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CHRONOTYPE, NURSING ACTIVITY AND GENDER: A SYSTEMATIC REVIEW

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ABSTRACT

Aim: To synthesise evidence about the effect of individual circadian preference (chronotype) and gender in the development of sleep and mood problems in nursing professionals.

Background: Shift workers are more prone to having unhealthy habits and unfavourable clinical conditions than non-shift workers. These associations are mediated by chronotype and gender differences have also been detected.

Design: A quantitative systematic review

Data sources: Electronic searches were performed in MEDLINE, Scopus, ScienceDirect and Web of Science from 1 July 2012 – 1 July 2017.

Review methods: A systematic review was conducted using the Cochrane Collaboration guidelines and two quality assessment tools: the National Heart, Lung and Blood Institute and GRADE. Inclusion criteria were quantitative studies where the sample consists entirely of nurses, analysing circadian rhythms or individual chronotype or gender and sleep/mood disturbances in nursing activity. The review was reported using the PRISMA statement.

Results: A total of 23 studies were included in the review (five cohort studies and 18 cross-sectional studies). Data on gender-specific attention were scarce (two studies) and showed a higher incidence of sleep problems. Female nurses with eveningness-oriented personality seem to be more prone to having sleep disorders, insomnia, fatigue and anxiety than male and morningness ones.

Conclusions: Evidence seems to show that female nurses with an evening-oriented preference suffer more problems of insomnia, sleepiness, fatigue and anxiety. The impact of our results may affect nurses, patient safety and the quality of clinical practice.

Keywords: chronobiology, circadian rhythm, chronotype, nursing, nursing activity, systematic review, gender, sleep, mood, patient safety.

SUMMARY STATEMENT

Why is this research/review need?

- Some unhealthy habits and unfavourable conditions have been shown to be associated with a late individual circadian preference.
- Gender differences by have been found in the development of sleep and mood symptoms or disorders
- Shift work is inexorably linked to nursing since patients need continuous assistance.

What are the key findings?

- Female nurses with an eveningness-oriented personality seem to be more prone to sleep disorders, insomnia, fatigue and anxiety.
- Some studies have reported that variables related to cognitive performance are more affected in women than in men.
- The determination of the type of individual circadian orientation is crucial for the well-being of the nursing professional, as well as for patient safety.

How should the findings be used to influence policy/practice/research/education?

- Developing gender-sensitive strategies to refine the work organisation in health-care professionals, as well as to consider individual circadian preferences.
- More research is needed to determine how the desynchronization of the circadian time structure is established among shift-work nurses, with special attention given to vigilance and oversight.

Introduction

The rhythmic expression of biological variables and the temporal organisation of biological rhythms represents an adaptation to rhythmic changes of the surrounding environment. Thus, biochemical, physiological and behavioural processes vary according to rhythmic patterns with a characteristic periodicity (Reinberg & Ashkenazi, 2003).

Most rhythms observed in nature and especially in humans, exhibit a circadian periodicity. A circadian rhythm can be defined as a set of molecular mechanisms on a transcriptional basis, based on both positive and negative feedback circuits, with a free period (so-called 'free-running') of about 24 h (Edery, 2000). This rhythm is controlled by so-called biological clocks (or circadian pacemakers or oscillators). These biological clocks are reset (acrophase or peak: Φ) and calibrated (period: $\tau = 24$ h) by environmental signals that also have a 24-h period, such as photic (sunrise/sunset) and non-photic (activity/rest or noise/silence) signals. These periodic environmental signals are called synchronizers, synchronising agents (entraining agents) or *zeitgebers* (Halberg et al., 1953; Toitou & Haus, 1992).

Background

Both the main biological clock and the peripheral clocks present in most organs can undergo desynchronizations, which is associated with potential health risks (Young & Bray, 2007). There are two main routes to desynchronizing the body's rhythms (Comperatore & Kruger, 1990): (a) fast, through the rapid crossing of multiple time zones (jet lag); and (b) slow, through feeding times, the timing of sports activities and shift work. These desynchronizing routes are characterized by a series of symptoms and disorders of variable entity, such as sleep disorders (e.g., delayed sleep, early awakening and fragmented sleep with frequent awakenings), headache, irritability, loss of concentration, dyspepsia and digestive difficulties (Tahghighi et al. 2017; Waterhouse, Reilly, Atkinson, & Edwards, 2007; Driscoll, Grunstein, & Rogers, 2007; Reid & Abbott, 2015; Manfredini, Manfredini, Fersini, & Conconi, 1998).

Horne and Ostberg established the existence of various circadian variations (so-called *chronotypes*) in people through the development of a 19-item self-assessment questionnaire (Horne & Ostberg, 1976). In general terms, a *chronotype* is mainly linked to the different sleep-wake cycles (an endogenous component of the circadian rhythm time structure [CTS]) (Argent, Benbenishty & Flaatten, 2015). Disruption of the CTS has been related to employee performance, accident vulnerability and health (Smolensky, Reinberg & Sackett-Lundeen, 2017). Several scales are used in the scientific community to determine a morningness-eveningness personality (Horne & Ostberg, 1976; Torsvall & Åkerstedt, 1980; Zavada, Gordijn, Beersma, Daan, & Roenneberg, 2005). Some unhealthy habits and unfavourable conditions have been shown to be associated with later chronotype and gender differences are often noted (Fabbian et al., 2016).

On the other hand, nursing activity is inexorably linked to shift work since patients need continuous assistance (24 h per day). In this context, it would be interesting to study how chronotype and gender might be related in this group of health-care professionals.

The review

Aims

The aim of this systematic review was to synthesise and evaluate evidence of the effects of chronotype and gender in the development of sleep and mood disorders or symptoms among nursing professionals.

Design

The Cochrane Handbook (version 5.1.0) (Higgins & Green, 2011) was used to guide review processes. The review was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline (Moher, Liberati, Tetzlaff, Altman, PRISMA Group, 2009).

Search methods

An electronic search was carried out using the following databases: MEDLINE, Scopus, ScienceDirect and Web of Science. Moreover, even if (to the best of our knowledge) no previous studies were available, the Cochrane and PROSPERO databases were checked for information about possible reviews addressing this topic.

