associated with more negative status incongruence compared with employment in other occupations, and (ii) status incongruence predicts mild-to-severe depressive symptoms and sickness absence.

Methods

Study sample

In this prospective study, we used data from two waves (2014 and 2016) of the Swedish Longitudinal Occupational Survey of Health (SLOSH), an open cohort representing an approximately nationally representative sample of the Swedish working population. Statistics Sweden has collected data every second year since 2006, and the respondents are invited to answer a self-completion questionnaire in two versions, one for those who work >30% of full time and another one for those who work less or not at all. More information on SLOSH can be found in the cohort profile (31). The SLOSH cohort comprised in total 20 316 individuals in 2014 and 19 360 individuals responded to the follow-up in 2016 (response rate 51%). For the present study, we selected participants who answered the questionnaire for those who work >30% in 2014 and who also responded to the questionnaire for those who work >30% or to the questionnaire for those who work less or not at all in 2016 (N=11 814; 42% men, 58% women). Of these, 3518 participants (29.8% of all; 11.3% of men, 43.3% of women) were employed in a HSO. Information on sickness absence in 2016 was obtained from the Longitudinal Integration Database for Health Insurance and Labor Market Studies (LISA), which is an integrated total population register of all residents in Sweden >16 years of age, provided by Statistics Sweden. Register data on sickness absence in 2016 was connected to register and self-reported data provided by SLOSH participants in 2014. The participants received written information about the study and, in accordance with Swedish regulation and practice, responding to and returning the survey indicated informed consent. The Regional Research Ethics Board in Stockholm approved the study (Dnr: 2017/236-3). The funding sources had no role in the writing of the manuscript or in the decision to submit it for publication.

Variables

HSO, status incongruence, and all covariates were measured in 2014 and the outcome measures in 2016. The variables were used as categorical unless stated otherwise.

Human service occupation

HSO was used as a dichotomous variable, with all other occupations used as the reference category. Data on the participants' occupations were based on the Swedish Standard Classification of Occupations (SSYK 2012) and obtained from register data. We used the same definition of HSO, developed in collaboration with several Swedish

authorities, as in a previous publication (2). In accordance with this definition we categorized "occupations in which contact with children, students, sick, older adults, or individuals with a vulnerable societal position is part of the daily work tasks" into HSO. Large professional groups in the present data material are teachers on all levels of the educational system and nurses and assistant nurses. Other professions included are, for example, physicians, psychologists, social workers, and priests.

Status incongruence

Status incongruence is calculated from register-based educational level and subjective social status and is a linear variable used as an outcome in the first step of our analyses and a predictor in the second step. Educational level was derived from register data and categorized into <9 years of education, <12 years of education, <3 years of university education, >3 years of university education, and post-graduate education. Subjective social status was measured using an illustration of a ladder next to the question "Think of this ladder as representing where people stand in our society. At the top of the ladder are the people who are the best off - those with the most money, most education and the best jobs. At the bottom are the people who are worst off - those who have the least money, least education, and the worst jobs or no job. The higher up you are on this ladder, the closer you are to the people at the very top and the lower you are, the closer you are to the people at the very bottom. Mark a large X on the rung where you think you stand (not in between the rungs)" (32). We used a new way of assessing status incongruence, that to our best knowledge has not been applied in previous incongruence research. The variable is the standardized residual obtained in a linear regression model, adjusted for age and gender, in which subjective social status was regressed on register-based educational level. The standardized residual for each individual was saved as a new linear variable in the dataset and used to indicate status incongruence in the following analyses. The variable ranges from -3.13-4.08. For pedagogical reasons, we have reversed the sign so that a positive value indicates that an individual has estimated his or her social status to be lower than what the regression model predicts (indicating negative status incongruence) and a negative value that the individual has estimated his or her social status as higher than what the model predicts. We are using the whole scale of status incongruence, as a linear variable, because we are interested in estimating also if employment in a human service profession may be associated with a less positive status incongruence than employment in a non-human service profession with equivalent educational requirements. For example, a medical doctor may rate his or her social status higher than what the regression model predicts (thus being given a low value), but a lawyer or civil engineer may rate his or her status to be even higher (thus being given an even lower value).

Outcome variables

The two outcome variables were chosen to capture a breadth of possible consequences of status incongruence among working individuals. Mild-to-severe depressive symptoms was measured with the Symptom Checklist Core Depression Scale (SCL-CD6), which is a 6-item subscale derived from the Symptom Checklist-90. The question "How much during the last week have you been troubled by..." is followed by six core symptoms of depression, namely "feeling blue/sad", "feeling no interest in things", "feeling low in energy", "feeling that everything is an effort", "worrying too much", and "blaming yourself for various things". The five response alternatives range from "not at all" to "very much" and the depression index score ranges from 0 (lowest) to 24 (highest) (33). In the present study, we used a cut-off of 10, proposed by Bech (34) to indicate mild symptoms of depression, which we have used in a previous study based on the same cohort (35). We categorized individuals with mild-to-severe symptoms of depression (values 10-24) into one group and the rest of the sample into the reference group (values 0-9). Sickness absence encompasses only absences lasting >14 days, for which all employed individuals can receive sickness benefit from the Swedish Social Insurance Agency. We used net days of sickness absence, a variable in which one day is equal either to one full day (100%) of sickness benefit (preventive sickness benefit, rehabilitation allowance, and occupational injury allowance), two days of sickness benefit of 50% or four days of 25%. We categorized the variable into either no or little sickness absence (0-30 days) and sickness absence (>31 days).

