



ADHD, sleep, chronotype and health in a large cohort of Dutch nurses

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1. Background

Attention-deficit/hyperactivity disorder (ADHD) is a chronic neurodevelopmental disorder characterized by inattention and/or hyperactivity/impulsivity leading to impaired functioning. Reported prevalence estimates are 5.0% among children (Polanczyk and Rohde, 2007), 4.4% among adults (Kessler et al., 2006) and 2.8% among older adults (Michielsen et al., 2012). ADHD is associated with functional impairment, poorer social functioning (Eakin et al., 2004; Hoza, 2007; Michielsen et al., 2015; Young et al., 2003) and more comorbid psychiatric (Kooij, 2017; Polyzoï et al., 2018) and somatic disorders (Du Rietz et al., 2020; Instanes et al., 2018).

In recent years, studies have focused on ADHD and its associations with sleep disorders, specifically with the delayed sleep phase disorder (DSPD) (Bijlenga et al., 2019; Coogan and McGowan, 2017). DSPD is a problem in which the circadian clock has a 24-h rhythm that is significantly delayed in its timing compared to the time of the world, and with respect to the individual's desired sleep-onset and rising times (American Psychiatric Association, 2013; van Geijlswijk et al., 2010). This can result in a persistent or recurrent misalignment between the patient's sleep and activity pattern with the dark and light cycle of the environment, and being unable to sleep at a desired earlier time in the evening, getting up on time in the morning and feeling tired during daytime. DSPD patients are often characterized as “night owls” and when tested with chronotype questionnaires, they score on the eveningness end of the scale (Okawa and Uchiyama, 2007). With a prevalence of 73–78%, DSPD is the most common sleep problem associated with ADHD among both children and adults (Bijlenga et al., 2019; Craig et al., 2017; Hittle and Gillespie, 2018; Van Veen et al., 2010). In contrast, it occurs in 3.3% of adolescents and 1.5–8.5% of adults from the general population without ADHD (Paine et al., 2014; Sivertsen et al., 2013).

DSPD and evening chronotype can lead to daytime sleepiness and to

sleep debt (Baron and Reid, 2014; Shirayama, 2003). Studies on the consequences of DSPD and sleep deprivation suggest a profound effect on physical processes that affect risk for obesity, diabetes, cardiovascular disease, alcohol use and psychiatric conditions such as depression and dementia (Baron and Reid, 2014; Bayon et al., 2014; Colten et al., 2006; Hittle and Gillespie, 2018; Kuna et al., 2022; Spira et al., 2014; Tobaldini et al., 2017). Poor sleep quality is a strong correlate of both migraine and non-migraine headache (Sullivan and Martin, 2017). ADHD in children and (older) adults is also associated with depression (Angold et al., 1999; Spencer et al., 1999; Wilens et al., 2002). A literature review describes a strong association between ADHD and being overweight or obese and with both type I and II diabetes (T1D and T2D) (Faraone et al., 2021).

Although research attention is increasing on the prevalence of delayed sleep phase disorder in ADHD and the associations of these disorders with somatic and psychiatric conditions (Bijlenga et al., 2011; van Andel et al., 2021), a study among a large cohort is lacking. Therefore, in this study we aim to further explore the associations between adult ADHD and poorer sleep quality, evening chronotype, depression, and somatic disorders such as migraine, obesity, T1D and T2D and chronic fatigue syndrome. To understand the association between adult ADHD and the above mentioned mental and somatic disorders, we aim to examine the putative mediating role of sleep quality and evening chronotype in this association. In this cross-sectional study data was used of the Nightingale Study, a large Dutch cohort study among female nurses (Pijpe et al., 2014).