The keywords used were (i) related to circadian rhythms: "chronotype", "morningness" and "eveningness"; (ii) according to gender: "female", "gender" and "women"; and (iii) associated with nursing activity: "nurs*", "nurses" and "nursing". The search strategy combined each search theme with the Boolean operator AND. The final strategy was: ((chronotype OR morningness OR eveningness) AND (female OR gender OR women) AND (nurs* OR nurses OR nursing)). In all the databases, the title/abstract/keywords were included in the search criteria. With the aim of not changing the search strategy in each database, we opted to perform a simple search rather than searching for MeSH terms. Also, the words "chronotype", "morningness" and "eveningness" are not heavily used and they have not yet been included as MeSH terms. No age limits or restriction of language were established.

Inclusion and exclusion criteria

We included original studies with the following variable: (i) observational studies (cross-sectional, cohort studies and case-control studies); (ii) studies where the sample consists entirely of nurses; and (iii) studies analysing circadian rhythms or individual chronotype or gender and sleep/mood disturbances in nursing activity.

We excluded: (i) other types of studies, such as systematic reviews, root case analyses, dissertations and editorials; (ii) studies not considering circadian rhythms or individual chronotype or gender and sleep/mood disorders in these health-care professionals; and (iii) studies published more than 5 years previously (1 July 2012 – 1July 2017).

Search outcome

Three reviewers reached a consensus regarding the search terms and databases that were used. Between 7 July 2017 and 15 July 2017, each reviewer independently carried out an electronic search in the databases above. Both reviewers arrived at the same results in each database: a total of 93 records (31 in MEDLINE, six in ScienceDirect, 33 in Scopus and 23 in Web of Science).

PRISMA recommendations were followed to report the search process (Moher et al. 2009). After removing those manuscripts that were duplicated (44 entries), we reviewed the remaining 49 articles, noting whether the title and abstract met the inclusion/exclusion criteria. At this step, the reviewers reached a consensus, considering 36 entries as acceptable. After reading the full-text of these 36 articles, we removed 13 for the following reasons: 12 were publications more than 5 years previously and one analysed the chronotype and sleep problems in nursing students exclusively. It was considered to include the manuscripts published in the last five years due to the exponential increase of the scientific literature in this period. However, the 12 articles that were excluded by this criterion have been detailed in the Supplementary Table 1. Finally, the total number of articles selected for the synthesis process was 23. The search process is shown in the PRISMA flow chart diagram (*Figure 1*).

Quality appraisal

The methodological quality of the selected articles was assessed by the same three researchers. Assessing the risk of bias is a part of the conduct and reporting of any systematic review. Observational studies are more susceptible to bias than experimental studies (particularly in participant allocation, outcome assessment). In this regard,

for assessing risk of bias of individual studies we used a quality assessment tool from the National Heart, Lung and Blood Institute for Observational Cohort and Cross-Sectional studies (National Heart, Lung and Blood Institute 2014a). This quality appraisal included the study question, study population, study participants' representation, sample size, exposure measures for the observational

studies, intervention, outcome measures, blinding of outcome assessors, follow-up (loss rate) and statistical analysis. The judgement of the risk of potential for selection, information, measurement bias or confounding is categorised as good, fair or poor (Supplementary Table 2 & 3). We assessed the quality of the evidence by applying the GRADE approach to determine the risk of bias, inconsistency, indirectness, imprecision and quality of evidence (Jaeschke et al., 2008).

Data extraction and synthesis

Twenty-three manuscripts met the inclusion criteria. The following information was extracted: author and publication year, study design, sample size and shift work, country, notes about gender predominance and chronotype and mean outcome associated to sleep or mood disorder. All descriptive statistics were used. To explore the association between gender and chronotype and sleep and mood disorder in nursing professionals in the included studies, study results were extracted in more detail. The data abstraction and synthesis processes were carried out independently by three reviewers. Disagreements were resolved by consensus. Due to the methodology and heterogeneity of included studies, it was not possible to carry out a meta-analysis so results were presented as a narrative summary (Higgins & Green, 2011).

Results

Overview of the studies

The 23 selected studies were observational: 18 were cross-sectional and the remaining were cohort studies (only five were prospective). According to sleep and mood disorder, the main findings are shown in Table 1 and Table 2.

Cohort studies

Four of the five cohort studies were prospective, only Vedaa et al. (2013) carried out a retrospective study (Vedaa, Bjorvatn, Magerøy, Thun, & Pallesen, 2013).

Association with gender

Four out of the five cohort studies had a predominance of women higher to 85% (Vedaa et al., 2016; Storemark, Fossum, Bjorvatn, Moen, Flo, Pallesen, 2013; Vedaa, Bjorvatn, Magerøy, Thun, & Pallesen, 2013; Saksvik-Lehouillier et al., 2012), with only that by Reinke et al. (2015) presenting a lower percentage (74%). Vedaa et al. (2013) found that gender predicted significant change in the Diurnal Type Scale (DTS), with women obtaining higher scores in the morning chronotype ($\beta = 0.65$; $p = 0.06$) (Vedaa, Bjorvatn, Magerøy, Thun, & Pallesen, 2013).

Association with chronotype

To determine chronotype, Reinke et al. (2015) used the Munich Chronotype Questionnaire for shift work score (MCTQshift) and the Diurnal Type Scale (DTS) was used in the remaining cohort studies (Vedaa et al., 2016; Storemark, Fossum, Bjorvatn, Moen, Flo, Pallesen, 2013; Vedaa, Bjorvatn, Magerøy, Thun, & Pallesen, 2013; Saksvik-Lehouillier et al., 2012).

Morningness was positively associated with sleep-related day shift tolerance ($\beta = 0.17$ (0.05); $p < 0.001$) (Storemark, Fossum, Bjorvatn, Moen, Flo, Pallesen, 2013), having children at home ($\beta = 0.42$ (0.21); $p < 0.01$) (Reinke, Ozbay, Dieperink, & Tulleken, 2015; Vedaa, Bjorvatn, Magerøy, Thun, & Pallesen, 2013), higher probability to nap before work (22.86% vs. 52.46%; $p = 0.004$) (Reinke, Ozbay, Dieperink, & Tulleken, 2015) and, together with positive spillover from work to family ($\beta = -0.11$; $p < 0.01$), predicted lower insomnia symptoms ($\beta = -0.09$; $p < 0.05$) (Vedaa et al., 2016). Higher DTS score (morningness personality) was also associated with the percentage of the full-time equivalent ($\beta = 0.05$; $p < 0.05$) and female gender. On the other hand, smaller DTS score (eveningness personality) was associated with higher number of night shifts over the past two years ($\beta = -0.06$; $p < 0.05$), whether the person had started smoking and consumed more alcohol ($\beta = -0.05$; $p < 0.05$) (Vedaa, Bjorvatn, Magerøy, Thun, & Pallesen, 2013). In general, morningness was negatively correlated with depression ($\beta = -0.14$; $p < 0.01$), sleepiness ($\beta = -0.13$; $p < 0.01$), fatigue ($\beta = -0.19$; p

< 0.01) and anxiety (β = -0.15; p < 0.05) after the second year of follow-up (Saksvik-Lehouillier et al., 2012).

