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Shift work and menstruation: A meta-analysis study

Fengying Hu[a,1], Cuiyun Wu[b,1], Yunfei Jia[a], Hualong Zhen[a], Hengshun Cheng[a], Fan Zhang[a], Liuqing Wang[b,**], Minmin Jiang[a,*]

[a] Department of Occupational Health and Environmental Health, School of Public Health, Anhui Medical University, Hefei, 230032, China
[b] The Third People's Hospital of Hefei, Hefei Third Clinical College of Anhui Medical University, Hefei, 230022, China

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ABSTRACT

Background: Shift work is a potential risk factor for women's reproductive health. Evidence suggests that shift work is associated with menstrual disorders, reproductive disturbances, and adverse pregnancy outcomes. However, previous studies did not systematically examine the results of menstrual irregularities, dysmenorrhea, and early menopause at the same time.
Objective: To determine the relationship between shift work and women's menstrual characteristics (e.g., irregular menstruation, dysmenorrhea, and early menopause).
Methods: Four databases (PubMed, Embase, Cochrane, and Web of Science) were searched up to December 2022. The study characteristics and risk assessment values of the literature were extracted from 21 studies that met the criteria. Odds ratios (ORs), relative risks (RRs), hazard ratios (HRs), and 95% confidence intervals (CIs) were calculated to assess the relationship between shift work exposure and menstruation. The included studies were evaluated for heterogeneity, publication bias, sensitivity analysis, and subgroup analysis.
Results: A total of 21 studies with 195,538 female participants, including 16 cross-sectional studies and 5 cohort studies, were included in this meta-analysis. According to the quality evaluation, the included research had high methodological quality. The overall ORs of shift work for the likelihood of irregular menstruation and dysmenorrhea were 1.30 (95% *CI*, 1.23–1.36) ($I^2 = 41.9\%$, $P < 0.05$) and 1.35 (95% *CI*, 1.04–1.75) ($I^2 = 73.0\%$, $P < 0.05$), respectively. There was a significant positive association between shift work and the risk of early menopause ($HR = 1.09$, 95% *CI*, 1.04–1.14), without significant heterogeneity ($I^2 = 0.0\%$, $P > 0.05$).
Conclusions: This meta-analysis indicated that shift workers have significantly higher odds of menstrual disorders, dysmenorrhea, and early menopause. This study focuses on female reproductive health and has broad implications for adjusting optimal working hours and shift schedules for female workers.

1. Background

The International Agency for Research on Cancer (IARC) defines working in shifts as a probable human carcinogen (group 2A) (IARC, 2019). It is any arrangement of working hours other than the standard daylight hours (generally 7 a.m. or 8 a.m. to 5 p.m. or 6 p.m.), including three types of shift work: permanent, continuous, with or without night shift work (Stevens et al., 2011). Shift work is essential for guaranteeing round-the-clock production and activities. It is commonly found in the health care, manufacturing, transportation, retail, and services sectors (Straif et al., 2007). Several adverse health effects may be associated with shift work. The results of epidemiological studies have shown that shift work is associated with an increased risk of breast cancer (Erren et al., 2010), diabetes (Shan et al., 2018), depression (Zhang et al., 2022), metabolic disturbances (Lim et al., 2018), and cardiovascular disease (Johnson et al., 2020). Moreover, studies have found a higher risk of adverse pregnancy outcomes and subsequent long-term disease in the offspring of female shift workers (Kader et al., 2022; Strohmaier et al., 2018).

In the workplace, environmental safety is crucial for safeguarding and promoting the well-being of professional women (Kumar et al., 2019). Workers are simultaneously exposed to a wide range of

* Corresponding author. School of Public Health, Anhui Medical University, 81 Meishan Road, Hefei, Anhui, 230032, China.
** Corresponding author. The Third People's Hospital of Hefei, Hefei Third Clinical College of Anhui Medical University, Hefei, 230022, China.
E-mail addresses: hfy22humb@163.com (F. Hu), wucuiyn3307@163.com (C. Wu), jyf2050@163.com (Y. Jia), hualong_zhen@163.com (H. Zhen), chenghengshun@163.com (H. Cheng), bbyxzhangfan@163.com (F. Zhang), wangliuqinghf@126.com (L. Wang), jiangmm0205@ahmu.edu.cn (M. Jiang).
[1] The authors consider that the first two authors should be regarded as joint first authors.

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hazardous factors in the workplace, including a variety of biological (viruses and bacteria), chemical (heavy metals and other chemicals), physical (light, high temperature, and noise), and occupational factors (shift work and workload) (Golmohammadi & Darvishi, 2019; Rim & Lim, 2014). The hazardous factors present in the working environment can cause serious harm to health (Cho & Kang, 2022). Long-term exposure to harmful occupational factors may lead to endometriosis, endometrial cancer, menstrual disorders, and other reproductive system diseases in women (Dutta et al., 2021). Female reproductive function is primarily regulated by the interaction of the hypothalamic-pituitary-ovarian axis (Doufas & Mastorakosa, 2000). Shift work stress has been shown to negatively affect the hypothalamic-pituitary-ovarian axis (Valsamakis et al., 2019), altering periodic changes in estrogen-progesterone secretion by the ovaries (Deligeoroglou & Creatsas, 2012), further leading to impairment of menstrual function. The main adverse effects of shift work on female menstrual function are irregular menstrual cycles, dysmenorrhea, premenstrual syndrome, early menopause, and infertility (Chung et al., 2005; Kahyaoglu Sut & Mestogullari, 2016; Stock & Schernhammer, 2019).

Previous epidemiological studies have explored the association between shift work and the risk of menstrual disorders (Lawson et al., 2011; Ok et al., 2019) but have reported inconsistent results. Lawson et al. used cross-sectional data from 71,077 nurses collected in the Nurses' Health Study II and observed a dose-response relationship between shift work and irregular menstrual cycles, with a 13% increased risk for every 12 months of shift work (Lawson et al., 2011). A survey with a sample size of 1521 conducted in Korea found that the weighted prevalence of irregular menstrual cycles in shift-work workers (18.36%) was 1.5 times higher than that in those who worked regular hours (12.02%) (Ok et al., 2019). Nevertheless, a study conducted in Norway with a sample size of 766 found that 15% of the study subjects reported irregular menstruation, but the logistic regression analysis of the association between irregular menstruation and night work was not statistically significant (Moen et al., 2015). Another 4-month cohort study with a sample size of 188 found no difference in dysmenorrhea, prolonged duration, or delayed menstrual cycles among shift nurses but a slightly lower risk of prolonged periods among women who rotated for more than 5 years (Amilcar Albert-Sabater et al., 2016).