Covariates

Depression symptoms, measured in 2014 with the scale described above but used as a continuous variable, were

adjusted for in models with mild-to-severe depressive symptoms in 2016 as the outcome. Any (>1) registerbased net day of sickness absence in 2014, as opposed to none, was adjusted for in models measuring register-based sickness absence >31 days in 2016 as the outcome. Age was categorized into <34, 35-44, 45-54, 55-64 and >65 years, and weekly working hours into <29, 30-39, 40-49, and >50 hours. Income was derived from register data and categorized into deciles. Because the income variable is affected by leaves from work, sickness absences and staying home with sick children were adjusted for in models including income. Self-reported sickness absence was measured with the question "Roughly how many days in total have you been on sick leave during the past 12 months?" with the response alternatives 0, 1-7, 8-30, 31-90 and >91 days and was adjusted for in these categories. Staying home with sick children was measured with the question "How many times over the past 12 months have you stayed home caring for a sick child?" with the response alternatives "not at all", "once", "two to three times", and "four times or more" used as the categories adjusted for. Job qualification match was measured with the question "Comparing your skills and knowledge with the job you do, do you think you are" ... with the following five options ... "over-qualified to a great extent", "over-qualified to some extent", "well qualified", "need some additional knowledge", "need a lot of additional knowledge".

The analyses were stratified by gender.

Analytical strategy

Differences between men and women in the distribution of study variables were calculated with Chi square test or analysis of variance. The first research question was analysed by building a gender-stratified linear regression model in two steps in which employment in a HSO, as compared with employment in any other occupation, was used as the predictor and status incongruence as the outcome. In the first step, the association was adjusted for age only and, in the second step, additionally for income, self-reported days of sickness absence, occasions staying home with sick child, working hours, and job qualification match. We conducted sensitivity analyses in which only participants working full-time were included (both >30 and >40 hours a week were considered). Standardized linear regression coefficients and 95% confidence intervals (CI) were reported. The second research question was analyzed, using all occupations together, with genderstratified binary logistic regression analyses in which status incongruence (2014) was the predictor and mildto-severe depressive symptoms and sickness absence >31 days respectively (2016) the outcomes. In a first step, the associations were adjusted for age only and, in a second step, additional adjustment was made for symptoms of depression/any day of register-based sickness absence as opposed to none in 2014. We furthermore conducted analyses of mild-to-severe depressive symptoms in 2016 in which cases of mild-to-severe depressive symptoms in 2014 were excluded (men N=699, women N=1390) as well as analyses using the cut-off in the SCL-CD6 of 16/17. A score >17 has been validated against diagnostic criteria to indicate major depression (36). In the latter analyses only individuals with a score <16 (no indication of depression) in 2014 were included. Odds ratios (OR) and 95% CI were reported. Sensitivity analyses were conducted assessing the association between status incongruence and mild-to-severe depressive symptoms/ sickness absence >31 days among employees in HSO only. Missing data were handled by the full information maximum likelihood. Model fit was estimated with the root mean square error of approximation (RMSEA), the Tucker-Lewis index (TLI), the comparative fit index (CFI), and the standardized root mean square residual (SRMR), with model fits suggested to be acceptable when RMSEA<0.08, TLI >0.90, and CFI >0.90, and SRMR<0.08 (37). Descriptive statistics were estimated in SPSS version 25 and the regression analyses conducted in MPLUS version 8.

Results

The distribution of the study variables is presented in table 1a and b. There were statistically significant gender differences in the distribution of all study variables except occasions taking care of sick children. The linear status incongruence variable ranged from -2.99-4.08 among men and -3.13-3.66 among women.

Employment in human service occupation and status incongruence

As shown in table 2 there were, among both men and women, statistically significant associations between employment in a HSO, compared with employment in other occupations, and more negative status incongruence. For men, employment in a HSO was associated with an increase of 0.08 (95% CI 0.05-0.11) standard deviations

towards more negative status incongruence in the age-adjusted model. For women, employment in a HSO was associated with an increase of 0.12 (95% CI 0.10-0.15) standard deviations. When adjustment for the additional covariates were introduced in the second step of the model the standardized coefficient decreased to 0.04 (95% CI 0.02-0.07) among men and 0.06 (95% CI 0.04-0.09) among women. Similar results were found in analyses including fulltime employed only. Model fit statistics were RMSEA 0.000, TLI 1.000, CFI 1.000, and SRMR 0.000.

Status incongruence and health outcomes

As shown in table 3, among men, each standard deviation increase towards more negative status incongruence in 2014 was associated with an OR of 1.18 (95% CI 1.08-1.29) of mild-to-severe depressive symptoms in 2016 in the model adjusted for a linear variable of depression symptoms at baseline. The corresponding numbers were for women OR 1.17 (95% CI 1.09-1.26). Results of analyses in which cases of mild-to-severe depressive symptoms at baseline were excluded (men N=699, women N=1390) showed OR of mild-to-severe depressive symptoms in 2016 of 1.36 (95% CI 1.221-1.52) for men and 1.32 (95% CI 1.20-1.44) for women. In analyses using the cut-off for major depression (respondents with major depression in 2014 excluded) each standard deviation increase towards more negative status incongruence in 2014 was associated with an OR of major depression in 2016 of 1.58 (95% CI 1.331-1.89) among men and 1.38 (95% CI 1.20-1.58) among women. Each standard deviation increase towards more negative status incongruence was furthermore associated with an OR of 1.40 (95% CI 1.23-1.59) of >31 days of register-based sickness absence in the fully adjusted model among men and OR 1.17 (95% CI 1.07-1.28) among women. Results were similar in models including employees in HSO only.

