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## Migraine, tension-type headache and medication-overuse headache in a large population of shift working nurses

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# Migraine, tension-type headache and medication-overuse headache in a large population of shift working nurses – a cross-sectional study

Bjørn Bjorvatn MD PhD[1,2], Ståle Pallesen PhD[2,3], Bente E. Moen MD PhD[1], Siri Waage PhD[1,2], Espen S. Kristoffersen MD PhD[4]

[1] Department of Global Public Health and Primary Care, University of Bergen, Norway.

[2] Norwegian Competence Center for Sleep Disorders, Haukeland University Hospital, Norway.

[3] Department of Psychosocial Science, University of Bergen, Norway.

[4] Department of General Practice, University of Oslo, Norway.

Corresponding author:

Bjørn Bjorvatn

Department of Global Public Health and Primary Care

University of Bergen

Kalfarveien 31, N-5018 Bergen

Norway

Phone: +4755586088

Fax: +4755586130

Email: bjorn.bjorvatn@uib.no

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**Key messages**

What is already known about this subject?

- Shift work is associated with poor sleep, and poor sleep may trigger headache. However, whether there is an association between shift work and headache is unclear.

What are the new findings?

- Tension-type headache was associated with high number of night shifts, but neither migraine, tension-type headache, nor medication-overuse headache were associated with work schedule. Several types of headaches were however associated with insomnia disorder and shift work disorder.

How might it impact on clinical practice in the foreseeable future?

- As no clear association was found between different types of headache and shift work schedules, headache may not be a major concern for the majority of shift workers.

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**ABSTRACT**

**Objectives**

To investigate associations between different types of headache and shift work.

**Methods**

1585 nurses with different work schedules (day work, two-shift rotation, night work, three-shift rotation) participated in a cohort study with annual surveys that started in 2008/2009. A comprehensive headache instrument was included in wave 6. Headaches were assessed according to the International Classification of Headache Disorders IIIb. Frequent headache (≥1 day per month), migraine, tension-type headache (TTH), chronic headache (headache >14 days per month), and medication-overuse headache (MOH, chronic headache + acute headache medication ≥10 days last month) comprised the dependent variables. Adjusted (for sex, age, percentage of full-time equivalent, marital status, children living at home) logistic regression analyses were conducted with work schedule, number of night shifts worked last year, number of quick returns (<11 hours in-between shifts) last year, shift work disorder (SWD), and insomnia disorder as predictors.

**Results**

Frequent headache, migraine, and chronic headache were associated with SWD (ORs 1.60 to 2.45) and insomnia disorder (ORs 1.55 to 3.03), but not with work schedule, number of night shifts or number of quick returns. TTH was only associated with >20 night shifts last year (OR 1.41). MOH was only associated with insomnia disorder (OR 7.62).

**Conclusions**

We found no association between different types of headache and work schedule. However, TTH was associated with high number of night shifts. Nurses with insomnia disorder and SWD reported higher prevalence of frequent headache, migraine, chronic headache and MOH (only insomnia) compared to nurses not having insomnia disorder and SWD, respectively.

**Keywords:** chronic headache, insomnia, shift work disorder, night work, quick returns

**Strengths and limitations of this study**

- A large and homogeneous sample of nurses with different work schedules
- Validated questionnaires for diagnosing different types of headache and sleep disorders

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- No clinical interviews by physicians
- Few nurses with some of the headache subtypes which limits statistical power in these analyses
- No conclusions about causality due to the cross-sectional design

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**INTRODUCTION**

Shift work is associated with impaired health, and several studies show that working shifts increase the risk of sleep disturbances, cardiovascular disease, metabolic disorders, and cancer.[1] Sleep disturbances are considered to be the most common complaints, especially among rotating shift workers and night workers.[2 3] Night workers are on duty during their biological resting phase and are enforced to schedule sleep to their biological active phase. This has been proposed as a causative factor for sleep and health problems.[1] Accordingly, studies suggest that the number of night shifts per year and the number of quick returns (defined at shifts with less than 11 hours in-between) per year are associated with increased risk of health complaints and sick leave.[4-6]

Recently, the focus on shift workers fulfilling the criteria for shift work disorder (SWD) has been intensified.[7-9] SWD is characterized by complaints of sleep problems and excessive sleepiness caused by work schedules overlapping with the habitual time for sleep.[7 10] This disorder affects 4.8-44.3% of nurses depending on type of work schedule.[11] SWD has been associated with impaired health, e.g. depression and hypertension.[7 9 11 12]

Few studies have specifically investigated the association between shift work and the presence and severity of headache. This is somewhat surprising, considering the association between sleep and headache.[13-15] One study from China reported that greater number of night shifts is positively associated with prevalence of headache,[16] and another study from Taiwan suggested that shift work increases the risk of migraine.[17] A Scandinavian study found an association between evening work, but not night work, and migraine.[15] The relationship between sleep and headache seems to be bidirectional. Lack of sleep can trigger headache, but sleep may also alleviate headache.[14] Disturbed sleep due to shift work is therefore likely to increase the risk of headache. The most common primary headaches in the general population are migraine and tension-type headache.[18] Most studies have focused on migraine and shift work,[14 15] although tension-type headache (TTH) is considered the most common form of headache with an estimated worldwide prevalence of approximately 40%.[18] The prevalence of migraine in the general population is 10-16%.[18 19] Chronic headache is defined as headache occurring more than 14 days per month and is present in 2-4% of the general population.[18-21] Medication-overuse headache (MOH) is a condition characterized by chronic headache and overuse of acute headache medications, usually defined as intake of acute pain or migraine

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medications 10 or more days per month.[20][22] The prevalence of medication-overuse headache in the general population is 1-2%, with more females being afflicted than males.[22][23]

As headache is common in the general population and since sleep loss, that often occurs concomitant with shift work, may trigger headache, we aimed to investigate whether different types of headache (i.e. migraine, TTH, chronic headache, MOH) were related to work schedules, number of night shifts, number of quick returns, SWD, and insomnia disorder, after adjusting for relevant confounders. Nurses comprise a large population of shift workers and are thereby suitable for such studies. We hypothesized that nurses involved in night and shift work would report a higher prevalence of headaches compared to day workers.

## METHODS

### Procedure and participants

The data stemmed from the ongoing longitudinal cohort study "SUrvey of Shift work, Sleep and Health (SUSSH)" among Norwegian nurses. The first data collection was conducted during winter 2008/2009 (wave 1) when a sample of 5400 nurses was randomly selected from the Norwegian Nurses Organisation's (NNO) membership roll and invited to participate. A total of 2059 (response rate = 38.1%) nurses completed the questionnaire at the first wave. In order to increase the study population, an additional sample of 906 newly educated nurses (response rate = 33.1%) was recruited in 2009. The total sample in wave 1 therefore included 2965 nurses, see details in Bjorvatn et al.[24] The nurses who responded to the first wave have been invited to participate in annual follow-ups by receiving questionnaires sent by postal mail with pre-paid envelopes for returning the completed forms. Up to two reminders were sent to nurses who did not respond. The nurses who returned the questionnaire took part in a lottery, in which 25 individuals won a gift card with a value of 500 NOK (~ 60 US $). The present study reports findings based on data from the sixth (2014) wave, in which the headache questionnaire was included. A total of 1991 out of 2869 eligible nurses completed the questionnaire at wave 6, yielding a response rate of 69.4%. Nurses that reported that they were no longer working as nurses at wave 6 were excluded from the analyses, leaving a total study population of 1585 nurses.

Demographics

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The demographic variables were assessed in wave 6, except for age and sex that were registered in wave 1. The nurses responded to questions about marital status (married/cohabiting; yes/no), children living at home (yes/no), percentage of full-time equivalent (<50%, 50-75%, 76-90%. >90% position), work schedule (day only, evening only, two-shift rotation (day and evening), night only, three-shift rotation (day, evening and night), and other schedules including night work), number of night shifts worked last year, and number of quick returns (defined as less than 11 hours between consecutive work shifts) worked last year. Few nurses worked "evening only" (n=6) and "other schedules including night shifts" (n=67), and these shifts were therefore excluded in the analysis of the association between work schedule and headache.

Headache

The comprehensive headache questionnaire was designed to determine whether the nurses suffered from headache, and fulfilled the International Classification of Headache Disorders (ICHD) IIIb criteria for migraine, tension-type headache (TTH) and medication-overuse headache (MOH).[20] The nurses were first screened: "Have you suffered from headache during the last year?", and only nurses who answered "yes" were asked to respond to the other headache items. The screening positive headache sufferers were asked to report frequency, attack duration, intensity and accompanying headache symptoms to classify migraine and TTH, accordingly. The diagnoses of migraine and TTH were mutually exclusive. Frequent headache was defined as headache ≥1 day per month, and chronic headache was defined as headache >14 days per month. MOH was defined as chronic headache and intake of acute headache medication ≥10 days last month. The questionnaire-based headache diagnoses used here have previously been validated in a large unselected general population sample.[19 25 26]

Shift work disorder (SWD)

SWD was measured with three previous used questions[10 11] based on the minimal criteria listed in the second edition of the International Classification of Sleep Disorders (ICSD-2).[27] The questions were: a) Do you experience either difficulties sleeping or experience excessive sleepiness? (yes/no), b) Is the sleep or sleepiness problem related to a work schedule that makes you work when you normally would sleep? (yes/no), c) Have you had this sleep or sleepiness problem related to the work schedule for at least one month? (yes/no). Participants were classified as having SWD if they endorsed all three questions.

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Insomnia disorder

Insomnia symptoms were evaluated with Bergen Insomnia Scale (BIS).[28] The BIS consists of six items, and was developed based on the diagnostic criteria for insomnia according to 4th and text revision version of the Diagnostic and Statistical Manual for Mental Disorders (DSM-IV-TR).[29] The items are scored along an eight-point scale indicating the number of days per week for which a specific insomnia symptom is experienced (0-7 days). The items refer to sleep onset (sleep latency exceeding 30 minutes), wake after sleep onset (more than 30 minutes), early morning awakening (more than 30 minutes), non-restorative sleep, daytime impairment, and dissatisfaction with sleep. The time frame is insomnia symptoms experienced during the past month. According to DSM-5 criteria,[30] insomnia disorder is defined as scoring 3 days per week or more on at least one of the first three items as well as 3 days per week or more on at least one of the latter two items. Missing responses to any of the insomnia questions were treated as not reporting that specific insomnia symptom. The scale has acceptable test-retest reliability, and good convergent and discriminative validity in relation to other self-report measures as well as to polysomnographic data.[28] Cronbach's alpha for the BIS was 0.83 in the present sample.

Ethics

The study was approved by the Regional Committee for Medical and Health Research Ethics of Western Norway (REK-West, no 088.08). Written informed consent was obtained from all participants.

Statistics

The statistical analyses were conducted with IBM SPSS Statistics 23 for Windows. The prevalence of frequent headache, migraine, TTH, chronic headache, and MOH in relation to the different work schedules, categories of night shifts and quick returns last year, SWD and insomnia disorder were explored by the Pearson chi-square tests (with Yates' correction for continuity when used in a 2 x 2 table). In addition, separate adjusted (with sex, age, percentage of full-time equivalent, marital status, children living at home as co-variates) logistic regression analyses were performed to assess different headaches (frequent headache, migraine, TTH, chronic headache, MOH) as dependent variables with work schedule (day only as a reference, compared to two-shift rotation, night only and three-shift rotation), number of night shifts last year (0, 1-20, >20 night shifts), number of quick returns last year

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(0, 1-20, >20 quick returns), SWD, and insomnia disorder as predictors. Significance level was set to .05.

