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## Global view of vasomotor symptoms and sleep disturbance in menopause: a systematic review

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### ABSTRACT

Studies have shown racial/ethnic differences in the prevalence of vasomotor symptoms (VMS), sleep disturbance and VMS treatment in menopause. To assess the reproducibility of these differences, we systematically reviewed observational studies, published in 2000–2021, reporting the prevalence/incidence of VMS, sleep disturbance or treatment use in menopausal women stratified by race/ethnicity. We screened 3799 records from PubMed and Embase and included 27 papers (19 studies). No incidence data were found. Prevalence data varied widely, but some common patterns emerged. In all five studies comparing VMS between Black women and White, Hispanic and/or East Asian women, the prevalence was highest in Black women and lowest in East Asian women. The prevalence of sleep disturbance overall was compared among Black, White and East Asian women in two study populations, and was highest in White women in both papers. Sleep disturbance was more common than VMS in East Asian women. In all four studies comparing hormone therapy use between White women and Black and/or East Asian women, treatment use was more common in White women. These results highlight the need for individualized counseling and treatment, outreach to under-served minorities, and standardized definitions and outcome measures for VMS and sleep disturbance for future studies.

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Systematic review; epidemiology; menopause; vasomotor symptoms; hot flashes; sleep; hormone therapy; race; ethnicity


### Introduction

Vasomotor symptoms (VMS; also referred to as hot flashes) are considered to be cardinal symptoms of menopause [1,2]. The prevalence of VMS has been reported to be 50–82% in US women who experience natural menopause [1], with symptoms lasting a median of 7.4 years, according to the US-based Study of Women's Health Across the Nation (SWAN) [3]. In a study of perimenopausal and postmenopausal women in the USA, 60% of participants reported seeking health care for their menopausal symptoms, with VMS being the most common symptoms discussed with a health-care professional [4].

Sleep disturbance is common in menopausal women and may occur alone or in combination with VMS [5,6]. Both sleep disturbance and VMS may substantially impair health-related quality of life [7]. Treatments for menopausal VMS and sleep disturbance include hormone therapy (HT) and non-hormonal pharmaceutical therapies (e.g. selective serotonin reuptake inhibitors for VMS and sedative hypnotics for sleep disturbance) [5,8]. In addition, many women with menopausal symptoms use complementary and alternative medicine (CAM) options such as mind–body therapies and herbal preparations [9].

Postmenopausal women account for a growing proportion of the global population [10], and menopause is the focus of increasing clinical interest, with the recent publication of the 2022 HT and 2023 non-HT position statements of the North American Menopause Society [11,12], new treatments for VMS showing promising results in clinical trials [13] and the recent approval of the neurokinin-3 receptor antagonist fezolinetant in the USA for the treatment of moderate to severe VMS due to menopause [14–16]. Data from the SWAN have previously shown differences between racial/ethnic groups in the prevalence of VMS and sleep disturbance and the treatment of VMS [17,18]. However, to the best of our knowledge, within the past 5 years there have been no systematic literature reviews (SLRs) comparing the prevalence of VMS or sleep disturbance between different racial or ethnic groups. We therefore performed an SLR of the prevalence and incidence of VMS and sleep disturbance in menopausal women worldwide, stratified by race/ethnicity, to obtain an overview of the current status of published research, to better understand the burden of menopause in different ethnic groups around the world, to assess whether racial/ethnic differences are reproducible across different studies (which

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would argue for race/ethnicity being an independent influencing factor) and to identify any evidence gaps. We also investigated the use of treatments for menopausal symptoms, to create awareness regarding the needs for care.

## Methods

This SLR was conducted as part of a broader set of searches assessing the prevalence and incidence of four menopausal symptoms (VMS, sleep disturbance, depression and joint pain) and treatment use in menopausal women. We chose to focus on VMS and sleep disturbance for the current analysis of symptoms by race/ethnicity, because whereas depression and joint pain are symptoms of multifactorial origin, VMS are the cardinal symptoms of menopause [1,2], while sleep disturbance (although also multifactorial in origin) has been linked to VMS [5] and is highly bothersome [19]. PubMed and Embase were searched on 27 April 2021 for epidemiological/observational studies reporting the prevalence or incidence of menopausal symptoms or treatments in menopausal or middle-aged women, published from 2000 to 2021. The search terms are presented in [Supplementary Tables 1 and 2](#). Duplicate citations were removed using EndNote software (Clarivate Analytics, Philadelphia, PA, USA) before screening.

Titles and abstracts were screened by a single reviewer to identify epidemiological/observational studies (primary research articles and meta-analyses) reporting the prevalence/incidence of VMS, sleep disturbance or treatment use in menopausal or middle-aged women stratified by race/ethnicity. Other article types (e.g. reviews), articles without abstracts, interventional studies, non-clinical studies, studies of subpopulations with comorbidities (e.g. women with diabetes), studies including only late postmenopausal women (with minimum age  $\geq 60$  years or mean age  $\geq 70$  years) and studies reporting only subtypes of sleep disturbance (e.g. sleep-disordered breathing) or sleep duration/time, rather than sleep disturbance, were excluded. For studies with multiple publications (such as the SWAN and the Women's Health Initiative Observational Study [WHI OS]), the publications describing the largest analysis sets and/or the most detailed information for a specific symptom/treatment of interest were selected for inclusion (the remainder were considered to be secondary papers and excluded). Data were extracted by menopausal status (e.g. premenopausal, perimenopausal and postmenopausal) if this information was available; data from study populations with mixed or unclear menopausal status were also documented.

Quality was assessed using the Joanna Briggs Institute Checklist for Prevalence Studies [20], with scores of 7–9, 4–6 and 0–3 considered to represent good, moderate and poor quality, respectively.

## Results

### Studies

In total, 6370 references were identified in the PubMed and Embase searches ([Supplementary Figure 1](#)). Of these, 2571 were duplicates, 3799 were screened, 75 potentially relevant

references were identified for full-text review and 27 papers (19 studies; [Table 1](#)) were included in the SLR. Quality was rated as good, moderate and poor in 21 papers, five papers and one paper, respectively ([Supplementary Table 3](#)). Although the included papers were published during 2000–2021, only two had a study period that ended in 2015 or later (out of a total of 21 papers with a reported study period). The results of each included study are presented in [Supplementary Table 4](#); overviews of prevalence data by race/ethnicity and menopausal status are presented in [Supplementary Tables 5–13](#).

### Vasomotor symptoms

The prevalence of VMS was reported by race/ethnicity in 17 papers on 13 studies (no incidence data were found). Eleven papers (nine studies) reported the prevalence of hot flashes [28–30,32,33,39,41–43,45,47], five papers (four studies) reported the prevalence of night sweats [30,32,33,42,47] and seven papers (five studies) reported the prevalence of VMS overall [21–23,31,33,37,40].

