Normal polysomnography parameters in healthy adults: a systematic review and meta-analysis

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Summary

Background Existing normal polysomnography values are not truly normative as they are based on small sample sizes due to the fact that polysomnography is expensive and burdensome to obtain. There is a clear need for a large sample of truly normative data for clinical management and research. This study is a comprehensive meta-analysis of adult polysomnography parameters scored using recent criteria and establishes normative values adjusted for age and sex.

Methods For this meta-analysis of adult polysomnography parameters, we searched Scopus for studies of any design published between Jan 1, 2007, and July 31, 2016, that reported polysomnographic parameters scored using recent American Academy of Sleep Medicine criteria (2007 or 2012) collected during an overnight level 1 in-laboratory sleep study in healthy controls. We excluded studies of patients with conditions or subjected to treatments that might affect sleep and studies not available in English. Study endpoints were the pooled estimates of 14 reported polysomnographic parameters. Estimates for each parameter were pooled using a random-effects meta-analysis. The influence of age and sex was ascertained using multivariate mixed-effects meta-regressions. This study is registered with PROSPERO, number CRD42017074319.

Findings Of 3712 articles, 169 studies, comprising 5273 participants, were eligible for inclusion. We report normative data stratified by age and sex. For each decade of age, total sleep time decreased by 10·1 min (95% CI 7·5 to 12·8), sleep efficiency decreased by 2·1% (1·5 to 2·6), wake after sleep onset increased by 9·7 min (6·9 to 12·4), sleep onset latency increased by 1·1 min (0·3 to 1·9), arousal index increased by 2·1 events per h (1·5 to 2·6), percentage of N1 sleep increased by 0·5% (0·1 to 0·8), apnea–hypopnea index increased by 1·2 events per h (0·9 to 1·4), mean oxygen saturation decreased by 0·6% (0·5 to 0·7), minimum oxygen saturation decreased by 1·8% (1·3 to 2·3), and periodic limb movement index increased by 1·2 events per h (0·8 to 1·6). Changes with age in the percentage of N2 sleep (0·0%, 95% CI –0·1 to 0·1), N3 sleep (–0·1%, –0·1 to 0·0), and rapid eye movement (REM) sleep (0·0%, –0·1 to 0·0) were not significant. Every 10% increase in the percentage of male participants was associated with reduced REM latency (0·9 min decrease, 95% CI 0·1 to 1·6) and mean oxygen saturation (0·1% decrease, 0·0 to 0·1), and greater arousal index (0·3 events per h, 0·0 to 0·5) and apnea–hypopnea index (0·2 events per h, 0·1 to 0·3).

Interpretation These normative values serve as a useful control reference for clinicians and for future research where it might be difficult to obtain polysomnographic controls. The resulting normative trends by age and sex might also be hypothesis-generating for a broad range of investigations.

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Introduction

Polysomnography has been scored using the Rechtschaffen and Kales criteria[1] for decades. These scoring criteria have been criticised because the rules had some subjectivity that reduced inter-rater reliability.[2] The manual was developed specifically for young, healthy adults and therefore lacked applicability to older adults (eg, >60 years) and various patient populations (eg, insomnia, parasomnias, narcolepsy, fibromyalgia, and sleep apnoea).[2,3] To address these criticisms, the American Academy of Sleep Medicine (AASM) published a modified scoring manual in 2007 that emphasised objectivity in scored parameters.[4] In 2012, the manual was updated to address concerns related to the scoring of respiratory events.[5] To date, the AASM criteria have facilitated improvement in inter-rater

reliability[6] and have become the standard for scoring sleep.

The differences in parameters obtained using the AASM criteria[4] compared with the Rechtschaffen and Kales rules[1] necessitate an appraisal of the normative values of sleep. For example, wake after sleep onset and the amount of time spent in different sleep stages changed significantly with the AASM criteria.[2] The availability of normative values based on key demographic characteristics, such as age and sex, would be of particular interest for clinical and research reference. Although investigators of research studies in a variety of conditions might wish to recruit a healthy control group for comparison, the high costs associated with in-laboratory polysomnography might preclude the inclusion of a healthy control group or limit participation to one night. Therefore, establishing reliable

Research in context

Evidence before this study

Several studies have explored the effect of age and sex on polysomnography parameters in healthy adults. However, inconsistent findings have been reported, probably related to small sample sizes. Thus far, only one meta-analysis has examined age-related and sex-related trends in sleep architecture; these findings pertained to sleep studies scored according to older scoring criteria and are not generalisable to sleep studies scored using more recent criteria. Using Scopus, we did a cited reference search for studies that referenced the 2007 American Academy of Sleep Medicine criteria and its subsequent 2012 update. We included studies published between Jan 1, 2007, and July 31, 2016, that evaluated healthy adults using level 1 overnight in-laboratory polysomnography. We excluded studies not available in English. The quality of each included cohort of healthy adults was assessed and pooled summary estimates were calculated for the polysomnography parameters of interest: total sleep time, sleep efficiency, wake after sleep onset, sleep onset latency, rapid-eye-movement (REM) latency, arousal index, percentage of total sleep time spent in each sleep stage (N1, N2, N3, and REM), apnea–hypopnea index, mean and minimum arterial oxygen saturation, and periodic limb movements index.

Added value of this study

To our knowledge, this meta-analysis is the largest analysis of published normative sleep data to date: we incorporate data from 169 published manuscripts that collectively examined 5273 healthy adults. We report robust summary values for 14 routine polysomnography parameters and the effect of age and sex on these parameters. We confirm and further define several of the age-related changes in sleep architecture previously reported. Finally, our meta-analysis also quantifies age-related and sex-related trends in the frequency of common physiological events (arousals, respiratory events, and periodic limb movements) in the sleep of healthy adults.

Implications of all the available evidence

This study provides many insights into how sleep changes with age and also illustrates sex differences. Our values provide normative data and report degrees of variance that may be helpful when preparing further research. These values will be useful in sleep clinics and for future research studies where cost could be prohibitive for obtaining polysomnography control data. The reported normative trends by age and sex are also hypothesis-generating for a broad range of investigations.

normative reference standards for first-night polysomnography would be helpful. Normative values could be a particularly valuable resource for studies exploring polysomnography abnormalities in different conditions, particularly if adequately adjusted normative values could be identified across age and sex.