2. Methods

2.1. Study sample

Data used for this study was collected in the Nightingale Study, a

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large Dutch prospective cohort study investigating the associations between occupational exposures and risk of chronic diseases among female nurses with a focus on the assessment of the association between shift work and breast cancer risk (Pijpe et al., 2014). Full details on sampling are described elsewhere (Pijpe et al., 2014). In summary, in 2010 the Netherlands Cancer Institute (NKI) and the Institute of Risk Assessment Sciences (IRAS) of the Utrecht University initiated the Nightingale study. Approval of the study procedures was obtained from the Institutional Review Board of the NKI. In the fall of 2011, 191,971 eligible women (i.e. registered as a nurse in the national healthcare professional registry, aged 18–65 years old, of Dutch residency) were invited through the national healthcare professional registry to complete an informed consent form and a web-based questionnaire on occupational exposures, including a detailed questionnaire on all aspects of shift work, and potential confounding factors. Between October 2011 and February 2012, 59,974 women (31%) responded. No data is available of the non-responders.

3. Measures

3.1. Nightingale questionnaire

For this study we had access to the following domains of the Nightingale questionnaire:

Socio-demographics, education, shift work, lifestyle, current sleep and current and lifetime disorders/illnesses.

Education items included lifetime work duration in years, highest nursing degree (secondary vocational, higher professional and university education).

Shift work items included night shift lifetime duration (in years and categorical), night shifts ever (no/yes).

Life style included Body Mass Index (BMI) at baseline that was calculated as measured body weight (kg) divided by measured height (m) squared, total number of years of smoking, smoking status (never/former/current), number of cigarettes per year, alcohol use (never/former/current), amount of alcohol units per week.

Current sleep was measured by the Medical Outcomes Study (MOS) Sleep Scale.

The 12 items of the MOS Sleep Scale measure sleep parameters across six domains. These domains are: (1) sleep disturbance, which measures the ability to fall asleep and maintain restful sleep (four items); (2) sleep adequacy, which measures the sufficiency of sleep in terms of sleeping enough to provide restoration of wakefulness (two items); (3) sleep quantity, which measures (in hours) the amount of sleep an individual has had each night (one item); (4) somnolence, which measures daytime drowsiness or sleepiness (three items); (5) snoring (one item); and (6) shortness of breath, or headache (one item) (27). Ten of the scale's 12 items are scored using a six-point response scale, one item uses a five-point Likert scale, and sleep quantity is an open-ended question recording the actual number of hours slept. All domains except sleep quantity are recalibrated on a 0–100 scale that represents the percentage of a particular sleep domain; sleep quantity is recorded as 0–24 h. Higher scores for the domains of sleep disturbance, somnolence and the sleep indices indicate less sleep problems, whereas lower scores for sleep quantity and sleep adequacy indicate worse sleep problems. The MOS-sleep scale was computed in an index which integrates the domains in a total sleep quality score.

Sleep aid use consisted of one question about using sleep medication to enhance sleep the past four weeks. The item used a six point response scale (ranging from always to never) and is recalibrated on a 0–100 scale, a low score meaning more medication use compared to a high score.

Chronotype self description is a nominal item consisting of 6 possible answers; morning type, more morning than evening type, more evening than morning type, evening type, no specific type, don't know. A dichotomous chronotype variable was computed (morning/evening

type). Respondents scoring on “I am clearly a morning person” and “more morning than evening person” were scored as morning type and respondents scoring on “I am clearly an evening person” and “more evening than morning person” were included in the new dichotomous variable.

Current or lifetime disorders/illnesses included T1D, T2D, migraine, chronic fatigue syndrome, ADHD and depression. The question “Has a doctor ever diagnosed you with any of the following illnesses and/or conditions (no/yes) ? If so, at what age first?“.

3.2. Statistical analyses

Differences in the characteristics of the respondents with and without ADHD were examined with Welch's *t*-test, and chi-squared tests for categorical variables. Effect size measures (Cohen's *d*) relating to the difference between nurses with and without ADHD on continuous variables and phi (ϕ) relating to the difference on categorical variables was determined. Effect sizes of $d = 0.2$ denotes a “small” effect, a value of $d = 0.5$ denotes a “medium” effect, and a value of $d = 0.8$ denotes a “large” effect. Effect size of $\phi \leq 0.2$ denotes a “small” effect, $0.2 < \phi \leq 0.6$ a “medium effect” and $0.6 < \phi$ a large effect. Logistic regression analyses were performed to assess the association between depression, T1D, T2D, migraine and chronic fatigue syndrome and ADHD. Two models were used in the logics regression analyses; in the first model age and lifetime work were included as covariates. In de second model chronotype, night shifts and total sleep problems were additionally added as covariates to the model. These analyses were carried out with IBM SPSS v25.