Although VMS and hot flashes are synonyms, and night sweats are generally understood to be hot flashes that occur at night, two studies reported a lower prevalence of hot flashes than VMS or night sweats [30,33], suggesting that the term 'hot flashes' was used in these two studies as daytime VMS or hot flashes occurring during the day, in contrast to the common understanding.

Instruments used to identify women with VMS included the Menopause Rating Scale [37,40], the Women's Health Questionnaire [42] and the first question of the Cervantes 10-item scale [39]. Other studies used study-specific questionnaires. Recall periods ranged from 2 weeks [21–23,41,43] to ever [32,33]; four studies did not specify a recall period [37,39,40,42].

Menopausal status was mixed/unclear in eight papers (eight studies) [21,37,39–41,43,45,47]; the remaining papers reported data for premenopausal women (three papers [three studies]) [22,30,33], premenopausal to early perimenopausal women [28], perimenopausal women [30], perimenopausal to postmenopausal women (two papers [two studies]) [32,42], late perimenopausal to postmenopausal women [28], postmenopausal women (two papers [two studies]) [30,31], women in the transition phase from premenopause to early perimenopause, early to late perimenopause and late perimenopause to postmenopause [22], and women in specific time frames relative to their natural last menstrual period (–14 to –1 years, 0–5 years and 6–14 years [29]). One paper reported the prevalence of VMS by their trajectory over the menopausal transition (persistently low, early onset, late onset and persistently high) [23]. The two postmenopausal study populations had mean ages of 63 years (WHI OS;  $n=87,783$  postmenopausal women) [31] and 50.5 years (the MetroNet study;  $n=46$  postmenopausal women) [30].

The reported prevalence of VMS varied widely (hot flashes, 18–98%; night sweats, 13–79%; VMS overall, 18–93%) (see [Supplementary Tables 4–7](#)). Nevertheless, some common patterns emerged when comparing different racial/ethnic groups. For example, five studies (SWAN [21–23], WHI OS [31], Lifetime

Table 1. Summary of included studies.

Authors, publication year (study) [reference]	Design, number of participants (time of study)	Country	Study population	Menopause stages/definitions	Symptoms/treatments reported
Gold et al., 2000 (SWAN) [21]	Prospective cross-sectional, n = 12,425 (1995–1997)	USA	Women aged 40–55 years (Black, Chinese, Hispanic, Japanese, and White), excluding those whose menstrual periods had stopped because of medication, radiotherapy, pregnancy or lactation, or extreme weight change, or who reported use of exogenous female hormones in past 3 months	NA <sup>a</sup>	VMS: reported as any hot flashes/night sweats in past 2 weeks
Gold et al., 2006 (SWAN) [22]	Prospective longitudinal, n = 3198 (1996–2002)	USA	Women aged 42–52 years (Black, Chinese, Hispanic, Japanese and White), with intact uterus and $\geq 1$ ovary, not currently using exogenous hormones affecting ovarian function, with menstrual period in previous 3 months	<p>Premenopause: menses in previous 3 months and no change in menstrual regularity in preceding year</p> <p>Early perimenopause: menses in previous 3 months and changes in regularity in past year</p> <p>Late perimenopause (non-surgical): no menses in previous 3 months but menses in preceding 11 months</p> <p>Postmenopause (non-surgical): <math>\geq 12</math> months of amenorrhea</p> <p>Transition phase: first visit at which a change in menopausal status was observed</p>	VMS: reported as any VMS in past 2 weeks and VMS on $\geq 6$ days in past 2 weeks
Tepper et al., 2016 (SWAN) [23]	Prospective longitudinal, n = 1455 (1996–2013)	USA	See Gold et al., 2006 [22]. Analysis included non-pregnant, non-lactating women who experienced natural menopause and women who stopped hormone use and had menstrual bleeding after a 6-month washout period and then $\geq 12$ consecutive months of amenorrhea	<p>Study of symptom trajectory across menopausal transition (12 years before to 15 years after natural FMP). FMP identified at the first visit when a woman had no menses for <math>\geq 12</math> months; date of FMP was date of last reported menstrual period</p>	VMS: reported as persistently low VMS (with slight increase around FMP), early-onset VMS (decreasing immediately after FMP), late-onset VMS (sharp increase just after FMP followed by decrease) and persistently high VMS; VMS defined as hot flashes or night sweats
Kravitz et al., 2003 (SWAN) [24]	Prospective cross-sectional, n = 12,603 (1995–1997)	USA	Women in the SWAN aged 40–55 years (Black, Chinese, Hispanic, Japanese and White) who responded to the question ‘Over the past 2 weeks, have you experienced difficulty sleeping (no/yes)?; could be categorized as premenopausal, early or late perimenopausal, or naturally or surgically postmenopausal and, if premenopausal or perimenopausal, had not taken reproductive hormones during previous 3 months. Exclusion criteria: pregnancy; periods stopped in past 12 months because of pregnancy or breast-feeding; periods stopped because of medication or severe weight loss or illness; missing information regarding hysterectomy/oophorectomy; hysterectomy without bilateral oophorectomy and not on HT	<p>Premenopause: menstrual period in previous 3 months and no irregularity</p> <p>Early perimenopause: menstrual period in previous 3 months and irregularity in past 12 months compared with preceding year</p> <p>Late perimenopause: menses in past 12 months but not in past 3 months</p> <p>Natural postmenopause: no menstrual period in past 12 months</p> <p>Surgical postmenopause: bilateral ovariectomy</p> <p>Postmenopause on HT: HT in previous 3 months</p>	Sleep disturbance: reported as difficulty sleeping in past 2 weeks Treatment: postmenopausal HT in previous 3 months
Solomon et al., 2020 (SWAN) [25]	Prospective longitudinal, n = 3082 (1996–2016)	USA	See Gold et al., 2006 [22]. Exclusion criteria: pregnancy; lactation; reproductive hormone use in previous 3 months	<p>Premenopause or early perimenopause (at baseline): menstrual period in previous 3 months</p>	Sleep disturbance: reported as difficulties with falling asleep, staying asleep or early morning waking on 3–7 nights/week during past 2 weeks, assessed annually or biennially Treatment: sleep medication use

(Continued)

Table 1. Continued.