Discussion

The main findings of the present study were that employment in a HSO, compared with employment in other occupations, was associated with more negative status incongruence and that negative status incongruence in turn was associated with higher odds of self-reported mild-to-severe depressive symptoms and register-based sickness absence >31 days two years later.

Employment in human service occupation and status incongruence

Women and men in HSO rate their social status somewhat lower than employees in other occupations with equivalent educational backgrounds on the Swedish labor market. The effect size is rather small, but on the other hand it affects a large part of the working population. Income was strongly associated with status incongruence. In the theory of relative deprivation, experienced negative status incongruence has been discussed to be related to a perception of distributive injustice and to a discrepancy between investments (in terms of education, for example) and rewards (in terms of financial situation, for example) (18). HSO employees who are underpaid in relation to other professions with corresponding educational requirements (38) may, in accordance with this theory, experience a discrepancy between investments, in terms of their educational background and rewards, in terms of their salaries. However, the association between employment in a HSO and negative status incongruence could not fully be explained only by income or the other included covariates. Subjective social status is a measure that theoretically goes beyond that of socioeconomic position in terms of access to power and resources and indicates a sense of value in the society to which one belongs (5). Based on findings from the Whitehall study in Britain, Singh-Manoux et al (22) argue that subjective social status appears to more fully reflect the total sociocultural circumstances of the individual than other broad objective measures of socioeconomic position. In line with this argument, our results suggest that HSO employees in Sweden may find the work they do is not valued by the society to which they belong to the same extent as employees with equivalent educational backgrounds in other occupations. This could be due to that women's work, according to theory (4, 5), is generally less valued than men's work by society at large, and could also be associated with the continuous cuts in resources to the human service sector since the middle of the 1990s with deteriorating working conditions as a consequence (39). To what extent negative status incongruence as measured in the present study affects the association between psychosocial work stressors and health outcomes (25-29) is a research question that should be explored further. For example, high job demands may be more strongly associated with negative mental health outcomes depending on the social status of the job demands per se, whether oriented towards caring for others (lower status) or towards data or technical skills (higher status).

The implication of status incongruence for health outcomes

The odds of mild-to-severe depressive symptoms decreased markedly in both genders with the introduction of adjustment for depression symptoms at baseline whereas sickness absence >31 days remained relatively unchanged with the introduction of baseline adjustment for sickness absence >1 day. This may not be surprising since both depression symptoms and subjective social status are self-reported and may be interrelated, whereas sickness absence is register-based. The adjusted results may be considered as conservative since a reverse association between the variables is also plausible, ie, that depression symptoms and sickness absence affect experienced social status negatively over time. The effect of status incongruence on mild-to-severe depressive symptoms and depression was evident also after excluding cases of the respective outcome at baseline. The present study supports the results of several previous ones of various more traditional measures of status incongruence, reporting associations with outcomes such as mental well-being (17), depression symptoms (13, 16), poor self-rated health (15), and risk of cardiovascular disease (14). In the present study, the odds of sickness absence >31 days for each standard deviation increase in negative status incongruence is particularly high among men.

Strengths and limitations

Besides the strength of the prospective design and high-quality data used in the present study, it gives a novel contribution with its focus on social status associated with typically female gendered occupations in relation to educational requirements and a measure of social status that may more adequately capture an individual's total sociocultural life circumstances. This may be particularly relevant for studies of value or esteem associated with differently gendered occupations. However, the measure of status incongruence used in the study has not been used before. Although it is based on educational level derived from register data and a validated scale of subjective social status, future research may prove the usefulness of this scale for other research questions. There is a selective drop out from the SLOSH cohort; more women, well-educated, Swedish-born, and employees in the public sector remain in the cohort. Although gender, education and, to some extent, sector (through HSO) is taken into consideration in the analyses of the present study, the results cannot be generalized to the Swedish working population as a whole. The measure of sickness absence is non-specific and no conclusions can be drawn regarding specific diagnoses. The measure of mild-to-severe depressive symptoms is furthermore self-reported. However, the longer version of the scale, the SCL depression scale, has been validated against clinical diagnostic interviews and found to be robust (36).

Concluding remarks

Status incongruence is somewhat higher among HSO than other occupations and is associated with increased odds of depressive symptoms and register-based sickness absence. The possible moderating role of status incongruence in the association between established work stressors and negative health outcomes should be investigated in future studies. Arenas to target with interventions may be the gender-segregated labor market, the wage distribution in HSO, and more generally social status associated with gender.

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Declaration of interests

The authors declare no conflicts of interest.

Sidebar

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DETAILS

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Breast cancer specialists' perspective on their role in their patients' return to work: A qualitative study

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ABSTRACT (ENGLISH)

Objectives This study aimed to explore the views of breast cancer (BC) specialists as to their role in the return-to-work (RTW) process of their BC patients. **Methods** A qualitative study using semi-structured interviews was conducted in a sample of 20 BC specialists selected according to age, gender, medical specialty (medical oncology, radiation oncology, gynecological surgery), and healthcare organization (regional cancer center, university or private hospital). All interviews were audiotaped and transcribed for qualitative thematic content analysis. **Results** BC specialists had heterogeneous representations and practices regarding their role in their patients' RTW process, ranging from non-involvement to frequent discussion. Most BC specialists had concerns regarding the "right time and right way" to address patient's RTW. They hardly mentioned workplace and job factors as potential barriers but rather stressed motivation. The main reported barriers to involvement in the RTW process were lack of time, lack of knowledge, lack of skills, and a professional attitude exclusively focused on cancer care issues. **Conclusion** While our study showed varying representations and practices among BC specialists, participants consistently identified barriers in supporting BC survivors' RTW. The results will guide the development of an intervention to facilitate the role of BC specialists in the RTW process as part of a multicomponent intervention to facilitate BC survivors' RTW.