The purpose of this meta-analysis was to determine the relationship between shift work and women's menstrual characteristics (e.g., irregular menstruation, dysmenorrhea, and early menopause) by collecting the literature of cross-sectional and cohort study designs. Integrating the existing evidence of the impact of shift work on women's menstrual function provides valuable insights for the reproductive health of professional women.

2. Materials and methods

2.1. Literature search

Until December 2022, four databases (PubMed, Embase, Cochrane, and Web of Science) were searched. The search strategy used the following keywords and/or Medical Subject Heading (MeSH) terms: "shift work", "shift work schedule", "night shift work", "night work", "rotating shift work", "evening shift work", "rotating shift" and "menstruation", "menstruation disturbances", "dysmenorrhea", "menstrual cycle", "menopause", etc. The detailed search strategy is provided in Supplemental Table 1. All human studies that described shift work (any work outside of fixed-day work), menstrual disorders, dysmenorrhea, and menopause were eligible, without restrictions on publication date, study design status, or language. References of all included primary and review articles were checked.

2.2. Inclusion and exclusion criteria

Inclusion criteria were determined prior to the literature search. All studies were included regardless of sample size and follow-up duration.

Inclusion criteria: (1) subjects were female workers with shift work experience; shift work was defined as any shift work performed outside normal working hours (8:00 a.m. to 6:00 p.m.); (2) the subject reported the occurrence of menstrual disorders, dysmenorrhea, or menopause; (3) studies reported odds ratios (ORs), relative risks (RRs), or hazard ratios (HRs) with 95% confidence intervals (CIs); (4) moderate- or high-quality studies were included; (5) studies used cross-sectional or cohort study designs.

Exclusion criteria: (1) animal experiment; (2) gynecological diseases or syndromes other than menstruation (e.g., endometriosis, polycystic ovary syndrome, infertility, etc.); (3) non-English literature, reviews, case reports, and conference abstracts were excluded.

2.3. Date extraction and quality assessment

The following items were extracted from each study: the author's name, publication year, country where the study was conducted, the main characteristics of the study population (e.g., age, sample size, follow-up duration, types of shift work schedules), the study outcomes, the estimated risk of the study, and adjusted confounders.

The Newcastle-Ottawa Scale (NOS) was used to evaluate the quality of cohort studies (Luchini et al., 2021; Stang, 2010). We primarily assessed the representativeness of the study population, comparability between groups, duration of follow-up, exposures, and outcomes. The scale assigns a maximum of 9 points to each study, with studies scoring at least 7 points being classified as high-quality studies, 4 to 6 points as moderate-quality studies, and studies scoring 3 or less as low-quality studies. The quality of the cross-sectional study was evaluated by the Agency for Healthcare Research and Quality (AHRQ). There are 11 evaluation criteria: (1) define the source of information; (2) clarify the inclusion and exclusion criteria of research objects; (3) indicate the inclusion time of research subjects; (4) indicate whether or not subjects were consecutive; (5) indicate if evaluators of subjective components of the study were masked to other aspects of the status of the participants; (6) describe any assessments undertaken for quality assurance purposes; (7) describe the characteristics of excluded objects in data analysis; (8) describe how confounding was assessed and/or controlled; (9) explain how missing data were handled in the analysis; (10) summarize patient response rates and the completeness of data collection; and (11) clarify the expected follow-up and the percentage of patients with incomplete data or follow-up. There are 11 items in the AHRQ, and the scoring method for each item is 1 point for "yes", 0 points for "no" or "unclear". The score of each item is added up to the total score, which ranges from 0 to 11 points. Scores of 0–3 were considered low quality, 4 to 7 moderate quality, and 8 to 11 high quality (Hu et al., 2015).

2.4. Data synthesis and analysis

All statistical analyses were performed using Stata 15.0. The adjusted ORs, RRs, HRs, and 95% CIs were extracted from the included articles. The effect values were logarithmically converted before being included in the final meta-analysis. If the studies did not directly provide risk estimates, ORs were calculated by extracting data from fourfold tables. Heterogeneity was presented with a calculated I-squared (I^2) index (Higgins & Thompson, 2002). I^2 values of 25%, 50%, and 75% represented low, moderate, and high heterogeneities, respectively (Spineli & Pandis, 2020). We used a fixed-effects model if the I^2 index was less than 50%; otherwise, a random-effects model was used.

2.5. Publication bias

We applied Egger's and Begg's tests to investigate whether publication bias existed in the studies, and $P < 0.05$ was used to test for significant publication bias. When the results of the two tests were contradictory, we preferentially used the results of Egger's test because it is more sensitive. To further verify the existence of publication bias, the trim and fill method was implemented by using the metatrim command of Stata software (Weinhandl & Duval, 2012). The meta-analysis was performed again after a part of the study was supplemented by the trim and fill method (Luo et al., 2022). If the estimated combined effect size did not change significantly, it indicated that publication bias had little influence.

2.6. Sensitivity analysis

Due to the expected heterogeneity of the studies, a sensitivity analysis was planned to evaluate the stability of the study results. Subgroup analysis was performed if the heterogeneity was large after pooling the effect size. Subgroup analysis was performed according to age (≤30 years, >30 years), sample size (n ≤ 400, 400 < n ≤ 800, n > 800), type of shift work (any shift work, rotating shift work, rotating night shifts, two/three rotating shifts), study design (cross-sectional, cohort study), and study quality (high quality, moderate quality).