Authors, publication year (study) [reference]	Design, number of participants (time of study)	Country	Study population	Menopause stages/definitions	Symptoms/treatments reported
Kravitz et al., 2008 (SWAN) [26]	Prospective longitudinal, n = 3045 (NR)	USA	See Gold et al., 2006 [22]. Exclusion criteria: pregnancy; reproductive hormone use in previous 3 months	Perimenopause or early postmenopause (at baseline); menstrual period in previous 3 months	Sleep disturbance: reported as trouble falling asleep $\geq 3$ times/week in past 2 weeks, waking up several times $\geq 3$ times/week in past 2 weeks and waking up early $\geq 3$ times/week in past 2 weeks Treatment: HT
Kazlauskaite et al., 2015 (SWAN with additional premenopausal women) [27]	Cross-sectional analysis of baseline data in prospective cohort study, n = 393 (2000–2008)	USA	Black and White participants of the SWAN at Chicago site, plus 138 additional premenopausal women. Exclusion criteria: hysterectomy; diabetes; no longitudinal intra-abdominal adipose tissue data	Perimenopause (at baseline): regular menstruations within past 3 months (Only 63% were premenopausal at initial evaluation; menopausal status of remainder was NR but hysterectomy was excluded)	
Freeman et al., 2005 (POAS) [28]	Prospective longitudinal, n = 436 (1996–2002 [6-year follow-up])	USA	Black and White women aged 35–47 years with menstrual cycles in normal range (22–35 days) for previous 3 months at baseline, with intact uterus and $\geq 1$ ovary. Exclusion criteria: current use of hormonal or psychotropic medications; pregnancy or breast-feeding; serious health problems known to compromise ovarian function; alcohol or drug abuse within past year	Perimenopause: regular menstrual cycles in normal range Early transition: change in cycle length of $\geq 7$ days from participant's baseline (at enrollment) for $\geq 2$ cycles in study Late transition: 3–11 months amenorrhea during study Postmenopause: $\geq 12$ months amenorrhea	VMS: reported as hot flashes in past month at 4, 5 and 6 years of follow-up
Freeman et al., 2014 (POAS) [29]	Prospective longitudinal, n = 255 (1996–2012)	USA	Women in POAS who reached natural menopause during a 16-year follow-up period (Black and White)	Data reported by time relative to natural FMP (–14 to –1 years, 0–5 years and 6–14 years). FMP identified after $\geq 12$ months without menstrual bleeding	VMS: reported as moderate/severe hot flashes in past month or year (unclear from text)
Xu et al., 2005 (MetroNet) [30]	Prospective cross-sectional, n = 237 (2000–2001)	USA	Black and White women aged between 40 and 55 years presenting at primary care clinics. Women who reported surgical menopause (hysterectomy and/or oophorectomy) were excluded from analyses of symptoms	Perimenopause: regular menstrual periods in previous 12 months Perimenopause (non-surgical): no period in previous 3 months, but $\geq 1$ menstruation in previous 12 months Postmenopause (non-surgical): no period in previous 12 months	VMS: reported as hot flashes/flushes in past 6 months and night sweats in past 6 months Sleep disturbance: reported as difficulty sleeping in past 6 months
Harrington et al., 2018 (WHI OS) [31]	Prospective longitudinal, n = 87,783 (NR)	USA	WHI OS participants. Exclusion criteria: missing baseline VMS data; history of venous thrombosis; missing number of days of follow-up; anticoagulant use. Studied racial/ethnic groups: American Indian/Alaskan Native; Asian/Pacific Islander; Black; Hispanic; White not of Hispanic origin; other; unknown	Perimenopause (not defined)	VMS: reported as hot flashes or night sweats in last 4 weeks at baseline
Reed et al., 2013 (LEAVES) [32]	Prospective cross-sectional, n = 5634 (2010–2011)	USA	Perimenopausal and postmenopausal women aged 45–58 years who had been enrolled in Group Health for $\geq 1$ year, received care at a Group Health-owned facility, and resided within 50 miles of the research clinic. Exclusion criteria: hormone use; intestinal or malabsorption syndromes; colectomy; cancer; antibiotic use in prior 3 months. Studied racial/ethnic groups: White; Black; American Indian; Asian Indian; Chinese; Filipino; Japanese; Vietnamese; Other Asian; Hawaiian/other Pacific Islander; Mixed; other; non-Hispanic White; Hispanic	Perimenopause and postmenopause: skipped $\geq 1$ menses in past 12 months or absence of menses for $> 12$ months	VMS: reported as hot flashes ever and night sweats ever Treatment: prior postmenopausal HT (women who used systemic estrogen and/or progestin, selective estrogen receptor modulators or oral contraceptives in prior 6 months were excluded)