FULL TEXT

Headnote

Objectives This study aimed to explore the views of breast cancer (BC) specialists as to their role in the return-to-work (RTW) process of their BC patients.

Methods A qualitative study using semi-structured interviews was conducted in a sample of 20 BC specialists selected according to age, gender, medical specialty (medical oncology, radiation oncology, gynecological surgery),

and healthcare organization (regional cancer center, university or private hospital). All interviews were audiotaped and transcribed for qualitative thematic content analysis.

Results BC specialists had heterogeneous representations and practices regarding their role in their patients' RTW process, ranging from non-involvement to frequent discussion. Most BC specialists had concerns regarding the "right time and right way" to address patient's RTW. They hardly mentioned workplace and job factors as potential barriers but rather stressed motivation. The main reported barriers to involvement in the RTW process were lack of time, lack of knowledge, lack of skills, and a professional attitude exclusively focused on cancer care issues.

Conclusion While our study showed varying representations and practices among BC specialists, participants consistently identified barriers in supporting BC survivors' RTW. The results will guide the development of an intervention to facilitate the role of BC specialists in the RTW process as part of a multicomponent intervention to facilitate BC survivors' RTW.

Key terms breast cancer survivor; general practitioner; intervention mapping; psychosocial, occupational physician; oncology; RTW.

Breast cancer (BC) is the most common cancer in women worldwide (1), with good prognosis and 5-year survival rates exceeding 80% (2-4). Due to increasing BC incidence (including in younger women), increasing survival and the raising of the retirement age (5), the number of BC survivors expected to return to work (RTW) is raising and becoming a growing issue in BC care. Overall, about 40% of BC survivors are estimated to be of working age (<65 years old) (6).

RTW after BC is influenced by many factors, acting both as barriers and facilitators. These factors are linked to individual BC survivor characteristics such as age and education, cancer characteristics such as type and stage, treatment characteristics such as type of surgery and use of adjuvant chemotherapy, and the BC survivor's environment (family, workplace) (7, 8). Physical and cognitive limitations may impact ability to work (9, 10). Changes in the workplace during sick leave may mean that patients lose their bearings (9, 10) and increase negative feelings and anxiety (9-12). Qualitative surveys highlighted many uncertainties faced by BC survivors and emphasized changes in their career goals during and after active BC treatment (9-11, 13).

Furthermore, women report insufficient guidance from their healthcare practitioners on work-related issues (11, 13, 14), and feel abandoned by the healthcare system at the end of their active treatment. Lack of communication between hospital and general practitioners (GP) during follow-up has also been reported, as well as lack of communication with occupational health services (15). These issues are likely to influence the RTW process (16, 17).

In the workplace, social support from colleagues and managers and job accommodation are positively associated with RTW rates and sustained employment after cancer (7, 18, 19). Although interventions to promote RTW after BC have been developed, workplace involvement and job accommodation are rarely organized (2022). Coordination between hospital, community, and occupational physicians (OP) needs improving to fill the gap between the end of active treatment and RTW (13).

BC survivors meet various specialists during hospital-based treatment, usually in the following order: surgeons, medical oncologists, and radiation oncologists. In France, in addition to the compulsory RTW consultation at resumption of work, a pre-RTW consultation with the OP is mandatory for a sick leave of >3 months regardless of the underlying medical condition (23). This pre-RTW consultation, aiming to address the conditions of the resumption of work and possible adaptations needed, is organized as early as possible before the end of the sick leave on request by the patient himself or his/her treating physician. The BC specialist, in charge of prescribing the sick leave and evaluating the patient's ability to resume work from the oncology perspective, plays a major role in this process. However, only 37% of cancer patients who returned to their job and 14% of those who went to another job after cancer had such a consultation (24). This suggests a lack of referral to the OP and potential lack of commitment of cancer specialists regarding RTW issues for BC survivors. Although RTW after (breast) cancer has been previously explored from the patient, GP and workplace perspectives (25-28), the experience and perceptions of BC specialists on their role in RTW issues has been mostly unexplored.

The main objective of the present qualitative study was to explore the perspective of BC specialists regarding their perceived professional role toward the RTW needs of their BC patients. Secondary objectives were to identify barriers and facilitators for teamwork between BC specialists and GP and OP in the RTW process.

Methods

A qualitative approach with semi-structured interviews was adopted to explore BC specialists' point of view in depth. This qualitative study is part of the FASTER program conducted in France, which aims to develop a multi-component intervention to facilitate and sustain RTW after BC, following the six steps of the intervention mapping (IM) protocol (29, 30). The study is part of the first step, consisting of a health-needs assessment to develop a logic model of the problem and define intervention objectives. The results are expected to contribute to the subsequent steps of the IM protocol in order to develop, implement, and evaluate a multi-stage intervention involving BC specialists and other stakeholders in the RTW process. More specifically, these results will identify the behaviors of cancer specialists that should be modified by the intervention to facilitate the RTW process.

Setting

The study was conducted in the urban area of Lyon, France, which comprises three types of cancer-care facilities for 1.8 million inhabitants: a regional cancer center, a consortium of university public hospitals, and private hospitals. Approximately 1700 new BC cases are diagnosed each year in this area.

Sampling

A purposive sampling strategy was followed to include a balanced sample of participants intended to represent the variety of BC specialists, which patients encounter. Sampling criteria comprised gender, age, specialty (medical oncology, radiation oncology, and gynecological surgery), and healthcare organization (regional cancer center, university hospital, and private hospital). The second author identified the first participants, who in turn identified other possible participants in a snowball progression. New participants were chosen and contacted on an ongoing basis according to the sampling criteria, until data saturation defined as the point at which interviews did not bring important additional information (31).