**RESULTS**

Demographic characteristics are presented in Table 1. Most of the nurses were females (90.5%) and mean age in wave 1 was 32.5 years (SD=8.5). Three-shift and two-shift rotation were the most common work schedules (Table 1). Mean number of night shifts last year was 23.5 (SD=36.7) and mean number of quick returns last year was 33.4 (SD=35.4). Shift work disorder and insomnia disorder were present in 27.3% and 31.7% of the nurses, respectively. In total, 56.0% of the nurses (n=885) reported headache complaints during the last year, and 48.1% (n=763) frequent headache (≥1 day per month). Migraine, TTH, chronic headache, and MOH were present in 19.6% (n=302), 27.9 (n=435), 2.3% (n=37), and 1.2% (n=19) of the total sample of nurses, respectively (Table 1).

We did not find any significant differences between the prevalence of frequent headache, migraine, TTH, chronic headache or MOH across work schedules (Table 2). Similarly, logistic regression analyses with adjustment for sex, age, percentage of full-time equivalent, marital status, and children living at home, revealed no association between the different headache types and work schedule (Table 3).

The prevalence of TTH was higher in nurses working night shifts last year compared to those not working night shifts, but we found no association between frequent headache, migraine, chronic headache or MOH and number of night shifts last year (Table 2). Similarly, in the adjusted logistic regression analysis, TTH was significantly associated with >20 night shifts last year (OR=1.41) (Table 3). There were no associations between the different headache types and number of quick returns last year (Tables 2 and 3).

The prevalence of frequent headache, migraine, and chronic headache were all clearly higher among nurses with SWD compared to nurses without SWD (Table 2). Furthermore, adjusted logistic regression analyses revealed that frequent headache, migraine, and chronic headache all were significantly associated with SWD, with odd ratios ranging from 1.60 to 2.45 (Table 3). TTH and MOH were not significantly associated with SWD (Tables 2 and 3).

The prevalence of frequent headache, migraine, chronic headache, and MOH were all clearly higher among nurses with insomnia disorder compared to nurses without insomnia disorder (Table 2). These findings were also present in the adjusted logistic regression analyses, with odds ratios ranging from 1.55 to 7.62 (Table 3). The only headache type that was not associated with insomnia disorder was TTH (Tables 2 and 3).

**DISCUSSION**

The present study showed that nurses with different work schedules reported similar prevalence of frequent headache, migraine, TTH, chronic headache, and MOH. These findings did thus not support our hypothesis that shift working nurses would report higher prevalence of headaches than day workers. However, nurses with high number of night shifts during the last year reported higher prevalence of TTH than nurses with no night shifts. Furthermore, nurses with SWD and insomnia disorder reported higher prevalence of most types of headache compared to nurses without SWD and insomnia disorder, respectively.

We hypothesized that night and shift work would be associated with higher prevalence of headaches. This was based on the well-known association between lack of sleep and headache.[14 31] It is well known that both rotating shift work schedules and night work normally will cause circadian rhythm misalignment and sleep deprivation.[8 32 33] In line with this, a Chinese study showed that number of night shifts was positively associated with prevalence of different types of headache.[16] However, a recent Danish study did not find any association between treatment-seeking migraine and night work or variable working hours.[15] In the latter study, only fixed evening work was found to be associated (positively) with migraine. One possible explanation for the lack of association between headaches and work schedules in the present study may be the "healthy shift worker effect". This is based on the assumption that shift workers have better health than those who avoid or quit shift work.[34] Hence, nurses with headaches may be more reluctant to work shifts or quit shift work more frequently than others, leading to underestimates of the possible negative effects of shift work in studies like the present one.

Similarly, the number of night shifts worked the last year was not associated with frequent headache, migraine, chronic headache, or MOH. However, TTH was associated with high number of night shifts. This finding suggests that there may be different sleep-headache

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mechanisms in TTH than in e.g. migraine.[35] In line with this, a polysomnography study found that TTH patients need more sleep than healthy controls, and that inadequate sleep may contribute to increased pain sensitivity in TTH.[36] Furthermore, a high number of night shifts may not necessarily only cause sleep deprivation, but may also be experienced as stressful and thereby precipitate TTH. High work stress is a risk factor for primary headaches, especially tension-type headache.[16 37] Whether circadian misalignment in itself (often occurring among shift and night workers) triggers headaches is not known, and this topic should receive more attention in the future.

Many Norwegian nurses with rotating shift schedules have quick returns (defined as shifts separated by less than 11 hours) in their roster. For the nurses, most quick returns involve working an evening shift followed by a day shift. Such short rest in-between shifts typically cause sleep deprivation and health problems.[4 5] However, we found no association between headaches and quick returns. This suggests that short-term sleep deprivation, as seen with quick returns, may not pose a major problem in relation to headache risk. This was found even though a high percentage of the nurses reported frequent quick returns.

In the present study, frequent headache, migraine, and chronic headache were all associated with SWD. These novel findings suggest that nurses who do not cope well with shift work are at increased risk of other health complaints like headaches. However, our study cannot say anything about cause-and-effect. That is, it may be that headache increases the risk of SWD. Future studies should consequently focus on whether there may be common vulnerability factors (e.g. genetic, health behaviour, etc.) between headaches and sleep related disorders. Interestingly, TTH was not associated with SWD, suggesting that different pathophysiological mechanisms may be involved across the different types of headaches.

Insomnia disorder was associated with all headache types, except TTH, which is in line with the findings from several other studies.[14 38 39] However, few studies have used formal diagnostic criteria for insomnia disorder, like the present study. Thus, one major asset with the present study was the use of ICSD and ICHD criteria for sleep disorders and headache classification, respectively. Surprisingly, TTH was not associated with insomnia disorder in our study, in contrast to two other population-based studies.[31 40] However, none of those studies used the formal diagnostic criteria for insomnia disorder. MOH was significantly associated with insomnia disorder, but not with any of the work-related variables. In fact, our

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data indicate that nurses with insomnia disorder had more than 7 times higher risk of MOH than those without insomnia disorder. This strong association warrants further studies.

**Strenghts and limitations**

The present study was based on a large and homogeneous sample of nurses that limits the influence from possible confounding variables. Other strengths were the use of validated headache diagnoses and a validated insomnia scale as well as criteria-based SWD diagnostics. Furthermore, the study did not have a primary focus on headache, it was one of many health outcomes. Thus, a possible selection bias related to headache was unlikely. In terms of limitations, it should be noted that the response rate in the first wave was low, which may make the interpretation of the data and conclusions less generalizable. Still, the response rate in wave 6 where the headache questionnaire was included was high. Due to the high number of participants in our survey, it was not feasible to apply the gold standard, i.e. a clinical interview by a physician experienced in headache and sleep diagnostics. For the same reason, prospective headache and sleep diaries were not feasible. However, the questionnaire-based headache diagnostic procedures have been included in several previous large population-based studies and have been validated against clinical interviews with a high degree of agreement.[19 25 26] The prevalence of the different headaches reported in the present study were similar to those reported previously,[16 18 19 21 23] strengthening the assumption of representativeness of the study population. The number of participants with chronic headache and MOH were low, limiting the statistical power in these analyses. Finally, it should be noted that the cross-sectional design does not permit any conclusions about causality in the relationship between headaches and work variables.

**Conclusion**

We found no association between different types of headache and work schedule or quick returns. TTH was however associated with high number of night shifts, but not any of the other work variables. Nurses with SWD reported higher prevalence of frequent headache, migraine, and chronic headache compared to nurses not having SWD. Similarly, nurses with insomnia disorder, compared to those without, reported higher prevalence of all types of headache, except TTH. Further research should be longitudinal in order to study causality/directionality between headaches and work variables.

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**Competing interests statement**

None declared.

**Data sharing**

No additional data available.

**Contributorship statement**

BB: contributed to the design of the study, data collection, data analysis, drafted the paper, and approved the final version.

SP: contributed to the design of the study, data collection, data analysis, revised the paper, and approved the final version.

BEM: contributed to the design of the study, data collection, data analysis, revised the paper, and approved the final version.

SW: contributed to the design of the study, data collection, data analysis, revised the paper, and approved the final version.

ESK: contributed to the design of the study, data analysis, revised the paper, and approved the final version.

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Table 1. Characteristics of the Norwegian nurses in the study.

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| Sex (n=1578): Female | 90.5% |
| Age in wave 1 (n=1583): mean (SD) | 32.5 (8.5) years |
| Percentage of full-time equivalent (n=1536): | |
| <50% | 3.9% |
| 50-75% | 20.3% |
| 76-90% | 16.5% |
| >90% | 59.2% |
| Married/cohabiting (n=1582): Yes | 76.5% |
| Children living at home (n=1578): Yes | 63.3% |
| Work schedule (n=1532): | |
| Day only | 19.3% |
| Evening only | 0.4 |
| Two-shift rotation | 32.4% |
| Night shift only | 6.6% |
| Three-shift rotation | 36.9% |
| Other schedules including night shifts | 4.4% |
| Number of night shifts last year (n=1534): | |
| 0 night shifts | 39.8% |
| 1-20 night shifts | 26.1% |
| >20 night shifts | 34.0% |
| Number of quick returns last year (n=1511): | |
| 0 quick returns | 22.6% |
| 1-20 quick returns | 25.2% |
| >20 quick returns | 52.2% |
| Shift work disorder (n=1567): Yes | 27.3% |
| Insomnia disorder (n=1585): Yes | 31.7% |
| Headache last year (n=1579): Yes | 56.0% |
| Frequent headache (≥1 day per month) (n=1585): Yes | 48.1% |
| Migraine (n=1537): Yes | 19.6% |
| Tension-type headache (n=1559): Yes | 27.9% |
| Chronic headache (n=1577): Yes | 2.3% |
| Medication-overuse headache (n=1579): Yes | 1.2% |

SD, standard deviation.  n, number of nurses.

Table 2. Prevalence of different types of headache complaints among Norwegian nurses.

| | Frequent headache[1] % (n) | Migraine % (n) | Tension-type headache % (n) | Chronic headache[2] % (n) | Medication-overuse headache % (n) |
|---|---|---|---|---|---|
| Work schedule (n=1415-1459): | 0.2[a], p=.979 | 2.5[a], p=.472 | 3.5[a], p=.321 | 2.3[a], p=.510 | 1.7[a], p=.637 |
| Day only | 47.3 (140) | 22.6 (65) | 24.5 (71) | 1.7 (5) | 1.0 (3) |
| Two-shift rotation | 48.7 (242) | 20.3 (98) | 26.1 (129) | 3.2 (16) | 1.6 (8) |
| Night shift only | 47.5 (48) | 16.3 (16) | 29.0 (29) | 2.0 (2) | 2.0 (2) |
| Three-shift rotation | 47.6 (269) | 18.8 (103) | 29.9 (165) | 2.1 (12) | 0.9 (5) |
| Night shifts last year (n=1489-1534): | 3.4[a], p=.180 | 3.3[a], p=.188 | 6.9[a], p=.032 | 0.4[a], p=.813 | 1.1[a], p=.578 |
| 0 night shifts | 47.8 (292) | 21.9 (130) | 24.4 (147) | 2.6 (16) | 1.5 (9) |
| 1-20 night shifts | 44.6 (179) | 18.0 (70) | 30.0 (118) | 2.0 (8) | 0.8 (3) |
| >20 night shifts | 50.8 (265) | 18.1 (92) | 30.9 (159) | 2.3 (12) | 1.2 (6) |
| Quick returns last year (n=1465-1511): | 0.2[a], p=.902 | 1.5[a], p=.480 | 2.4[a], p=.296 | 0.2[a], p=.885 | 0.8[a], p=.666 |
| 0 quick returns | 47.4 (162) | 22.1 (73) | 24.8 (83) | 2.1 (7) | 1.2 (4) |
| 1-20 quick returns | 48.8 (186) | 18.9 (70) | 29.6 (111) | 2.4 (9) | 0.8 (3) |
| >20 quick returns | 48.7 (384) | 19.1 (146) | 28.8 (224) | 2.5 (20) | 1.4 (11) |
| Shift work disorder (n=1521-1567): | 36.9[a], p<.0005 | 11.3[a], p=.001 | 1.6[a], p=.208 | 5.7[a]. p=.017 | 0.5[a], p=.491 |
| No | 43.4 (494) | 17.7 (197) | 26.9 (301) | 1.8 (20) | 1.1 (12) |
| Yes | 60.7 (260) | 25.6 (104) | 30.2 (127) | 4.0 (17) | 1.6 (7) |
| Insomnia disorder (n=1537-1585): | 25.1[a], p<.0005 | 10.1[a], p=.001 | 0.0[a], p=.983 | 9.7[a], p=.002 | 15.6[a], p<.0005 |
| No | 43.8 (474) | 17.4 (184) | 28.0 (297) | 1.5 (16) | 0.5 (5) |
| Yes | 57.5 (289) | 24.5 (118) | 27.8 (138) | 4.2 (21) | 2.8 (14) |

[1]Headache ≥1 days per month. [2]Headache >14 days per month.
[a]Pearson Chi-square, with Yates' correction for continuity when used in a 2x2 table.
Significant findings are shown in **bold**.