Reed et al., 2014 (LEAVeS) [33]	Prospective cross-sectional, <i>n</i> = 1513 (2010–2011)	USA	Premenopausal women aged 45–56 years. Other eligibility criteria were as described in Reed et al., 2013 [32]	Premenopause: regular menses (no skipped period in past 12 months)	VMS: reported as hot flashes ever, night sweats ever and VMS ever
Gaston et al., 2019 (Sister Study) [34]	Retrospective cross-sectional analysis of baseline data from a prospective cohort study, <i>n</i> = 38,007 (2003–2009)	USA	Women aged 35–74 years without breast cancer with a sister diagnosed with breast cancer. Women were excluded if they self-identified as any race/ethnicity other than White, Black or Hispanic/Latina; were currently pregnant, breastfeeding or with pre-existing medical conditions; were current shift workers; or were missing values or had unknown timing of excluded medical conditions	Premenopausal and postmenopausal: self-reported (not further defined)	Sleep disturbance: reported as difficulty falling asleep (taking ≥30 min to fall asleep on average), difficulty staying asleep (awakening ≥3 times per night/day, ≥3 nights/days per week) and insomnia symptoms (difficulty falling or staying asleep) Treatment: sleep medication use; HT use
Shadyab et al., 2015 [35]	Retrospective cross-sectional, <i>n</i> = 1609 (1992–1999)	USA	White, Filipina and Black community-dwelling, postmenopausal women aged 50–86 years	Postmenopause (not defined)	Treatment: current insomnia medication
Keenan et al., 2003 (CAMPS) [36]	Prospective cross-sectional, <i>n</i> = 2602 (1997–1998)	USA	Women aged ≥45 years with complete data on current age and menopausal status (White non-Hispanic, Black non-Hispanic and Hispanic)	NA <sup>a</sup>	Treatment: conventional therapies <sup>b</sup> alone or in combination for ≥3 months, complementary and alternative medicine therapies: alone or in combination for ≥ 3 months, both types and neither type VMS: reported as hot flushes, sweating Sleep disturbance: reported as sleeping problems (MRS)
Monterrosa et al., 2008 [37]	Prospective and retrospective cross-sectional, <i>n</i> = 578 (2006–2007 [dates of REDLINC III–IV NR])	Colombia	Healthy Afro-Colombian and non-Afro-Colombian women aged 40–59 years (data for non-Afro-Colombian women were taken from REDLINC III–IV)	NA <sup>a</sup>	Sleep disturbance: reported as insomnia (score ≥6 on Athens Insomnia Scale)
Monterrosa-Castro et al., 2013 [38]	Prospective cross-sectional, <i>n</i> = 1325 (2009–2011)	Colombia	Colombian women aged 40–59 years (Mestizo [Hispanic], indigenous [direct descendants of native Zenu] or Black [direct African descendants]). Exclusion criteria: refused participation; did not complete socio-demographic questionnaire or incapable of understanding its content; surgery in last 6 months; cancer; other serious illness	NA <sup>a</sup>	VMS: reported as hot flushes present (first question of Cervantes 10-item scale) Treatment: phytoestrogen VMS: reported as hot flushes/sweating Sleep disturbance: reported as sleeping disorders (MRS) VMS: reported as hot flash in past 2 weeks
Salazar-Pousada et al., 2017 [39]	Prospective cross-sectional, <i>n</i> = 864 (2015–2016)	Colombia, Peru, Ecuador and Paraguay	Women aged 40–65 years (Afro-Colombian from Colombia, Mestizo [Hispanic] from Ecuador and Paraguay, and Quechua [high altitude] from Peru)	NA <sup>a</sup>	
Ojeda et al., 2014 [40]	Prospective cross-sectional, <i>n</i> = 771 (NR)	Peru	Healthy Hispanic-Mestizo or Quechua women aged between 40 and 59 years living in District of El Cusco (between 2500 m and 3500 m above sea level)	NA <sup>a</sup>	
Brown et al., 2009 (HWHS) [41]	Prospective cross-sectional, <i>n</i> = 527 (2004–2008)	Hawaii, USA	Women of European American or Japanese American ethnicity, aged 45–55 years, living in Hilo, Hawaii, not using exogenous hormones	NA <sup>a</sup>	
Gupta et al., 2006 [42]	Prospective cross-sectional, <i>n</i> = 153 (NR)	UK and India	Perimenopausal and postmenopausal South Asian (India and UK) and White (UK) women aged 45–55 years without history of severe, physically disabling medical or surgical conditions, dementia, major psychotic or affective disorders	Perimenopause: irregular menstruation but ≥1 spontaneous period in last 12 months Postmenopause: no menstruation for past 12 months	VMS: reported as hot flushes and night sweats (separately; Women's Health Questionnaire)

(Continued)

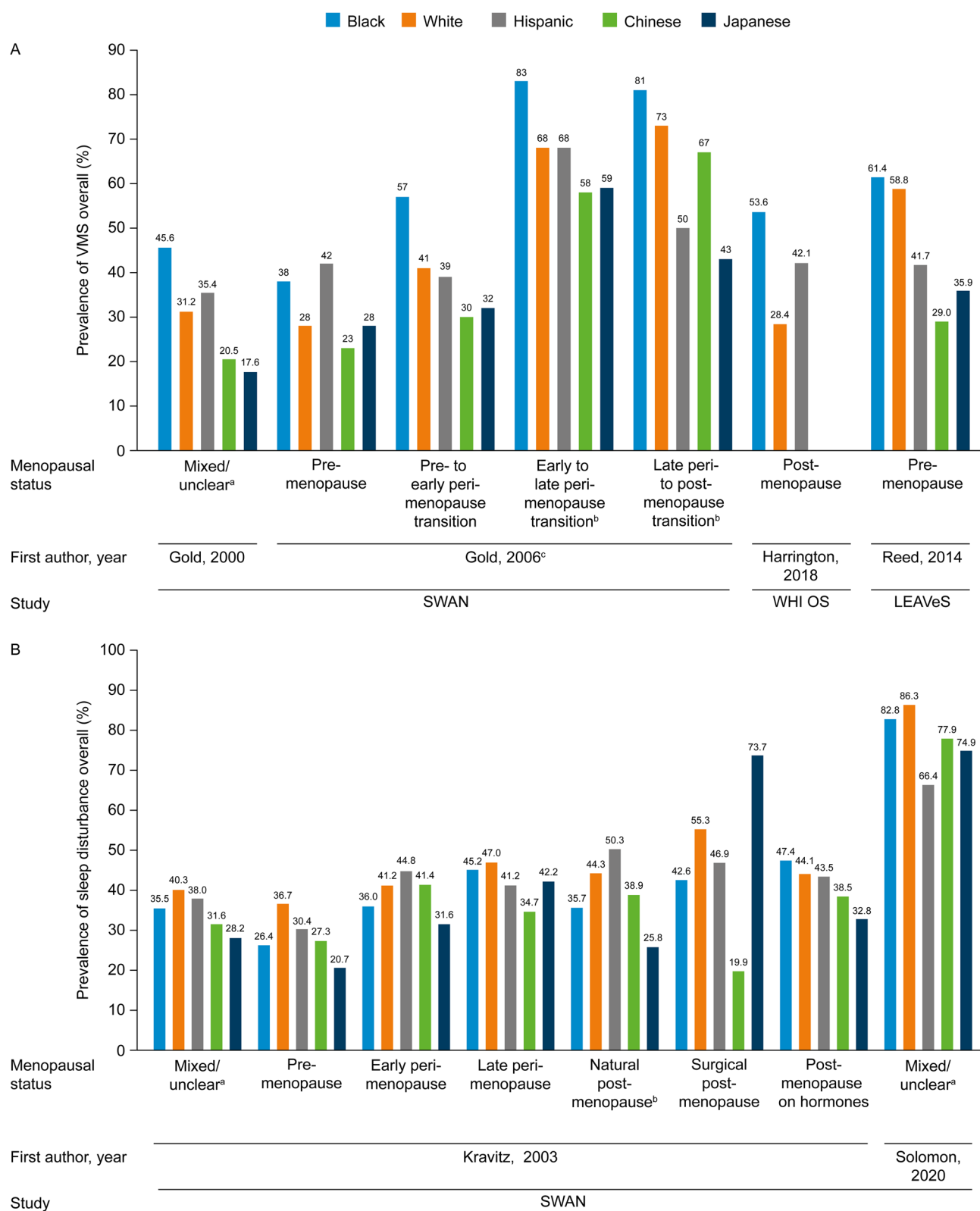
Table 1. Continued.