Several studies have explored the effect of age and sex on polysomnography parameters and inconsistent findings have been reported.[7–9] The discrepancies found between studies probably reflect small sample sizes as well as methodological differences. The purpose of this study was to do a comprehensive meta-analysis of commonly used polysomnography parameters, scored using the 2007[4] and updated 2012[5] AASM criteria, with the goal of establishing a robust updated set of values pertaining to the relationship of age and its interaction with sex in healthy adults; we also secondarily examined the effect of the night of sleep study in the laboratory. We thought this resource could have broad applicability to clinicians and to future research endeavours that require normal polysomnography comparisons.

Methods

Search strategy and selection criteria

In this systematic review and meta-analysis, we evaluated the nocturnal sleep parameters of healthy adults who participated in published polysomnographic studies of any design that met the following criteria: (1) included a healthy control group of adults (mean age ≥18 years), defined as a group of participants with no known potentially confounding health conditions or exposure to unnatural sleep environments; (2) reported the mean age or sex distribution for the healthy controls; for two studies[10,11] that only reported age ranges (which were all ≤5 years between the oldest and youngest participant), the midpoint of the range was estimated to be the mean; (3) did an overnight level 1 in-laboratory sleep study (as defined by the American Sleep Disorders Association[12]); (4) reported at least one of the following sleep parameters with a mean and SD: total sleep time, sleep efficiency, wake after sleep onset, sleep onset latency, rapid eye movement (REM) latency, total arousal index, percentage of total sleep time spent in each stage of sleep (N1, N2, N3, REM), apnea–hypopnea index (AHI), mean oxygen saturation during sleep (SaO_2), minimum SaO_2, and periodic limb movement index (PLMI); and (5) scored sleep parameters according to the 2007 AASM Manual for the Scoring of Sleep and Associated Events[4] or the subsequent revision to these guidelines.[5] For publications which cited both the 1968 Rechtschaffen and Kales criteria[1] and 2007 AASM criteria[4] (or its subsequent revision[5]), only parameters scored using the AASM criteria[4,5] were included.

We excluded studies in which participants were recruited from sleep laboratory practices, were subjected to experimental treatments that might have affected sleep (eg, heat or noise), were hospital inpatients, performed shift work, or were patients with conditions that could affect sleep. A non-exhaustive list of excluded health conditions and experimental treatments is provided in
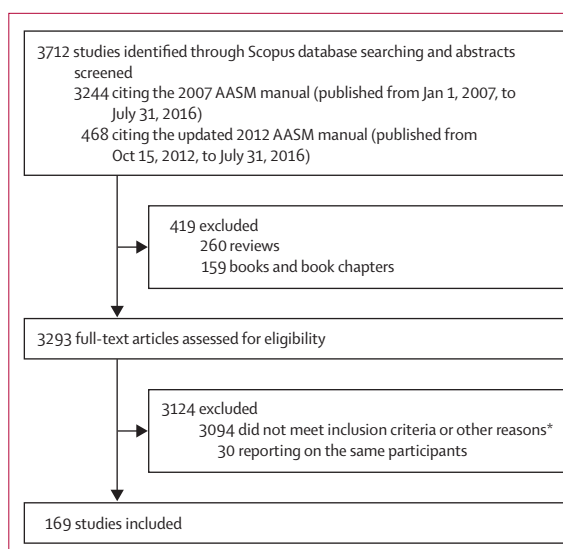
the appendix; in addition to sleep disorders (eg, insomnia, narcolepsy, sleep apnoea), these included obesity (body-mass index [BMI] >30 m²), pregnancy, neurological conditions such as Alzheimer's disease, Parkinson's disease, or epilepsy, and psychiatric conditions such as anxiety or depression, among others. We also excluded studies if they used level 2, 3, or 4 home sleep apnoea tests[12] or reported insufficient information about the participants (ie, health or demographics). For studies reporting on the same group of participants, we included only the cohort reporting the largest sample size to prevent overlap in the individuals.

We did our literature search using a cited reference search in Scopus to identify articles that cited the AASM 2007 scoring manual[4] or its subsequent revision.[5] We chose a cited reference search over a keyword search because they are more sensitive than keyword searches in identifying studies using specific measurement instruments, such as the AASM scoring manual.[13] We restricted our search to articles published between Jan 1, 2007, and July 31, 2016, and excluded studies that were not available in English. All papers were initially manually reviewed by one author (MIB, TJ, JI, or AM). Articles selected for inclusion by each coauthor were then re-reviewed by another co-author (MIB, TJ, JI, or AM) to confirm eligibility. Concerns regarding the suitability of data to be included were resolved after discussions with the lead author (MIB). The study protocol is available online.

Data analysis

We extracted data pertaining to the healthy control group from each included study for demographic parameters, sleep parameters, and sample size. For a covariate to be included in our analyses, it needed to be present in at least 60% of studies. For demographic parameters, age and BMI were recorded as mean (SD), sex as the percentage of male participants, and race as per the proportions provided. For sleep parameters, we recorded each reported parameter as mean (SD). We also extracted information concerning whether the polysomnography parameters were recorded during the first night, subsequent night, or as a multiple night average (if provided) and whether participants slept on a fixed or habitual schedule during the nights of the polysomnography (if provided). For two studies[14,15] that reported multiple nights, we recorded only the data pertaining to the first night, because this would be representative of a patient coming to a laboratory for clinical evaluation. For any single study, if there was more than one healthy control group or if healthy participants were divided into multiple groups, we recorded the data for each group independently.

The endpoints of this meta-analysis were the pooled estimates of 14 polysomnography parameters: total sleep time, sleep efficiency (proportion of total time in bed spent asleep), wake after sleep onset (length of periods of wakefulness occurring after sleep onset), sleep onset latency (time from lights out to sleep onset), REM latency (time from sleep onset to REM onset), arousal index (frequency of arousals per hour of sleep), percentage of total sleep time spent in each sleep stage (N1, N2, N3, and REM), AHI (frequency of apnoeic or hypopnoeic events per hour of sleep), mean SaO_2, minimum SaO_2, and PLMI (frequency of periodic limb movements per hour of sleep).