In the associations between ADHD (independent variable) and one of the dependent variables (depression, T1D, T2D, migraine and chronic fatigue syndrome), total quality of sleep, and chronotype were added separately as a mediator in the single mediator analyses in the cross-sectional data. Mediation analysis using path analysis with bootstrapping was used for data analysis. A total of four regression parameters were estimated using bootstrap procedures: 1) of the mediator regressed on the predictor variable (a path); 2) of the mediator regressed on the outcome variable (b path); 3) of the outcome variable regressed on the predictor variable (direct effect, c path); and 4) of the parameter representing the indirect effect of the predictor on the outcome via the mediator (c' path). The indirect effect refers to the ab pathway. Fig. 1 shows the model of the simple mediation. The statistical program R using the package Lavaan was employed (Rosseel, 2012). The categorical variable chronotype (morning or evening type) was included as mediator in the regression model as dummy coded variable (morning = 0; evening = 1). The effect sizes for each indirect path was calculated with ϵ (v), a novel measure of effect size of mediation analysis (Lachowicz et al., 2018).

4. Results

Descriptive statistics of the sample are presented in Table 1. Of the 59,944 nurses, 202 reported to be diagnosed with ADHD by a doctor (0.3%). Nurses with ADHD were significantly younger than nurses without ADHD, $p < 0.001$, $d = 0.28$ and worked significantly less years than nurses without ADHD $p = 0.003$, $d = 0.21$. When corrected for age and years of work, nurses with ADHD reported to have worked significantly less years in night shifts compared to nurses without ADHD ($\beta = -1.33$ $t(43062) = -2.04$, $p = 0.04$).

Nurses with ADHD reported significantly more T1D ($p < 0.001$, $\phi = 0.10$), T2D ($p < 0.001$, $\phi = 0.01$), migraine ($p < 0.001$, $\phi = 0.01$), chronic fatigue syndrome ($p < 0.001$, $\phi = 0.09$) and depression ($p < 0.001$, $\phi = 0.09$).

Nurses with ADHD reported significantly worse on all sleep domains; sleep disturbances, sleep adequacy, somnolence, snoring and shortness of breath (see Table 1), and lower on the total quality of sleep item than nurses without ADHD ($p < 0.001$, $d = 0.77$). In addition, nurses with ADHD used significantly more sleep aids ($p < 0.001$, $\phi = 0.01$), and