Authors, publication year (study) [reference]	Design, number of participants (time of study)	Country	Study population	Menopause stages/definitions	Symptoms/treatments reported
Dhanoya et al., 2016 [43]	Prospective cross-sectional, n = 108 (NR)	UK and Bangladesh	Eligibility criteria included: age 40–59 years, no exogenous hormone use in last 3 months, not lactating or pregnant, no history of oophorectomy, hysterectomy, thyroid disease, polycystic ovaries or type 1 diabetes. Studied racial/ethnic groups were European (UK) and South Asian (UK [migrated from Bangladesh as adults] and Bangladesh)	NA <sup>a</sup>	VMS: reported as hot flashes in past 2 weeks Treatment: HT
Soh et al., 2020 (SEED) [44]	Retrospective cross-sectional, n = 3408 (Chinese, 2009–2011; Indian, 2007–2009; Malay, 2004–2006)	Singapore	Population-based cohorts of Malay, Indian and Chinese women aged 40–80 years. Women with missing data on age of menstruation cessation, HRT usage and history of oophorectomy were excluded	NA <sup>a</sup>	Treatment: HT
Blumstein et al., 2012 (WHMINSI) [45]	Prospective cross-sectional, n = 811 (2004–2006)	Israel	Women aged 45–64 years (long-term Jewish residents, Jewish immigrants from former Soviet Union who arrived after 1989 and Arab Israelis)	NA <sup>a</sup>	VMS: reported as hot flashes in past 6 months
Madaeva et al., 2020 [46]	Prospective cross-sectional, n = 542 (NR)	Russia	Buryat and White women either in perimenopause and aged 45–55 years or in postmenopause and aged 56–60 years. Exclusion criteria: use of hormone replacement therapy; exacerbation of chronic disease; diabetes mellitus; history of chronic sleep disorder; use of hypnotics in last 2 weeks; 'surgical menopause'; 'evening' chronotype; 'shift work'	Perimenopause: changes in menstrual cycle (oligomenorrhea or absence of menstrual function for 12 months); ultrasound data showing non-functional endometrium; depletion of ovarian follicular apparatus Postmenopause: absence of menstrual function for >24 months; follicle-stimulating hormone level >20 mIU/ml; luteinizing/follicle-stimulating hormone index <1; ultrasound studies showing thin, non-functional endometrium, M echo ≤0.3 cm; absence of ovarian follicular apparatus	Sleep disturbance: reported as sleep disorders, difficulty going to sleep, frequent nocturnal waking (>2 times/night), difficulty waking in morning and insomnia (Insomnia Severity Index 0–7 [none], 8–14 [mild], 15–21 [moderate], 22–28 [severe])
Mishra et al., 2002 (ALSWH) [47]	Prospective cohort, n = 8466 (1996–1998)	Australia	Women born from 1946 to 1951 (aged 45–50 years in 1996) selected randomly from Medicare Australia database who responded to Survey 1 (1996) and Survey 2 (1998). Country/region of birth (Australia, other English-speaking country, Europe or Asia) used as proxy for ethnicity. Exclusion criteria: hysterectomy or oophorectomy; response to short version of Survey 2; country of birth not stated or not readily categorized	NA <sup>a</sup>	VMS: reported as hot flushes sometimes or often in past 12 months and night sweats sometimes or often in past 12 months Sleep disturbance: reported as difficulty sleeping sometimes or often in past 12 months Treatment: HT at Survey 2

<sup>a</sup>Population not selected by menopausal stage and symptoms/treatments not reported by menopausal stage in racial/ethnic subgroups.

<sup>b</sup>Estrogen, estrogen+progestin, progestin/progesterone, androgen.

<sup>c</sup>Vitamins/minerals, increased amount of physical activity, herbal remedy, soy foods, body/mind techniques, body work, melatonin, acupuncture, self-help group, dehydroepiandrosterone. ALSWH, Australian Longitudinal Study on Women's Health; CAMPS, Conventional, Complementary and Alternative Menopausal Practices Survey; FMP, final menstrual period; HT, hormone therapy; HWHS, Hilo Women's Health Study; LEAVES, Lifetime Exposures And Vasomotor Symptoms; MRS, Menopause Rating Scale; NA, not applicable; NR, not reported; POAS, Penn Ovarian Aging Study; REDLINC, Collaborative Group for Research of the Climacteric in Latin America; SEED, Singapore Epidemiology of Eye Diseases; SWAN, Study of Women's Health Across the Nation; VMS, vasomotor symptoms; WHI OS, Women's Health Initiative Observational Study; WHMINSI, Women's Health in Midlife National Study in Israel.



**Figure 1.** Prevalence of (A) VMS overall and (B) sleep disturbance overall in studies comparing Black women with White, Hispanic and/or East Asian (Chinese and Japanese) women. Sleep disturbance data are from the SWAN cross-sectional [24] and longitudinal [25] study populations. <sup>a</sup>Symptom not reported by menopausal stage. <sup>b</sup>Non-surgical menopause only. <sup>c</sup>Data published as graph only; prevalence values estimated using Graph Grabber v2.0 (Quintessa, UK). LEAVeS, Lifetime Exposures And Vasomotor Symptoms; SWAN, Study of Women's Health Across the Nation; VMS, vasomotor symptoms; WHI OS, Women's Health Initiative Observational Study.

Exposures And Vasomotor Symptoms [LEAVeS] study [32,33], Penn Ovarian Aging Study [POAS] [28] and MetroNet study [30]) compared the prevalence of hot flashes, night sweats or

VMS overall between Black women and White, Hispanic and/or East Asian (Japanese and Chinese) women; all showed the highest prevalence in Black women, while East Asian women



had the lowest prevalence (dependent on menopausal stage in the SWAN [22] and the MetroNet study [30]). Data for VMS overall are shown in Figure 1A. A separate POAS analysis showed a higher prevalence of moderate/severe hot flashes in Black women than in White women among those with a body mass index (BMI) <30 kg/m<sup>2</sup>, but not among those with a BMI ≥30 kg/m<sup>2</sup> [29].

Women of South Asian ethnicity and White women were compared in the US-based LEAVeS study [32,33] and the studies by Gupta et al. [42] and Dhanoya et al. [43], which were both conducted in the UK and in Asia. Interestingly, Gupta et al. found that the prevalence of hot flashes was higher among Asian Indian women in the UK, but lower among Asian women in India, compared with White women in the UK, suggesting environmental or sociocultural influences [42]. A similar pattern was observed for night sweats. By contrast, Dhanoya et al. found a higher prevalence of hot flashes in Bangladeshi women, regardless of their location (Bangladesh or the UK), compared with European women in the UK [43]. Conversely, the LEAVeS study showed a lower prevalence of hot flashes and night sweats in Asian Indian women than in White women in both premenopausal and perimenopausal to postmenopausal subgroups [32,33].