3. Results

3.1. Study characteristics

Flow diagram of the systematic review process is presented in Fig. 1. The meta-analysis of PRISMA guidelines was applied to this study (Page et al., 2021). A total of 26,152 articles were retrieved. After using the Endnote document manager to delete 9693 duplicate articles, irrelevant research was excluded by reading the title and abstract, and 71 possibly relevant complete papers were retrieved. Fifty studies were excluded because 10 articles were non-English literature, 5 articles did not address the outcome of attention, 4 articles used univariate analysis methods, 13 articles had no extractable data, 11 articles were reviews, and 8 articles were conference abstracts. Finally, 21 articles met the inclusion criteria, among which 16 articles focused on menstrual disorders (Attarchi et al., 2013; Chung et al., 2005; Hatch et al., 1999; Jiang et al., 2019; Kwak & Kim, 2018; Labyak et al., 2002; Lawson et al., 2011, 2015; Lim et al., 2016; Mayama et al., 2020; Mirfat, 2016; Moen et al., 2015; Ok et al., 2019; Song et al., 2022; Su et al., 2008; Wang et al., 2016), 8 articles reported the occurrence of dysmenorrhea (Amilcar Albert-Sabater et al., 2016; Attarchi et al., 2013; Chiu et al., 2017; Chung et al., 2005; Jiang et al., 2019; Mayama et al., 2020; Mirfat, 2016; Sznajder et al., 2014), and 2 articles reported menopause (Khan et al., 2022; Stock et al., 2019).

The main characteristics of the 21 eligible articles are shown in

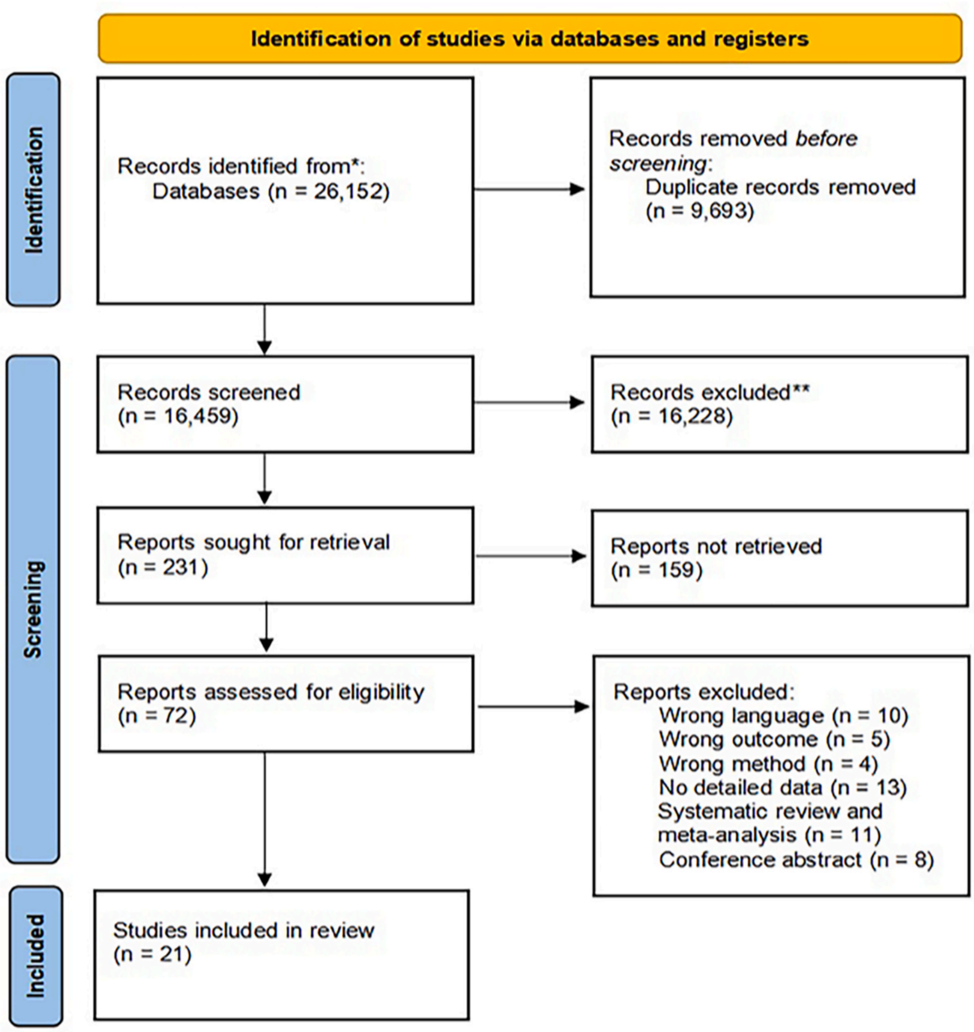

Fig. 1. Flow diagram of the systematic review process.

Table 1
The main characteristics of the 21 eligible articles.

Author	Year	Area	Study design	Sample size	Age of the study population	Definition of shift work	Shift schedule type	Outcome type	Effect value and 95% CI	Confounders adjustment	Quality
Hatch	1999	America	Cross-sectional study	124	Mean age 34 years	Any shift work other than fixed day shifts, including fixed night shifts and rotating shifts.	Any shift work	Irregular menstruation	OR = 1.3 (0.56–3.02)	Age, smoking, and drinking	Moderate
Labyak	2002	America	Cross-sectional study	68	22–30 Mean age 29.97 years	Shift work includes night shift (3:30 a.m.–12:00 a.m.) or night shift (12:00 a.m.–8:00 a.m.).	Any shift work	Irregular menstruation	OR = 2.07 (0.6–7.13)	Average sleep latency, number of awakenings from sleep, and sleep length	High
Chung	2005	Asia	Cross-sectional study	151	21–44 Mean age 27.7 years	Work shifts include day shift, evening shift, and night shift.	Any shift work	Irregular menstruation Dysmenorrhea	OR = 2.22 (1.12–4.40) OR = 1.90 (0.94–3.83)	Age, education, marital status, and working hours	Moderate
Su	2008	Asia	Prospective study	329	Mean age 24.3 years	The 12-hour rotation schedule includes day and night shifts without transition.	Two rotating shifts	Irregular menstruation	OR = 1.71 (1.03–2.88)	Shift-work history, employment duration, coffee consumption, and preemployment menstrual cycle irregularity	Moderate
Lawson	2011	America	Cohort study	71,077	28–45 Mean age 37.8 years	Any shift work other than regular day shift, evening shift, night shift, or rotating shifts, three or more nights per month.	Rotating shift work	Irregular menstruation Short cycle <21d Long cycle >40d	RR = 1.23 (1.14–1.33) RR = 1.27 (0.90–1.62) RR = 1.49 (1.19–1.87)	Age, BMI, age at menarche, parity, race, ethnicity, smoking status, alcohol consumption, and physical activity	High
Attarchi	2013	Asia	Cross-sectional study	406	22–43 Mean age 31.3 years	Any shift work other than the fixed day shift, including the fixed night shift.	Rotating shift work	Irregular menstruation Short cycle <21d Long cycle >35d Dysmenorrhea	OR = 5.54 (2.78–11.02) OR = 4.64 (1.65–13.10) OR = 3.51 (1.70–7.24) OR = 2.48 (1.57–3.89)	Age at menarche, regular exercise, marital status, age, BMI, work experience, self-perceived job satisfaction, and self-perceived job stress	Moderate
Sznajder	2014	Asia	Cross-sectional study	651	Mean age 28 years	Any shift work other than regular daytime hours.	Rotating night shifts	Dysmenorrhea	OR = 1.36 (0.90–2.05)	Age, children, marital status	Moderate
Lawson	2015	America	Cross-sectional study	6309	21–45 Mean age 35.2 years	The shift schedule includes day only, night only, night only, night rotation, and no night rotation.	Rotating night shifts	Irregular menstruation Long cycle <21d Short cycle >32d	OR = 1.43 (1.26–1.62) OR = 1.75 (0.98–3.12) OR = 1.28 (1.03–1.61)	Age, smoking, BMI, physical activity, parity, age at menarche, race, and ethnicity	High
Moen	2015	Europe	Cross-sectional study	766	21–50 Mean age 33 years	Shift schedules include three shifts: day only, evening only, night only, day and night only.	Three rotating shifts	Irregular menstruation Long cycle >34d	OR = 1.3 (0.90–2.00) OR = 0.4 (0.00–3.40)	Age, BMI, alcohol consumption, cups of coffee/tea/cola, smoking	High
Sabater	2016	Europe	Prospective study 4 months	188	Mean age 33.7 years	The shift schedules include morning shift, afternoon or	Rotating shift work	Dysmenorrhea	OR = 1.35 (0.74–2.46)	Age, marital status, menarche age, BMI, smoking	moderate