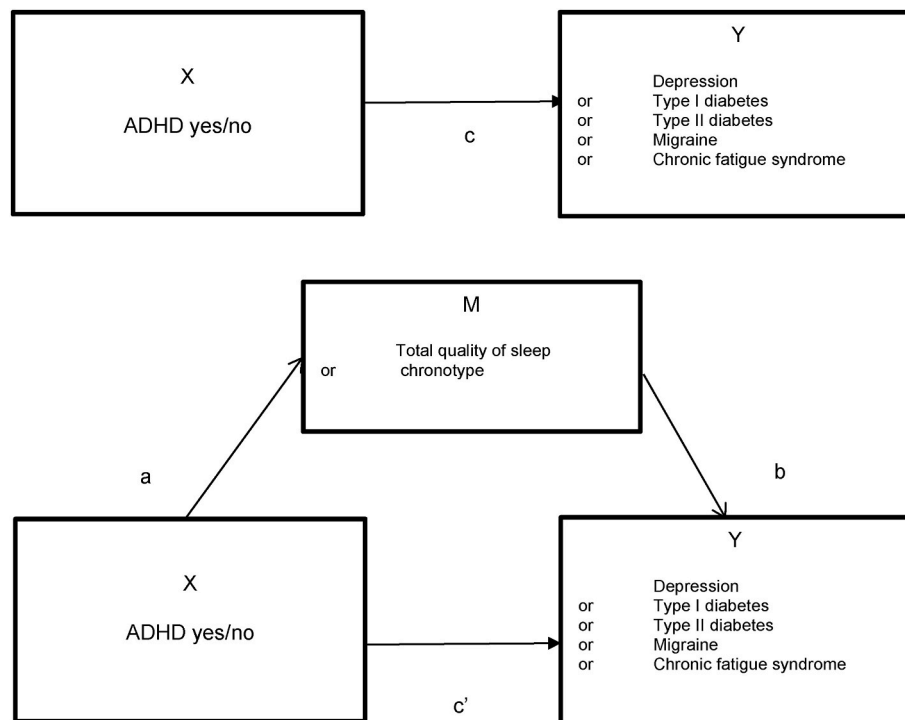


Fig. 1. The simple mediation model in which X transmits an effect on Y directly, as well as indirectly through M.

reported significantly less hours of sleep than nurses without ADHD ($p < 0.001$, $d = 0.78$). In nurses with ADHD a significant association was found with evening chronotype, compared to nurses without ADHD ($p = 0.005$, $\phi = 0.01$).

Table 2 shows the association between ADHD and depression, T1D, T2D, migraine and chronic fatigue syndrome. The logistic regression analyses showed that ADHD, after adjustment of age, lifetime work (in years) chronotype, night shifts (in years) and sleep problems, was significantly associated with migraine ($p = 0.002$, OR = 2.0 (95% CI: 1.3–3.2)), T1D ($p < 0.001$, OR = 26.8 (95% CI 12.4–58.1)), T2D ($p < 0.0001$, OR = 9.8 (95% CI 4.9–19.7)), depression ($p < 0.0001$, OR = 7.2 (95% CI 4.8–10.8)) and chronic fatigue syndrome ($p < 0.0001$ OR = 680 (95% CI 3.2–14.3)).

The results of the single mediation analyses of the relationship between ADHD and depression, diabetes, migraine and chronic fatigue syndrome through sleep quality and chronotype are presented in Table 3. The single mediation analyses shows that the relationship between ADHD and depression, ADHD and T2D, ADHD and migraine and ADHD and chronic fatigue syndrome was mediated by sleep quality, but not in the association between ADHD and T1D. ADHD and depression were also mediated by chronotype.

5. Discussion

This study examines the association between ADHD, sleep quality, evening chronotype, depression, migraine, T1D, T2D and chronic fatigue syndrome in a large sample of nurses. The findings of this study show that nurses with ADHD report poorer sleep quality and more evening chronotype than nurses without ADHD. Nurses with ADHD had a higher risk of developing lifetime depression, T1D and T2D, migraine and chronic fatigue syndrome, also when adjusted for confounding variables. The results suggest that poor sleep quality mediates the relationship between ADHD and depression, T2D, migraine and chronic fatigue syndrome, but not in the relationship between ADHD and T1D. The relationship between ADHD and depression also seems to be mediated by evening chronotype.

The associations are in line with other studies among adults with

ADHD, where ADHD was associated with more depression and chronic fatigue syndrome (Bélanger et al., 2018; Chen, M.H. et al., 2018; Chen, Q. et al., 2018; Instanes et al., 2018; Sáez-Francàs et al., 2012; Schredl et al., 2007; Simon et al., 2013). In addition, the outcome of ADHD in nurses being associated with poorer sleep quality and evening chronotype is also in line with the literature on adults with ADHD (Bijlenga et al., 2019; McGowan et al., 2016). The prevalence of evening chronotype among nurses with ADHD (25.9%) is lower than the prevalence found in the study of Bijlenga et al. (63.9% (extreme) evening chronotype in subjects with ADHD) and in the study of Van Veen et al. where 78% of subjective delayed sleep confirmed with actigraphy (Bijlenga et al., 2013; Van Veen et al., 2010). This difference may be explained by the clinical sample used in the studies of Van Veen et al. and Bijlenga et al.