Sleep and mood disorders

All selected cohort studies, except Reinke et al. (2015), found that sleep and mood disorders are consequences of the interaction between the individual/familiar (hardiness or languidity, having children, female gender) or work (percentage of the full-time equivalent) behavioural patterns, rather than a precursor to them (Vedaa et al., 2016). On the other hand, Reinke et al. (2015), with the smallest sample (N = 96) of the five selected cohort studies, found that there is no decrease in surveillance or safety when solving problems for both chronotypes (Reinke, Ozbay, Dieperink, & Tulleken, 2015).

Cross-sectional studies

Eighteen cross-sectional studies were selected.

Association with gender

The majority of cross-sectional studies (13 out of 18) (Yoshizaki et al., 2016; Peplonska, Bukowska, Ukowska, Gromadzinska, & Zienolddiny, 2016; Guerra et al., 2016; Lee et al., 2015; Selvi, Karakas, Boysan, & Selvi, 2014; Geiger-Brown et al., 2014; Yazdi, Haghighi, Javadi, & Rikhtegar, 2014; de Souza, Tavares, Macedo, Moreira, & Lautert, 2012; De Martino, Abreu, Barbosa, & Teixeira, 2013; Moreno, Marqueze, Lemos, Soares, & Lorenzi-Fillho, 2012; Chung, Liu, Lee, & Hsu, 2013) used the Horne-Otsberg Morningness-Eveningness Questionnaire (MEQ) to determine the circadian preference. Costa et al. (2014) and Korompeli et al. (2014) employed the Standard Shiftwork Index (SSI). The Diurnal Type Scale was used by Jung et al. (2015) and Petrov et al. (2014).

Six studies employed samples with only females (Yoshizaki et al., 2016; Peplonska, Bukowska, Ukowska, Gromadzinska, & Zienolddiny, 2016; Futenma et al., 2015; Petrov, Clarck, Molzof, Johnson, Cropsey, & Gamble, 2014; Yazde et al., 2014; Chung, Liu, Lee, & Hsu, 2013). Some authors opted for this approach because the proportion of men was low (Yoshizaki et al., 2016; Futenma et al., 2015) or because their inclusion modified the results for a dependent variable (e.g., the food behaviour questionnaire) (Yoshizaki et al. 2016). In all other studies, except Geiger-Browen et al. (2014) and Asaoka et al. (2013), who do not provide this data, the sample was predominantly composed of women, accounting for 86.5% (Korompeli, Muurlink, Tzvara, Velonakis, Lemonidou, & Sourtzi, 2014) to 98% (Jung & Lee, 2015) of the sample.

A gender-specific analysis was developed in only two articles (Korompeli, Muurlink, Tzvara, Velonakis, Lemonidou, & Sourtzi, 2014; Selvi, Karakas, Boysan, & Selvi, 2014). Korompeli et al. (2014) found that women had more sleep problems ($\beta = 5.95$ (1.75); $p < 0.01$) and experienced more digestive ($\beta = 2.32$ (0.75); $p < 0.01$) and cardiovascular problems ($\beta = 4.1$ (0.76); $p < 0.01$) than men. Also, women had higher scores on the general health questionnaire (GHQ) ($\beta = 2.62$ (1.01); $p < 0.05$) and on the cognitive anxiety sub-scale ($\beta = 2.40$ (1.06); $p < 0.05$) and had less shift time satisfaction ($\beta = -6.70$ (2.31); $p < 0.05$). In addition, women presented higher scores in the questionnaires for engagement/disengagement ($\beta = 5.00$ (1.68); $p < 0.01$ / $\beta = 5.16$ (1.77); $p < 0.01$), languidity ($\beta = 3.90$ (1.01); $p < 0.001$) and neuroticism ($\beta = 1.50$ (0.47); $p < 0.01$) and less flexibility ($\beta = -2.01$ (0.89); $p < 0.05$). However, no significant differences were found with respect to impulsivity ($\beta = -0.02$; $p = 0.72$) (Selvi, Karakas, Boysan, & Selvi, 2014).

In the studies exclusively consisting of women, the authors found that *eveningness* was associated with: (i) poor eating behaviours (less balanced diets [$\beta = -0.338$; $p < 0.05$] and abnormal eating patterns [$\beta = -0.196$; $p = 0.051$]) in shift-workers (Yoshizaki et al., 2016); (ii) predisposition to use hypnotics ($p < 0.001$) (Futenma et al., 2015), (iii) adaptive sleep strategies (sleep interruption and incomplete interruption) ($p < 0.01$) (Petrov, Clarck, Molzof, Johnson, Cropsey, & Gamble, 2014); and (iv) poor sleep quality (Odds Ratio [OR] = 2.1; 95% Confident Interval [95% CI] = 1.8–2.9; p =

0.004) (Yazdi, Haghighi, Javadi, & Rikhtegar, 2014). Indeed, Chung et al. (2013) showed that morningness-eveningness ($\beta = -0.22$; $p < 0.05$) through sleep hygiene (behavioural) ($\beta = 0.31$; $p < 0.001$) and menstrual distress ($\beta = 0.14$; $p < 0.05$) and mood states (psychological) ($\beta = 0.27$; $p < 0.001$) influenced sleep quality. The association between menstrual distress and morning chronotype was also studied by Peplonska et al. (2016), showing that higher total number of years of night shift work was associated with higher estradiol concentration ($p < 0.001$).

Association with chronotype

Eveningness personality was associated with high levels of emotional disturbances ($\beta = 0.07$ (0.03); $p < 0.001$) and vulnerability to insomnia ($\beta = 0.04$ (0.01); $p < 0.001$) and was correlated with poor sleep quality (Lee et al., 2015) and higher score on the impulsivity scale ($\beta = -0.18$; $p < 0.05$) (Selvi, Karakas, Boysan, & Selvi, 2014). This chronotype was associated with fatigue ($\beta = -0.06$; $p < 0.001$) and depression ($\beta = -0.18$; $p < 0.05$) (Jung & Lee, 2015), as well as with lesser sleep time ($r = -0.60$; $p < 0.001$) (De Martino, Abreu, Barbosa, & Teixeira, 2013). In rotation shift nurses, a late chronotype was associated with shift work disorders (OR = 1.67 (1.16 – 2.36); $p < 0.01$) (Asaoka et al., 2013) and sleep disturbances ($\beta = -2.07$; $p < 0.05$) in those working on 3 × 8 rotation shifts (Costa, Anelli, Castellini, Fustinoni, & Neri, 2014). Worse scores in the physical domain of quality of life (WHOQOL) were detected for *eveningness* nurses ($p = 0.003$) (de Souza, Tavares, Macedo, Moreira, & Lautert, 2012).