We pooled study estimates of each parameter using a random-effects generic inverse meta-analysis; means and SEs (computed from SDs and sample sizes) were used as input parameters.[16] For all of these meta-analyses, we used the DerSimonian-Laird estimator[17] because it does not rely on the assumption that study estimates are normally distributed.[18] Heterogeneity in study estimates of parameters was assessed using Cochran's Q test, and a p value of less than 0·10 was considered to represent evidence of heterogeneity.[19] To quantify heterogeneity, we used an I^2 statistic estimate;[20] an I^2 value greater than 50% was considered to indicate substantial heterogeneity.[21]

We attempted to explain heterogeneity through several moderators: mean age, sex, and night of sleep study. We stratified the included cohorts of healthy adults into subgroups based on mean age (18–34, 35–49, 50–64, 65–79, and ≥80 years), sex composition (both sexes, women only, and men only), and night of sleep study (first night *vs* second night or later); a random effects meta-analysis was then used to pool estimates of parameters within each subgroup. On the basis of these

Figure 1: **Flow diagram of selection of included studies**
AASM=American Sleep Disorders Association. *Reasons for exclusion of the 3094 studies were: lack of a healthy control group (n=1427), nocturnal sleep parameters not reported (n=789), mean age of participants less than 18 years (n=537), polysomnography was not level 1 (n=117), full-text article not available (n=106), polysomnography not scored using AASM standards (n=52), not available in English (n=47), and insufficient information about participants who underwent polysomnography or non-analysable data (n=19).

	Number of studies	Number of participants			
		Total	Male	Female	Sex not reported
All studies	169	5273	2725	2454	94
Country					
Australia	8 (5%)	88 (2%)	57 (2%)	31 (1%)	0
Austria	2 (1%)	62 (1%)	29 (1%)	33 (1%)	0
Belgium	5 (3%)	91 (2%)	54 (2%)	37 (2%)	0
Brazil	11 (7%)	1286 (24%)	577 (21%)	665 (27%)	44 (47%)
Canada	8 (5%)	251 (5%)	109 (4%)	117 (5%)	25 (27%)
China	11 (7%)	240 (5%)	120 (4%)	110 (4%)	10 (11%)
Denmark	4 (2%)	73 (1%)	31 (1%)	42 (2%)	0
Egypt	1 (1%)	20 (<1%)	15 (1%)	5 (<1%)	0
England	3 (2%)	92 (2%)	65 (2%)	27 (1%)	0
Finland	3 (2%)	51 (1%)	20 (1%)	31 (1%)	0
France	10 (6%)	219 (4%)	149 (5%)	70 (3%)	0
Germany	6 (4%)	207 (4%)	108 (4%)	99 (4%)	0
Hungary	1 (1%)	79 (1%)	79 (3%)	0	0
India	4 (2%)	95 (2%)	45 (2%)	50 (2%)	0
Italy	11 (7%)	266 (5%)	120 (4%)	146 (6%)	0
Japan	3 (2%)	34 (1%)	30 (1%)	4 (<1%)	0
Netherlands	6 (4%)	94 (2%)	60 (2%)	34 (1%)	0
Norway	1 (1%)	22 (<1%)	0	22 (1%)	0
Russia	1 (1%)	6 (<1%)	6 (<1%)	0	0
Saudi Arabia	2 (1%)	16 (<1%)	16 (1%)	0	0
Singapore	1 (1%)	14 (<1%)	7 (<1%)	7 (<1%)	0
South Korea	5 (3%)	110 (2%)	100 (4%)	10 (<1%)	0
Spain	2 (1%)	24 (<1%)	16 (1%)	8 (<1%)	0
Sweden	1 (1%)	24 (<1%)	11 (<1%)	13 (1%)	0
Switzerland	7 (4%)	99 (2%)	64 (2%)	35 (1%)	0
Taiwan	4 (2%)	67 (1%)	48 (2%)	19 (1%)	0
Thailand	1 (1%)	350 (7%)	181 (7%)	169 (7%)	0
Tunisia	1 (1%)	55 (1%)	43 (2%)	12 (<1%)	0
Turkey	6 (4%)	149 (3%)	80 (3%)	69 (3%)	0
USA	40 (24%)	1089 (21%)	485 (18%)	589 (24%)	15 (16%)
Night on which polysomnography was obtained					
First night	86 (51%)	3053 (58%)	1583 (58%)	1376 (56%)	94 (100%)
Second night or later	51 (30%)	1192 (23%)	544 (20%)	648 (26%)	0
Average of first and later night, or unknown	32 (19%)	1028 (19%)	598 (22%)	430 (18%)	0
Sleep schedule					
Habitual	60 (36%)	2471 (47%)	1067 (39%)	1379 (56%)	25 (27%)
Fixed	24 (14%)	566 (11%)	331 (12%)	235 (10%)	0
Unknown	85 (50%)	2236 (42%)	1327 (49%)	840 (34%)	69 (73%)

Table 1: **Characteristics of the 169 included studies (n=5273)**

pooled estimates, we present normative data as means with 95% CIs (that would be of use to researchers interested in aggregate data) and 95% prediction intervals[22] (that would be useful for clinicians assessing individual polysomnography parameters; see appendix for details).

To ascertain the significance of moderator-related trends in sleep parameters, we used multivariate mixed-effects meta-regression models (see appendix for details). Finally, using mixed-effects meta-regression models, we also estimated changes in sleep associated with age subgroups stratified by sex.

Risk of publication bias was not applicable; however, we appraised the quality of each included study based on whether sleep, medical, or psychiatric disorders were explicitly excluded and whether the study cohort was recruited from a population-based study (appendix). To assess whether quality-related variables affected trends in our sleep parameters, we additionally controlled for these in mixed-effects meta-regressions in a secondary analysis. We also tested the robustness of findings with influence analyses (see appendix for details).

We did our meta-analysis using R, version 3.3.1, using the metafor and meta packages.[23–25] This study is registered with PROSPERO, number CRD42017074319.

Role of the funding source

There was no funding source for this study. The corresponding author had full access to all the data and the final responsibility to submit for publication.

Results

We reviewed 3712 potentially eligible articles and ultimately included 169 studies (figure 1). Demographic characteristics of included participants and methodological features of included studies are summarised in table 1. Our quality appraisal for each study is presented in the appendix, as well as a listing of the demographics and variables extracted from each of the included studies.

The included studies represented 202 healthy control groups and a total sample size of 5273 participants. 196 (97%) groups had their polysomnography scored according to the 2007 AASM criteria[4] whereas the remaining six (3%) had their polysomnography scored according to the updated 2012 AASM criteria.[5] The youngest control group had a mean age of 19 years (SD 4) whereas the oldest group had a mean age of 92 years (6). Sex composition was relatively balanced with 2725 (52%) of 5273 participants being male and 2454 (46%) female; the sexes of 94 (2%) participants were unreported (table 1). Mean BMI was only reported for 108 (53%) control groups (range 20–30 kg/m²) and was not included in our analyses. Likewise, race was also infrequently reported and not further analysed.