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Table 1 (*continued*)

Author	Year	Area	Study design	Sample size	Age of the study population	Definition of shift work	Shift schedule type	Outcome type	Effect value and 95% CI	Confounders adjustment	Quality
						evening shift, and night shift.					
Lim	2016	Asia	Cross-sectional study	231	21–45 Mean age 31.6 years	Any work outside the regular daytime hours	Rotating shift work	Irregular menstruation Short cycle <25d Long cycle ≥35d	OR = 1.26 (0.68–2.36) OR = 2.57 (1.01–7.24) OR = 0.91 (0.45–1.81)	Age, BMI, race, education, stress levels, having given birth in the last 5 years	High
El-Kashif	2016	Africa	Cross-sectional study	100	25–30	Shifts include the fixed day shift and the fixed night shift (alternating morning, afternoon, and night).	Rotating shift work	Irregular menstruation Dysmenorrhea	OR = 0.98 (0.41–2.33) OR = 2.02 (0.60–6.88)	Age, BMI, educational level, marital status, number of children, and years of experience	High
Wang	2016	Asia	Cross-sectional study	473	21–46	Any shift work other than the fixed time (8:00 a.m.–17:00 p.m.)	Rotating shift work	Irregular menstruation	OR = 1.79 (0.94–3.4)	Age, BMI, and perceived job satisfaction	High
Chiu	2017	Asia	Cross-sectional study	420	22–48	Any shift work other than regular daytime hours	Three rotating shifts	Dysmenorrhea	OR = 2.07 (1.01–4.21)	age, marital status, attitude toward menstruation	High
Kwak	2018	Asia	Cross-sectional study	4731	19–54	Shifts include evening and night work, regular day, day and night shift, 24-h shift work, split shift, irregular shift, and others.	Any shift work	Irregular menstruation	OR = 1.39 (1.03–1.88)	Age, BMI, marital status, smoking, drinking, regular physical activity, stress, and education	Moderate
Zhao	2019	Asia	Cross-sectional study	12,881	18–50	Shifts include fixed night work, rotating shifts, and daytime work.	Night shift work Rotating shift work	Irregular menstruation Dysmenorrhea	OR = 1.20 (1.06–1.35) OR = 1.20 (1.05–1.30)	Age, marriage, education level, income, tobacco smoking, and alcohol drinking	High
Guseul	2019	Asia	Cross-sectional study	1521	19–50	Any shift work other than the fixed work schedule (6:00 a.m.–18:00 a.m.)	Any shift work	Irregular menstruation	OR = 1.54 (1.03–2.26)	Age, education, household income, smoking status, alcohol consumption, and obesity	High
Stock	2019	America	cohort study	80,840	25–42	Rotating night shift work	1–9 mos 10–19 mos >20 mos	Menopause The mean age of natural menopause was 50 (SD 4.0 years).	HR = 1.06 (1.00–1.12) HR = 1.10 (1.01–1.21) HR = 1.09 (0.02–1.16)	Age, alcohol consumption, BMI, physical activity, smoking status, oral contraceptive use, parity, age at first birth, total time breastfed, sleep, and age at menarche	High
Mayama	2020	Asia	Cross-sectional study	1249	45–80	Any shift work other than regular daytime hours	Rotating night shifts	Irregular menstruation Dysmenorrhea	OR = 1.79 (1.36–2.34) OR = 1.26 (0.98–1.62)	Age, BMI, hospital size, and the department in which women worked	Moderate
Khan	2022	America	Cohort study 3 years	3688	45–80 Mean age 48.9 years	Any shift work other than regular daytime hours	Rotating night shifts	Menopause	HR = 1.27 (0.72–2.24) HR = 0.64 (0.46–0.89)	Age, BMI, ethnicity, education level, marital status, total annual household income, smoking status, alcohol consumption, self-reported status of type 2 diabetes,	High

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Table 1 (*continued*)

Author	Year	Area	Study design	Sample size	Age of the study population	Definition of shift work	Shift schedule type	Outcome type	Effect value and 95% CI	Confounders adjustment	Quality
										hypertension, and cardiovascular disease	
Song	2022	Asia	Cross-sectional study	9335	22–45 Mean age 30.83 years	Any shift work other than regular daytime hours	Rotating night shifts	Irregular menstruation	OR = 1.19 (1.01–1.39)	Age, age at menarche, parity, vigorous physical activity, alcohol consumption	High

Abbreviations: OR (odds ratio), RR (relative risks), HR (hazard ratio), CI (confidence interval), BMI (body mass index), short/long cycle (length of menstrual cycle). Study quality was assessed by the Newcastle-Ottawa Scale (NOS) and the Agency for Healthcare Research Quality (AHRQ).