Data collection

Semi-structured interviews were preferred to focus groups so as to minimize the risk of dominant personalities and social desirability bias. An interview guide was drawn up based on the most common themes mentioned in literature reviews on RTW after (breast) cancer (10, 12), and on the clinical experience of the authors in medical oncology, general practice, and occupational medicine. All the researchers discussed the interview guide, and it was adjusted during the data collection process to modify wording and incorporate new important themes. The themes of the final interview guide are shown in table 1.

Two residents in general practice conducted the interviews (AK and CJ), following training by a senior researcher (JBF) who also discussed their field notes and interview transcriptions after each interview. All interviews were conducted face-to-face in the participant's usual work setting, between 22 December 2015 and 26 July 2016. Median duration was 43 minutes (range, 31-97 minutes). Data saturation was obtained after 20 interviews.

Data analysis

All interviews were audiotaped, transcribed verbatim, and pseudonymized for any information identifying person or place. Qualitative thematic content analysis was performed using the MAXQDA v11 (VERBI Software GmbH, Berlin, Germany). Analysis first proceeded deductively, with a coding tree adapted from the themes of the interview guide. In a second step, new categories were created inductively to analyze data which did not fit the initial categories. Sub-categories were also created to refine the analysis of categories in which content was deemed too heterogeneous. Each interview was analyzed in depth (intra-case analysis) and summarized in a concise format that was used secondarily for transversal (intercase) analysis. Data saturation was reached progressively. After discussion, it was decided to stop the data collection after 20 interviews (31). At the end of the process, the researchers discussed the results with two participants, who recognized themselves in the results and provided more details that were included in the final results.

Ethics

No identifying patient information were accessed for the study. All participating physicians were provided with an information leaflet. Written informed consent was obtained from all participants. The study received local review board approval (IRB n° 00009118).

Results

Participants

The characteristics of the 20 participants are presented in table 2. The sample was composed of 12 female and 8 male physicians, aged 30-39 (N=9), 40-49 (N=6) and >50 years (N=5). They worked in public hospitals (N=9), private hospitals (N=5), or the regional cancer center (N=6). Their specialties were medical oncology (N=8), radiation oncology (N=6), and gynecological surgery (N=6).

Various representations of the importance of work issues for the doctor-patient encounter

The respondents offered diverse representations of the relevance of the patient's work and RTW issues in the doctor-patient encounter. They reported varying practices of how to address work issues with their patients, ranging from almost total absence of consideration to frequent discussions about the patient's work.

"But we are entirely involved in treatment in one way or another, or in prevention. And the relationship to work, almost never." (Surgeon)

"So, if you want to discuss this subject with patients, there are virtually permanent discussions." (Medical oncologist)

Shared concerns

There was no single approach to the timing and way to address work-related issues with patients. Surgeons tended to address the occupational consequences of specific techniques beforehand, or at follow-up in case of secondary breast reconstruction.

Medical oncologists reported raising work-related issues before or after chemotherapy but never during the chemotherapy itself. Radiation oncologists considered themselves to be in the best position to raise work-related issues at the end of radiotherapy, deemed to constitute the end of "heavy treatment". Many participants shared concerns about the "right time and right way" to address RTW with their patients given the variety of individual situations.

"We don't really know how to situate return to work during patient care, (...) well, I find it difficult to decide when to talk about return to work and what resources are available and already set up to help the patients with that."

(Medical oncologist)

Perceived barriers, needs, and facilitators for RTW

Perceived barriers, needs, and facilitators are listed in table 3. The need for better continuity of care at the end of curative treatment was reported as being important. Several respondents mentioned that BC patients asked for their permission before returning to work. BC specialists stated that, even if they could identify treatment side-effects, they did not ask their patients about their potential impact as barriers to return to work and sometimes minimize them.

"Well, with radiotherapy, there's no... Normally after a patient who has had breast irradiation, there's no problem for her to go back to work afterwards." (Radiation oncologist)

"No, no, I don't think I'm looking for them, the side-effects. You look for them (...) in daily activities. But specifically their impact on work, no." (Medical oncologist)

"So I'll ask her "Is there anything worrying you in your daily life?" But in terms of returning to work... [Coughing]. No, to be honest, no." (Surgeon)

Physical demands of the job, psychological pressure, and adversarial relations in the workplace were hardly mentioned as potential barriers to RTW. The influence of pain, anxiety, or depressive disorders as potential barriers to RTW was rarely mentioned. While the physicians emphasized the importance of social support from colleagues and employers (table 3), the possible role of the OP in this respect was never mentioned.

Professional practices of BC specialists

BC specialists reported a lack of opportunity to discuss work-related issues of their patients. Work and RTW issues were never on the agenda of the weekly multidisciplinary meeting, which was exclusively dedicated to treatment

issues.

[Concerning other oncologists]: "No, very rarely, because we're entirely on the, concerned about, like, managing the disease and treatments." (Medical oncologist)

"But it's true we don't talk about it. (...) It's true that it's not an issue." (Radiation oncologist)

Most respondents agreed as to the importance of the GP and OP regarding RTW. However, they were unable to say precisely what role they could have. They reported mentioning them to their patients as possible contact persons for RTW issues. However, they themselves never took the initiative to contact the OP or GP, except for one medical oncologist.