86 (51%) of 169 studies had a polysomnography obtained during the first night whereas 51 (30%) had a polysomnography obtained during later nights; for the remaining studies, first-night data was averaged with that of later nights or the night of the sleep study was not clear. Finally, whether participants could adhere to their typical habitual sleep schedule or were subjected to a fixed schedule during their polysomnography recording

	Total sleep time, min	Sleep efficiency	Wake after sleep onset, min	Duration of sleep stages (percentage of total sleep time)			
				N1	N2	N3	REM
Total sample	394·6 (388·4–400·8); k=158	85·7% (84·8–86·6); k=147	48·2 (43·8–52·6); k=94	7·9% (7·3–8·5); k=104	51·4% (50·2–52·6); k=104	20·4% (19·0–21·8); k=107	19·0% (18·5–19·6); k=108
Mean age, years							
18–34	410·6 (404·5–416·6); k=76	89·0% (88·0–90·0); k=65	32·1 (28·2–36·1); k=42	6·0% (5·3–6·7); k=38;	51·3% (49·6–52·9); k=39	21·4% (20·0–22·8); k=42	19·8% (18·8–20·8); k=44
35–49	386·6 (371·4–401·9); k=32	85·4% (83·7–87·1); k=35	51·1 (41·1–61·1); k=22	8·0% (6·9–9·2); k=23	52·2% (50·6–53·8); k=24	20·4% (18·5–22·2); k=23	19·3% (18·2–20·3); k=24
50–64	372·0 (358·1–85·89); k=26	83·2% (81·0–85·4); k=27	64·0 (55·1–72·9); k=17	8·7% (7·3–10·0); k=22	52·8% (49·8–55·8); k=22	18·1% (15·0–21·2); k=23	18·7% (17·8–19·6); k=23
65–79	346·0 (326·7–365·4); k=17	77·5% (73·0–81·9); k=16	77·1 (57·3–96·9); k=12	9·3% (7·0–11·6); k=11;	53·3% (50·0–56·7); k=11	19·9% (17·8–22·1); k=11	17·7% (16·9–18·5); k=10
≥80	198·6 (142·5–254·7); k=1	45·7% (33·7–57·7); k=1	NA	27·5% (15·0–40·0); k=1	43·5% (37·8–49·2); k=1	19·1% (8·3–29·9); k=1	9·9% (4·4–15·4); k=1
Sex							
Both	405·2 (398·8–411·7); k=101	86·7% (85·5–87·8); k=96	43·3 (37·9–48·8); k=56	9·7% (8·7–10·6); k=59	50·6% (48·7–52·5); k=59	19·5% (17·5–21·4); k=62	19·2% (18·5–19·9); k=63
Men only	374·6 (357·3–392·0); k=30	84·3% (82·0–86·6); k=27	51·8 (42·1–61·4); k=20	5·3% (4·5–6·1); k=23	52·1% (50·2–53·9); k=24	21·0% (19·5–22·4); k=24	19·9% (18·5–21·2); k=24
Women only	356·0 (337·3–374·8); k=19	84·1% (81·6–86·5); k=20	55·0 (46·3–63·7); k=17	4·2% (3·6–4·7); k=16	55·1% (54·0–56·3); k=16	22·1% (20·8–23·4); k=17	18·6% (17·9–19·3); k=17
Night of sleep study							
First night	371·6 (361·8–381·3); k=89	84·2% (83·0–85·4); k=88	52·7 (46·7–58·7); k=57	7·0% (6·4–7·5); k=63	52·1% (50·8–53·3); k=69	20·7% (19·6–21·8); k=69	18·3% (17·7–18·8); k=68
Second night or later	419·7 (412·0–427·4); k=48	89·3% (88·0–90·5); k=39	37·9 (30·6–45·2); k=26	6·9% (5·6–8·3); k=23	48·2% (45·7–50·8); k=24	22·3% (18·5–26·2); k=25	21·4% (20·0–22·7); k=26

Variable k represents the number of control groups combined to reach the pooled estimate; the corresponding number of participants for each estimate is included in the appendix. Some studies included more than one control group. REM=rapid eye movement. NA=no studies available for this variable at this age cutoff.

Table 2: Means with 95% CIs for total sleep time, sleep efficiency, wake after sleep onset, and duration of sleep stages for total sample and by age, sex, and night of sleep study based on random-effects models

was not specified in 85 (50%) studies and was not included in our analyses.

Heterogeneity in study estimates was substantial (appendix), with I^2 values ranging from 81·6% (REM latency) to 98·3% (total sleep time). We report pooled estimates between subgroups with normative data for sleep parameters: 95% CIs (tables 2, 3) and 95% prediction intervals (appendix).

Parameters that significantly declined with age were the total sleep time, sleep efficiency, mean SaO_2, and minimum SaO_2. For each decade of age, total sleep time decreased an average of 10·1 min (95% CI 7·5 to 12·8), sleep efficiency by 2·1% (1·5 to 2·6), mean SaO_2 by 0·6% (0·5 to 0·7), and minimum SaO_2 by 1·8% (1·3 to 2·3; figure 2; table 4; appendix). By contrast, sleep parameters that significantly increased with age consisted of wake after sleep onset, sleep onset latency, arousal index, percentage of N1 in total sleep time, AHI, and PLMI. For each decade of age, wake after sleep onset increased an average of 9·7 min (6·9 to 12·4), sleep onset latency by 1·1 min (0·3 to 1·9), arousal index by 2·1 events per h (1·5 to 2·6), percentage of N1 by 0·5% (0·1 to 0·8), AHI by 1·2 events per h (0·9 to 1·4), and PLMI by 1·2 events per h (0·8 to 1·6; figure 3; table 4;

appendix). Changes in the percentage of N2 (0·0%, 95% CI −0·1 to 0·1), N3 (−0·1%, −0·1 to 0·0), and REM (0·0%, −0·1 to 0·0) with age did not reach statistical significance (appendix). The overall effect of these changes is a decline in sleep duration with age, with more time spent in N1 sleep and a non-statistically significant trend for less time spent in stages N3 and REM sleep (figure 4).

