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Work-related mental fatigue, physical activity and risk of insomnia symptoms: Longitudinal data from the Norwegian HUNT Study

Running head: Mental fatigue, physical activity and insomnia

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ABSTRACT

Objective/Background: To examine the prospective association between work-related mental fatigue and risk of insomnia symptoms, and if leisure time physical activity modifies this association.

Participants: A total of 8,464 women and 7,480 men who participated in two consecutive surveys of the Norwegian HUNT study.

Methods: The study comprises longitudinal data on persons who were vocationally active and without insomnia symptoms at baseline in 1995-1997. We used a modified Poisson regression model to calculate adjusted risk ratios (RRs) with a 95% confidence interval (CI) for insomnia symptoms at follow-up in 2006-2008 associated with work-related mental fatigue and leisure time physical activity at baseline.

Results: Women and men who always experienced mental fatigue after a workday had RRs of insomnia symptoms of 2.55 (95% CI 1.91-3.40) and 2.61 (95% CI 1.80-3.78), respectively, compared to workers who never or seldom had this experience. There was no strong modifying effect of leisure time physical activity on this association, but workers who always experienced mental fatigue had a RR of insomnia symptoms of 3.17 (95% CI 2.28-4.40) if they reported low physical activity and a RR of 2.52 (95% 1.89-3.39) if they reported high physical activity.

Conclusion: This study shows that work-related mental fatigue, caused by high cognitive workload, is a strong risk factor for insomnia symptoms. There was no clear modifying effect of leisure time physical activity but workers who experienced excessive work-related fatigue accompanied by low physical activity had the highest risk of insomnia symptoms.

Key words: Psychosocial work demands, work exposure, sleep problems, occupational health

INTRODUCTION

Insomnia symptoms are common in the working population (Kuppermann et al., 1995; Linton & Bryngelsson, 2000; Yong, Li, & Calvert, 2017) and may have several negative consequences, such as increased risk of work-related injuries (Uehli et al., 2014) and reduced productivity (Rosekind et al., 2010), leading to increased costs for the employers and the community (Godet-Cayre et al., 2006). Furthermore, insomnia is associated with increased risk of several adverse health outcomes, including cardiovascular disease, type 2 diabetes, hypertension, musculoskeletal pain, and mental disorders (Anothaisintawee, Reutrakul, Van Cauter, & Thakkinstian, 2015; Ayas et al., 2003; Cappuccio, Cooper, D'Elia, Strazzullo, & Miller, 2011; Cappuccio, D'Elia, Strazzullo, & Miller, 2010; Dew et al., 2003; Sivertsen, Krokstad, Øverland, & Mykletun, 2009; Stranges et al., 2010; Uhlig, Sand, Nilsen, Mork, & Hagen, 2018; Vgontzas, Liao, Bixler, Chrousos, & Vela-Bueno, 2009). The negative consequences of insomnia symptoms for both the society and affected individuals underscore the importance of identifying modifiable risk factors. This knowledge will provide important input for developing evidence-based interventions that target factors known to cause insomnia symptoms.

Adverse psychosocial work stressors are associated with increased risk of sleep problems (de Lange et al., 2009; Jansson & Linton, 2006; Linton, 2004; Ota et al., 2009; Ribet & Derriennic, 1999; Van Laethem, Beckers, Kompier, Dijksterhuis, & Geurts, 2013). The mechanisms underlying this association are complex and not entirely clear but it has been shown that cognitive arousal due to work-related stress (Linton, 2004) and accumulated fatigue due to repeated exposure to high work demands increase the risk of insomnia symptoms (Skarpsno, Nilsen, Sand, Hagen, & Mork, 2018). Other studies have shown that high cognitive work demands are associated with sustained psychophysiological activation (Geurts & Sonnentag,

2006) and excessive mental fatigue (Mizuno et al., 2011). Further, exposure to high cognitive work demands may elicit different mental responses across individuals (Too & Butterworth, 2018), and the long-term influence on insomnia symptoms may thereby depend on the coping capacity of the individual worker (Otsuka et al., 2017). Perceived work-related mental fatigue may therefore be a relevant and sensitive measure to capture the impact of cognitive workload imposed on the individual worker, and consequently, provide insight about the potential link between psychosocial work stressors and risk of insomnia symptoms.

Leisure time physical activity may improve the capacity to cope with adverse psychosocial work demands (Arvidson, Borjesson, Ahlborg, Lindegard, & Jonsdottir, 2013) and protect against undue work-related fatigue (Puetz, 2006). Furthermore, previous studies report positive effects of physical activity on sleep (Morgan, 2003; Ohida et al., 2001; Youngstedt & Kline, 2006), and physically active people may have less problems falling asleep, less nocturnal awakenings and improved restorative sleep (Flausino, Da Silva Prado, de Queiroz, Tufik, & de Mello, 2012; King et al., 2008; Loprinzi & Cardinal, 2011; Soltani et al., 2012). In a recent study, we showed that leisure time physical activity is inversely associated with non-restorative sleep while occupational physical activity is positively and dose-dependently associated with insomnia symptoms (Skarpsno, Mork, Nilsen, Jorgensen, & Holtermann, 2018). It is therefore conceivable that workers who are physically active during leisure time are less likely to develop insomnia symptoms (Otsuka et al., 2017). To gain further knowledge about the joint effect of work-related mental fatigue and leisure time physical activity may therefore be valuable for improved prevention of insomnia among workers.

The aim of this population-based study was twofold. First, to prospectively examine the association between work-related mental fatigue and risk of insomnia symptoms, and second, to

explore if leisure time physical activity modifies this association. Since women and men may perceive psychosocial work exposures differently (Eng et al., 2011), we explored the sex-specific association between work-related mental fatigue and risk of insomnia symptoms.