One of the main findings is that poor sleep quality plays a mediating role in the associations between ADHD and depression, migraine, T2D and chronic fatigue syndrome. Previous research in population based samples showed that short sleep and insomnia play a mediating role between persistent pain and depression (Campbell et al., 2013), and between depression and hypertension (hypertension and diabetes are both end results of the metabolic syndrome) (Cheung and Li, 2012; Gangwisch et al., 2010). Short sleep is associated with reduced immune response to pathogens and inflammation (Besedovsky et al., 2019) and to lower glucose tolerance and thyrotropin concentrations, higher evening cortisol levels and increased activity of the sympathetic nervous system (Spiegel et al., 1999). Decreased carbohydrate tolerance and increased sympathetic tone are well-recognised risk factors for the development of hypertension (Spiegel et al., 1999). Short sleep duration is associated with increased appetite by decreasing leptin levels and increasing ghrelin levels (Spiegel et al., 2004), and has been identified as a significant risk factor for diabetes (Gangwisch et al., 2007). Since poor sleep quality plays a mediating role in women with ADHD and T2D, migraine and chronic fatigue syndrome, it is important to understand the etiology of their poor sleep quality, to hopefully prevent the development of comorbid disorders in the future.

The strong association between ADHD and T1D is in accordance with a German and Swedish study where ADHD was 40% more likely to be

Table 1
Demographic and health characteristics of Dutch nurses with and without ADHD.

	ADHD (Total N = 202)		No ADHD (Total N = 59.742)		P value
Age at baseline (mean, SD)	43.8	10.8	46.9	11.0	<0.001
Lifetime work duration, no. years, (mean, SD)	20.0	10.4	22.2	10.8	0.003
Highest nursing degree (N %)					
Secondary vocational education	154	(76.2)	46413	(77.7)	
Higher professional education	48	(23.8)	13317	(22.3)	
University education	0	(0)	12	(0)	
Night shifts lifetime duration no. years, (mean, SD)	7.03	6.69	8.89	8.99	<0.001
Night shifts ever N (%)	165	(81.3)	48605	(81.4)	0.99
BMI at baseline (mean, SD)	25.2	5.00	24.9	4.12	0.32
Total number of years smoking (mean, SD)	16.7	9.38	17.1	10.9	0.69
Total glasses of alcohol per week (mean, SD)	3.42	5.11	3.78	5.14	0.32
Total quality of sleep (mean, SD) ^a	61.6	15.2	71.4	12.7	<0.001
Subscale sleep disturbances (mean, SD) ^a	50.6	13.8	55.8	11.3	<0.001
Subscale sleep adequacy (mean, SD) ^a	45.2	22.7	59.3	21.4	<0.001
Subscale sleep somnolence (mean, SD) ^a	68.9	19.0	76.3	15.4	<0.001
Subscale sleep snoring (mean, SD) ^a	65.9	28.8	71.7	24.2	0.006
Subscale sleep shortness of breath (mean, SD) ^a	83.4	20.3	89.7	16.4	<0.001
Sleep aid use (mean, SD)	78.3	32.3	92.5	18.3	<0.001
Type 1 diabetes N (%)	22	(10.9)	190	(0.3)	<0.001
Type 2 diabetes N (%)	25	(12.4)	789	(1.3)	<0.001
Migraine N (%)	53	(26.2)	6001	(10.0)	<0.001
Chronic fatigue syndrome N (%)	26	(12.9)	364	(0.6)	<0.001
Lifetime depression yes N (%)	100	(49.5)	4646	(7.8)	<0.001
Chronotype self description N (%)					
Morning	27	(14.3)	7416	(13.4)	
More morning than evening	36	(17.9)	13476	(24.3)	
More evening than morning	39	(19.4)	12924	(23.3)	
Evening	52	(25.9)	6225	(11.2)	
No specific	42	(20.9)	14766	(26.7)	
Don't know	5	(2.5)	594	(1.1)	

^a range 0–100, high scores defines a more favorable health state.