Male sex was associated with lower REM latency and mean SaO_2. For every 10% increase in the percentage of male participants, REM latency decreased by an average of 0·9 min (95% CI 0·1–1·6) and mean SaO_2 by 0·1% (0·0–0·1). Conversely, male sex was associated with higher mean arousal index and AHI, with arousal index increasing by an average of 0·3 events per h (0·0–0·5) and AHI by 0·2 events per h (0·1–0·3) for every 10% increase in the percentage of male participants. Sex-related trends, along with stratification for significant moderators (ie, night of sleep study for REM latency and mean age for arousal index, AHI, and mean SaO_2), are presented in the appendix.

When considering the effect of age on the sleep parameters when stratified by sex, we found significant decreases in total sleep time and sleep efficiency (with

	Sleep onset latency, min	REM latency, min	Arousal index, events per h	AHI, events per h	Mean SaO$_2$	Minimum SaO$_2$	PLMI, events per h
Total sample	15·4 (14·2–16·7); k=124	97·4 (93·9–100·8); k=89	12·6 (11·8–13·3); k=89	2·9 (2·6–3·1); k=99	95·0% (94·7–95·3); k=48	89·2% (88·5–89·9); k=58	2·5 (2·1–2·9); k=58
Mean age, years							
18–34	14·3 (12·5–16·1); k=58	96·4 (91·0–101·8); k=42	9·6 (8·8–10·5); k=32	1·6 (1·2–2·0); k=28	96·2% (95·9–96·5); k=15	91·8% (91·3–92·3); k=17	1·1 (0·6–1·6); k=11
35–49	14·4 (12·3–16·6); k=25	93·4 (88·9–98·0); k=18	12·5 (10·7–14·2); k=25	3·1 (2·5–3·7); k=28	95·3% (94·7–95·8); k=13	90·5% (89·3–91·7); k=19	3·1 (1·9–4·3); k=14
50–64	15·7 (13·7–17·8); k=19	101·3 (92·8–109·7); k=14	16·5 (14·9–18·2); k=19	4·2 (3·6–4·8); k=28	94·3% (93·9–94·7); k=11	87·0% (84·7–89·3); k=12	6·2 (4·1–8·3); k=15
65–79	19·5 (15·2–23·8); k=16	99·7 (85·6–113·8); k=11	18·8 (15·3–22·3); k=9	15·5 (12·9–18·2); k=10	93·3% (93·0–93·7); k=7	84·0% (83·0–85·0); k=7	8·5 (4·9–12·1); k=8
≥80	41·4 (14·2–68·6); k=1	182·0 (118·6–245·4); k=1	31·6 (15·4–47·8); k=1	30·3 (12·3–48·3); k=1	94·2% (92·5–95·9); k=1	88·0% (84·3–91·7); k=1	14·6 (5·6–23·4); k=1
Sex							
Both	15·4 (13·7–17·1); k=76	96·7 (91·9–101·6); k=44	11·3 (10·3–12·4); k=47	2·2 (1·9–2·5); k=54	95·4% (94·8–95·9); k=14	91·7% (90·9–92·4); k=21	4·4 (3·4–5·4); k=26
Men only	14·7 (13·0–16·4); k=25	92·5 (85·8–99·2); k=24	14·5 (12·6–16·5); k=20	5·2 (4·2–6·1); k=23	94·7% (94·3–95·1); k=18	87·9% (86·6–89·2); k=19	2·1 (1·3–3·0); k=16
Women only	13·5 (11·8–15·1); k=20	99·5 (95·2–103·9); k=20	12·7 (11·1–14·4); k=15	3·1 (2·4–3·8); k=16	95·0% (94·5–95·6); k=14	87·6% (86·0–89·3); k=14	2·1 (1·4–2·8); k=15
Night of sleep study*							
First night	14·7 (13·3–16·1); k=68	99·5 (96·1–103·0); k=49	13·5 (12·5–14·6); k=62	3·4 (3·1–3·8); k=72	95·0% (94·7–95·3); k=40	89·0% (88·1–89·8); k=49	2·2 (1·8–2·6); k=45
Second night or later	14·4 (12·3–16·4); k=41	87·3 (82·4–92·2); k=28	9·6 (8·0–11·2); k=14	..	..	..	..

Variable *k* represents number of control groups combined to reach the pooled estimate; the corresponding number of participants for each estimate is included in the appendix. Some studies included more than one control group. REM=rapid eye movement. AHI=apnea–hypopnea index. SaO$_2$=arterial oxygen saturation. PLMI=periodic limb movement index. *Most studies reporting AHI, mean and minimum SaO$_2$, and PLMI were first-night studies and those remaining predominantly provided average values across the first night and a subsequent night or did not specify the night of study; therefore, we did not include night of study as a covariate for these four sleep parameters in our mixed-effects model and report only the pooled estimates for first-night studies.

Table 3: **Means with 95% CIs for sleep onset latency, REM latency, arousal index, AHI, mean and minimum SaO$_2$, and PLMI for total sample and by age, sex, and night of sleep study based on random-effects models**

corresponding increases in wake after sleep onset) in both sexes in the 50–64 year age group compared to the 18–34 year age group (appendix). However, a significant increase in sleep onset latency associated with older age was observed in women but not in men (appendix).

Compared with first-night sleep studies, studies done on later nights reported significantly higher total sleep time, sleep efficiency, and percentage of REM. For studies performed on later nights, total sleep time was higher by an average of 38·3 min (95% CI 29·4–47·2), sleep efficiency by 2·7% (0·9–4·4), and percentage of REM sleep by 3·5% (2·3–4·7). By contrast, percentage of N2 sleep and REM latency were significantly lower in studies done on later nights, by an average of 3·7% (1·1–6·2) for percentage of N2 sleep and 11·1 min (4·4–17·9) for REM latency (table 4).

Because total sleep time and sleep efficiency were significantly modulated by both age and night of sleep study, we further stratified our normative data for these variables by age and night of sleep study (appendix). Furthermore, because REM latency was significantly affected by both sex and night of sleep study, we also further stratified our REM latency data by sex and night of sleep study (appendix).

Trends with age, sex, and night of sleep study generally remained unchanged after controlling for the quality of included cohorts (ie, whether studies explicitly excluded participants with sleep, medical, or psychiatric disorders and whether the study cohort was recruited from a population-based study) in mixed-effects models during a secondary analysis (appendix). Most pooled estimates and mixed-effects models were also robust, as confirmed through influence analyses (details on the influence analyses are available in the appendix; results are not shown but are available upon request). Exceptions were seen with AHI: pooled estimates and the mixed-effects model for the mean AHI of control groups with an age greater than 50 years were not robust (appendix).