METHODS

Study population

This prospective study utilized longitudinal data from the second (1995-1997) and third (2006-2008) survey of the HUNT Study. All inhabitants aged 20 years or older residing in Nord-Trøndelag County in Norway have been invited to participate in the HUNT Study. In HUNT2, 93,898 people were invited to participate, and 65,237 (69.5%) accepted the invitation. In HUNT3 93,860 people were invited and 50,839 (54.1%) accepted the invitation. Information on lifestyle and health-related factors was collected by questionnaires and a clinical examination at both HUNT2 and HUNT3. More detailed information about the HUNT Study can be found at http://www.ntnu.edu/hunt.

For the purpose of the current study, we used data from 36,984 persons who participated in both HUNT2 and HUNT3. Of these, we excluded 8,951 persons who were not vocationally active at HUNT2. Further, we excluded 2,153 persons who were ≥60 years at HUNT2, since they most likely would retire from work during the follow-up period (usual retirement age in Norway is 67 years). We also excluded 2,164 persons who reported insomnia symptoms and 931 persons who reported use of sedatives and/or sleeping medicine at baseline in HUNT2. Further, we excluded 4,170 persons with incomplete information on work-related mental fatigue at HUNT2. Out of the remaining 18,615 persons, 15,944 answered relevant insomnia questions in both surveys. The prospective analysis was therefore based on information from 8,464 women

and 7,480 men aged 20-60 years, who were vocationally active and without insomnia symptoms at the time of HUNT2.

All participants signed a written consent, and the study was approved by the Regional Committee for Ethics in Medical Research (project no. 2014/612 REK midt). The study was carried out according to the Declaration of Helsinki.

Insomnia symptoms

Insomnia symptoms at baseline in HUNT2 were assessed by two questions: "Have you had problems falling asleep during the last month?" and "During the last month, did you ever wake up too early, not being able to fall asleep again?" with four responses options on each question: "Never", "Occasionally", "Often", and "Almost every night". Participants who reported "Never" or "Occasionally" on both questions were considered unlikely to have insomnia at baseline and were included into the study. Participants who reported "Often" or "Almost every night" on one or both of the questions were excluded from the current study.

At follow-up in HUNT3, insomnia symptoms were assessed by the following four questions: 1) "How often during the last three months have you had difficulty falling asleep at night?", 2) "How often during the last three months have you woken up repeatedly during the night?", 3) "How often during the last three months have you woken too early and couldn't get back to sleep?", and 4) "How often during the last three months have you felt sleepy during the day?", with three response options on each question: "Never/seldom", "Sometimes" and "Several times a week". Participants were classified with insomnia symptoms if they answered, "Several times a week" on at least one of the questions 1-3, and 'Several times a week' on question 4. The information retrieved from these four questions approximates the information

necessary to diagnose insomnia according to the DSM-V criteria (American Psychiatric Association, 2013). The independent associations for each of the insomnia questions were also investigated. For this analysis, "Several times a week" was used to indicate increased risk for each item.

Mental fatigue

Work-related mental fatigue at baseline in HUNT2 was assessed by the question "Does your work require so much concentration and attention that you often feel worn out after a day's work?" with the response options: "Yes, nearly always", "Quite often", "Seldom", and "Never, or almost never". We then classified participants into three categories: Never/seldom fatigued (never or almost never/seldom), often fatigued (quite often) and always fatigued (yes, nearly always).

Leisure time physical activity

Leisure time physical activity at baseline in HUNT2 was assessed by the question: "How much of your leisure time have you been physically active during the last year? (Think of a weekly average for the year. Your commute to work counts as leisure time)". The participants were then asked to specify number of hours per week of light (no sweating or heavy breathing) and/or hard (sweating and heavy breathing) physical activity with the response options: "None", "Less than 1 hour", "1-2 hours" and "3 or more hours" for both light and hard activity. Based on this information, we constructed a new variable with two categories combining information on light and hard activity: low leisure time physical activity (≤2 h light and no hard activity) and high leisure time physical activity (>2 h light and/or any hard activity).

Other variables

The Hospital Anxiety and Depression Scale (HADS) was used to assess symptoms of anxiety and depression. HADS is a validated self-rating questionnaire including seven questions on anxiety and seven questions on depression (Bjelland, Dahl, Haug, & Neckelmann, 2002). As recommended, the cutoff score was set to ≥8 on both anxiety and depression and were dichotomized as presence or no presence of anxiety or depression (Bjelland et al., 2002). Education was assessed by the question: "What is your highest level of education?", and were divided in four categories: "primary school", "high school" "college ≤4 years" and "college >4 years". Shift work was assessed by the question: "Do you work shifts, at night, or on call?", with two response options "no" and "yes". Participants were asked to indicate number of working hours based on the following question: "How many hours of paid work do you have a week?". The answers were dichotomized into "<45 hours" and "≥45 hours"). Physical work demands were assessed by the questions: "How would you describe your work?", with the response options: "Mostly sedentary work (e.g. at a desk, on an assembly line)", "Much walking at work (e.g. delivery work, light industrial work, teaching)", "Much walking or lifting at work (e.g. postman, nurse, construction work)", and "Heavy physical work (e.g. forestry work, heavy agricultural work, heavy construction)". At follow-up in HUNT3, sleep apnea was assessed by the following question: "How often during the last three months have you stopped breathing when you were sleeping (sleep apnea)?", with the response options: "Never/seldom", "Sometimes" and "Several times a week". Participants were classified with symptoms of sleep apnea if they answered "Sometimes" or "Several times a week".