Table 1. Overall, the included studies were published between 1999 and 2022, including 16 cross-sectional studies and 5 cohort studies with sample sizes ranging from 68 to 80,840 women. A total of 195,538 female workers' basic information was collected. There were twelve studies from Asia, six from the Americas, two from Europe, and only one from Africa. Overall, 13 studies were from developed countries and 8 from developing countries. The subjects were mostly nurses, doctors, office workers, and factory workers, with an age range from 18 to 80 years. Shift definitions and shift types were reported in the 21 studies included. The length and regularity of the menstrual cycle were taken into account in four studies with a menstrual disorder outcome. All studies adjusted for potential confounding factors to provide adjusted odds ratios. According to the quality evaluation, 8 studies were of moderate quality, and 13 were of high quality (Supplemental Table 2 and Table 3).

3.2. Irregular menstruation

Shift work was found to increase the risk of menstrual disorders in female workers ($OR = 1.30$, 95% CI, 1.23–1.36, $P < 0.05$) according to pooled data from 16 studies. There was no significant heterogeneity ($I^2 = 41.9\%$, $P < 0.05$), and the fixed-effects model was used for the meta-analysis (Fig. 2). The results of Egger's test ($t = 2.63$, $P < 0.05$) and Begg's test ($z = 0.81$, $P > 0.05$) were contradictory. The risk of publication bias was unrevealed after adjusting by the trim and fill method ($OR = 1.29$, 95% CI, 1.16–1.44) (Fig. 3).

The results of subgroup analysis showed that shift work increased the risk of menstrual disorders by 70% ($OR = 1.70$, 95% CI, 1.23–2.34) in women aged ≤30 years, and shift work exposure for women aged over 30 increased the risk of menstrual disorders by 30% ($OR = 1.30$, 95% CI, 1.21–1.40). In the cross-sectional study, the combined OR was 1.34 (95% CI, 1.26–1.44). The combined OR of the cohort study was 1.24 (95% CI, 1.15–1.34). Both moderate-quality and high-quality studies showed that shift work exposure increased the risk of menstrual

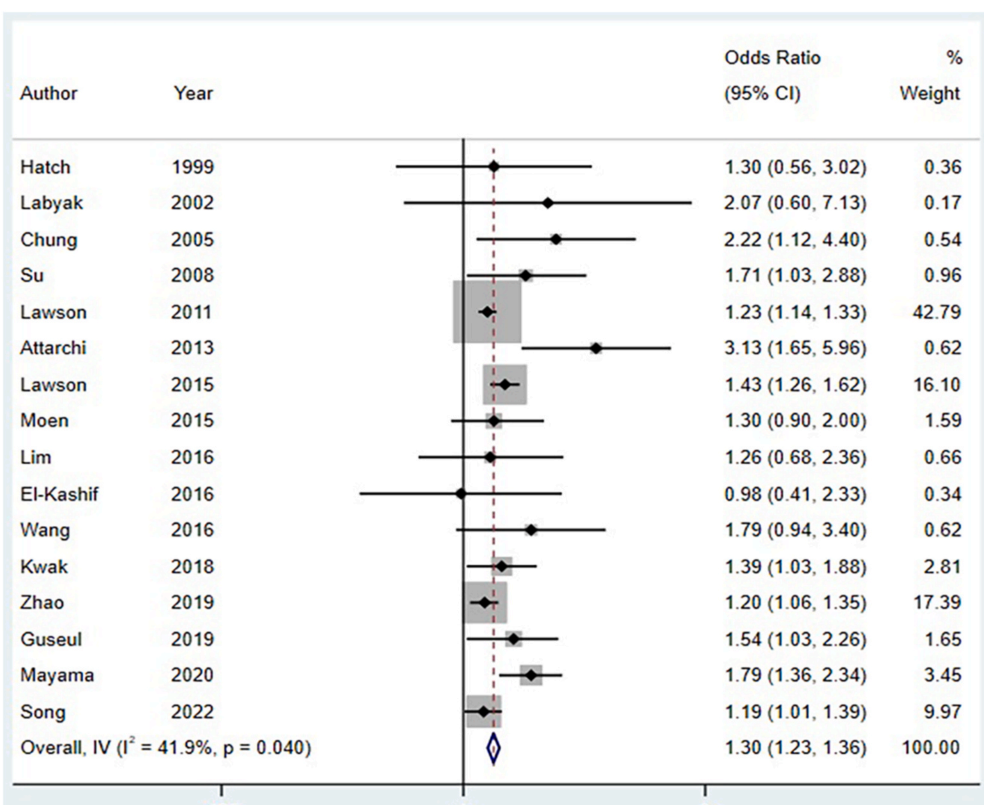

Fig. 2. Results of meta-analysis on irregular menstruation (fixed-effects model). Gray squares represent the point estimate of each study. OR: odds ratio. I-squared is the Higgins I^2 index. Horizontal bars represent the 95% CI line. The diamond represents the mean of effect sizes obtained by the meta-analysis.