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Table 3. Separate adjusted logistic regression analyses with different headache types as the dependent variables among Norwegian nurses.

| Independent variables | Frequent headache[1] OR (95% CI)[a] n=1439-1519 | Migraine OR (95% CI)[a] n=1398-1476 | Tension-type headache OR (95% CI)[a] n=1416-1495 | Chronic headache[2] OR (95% CI)[a] n=1432-1512 | Medication-overuse headache OR (95% CI)[a] n=1434-1514 |
|---|---|---|---|---|---|
| Work schedule | | | | | |
| Day only | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Two-shift | 1.07 (0.80-1.44) | 0.89 (0.62-1.28) | 1.11 (0.79-1.57) | 1.91 (0.68-5.32) | 1.49 (0.39-5.80) |
| Night only | 1.07 (0.65-1.77) | 0.75 (0.39-1.44) | 1.30 (0.74-2.28) | 1.18 (0.20-6.88) | 2.39 (0.32-17.65) |
| Three-shift | 1.01 (0.76-1.35) | 0.79 (0.55-1.14) | 1.31 (0.94-1.83) | 1.22 (0.42-3.56) | 0.86 (0.20-3.70) |
| Number of night shifts | | | | | |
| 0 night shifts | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| 1-20 night shifts | 0.86 (0.66-1.11) | 0.78 (0.56-1.09) | 1.27 (0.95-1.70) | 0.73 (0.30-1.74) | 0.51 (0.14-1.95) |
| >20 night shifts | 1.15 (0.90-1.47) | 0.80 (0.58-1.09) | **1.41 (1.07-1.86)** | 0.82 (0.38-1.80) | 0.78 (0.27-2.29) |
| Number of quick returns | | | | | |
| 0 quick returns | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| 1-20 quick returns | 1.09 (0.81-1.46) | 0.83 (0.57-1.21) | 1.30 (0.92-1.82) | 1.12 (0.41-3.05) | 0.66 (0.15-3.01) |
| >20 quick returns | 1.06 (0.82-1.39) | 0.81 (0.58-1.12) | 1.23 (0.91-1.67) | 1.21 (0.50-2.95) | 1.18 (0.37-3.83) |
| Shift work disorder | | | | | |
| No | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Yes | **2.04 (1.62-2.59)** | **1.60 (1.21-2.12)** | 1.19 (0.92-1.54) | **2.45 (1.25-4.80)** | 1.67 (0.64-4.40) |
| Insomnia disorder | | | | | |
| No | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Yes | **1.79 (1.43-2.23)** | **1.55 (1.18-2.02)** | 1.01 (0.79-1.29) | **3.03 (1.54-5.95)** | **7.62 (2.48-23.41)** |

[1]Headache ≥1 days per month. [2]Headache >14 days per month.

[a]Separate logistic regression analyses for each independent variable with adjustment for sex, age, percentage of full-time equivalent, marital status, and children living at home.

Significant findings are shown in **bold**.

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STROBE Statement—checklist of items that should be included in reports of observational studies

| | Item No | Recommendation |
|---|---|---|
| **Title and abstract** | 1 | (*a*) Indicate the study's design with a commonly used term in the title or the abstract |
| | | (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found |
| See page 1 and 3 | | |
| **Introduction** | | |
| Background/rationale | 2 | Explain the scientific background and rationale for the investigation being reported |
| See page 5 and 6 | | |
| Objectives | 3 | State specific objectives, including any prespecified hypotheses |
| See page 6 | | |
| **Methods** | | |
| Study design | 4 | Present key elements of study design early in the paper |
| See page 6 and 7 | | |
| Setting | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection |
| See page 6 and 7 | | |
| Participants | 6 | (*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up |
| | | *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls |
| | | *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants |
| | | (*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed |
| | | *Case-control study*—For matched studies, give matching criteria and the number of controls per case |
| See page 6 | | |
| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable |
| See page 7 and 8 | | |
| Data sources/ measurement | 8* | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group |
| See page 6, 7 and 8 | | |
| Bias | 9 | Describe any efforts to address potential sources of bias |
| See page 12 | | |
| Study size | 10 | Explain how the study size was arrived at |
| See page 6 | | |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why |
| See page 8 | | |
| Statistical methods | 12 | (*a*) Describe all statistical methods, including those used to control for confounding |
| | | (*b*) Describe any methods used to examine subgroups and interactions |

(*c*) Explain how missing data were addressed

(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed

*Case-control study*—If applicable, explain how matching of cases and controls was addressed

*Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy

(*e*) Describe any sensitivity analyses

See page 8 and 9

**Results**

| Participants | 13* | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed |
| | | (b) Give reasons for non-participation at each stage |
| | | (c) Consider use of a flow diagram |

See page 9

| Descriptive data | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders |
| | | (b) Indicate number of participants with missing data for each variable of interest |
| | | (c) *Cohort study*—Summarise follow-up time (eg, average and total amount) |

Page 9 and 17

| Outcome data | 15* | *Cohort study*—Report numbers of outcome events or summary measures over time |
| | | *Case-control study*—Report numbers in each exposure category, or summary measures of exposure |
| | | *Cross-sectional study*—Report numbers of outcome events or summary measures |

Page 9 and 10

| Main results | 16 | (*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included |
| | | (*b*) Report category boundaries when continuous variables were categorized |
| | | (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period |

Page 18 and 19

| Other analyses | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses |

Page 18 and 19

**Discussion**

| Key results | 18 | Summarise key results with reference to study objectives |

Page 10

| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias |

Page 12

| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence |

Page 10-12

| Generalisability | 21 | Discuss the generalisability (external validity) of the study results |

Page 12

**Other information**

| | | |
|---|---|---|
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based |

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*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

# BMJ Open

# Migraine, tension-type headache and medication-overuse headache in a large population of shift working nurses

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# Migraine, tension-type headache and medication-overuse headache in a large population of shift working nurses – a cross-sectional study

Bjørn Bjorvatn MD PhD[1,2], Ståle Pallesen PhD[2,3], Bente E. Moen MD PhD[1], Siri Waage PhD[1,2], Espen S. Kristoffersen MD PhD[4]

[1] Department of Global Public Health and Primary Care, University of Bergen, Norway.

[2] Norwegian Competence Center for Sleep Disorders, Haukeland University Hospital, Norway.

[3] Department of Psychosocial Science, University of Bergen, Norway.

[4] Department of General Practice, University of Oslo, Norway.

Corresponding author:

Bjørn Bjorvatn

Department of Global Public Health and Primary Care

University of Bergen

Kalfarveien 31, N-5018 Bergen

Norway

Phone: +4755586088

Fax: +4755586130

Email: bjorn.bjorvatn@uib.no

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**Key messages**

What is already known about this subject?

- Shift work is associated with poor sleep, and poor sleep may trigger headache. However, whether there is an association between shift work and headache is unclear.

What are the new findings?

- Tension-type headache was associated with high number of night shifts, but neither migraine, tension-type headache, nor medication-overuse headache were associated with work schedule. Several types of headaches were however associated with insomnia disorder and shift work disorder.

How might it impact on clinical practice in the foreseeable future?

- As no clear association was found between different types of headache and shift work schedules, headache may not be a major concern for the majority of shift workers.

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**ABSTRACT**

**Objectives**

To investigate associations between different types of headache and shift work.

**Design, participants and outcome measures**

Nurses with different work schedules (day work, two-shift rotation, night work, three-shift rotation) participated in a cohort study with annual surveys that started in 2008/2009. In 2014 (wave 6), a comprehensive headache instrument was included in the survey, in which 1585 nurses participated. Headaches were assessed according to the International Classification of Headache Disorders IIIb. Frequent headache (≥1 day per month), migraine, tension-type headache, chronic headache (headache >14 days per month), and medication-overuse headache ( chronic headache + acute headache medication ≥10 days last month) comprised the dependent variables. Adjusted (for sex, age, percentage of full-time equivalent, marital status, children living at home) logistic regression analyses were conducted with work schedule, number of night shifts worked last year, number of quick returns (<11 hours in-between shifts) last year, shift work disorder, and insomnia disorder as predictors.

**Results**

Frequent headache, migraine, and chronic headache were associated with shift work disorder (OR 2.04, 1.62-2.59; 1.60, 1.21-2.12; 2.45, 1.25-4.80, respectively) and insomnia disorder (OR 1.79, 1.43-2.23; 1.55, 1.18-2.02; 3.03, 1.54-5.95, respectively), but not with work schedule, number of night shifts or number of quick returns. Tension-type headache was only associated with >20 night shifts last year (OR 1.41, 1.07-1.86). Medication-overuse headache was only associated with insomnia disorder (OR 7.62, 2.48-23.41).

**Conclusions**

We did not find any association between different types of headache and work schedule. However, tension-type headache was associated with high number of night shifts. Nurses with sleep disorders (insomnia disorder and shift work disorder) reported higher prevalence of frequent headache, migraine, chronic headache and medication-overuse headache (only insomnia) compared to nurses not having insomnia disorder and shift work disorder, respectively.

**Keywords:** chronic headache, insomnia, shift work disorder, night work, quick returns

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**Strengths and limitations of this study**

- A large and homogeneous sample of nurses with different work schedules
- Validated questionnaires for diagnosing different types of headache and sleep disorders
- No clinical interviews by physicians
- Few nurses with some of the headache subtypes which limits statistical power in these analyses
- No conclusions about causality due to the cross-sectional design

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**INTRODUCTION**

Shift work is associated with impaired health, and several studies show that working shifts increase the risk of sleep disturbances, cardiovascular disease, metabolic disorders, and cancer.[1] Sleep disturbances are considered to be the most common complaints, especially among rotating shift workers and night workers.[2 3] Night workers are on duty during their biological resting phase and are enforced to schedule sleep to their biological active phase. This has been proposed as a causative factor for sleep and health problems.[1] Accordingly, studies suggest that the number of night shifts per year and the number of quick returns (defined at shifts with less than 11 hours in-between) per year are associated with increased risk of health complaints and sick leave.[4-7]

Recently, the focus on shift workers fulfilling the criteria for shift work disorder (SWD) has been intensified.[8-10] SWD is characterized by complaints of sleep problems and excessive sleepiness caused by work schedules overlapping with the habitual time for sleep.[8 11] This disorder affects 4.8-44.3% of nurses depending on type of work schedule.[12] SWD has been associated with impaired health, e.g. depression and hypertension.[8 10 12 13]

Few studies have specifically investigated the association between shift work and the presence and severity of headache. This is somewhat surprising, considering the association between sleep and headache.[14-16] Many of the existing studies suffer from methodological limitations, such as low number of participants (<300) [17-19] and not using validated headache questions.[17-21] One study from China reported that greater number of night shifts is positively associated with prevalence of headache,[22] and another study from Taiwan suggested that shift work increases the risk of migraine.[23] A Scandinavian study found an association between evening work, but not night work, and migraine.[16] The relationship between sleep and headache seems to be bidirectional. Lack of sleep can trigger headache, but sleep may also alleviate headache.[15] Disturbed sleep due to shift work is therefore likely to increase the risk of headache. The most common primary headaches in the general population are migraine and tension-type headache.[24] Most studies have focused on migraine and shift work,[15 16] although tension-type headache (TTH) is considered the most common form of headache with an estimated worldwide prevalence of approximately 40%.[24] The prevalence of migraine in the general population is 10-16%.[24 25] Chronic headache is defined as headache occurring more than 14 days per month and is present in 2-4% of the general population.[24-27] Medication-overuse headache (MOH) is a condition characterized by chronic headache and overuse of

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acute headache medications, usually defined as intake of acute pain or migraine medications 10 or more days per month.[26 28] The prevalence of medication-overuse headache in the general population is 1-2%, with more females being afflicted than males.[28 29]

As headache is common in the general population and since sleep loss, that often occurs concomitant with shift work, may trigger headache, we aimed to investigate whether different types of headache (i.e. migraine, TTH, chronic headache, MOH) were related to work schedules, number of night shifts, number of quick returns, SWD, and insomnia disorder. Nurses comprise a large population of shift workers and are thereby suitable for such studies. We hypothesized that nurses involved in night and shift work would report a higher prevalence of headaches compared to day workers.