Statistical analysis

A modified Poisson regression was used to estimate risk ratios (RRs) of insomnia symptoms associated with work-related mental fatigue. Participants who reported that they "often" or "always" experienced work-related mental fatigue were compared to the reference group who reported to experience work-related mental fatigue "never/seldom". The precision of the RRs was assessed by 95% confidence intervals (CIs) using robust variance estimation. All associations were stratified by sex and adjusted for potential confounding by age (20-29, 30-39, 40-49, 50-59 years), HADS score (0-7, 8-21, unknown), education (primary school, high school, college ≤4 years, college >4 years, unknown), shift work (no, yes and unknown), working hours (<45 hours, ≥45 hours and unknown), and physical work demands (mostly sedentary, much walking, much walking or lifting, heavy physical work, unknown).

We estimated the joint effect of work-related mental fatigue and leisure time physical activity on risk of insomnia symptoms using physically active workers who experienced work-related mental fatigue "never/seldom" as the reference group. Further, these analyses were conducted on a pooled sample adjusting for sex (women, man). Potential effect modification between the variables was assessed as departure from additive effects calculating the relative excess risk due to interaction (RERI) (Andersson, Alfredsson, Kallberg, Zdravkovic, & Ahlbom, 2005). We calculated RERI estimates with 95% CIs from the following equation: $RERI = RR_{\text{low physical activity and always mental fatigue}} - RR_{\text{high physical activity and always mental fatigue}} - RR_{\text{low physical activity and never/seldom mental fatigue}} + 1$ i.e., RERI >0 indicate a synergistic effect beyond an additive effect.

Since daytime sleepiness may indicate a specific subset of individuals with insomnia or other sleep disorders, we conducted two supplementary analyses to assess the robustness of the

results. First, we excluded workers with self-reported symptoms of sleep apnea. Second, we excluded workers with "daytime sleepiness" from the insomnia definition.

All statistical analyses were performed using Stata for Windows, version 13.1 (StataCorp LP, College Station, Texas).

RESULTS

At follow-up in HUNT3, 471 (5.6%) women and 287 (3.8%) men reported insomnia symptoms. Table 1 shows baseline characteristics of the study population stratified by sex and work-related mental fatigue. The proportion of workers who "always" experience mental fatigue from work was 7.0% among women and 5.9% among men.

TABLE 1

Table 2 shows the associations between work-related mental fatigue and risk of insomnia symptoms. Women and men who always experienced mental fatigue after work had a threefold increased risk of insomnia symptoms, with RRs of 2.55 (95% CI 1.91-3.40) and 2.61 (95% CI 1.80-3.78), respectively. Furthermore, work-related mental fatigue was associated with increased risk of all symptoms used in the classification of insomnia (Supplementary table I). The association was somewhat stronger for "daytime sleepiness" than the other symptoms while the weakest association was found for "waking up too early".

TABLE 2

Table 3 shows the joint effect of work-related mental fatigue and leisure time physical activity on risk of insomnia symptoms. Compared to workers with high leisure time physical activity and who "never/seldom" experienced work-related mental fatigue, workers who "always" experience mental fatigue after work had a RR of 3.17 (95% CI 2.28-4.40) if they reported low leisure time

physical activity, and a RR of 2.52 (95% 1.89-3.39) if they reported high leisure time physical activity levels. This corresponds to a RERI of 0.41 (95% CI -0.80-1.60). RERI estimates for the association with the separate symptoms used in the classification of insomnia symptoms ranged between 0.01 and 0.37 (Supplementary Table II).

TABLE 3

Supplementary analyses

The exclusion of workers with self-reported symptoms of sleep apnea had negligible influence on the association between work-related mental fatigue and risk of insomnia symptoms among women while the association was strengthened among men (i.e., men who always experienced mental fatigue had a RR of 2.98 [95% CI 1.91-4.63]). This exclusion had negligible influence on the estimates in the analysis of joint effect. The association between work-related mental fatigue and insomnia symptoms became somewhat attenuated when removing "daytime sleepiness" as a criterion in the definition of insomnia symptoms, i.e., compared with workers without work-related mental fatigue, women and men who reported always to be mentally fatigued had RRs of insomnia symptoms of 1.59 (95% CI 1.39-1.81) and 1.66 (95% CI 1.37-2.01), respectively (Supplementary Table III). Further, workers who "always" experienced mental fatigue had a RR of 1.67 (95% CI 1.38-2.01) if they reported low leisure time physical activity, and a RR of 1.54 (95% 1.32-1.80) if they reported high leisure time physical activity levels, compared to workers with high leisure time physical activity and who "never/seldom" experienced work-related mental fatigue.

DISCUSSION

The main finding in the current study is the positive and strong association between work-related mental fatigue and risk of insomnia symptoms. Women and men who always experienced mental fatigue in relation to work had more than a twofold increased risk of insomnia symptoms compared to workers who never experienced work-related mental fatigue. Our analysis of joint effects showed that leisure time physical activity had minor modifying influence on the adverse association between work-related mental fatigue and risk of insomnia symptoms, but workers with the combination of excessive fatigue and low leisure time physical activity had the highest risk of insomnia symptoms.