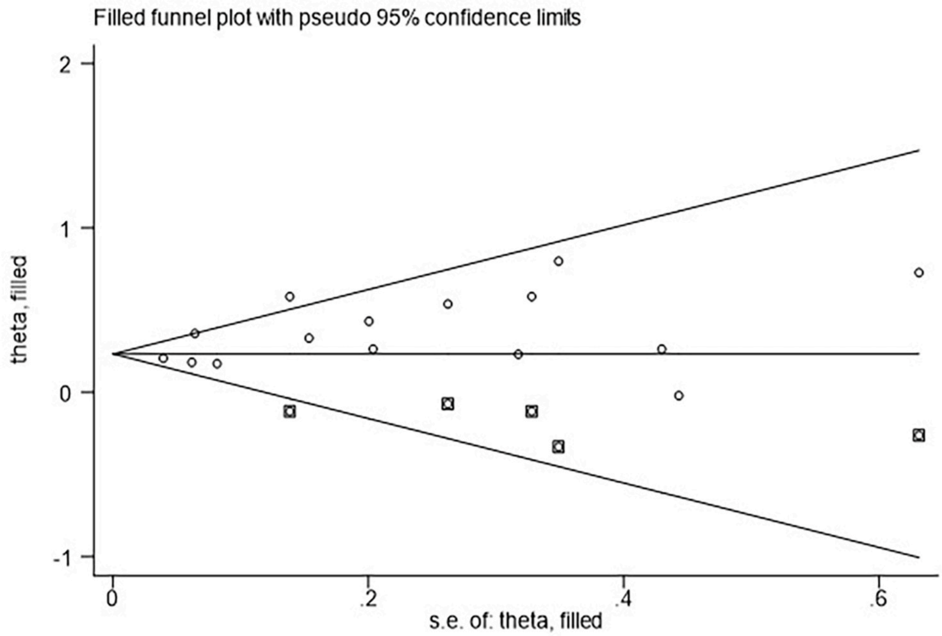

Fig. 3. Results of the trimming and filling test for publication bias (trim and fill method). Trim and fill analysis: The data from five virtual studies were automatically included. Meta-analysis was performed again. Test for heterogeneity: $Q = 44.857$ on 20 degrees of freedom ($P = 0.001$) (*OR* = 1.29, 95% *CI*, 1.16–1.44).

disorders (*OR* = 1.71, 95% *CI*, 1.44–2.03, and *OR* = 1.26, 95% *CI*, 1.20–1.33, respectively). In addition, different types of shift exposure were also significantly associated with the risk of menstrual disorders: any shift work (*OR* = 1.51, 95% *CI*, 1.22–1.57), rotating shift work (*OR* = 1.23, 95% *CI*, 1.14–1.33), rotating night shifts (*OR* = 1.34, 95% *CI*, 1.16–1.55), and two/three rotating shifts (*OR* = 1.44, 95% *CI*, 1.05–1.98). Studies with different sample sizes also demonstrated this relationship: $n \leq 400$ (*OR* = 1.54, 95% *CI*, 1.15–2.06), $400 < n \leq 800$ (*OR* = 1.40, 95% *CI*, 1.12–1.78), and $n > 800$ (*OR* = 1.31, 95% *CI*, 1.19–1.45) (Table 2).

3.3. Dysmenorrhea

Pooled multivariable analysis showed that the effect of shift work on dysmenorrhea remained significant (*OR* = 1.35, 95% *CI*, 1.04–1.75, $P < 0.05$), with significant heterogeneity ($I^2 = 73.0\%$, $P < 0.05$) (Fig. 4). Egger's test ($t = 0.432$, $P > 0.05$) and Begg's test ($z = 1.88$, $P > 0.05$) showed no evidence of publication bias.

The association between shift work and dysmenorrhea was statistically significant only in the following subgroups: age >30 years (*OR* = 1.47, 95% *CI*, 1.14–1.90), sample size ≤400 (*OR* = 1.61, 95% *CI*, 1.05–2.47) or > 800 (*OR* = 1.21, 95% *CI*, 1.08–1.37), rotating night shifts (*OR* = 1.29, 95% *CI*, 1.04–1.59), two/three rotating shifts (*OR* = 2.07, 95% *CI*, 1.01–4.23), cross-sectional study (*OR* = 1.35, 95% *CI*, 1.02–1.80) and moderate research quality (*OR* = 1.55, 95% *CI*, 1.19–2.03) (Table 2).

3.4. Menopause

Both studies in which the outcome was menopause used Cox proportional hazards models to generate *HRs* and 95% *CIs*. Women's natural menopause age is influenced by shift exposure. Among women over 45 years old, the circadian rhythm disorder caused by shift work may increase the risk of early menopause by 9%. The pooled risk estimate between night shift work and menopause was 1.09 (95% *CI*, 1.04–1.14), with a low level of statistical heterogeneity ($I^2 = 0.0\%$, $P > 0.05$) (Fig. 5).

3.5. Sensitivity analysis

The sensitivity analysis revealed that there was no significant difference in the amount of combined effects after excluding each piece of literature one by one (Supplemental Fig. 1 and Fig. 2). Therefore, the results of the meta-analysis are relatively stable. After removing the two studies published by Attarchi (Attarchi et al., 2013) and Wang (Wang et al., 2016), the heterogeneity of menstrual disorder outcomes decreased from 41.9% to 25.9% (*OR* = 1.29, 95% *CI*, 1.22–1.35, $I^2 = 25.9\%$) (Supplemental Fig. 3), and the heterogeneity of dysmenorrhea outcomes decreased from 73.0% to 0.0% (*OR* = 1.26, 95% *CI*, 1.13–1.41, $I^2 = 0.0\%$) (Supplemental Fig. 4). This may be one of the causes of heterogeneity.

4. Discussion

The results of this meta-analysis study showed that rotating shift workers have a higher risk of developing menstrual irregularity, dysmenorrhea, and early menopause. Compared with those who worked fixed-day shifts, the likelihood of menstrual disorders, dysmenorrhea, and early menopause among shift workers increased by 1.30, 1.35, and 1.09 times, respectively. Subgroup analysis found that shift work exposure was associated with an increased risk of menstrual dysfunction. The results revealed that it is necessary to develop a reasonable shift schedule for female workers in the future to reduce the level of occupational hazards.

A meta-analysis of shift work and female reproductive health published in 2014 found that shift workers had a high incidence of menstrual disruption (*OR* = 1.22, 95% *CI*, 1.15–1.29) (Stocker et al., 2014). Another meta-analysis that pooled data on menstrual disturbances from 12 studies confirmed a greater risk of irregular menstruation among shift workers (*OR* = 1.35, 95% *CI*, 1.28–1.42), especially women under 30 years of age (*OR* = 1.66, 95% *CI*, 1.13–2.44) (Chang & Chang, 2021). The strengths of our meta-analysis methodology over these studies included comprehensive searching, multifaceted subgroup analysis, and cross-occupation data collection, which improved universality and generalizability. Meanwhile, considering the influence of shift work on the natural menopause age of women, we conducted a pooled analysis of

Table 2
Subgroup analysis of the relationship between shift exposure and menstruation.