On the other hand, *moningness* was associated with higher scores in the psychological ($p = 0.02$), social ($p = 0.01$) and general domains ($p = 0.01$) of WHOQOL (de Souza, Tavares, Macedo, Moreira, & Lautert, 2012); greater work satisfaction ($\beta = 0.27$ (0.26); $p = 0.03$) and sleep quality ($\beta = -5.56$ (2.64); $p < 0.001$) (Moreno, Marqueze, Lemos, Soares, & Lorenzi-Fillho, 2012); higher shift work tolerance ($\beta = 0.09$; $p < 0.05$) (Jung & Lee, 2015); and less average sleepiness in shifts with greater temporal demand ($\beta = -0.08$ (0.07); $p < 0.05$) (Geiger-Brown et al., 2014). Otherwise, Saksvik-Lehouillier et al. (2013) found that nurses with morning chronotype and with less than 1 year of

experience working night shifts were more prone to general Shift Work Disorder (SWD) (β = 0.15 (0.08); $p < 0.05$), whereas more experienced nurses presented lesser scores on languidity (β = -0.29 (0.05); $p < 0.01$) and caffeine consumption (β = -0.12 (0.08); $p < 0.05$) and higher scores in flexibility (β = 0.13 (0.05); $p < 0.05$) (Korompeli, Muurlink, Tzvara, Velonakis, Lemonidou, & Sourtzi, 2014).

Sleep and mood disorders

Seven manuscripts presented results associated with mood disorders (Yoshizaki et al., 2016; Jung & Lee, 2015; Selvi, Karakas, Boysan, & Selvi, 2014; de Souza, Tavares, Macedo, Moreira, & Lautert, 2012; Saksvik-Lehouillier et al., 2012; Korompeli, Muurlink, Tzvara, Velonakis, Lemonidou, & Sourtzi, 2014; Chung, Liu, Lee, & Hsu, 2013). Korompeli et al. (2014) and Chung et al. (2013) also showed some results regarding sleep problems.

Higher levels of self-esteem (β = -0.22; $p < 0.001$) (Jung & Lee, 2015) and hardiness (Saksvik-Lehouillier et al., 2012) were associated with higher shift work tolerance (sleepiness [β = -0.17; $p < 0.01$], fatigue [β = -0.27; $p < 0.01$], anxiety [β = -0.34; $p < 0.01$] and depression) [β = -0.38; $p < 0.01$]). Behavioural and lifestyle factors can trigger effect of mood (Korompeli, Muurlink, Tzvara, Velonakis, Lemonidou, & Sourtzi, 2014). On the other hand, mood mediates, together with sleep hygiene practices, in the effect of the chronotype (Sobel test: 2.40; $p < 0.05$). Also both varibles and menstrual distress (Sobel test: 3.31; $p < 0.05$) mediate in sleep quality (Sobel test: 1.98; $p < 0.05$) (Chung, Liu, Lee, & Hsu, 2013). In fact, nurses working with shifts in agreement with personal chronotype showed higher scores ($p < 0.03$) in the WHOQOL 'environment' field than those disagreeing (de Souza, Tavares, Macedo, Moreira, & Lautert, 2012). Also, chronotype influenced attention deficit (β = -0.16; $p < 0.05$), hyperactivity (β = -0.15; $p < 0.01$) and impulsivity (β = -0.18; $p < 0.05$) (Selvi, Karakas, Boysan, & Selvi, 2014).

Low levels of sleep quality were reported in postmenopausal women (Peplonska, Bukowska, Ukowska, Gromadzinska, & Zienolddiny, 2016) and those shift nurses with a lack of physical exercise (68%) (De Martino, Abreu, Barbosa, & Teixeira, 2013). Compared with eveningness nurses,

greater job satisfaction was found in morningness-oriented nurses (β = 0.27 (0.26); p = 0.03) and with greater sleep quality (β = -5.56 (2.64); p < 0.001) (Moreno, Marqueze, Lemos, Soares, & Lorenzi-Fillho, 2012).

Those nurses with high levels of emotional disturbances (β = 0.30 (0.05); p < 0.001) and insomnia vulnerability (β = 0.18 (0.03); p < 0.001) had higher risk of sleep problems (Lee et al. 2015). Sleep disturbance was associated with hypnotic use (OR = 1.93 (1.09–3.42); p = 0.02) (Futenma et al., 2015); using more adaptive strategies (p < 0.01) (Petrov, Clarck, Molzof, Johnson, Cropsey, & Gamble, 2014), working in shifts (β = 1.90 (0.97); p < 0.05), being married (β = 4.28 (1.85); p < 0.03), living with a partner (β = 6.25 (2.77); p < 0.05) and presenting a chronic disease (β = 4.16 (1.22); p < 0.001) (Korompeli, Muurlink, Tzvara, Velonakis, Lemonidou, & Sourtzi, 2014); and languidity to overcome drowsiness (β = 0.23; p < 0.02) and flexibility of sleeping habits (β = -0.16; p < 0.05) during the morning shifts (Costa, Anelli, Castellini, Fustinoni, & Neri, 2014). Those with symptoms of sleep disturbance and with a somnolence trait had increased sleepiness (Geiger-Brown et al. 2014).

Risk of bias

In Supplementary Tables 2 and 3 are shown the quality appraisals for individual studies. In general, the overall quality rating ranged as good or fair. On the other hand, we also used the GRADE approach (Table 3). Due to the heterogeneity of the variables provided by the selected articles, we determined only the quality of evidence for chronotype (morningness/eveningness) and female gender. For both variables, we found a very low certainty, especially determined by not explanation of losses in follow-up of subjects, differences in comparator (type of shift), not optimal sample size and differences in outcome variables.

Discussion

To our knowledge, this is the first systematic review focused on detecting a possible relationship between nursing activity, *chronotype*, gender and sleep and mood disorders. Our findings could be read merely as slight associations. However, we propose that female nurses with an evening-oriented personality present higher sleep and mood problems.