## METHODS

### Procedure and participants

The data stemmed from the ongoing longitudinal cohort study "SUrvey of Shift work, Sleep and Health (SUSSH)" among Norwegian nurses. The first data collection was conducted during winter 2008/2009 (wave 1) when a sample of 5400 nurses was randomly selected from the Norwegian Nurses Organisation's (NNO) membership roll and invited to participate. A total of 2059 (response rate = 38.1%) nurses completed the questionnaire at the first wave. In order to increase the study population, an additional sample of 906 newly educated nurses (response rate = 33.1%) was recruited in 2009. The total sample in wave 1 therefore included 2965 nurses, see details in Bjorvatn et al.[30] The nurses who responded to the first wave have been invited to participate in annual follow-ups by receiving questionnaires sent by postal mail with pre-paid envelopes for returning the completed forms. Up to two reminders were sent to nurses who did not respond. The nurses who returned the questionnaire took part in a lottery, in which 25 individuals won a gift card with a value of 500 NOK (~ 60 US $). The present study reports findings based on data from the sixth (2014) wave, in which the headache questionnaire was included. A total of 1991 out of 2869 eligible nurses completed the questionnaire at wave 6, yielding a response rate of 69.4%. Nurses that reported that they were no longer working as nurses at wave 6 were excluded from the analyses, leaving a total study population of 1585 nurses.

Demographics

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The demographic variables were assessed in wave 6, except for age and sex that were registered in wave 1. The nurses responded to questions about marital status (married/cohabiting; yes/no), children living at home (yes/no), percentage of full-time equivalent (<50%, 50-75%, 76-90%. >90% position), work schedule (day only, evening only, two-shift rotation (day and evening), night only, three-shift rotation (day, evening and night), and other schedules including night work), number of night shifts worked last year, and number of quick returns (defined as less than 11 hours between consecutive work shifts) worked last year. Few nurses worked "evening only" (n=6) and "other schedules including night shifts" (n=67), and these shifts were therefore excluded in the analysis of the association between work schedule and headache.

Headache

The comprehensive headache questionnaire was designed to determine whether the nurses suffered from headache, and fulfilled the International Classification of Headache Disorders (ICHD) IIIb criteria for migraine, tension-type headache (TTH) and medication-overuse headache (MOH).[26] The nurses were first screened: "Have you suffered from headache during the last year?", and only nurses who answered "yes" were asked to respond to the other headache items. The screening positive headache sufferers were asked to report frequency, attack duration, intensity and accompanying headache symptoms to classify migraine and TTH, accordingly. The diagnoses of migraine and TTH were mutually exclusive. Frequent headache was defined as headache ≥1 day per month, and chronic headache was defined as headache >14 days per month, independently of the underlying subtype of headache. MOH was defined as chronic headache and intake of acute headache medication ≥10 days last month. The questionnaire-based headache diagnoses used here have previously been validated in a large unselected general population sample.[25 31 32]

Shift work disorder (SWD)

SWD was measured with three previous used questions[11 12] based on the minimal criteria listed in the second edition of the International Classification of Sleep Disorders (ICSD-2).[33] The questions were: a) Do you experience either difficulties sleeping or experience excessive sleepiness? (yes/no), b) Is the sleep or sleepiness problem related to a work schedule that makes you work when you normally would sleep? (yes/no), c) Have you had this sleep or sleepiness problem related to the work schedule for at least one month? (yes/no). Participants were classified as having SWD if they endorsed all three questions.

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Insomnia disorder

Insomnia symptoms were evaluated with Bergen Insomnia Scale (BIS).[34] The BIS consists of six items, and was developed based on the diagnostic criteria for insomnia according to 4th and text revision version of the Diagnostic and Statistical Manual for Mental Disorders (DSM-IV-TR).[35] The items are scored along an eight-point scale indicating the number of days per week for which a specific insomnia symptom is experienced (0-7 days). The items refer to sleep onset (sleep latency exceeding 30 minutes), wake after sleep onset (more than 30 minutes), early morning awakening (more than 30 minutes), non-restorative sleep, daytime impairment, and dissatisfaction with sleep. The time frame is insomnia symptoms experienced during the past month. According to DSM-5 criteria,[36] insomnia disorder is defined as scoring 3 days per week or more on at least one of the first three items as well as 3 days per week or more on at least one of the latter two items. Missing responses to any of the insomnia questions were treated as not reporting that specific insomnia symptom. The scale has acceptable test-retest reliability, and good convergent and discriminative validity in relation to other self-report measures as well as to polysomnographic data.[34] Cronbach's alpha for the BIS was 0.83 in the present sample.

Ethics

The study was approved by the Regional Committee for Medical and Health Research Ethics of Western Norway (REK-West, no 088.08). Written informed consent was obtained from all participants.

Patient and public involvement

The questionnaire was developed by a group of researchers experienced with shift work and shift work related problems. The participating nurses were not involved in the design, recruitment or conduct of the study. The results will be disseminated to the study participants in the yearly report we send to the journal of the Norwegian nurses. Here we address last year's published data from the cohort study. In addition, the results will appear on a designated website – www.sussh.no (after publication).

Statistics

The statistical analyses were conducted with IBM SPSS Statistics 23 for Windows. The prevalence of frequent headache, migraine, TTH, chronic headache, and MOH in relation to

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the different work schedules, categories of night shifts and quick returns last year, SWD and insomnia disorder were explored by the Pearson chi-square tests (with Yates' correction for continuity when used in a 2 x 2 table). In addition, separate adjusted (with sex, age, percentage of full-time equivalent, marital status, children living at home as co-variates) logistic regression analyses were performed to assess different headaches (frequent headache, migraine, TTH, chronic headache, MOH) as dependent variables with work schedule (day only as a reference, compared to two-shift rotation, night only and three-shift rotation), number of night shifts last year (0, 1-20, >20 night shifts), number of quick returns last year (0, 1-20, >20 quick returns), SWD, and insomnia disorder as predictors. Significance level was set to .05.

**RESULTS**

Demographic characteristics are presented in Table 1. Most of the nurses were females (90.5%) and mean age in wave 1 was 32.5 years (SD=8.5). Three-shift and two-shift rotation were the most common work schedules (Table 1). Mean number of night shifts last year was 23.5 (SD=36.7) and mean number of quick returns last year was 33.4 (SD=35.4). Shift work disorder and insomnia disorder were present in 27.3% and 31.7% of the nurses, respectively. In total, 56.0% of the nurses (n=885) reported headache complaints during the last year, and 48.1% (n=763) frequent headache (≥1 day per month). Migraine, TTH, chronic headache, and MOH were present in 19.6% (n=302), 27.9 (n=435), 2.3% (n=37), and 1.2% (n=19) of the total sample of nurses, respectively (Table 1).

We did not find any significant differences between the prevalence of frequent headache, migraine, TTH, chronic headache or MOH across work schedules (Table 2). Similarly, logistic regression analyses with adjustment for sex, age, percentage of full-time equivalent, marital status, and children living at home, revealed no association between the different headache types and work schedule (Table 3).

The prevalence of TTH was higher in nurses working night shifts last year compared to those not working night shifts, but we found no association between frequent headache, migraine, chronic headache or MOH and number of night shifts last year (Table 2). Similarly, in the adjusted logistic regression analysis, TTH was significantly associated with >20 night shifts

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last year (OR=1.41, 1.07-1.86) (Table 3). There were no associations between the different headache types and number of quick returns last year (Tables 2 and 3).

The prevalence of frequent headache, migraine, and chronic headache were all clearly higher among nurses with SWD compared to nurses without SWD (Table 2). Furthermore, adjusted logistic regression analyses revealed that frequent headache, migraine, and chronic headache all were significantly associated with SWD, with odd ratios 2.04, 1.62-2.59; 1.60, 1.21-2.12; 2.45, 1.25-4.80, respectively (Table 3). TTH and MOH were not significantly associated with SWD (Tables 2 and 3).

The prevalence of frequent headache, migraine, chronic headache, and MOH were all clearly higher among nurses with insomnia disorder compared to nurses without insomnia disorder (Table 2). These findings were also present in the adjusted logistic regression analyses, with OR 1.79, 1.43-2.23; 1.55, 1.18-2.02; 3.03, 1.54-5.95, 7.62, 2.48-23.41, respectively (Table 3). The only headache type that was not associated with insomnia disorder was TTH (Tables 2 and 3).

## DISCUSSION

The present study showed that nurses with different work schedules reported similar prevalence of frequent headache, migraine, TTH, chronic headache, and MOH. These findings did thus not support our hypothesis that shift working nurses would report higher prevalence of headaches than day workers. However, nurses with high number of night shifts during the last year reported higher prevalence of TTH than nurses with no night shifts. Furthermore, nurses with SWD and insomnia disorder reported higher prevalence of most types of headache compared to nurses without SWD and insomnia disorder, respectively.

We hypothesized that night and shift work would be associated with higher prevalence of headaches. This was based on the well-known association between lack of sleep and headache.[15 37] It is well known that both rotating shift work schedules and night work normally will cause circadian rhythm misalignment and sleep deprivation.[9 38 39] In line with this, a Chinese study showed that number of night shifts was positively associated with prevalence of different types of headache.[22] However, a recent Danish study did not find any association between treatment-seeking migraine and night work or variable working hours.[16]

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In the latter study, only fixed evening work was found to be associated (positively) with migraine. One possible explanation for the lack of association between headaches and work schedules in the present study may be the "healthy shift worker effect". This is based on the assumption that shift workers have better health than those who avoid or quit shift work.[40] Hence, nurses with headaches may be more reluctant to work shifts or quit shift work more frequently than others, leading to underestimates of the possible negative effects of shift work in studies like the present one.

Similarly, the number of night shifts worked the last year was not associated with frequent headache, migraine, chronic headache, or MOH. However, TTH was associated with high number of night shifts. This finding suggests that there may be different sleep-headache mechanisms in TTH than in e.g. migraine.[41] In line with this, a polysomnography study found that TTH patients need more sleep than healthy controls, and that inadequate sleep may contribute to increased pain sensitivity in TTH.[42] Furthermore, a high number of night shifts may not necessarily only cause sleep deprivation, but may also be experienced as stressful and thereby precipitate TTH. High work stress is a risk factor for primary headaches, especially tension-type headache.[22 43] Whether circadian misalignment in itself (often occurring among shift and night workers) triggers headaches is not known, and this topic should receive more attention in the future.

Many Norwegian nurses with rotating shift schedules have quick returns (defined as shifts separated by less than 11 hours) in their roster. For the nurses, most quick returns involve working an evening shift followed by a day shift. Such short rest in-between shifts typically cause sleep deprivation and health problems.[4 5] However, we found no association between headaches and quick returns. This was surprising, and may suggest that short-term sleep deprivation, as seen with quick returns, may not pose a major problem in relation to headache risk. This lack of association was found even though a high percentage of the nurses reported frequent quick returns.