Subgroup	Irregular menstruation			Dysmenorrhea		
	Number of studies (n)	*OR* (95% *CI*)	*P-value*	Number of studies (n)	*OR* (95% *CI*)	*P-value*
Age of study subjects						
≤30	5	1.70 (1.23, 2.34)	<0.05	4	1.19 (0.61, 2.32)	>0.05
>30	11	1.30 (1.21, 1.40)	<0.05	5	1.47 (1.14, 1.90)	<0.05
Sample size						
≤400	6	1.54 (1.15, 2.06)	<0.05	3	1.61 (1.05, 2.47)	<0.05
400< **N** ≤ 800	3	1.40 (1.12, 1.76)	<0.05	4	1.37 (0.67, 2.80)	>0.05
>800	6	1.31 (1.19, 1.45)	<0.05	2	1.21 (1.08, 1.37)	<0.05
Shift type						
Any shift work	5	1.51 (1.22, 1.87)	<0.05	1	1.90 (0.94, 3.84)	–
Rotating shift work	4	1.23 (1.14, 1.33)	<0.05	5	1.26 (0.78, 2.05)	>0.05
Rotating night shifts	4	1.34 (1.16, 1.55)	<0.05	2	1.29 (1.04, 1.59)	<0.05
Two /three rotating shifts	2	1.44 (1.05, 1.98)	<0.05	1	2.07 (1.01, 4.23)	–
Study design						
Cross-sectional study	14	1.34 (1.26, 1.44)	<0.05	8	1.35 (1.02, 1.80)	<0.05
Cohort study	2	1.24 (1.15, 1.34)	<0.05	1	1.35 (0.74, 2.46)	–
Study quality						
High quality	10	1.26 (1.20, 1.33)	<0.05	5	1.15 (0.65, 2.02)	>0.05
Moderate quality	6	1.71 (1.44, 2.03)	<0.05	4	1.55 (1.19, 2.03)	<0.05

menopausal data for the first time, which has important implications for the health care of middle-aged women.

Menstrual disorders in shift workers may be caused by abnormal circadian clock gene expression (Reszka et al., 2013) and sex hormone secretion (Bracci et al., 2014), which is an existing public health problem. Circadian rhythms are biological oscillations proceeding on a daily cycle (Gentry et al., 2021). Most organisms have evolved circadian clocks that exhibit patterns of behavior following an endogenous 24-h rhythm (Jagannath et al., 2017). Irregular work schedules can disrupt human circadian rhythms and alter the sleep-wake cycle, thereby altering the physiological cycle. In addition, when working at night, people are exposed to many physical hazards, such as noise, light exposure, low temperatures, radiation, etc. These hazards are also likely to interfere with physiological parameters, leading to menstrual cycle disturbances and ovarian dysfunction (Cable et al., 2021; Miguet et al., 2020).

During the menstrual period, shift workers were often accompanied by physical discomfort and mood swings such as abdominal pain, diarrhea, back pain, fatigue, irritability, anxiety, and poor concentration (Choi et al., 2010). This may be affected by the decline in ovarian function and estrogen and progesterone levels during the menstrual period (Yen et al., 2019). Shift-work stress may aggravate these symptoms. Conversely, these physical and emotional symptoms will also have a negative impact on the absenteeism rate, work status, quality of life, and satisfaction of workers. More studies on the adverse effects of shift work on female reproductive health are needed to explore the mechanism of menstrual disorder caused by circadian rhythm disorder in shift workers and to provide the basis for maximizing the solution of occupational hazards and improving the health status of the occupational population.

This meta-analysis was subject to heterogeneity. A possible explanation for this might be that differences between studies persisted despite strict inclusion criteria. First, this study included different types of study designs with variable data collection, possibly contributing to heterogeneity. Structured questionnaires were used for study subjects to self-report shift work and hours worked, which increases the risk of recall bias and affects the accuracy of the data. Follow-up bias and participation rates of less than 80% in observational studies were other shortcomings of some studies (Chung et al., 2005; Hatch et al., 1999; Moen et al., 2015). The adjusted confounding factors in the study were different. Age, BMI, smoking, drinking, education, physical activity, and sleep quality were the main confounding factors. Factors such as past disease history, work pressure, consumption of tea or caffeine, and other factors that may have a certain impact on the endocrine system of shift workers are easy to ignore. Therefore, the impact of other potential unmeasured confounding factors on the research results cannot be eliminated. In addition, we did not limit the sample size of the study when screening the literature. There are two small sample studies (sample size ≤100) (Labyak et al., 2002; Mirfat, 2016), which lacked sufficient representation of the population.

In the screening process, we only searched studies published in English. Studies published in other languages especially from low- and middle-income countries (LMICs) are limited. Only eight of the 21 included studies were from developing countries, and the rest were from developed countries. The limited representation of LMICs in the studies highlights the need for more reports on menstrual behavior in these regions. Women in different cultures present and resolve menstruation differently, indicating sociocultural and spatial-geographical differences (Kaur et al., 2018; Majeed et al., 2022). Compared with professional women in developing countries and low-income countries, the menstrual behavior of women in developed countries is mainly manifested by the differences in the timing of menarche, dysmenorrhea degree, and menstrual cycle length (Mavhu et al., 2021). Challenges to good menstrual practices in LMICs are due to socio-economic, educational, religious, and cultural constraints (Myers et al., 2019; Sommer et al., 2016). Poor hygiene habits can cause reproductive tract infections and urinary tract infections in females (Ramachandra et al., 2016). There is a need for more research that specifically focuses on working women in LMICs. By understanding the unique challenges faced by women in these regions, we can develop targeted interventions and policies that promote good menstrual practices and improve overall health outcomes.

Second, the duration of shift work exposure varied among studies due to age and region differences in the study population. Most of the literature failed to consistently report distinctions between various shift types. Inconsistent standards for the measurement of shift work exposure and the definition of shift work varied across studies. Therefore, the distribution of menstrual disorders across shift types has not been clearly demonstrated. The menstrual cycle is the interval of time from the beginning of one menstrual period to the next, with irregular patterns defined as 7-day variability during the cycle. However, misclassification of cycle length is a possibility in current studies, which may cause bias in cycle length measurement. In addition, women may decide to leave work if they experience rostering-related menstrual symptoms, which may lead to other healthier workers entering the workplace, resulting in a "healthy worker effect" (Brown et al., 2017). With some studies having a follow-up period of more than 20 years (Jiang et al., 2019; Lawson et al., 2011), it is not easy to know when the shift work started in the first