Table 2
Associations between ADHD and somatic diseases and depression in female nurses.

	ADHD diagnosis					
	Model 1			Model 2		
	OR	95% CI	p	OR	95% CI	p
Migraine	3.4	2.4–4.9	<0.001	2.0	1.3–3.2	0.002
Type 1 Diabetes	39.9	23.0–69.1	<0.001	26.8	12.4–58.1	<0.001
Type 2 Diabetes	16.9	10.1–28.2	<0.001	9.8	4.9–19.7	<0.001
Depression	13.7	9.9–19.0	<0.001	7.2	4.8–10.8	<0.001
Chronic fatigue syndrome	22.4	13.5–37.3	<0.001	6.8	3.2–14.3	<0.001

Model 1: adjusted for age, life time work, years night shifts.

Model 2: adjusted for age, lifetime work, chronotype, night shifts and sleep problems.

diagnosed among children with T1D (Butwicka et al., 2015; Kapellen et al., 2016), yet the found OR, after adjustment for covariates, in our study is higher than in other studies. It is well known that in the etiology of T1D autoimmune destruction of pancreatic beta cells plays an important role (Masini et al., 2021). A recent focus of research is the role of a possible underlying autoimmune dysregulation that may have an

etiological role in ADHD symptoms and associated somatic diseases, such as allergies, food intolerance, irritable bowel syndrome, asthma, arthritis, migraine, dysautonomia and hypermobility (Csecs et al., 2022; Monaco et al., 2022; Song et al., 2020). Our hypothesis is that nurses with ADHD, late chronotype, with a stressful emotional and physical job, might have an underlying autoimmune dysregulation, which may explain the strong relation between ADHD and T1D. So far, no study has examined role of autoimmune dysregulation in ADHD and somatic diseases; this intriguing new area of research deserves more research attention.

With regards to the mediating role of quality of sleep between ADHD and depression, the association between poor sleep quality and depression is considered to be bidirectional (Alvaro et al., 2013; de Feijter et al., 2021). Cross-sectional and longitudinal studies reported poor sleep to be predictive for onset and recurrence of depression, and depressive symptoms to be predictive for development and worsening of sleep disturbances (Bao et al., 2017; de Feijter et al., 2021). In addition, our results show that depression among nurses with ADHD can be partially explained by the increased prevalence of evening chronotype in this group. The association between evening chronotype and depressive symptoms is well established (Au and Reece, 2017) and a longitudinal study among students found that poor sleep quality mediated the relationship between chronotype and depressive symptoms (Van den Berg et al., 2018). Future studies concerning ADHD and depression should also include chronotype and sleep.

An interesting result in this study is that nurses with ADHD worked less night shifts than nurses without ADHD, despite reporting being more often an evening chronotype. A mismatch of chronotype to shift timing seems to be predictive for disease (Hittle and Gillespie, 2018). A possible explanation why nurses with ADHD worked less night shifts may be that persons with ADHD are more sensitive to the repeated change in working hours and choose not to work in night shifts. More research is necessary to duplicate the finding that persons with ADHD work less shifts, investigate the possible reasons and examine the role of misalignment of chronotype and work in persons with ADHD.

6. Limitations

Due to the cross-sectional nature of the study, we are limited in drawing strong causal conclusions including statements about mediation. Longitudinal studies are needed to further determine the direction of effects of ADHD, depression and quality of sleep. Another limitation is that psychological disorders and chronotype were self-reported. Since girls and women are still often underdiagnosed with ADHD compared to boys and men (Hinshaw et al., 2022) it is likely that women with ADHD in this study were underdiagnosed. This may have led to underreporting of ADHD in this female sample (0.3%) compared to the pooled prevalence of 2.8 % of ADHD in adults found in a meta-analysis (Fayyad et al., 2017). Women with severe ADHD were more likely to be detected in this study and these women are more likely to have more sleep disturbances and comorbidities compared to women with milder ADHD. Therefore, we cannot rule out that a distortion of the results has occurred due to selection bias. In addition, it is unknown if the nurses received treatment for their ADHD, depression and/or somatic problems. Other (comorbid) psychiatric diagnoses such as delayed sleep phase disorder, anxiety, PTSD and/or bipolar disorder were not included in this study. Finally, no data was available on other somatic disorders.