In the present study, frequent headache, migraine, and chronic headache were all associated with SWD. These novel findings suggest that nurses who do not cope well with shift work are at increased risk of other health complaints like headaches. However, our study cannot say anything about cause-and-effect. That is, it may be that headache increases the risk of SWD. Future studies should consequently focus on whether there may be common vulnerability

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factors (e.g. genetic, health behaviour, etc.) between headaches and sleep related disorders. Interestingly and surprisingly, TTH was not associated with SWD, suggesting that different pathophysiological mechanisms may be involved across the different types of headaches. This issue warrants further studies.

Insomnia disorder was associated with all headache types, except TTH, which is in line with the findings from several other studies.[15 44 45] However, few studies have used formal diagnostic criteria for insomnia disorder, like the present study. Thus, one major asset with the present study was the use of ICSD and ICHD criteria for sleep disorders and headache classification, respectively. Surprisingly, TTH was not associated with insomnia disorder in our study, in contrast to two other population-based studies.[37 46] However, none of those studies used the formal diagnostic criteria for insomnia disorder. Lack of association between insomnia disorder and TTH may be related to methodological limitations, but suggests the need for more research, and especially studies with a longitudinal design. MOH was significantly associated with insomnia disorder, but not with any of the work-related variables. In fact, our data indicate that nurses with insomnia disorder had more than 7 times higher risk of MOH than those without insomnia disorder. This strong association warrants further studies.

**Strengths and limitations**

The present study was based on a large and homogeneous sample of nurses that limits the influence from possible confounding variables. Other strengths were the use of validated headache diagnoses and a validated insomnia scale as well as criteria-based SWD diagnostics. Furthermore, the study did not have a primary focus on headache, it was one of many health outcomes. Thus, a possible selection bias related to headache was unlikely. In terms of limitations, it should be noted that the response rate in the first wave was low, which may make the interpretation of the data and conclusions less generalizable. Still, the response rate in wave 6 where the headache questionnaire was included was high. Due to the high number of participants in our survey, it was not feasible to apply the gold standard, i.e. a clinical interview by a physician experienced in headache and sleep diagnostics. For the same reason, prospective headache and sleep diaries were not feasible. However, the questionnaire-based headache diagnostic procedures have been included in several previous large population-based studies and have been validated against clinical interviews with a high degree of agreement.[25 31 32] A limitation of the headache questionnaire is that migraine and TTH are

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mutually exclusive, i.e. the questionnaire only allows the participant to be diagnosed with the most bothersome headache subtype even though some might suffer from both migraine and TTH [25]. It is possible that differences between migraine and TTH are underestimated owing to the presence of people with TTH in the migraine group and vice versa, making the two groups more similar than they actually are. Thus, some caution is needed when interpreting the results. As migraine is hierarchically more important in the headache classification [26] than TTH, it is possible that there is an underestimation of TTH in the sample. However, the prevalence of the different headaches reported in the present study is similar to those reported previously,[22 24 25 27 29] strengthening the assumption of representativeness of the study population. The number of participants with chronic headache and MOH were low, limiting the statistical power in these analyses. We adjusted for several confounders known to influence shift work and headache, however, many other relevant factors were not adjusted for, e.g. physical inactivity, stress, and psychological disturbances. Lack of such adjustment should be taken into consideration when interpreting the results. Finally, it should be noted that the cross-sectional design does not permit any conclusions about causality in the relationship between headaches and work variables.

**Conclusion**

We found a significant association between headaches and SWD and insomnia disorder in our cohort of nurses. In fact, nurses with SWD reported higher prevalence of frequent headache, migraine, and chronic headache compared to nurses not having SWD. Similarly, nurses with insomnia disorder, compared to those without, reported higher prevalence of all types of headache, except TTH. Although we did not find any association between different types of headache and work schedule or quick returns, TTH was associated with high number of night shifts. Future longitudinal research should be conducted in order to investigate the causality/directionality of association between headaches and work variables.

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## Competing interests statement

None declared.

## Data sharing

No additional data available.

## Contributorship statement

BB: contributed to the design of the study, data collection, data analysis, drafted the paper, and approved the final version.

SP: contributed to the design of the study, data collection, data analysis, revised the paper, and approved the final version.

BEM: contributed to the design of the study, data collection, data analysis, revised the paper, and approved the final version.

SW: contributed to the design of the study, data collection, data analysis, revised the paper, and approved the final version.

ESK: contributed to the design of the study, data analysis, revised the paper, and approved the final version.

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Table 1. Characteristics of the Norwegian nurses in the study.

| Sex (n=1578): Female | 90.5% |
|---|---|
| Age in wave 1 (n=1583): mean (SD) | 32.5 (8.5) years |
| Percentage of full-time equivalent (n=1536): | |
|   <50% | 3.9% |
|   50-75% | 20.3% |
|   76-90% | 16.5% |
|   >90% | 59.2% |
| Married/cohabiting (n=1582): Yes | 76.5% |
| Children living at home (n=1578): Yes | 63.3% |
| Work schedule (n=1532): | |
|   Day only | 19.3% |
|   Evening only | 0.4 |
|   Two-shift rotation | 32.4% |
|   Night shift only | 6.6% |
|   Three-shift rotation | 36.9% |
|   Other schedules including night shifts | 4.4% |
| Number of night shifts last year (n=1534): | |
|   0 night shifts | 39.8% |
|   1-20 night shifts | 26.1% |
|   >20 night shifts | 34.0% |
| Number of quick returns last year (n=1511): | |
|   0 quick returns | 22.6% |
|   1-20 quick returns | 25.2% |
|   >20 quick returns | 52.2% |
| Shift work disorder (n=1567): Yes | 27.3% |
| Insomnia disorder (n=1585): Yes | 31.7% |
| Headache last year (n=1579): Yes | 56.0% |
| Frequent headache (≥1 day per month) (n=1585): Yes | 48.1% |
| Migraine (n=1537): Yes | 19.6% |
| Tension-type headache (n=1559): Yes | 27.9% |
| Chronic headache (n=1577): Yes | 2.3% |
| Medication-overuse headache (n=1579): Yes | 1.2% |

SD, standard deviation.  n, number of nurses.

Table 2. Prevalence of different types of headache complaints among Norwegian nurses.

| | Frequent headache[1] % (n) | Migraine % (n) | Tension-type headache % (n) | Chronic headache[2] % (n) | Medication-overuse headache % (n) |
|---|---|---|---|---|---|
| Work schedule (n=1415-1459): | 0.2[a], p=.979 | 2.5[a], p=.472 | 3.5[a], p=.321 | 2.3[a], p=.510 | 1.7[a], p=.637 |
| Day only | 47.3 (140) | 22.6 (65) | 24.5 (71) | 1.7 (5) | 1.0 (3) |
| Two-shift rotation | 48.7 (242) | 20.3 (98) | 26.1 (129) | 3.2 (16) | 1.6 (8) |
| Night shift only | 47.5 (48) | 16.3 (16) | 29.0 (29) | 2.0 (2) | 2.0 (2) |
| Three-shift rotation | 47.6 (269) | 18.8 (103) | 29.9 (165) | 2.1 (12) | 0.9 (5) |
| Night shifts last year (n=1489-1534): | 3.4[a], p=.180 | 3.3[a], p=.188 | **6.9[a], p=.032** | 0.4[a], p=.813 | 1.1[a], p=.578 |
| 0 night shifts | 47.8 (292) | 21.9 (130) | 24.4 (147) | 2.6 (16) | 1.5 (9) |
| 1-20 night shifts | 44.6 (179) | 18.0 (70) | 30.0 (118) | 2.0 (8) | 0.8 (3) |
| >20 night shifts | 50.8 (265) | 18.1 (92) | 30.9 (159) | 2.3 (12) | 1.2 (6) |
| Quick returns last year (n=1465-1511): | 0.2[a], p=.902 | 1.5[a], p=.480 | 2.4[a], p=.296 | 0.2[a], p=.885 | 0.8[a], p=.666 |
| 0 quick returns | 47.4 (162) | 22.1 (73) | 24.8 (83) | 2.1 (7) | 1.2 (4) |
| 1-20 quick returns | 48.8 (186) | 18.9 (70) | 29.6 (111) | 2.4 (9) | 0.8 (3) |
| >20 quick returns | 48.7 (384) | 19.1 (146) | 28.8 (224) | 2.5 (20) | 1.4 (11) |
| Shift work disorder (n=1521-1567): | **36.9[a], p<.0005** | **11.3[a], p=.001** | 1.6[a], p=.208 | **5.7[a]. p=.017** | 0.5[a], p=.491 |
| No | 43.4 (494) | 17.7 (197) | 26.9 (301) | 1.8 (20) | 1.1 (12) |
| Yes | 60.7 (260) | 25.6 (104) | 30.2 (127) | 4.0 (17) | 1.6 (7) |
| Insomnia disorder (n=1537-1585): | **25.1[a], p<.0005** | **10.1[a], p=.001** | 0.0[a], p=.983 | **9.7[a], p=.002** | **15.6[a], p<.0005** |
| No | 43.8 (474) | 17.4 (184) | 28.0 (297) | 1.5 (16) | 0.5 (5) |
| Yes | 57.5 (289) | 24.5 (118) | 27.8 (138) | 4.2 (21) | 2.8 (14) |

[1]Headache ≥1 days per month. [2]Headache >14 days per month.
[a]Pearson Chi-square, with Yates' correction for continuity when used in a 2x2 table.
Significant findings are shown in **bold**.

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Table 3. Separate adjusted logistic regression analyses with different headache types as the dependent variables among Norwegian nurses.

| Independent variables | Frequent headache[1] OR (95% CI)[a] n=1439-1519 | Migraine OR (95% CI)[a] n=1398-1476 | Tension-type headache OR (95% CI)[a] n=1416-1495 | Chronic headache[2] OR (95% CI)[a] n=1432-1512 | Medication-overuse headache OR (95% CI)[a] n=1434-1514 |
|---|---|---|---|---|---|
| Work schedule | | | | | |
| Day only | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Two-shift | 1.07 (0.80-1.44) | 0.89 (0.62-1.28) | 1.11 (0.79-1.57) | 1.91 (0.68-5.32) | 1.49 (0.39-5.80) |
| Night only | 1.07 (0.65-1.77) | 0.75 (0.39-1.44) | 1.30 (0.74-2.28) | 1.18 (0.20-6.88) | 2.39 (0.32-17.65) |
| Three-shift | 1.01 (0.76-1.35) | 0.79 (0.55-1.14) | 1.31 (0.94-1.83) | 1.22 (0.42-3.56) | 0.86 (0.20-3.70) |
| Number of night shifts | | | | | |
| 0 night shifts | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| 1-20 night shifts | 0.86 (0.66-1.11) | 0.78 (0.56-1.09) | 1.27 (0.95-1.70) | 0.73 (0.30-1.74) | 0.51 (0.14-1.95) |
| >20 night shifts | 1.15 (0.90-1.47) | 0.80 (0.58-1.09) | **1.41 (1.07-1.86)** | 0.82 (0.38-1.80) | 0.78 (0.27-2.29) |
| Number of quick returns | | | | | |
| 0 quick returns | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| 1-20 quick returns | 1.09 (0.81-1.46) | 0.83 (0.57-1.21) | 1.30 (0.92-1.82) | 1.12 (0.41-3.05) | 0.66 (0.15-3.01) |
| >20 quick returns | 1.06 (0.82-1.39) | 0.81 (0.58-1.12) | 1.23 (0.91-1.67) | 1.21 (0.50-2.95) | 1.18 (0.37-3.83) |
| Shift work disorder | | | | | |
| No | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Yes | **2.04 (1.62-2.59)** | **1.60 (1.21-2.12)** | 1.19 (0.92-1.54) | **2.45 (1.25-4.80)** | 1.67 (0.64-4.40) |
| Insomnia disorder | | | | | |
| No | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Yes | **1.79 (1.43-2.23)** | **1.55 (1.18-2.02)** | 1.01 (0.79-1.29) | **3.03 (1.54-5.95)** | **7.62 (2.48-23.41)** |

[1]Headache ≥1 days per month. [2]Headache >14 days per month.
[a]Separate logistic regression analyses for each independent variable with adjustment for sex, age, percentage of full-time equivalent, marital status, and children living at home.
Significant findings are shown in **bold**.