The endogenous circadian clock generates daily variations of physiological and behavioural functions; moreover, individual human differences are also deeply influenced by the day-night cycle. In the 1970s, Horne and Ostberg showed possible individual differences in circadian attitudes (Horne & Ostberg, 1976). Mood, alertness, appetite and task performance – all psychological and behavioural variables – were shown to have a circadian pattern (Monk, Buysse & Reynolds, 1997). Different circadian patterns have been shown to have significant differences when comparing morning and evening types. Moreover, it has been demonstrated that chronotype is associated with a circadian gene polymorphism. The length of the repeat region of the *Per3* gene has been suggested as a potential genetic marker for extreme diurnal preference and might, therefore, influence the morningness/eveningness dimension (Archer et al. 2003). People who consistently prefer diurnal activity are defined as morning types, while those who prefer nocturnal activities are defined as evening types (Benedito- Silva, Menna- Barreto, Marques, & Tenreiro, 1990). A complex interaction among social, geographic and genetic factors determine the morningness/eveningness dimension; it has been reported that increasing age and female gender are associated with morningness (Carrier, Monk, Buysse, & Kupfer, 1997). The impact of different phase shift and, consequently, of work shift on health is a matter of debate; whereas morbidity (especially to sleep and mood disorders) appears to be more frequent in eveningness people. The authors tested the potential association between polymorphisms in circadian clock-related genes, seasonal affective disorder (SAD), seasonality (seasonal variations in mood and behaviour) and diurnal preference (morningness-eveningness tendencies) and found a possible involvement of circadian clock-related polymorphisms both in susceptibility to SAD and diurnal preference (Johansson et al. 2003). Disruptions in the sleep-wake cycle frequently characterise affective illness, linking the latter to sleep-wake and circadian rhythm

disturbance. Ashman et al. (1999) compared social rhythms and mood in patients with rapid cycling bipolar disorder against healthy control subjects. These patients showed a phase delay in the timing of morning activities during depression compared with hypomania or euthymia. Moreover, the timing of five (mostly morning) activities were phase delayed in patients compared with control subjects. These findings suggest that mood disorders are associated with a breakdown in the organisation of the ultradian rhythm (Ashman et al. 1999). Evening types have also been reported to be more frequent in depressive college students (Chelminski, Ferraro, Petros & Plaud, 1999). Hidalgo et al. (2009) evaluated the relationship between chronotype and the range of depressive symptoms, controlling for the effect of potential confounding variables and identified an association between evening typology and depressive symptoms in healthy subjects (Hidalgo, Caumo, Posser, Coccaro, Camozzato, & Chaves, 2009).

In agreement with the above-cited studies, we found an association between evening type and depressive symptoms in a restricted sample, namely shift working nurses.

Shift works can profoundly disrupt the body's circadian system, resulting in negative health consequences, such as metabolic syndrome and changes in body composition, negative psychological events, such as depression, anxiety and behavioural problems (Antypa, Vogelzangs, Meesters, Schoevers, & Penninx, 2016; Bei, Wiley, Trindler, & Manber, 2015; Koo et al., 2016; Siqueira, Griep, Rotember, Silva-Costa, & Mendes da Fonseca, 2016; Reutrakul & Knutson, 2015; Vetter, Devore, Ramin, Speizer, Willett, & Schernhammer, 2015; Wennman, Kronholm, Partonen, Peltonen, Vasankari, & Borudulin, 2015; Wong, Hasler, Kamarck, Muldoon, & Manuck, 2015; Manfredini, Fabbian, Cappadona, & Modesti, 2018) and cancer and sleep problems (Papantoniou et al., 2015; Akerstedt, Nordin, Alfredsson, Westerholm, & Kecklun, 2010; Bjorvatn, Magerøy, Moen, Pallesen, & Waage, 2015; Kecklund & Axelsson, 2016). These problems have been reported to be particularly prevalent in women (Li & Singh, 2014; Heller, Dogan, Schulz, & Reetz, 2014)

Generally, most shift work studies have been focused on male populations (Boivin, Trembaly, & James, 2007; Akerstedt & Knutsson, 1997; Kuljis et al., 2013). Labyak et al. (2002) found that women nurses working in shifts had sleep disturbance leading to menstrual irregularities and

reproductive disturbances, which were related to the negative impact of shift work on women's hormonal system. *Chronotype* and menstrual distress, through sleep hygiene and mood states, have been established as mediators of sleep quality (Chung, Liu, Lee, & Hsu, 2013). Moreover, greater time doing night shift work has been associated with higher estradiol concentration (Peplonska, Bukowska, Ukowska, Gromadzinska, & Zienolddiny, 2016).

It should be noted that the prevalence of women among nurses is high. Nineteen of the selected studies were based on a sample population consisting of greater than 85% women.

Familiar behavioural patterns have been related to sleep and mood disorders (Vedaa et al., 2016). Lowson & Arber (2014) reported that having some children at home (Reinke, Ozbay, Dieperink, & Tulleken, 2015; Vedaa, Bjorvatn, Magerøy, Thun, & Pallesen, 2013), a positive work-to-family transition (Vedaa et al. 2016) or obtaining social domains of quality of life (de Souza, Tavares, Macedo, Moreira, & Lautert, 2012) could affect the *chronotype*, orienting towards a lark chronotype. On the other hand, being married or living with a partner were associated with sleep disturbance and an eveningness chronotype (Korompeli, Muurlink, Tzvara, Velonakis, Lemonidou, & Sourtzi, 2014).

Psychosocial and lifestyle factors, such as higher level of self-esteem (Jung & Lee, 2015) or hardiness (Saksvik-Lehouillier et al. 2012), are associated with higher shift work tolerance and a morningness-oriented personality. On the contrary, emotional disturbances (Lee et al. 2015), attention deficit, hyperactivity and impulsivity (Selvi, Karakas, Boysan, & Selvi, 2014), smoking or consuming more alcohol (Vedaa, Bjorvatn, Magerøy, Thun, & Pallesen, 2013), lack of activity (De Martino, Abreu, Barbosa, & Teixeira, 2013), taking hypnotics (Futenma et al. 2015) and abnormal eating patterns (Yoshizaki et al. 2016) predisposed to an evening chronotype and sleep disorder (sleepiness or insomnia), fatigue and anxiety.