7. Conclusions

The findings suggest that nurses with ADHD have more lifetime depression, poorer health, poorer quality of sleep and more self reported evening chronotype than nurses without ADHD. In addition, poorer sleep quality was a mediator in the association between ADHD and depression, T2D, migraine and chronic fatigue. Evening chronotype was also a mediator between ADHD and depression. The results imply that

Table 3

Single mediation of the relationship between ADHD and depression, diabetes, migraine and chronic fatigue syndrome through sleep quality and chronotype.^a

Mediating variable (M)	Outcome variable (Y)	Total effect (c)		Effect of X on M (a)		Effect of M on Y (b)		Direct effect (c')		Indirect effect (ab)		95%CI (ab)	v
		b	p	B	p	B	P	B	P	B	p		
Total quality of sleep	Depression	1.17	0.0	-9.76	0.0	-0.02	0.0	1.37	0.0	0.20	0.0	(0.17–0.23)	<0.05
		1.18	0.0	0.52	0.0	0.12	0.0	1.24	0.0	0.06	0.0	(0.02–1.03)	<0.05
Total quality of Sleep	Type I diabetes	1.40	0.0	-9.75	0.0	-0.001	0.64	1.41	0.0	0.009	0.64	(-0.01 – 0.05)	
		1.08	0.0	0.52	0.0	0.02	0.72	1.09	0.0	0.01	0.72	(-0.05-0.07)	
Total quality of sleep	Type II diabetes	0.90	0.0	-9.76	0.0	-0.01	0.0	0.95	0.0	0.05	0.0	(0.03–0.07)	<0.05
		0.30	0.25	0.52	0.0	0.07	0.03	0.34	0.19	0.04	0.06	(-0.001-0.08)	
Total quality of sleep	Migraine	0.49	0.0	-9.76	0.0	-0.01	0.0	0.61	0.0	0.12	0.0	(0.10–0.15)	<0.05
		0.41	0.01	0.52	0.0	-0.004	0.84	0.41	0.01	-0.002	0.84	(-0.02-0.02)	
Total quality of sleep	Chronic fatigue syndrome	1.08	0.0	-9.76	0.0	-0.02	0.0	1.30	0.0	0.22	0.0	(0.18–0.26)	<0.05
		1.26	0.0	0.28	0.0	0.02	0.58	1.26	0.0	0.004	0.59	(-0.01-0.02)	

^a Single mediation was performed between ADHD with each one of the outcome variables, where total quality of sleep, and chronotype were added separately as a mediator in the single mediator analyses.

nurses with ADHD have more mental, somatic and sleep complaints than nurses without ADHD. Employers, nurses and general practitioners should be more aware of the health impact of poor quality of sleep and evening chronotype. And when examining the relationship between ADHD and depression, it is recommended to include chronotype in the study. Still, many unresolved issues remain. Most importantly future research should focus on the role of shift work, chronotype in relation to ADHD, health outcomes and social jet lag, since both shift work and having an evening chronotype have serious negative mental and somatic health consequences.

CRedit authorship contribution statement

M. Michielsen: Formal analysis, Visualization, Writing – original draft. **M.N. Böhmer:** Validation, Writing – review & editing. **R.C.H. Vermeulen:** Conceptualization, Writing – review & editing. **J.J. Vlaanderen:** Conceptualization, Project administration, Writing – review & editing. **A.T.F. Beekman:** Writing – review & editing. **J.J.S. Kooij:** Conceptualization, Supervision, Writing – review & editing.

Declaration of competing interest

All authors declare none.

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