Discussion

In this systematic review and meta-analysis, we report robust summary values for 14 routine polysomnography parameters with the effect of age and sex. We also secondarily evaluated the influence of night of sleep study. Our analyses reveal that total sleep time and sleep efficiency decline with age, whereas sleep onset latency and wake after sleep onset increase; the frequency of common physiological events (arousals, respiratory
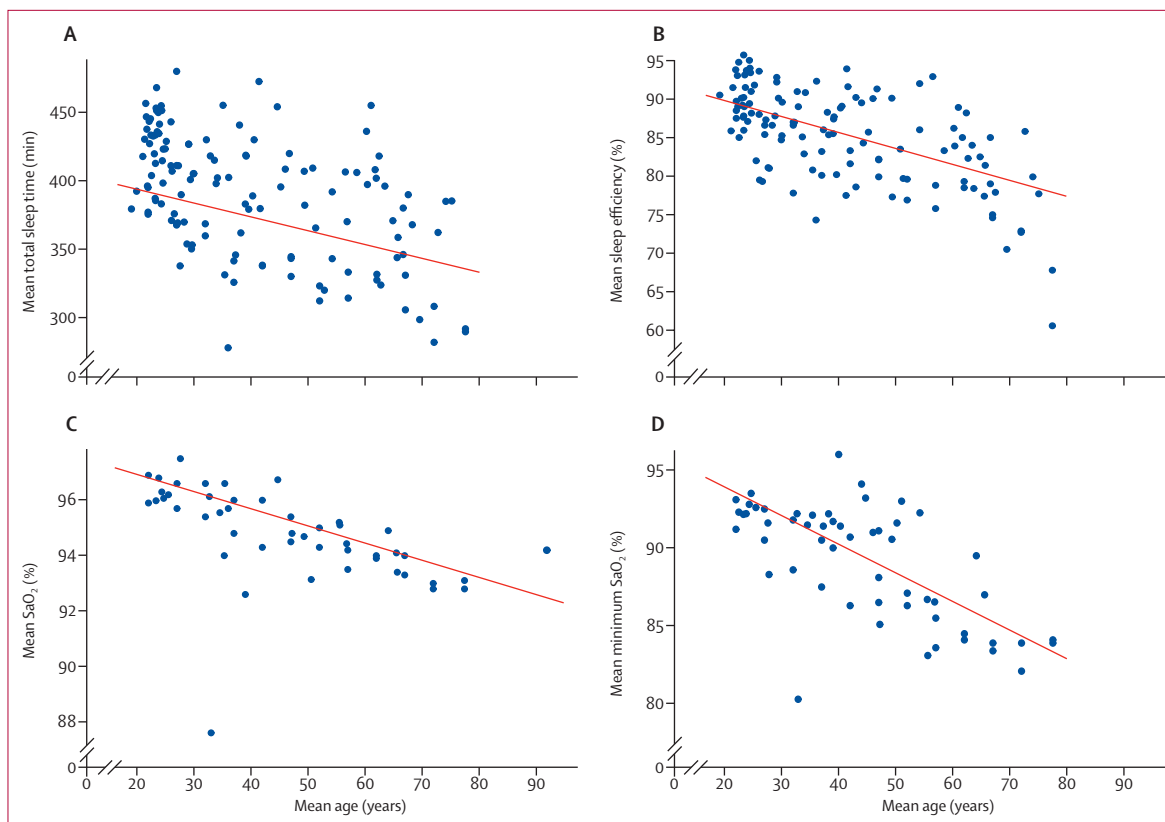
Figure 2: The effect of age on sleep parameters: age-related decreases
The effect of age is shown on total sleep time (A), sleep efficiency (B), mean SaO$_2$ (C), and minimum SaO$_2$ (D). Each dot represents data from a study included in our meta-analysis with a fitted mixed-effects meta-regression line placed over the datapoints. SaO$_2$=oxygen saturation during sleep.

	Change per 10 years of ageing	Change for every 10% increase in percentage of male participants	Change when sleep study was done on second or later night compared with first night	Appendix table reporting normative data as prediction intervals
Total sleep time, min	−10·1 (−12·8 to −7·5); p<0·0001	..	38·3 (29·4 to 47·2); p<0·0001	Table 3A*, p 8
Sleep efficiency	−2·1% (−2·6 to −1·5); p<0·0001	..	2·7% (0·9 to 4·4); p=0·0037	Table 3A*, p 8
Wake after sleep onset, min	9·7 (6·9 to 12·4); p<0·0001	..	..	Table 3A, p 8
Sleep onset latency, min	1·1 (0·3 to 1·9); p=0·0051	..	..	Table 3B, p 9
REM latency, min	..	−0·9 (−1·6 to −0·1); p=0·027	−11·1 (−17·9 to −4·4); p=0·0012	Table 3B†, p 9
Arousal index, events per h	2·1 (1·5 to 2·6); p<0·0001	0·3 (0·0 to 0·5); p=0·029	..	Table 3B‡, p 9
Percentage of total sleep time in sleep stages				
N1	0·5% (0·1 to 0·8); p=0·0069	..	..	Table 3C, p 10
N2	..	..	−3·7% (−6·2 to −1·1); p=0·0051	Table 3C, p 10
N3	..	..	..	Table 3C, p 10
REM	..	..	3·5% (2·3 to 4·7); p<0·0001	Table 3C, p 10
AHI, events per h	1·2 (0·9 to 1·4); p<0·0001	0·2 (0·1 to 0·3); p=0·00043	..	Table 3D‡, p 11
Mean SaO₂	−0·6% (−0·7 to −0·5); p<0·0001	−0·1% (−0·1 to 0·0); p=0·0017	..	Table 3D‡, p 11
Minimum SaO₂	−1·8% (−2·3 to −1·3); p<0·0001	..	..	Table 3D, p 11
PLMI, events per h	1·2 (0·8 to 1·6); p<0·0001	..	..	Table 3D, p 11

Significant mixed-effects coefficients are reported as estimate (95% CI); p value. A full summary including non-significant values is available in the appendix (p 33). Because most studies reporting AHI, mean and minimum SaO$_2$, and PLMI were first-night studies, only mean age and percentage of male participants were included in mixed-effects models. REM=rapid eye movement. AHI=apnea–hypopnea index. SaO$_2$=arterial oxygen saturation. PLMI=periodic limb movement index. *See appendix (p 20) for data stratified by age and night of sleep study. †See appendix (p 21) for data stratified by sex and night of sleep study. ‡Due to low number of studies reporting male and female parameters separately, normative data stratified by age and sex was not tabulated.