In agreement with Korompeli et al. (2014), shift-work affects female nurses, especially if they suffer because of older age, chronic diseases and domestic responsibilities. Similar findings have been reported by various authors (Yu, Yun, & Ahn, 2015; Nielsen, 2010). Therefore, increasing social support (Kageyama, Kobayashi, & Abe-Gotoh, 2011) and established good lifestyles (i.e., balanced

diet and physical activity) should be encouraged, thereby preventing the development of sleep and mood problems.

Indeed, work behavioural pattern (i.e., higher probability to nap before work) (Reinke, Ozbay, Dieperink, & Tulleken, 2015) or using of more adaptive strategies for shift-working (Petrov, Clarck, Molzof, Johnson, Cropsey, & Gamble, 2014) could help nurses. Asaoka et al. (2013), among 1021 Japanese nurses, found that SWD can be mostly prevented by lessening the amount time spent in night work, ensuring nap opportunities during night work and reducing the disruption of circadian rhythms. A recent study (Giorgi et al. 2017) found that nurses with SWD reported higher errors/accident rates (traffic accidents, procedural errors at work and work injuries). Santhi et al. (2016) evaluated the contribution to brain function due to the sleep-wake cycle and circadian rhythmicity in men and women and how it varies across cognitive domains and subjective dimensions. These authors found that effort showed the largest circadian modulation, whereas accuracy exhibited the largest gender difference in circadian modulation. Gender differences could not be explained by their study design; however, these authors suggested an impact of circadian rhythmicity and sex on waking cognition (Santhi, Lazar, McCabe, Lo, & Groeger, 2016). These novel aspects of gender-specific differences in personal performances should rise growing interest. To ensure the safety of patient and nurses, as well as the quality of clinical practice, educators and clinical preceptors should develop effective strategies (e.g, relaxation) to improve nursing students' sleep quality and integrate sleep education into nursing curricula to further advance the students' sleep knowledge in educational programs and practice (Huang, Liao, Chang, & Lai, 2017).

Limitations

Although an exhaustive electronic search without language limitations was conducted, we could not exclude the possibility that the number of selected studies was limited by our decision not to included the grey literature. Even though three important databases were analysed and relevant information was obtained in such a particular population. On the other hand, the search strategy might not be fully comprehensive. However, the methodological quality *per se* was not determined due to the limited

number and nature of the selected studies. We used the quality assessment tool from the National Heart, Lung and Blood Institute and the GRADE approach to obtain a clear and pragmatic interpretation for clinicians, patients and policymakers.

Conclusions

Our study findings reinforce the need to develop specific strategies to refine how we organise the work of health-care professionals, as well as to consider the individual circadian preferences of these workers. Our results clearly showed that the health status of nurses should be carefully evaluated. Moreover, it is important to consider that the well-being of nurses affects the quality of clinical practice and ultimately, patients' safety.

Personal chronotype, mediated mainly by individual, familiar and work behavioural factors and coupled with gender, represent variables of great interest in attempts to prevent sleep and mood disorder in nursing workers. This systematic review, although in the presence of limited data, shows that female nurses with eveningness-oriented personality seem to be more prone to having sleep disorders, insomnia, fatigue and anxiety than male and morningness ones.

Therefore, our findings support the need for further investigations addressing the adaptation of shift work to the individual chronotype, especially among healthcare professionals. Specifically, prospective cohort studies are recommended (with several measures), trying to avoid significant losses of follow-up and with homogeneous samples in terms of gender, age and work shifts. The determination of the type of individual circadian orientation is crucial for the well-being of the nursing professional, as well as for patient safety.

Author Contributions:

All authors have agreed on the final version and meet at least one of the following criteria (recommended by the ICMJE):

1) substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data;

2) drafting the article or revising it critically for important intellectual content.

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Table 1. Main findings for cross-sectional selected studies (1/5)

Author	Sample	Country	Notes about gender	Notes about chronotype	Sleep and mood disorder
(1) Yoshizaki et al. 2016	162 rotating nurses (39: D workers; 123: shift workers)	Japan	Total sample: women	E-type: less balanced diets (β=-0.338, p<0.05) and abnormal eating patterns (β=-0.196, p=0.051) in shift workers	Associations between rotating shift work, diurnal preference and eating behaviour.
(2) Peplonska et al. 2016	345 pre- and 187 post-menopausal nurses (263: rotating N shift-workers; and 269: D-workers)	Poland	Total sample: women	M-type: Positive association between estradiol and current night work status (p=0.019), night work frequency (p=0.012) and night work duration (p<0.001).	Higher scores for PSQI in postmenopausal women than premenopausal Chronotype: modifier of estradiol association among postmenopausal women
(3) Guerra et al. 2016	168 nurses (41% M-shift, 17.3% A- shift and 41.7% midnight)	Brazil	Predominance of women (94.1%)	Prevalence of N-type (55.6%)	Health professionals have sleep problems but do not have low quality of life or mood disturbance scores
(5) Lee et al. 2015	398 shift-work nurses	Taiwan	Predominance of women (97.5%)	E-type: high levels of emotional disturbances (β=0.07, p<0.001) and vulnerability to insomnia (β=0.04, p<0.001) correlated with poor sleep quality	High levels of emotional disturbances and vulnerability to insomnia have a higher risk of sleep disturbance.
(6) Futenma et al. 2015	997 rotating shift work nurses	Japan	Total sample: women.	E-type: higher use of hypnotics (OR 2.047; p=0.006)	E-type (p=0.006), age>27 years (p<0.001), presence of depression (p>0.001) and insomnia (p=0.023) associated with hypnotic use

E: evening; M: morning; N: Neutral; A: Afternoon; D: Day; N: Night; PSQI: Pittsburgh Sleep Quality Index

Table 1. Main findings for cross-sectional selected studies (2/5)

Author	Sample	Country	Notes about gender	Notes about chronotype	Sleep and mood disorder
(8) Jung et al. 2015	660 rotating shift-work nurses	South Korea	Predominance of women (98%)	M-type: negatively correlated with fatigue (β=-0.06, p<0.001) and depression (β=0.18, p<0.05). Positive correlation with shift work tolerance (β=0.09, p<0.05).	Age, M-type, self-esteem, social support, work stress, alcohol consumption, physical activity and n. of night hours associated with SWT
(9) Selvi et al. 2014	206 nurses (79 D and 127 N-shift workers)	Turkey	Predominance of women (91.1%): No differences: impulsivity	E-type: higher scores on impulsivity scale (β -0.18; p<0.05)	Attention deficit (β -0.16; p<0.05), hyperactivity (β -0.15; p<0.01) and impulsivity (β -0.18; p<0.05) change according to the chronotype
(10) Petrov et al. 2014	213 N-shift nurses	United State of America	Total sample: women	E-type was associated with adaptive sleep strategies: sleep interruption and incomplete interruption (2.8 [1.7]; p<0.01)	More adaptive strategies were associated with less sleep disturbance (18.8 [3.9]; p<0.01), E-type and fewer cardiovascular problems (15.1 [5.0]; p<0.05)
(11) Costa et al. 2014	294 nurses + 30 nurses. Different shifts: 3x8X5; 3x8x6; 2x12	Italy	Predominance of women (68% in ICUs and 75% in PSWs)	E-type: Sleep problems (β 0.23; p<0.02) and non-flexibility of sleep habits (β -0.16; p<0.05) in the morning shift	E-type, difficulty in overcoming sleepiness, non-flexibility in sleep habits and older age in nurses in 3x8 rotations