Different methods for assessing cognitive workload along with different study designs limit the possibility to compare our results with previous findings. Previous longitudinal studies have shown that psychosocial work stressors are associated with increased risk of poor sleep (de Lange et al., 2009; Jansson & Linton, 2006; Linton, 2004; Ota et al., 2009; Ribet & Derriennic, 1999; Van Laethem et al., 2013). A possible explanation for these findings is that prolonged exposure to high cognitive work demands results in sustained psychophysiological activation. For instance, sustained activation of the sympathetic nervous system leads to accumulation of fatigue (Geurts & Sonnentag, 2006) that in turn increases the risk of sleep disturbances (Michael H. Bonnet & Arand, 2010). Common symptoms of insufficient recovery and accumulated fatigue is elevated heart rate, undue fatigue and persistent sleep problems (Sluiter, Frings-Dresen, van der Beek, & Meijman, 2001). Interestingly, it has been shown that the effect of stressors vary considerably between individuals and the typical response among susceptible individuals is elevated sympathetic activation and poor sleep (M. H. Bonnet & Arand, 2003; Otsuka et al., 2017). It is therefore conceivable that the ability to cope with repeated and prolonged exposure to

high cognitive work demands vary between individuals. The individual's subjective response to the exposure may therefore be a more appropriate measure to determine the health effects of psychosocial work demands. This idea is supported by a recent study, showing that individual perception of work-related physical fatigue is strongly associated with increased risk of insomnia irrespective of physical work demands (Skarpsno, Nilsen, et al., 2018). The current study expands on these findings by showing that perceived mental fatigue is a strong risk factor for insomnia symptoms. However, it should be noted that we used a question about feeling of sleepiness as a proxy for the daytime consequence of insomnia symptoms, and it is possible that this introduces a less precise outcome measure (i.e., an increased risk of misclassification). Moreover, it is also possible that other sleep disorders than insomnia (e.g., sleep apnea) influence the score of daytime sleepiness. In a sensitivity analysis excluding daytime sleepiness, the association between work-related mental fatigue and insomnia symptoms became somewhat attenuated; however, work-related mental fatigue was still positively and strongly associated with risk of insomnia symptoms. Furthermore, removing participants with self-reported sleep apnea had negligible influence on the results. Thus, reducing work-related mental fatigue seems to be an important target for measures aimed at reducing incidence of insomnia symptoms in the working population.

Work organization and the nature of work could also have influenced the association between work-related mental fatigue and insomnia symptoms. Previous studies have shown that low job control and low social support (Kim et al., 2011; Runeson, Lindgren, & Wahlstedt, 2011), job insecurity (Kim et al., 2011) and negative emotional experiences at work (J. B. Park, Nakata, Swanson, & Chun, 2013) are associated with insomnia symptoms. For instance, workers going from slow work and high decision authority to fast work and low decision authority are

more susceptible to develop sleep problems and fatigue (de Lange et al., 2009). Different levels of decision authority in combination with psychosocial work stressors may therefore lead to an overload response. Although the current study indicates a strong association between work-related mental fatigue and risk of insomnia symptoms, we cannot exclude the possibility that other work stressors influenced our findings. For instance, it has been suggested that cognitive intrusion caused by stressful exposures increases the risk of insomnia (Drake, Pillai, & Roth, 2014). Rumination and worrying thoughts may be factors that mediate the negative effects of work stress into poor sleep (Berset, Elfering, Lüthy, Lüthi, & Semmer, 2011). This view is supported by a cognitive model of insomnia, suggesting that negatively toned cognitive activity, autonomic arousal and distress are factors that may contribute to insomnia (Harvey, 2002). Further, some evidence indicates that premorbid sleep reactivity and hyperarousal play important roles in the aetiology of insomnia (Kalmbach et al., 2018). Cognitive detachment and mental recovery may therefore explain the association between high cognitive workload and development of insomnia symptoms (Berset et al., 2011; Geurts & Sonnentag, 2006). Some workplace interventions have demonstrated promising results for reducing psychological distress and insomnia symptoms in specific populations with high work stress and insomnia (Yamamoto et al., 2016). Thus, interventions aimed at reducing adverse psychosocial work stress may help to reduce the risk of insomnia.

To the best of our knowledge, no studies have investigated if leisure time physical activity influences the association between work-related mental fatigue and risk of insomnia. Although we found no clear interaction, our analysis of the joint effect of mental fatigue and leisure time physical activity showed that the adverse effect of mental fatigue on risk of insomnia was slightly weaker in people who reported high leisure time physical activity compared to those

who reported low physical activity. These results are in line with a recent study, showing that low-intensity aerobic exercise may reduce overall fatigue among workers with symptoms of work-related fatigue (de Vries, van Hooff, Guerts, & Kompier, 2017). The underlying mechanism for this association is not entirely clear, but it is likely that regular exercise improves sleep quality (Smagula et al., 2015) and thereby the recovery process from fatiguing work. For instance, both experimental and observational studies suggest that physical activity have a weak, but beneficial effect on sleep onset latency, wake time after sleep onset, and total sleep time in people without insomnia (Flausino et al., 2012; Loprinzi & Cardinal, 2011; Soltani et al., 2012). Furthermore, leisure time physical activity may also improve psychological health and well-being (S. Park, 2014; Teychenne, Costigan, & Parker, 2015), which in turn may reduce the risk of insomnia symptoms (Smagula et al., 2015). However, it should be noted that leisure time physical activity and work-related mental fatigue were measured at the same time, and we cannot exclude the possibility that these results could reflect that workers who better withstand high mental work demands are also able to maintain a higher level of leisure time physical activity.

Strengths of the current study include the prospective design, the large working population, and the possibility to adjust for several potentially confounding variables with known impact on insomnia symptoms. Importantly, we excluded workers at baseline with insomnia symptoms and workers who used sedative and/or sleep medication. Further, the insomnia questions in HUNT3 have been found to have acceptable reliability (Engstrøm et al., 2011) Finally, it should be noted that there were minor differences between workers included in the current study compared to those with missing information about insomnia at follow-up.