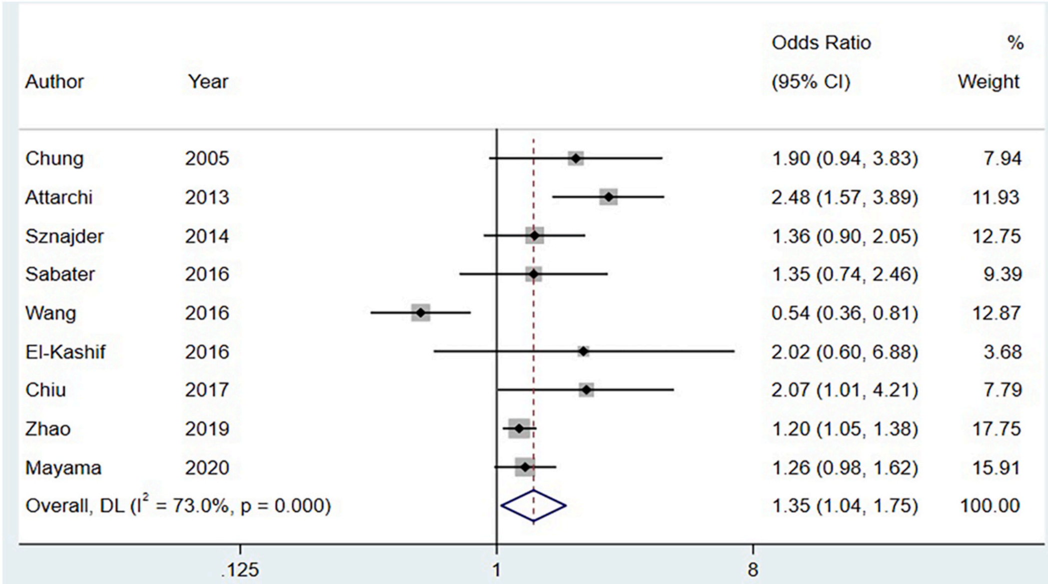

Fig. 4. Results of meta-analysis on dysmenorrhea (random-effects model). Gray squares represent the point estimate of each study. OR: odds ratio. I-squared is the Higgins I^2 index. Horizontal bars represent the 95% *CI* line. The diamond represents the mean of effect sizes obtained by the meta-analysis.

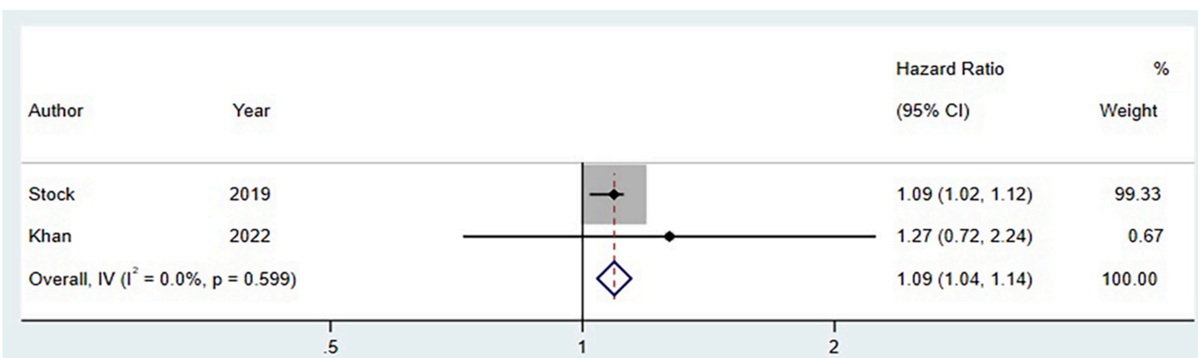

Fig. 5. Results of meta-analysis on menopause (fixed-effects model). Gray squares represent the point estimate of each study. HR, hazard ratio. I-squared is the Higgins I2 index. Horizontal bars represent the 95% CI line. The diamond represents the mean of effect sizes obtained by the meta-analysis.

two years of the survey, meaning that workers may have moved from one type of shift work to another. Ignoring the "healthy worker effect" in assessing overall disease incidence among shift workers (Li & Sung, 1999), the association between shift work exposure and menstrual disorders would not be truly reflected.

Finally, the observed effects may be multifactorial. Depressive symptoms (Barsom et al., 2004), work stress (Laszlo et al., 2008), obesity (Wei et al., 2009), an unhealthy diet (Huhmann, 2020), and decreased physical activity (Kim et al., 2022) have all been identified as causes of menstrual problems. Functional hypothalamic amenorrhea in patients with eating disorders inhibits the hypothalamic-pituitary-ovarian axis, resulting in decreased estrogen (Milano et al., 2022). Poor lifestyles, such as frequent consumption of junk food and fast food, can also contribute to menstrual morbidities (Vyver et al., 2008). The etiology of menstrual dysfunction is multifaceted. The association between shift work and menstruation may be mediated by social, psychological, physiological, and environmental factors. Limited studies have done further mediation analyses of these factors as confounders or mediators. Further research is needed to better understand the mechanisms behind this association and to develop effective interventions to improve menstrual health in shift workers.

There is evidence of an exposure-response relationship between the frequency of shift work and menstrual cycle length (Lawson et al., 2011; Mayama et al., 2020). However, due to the limited number of studies and the poorly defined menstrual cycle length, it is not possible to quantify this in our meta-analysis. The dose-response relationship should be emphasized in future research. Therefore, higher quality studies are needed to determine the effects of shift work exposure on the reproductive health of female workers. Subsequent studies are needed to accurately report the amount of shift work exposure, the type of shift schedule, and the duration of shift work. Furthermore, the literature on the risk of menopause in shift-work women in the current database is insufficient. Prospective studies can be conducted to observe the effects of shift work on the timing of menopause in female workers.

Credit author statement

All authors contributed significantly to this study. Fengying Hu: conceptualization, methodology, software, date Analysis, writing-original draft. Cuiyun Wu: data curation, date analysis, writing-original draft. Yunfei Jia: conceptualization, methodology, software. Hualong Zhen: conceptualization, methodology, software. Hengshun Cheng: data curation, writing - review & editing. Fan Zhang: writing - review & editing. Liuqing Wang: resources, writing-review & editing. Minmin Jiang: funding acquisition, resources, supervision, writing-review & editing, final approval of the version to be published.

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The authors have no competing interests to declare.

Data availability

Data will be made available on request.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ssmph.2023.101542.

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