E: evening; M: morning; D: Day; N: Night; SWT: Shift Work Tolerance; ICU: Intensive Care Unit; PSW: Poli-Specialistic Wards,

Table 1. Main findings for cross-sectional selected studies (3/5)

Author	Sample	Country	Notes about gender	Notes about chronotype	Sleep and mood disorder
(13) Korompeli et al. 2014	365 nurses and nursing assistants working in shifts	Greece	Predominance of women (86.5%). W: more sleep (β 5.95; p<0.01), digestive (β 2.32; p<0.01) and cardiovascular problems (β 4.1; p<0.01). Higher scores on the GHQ (β 2.62; p<0.05), cognitive anxiety sub-scale (β 2.40; p<0.05) and less satisfaction working (β -6.70; p<0.05). Higher scores in coping, languidity, flexibility, and neuroticism.	M-type: higher scores on the disconnection and languidity scales (those with more years of work experience) (β -0.29; p<0.01)	Nursing shifts most directly affect: female nurses, who have chronic illness, older age and household responsibilities.
(14) Geiger-Brown et al. 2014	40 nurses with 12-hour shifts	United State of America	No data	M-chronotype and shifts with greater temporal demand: less sleepiness (β -0.08; p<0.05)	Nocturnal shifts, on the third night (when compared with the first one), symptoms of sleep disturbance and somnolent trait on the Epworth scale: higher sleepiness
(15) Yazdi et al. 2014	160 with 8-hour shift	Iran	Total sample: women	E-type: poorer sleep quality (OR 2.1 [1.8-2.9]; p=0.004)	E-type: poorer sleep quality. No differences between work shift and the nurses' age.

E: evening; M: morning; D: Day; N: Night; W: Women; GHQ: General Health Questionnaire

Table 1. Main findings for cross-sectional selected studies (4/5)

Author	Sample	Country	Notes about gender	Notes about chronotype	Sleep and mood disorder
(16) Chung et al. 2013	338 rotating shift-work nurses	Taiwan	Total sample: women	No data	Sleep hygiene practices (β 0.31; p<0.001) and mood (β 0.27; p<0.001) mediate the effect of chronotype (β -0.22; p<0.05) and menstrual alteration (β 0.14; p<0.05) in sleep quality.
(18) De Souza et al. 2012	101 nursing professionals. Fixed M or B	Brazil	Predominance of women (90.6%)	E-type: worse scores in the physical domain of WHOQOL (66.3 [10.1]; p=0.003). M-type: higher scores in the psychological (65.4 [9.6]; p=0.02), social (56.7 [17.2]; p=0.01) and general of WHOQOL (67.2 [12.8]; p=0.01)	Agreeing with their chronotypes: higher scores on the WHOQOL 'environment' field that those that disagreeing. (67.01 [10.83]; p<0.03)
(19) De Martino et al. 2013	60 nurses with 8-hour shift	Portugal	Predominance of women (88,33%)	M-type: less sleep time (r -0.60; p< 0.001)	Poorer sleep quality: lack of physical exercise, work shifts, and specific work for patient care
(20) Asaoka et al. 2013	1202 nurses (727 working 2-shifts, 315 3-shifts)	Japan	No data	E-type: higher SWD (OR 1.67 [1.16 – 2.36]; p<0.01)	Failure to perform naps during the night shift, higher hours of night work and a E-type: higher SWD

E: evening; M: morning; D: Day; WHOQOL: Quality of Life; SWD: Shift Work Distress

Table 1. Main findings for cross-sectional selected studies (5/5)

Author	Sample	Country	Notes about gender	Notes about chronotype	Sleep and mood disorder
(21) Saksvik-Lehouillier et al. 2013	749 nurses (322: <1 year of night shift experience, 427: >1 year)	Norway	Predominance of women (91.3% new; 87.5% experienced)	M-type: higher general SWD for new nurses (<1-year of night shift) (β 0.15 (0.08); p<0.05)	Young and hardiness: tolerance to work shifts. For the experienced one: languidity (β -0.29 (0.05); p<0.01, hours of work per week and caffeine consumption (β -0.12 (0.08); p<0.05) associated negatively, but flexibility positively (β 0.13 (0.05); p<0.05).
(23) Moreno et al. 2012	514 nurses (314 D-shift, 200 N-shift)	Brazil	Predominance of women (89% D-shift; 83% N-shift)	M-type: predictor of job satisfaction in D-workers (β 0.27 (0.26); p=0.03)	D-workers: greater M-type and quality of sleep (β -5.56 (2.64); p<0.001), greater job satisfaction. N-workers: satisfaction associated with sleep quality (β -5.56 (2.64); p<0.001) and hospital experience (β 0.27 (0.26); p=0.03)

E: evening; M: morning; D: Day; N: Night.