Some limitations should be considered when interpreting the results of the current study. First, the question used to assess work-related mental fatigue has not been validated. Second, the

classification of leisure time physical activity was based on self-reports. Third, the classification of insomnia in HUNT2 was less specific than in HUNT3 in terms of resembling the DSM-V criteria (American Psychiatric Association, 2013). The questions in HUNT2 did not include information about nighttime awakenings or daytime impairments, and it is possible that some of the participants had these symptoms at baseline. Further, the questions in HUNT2 only refer to symptoms the last month and we cannot differentiate between short-term and chronic insomnia (symptoms that persist for at least three months). In HUNT3, we had additional information about difficulty maintaining sleep and daytime sleepiness. However, we used a question about feeling of sleepiness (not actual sleepiness) as a proxy for the daytime consequence of insomnia symptoms. Thus, it is uncertain whether the question in HUNT3 about daytime sleepiness is a good measure of distress or impairment in social, occupational, educational, academic, behavioral, or other important areas of functioning. Moreover, the response option "several times a week" has been shown to include people who have sleep problems twice a week or more (Engstrøm et al., 2011), while the DSM-V criteria requires the symptoms to be present three times or more per week. Our questions do not capture whether the insomnia symptoms occur regardless of the presence of a coexisting mental or medical conditions. However, we tried to make the classification of insomnia at HUNT3 more specific by excluding participants with self-reported symptoms of sleep apnea. Unfortunately, we have no data on continuity of work, changes in employment status, exposure variation or the progression of fatigue, leisure time physical activity and insomnia symptoms during the follow-up period. Further, we have no information about work stress or other psychosocial work factors that could potentially confound or mediate the association between work-related mental fatigue and insomnia. Thus, we cannot exclude the possibility that the influence of other unmeasured and unknown work stressors have

biased our results. Future prospective studies should therefore include more information about psychosocial work stressors that could potentially influence the association between mental fatigue and insomnia. Further, disentangling the complex association between work-related mental fatigue and insomnia require longitudinal data with repeated measurements of these factors. Finally, future studies should include objective measurements of all dimensions of leisure time physical activity and more comprehensive sleep questionnaire batteries.

In conclusion, the current study indicates that excessive work-related mental fatigue is positively and strongly associated with risk of insomnia in both women and men. There was no clear modifying effect of leisure time physical activity, but workers with the combination of excessive fatigue and low physical activity had the highest risk of insomnia. Reduction of work-related mental fatigue, caused by high cognitive workload, may represent an important target for preventive measures aimed at reducing the incidence of insomnia in the working population.

REFERENCES

American Psychiatric Association. (2013). *Diagnostic and Statistical Manual of Mental Disorders, 5th edn.* : American Publishing, Washington, DC.

Andersson, T., Alfredsson, L., Kallberg, H., Zdravkovic, S., & Ahlbom, A. (2005). Calculating measures of biological interaction. *European Journal of Epidemiology, 20*(7), 575-579. doi:10.1007/s10654-005-7835-x

Anothaisintawee, T., Reutrakul, S., Van Cauter, E., & Thakkinstian, A. (2015). Sleep disturbances compared to traditional risk factors for diabetes development: Systematic review and meta-analysis. *Sleep Medicine Reviews, 30,* 11-24. doi:10.1016/j.smrv.2015.10.002

Arvidson, E., Borjesson, M., Ahlborg, G., Jr., Lindegard, A., & Jonsdottir, I. H. (2013). The level of leisure time physical activity is associated with work ability-a cross sectional and prospective study of health care workers. *BMC Public Health, 13,* 855. doi:10.1186/1471-2458-13-855

Ayas, N. T., White, D. P., Al-Delaimy, W. K., Manson, J. E., Stampfer, M. J., Speizer, F. E., . . . Hu, F. B. (2003). A prospective study of self-reported sleep duration and incident diabetes in women. *Diabetes Care, 26*(2), 380-384. doi:10.2337/diacare.26.2.380

Berset, M., Elfering, A., Lüthy, S., Lüthi, S., & Semmer, N. K. (2011). Work stressors and impaired sleep: rumination as a mediator. *Stress and Health, 27*(2), e71-e82. doi:doi:10.1002/smi.1337

Bjelland, I., Dahl, A. A., Haug, T. T., & Neckelmann, D. (2002). The validity of the Hospital Anxiety and Depression Scale. An updated literature review. *Journal of Psychosomatic Research, 52*(2), 69-77. doi:10.1016/S0022-3999(01)00296-3

Bonnet, M. H., & Arand, D. L. (2003). Situational insomnia: consistency, predictors, and outcomes. *Sleep, 26*(8), 1029-1036. doi:10.1093/sleep/26.8.1029

Bonnet, M. H., & Arand, D. L. (2010). Hyperarousal and insomnia: State of the science. *Sleep Medicine Reviews, 14*(1), 9-15. doi:10.1016/j.smrv.2009.05.002

Cappuccio, F. P., Cooper, D., D'Elia, L., Strazzullo, P., & Miller, M. A. (2011). Sleep duration predicts cardiovascular outcomes: a systematic review and meta-analysis of prospective studies. *European Heart Journal, 32*(12), 1484-1492. doi:10.1093/eurheartj/ehr007

Cappuccio, F. P., D'Elia, L., Strazzullo, P., & Miller, M. A. (2010). Quantity and quality of sleep and incidence of type 2 diabetes: a systematic review and meta-analysis. *Diabetes Care, 33*(2), 414-420. doi:10.2337/dc09-1124

de Lange, A. H., Kompier, M. A., Taris, T. W., Geurts, S. A., Beckers, D. G., Houtman, I. L., & Bongers, P. M. (2009). A hard day's night: a longitudinal study on the relationships among job demands and job control, sleep quality and fatigue. *Journal of Sleep Research, 18*(3), 374-383. doi:10.1111/j.1365-2869.2009.00735.x

de Vries, J. D., van Hooff, M. L., Guerts, S. A., & Kompier, M. A. (2017). Exercise to reduce work-related fatigue among employees: a randomized controlled trial. *Scandinavian Journal of Work, Environment & Health, 43*(4), 337-349. doi:10.5271/sjweh.3634