"(...) but, the question of returning to work, quite honestly, we don't even discuss it with the social worker." (Medical oncologist)

Overall, BC specialists described their role as dedicated to cancer care and cure, predominantly as technical expertise, leaving little room for psychological or survivorship issues. There was no difference in this regard between surgeons, medical oncologists, and radiation oncologists.

"(...) we are entirely involved in the management of the disease and treatment." (Surgeon)

"That is, once the chemo is over, the radiotherapy is over, the surgery has been done, so the person is supposed to get back to normal life, and for us the work has been done" (Medical oncologist)

Lack of time, lack of training and sometimes lack of interest were mentioned about patients' work-related issues.

Several respondents expressed their inability to meet the work-related expectations of BC patients.

"Well, you see, it's complicated, because at the same time, we have to tie up the health aspect; they ask us questions about the prognosis for their disease. And at the same time, we have to answer about work, the legal aspect, which we are not necessarily familiar with either, you see." (Medical oncologist)

Ways to improve BC specialists' involvement in survivors' return to work

The main barriers to the involvement of BC specialists in their patients' RTW issues included (i) lack of time, (ii) lack of knowledge, especially regarding RTW procedures and legislation, (iii) the potential barriers to RTW, (iv) the role of the various actors involved in the RTW process, particularly GP and OP, (v) lack of awareness of the importance of work to their patients, and (vi) a professional attitude exclusively focused on care and cure objectives.

The participants offered no practical solutions to the removal of these barriers. Only one medical oncologist mentioned the possibility of integrating work-related issues in the personalized treatment plan of the patients.

"Maybe we should say: "So, then, about three or four months after the end of the radiotherapy, you should get back to work, well considering that could be as a therapeutic half-time, but we'll talk about it again, it's much too early, first of all let's start the treatment, you need to be on the road to recovery first." (Medical oncologist)

BC specialists' views according to gender and medical specialty

All the respondents expressed an interest in the study and willingly shared their personal limitations regarding RTW in cancer patients during the interviews. None expressed negative feelings about the risk of being judged or stigmatized. No specificities were identified in terms of respondents' age or type of healthcare facility.

"I think what is interesting about this study is that it raises questions that I think are untypical. In any case untypical (...) for a cancer specialist who is used to (...) being immersed in a cancer research environment. Because precisely (...) the theme (...) is not directly the one we deal with on a daily basis, which is optimizing patient treatment."

(Medical oncologist)

Female and male BC specialists sometimes expressed different views. Female specialists said they participated in the study due to a desire to improve their practice, whereas male participants rather expressed their interest in scientific research. Females particularly stressed BC survivors' need for cognitive rehabilitation. Only females mentioned the patients' need to take some time for themselves, to have treatment schedules adapted to their occupational needs, and the fact that they encounter barriers in the workplace due to physical demands or psychological pressure. Males, in contrast, stressed the importance of the patient's personal motivation and temperament in RTW.

BC specialists minimized the side-effects of the treatments they prescribed, ie, medical oncologists understated the

side-effects of chemotherapy, whereas radiation oncologists minimized the side-effects of radiotherapy. During feedback with two interviewees, this finding was confirmed and commented on in terms of medical liability.

"Afterwards, what's true, and it's really true, in oncology, it's never your fault, when a patient has a symptom, it's always the other specialist's fault. Always." (Medical oncologist)

"And there, I think, there's also a forensic problem. You can't be responsible for a problem, uh, the patient has... because in the last analysis, there's the insurance, you know." (Medical oncologist)

Discussion

Main findings

While there is a growing body of studies on RTW issues in cancer patients, the present study is to the best of our knowledge the first specifically to examine BC specialists' perspective on their role in BC survivors' RTW. This qualitative study revealed varying attitudes and practices in BC specialists regarding the relevance of work and return to work issues in the doctor-patient relationship and their role in the patients RTW process. Overall, the BC specialists perceived their role as limited and mainly restricted to management of disease and treatment-related side effects. Participants unanimously expressed difficulties in supporting BC survivors in their RTW in collaboration with GP and OP. The participants consistently identified the following main obstacles: lack of time and awareness of the importance of work for their patients, lack of skills and personal efficacy, as well as professional practices centered on treatment and cure, leaving little room for psychological and occupational issues. Despite these recognized difficulties, specialists also stressed that BC survivors frequently asked them for advice before returning to work.

Barriers and facilitators in the RTW process

Certain participants mentioned treatment side-effects and sequelae as obstacles to RTW, in agreement with the literature (14, 32). Others, however, minimized this and in their consultations did not assess the occupational impact of cancer and treatment, consistent with other reports (33). The majority, on the other hand, cited the determining role of the patient's personality in the RTW process. Factors relating to the workplace environment were rarely mentioned, despite the scientific evidence, especially in case of cognitive disorder or lymphedema limiting work ability (32).

BC specialists' working environment, training, and professional role

The present study found a mismatch between BC specialists' practices and their patients' expectations in terms of support needed in the RTW process following BC (34). This is in line with other reports stating that BC specialists fail to take account of a variety of cancer survivors' needs including, their occupational concerns (5, 28, 35-40). This may be related to factors concerning BC specialists' working environment and medical training. It also raises the question of whether BC specialists should take on a more supportive role in the RTW process.