Table 4: Summary of significant changes in sleep parameters by age, sex, and night of the sleep study
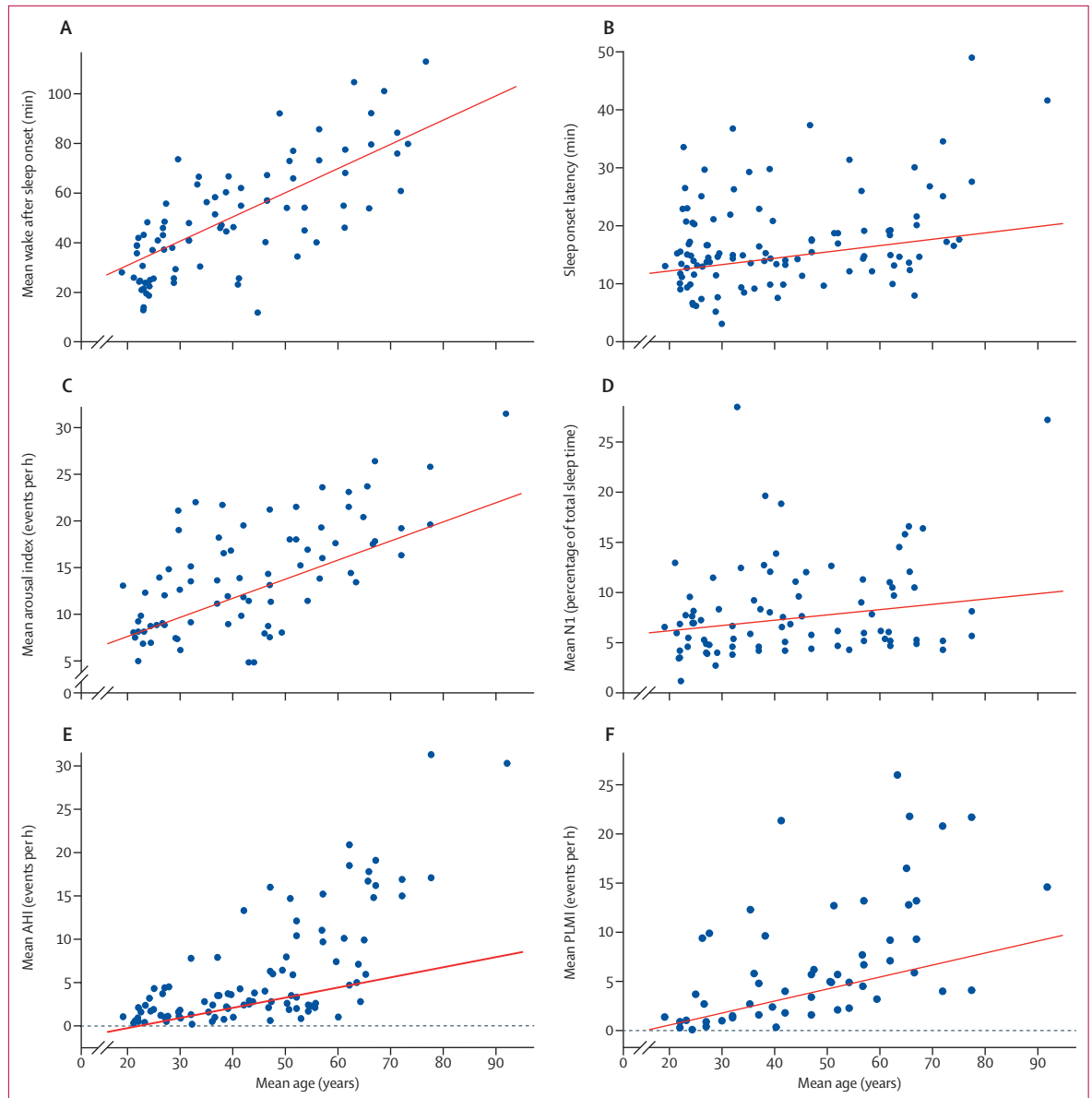
Figure 3: **The effect of age on sleep parameters: age-related increases**
The effect of age is shown on wake after sleep onset (A), sleep onset latency (B), arousal index (C), percentage of total sleep time spent in stage N1 (D), AHI (E), and PLMI (F). Each dot represents data from a study included in our meta-analysis with a fitted mixed-effects meta-regression line placed over the datapoints. AHI=apnea–hypopnea index. PLMI=periodic limb movement index.

events [ie, AHI], and periodic limb movements) during sleep increases with age whereas nocturnal oxygen saturation decreases; male sex is associated with increased sleep-disordered breathing (as assessed by the AHI and mean SaO_2, even though patients with pathological clinical apnoea were excluded), increased arousal index, and reduced REM latency; and finally, key polysomnography parameters (eg, total sleep time, sleep efficiency, REM percentage and latency, and percentage of N2) are affected by the night of the study on which polysomnography is performed.

We confirm and further define several of the age-related changes in sleep architecture reported by Ohayon and colleagues[7] in their meta-analysis of sleep data scored according to the Rechtschaffen and Kales criteria.[1] As shown in figure 4, we similarly show age-related decreases in total sleep time and sleep efficiency that were accompanied by increases in wake after sleep onset and sleep onset latency; we also report an age-related increase in N1 sleep, as well as a non-significant decrease in N3 and REM sleep. One difference in our findings is that we found no age-related changes in

REM latency and percentage of N2. Of note, Ohayon and colleagues[7] found that if they included studies that did not exclude participants with psychiatric disorders or subjected participants to a fixed (ie, non-habitual) sleep schedule, the age-related changes in N2 sleep and REM latency were not observed. In our study, the findings remained the same when we controlled for studies that explicitly excluded psychiatric disorders. We could not control for sleep schedule because this was infrequently reported.