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STROBE Statement—checklist of items that should be included in reports of observational studies

| | Item No | Recommendation |
|---|---|---|
| **Title and abstract** | 1 | (*a*) Indicate the study's design with a commonly used term in the title or the abstract |
| | | (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found |
| See page 1 and 3 | | |
| **Introduction** | | |
| Background/rationale<br>See page 5 and 6 | 2 | Explain the scientific background and rationale for the investigation being reported |
| Objectives<br>See page 6 | 3 | State specific objectives, including any prespecified hypotheses |
| **Methods** | | |
| Study design<br>See page 6 and 7 | 4 | Present key elements of study design early in the paper |
| Setting<br><br>See page 6 and 7 | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection |
| Participants | 6 | (*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up<br>*Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls<br>*Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants |
| | | (*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed<br>*Case-control study*—For matched studies, give matching criteria and the number of controls per case |
| See page 6 | | |
| Variables<br><br>See page 7 and 8 | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable |
| Data sources/<br>measurement<br><br>See page 6, 7 and 8 | 8* | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group |
| Bias<br>See page 12 | 9 | Describe any efforts to address potential sources of bias |
| Study size<br>See page 6 | 10 | Explain how the study size was arrived at |
| Quantitative variables<br><br>See page 8 | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why |
| Statistical methods | 12 | (*a*) Describe all statistical methods, including those used to control for confounding |
| | | (*b*) Describe any methods used to examine subgroups and interactions |

|  | | |
|---|---|---|
| | | (*c*) Explain how missing data were addressed |
| | | (*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed |
| | | *Case-control study*—If applicable, explain how matching of cases and controls was addressed |
| | | *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy |
| | | (*e*) Describe any sensitivity analyses |
| See page 8 and 9 | | |

**Results**

| Participants | 13* | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed |
|---|---|---|
| | | (b) Give reasons for non-participation at each stage |
| | | (c) Consider use of a flow diagram |
| See page 9 | | |
| Descriptive data | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders |
| | | (b) Indicate number of participants with missing data for each variable of interest |
| | | (c) *Cohort study*—Summarise follow-up time (eg, average and total amount) |
| Page 9 and 17 | | |
| Outcome data | 15* | *Cohort study*—Report numbers of outcome events or summary measures over time |
| | | *Case-control study—*Report numbers in each exposure category, or summary measures of exposure |
| | | *Cross-sectional study—*Report numbers of outcome events or summary measures |
| Page 9 and 10 | | |
| Main results | 16 | (*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included |
| | | (*b*) Report category boundaries when continuous variables were categorized |
| | | (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period |
| Page 18 and 19 | | |
| Other analyses | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses |
| Page 18 and 19 | | |

**Discussion**

| Key results | 18 | Summarise key results with reference to study objectives |
|---|---|---|
| Page 10 | | |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias |
| Page 12 | | |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence |
| Page 10-12 | | |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results |
| Page 12 | | |

**Other information**

| | | |
|---|---|---|
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based |

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*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

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## Migraine, tension-type headache and medication-overuse headache in a large population of shift working nurses - a cross-sectional study in Norway

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# Migraine, tension-type headache and medication-overuse headache in a large population of shift working nurses – a cross-sectional study in Norway

Bjørn Bjorvatn MD PhD[1,2], Ståle Pallesen PhD[2,3], Bente E. Moen MD PhD[1], Siri Waage PhD[1,2], Espen S. Kristoffersen MD PhD[4]

[1] Department of Global Public Health and Primary Care, University of Bergen, Norway.

[2] Norwegian Competence Center for Sleep Disorders, Haukeland University Hospital, Norway.

[3] Department of Psychosocial Science, University of Bergen, Norway.

[4] Department of General Practice, University of Oslo, Norway.

Corresponding author:

Bjørn Bjorvatn

Department of Global Public Health and Primary Care

University of Bergen

Kalfarveien 31, N-5018 Bergen

Norway

Phone: +4755586088

Fax: +4755586130

Email: bjorn.bjorvatn@uib.no

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**ABSTRACT**

**Objectives**

To investigate associations between different types of headache and shift work.

**Design, participants and outcome measures**

Nurses with different work schedules (day work, two-shift rotation, night work, three-shift rotation) participated in a cohort study with annual surveys that started in 2008/2009. In 2014 (wave 6), a comprehensive headache instrument was included in the survey, in which 1585 nurses participated. Headaches were assessed according to the International Classification of Headache Disorders IIIb. Frequent headache (≥1 day per month), migraine, tension-type headache, chronic headache (headache >14 days per month), and medication-overuse headache ( chronic headache + acute headache medication ≥10 days last month) comprised the dependent variables. Adjusted (for sex, age, percentage of full-time equivalent, marital status, children living at home) logistic regression analyses were conducted with work schedule, number of night shifts worked last year, number of quick returns (<11 hours in-between shifts) last year, shift work disorder, and insomnia disorder as predictors.

**Results**

Frequent headache, migraine, and chronic headache were associated with shift work disorder (OR 2.04, 95% CI 1.62-2.59; 1.60, 1.21-2.12; 2.45, 1.25-4.80, respectively) and insomnia disorder (OR 1.79, 95% CI 1.43-2.23; 1.55, 1.18-2.02; 3.03, 1.54-5.95, respectively), but not with work schedule, number of night shifts or number of quick returns. Tension-type headache was only associated with >20 night shifts last year (OR 1.41, 95% CI 1.07-1.86). Medication-overuse headache was only associated with insomnia disorder (OR 7.62, 95% CI 2.48-23.41).

**Conclusions**

We did not find any association between different types of headache and work schedule. However, tension-type headache was associated with high number of night shifts. Nurses with sleep disorders (insomnia disorder and shift work disorder) reported higher prevalence of frequent headache, migraine, chronic headache and medication-overuse headache (only insomnia) compared to nurses not having insomnia disorder and shift work disorder, respectively.

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**Strengths and limitations of this study**

- A large and homogeneous sample of nurses with different work schedules
- Validated questionnaires for diagnosing different types of headache and sleep disorders
- No clinical interviews by physicians
- Few nurses with some of the headache subtypes which limits statistical power in these analyses
- No conclusions about causality due to the cross-sectional design

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## INTRODUCTION

Shift work is associated with impaired health, and several studies show that working shifts increase the risk of sleep disturbances, cardiovascular disease, metabolic disorders, and cancer.[1] Sleep disturbances are considered to be the most common complaints, especially among rotating shift workers and night workers.[2 3] Night workers are on duty during their biological resting phase and are enforced to schedule sleep to their biological active phase. This has been proposed as a causative factor for sleep and health problems.[1] Accordingly, studies suggest that the number of night shifts per year and the number of quick returns (defined at shifts with less than 11 hours in-between) per year are associated with increased risk of health complaints and sick leave.[4-7]

Recently, the focus on shift workers fulfilling the criteria for shift work disorder (SWD) has been intensified.[8-10] SWD is characterized by complaints of sleep problems and excessive sleepiness caused by work schedules overlapping with the habitual time for sleep.[8 11] This disorder affects 4.8-44.3% of nurses depending on type of work schedule.[12] SWD has been associated with impaired health, e.g. depression and hypertension.[8 10 12 13]

Few studies have specifically investigated the association between shift work and the presence and severity of headache. This is somewhat surprising, considering the association between sleep and headache.[14-16] Many of the existing studies suffer from methodological limitations, such as low number of participants (<300) [17-19] and not using validated headache questions.[17-21] One study from China reported that greater number of night shifts is positively associated with prevalence of headache,[22] and another study from Taiwan suggested that shift work increases the risk of migraine.[23] A Scandinavian study found an association between evening work, but not night work, and migraine.[16] The relationship between sleep and headache seems to be bidirectional. Lack of sleep can trigger headache, but sleep may also alleviate headache.[15] Disturbed sleep due to shift work is therefore likely to increase the risk of headache. The most common primary headaches in the general population are migraine and tension-type headache.[24] Most studies have focused on migraine and shift work,[15 16] although tension-type headache (TTH) is considered the most common form of headache with an estimated worldwide prevalence of approximately 40%.[24] The prevalence of migraine in the general population is 10-16%.[24 25] Chronic headache is defined as headache occurring more than 14 days per month and is present in 2-4% of the general population.[24-27] Medication-overuse headache (MOH) is a condition characterized by chronic headache and overuse of

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acute headache medications, usually defined as intake of acute pain or migraine medications 10 or more days per month.[26 28] The prevalence of medication-overuse headache in the general population is 1-2%, with more females being afflicted than males.[28 29]

As headache is common in the general population and since sleep loss, that often occurs concomitant with shift work, may trigger headache, we aimed to investigate whether different types of headache (i.e. migraine, TTH, chronic headache, MOH) were related to work schedules, number of night shifts, number of quick returns, SWD, and insomnia disorder. Nurses comprise a large population of shift workers and are thereby suitable for such studies. We hypothesized that nurses involved in night and shift work would report a higher prevalence of headaches compared to day workers.

## METHODS

### Procedure and participants

The data stemmed from the ongoing longitudinal cohort study "SUrvey of Shift work, Sleep and Health (SUSSH)" among Norwegian nurses. The first data collection was conducted during winter 2008/2009 (wave 1) when a sample of 5400 nurses was randomly selected from the Norwegian Nurses Organisation's (NNO) membership roll and invited to participate. A total of 2059 (response rate = 38.1%) nurses completed the questionnaire at the first wave. In order to increase the study population, an additional sample of 906 newly educated nurses (response rate = 33.1%) was recruited in 2009. The total sample in wave 1 therefore included 2965 nurses, see details in Bjorvatn et al.[30] The nurses who responded to the first wave have been invited to participate in annual follow-ups by receiving questionnaires sent by postal mail with pre-paid envelopes for returning the completed forms. Up to two reminders were sent to nurses who did not respond. The nurses who returned the questionnaire took part in a lottery, in which 25 individuals won a gift card with a value of 500 NOK (~ 60 US $). The present study reports findings based on data from the sixth (2014) wave, in which the headache questionnaire was included. A total of 1991 out of 2869 eligible nurses completed the questionnaire at wave 6, yielding a response rate of 69.4%. Nurses that reported that they were no longer working as nurses at wave 6 were excluded from the analyses, leaving a total study population of 1585 nurses.

Demographics and work-related factors

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The demographic variables were assessed in wave 6, except for age and sex that were registered in wave 1. The nurses responded to questions about marital status (married/cohabiting; yes/no), children living at home (yes/no), percentage of full-time equivalent (<50%, 50-75%, 76-90%. >90% position), work schedule (day only, evening only, two-shift rotation (day and evening), night only, three-shift rotation (day, evening and night), and other schedules including night work), number of night shifts worked last year, and number of quick returns (defined as less than 11 hours between consecutive work shifts) worked last year. Few nurses worked "evening only" (n=6) and "other schedules including night shifts" (n=67), and these shifts were therefore excluded in the analysis of the association between work schedule and headache.