The working environment of BC survivors is characterized by an insufficient number of professionals to manage an increasing number of complex patients requiring individualized treatments (41). Treatments are so heavy that RTW may seem to be a secondary consideration. At the same time, patient information requires more time and attention, resulting in severe time limits, with an average consultation time that is too short to deal with anything unrelated to diagnosis, disease, prognosis, treatment and treatment options, and side-effects. Moreover, current guidelines and personalized post-cancer plans make no mention of occupational factors among the various fields the BC specialist is supposed to deal with, even though the guidelines do acknowledge maintenance of employment as a major post-cancer issue (42, 43). Finally, mean age at BC diagnosis is around 61 years, so that many patients are not concerned by occupational questions (6, 44). It would thus seem that BC specialists' practices depend on aspects of their working environment and patient characteristics. Yet, the increase of younger women with BC, increased BC survival as well as growing female employment rates and raising retirement age in many countries is leading to a change in BC patient profile with an increasing number of BC survivors concerned by RTW issues (5, 45, 46). BC specialists' initial and continuous training focuses on diagnosis, prognosis, and treatment, with ever increasing technicity, especially in the fields of imaging, biology, and precision medicine. The psychological, social and occupational impact of cancer is little dealt with. This results in lack of knowledge of conditions and legislation regarding work and the various actors and provisions that can be brought into play to facilitate RTW. It also results in

a lack of competence to deal with patients' occupational issues, and a perceived lack of self efficacy in this regard, which could explain why participants did not mention factors related to their patients' working environment as barriers to RTW. Hence, the lack of consideration of RTW issues may be related more to the general barriers in the delivery of psychosocial care to cancer survivors as well as the lack of consideration for psychosocial issues by the healthcare system (28, 40). The lack of RTW help was among the numerous unmet psychological needs identified by cancer patients (22, 39, 40), and inter-relationships exists among poor psychosocial well-being and lower rates of return to work and/or impaired ability to work in cancer survivors (9, 22).

The present findings also point to a lack of communication between BC specialists and other professionals, such as GP, OP and social workers, regarding BC survivors' RTW. This is doubtless multifactorial, involving a lack of time on all sides and insufficient training, habits, and value attached to multidisciplinary teamwork beyond cancer treatment (47). While the communication among healthcare professionals for cancer survivor follow-up, as well as the role of communication between occupational health, employers and colleagues to managing RTW has been identified as key in the cancer survivor in the literature (28, 37, 48, 49), the communication between BC specialists and other professionals regarding RTW has not received much attention. The follow-up of cancer survivors involves different healthcare professionals and the transition from hospital to primary care faces various barriers, including communication but also sometimes patient preference (50). Consistent with the results from our study, GPs have identified the lack of communication and information from BC specialists in the hospital as a barrier to appropriately advice patients on RTW, resulting in sometimes conflicting guidance (28). In the specific field of occupational rehabilitation after cancer, the gap between hospital and community physicians is accentuated by the lack of guidelines as to respective professional roles and the articulation with occupational health services in facilitating RTW (28, 37, 49). These findings are applicable across numerous developed countries, leading to the need of improving collaboration and communication between hospital, community, and occupational professionals to improve continuity of care and adequate RTW guidance for cancer patients (28, 37, 50-53). In accordance with what has been suggested for cancer survivor care more generally, this role should be played by (health) professionals other than BC specialists (37, 49-51, 54) as has been suggested, BC specialists' training and working environment are combined to place them in a difficult position to advise patients on RTW. Despite their patients' expectations (14), they are neither sufficiently trained nor well placed to provide RTW advice themselves. Their professional role focusses the priority on cure and prevention of recurrence, in the context of high demand to keep their knowledge up to date and keep patients informed despite severe lack of time and increasing workload (41, 43).

Implications for healthcare practice and organization

The barriers identified do not seem to be specifically related to the French healthcare system and are in line with findings from other countries (28, 37, 52-54). Lack of communication among healthcare professionals, insufficient knowledge about work-related concerns, and limited resources were recurring themes in these studies.

Better integration of RTW issues in the management of BC patients requires better definitions of healthcare professionals' respective roles. Overcoming the barriers between hospital, community medicine, and occupational health requires improving communication and collaboration so as to improve continuity of care, rehabilitation, and RTW. While the role of BC specialists is limited by the many demands and workload related to cancer care, they should have a determining role in informing their patients of the importance of work in the recovery process and the persons and resources available to help them with this, as well as transmitting the relevant information to other healthcare providers, such as the patient's GP (28), to ensure continuity of care.

The present study's results suggest several means of improving BC specialists' practices in the support to RTW. Our results point out the need to enhance BC specialists' awareness and knowledge by means of targeted information on the importance of work for their patients and of the roles of the different professionals (52, 53); this in turn will enhance their self-efficacy and may lead to a change in behavior. As regards their working environment, finding more time to address RTW may be unrealistic, but guidelines and tools as a support to inform patients and enhance liaison with other professionals could usefully be developed. Also, means of remuneration for collaboration between the different professionals of this orphan issue in the current cancer care process should be explored.

Perspectives for integration in FASTRACS

The results from this study contributed to designing the FASTRACS RTW multicomponent intervention, in particular the steps of intervention mapping and setting up behavioral change matrices by helping to formulate performance objectives for behaviors to be encouraged in BC specialists (55). The first target for the BC specialists is to provide a minimum of advice to patients regarding the importance of RTW for recovery from cancer, relevant resource persons and the usefulness of calling upon these resource persons (GP, OP, social worker, and RTW counsellors). The second is to refer the patient at the end of radiation therapy to a transitional consultation with their GP with a specific liaison letter. According to the logic model of the problem (55), the next step is for the GP to refer the patient to a pre-RTW consultation with an OP to assess work ability and adapt working conditions and time so as to facilitate RTW.