The highest prevalence values for hot flashes (98%) and overall VMS (93%) were reported in two studies of Quechua women in Peru [39,40].

Native American and White women were compared in two studies (the WHI OS and the LEAVeS study). Both studies found a higher prevalence of VMS in the Native American group [31,33].

Other combinations of racial/ethnic groups were each compared in single studies. A study by Monterrosa et al. conducted in Colombia found that about half of Afro-Colombian and non-Afro-Colombian women aged 40–59 years had hot flashes/sweating (53.2% and 54.9%, respectively) [37]. The Hilo Women's Health Study in Hawaii compared women of European American and Japanese American ethnicity, aged 45–55 years, and showed a higher prevalence of hot flashes in the previous 2 weeks in the European American group (43.9% vs 30.9%) [41]. The Australian Longitudinal Study on Women's Health, which included women aged 45–50 years and used country of birth as a proxy for ethnicity, found a lower prevalence of hot flashes and night sweats (sometimes or often in the previous 12 months) in women born in Asia (hot flashes, 21.5%; night sweats, 13.0%) compared with women born in Australia, other English-speaking countries or Europe (hot flashes, 28.4–31.2%; night sweats, 22.1–24.7%) [47]. In the Women's Health in Midlife National Study in Israel, population estimates (projected from sample data) of the prevalence of hot flashes in the previous 6 months in women aged 45–64 years were 37.6% in long-term Jewish residents, 21.6% in Jewish immigrants and 32.6% in Arab Israelis [45].

### Sleep disturbance

The prevalence of sleep disturbance was reported by race/ethnicity in 10 papers on eight studies (no incidence data were found). Three papers (three studies) reported the

prevalence of difficulty falling asleep [26,34,46], three papers (three studies) reported the prevalence of frequent waking [26,34,46], two papers (two studies) reported the prevalence of problems with morning waking [26,46] and nine papers (eight studies) reported the prevalence of sleep disturbance overall (also described as sleep problems/disorders/difficulties or insomnia) [24,25,30,34,37,38,40,46,47].

Frequent waking was defined as waking up several times a night on ≥3 occasions per week [26], waking up ≥3 times per night at an unspecified frequency per week [46] or waking up ≥3 times per night/day on ≥3 occasions per week [34]. Problems with morning waking were defined as early waking ≥3 times per week [26] or difficulty with morning waking (frequency not specified) [46].

Instruments used to identify women with sleep disturbance included the Menopause Rating Scale [37,40], the Athens Insomnia Scale [38] and the Insomnia Severity Index [46]. Other studies used study-specific questionnaires. Recall periods ranged from 2 weeks [24–26] to 12 months [47]; five studies did not specify a recall period [34,37,38,40,46].

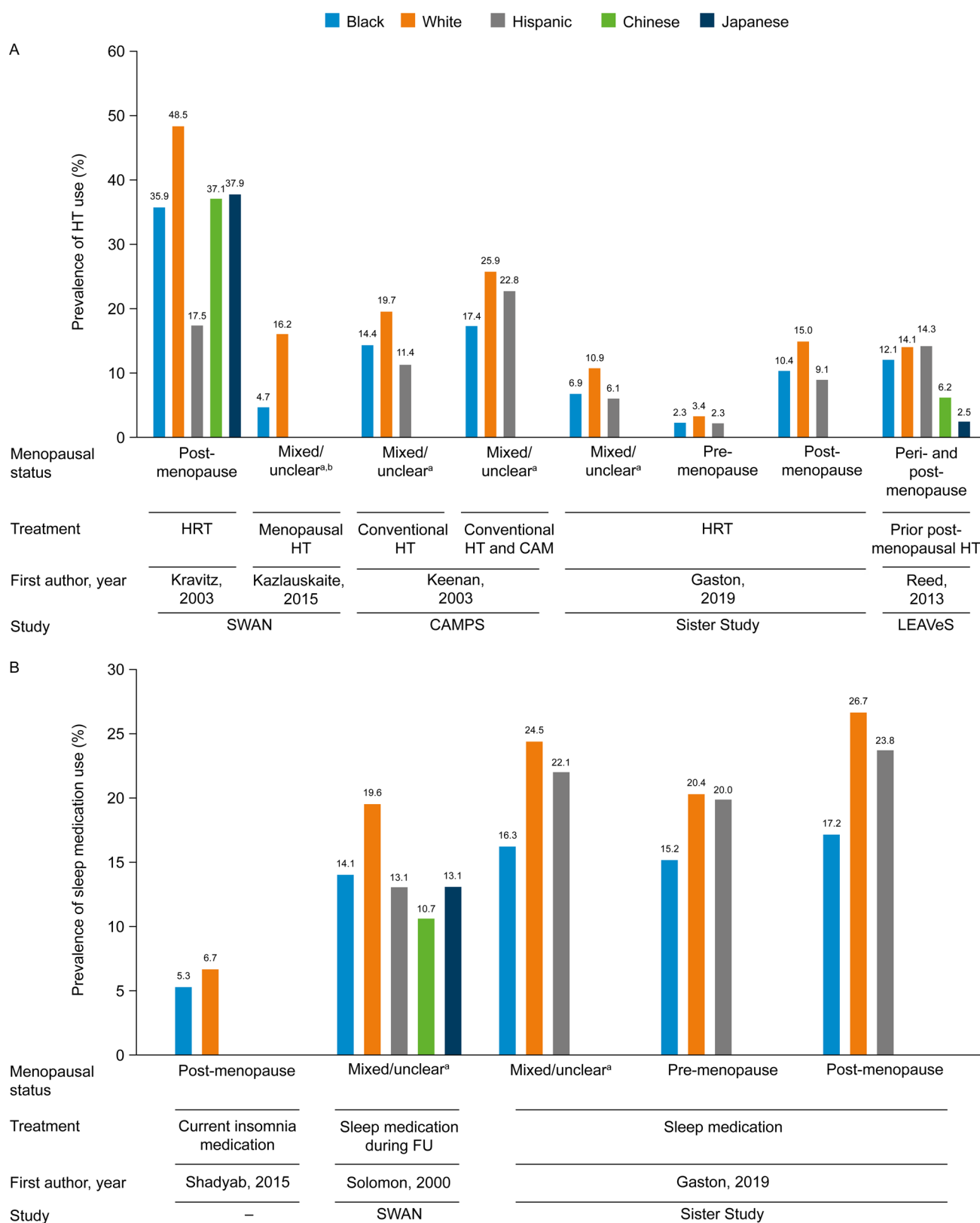
Data on the prevalence of sleep disturbance were reported for women with mixed/unclear menopausal status in eight papers (six studies) [24–26,34,37,38,40,47], for premenopausal women in three papers (three studies) [24,30,34], for perimenopausal women in three papers (three studies) [24,30,46] and for postmenopausal women in four papers (four studies) [24,30,34,46]. One paper reported prevalence data by cause of menopause (surgical vs. natural) [24].