Table 2. Main findings for cohort selected studies

Author	Sample	Country	Notes about gender	Notes about chronotype	Sleep and mood disorder
(4) Vedaa et al. 2016	799 nurses shift-workers	Norway	Predominance of women (90%)	M-type with positive spillover from work-to-family lower insomnia symptoms (β -0.09; p<0.05)	Insomnia: consequence of individual and work-related factors, rather than a precursor to them
(7) Reinke et al. 2015	96 N-shift-work nurses	Holland	Predominance of women (73.95%)	M-type: more likely to nap before work and have young children at home (β 0.42 (0.21); p < 0.01)	Both chronotypes: No decrease in surveillance or safety to solve problems
(12) Storemark et al. 2013	700 nurses with 3-rotating shifts	Norway	Predominance of women (91.5%). No significance was found	M-type: sleep-related D shift tolerance (β 0.17 (0.05); p < 0.001)	Hardiness and languidity predict the sleep-related shift work tolerance in all types of shifts. Flexibility and M-type depend on the shift
(17) Vedaa et al. 2013	1144 nurses	Norway	Predominance of women (91%). Gender predicted significantly change in the DTS. W: higher scores in the M-type	M-type: higher score in women (β 0.65; p=0.06)	Higher scores on the DTS: percentage of the full-time equivalent, having children, and the female gender. Smaller DTS: Higher number of night shifts over the past two years, starting smoking and consumed more alcohol
(22) Saksvik-Lehouillier et al. 2012	642 nurses with 3-rotating shifts	Norway	Total sample: women	M-type: Negatively correlated with sleepinesss (β -0.13; p <0.01), fatigue (β -0.19; p < 0.01) and anxiety (β -0.15; p < 0.05)	Personality factors, such as hardiness, can predict changes related to work tolerance during the period of one year

DTS: Diurnal Type Scale; E: evening; M: morning; D: Day; N: Night

Table 3. Quality of the evidence according the GRADE approach (based on our systematic review)

Certainty assessment							Impact	Certainty
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**		
Morningness chronotype (assessed with: MEQ, DTS and SSI)								
12	Observational studies (cross-sectional and cohort studies)	not serious [a]	not serious	serious [b]	serious [c]	none	- Positive association between estradiol and current night work status, night work frequency and night work duration. - Positive correlation with shift work tolerance, less sleepiness and gender - Higher scores on the disconnection and languidity scales (those with more years of work experience); higher scores in quality of life and job satisfaction	⊕◯◯◯ VERY LOW
Eveningness chronotype (assessed with: MEQ, DTS and SSI)								
9	Observational studies (cross-sectional studies)	serious [a]	not serious	serious [b]	serious [c]	none	- Poor eating behaviours and higher use of hypnotics - Higher Shift Work Disorder, less quality of life and higher score on impulsivity – Poorer sleep quality, less and non-flexibility of sleep habits	⊕◯◯◯ VERY LOW
Female gender								
2	observational studies (cross-sectional and cohort studies)	serious [a]	not serious	serious [d]	not serious	none	- More sleep, digestive and cardiovascular problems. - Higher scores on the coping, languidly, flexibility and neuroticism - Higher scores in the morningness chronotype	⊕◯◯◯ VERY LOW

Variables evaluated in different studies were heterogeneous, only chronotype and gender were evaluated. Note: a. There were losses of follow-up of subjects in the studies that were not explained; b. Differences in the comparator (type of shift); c. In several studies the sample size is not optimal; d. Differences in the outcome variables

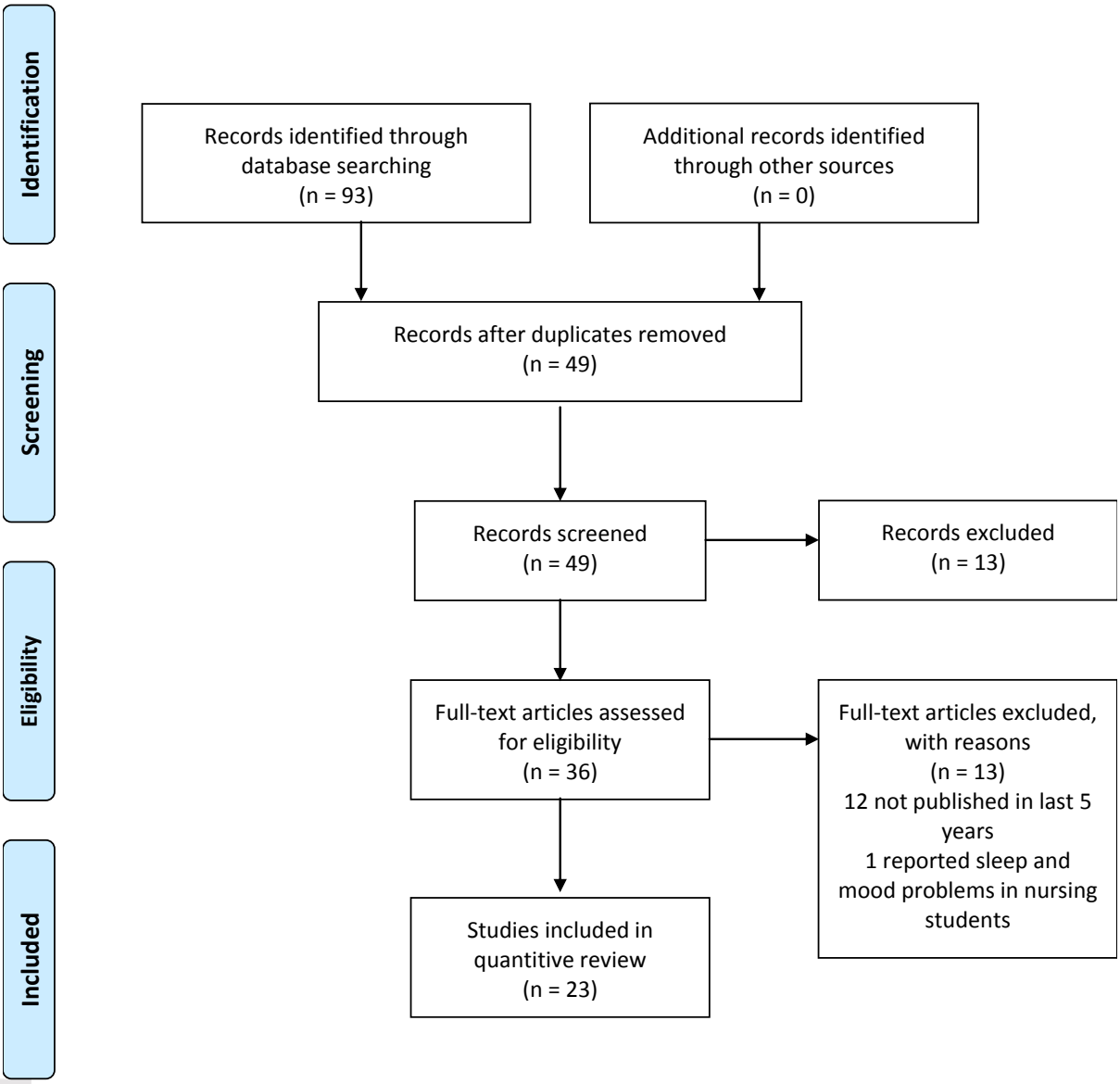

Figure 1. Flowchart of the inclusion procedure according to PRISMA