We postulate that the age-related decline in sleep duration is mainly due to a decreased ability to maintain rather than initiate sleep, as the wake after sleep onset increased by 9·7 min per decade of age while sleep onset latency only increased by 1·1 min per decade of age. As suggested by our analyses, the reduced ability to maintain sleep might partly manifest as age-related increases in the percentage of N1 sleep. Physiologically, this change could be driven by weakening of circadian regulation. Lifestyle changes associated with older age, such as an increase in daytime napping and decrease in physical activity, might also contribute.[26]

To our knowledge, our meta-analysis is the first to quantify age-related and sex-related trends in the frequency of common physiological events (arousals, respiratory events, and periodic limb movements) during sleep. We found that the frequency of respiratory events (as measured by the AHI) and periodic limb movements (as measured by PLMI) increase with advancing age, which is consistent with the increased presence of sleep-disordered breathing[27] and periodic limb movements during sleep[28] in older subjects in the general population. We also confirmed that male sex is associated with significantly higher arousal index and AHI and lower mean SaO_2, as has been established in prior research.[27] Our findings on the effect of age, stratified by sex, show that both sexes experience significant decreases in sleep quality at around 50 years of age but that women particularly exhibit prolonged sleep onset latency, suggesting that sex-related hormonal changes might play an important role;[29] this finding requires re-evaluation in larger studies given the limited statistical power for subgroup analyses in our study.

A unique feature of our meta-analysis was the inclusion of primarily first-night sleep studies; by contrast, Ohayon and colleagues[7] mostly analysed sleep studies done on the second night or later. Of importance, we confirmed a first-night effect: controlling for age and sex, first-night sleep studies reported reduced sleep duration, sleep efficiency and REM sleep, and greater REM latency and percentage of N2 sleep than did studies done on later nights. Because our included studies done on later nights had few participants older than 34 years of age, we could not ascertain the impact of the first-night effect on sleep later in adulthood.

We think our data are best described as predominantly normative rather than population-based because only
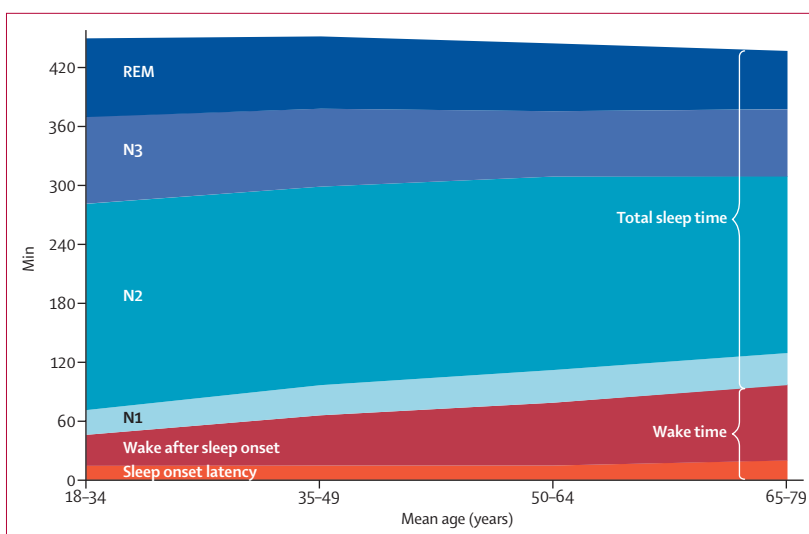

Figure 4: Sleep ontogeny graph
Age-related trends for sleep onset latency, wake after sleep onset, and stages N1, N2, N3, and REM sleep. REM=rapid eye movement.

23·3% (1230/5273) of the participants of our study sample were recruited from population-based studies and because we also explicitly excluded patients who had conditions known to affect sleep.

This meta-analysis has limitations. First, although we excluded patients with conditions known to affect sleep, some of the included study cohorts might have included participants with undiagnosed medical conditions, which might have led to overestimating the heterogeneity seen in the sleep parameters examined. High levels of unexplained statistical heterogeneity were seen in some sleep parameters (ie, AHI and arousal index); however, we are still confident in our findings because trends with age, sex, and night of sleep study generally remained unchanged after additionally controlling for the quality of included cohorts during secondary analyses. Furthermore, most pooled estimates and mixed-effects models remained stable as revealed by influence analyses. Second, the findings of our meta-analysis are statistically under-powered for older adults (≥65 years) due to the low numbers of studies and high level of clinical heterogeneity in this age group. Third, we could not provide robust normative values, stratified by both age and sex, for the arousal index, AHI, and mean SaO_2 due to an insufficient number of studies reporting male and female data separately. Fourth, the normative values for the AHI in older control groups (mean age ≥50 years) were not robust due to a high degree of variability in the mean AHI within this age group; this variability may have been attributed to variability in other factors, such as BMI and race, which could not be analysed due to insufficient reporting. Fifth, the normative values for AHI only reflect the 2007 AASM recommendation for scoring respiratory events in sleep, as insufficient studies reported respiratory data scored according to the updated 2012 AASM rules. The major

difference in the scoring of the AHI between the two guidelines was that the 2007 rules scored hypopneas associated with desaturation of at least 4%, whereas the revised 2012 criteria scored hypopneas associated with either desaturation of at least 3% or an arousal. A separate set of normative values for AHI based on the updated 2012 rules might have important clinical applications, because the 2007-derived and 2012-derived AHI values have recently been shown to provide unique but complementary information about risk for cardiovascular disease.[30] Sixth, our normative values for polysomnography parameters scored on the second night or later in the sleep laboratory are robust only for younger participants (mean age ≤34 years); normative values for older participants evaluated on these nights are statistically underpowered due to a low number of studies. Seventh, because BMI was not reported in a substantial number of studies, we cannot be confident that all healthy control groups had a mean BMI below 30kg/m². Finally, Scopus was the only database searched because it provides the most comprehensive and efficient database to pursue a cited reference search, covering 100% of the content available in MEDLINE and Embase and including a more expanded spectrum of journals compared with PubMed and Web of Science.[31] However, restricting our search to Scopus is one of several factors that could have limited the number of eligible studies, including the date range searched, the exclusion of studies not available in English and those reporting only medians with IQRs, and the absence of independent dual screening of studies considered for potential inclusion. However, our large sample size of more than 5000 participants and the robustness of our findings suggest that a larger number of studies was not necessary.

In summary, our meta-analysis is the largest analysis of published normative sleep data to date and provides robust control values for clinical use and various future research studies where it might be difficult to obtain polysomnographic controls. The summary values provide data to establish normative values in a variety of settings and suggest degrees of variance that could be helpful when preparing sample size calculations. The resulting normative trends by age and sex might also be hypothesis-generating for a broad range of investigations.

Contributors
BJM and MIB conceived of the idea for this review. MIB and TJ wrote the first draft of the manuscript. MIB, TJ, JI, and AM did the literature search and data extraction. TJ and TK did the statistical analyses. MIB, TJ, TK, and BJM interpreted the statistical analyses. All authors revised and approved the final manuscript.

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