Dew, M., Hoch, C., Buysse, D., Monk, T., Begley, A., Houck, P., . . . Reynolds, C. (2003). Healthy older adults' sleep predicts all-cause mortality at 4 to 19 years of follow-up. *Psychosomatic Medicine, 65*(1), 63-73. doi:10.1097/01.PSY.0000039756.23250.7C

Drake, C. L., Pillai, V., & Roth, T. (2014). Stress and sleep reactivity: a prospective investigation of the stress-diathesis model of insomnia. *Sleep, 37*(8), 1295-1304. doi:10.5665/sleep.3916

Eng, A., t Mannetje, A., McLean, D., Ellison-Loschmann, L., Cheng, S., & Pearce, N. (2011). Gender differences in occupational exposure patterns. *Occupational & Environmental Medicine, 68*(12), 888-894. doi:10.1136/oem.2010.064097

Engstrøm, M., Ødegård, S., Sand, T., Stovner, L., Zwart, J., & Hagen, K. (2011). The reliability of a new sleep screening questionnaire for large population-based studies: The third Nord-Trøndelag Health Study. *The Open Sleep Journal, 4*, 14-19. doi:10.2174/1874620901104010014

Flausino, N. H., Da Silva Prado, J. M., de Queiroz, S. S., Tufik, S., & de Mello, M. T. (2012). Physical exercise performed before bedtime improves the sleep pattern of healthy young good sleepers. *Psychophysiology, 49*(2), 186-192. doi:10.1111/j.1469-8986.2011.01300.x.

Geurts, S. A., & Sonnentag, S. (2006). Recovery as an explanatory mechanism in the relation between acute stress reactions and chronic health impairment. *Scandinavian Journal of Work, Environment & Health, 32*(6), 482-492. doi:10.5271/sjweh.1053

Godet-Cayre, V., Pelletier-Fleury, N., Le Vaillant, M., Dinet, J., Massuel, M. A., & Leger, D. (2006). Insomnia and absenteeism at work. Who pays the cost? *Sleep, 29*(2), 179-184. doi:10.1093/sleep/29.2.179

Harvey, A. G. (2002). A cognitive model of insomnia. *Behaviour Research and Therapy, 40*(8), 869-893. doi:10.1016/S0005-7967(01)00061-4

Jansson, M., & Linton, S. J. (2006). Psychosocial work stressors in the development and maintenance of insomnia: a prospective study. *Journal of Occupational Health Psychology, 11*(3), 241-248. doi:10.1037/1076-8998.11.3.241

Kalmbach, D. A., Cuamatzi-Castelan, A. S., Tonnu, C. V., Tran, K. M., Anderson, J. R., Roth, T., & Drake, C. L. (2018). Hyperarousal and sleep reactivity in insomnia: current insights. *Nature and Science of Sleep, 10*, 193-201. doi:10.2147/nss.s138823

Kim, H. C., Kim, B. K., Min, K. B., Min, J. Y., Hwang, S. H., & Park, S. G. (2011). Association between job stress and insomnia in Korean workers. *Journal of Occupational Health, 53*(3), 164-174. doi:10.1539/joh.10-0032-OA

King, A. C., Pruitt, L. A., Woo, S., Castro, C. M., Ahn, D. K., Vitiello, M. V., . . . Bliwise, D. L. (2008). Effects of Moderate-Intensity Exercise on Polysomnographic and Subjective Sleep Quality in Older Adults With Mild to Moderate Sleep Complaints. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences, 63*(9), 997-1004. doi:10.1093/gerona/63.9.997

Kuppermann, M., Lubeck, D. P., Mazonson, P. D., Patrick, D. L., Stewart, A. L., Buesching, D. P., & Fifer, S. K. (1995). Sleep problems and their correlates in a working population. *Journal of General Internal Medicine, 10*(1), 25-32.

Linton, S. J. (2004). Does work stress predict insomnia? A prospective study. *British Journal of Health Psychology, 9*(Pt 2), 127-136. doi:10.1348/135910704773891005

Linton, S. J., & Bryngelsson, I. L. (2000). Insomnia and Its Relationship to Work and Health in a Working-Age Population. *Journal of Occupational Rehabilitation, 10*(2), 169-183. doi:10.1023/a:1009408204694

Loprinzi, P. D., & Cardinal, B. J. (2011). Association between objectively-measured physical activity and sleep, NHANES 2005–2006. *Mental Health and Physical Activity, 4*(2), 65-69. doi:10.1016/j.mhpa.2011.08.001

Mizuno, K., Tanaka, M., Yamaguti, K., Kajimoto, O., Kuratsune, H., & Watanabe, Y. (2011). Mental fatigue caused by prolonged cognitive load associated with sympathetic hyperactivity. *Behavioral and Brain Functions, 7*, 17. doi:10.1186/1744-9081-7-17

Morgan, K. (2003). Daytime activity and risk factors for late-life insomnia. *Journal of Sleep Research, 12*(3), 231-238. doi:10.1046/j.1365-2869.2003.00355.x

Ohida, T., Kamal, A., Uchiyama, M., Kim, K., Takemura, S., Sone, T., & Ishii, T. (2001). The influence of lifestyle and health status factors on sleep loss among the Japanese general population. *Sleep, 24*(3), 333-338.