The reported prevalence of sleep disturbance varied widely (difficulty falling asleep, 7–69%; frequent waking, 9–84%; problems with morning waking, 6–64%; sleep disturbance overall, 20–86%) (Supplementary Tables 4 and 8–11). The prevalence of sleep disturbance overall was compared among Black, White and East Asian women in two study populations (SWAN cross-sectional and longitudinal phases) [24,25]; both showed the highest prevalence in White women and lowest prevalence in East Asian women, dependent on menopausal stage (Figure 1B). Sleep disturbance overall was more common than VMS overall in East Asian women but not in Black women.

Black, Hispanic and White women were compared in the Sister Study [34] and the SWAN [24,25], with inconsistent results: the prevalence of sleep disturbance overall was highest in White women and lowest/intermediate in Hispanic women in the SWAN, dependent on menopausal stage [24,25], but lowest in White women and highest in Hispanic women in the Sister Study [34]. Black and White women were also compared in the MetroNet study [30]: the prevalence of sleep disturbance overall was higher in White women in perimenopause and Black women in postmenopause.

Two studies in Colombia assessed the prevalence of sleep disturbance in women of different races/ethnicities aged 40–59 years: sleeping problems (Menopause Rating Scale) were reported in 54.7% and 60.5% of Afro-Colombian and non-Afro-Colombian women, respectively [37], and insomnia was reported in 29.9% of Mestizo women, 20.4% of Zenú indigenous women and 24.8% of Black women [38]. Among women aged 40–59 years in Peru, the prevalence of sleep problems (Menopause Rating Scale) was 72.9% and 71.8% in

Mestizo and Quechua women, respectively [40]. In a study of perimenopausal and postmenopausal women aged 45–60 years in Russia, the prevalence of sleep disturbance was 61.2% and 65.5%, respectively, in White women and 63.5% and 72.9%, respectively, in Buryat women; the most common complaint was difficulty going to sleep in White



**Figure 2.** Prevalence of (A) HT use and (B) sleep medication use in studies comparing Black women with White, Hispanic and/or East Asian (Chinese and Japanese) women. Prevalence was assessed in middle-aged/menopausal women overall (regardless of symptoms). <sup>a</sup>Treatment use not reported by menopausal stage. <sup>b</sup>Surgical hysterectomy was excluded. CAM, complementary and alternative medicine; CAMPS, Conventional, Complementary and Alternative Menopausal Practices Survey; FU, follow-up; HRT, hormone replacement therapy; HT, hormone therapy; LEAVeS, Lifetime Exposures And Vasomotor Symptoms; SWAN, Study of Women's Health Across the Nation.

perimenopausal women and frequent nocturnal waking in postmenopausal White women and perimenopausal and postmenopausal Buryat women [46]. In women aged 45–50 years in the Australian Longitudinal Study on Women's Health (which used country of birth as a proxy for ethnicity), difficulty sleeping in the previous 12 months was reported with a prevalence of 45.2%, 42.4%, 45.0% and 39.5% in those born in Australia, other English-speaking countries, Europe and Asia, respectively [47].

### Use of treatments

Use of treatments was reported by race/ethnicity in 10 papers on eight studies (Supplementary Tables 4, 12 and 13).

Use of HT or CAM was reported by race/ethnicity in eight papers on seven studies [24,27,32,34,36,39,44,47]. HT use was reported at the time of the survey in one study [47] and during the previous 3 months in one paper describing SWAN data [24]; the remaining papers did not specify a recall period. Seven papers (six studies) reported the use of HT (described in the papers as hormone replacement therapy, menopausal/postmenopausal HT or HT for menopausal symptoms) [24,27,32,34,36,44,47]. Some additional papers reported the use of HT but with no specific information on the regimen (at least one included oral contraceptives [31]) or on the symptoms that triggered the prescription, so these were not included in this review. One of the included papers describing HT use also reported the use of CAM for menopausal symptoms [36]. The remaining paper reported the use of phytoestrogen [39]. Treatment data were reported for women with mixed/unclear menopausal status in six papers (six studies) [27,34,36,39,44,47], for premenopausal women in one paper [34], for perimenopausal and postmenopausal women in one paper [32] and for postmenopausal women in two papers (two studies) [24,34].

HT use was compared between White women and Black and/or East Asian women in four studies (the SWAN [24,27], the Conventional, Complementary and Alternative Menopausal Practices Survey [CAMPS] [36], the Sister Study [34] and the LEAVeS study [32]). All four of these studies showed that HT use was more common in White women than in Black and/or East Asian women (Figure 2A).

Use of sleep medication was reported by race/ethnicity in three papers on three studies (a retrospective study by Shadyab et al. [35], the SWAN [25] and the Sister Study [34]). One study reported current insomnia medication use (sedative hypnotics) in postmenopausal women [35], one study reported current/recent sleep medication use (including trazodone, lorazepam, zolpidem, temazepam, doxepin, mirtazapine, triazolam, zaleplon, eszopiclone, flurazepam, ramelteon, brotizolam and estazolam) noted after or concurrent with a report of sleep disturbance at visits 1 or 2 years apart during ~20 years of follow-up across the menopausal transition [25] and the final study reported sleep medication use (not further specified) in premenopausal and postmenopausal women during the previous 6 weeks [34]. All three studies showed that sleep medication use was more common in White women than in Black women (Figure 2B). One of the

studies (SWAN) also assessed East Asian women, and showed that sleep medication use was less common in these women compared with White women [25]. The use of sleep medications increased more than three-fold over the period when women traversed the menopausal transition, from 2.5% to 8.0% of women who reported sleep disturbance. In addition to ethnicity, the depressive symptom score, hypertension, cancer status and trouble initiating sleep were associated with initiation of sleep medication among women reporting sleep disturbance in the SWAN [25].

### Discussion

The prevalence of VMS, sleep disturbance and use of HT/sleep medication showed a very high degree of variation across studies, menopausal stages and races/ethnicities in this SLR. Nevertheless, some common patterns emerged. VMS reporting was more prevalent in Black women than in White women, and less common in East Asian women. By contrast, HT use was more common in White women than in Black and East Asian women. Sleep disturbance was generally more commonly reported in White women than in East Asian women. Sleep medication use was more common in White women than in Black women and (based on a single study) East Asian women. Quality was rated as good or moderate for all but one of the included papers. The single poor-quality paper was included because it provided relevant data on South Asian women [43]; however, it has not influenced our conclusions (which focus on studies comparing Black, White and East Asian women).