Headache

The comprehensive headache questionnaire was designed to determine whether the nurses suffered from headache, and fulfilled the International Classification of Headache Disorders (ICHD) IIIb criteria for migraine, tension-type headache (TTH) and medication-overuse headache (MOH).[26] The nurses were first screened: "Have you suffered from headache during the last year?", and only nurses who answered "yes" were asked to respond to the other headache items. The screening positive headache sufferers were asked to report frequency, attack duration, intensity and accompanying headache symptoms to classify migraine and TTH, accordingly. The diagnoses of migraine and TTH were mutually exclusive. Frequent headache was defined as headache ≥1 day per month, and chronic headache was defined as headache >14 days per month, independently of the underlying subtype of headache. MOH was defined as chronic headache and intake of acute headache medication ≥10 days last month. The questionnaire-based headache diagnoses used here have previously been validated in a large unselected general population sample.[25 31 32]

Shift work disorder (SWD)

SWD was measured with three previous used questions[11 12] based on the minimal criteria listed in the second edition of the International Classification of Sleep Disorders (ICSD-2).[33] The questions were: a) Do you experience either difficulties sleeping or experience excessive sleepiness? (yes/no), b) Is the sleep or sleepiness problem related to a work schedule that makes you work when you normally would sleep? (yes/no), c) Have you had this sleep or sleepiness problem related to the work schedule for at least one month? (yes/no). Participants were classified as having SWD if they endorsed all three questions.

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Insomnia disorder

Insomnia symptoms were evaluated with Bergen Insomnia Scale (BIS).[34] The BIS consists of six items, and was developed based on the diagnostic criteria for insomnia according to 4th and text revision version of the Diagnostic and Statistical Manual for Mental Disorders (DSM-IV-TR).[35] The items are scored along an eight-point scale indicating the number of days per week for which a specific insomnia symptom is experienced (0-7 days). The items refer to sleep onset (sleep latency exceeding 30 minutes), wake after sleep onset (more than 30 minutes), early morning awakening (more than 30 minutes), non-restorative sleep, daytime impairment, and dissatisfaction with sleep. The time frame is insomnia symptoms experienced during the past month. According to DSM-5 criteria,[36] insomnia disorder is defined as scoring 3 days per week or more on at least one of the first three items as well as 3 days per week or more on at least one of the latter two items. Missing responses to any of the insomnia questions were treated as not reporting that specific insomnia symptom. The scale has acceptable test-retest reliability, and good convergent and discriminative validity in relation to other self-report measures as well as to polysomnographic data.[34] Cronbach's alpha for the BIS was 0.83 in the present sample.

Ethics

The study was approved by the Regional Committee for Medical and Health Research Ethics of Western Norway (REK-West, no 088.08). Written informed consent was obtained from all participants.

Patient and public involvement

The questionnaire was developed by a group of researchers experienced with shift work and shift work related problems. The participating nurses were not involved in the design, recruitment or conduct of the study. The results will be disseminated to the study participants in the yearly report we send to the journal of the Norwegian nurses. Here we address last year's published data from the cohort study. In addition, the results will appear on a designated website – www.sussh.no (after publication).

Statistics

The statistical analyses were conducted with IBM SPSS Statistics 23 for Windows. The prevalence of frequent headache, migraine, TTH, chronic headache, and MOH in relation to

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the different work schedules, categories of night shifts and quick returns last year, SWD and insomnia disorder were explored by the Pearson chi-square tests (with Yates' correction for continuity when used in a 2 x 2 table). In addition, separate adjusted (with sex, age, percentage of full-time equivalent, marital status, children living at home as co-variates) logistic regression analyses were performed to assess different headaches (frequent headache, migraine, TTH, chronic headache, MOH) as dependent variables with work schedule (day only as a reference, compared to two-shift rotation, night only and three-shift rotation), number of night shifts last year (0, 1-20, >20 night shifts), number of quick returns last year (0, 1-20, >20 quick returns), SWD, and insomnia disorder as predictors. Significance level was set to .05.

**RESULTS**

Demographic characteristics are presented in Table 1. Most of the nurses were females (90.5%) and mean age in wave 1 was 32.5 years (SD=8.5). Three-shift and two-shift rotation were the most common work schedules (Table 1). Mean number of night shifts last year was 23.5 (SD=36.7) and mean number of quick returns last year was 33.4 (SD=35.4). Shift work disorder and insomnia disorder were present in 27.3% and 31.7% of the nurses, respectively. In total, 56.0% of the nurses (n=885) reported headache complaints during the last year, and 48.1% (n=763) frequent headache (≥1 day per month). Migraine, TTH, chronic headache, and MOH were present in 19.6% (n=302), 27.9 (n=435), 2.3% (n=37), and 1.2% (n=19) of the total sample of nurses, respectively (Table 1).

We did not find any significant differences between the prevalence of frequent headache, migraine, TTH, chronic headache or MOH across work schedules (Table 2). Similarly, logistic regression analyses with adjustment for sex, age, percentage of full-time equivalent, marital status, and children living at home, revealed no association between the different headache types and work schedule (Table 3).

The prevalence of TTH was higher in nurses working night shifts last year compared to those not working night shifts, but we found no association between frequent headache, migraine, chronic headache or MOH and number of night shifts last year (Table 2). Similarly, in the adjusted logistic regression analysis, TTH was significantly associated with >20 night shifts

last year (OR 1.41, 95% CI 1.07-1.86) (Table 3). There were no associations between the different headache types and number of quick returns last year (Tables 2 and 3).

The prevalence of frequent headache, migraine, and chronic headache were all clearly higher among nurses with SWD compared to nurses without SWD (Table 2). Furthermore, adjusted logistic regression analyses revealed that frequent headache, migraine, and chronic headache all were significantly associated with SWD, with odd ratios 2.04, 95% CI 1.62-2.59; 1.60, 1.21-2.12; 2.45, 1.25-4.80, respectively (Table 3). TTH and MOH were not significantly associated with SWD (Tables 2 and 3).

The prevalence of frequent headache, migraine, chronic headache, and MOH were all clearly higher among nurses with insomnia disorder compared to nurses without insomnia disorder (Table 2). These findings were also present in the adjusted logistic regression analyses, with OR 1.79, 95% CI 1.43-2.23; 1.55, 1.18-2.02; 3.03, 1.54-5.95, 7.62, 2.48-23.41, respectively (Table 3). The only headache type that was not associated with insomnia disorder was TTH (Tables 2 and 3).

**DISCUSSION**

The present study showed that nurses with different work schedules reported similar prevalence of frequent headache, migraine, TTH, chronic headache, and MOH. These findings did thus not support our hypothesis that shift working nurses would report higher prevalence of headaches than day workers. However, nurses with high number of night shifts during the last year reported higher prevalence of TTH than nurses with no night shifts. Furthermore, nurses with SWD and insomnia disorder reported higher prevalence of most types of headache compared to nurses without SWD and insomnia disorder, respectively.

We hypothesized that night and shift work would be associated with higher prevalence of headaches. This was based on the well-known association between lack of sleep and headache.[15 37] It is well known that both rotating shift work schedules and night work normally will cause circadian rhythm misalignment and sleep deprivation.[9 38 39] In line with this, a Chinese study showed that number of night shifts was positively associated with prevalence of different types of headache.[22] However, a recent Danish study did not find any association between treatment-seeking migraine and night work or variable working hours.[16]

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In the latter study, only fixed evening work was found to be associated (positively) with migraine. One possible explanation for the lack of association between headaches and work schedules in the present study may be the "healthy shift worker effect". This is based on the assumption that shift workers have better health than those who avoid or quit shift work.[40] Hence, nurses with headaches may be more reluctant to work shifts or quit shift work more frequently than others, leading to underestimates of the possible negative effects of shift work in studies like the present one.

Similarly, the number of night shifts worked the last year was not associated with frequent headache, migraine, chronic headache, or MOH. However, TTH was associated with high number of night shifts. This finding suggests that there may be different sleep-headache mechanisms in TTH than in e.g. migraine.[41] In line with this, a polysomnography study found that TTH patients need more sleep than healthy controls, and that inadequate sleep may contribute to increased pain sensitivity in TTH.[42] Furthermore, a high number of night shifts may not necessarily only cause sleep deprivation, but may also be experienced as stressful and thereby precipitate TTH. High work stress is a risk factor for primary headaches, especially tension-type headache.[22 43] Whether circadian misalignment in itself (often occurring among shift and night workers) triggers headaches is not known, and this topic should receive more attention in the future.

Many Norwegian nurses with rotating shift schedules have quick returns (defined as shifts separated by less than 11 hours) in their roster. For the nurses, most quick returns involve working an evening shift followed by a day shift. Such short rest in-between shifts typically cause sleep deprivation and health problems.[4 5] However, we found no association between headaches and quick returns. This was surprising, and may suggest that short-term sleep deprivation, as seen with quick returns, may not pose a major problem in relation to headache risk. This lack of association was found even though a high percentage of the nurses reported frequent quick returns.

In the present study, frequent headache, migraine, and chronic headache were all associated with SWD. These novel findings suggest that nurses who do not cope well with shift work are at increased risk of other health complaints like headaches. However, our study cannot say anything about cause-and-effect. That is, it may be that headache increases the risk of SWD. Future studies should consequently focus on whether there may be common vulnerability

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factors (e.g. genetic, health behaviour, etc.) between headaches and sleep related disorders. Interestingly and surprisingly, TTH was not associated with SWD, suggesting that different pathophysiological mechanisms may be involved across the different types of headaches. This issue warrants further studies.

Insomnia disorder was associated with frequent headache, migraine, chronic headache, and medication-overuse headache, which is in line with the findings from several other studies.[15] [44 45] However, few studies have used formal diagnostic criteria for insomnia disorder, like the present study. Thus, one major asset with the present study was the use of ICSD and ICHD criteria for sleep disorders and headache classification, respectively. Surprisingly, TTH was not associated with insomnia disorder in our study, in contrast to two other population-based studies.[37 46] However, none of those studies used the formal diagnostic criteria for insomnia disorder. Lack of association between insomnia disorder and TTH may be related to methodological limitations, but suggests the need for more research, and especially studies with a longitudinal design. MOH was significantly associated with insomnia disorder, but not with any of the work-related variables. In fact, our data indicate that nurses with insomnia disorder had more than 7 times higher risk of MOH than those without insomnia disorder. This strong association warrants further studies.

**Strengths and limitations**

The present study was based on a large and homogeneous sample of nurses that limits the influence from possible confounding variables. Other strengths were the use of validated headache diagnoses and a validated insomnia scale as well as criteria-based SWD diagnostics. Furthermore, the study did not have a primary focus on headache, it was one of many health outcomes. Thus, a possible selection bias related to headache was unlikely. In terms of limitations, it should be noted that the response rate in the first wave was low, which may make the interpretation of the data and conclusions less generalizable. Still, the response rate in wave 6 where the headache questionnaire was included was high. Due to the high number of participants in our survey, it was not feasible to apply the gold standard, i.e. a clinical interview by a physician experienced in headache and sleep diagnostics. For the same reason, prospective headache and sleep diaries were not feasible. However, the questionnaire-based headache diagnostic procedures have been included in several previous large population-based studies and have been validated against clinical interviews with a high degree of agreement.[25 31 32] A limitation of the headache questionnaire is that migraine and TTH are

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mutually exclusive, i.e. the questionnaire only allows the participant to be diagnosed with the most bothersome headache subtype even though some might suffer from both migraine and TTH. [25] It is possible that differences between migraine and TTH are underestimated owing to the presence of people with TTH in the migraine group and vice versa, making the two groups more similar than they actually are. Thus, some caution is needed when interpreting the results. As migraine is hierarchically more important in the headache classification [26] than TTH, it is possible that there is an underestimation of TTH in the sample. However, the prevalence of the different headaches reported in the present study is similar to those reported previously, [22 24 25 27 29] strengthening the assumption of representativeness of the study population. The number of participants with chronic headache and MOH were low, limiting the statistical power in these analyses. In the logistic regressions we adjusted for several relevant confounders, like sex, age, percentage of full-time equivalent, marital status and children living at home, because such factors are known to influence shift work tolerance and headache. [12 21] However, other possible and relevant factors were not adjusted for, e.g. physical inactivity, stress, and psychological disturbances, [14 21] since data on these variables were not available. Lack of such adjustment should be taken into consideration when interpreting the results. Finally, it should be noted that the cross-sectional design does not permit any conclusions about causality in the relationship between headaches and work variables.