Study strengths and limitations

The strong point of the study lies in the measures taken to ensure validity according to the criteria implemented in qualitative research (56). Sampling enabled the research topic to be explored by varying participant characteristics and work contexts. Triangulation of researchers' disciplines (medicine, psychology, public health) was implemented at the design stage of the study topic, in drawing up the interview guide, and in analyzing and interpreting the results. Qualitative analysis software ensured the traceability of the analysis process and facilitated triangulation. Feedback from two participants corroborated and completed the researchers' interpretation. Data saturation was achieved progressively, with no significant new input during the last interviews. A logbook was updated by the two researchers who collected the data, enabling the non-verbal dimension and context to be included in analysis. The qualitative approach does not allow the present results to be considered representative of the practices of BC specialists as a whole. For them to be extrapolated, surveys of practice in larger representative samples will be needed, notably to confirm whether differences according to gender are real.

That interviews were conducted by two junior investigators may have impaired the richness of the data. This risk was limited by close supervision by one senior investigator. This particularity also had the advantage of reducing social desirability bias and perceived risk of being judged by a peer or senior researcher.

Extrapolation to contexts other than the French health system can only be made in the light of the specificities of the various systems. Barriers and facilitators to RTW after BC and the characteristics of cancer specialists' working environment are similar in many health systems; some countries, however, may have developed specific measures and organizational features to enhance specialists' involvement in accompanying RTW after cancer (57, 58).

Concluding remarks

The present qualitative survey of 20 BC specialist identified several limitations in their practice regarding accompaniment of RTW. These concerned individual characteristics but also medical training and restrictions in their working environment. Larger-scale surveys will be needed in order to describe more precisely BC specialists' RTW-related practices, their determining factors, and possible means of improvement. Any improvements must be integrated in the organization of healthcare so as to benefit all patients. This is the aim of the FASTRACS project: to develop an intervention to facilitate RTW after BC at the level of the AuvergneRhône-Alpes region of France.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional review board (n°IRB 00009118) and the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent was obtained from all individual participants included in the study, before taking part of the study.

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Sidebar

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DETAILS

Subject:	Motivation; Womens health; Potential barriers; Cancer; Cancer therapies; Intervention; Physicians; Content analysis; Hospitals; Researchers; Breast cancer; Oncology; Objectives; Radiation; Interviews; Representations; Patients; Qualitative analysis; Medical prognosis; Age; Surgery; Medical research; Data collection; Family physicians; Sick leave; Qualitative research
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What has been largely overlooked, however, is the fact that these approaches are only valid in linear models and rely on the assumption that there is no interaction between exposure and mediator on the outcome (6). ...]because the importance of controlling for mediator-outcome confounders was never mentioned in Baron & Kenny, many studies have neglected to account for potential confounding factors of the mediator-outcome relationship. ...]whereas a total effect can always be decomposed into a natural direct and indirect effect, controlled direct effects are estimated for every level of the mediator (which may differ substantially depending on the magnitude of the interaction effect between exposure and mediator). An alternative approach in mediation analysis is to quantify controlled direct effects that only rely on assumptions (i) and (iii): no uncontrolled exposure-outcome confounding and no uncontrolled mediator-outcome confounding. ...]some have argued that controlled direct effects are much more policy-relevant because they estimate the proportion of the total effect of the exposure on the outcome that could be eliminated by a specific intervention on the mediator (13, 14). ...]sensitivity analysis is helpful to assess the robustness of the results to potential violations of the underlying assumptions.

Korshøj, M., PhD, Hannerz, H., PhD., Marott, J. L., PhD., Schnohr, P., PhD., Prescott, E., PhD., Clays, E., PhD., & Holtermann, A., PhD. (2020). Does occupational lifting affect the risk of hypertension? cross-sectional and prospective associations in the copenhagen city heart study. *Scandinavian Journal of Work, Environment & Health*, 46(2), 188-197,188A. doi:<https://doi.org/10.5271/sjweh.3850>

Objective The aim of this study was to investigate cross-sectional and prospective associations between heavy occupational lifting and hypertension. **Methods** Data from the third, fourth and fifth examinations of the Copenhagen City Heart Study were included. Multivariable logistic regression models were applied to adjust for sex, age, body mass index (BMI), smoking, education, self-rated cardiorespiratory fitness, vital exhaustion and baseline blood pressure, and were used to estimate (i) the cross-sectional association between heavy occupational lifting and hypertension, defined as using anti-hypertensives or having a systolic blood pressure (SBP) >140 mmHg or diastolic blood pressure (DBP) >90 mmHg, and (ii) the prospective association between heavy occupational lifting and risk of becoming a systolic blood pressure case, defined as an above median change (from baseline to follow-up) and/or a shift from no use of anti-hypertensives at baseline to use of anti-hypertensives at a ten-year follow-up. **Results** Both cross-sectional odds ratio (OR) 1.06, 95% confidence interval (CI) 0.94-1.20] and prospective (OR 1.10, 95% CI 0.92-1.31) analysis indicated no relations. Explorative prospective analyses suggested linear associations between heavy occupational lifting and systolic blood pressure among participants using antihypertensives. Exposure to heavy occupational lifting tended to increase the incidence of hypertension (OR 1.30, 95% CI 0.97-1.73) among participants >50 years. **Conclusions** No associations were seen among the general population. Positive associations were seen among users of anti-hypertensives and participants >50 years, indicating these groups as vulnerable to increases in blood pressure when exposed to occupational lifting.

Lutz, N.,cand PhD., Clarys, P., PhD., Koenig, I.,cand PhD., Deliens, T., PhD., Taeymans, J., PhD., & Verhaeghe, N., PhD. (2020). Health economic evaluations of interventions to increase physical activity and decrease sedentary behavior at the workplace: A systematic review. *Scandinavian Journal of Work, Environment & Health*, 46(2), 127-142,127A. doi:<https://doi.org/10.5271/sjweh.3871>

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