The most recent previous SLRs on the prevalence of VMS and sleep disturbance by race/ethnicity were published more than 5 years ago [48,49]. Islam et al. found that the prevalence of VMS reported in Asian countries (particularly South Asian and Middle Eastern countries) was similar to that reported in western countries, based on indirect comparison between studies [48]. We focused on studies that compared racial/ethnic groups directly, and found a consistently lower prevalence of reported VMS in East Asian women than in White women, but mixed results for comparisons of reported VMS prevalence between South Asian and White women. Xu and Lang found that the prevalence of subjective sleep disturbance changed across the menopausal transition in Asian and White women but not Hispanic women [49]. The authors noted that their findings were consistent with those of the cross-sectional SWAN analysis [24] for Asian and White women but not for Hispanic women, and suggested that this may be because of differences in geographic location/environmental factors: the Hispanic women in the SWAN were based in the USA whereas the Hispanic women included in the SLR by Xu and Lang were based in other countries.

Many factors have been previously reported to influence VMS and sleep. Factors associated with an increased likelihood of VMS include not only menopausal status (perimenopause, postmenopause or surgical menopause vs. premenopause) and use of HT but also age (with a negative regression coefficient reported for age squared), high BMI,

depression, anxiety, poor physical health, high perceived stress, active and passive smoking, and (in immigrant populations) acculturation [50]. Differences in perception and tolerance of temperature change have also been suggested to contribute to the difference in reported VMS prevalence between Black and White women [51]. In the SWAN, lower educational attainment and higher perceived stress (which were more common among Black women than White women) were associated with a longer duration of VMS [18]. As discussed by Harlow et al., social disadvantage among Black women – likely related to structural racism – is an important driver of disparities in midlife health between Black and White women in the USA [18]. Sleep disturbance associated with menopause is influenced by multiple factors including hormonal changes, VMS, mood disorders and other age-related conditions (e.g. obesity, cancer, gastroesophageal reflux, urinary incontinence and nocturnal micturition, thyroid dysfunction, chronic pain syndromes and fibromyalgia) [5], as well as financial hardship, number of stressful life events and physical inactivity [18]. These numerous influencing factors, together with differences in study design, may have contributed to the high degree of variability in the prevalence of reported VMS and sleep disturbance seen across studies and races/ethnicities in our SLR.

Sleep medication use reflected the prevalence of reported sleep disturbance in the SWAN. By contrast, Black women were more likely to report VMS but less likely to use HT than White women in the SWAN, the CAMPS, the Sister Study and the LEAVeS study. These are all US-based studies. According to the 2019 National Healthcare Quality and Disparities Report in the USA, Black people received a lower quality of care than White people for about 40% of quality measures [52]. The relatively low use of HT in Black women may be partly related to this disparity in care. Studies conducted in the late 1990s and early 2000s identified racial disparities in the content of physician counseling on HT [53], the likelihood of receiving a recommendation for HT from a physician [54] and the rate of HT prescription [55]. Black women were found to be more likely than White women to rely on family for information about the menopause [56], and Black race was associated with a reduced likelihood of HT awareness (independent of educational level) [57]. More recent studies suggest that Black women are less likely to have their menopausal symptoms documented in their medical records [58] and less likely to accept HT for menopausal symptom management [59] than White women. Structural racism contributes to the disparities in health care between Black and White women in the USA [60]. For example, disinvestment in Black neighborhoods limits access to health-care resources; a recent study of the four largest cities in the USA showed that pharmacy deserts and pharmacy closures were more common in Black and Latino neighborhoods than in other neighborhoods [61].

Sleep disturbance was more commonly reported than VMS in East Asian women in our SLR. This finding is consistent with a previous SLR focusing on Asian populations in which physical menopausal symptoms (including musculoskeletal symptoms and sleep disturbance) had the highest prevalence, followed by psychological symptoms, VMS and

sexual symptoms [62]. The different patterns of reported VMS and sleep disturbance across racial/ethnic groups argue against sleep disturbance being purely a consequence of VMS in menopausal women.

Our SLR is limited by the heterogeneity of the included studies, which assessed women from different geographical locations and applied different inclusion/exclusion criteria. Study populations had different age ranges, and some studies excluded women who were using exogenous reproductive hormones and/or women who had undergone hysterectomy and/or oophorectomy. Another source of heterogeneity is the lack of a universal definition for each menopausal symptom of interest. For example, sleep disturbance overall was reported using different terms (difficulty sleeping, sleep problems/disorders or insomnia) based on different instruments (including the Athens Insomnia Scale, the Insomnia Severity Index and the Menopause Rating Scale). Recall periods ranged from current to ever, and were not specified in a substantial number of studies. Only two of the included studies provided information on the use of CAM for the treatment of menopausal symptoms [36,39]. Where consistent patterns in symptom/treatment reporting were observed, the reasons for the differences between racial/ethnic groups are unclear and could include socioeconomic, educational and health-care access disparities, which may in some cases be driven by structural racism. To identify the reasons behind racial/ethnic differences in symptom/treatment reporting, these factors should be considered in cohort studies worldwide and quality assessment adapted accordingly. Finally, our SLR focused on only two symptoms of menopause; other important symptoms such as declining sexual function may also show disparities across racial/ethnic groups, as suggested by data from the SWAN [17].

## Conclusions

In epidemiological/observational studies that compared the prevalence of menopausal symptoms and treatment use across different races/ethnicities, Black women were more likely to report VMS but less likely to use HT than White women. This discrepancy may reflect ethnocultural health beliefs and/or gaps in care. In addition, sleep disturbance was more commonly reported than VMS in East Asian women but not in Black women. These results highlight the need for individualized counseling and treatment, and the need for outreach to under-served minorities.

The prevalence of reported VMS, sleep disturbance, and use of HT and sleep medication was highly variable across studies and races/ethnicities. The variation may be related to genetic and psychosocial factors and culturally determined health beliefs and perceptions. Differences in study design (including differences in patient questionnaires, symptom definitions/interpretations and recall periods) are also potential sources of variation. Evidence gaps include the lack of incidence data stratified by race/ethnicity (meaning causality between sleep disturbance and menopause cannot be inferred) and the scarcity of recent data (collected in 2015 or later). Standardized definitions and validated clinical outcome measures for VMS and sleep disturbance are needed for



future studies comparing the prevalence and incidence of menopausal symptoms across racial/ethnic groups. Further evaluation of racial/ethnic differences in other menopausal symptoms such as declining sexual function is also warranted.

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## Data availability statement

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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