Ota, A., Masue, T., Yasuda, N., Tsutsumi, A., Mino, Y., Ohara, H., & Ono, Y. (2009). Psychosocial job characteristics and insomnia: a prospective cohort study using the Demand-Control-Support (DCS) and Effort-Reward Imbalance (ERI) job stress models. *Sleep Medicine, 10*(10), 1112-1117. doi:10.1016/j.sleep.2009.03.005

Otsuka, Y., Kaneita, Y., Itani, O., Nakagome, S., Jike, M., & Ohida, T. (2017). Relationship between stress coping and sleep disorders among the general Japanese population: a nationwide representative survey. *Sleep Medicine, 37*, 38-45. doi:10.1016/j.sleep.2017.06.007

Park, J. B., Nakata, A., Swanson, N. G., & Chun, H. (2013). Organizational factors associated with work-related sleep problems in a nationally representative sample of Korean workers. *International Archives of Occupational and Environmental Health, 86*(2), 211-222. doi:10.1007/s00420-012-0759-3

Park, S. (2014). Associations of physical activity with sleep satisfaction, perceived stress, and problematic Internet use in Korean adolescents. *BMC Public Health, 14*(1), 1143. doi:10.1186/1471-2458-14-1143

Puetz, T. W. (2006). Physical activity and feelings of energy and fatigue: epidemiological evidence. *Sports Medicine, 36*(9), 767-780. doi:10.2165/00007256-200636090-00004

Ribet, C., & Derriennic, F. (1999). Age, working conditions, and sleep disorders: a longitudinal analysis in the French cohort E.S.T.E.V. *Sleep, 22*(4), 491-504. doi:10.1093/sleep/22.4.491

Rosekind, M. R., Gregory, K. B., Mallis, M. M., Brandt, S. L., Seal, B., & Lerner, D. (2010). The Cost of Poor Sleep: Workplace Productivity Loss and Associated Costs. *Journal of Occupational and Environmental Medicine, 52*(1), 91-98. doi:10.1097/JOM.0b013e3181c78c30

Runeson, R., Lindgren, T., & Wahlstedt, K. (2011). Sleep problems and psychosocial work environment among Swedish commercial pilots. *American Journal of Industrial Medicine, 54*(7), 545-551. doi:10.1002/ajim.20943

Sivertsen, B., Krokstad, S., Øverland, S., & Mykletun, A. (2009). The epidemiology of insomnia: Associations with physical and mental health.: The HUNT-2 study. *Journal of Psychosomatic Research, 67*(2), 109-116. doi:10.1016/j.jpsychores.2009.05.001

Skarpsno, E. S., Mork, P. J., Nilsen, T. I. L., Jorgensen, M. B., & Holtermann, A. (2018). Objectively measured occupational and leisure-time physical activity: cross-sectional associations with sleep problems. *Scandinavian Journal of Work, Environment & Health, 44*(2), 202-211. doi:10.5271/sjweh.3688

Skarpsno, E. S., Nilsen, T. I. L., Sand, T., Hagen, K., & Mork, P. J. (2018). Physical work exposure, chronic musculoskeletal pain and risk of insomnia: longitudinal data from the HUNT study, Norway. *Occupational and Environmental Medicine, 75*(6), 421-426. doi:10.1136/oemed-2018-105050

Sluiter, J. K., Frings-Dresen, M. H., van der Beek, A. J., & Meijman, T. F. (2001). The relation between work-induced neuroendocrine reactivity and recovery, subjective need for recovery, and health status. *Journal of Psychosomatic Research, 50*(1), 29-37. doi:10.1016/S0022-3999(00)00213-0

Smagula, S. F., Reynolds, C. F., 3rd, Ancoli-Israel, S., Barrett-Connor, E., Dam, T. T., Hughes-Austin, J. M., . . . Cauley, J. A. (2015). Sleep Architecture and Mental Health Among Community-Dwelling Older Men. *The journals of Gerontology, 70*(5), 673-681. doi:10.1093/geronb/gbt125

Soltani, M., Haytabakhsh, M. R., Najman, J. M., Williams, G. M., O'Callaghan, M. J., Bor, W., . . . Clavarino, A. (2012). Sleepless nights: the effect of socioeconomic status, physical activity, and lifestyle factors on sleep quality in a large cohort of Australian women. *Archives of Women's Mental Health, 15*(4), 237-247. doi:10.1007/s00737-012-0281-3

Stranges, S., Dorn, J. M., Cappuccio, F. P., Donahue, R. P., Rafalson, L. B., Hovey, K. M., . . . Trevisan, M. (2010). A population-based study of reduced sleep duration and hypertension: the strongest association may be in premenopausal women. *Journal of Hypertension, 28*(5), 896-902. doi:10.1097/HJH.0b013e328335d076

Teychenne, M., Costigan, S. A., & Parker, K. (2015). The association between sedentary behaviour and risk of anxiety: a systematic review. *BMC Public Health, 15*(1), 513. doi:10.1186/s12889-015-1843-x

Too, L. S., & Butterworth, P. (2018). Psychosocial Job Stressors and Mental Health: The Potential Moderating Role of Emotion Regulation. *Journal of Occupational and Environmental Medicine, 60*(10), e518-e524. doi:10.1097/jom.0000000000001416

Uehli, K., Mehta, A. J., Miedinger, D., Hug, K., Schindler, C., Holsboer-Trachsler, E., . . . Künzli, N. (2014). Sleep problems and work injuries: A systematic review and meta-analysis. *Sleep Medicine Reviews, 18*(1), 61-73. doi:10.1016/j.smrv.2013.01.004

Uhlig, B. L., Sand, T., Nilsen, T. I., Mork, P. J., & Hagen, K. (2018). Insomnia and risk of chronic musculoskeletal complaints: longitudinal data from the HUNT study, Norway. *BMC Musculoskeletal Disorders, 19*(1), 128. doi:10.1186/s12891-018-2035-5

Van Laethem, M., Beckers, D. G., Kompier, M. A., Dijksterhuis, A., & Geurts, S. A. (2013). Psychosocial work characteristics and sleep quality: a systematic review of longitudinal and intervention research. *Scandinavian Journal of Work, Environment & Health, 39*(6), 535-549. doi:10.5271/sjweh.3376