**Conclusion**

We found a significant association between headaches and SWD and insomnia disorder in our cohort of nurses. In fact, nurses with SWD reported higher prevalence of frequent headache, migraine, and chronic headache compared to nurses not having SWD. Similarly, nurses with insomnia disorder, compared to those without, reported higher prevalence of all types of headache, except TTH. Although we did not find any association between different types of headache and work schedule or quick returns, TTH was associated with high number of night shifts. Future longitudinal research should be conducted in order to investigate the causality/directionality of association between headaches and work variables.

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**Competing interests statement**

None declared.

**Data sharing**

No additional data available.

**Contributorship statement**

BB: contributed to the design of the study, data collection, data analysis, drafted the paper, and approved the final version.

SP: contributed to the design of the study, data collection, data analysis, revised the paper, and approved the final version.

BEM: contributed to the design of the study, data collection, data analysis, revised the paper, and approved the final version.

SW: contributed to the design of the study, data collection, data analysis, revised the paper, and approved the final version.

ESK: contributed to the design of the study, data analysis, revised the paper, and approved the final version.

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Table 1. Characteristics of the Norwegian nurses in the study.

| | |
|---|---|
| Sex (n=1578): Female | 90.5% |
| Age in wave 1 (n=1583): mean (SD) | 32.5 (8.5) years |
| Percentage of full-time equivalent (n=1536): | |
| <50% | 3.9% |
| 50-75% | 20.3% |
| 76-90% | 16.5% |
| >90% | 59.2% |
| Married/cohabiting (n=1582): Yes | 76.5% |
| Children living at home (n=1578): Yes | 63.3% |
| Work schedule (n=1532): | |
| Day only | 19.3% |
| Evening only | 0.4 |
| Two-shift rotation | 32.4% |
| Night shift only | 6.6% |
| Three-shift rotation | 36.9% |
| Other schedules including night shifts | 4.4% |
| Number of night shifts last year (n=1534): | |
| 0 night shifts | 39.8% |
| 1-20 night shifts | 26.1% |
| >20 night shifts | 34.0% |
| Number of quick returns last year (n=1511): | |
| 0 quick returns | 22.6% |
| 1-20 quick returns | 25.2% |
| >20 quick returns | 52.2% |
| Shift work disorder (n=1567): Yes | 27.3% |
| Insomnia disorder (n=1585): Yes | 31.7% |
| Headache last year (n=1579): Yes | 56.0% |
| Frequent headache (≥1 day per month) (n=1585): Yes | 48.1% |
| Migraine (n=1537): Yes | 19.6% |
| Tension-type headache (n=1559): Yes | 27.9% |
| Chronic headache (n=1577): Yes | 2.3% |
| Medication-overuse headache (n=1579): Yes | 1.2% |

SD, standard deviation.  n, number of nurses.

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Table 2. Prevalence of different types of headache complaints among Norwegian nurses.

| | Frequent headache[1] % (n) | Migraine % (n) | Tension-type headache % (n) | Chronic headache[2] % (n) | Medication-overuse headache % (n) |
|---|---|---|---|---|---|
| Work schedule (n=1415-1459): | 0.2[a], p=.979 | 2.5[a], p=.472 | 3.5[a], p=.321 | 2.3[a], p=.510 | 1.7[a], p=.637 |
| Day only | 47.3 (140) | 22.6 (65) | 24.5 (71) | 1.7 (5) | 1.0 (3) |
| Two-shift rotation | 48.7 (242) | 20.3 (98) | 26.1 (129) | 3.2 (16) | 1.6 (8) |
| Night shift only | 47.5 (48) | 16.3 (16) | 29.0 (29) | 2.0 (2) | 2.0 (2) |
| Three-shift rotation | 47.6 (269) | 18.8 (103) | 29.9 (165) | 2.1 (12) | 0.9 (5) |
| Night shifts last year (n=1489-1534): | 3.4[a], p=.180 | 3.3[a], p=.188 | **6.9[a], p=.032** | 0.4[a], p=.813 | 1.1[a], p=.578 |
| 0 night shifts | 47.8 (292) | 21.9 (130) | 24.4 (147) | 2.6 (16) | 1.5 (9) |
| 1-20 night shifts | 44.6 (179) | 18.0 (70) | 30.0 (118) | 2.0 (8) | 0.8 (3) |
| >20 night shifts | 50.8 (265) | 18.1 (92) | 30.9 (159) | 2.3 (12) | 1.2 (6) |
| Quick returns last year (n=1465-1511): | 0.2[a], p=.902 | 1.5[a], p=.480 | 2.4[a], p=.296 | 0.2[a], p=.885 | 0.8[a], p=.666 |
| 0 quick returns | 47.4 (162) | 22.1 (73) | 24.8 (83) | 2.1 (7) | 1.2 (4) |
| 1-20 quick returns | 48.8 (186) | 18.9 (70) | 29.6 (111) | 2.4 (9) | 0.8 (3) |
| >20 quick returns | 48.7 (384) | 19.1 (146) | 28.8 (224) | 2.5 (20) | 1.4 (11) |
| Shift work disorder (n=1521-1567): | **36.9[a], p<.0005** | **11.3[a], p=.001** | 1.6[a], p=.208 | **5.7[a]. p=.017** | 0.5[a], p=.491 |
| No | 43.4 (494) | 17.7 (197) | 26.9 (301) | 1.8 (20) | 1.1 (12) |
| Yes | 60.7 (260) | 25.6 (104) | 30.2 (127) | 4.0 (17) | 1.6 (7) |
| Insomnia disorder (n=1537-1585): | **25.1[a], p<.0005** | **10.1[a], p=.001** | 0.0[a], p=.983 | **9.7[a], p=.002** | **15.6[a], p<.0005** |
| No | 43.8 (474) | 17.4 (184) | 28.0 (297) | 1.5 (16) | 0.5 (5) |
| Yes | 57.5 (289) | 24.5 (118) | 27.8 (138) | 4.2 (21) | 2.8 (14) |

[1]Headache $\geq 1$ days per month. [2]Headache >14 days per month.
[a]Pearson Chi-square, with Yates' correction for continuity when used in a 2x2 table.
Significant findings are shown in **bold**.

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Table 3. Separate adjusted logistic regression analyses with different headache types as the dependent variables among Norwegian nurses.

| Independent variables | Frequent headache[1] OR (95% CI)[a] n=1439-1519 | Migraine OR (95% CI)[a] n=1398-1476 | Tension-type headache OR (95% CI)[a] n=1416-1495 | Chronic headache[2] OR (95% CI)[a] n=1432-1512 | Medication-overuse headache OR (95% CI)[a] n=1434-1514 |
|---|---|---|---|---|---|
| Work schedule | | | | | |
| Day only | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Two-shift | 1.07 (0.80-1.44) | 0.89 (0.62-1.28) | 1.11 (0.79-1.57) | 1.91 (0.68-5.32) | 1.49 (0.39-5.80) |
| Night only | 1.07 (0.65-1.77) | 0.75 (0.39-1.44) | 1.30 (0.74-2.28) | 1.18 (0.20-6.88) | 2.39 (0.32-17.65) |
| Three-shift | 1.01 (0.76-1.35) | 0.79 (0.55-1.14) | 1.31 (0.94-1.83) | 1.22 (0.42-3.56) | 0.86 (0.20-3.70) |
| Number of night shifts | | | | | |
| 0 night shifts | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| 1-20 night shifts | 0.86 (0.66-1.11) | 0.78 (0.56-1.09) | 1.27 (0.95-1.70) | 0.73 (0.30-1.74) | 0.51 (0.14-1.95) |
| >20 night shifts | 1.15 (0.90-1.47) | 0.80 (0.58-1.09) | **1.41 (1.07-1.86)** | 0.82 (0.38-1.80) | 0.78 (0.27-2.29) |
| Number of quick returns | | | | | |
| 0 quick returns | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| 1-20 quick returns | 1.09 (0.81-1.46) | 0.83 (0.57-1.21) | 1.30 (0.92-1.82) | 1.12 (0.41-3.05) | 0.66 (0.15-3.01) |
| >20 quick returns | 1.06 (0.82-1.39) | 0.81 (0.58-1.12) | 1.23 (0.91-1.67) | 1.21 (0.50-2.95) | 1.18 (0.37-3.83) |
| Shift work disorder | | | | | |
| No | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Yes | **2.04 (1.62-2.59)** | **1.60 (1.21-2.12)** | 1.19 (0.92-1.54) | **2.45 (1.25-4.80)** | 1.67 (0.64-4.40) |
| Insomnia disorder | | | | | |
| No | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Yes | **1.79 (1.43-2.23)** | **1.55 (1.18-2.02)** | 1.01 (0.79-1.29) | **3.03 (1.54-5.95)** | **7.62 (2.48-23.41)** |

[1]Headache ≥1 days per month. [2]Headache >14 days per month.
[a]Separate logistic regression analyses for each independent variable with adjustment for sex, age, percentage of full-time equivalent, marital status, and children living at home.
Significant findings are shown in **bold**.

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STROBE Statement—checklist of items that should be included in reports of observational studies

| | Item No | Recommendation |
|---|---|---|
| **Title and abstract** | 1 | (*a*) Indicate the study's design with a commonly used term in the title or the abstract |
| | | (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found |
| See page 1 and 3 | | |
| **Introduction** | | |
| Background/rationale  See page 5 and 6 | 2 | Explain the scientific background and rationale for the investigation being reported |
| Objectives  See page 6 | 3 | State specific objectives, including any prespecified hypotheses |
| **Methods** | | |
| Study design  See page 6 and 7 | 4 | Present key elements of study design early in the paper |
| Setting   See page 6 and 7 | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection |
| Participants | 6 | (*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants |
| | | (*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case |
| See page 6 | | |
| Variables   See page 7 and 8 | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable |
| Data sources/ measurement   See page 6, 7 and 8 | 8* | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group |
| Bias  See page 12 | 9 | Describe any efforts to address potential sources of bias |
| Study size  See page 6 | 10 | Explain how the study size was arrived at |
| Quantitative variables   See page 8 | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why |
| Statistical methods | 12 | (*a*) Describe all statistical methods, including those used to control for confounding |
| | | (*b*) Describe any methods used to examine subgroups and interactions |

(*c*) Explain how missing data were addressed

(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed

*Case-control study*—If applicable, explain how matching of cases and controls was addressed

*Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy

(*e*) Describe any sensitivity analyses

See page 8 and 9

**Results**

| Participants | 13* | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed |
| | | (b) Give reasons for non-participation at each stage |
| | | (c) Consider use of a flow diagram |
| See page 9 | | |
| Descriptive data | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders |
| | | (b) Indicate number of participants with missing data for each variable of interest |
| | | (c) *Cohort study*—Summarise follow-up time (eg, average and total amount) |
| Page 9 and 17 | | |
| Outcome data | 15* | *Cohort study*—Report numbers of outcome events or summary measures over time |
| | | *Case-control study—*Report numbers in each exposure category, or summary measures of exposure |
| | | *Cross-sectional study—*Report numbers of outcome events or summary measures |
| Page 9 and 10 | | |
| Main results | 16 | (*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included |
| | | (*b*) Report category boundaries when continuous variables were categorized |
| | | (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period |
| Page 18 and 19 | | |
| Other analyses | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses |
| Page 18 and 19 | | |

**Discussion**

| Key results Page 10 | 18 | Summarise key results with reference to study objectives |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias |
| Page 12 | | |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence |
| Page 10-12 | | |
| Generalisability Page 12 | 21 | Discuss the generalisability (external validity) of the study results |

**Other information**

| | | |
|---|---|---|
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based |

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\*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.