Vgontzas, A., Liao, D., Bixler, E., Chrousos, G., & Vela-Bueno, A. (2009). Insomnia with Objective Short Sleep Duration is Associated with a High Risk for Hypertension. *Sleep, 32*(4), 491-497. doi:10.5665/sleep/32.4.491

Yamamoto, M., Sasaki, N., Somemura, H., Nakamura, S., Kaneita, Y., Uchiyama, M., & Tanaka, K. (2016). Efficacy of sleep education program based on principles of cognitive behavioral therapy to alleviate workers' distress. *Sleep and Biological Rhythms, 14*(2), 211-219. doi:10.1007/s41105-015-0045-3

Yong, L. C., Li, J., & Calvert, G. M. (2017). Sleep-related problems in the US working population: prevalence and association with shiftwork status. *Occupational and Environmental Medicine, 74*(2), 93-104. doi:10.1136/oemed-2016-103638

Youngstedt, S., & Kline, C. (2006). Epidemiology of exercise and sleep. *Sleep and Biological Rhythms., 4*(3), 215-221. doi:10.1111/j.1479-8425.2006.00235.x

TABLES

Table 1. Baseline characteristics of the study population stratified by sex and work-related mental fatigue.

	Women			Men		
	Work-related mental fatigue			Work-related mental fatigue		
	Never	Often	Always	Never	Often	Always
Persons, % (no.)	3,680	4,185	599	3,394	3,641	445
Age, mean±SD	42.0±9.6	41.9±9.2	42.6±9.4	43.4±9.8	43.7±9.0	43.1±9.6
Higher education, % (no.)[a]	19.2 (707)	37.8 (1,583)	42.7 (256)	23.4 (793)	30.1 (1,097)	26.5 (118)
Shift work, % (no.)	20.0 (735)	28.6 (1,196)	33.2 (199)	18.9 (641)	18.4 (669)	22.3 (99)
Work hours, mean±SD	28.0 (10.6)	31.1 (9.3)	32.3 (9.1)	37.9 (9.6)	39.2 (9.2)	40.6 (12.9)
Physical activity, % (no.)						
Low[b]	35.9 (1,281)	34.9 (1,436)	34.7 (204)	28.2 (937)	28.1 (1,009)	35.8 (156)
High[c]	64.2 (2,292)	65.1 (2,675)	65.3 (384)	71.8 (2,388)	72.0 (2,588)	64.2 (280)
Physical work demands, % (no.)						
Mostly sedentary	25.0 (919)	30.0 (1,254)	26.0 (156)	28.4 (963)	35.1 (1,279)	33.7 (150)
Much walking	39.2 (1,442)	33.8 (1,414)	36.1 (216)	23.7 (803)	25.0 (911)	21.8 (97)
Much walking and lifting	30.3 (1,115)	33.2 (1,391)	33.9 (203)	23.1 (784)	18.4 (670)	18.0 (80)
Heavy physical work	3.5 (130)	2.2 (91)	2.8 (17)	23.8 (807)	20.7 (754)	25.6 (114)

Abbreviations: SD, standard deviation

[a] College or higher

[b]Defined as ≤2h light and no hard activity per week

[c]Defined as >2h light and any hard activity per week

Table 2. Risk of insomnia at 11-year follow-up associated with work-related mental fatigue stratified by sex.

Frequency of mental fatigue	Women				Men			
	No. of persons	No. of cases	Age-adjusted, RR[a]	Multi-adjusted, RR[b] (95% CI)	No. of persons	No. of cases	Age-adjusted, RR[a]	Multi-adjusted, RR[b] (95% CI)
Seldom/never fatigued	3,680	142	1.00 (ref.)	1.00 (ref.)	3,394	90	1.00 (ref.)	1.00 (ref.)
Often fatigued	4,185	265	1.64	1.59 (1.29-1.95)	3,641	158	1.62	1.48 (1.14-1.92)
Always fatigued	599	64	2.81	2.55 (1.91-3.40)	445	39	3.28	2.61 (1.80-3.78)

Abbreviations: CI, confidence interval; RR, risk ratio

[a] Adjusted for age (20-29 years, 30-39 years, 40-49 years, 50-59 years).

[b] Multi-adjusted for age (20-29 years, 30-39 years, 40-49 years, 50-59 years), HADS (no depression and no anxiety, depression and/or anxiety, unknown), education (primary school, high school, college ≤4 years, college >4 years, unknown), shift work (no, yes,

unknown), working hours (<45, ≥45, unknown), and physical work demands (mostly sedentary, much walking, much walking and lifting, heavy physical work, unknown).

Table 3. Risk of insomnia at 11-year follow-up associated with the joint effect of work-related mental fatigue and leisure time physical activity.

	High physical activity[a]			Low physical activity[b]		
Frequency of mental fatigue	No. of persons	No. of cases	Multi-adjusted, RR (95% CI)[c]	No. of persons	No. of cases	Multi-adjusted, RR (95% CI)[c]
Seldom/never fatigued	4,680	140	1.00 (ref.)	2,218	87	1.24 (0.95-1.61)
Often fatigued	5,263	285	1.70 (1.39-2.07)	2,445	129	1.60 (1.26-2.02)
Always fatigued	664	61	2.52 (1.89-3.39)	360	41	3.17 (2.28-4.40)

Abbreviations: CI, confidence interval; RR, risk ratio

[a] >2h light and any hard activity

[b] ≤2h light and no hard activity

[c] Multi-adjusted for age (20-29 years, 30-39 years, 40-49 years, 50-59 years), HADS (no depression and no anxiety, depression and/or anxiety, unknown), education (primary school, high school, college ≤4 years, college >4 years, unknown), shift work (no, yes,

unknown), working hours (<45, ≥45, unknown), and physical work demands (mostly sedentary, much walking, much walking and lifting, heavy physical work, unknown).