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nature human behaviour

ARTICLES

https://doi.org/10.1038/s41562-020-00965-x

Sleep characteristics across the lifespan in 1.1 million people from the Netherlands, United Kingdom and United States: a systematic review and meta-analysis

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We aimed to obtain reliable reference charts for sleep duration, estimate the prevalence of sleep complaints across the lifespan and identify risk indicators of poor sleep. Studies were identified through systematic literature search in Embase, Medline and Web of Science (9 August 2019) and through personal contacts. Eligible studies had to be published between 2000 and 2017 with data on sleep assessed with questionnaires including ≥100 participants from the general population. We assembled individual participant data from 200,358 people (aged 1–100 years, 55% female) from 36 studies from the Netherlands, 471,759 people (40–69 years, 55.5% female) from the United Kingdom and 409,617 people (≥18 years, 55.8% female) from the United States. One in four people slept less than age-specific recommendations, but only 5.8% slept outside of the 'acceptable' sleep duration. Among teenagers, 51.5% reported total sleep times (TST) of less than the recommended 8–10 h and 18% report daytime sleepiness. In adults (≥18 years), poor sleep quality (13.3%) and insomnia symptoms (9.6–19.4%) were more prevalent than short sleep duration (6.5% with TST < 6 h). Insomnia symptoms were most frequent in people spending ≥9 h in bed, whereas poor sleep quality was more frequent in those spending <6 h in bed. TST was similar across countries, but insomnia symptoms were 1.5–2.9 times higher in the United States. Women (≥41 years) reported sleeping shorter times or slightly less efficiently than men, whereas with actigraphy they were estimated to sleep longer and more efficiently than man. This study provides age- and sex-specific population reference charts for sleep duration and efficiency which can help guide personalized advice on sleep length and preventive practices.

Poor sleep is common and increasingly recognized as a potentially modifiable risk factor for various physical and mental health problems[1,2]. Yet, sleep has received little attention from a public health perspective. This may partly be due to the lack of valid descriptions of typical sleep patterns in the general population. Estimating reference ranges for sleep duration can help compare an

A full list of affiliations appears at the end of the paper.

Table 1 | Time in bed, total sleep time and sleep efficiency, stratified by age and sex

Strata by age and sex	Time in bed (h)		Total sleep time (h)		Sleep efficiency (%)	
	Studies (20, 1998–2013)[a]		Studies (15, 1993–2015)		Studies (15, 2002–2013)	
	n	Mean ± s.d.	*n*	Mean ± s.d.	*n*	Mean ± s.d.
1–2 years						
Total	3,240	11.7 ± 0.72	-	-	-	-
Male	1,594	11.6 ± 0.73	-	-	-	-
Female	1,646	11.7 ± 0.70	-	-	-	-
3–5 years						
Total	6,421	11.5 ± 0.6	1,266	11.6 ± 0.6	1,183	99 ± 2
Male	3,241	11.4 ± 0.6	653	11.5 ± 0.6	604	99 ± 2
Female	3,180	11.5 ± 0.6	613	11.6 ± 0.6	579	99 ± 3
6–13 years						
Total	18,905	10.8 ± 0.9	8,377	10.6 ± 1.0	6,931	97 ± 5
Male	9,477	10.7 ± 0.8	4,185	10.5 ± 0.9	3,461	97 ± 5
Female	9,420	10.8 ± 0.9	4,189	10.6 ± 1.1	3,468	97 ± 5
14–17 years						
Total	3,747	8.8 ± 0.8	513	7.7 ± 1.1	509	91 ± 8
Male	1,745	8.7 ± 0.8	189	7.9 ± 1.0	186	92 ± 7
Female	2,000	8.8 ± 0.8	324	7.6 ± 1.1	323	91 ± 8
18–25 years						
Total	1,174	8.3 ± 1.2	5,192	7.5 ± 1.1	-	-
Male	588	8.0 ± 1.2	2,049	7.4 ± 1.1	-	-
Female	606	8.5 ± 1.1	3,143	7.6 ± 1.0	-	-
26–40 years						
Total	23,896	8.0 ± 0.9	38,635	7.2 ± 0.9	21,204	89 ± 9
Male	9,938	7.7 ± 0.9	16,182	7.1 ± 0.9	8,678	90 ± 8
Female	13,931	8.1 ± 0.8	22,453	7.3 ± 1.0	12,526	89 ± 10
41–65 years						
Total	51,086	7.8 ± 0.9	93,837	7.0 ± 1.1	49,513	90 ± 10
Male	21,235	7.5 ± 0.9	40,603	6.9 ± 1.0	20,570	92 ± 9
Female	29,851	7.9 ± 0.9	53,234	7.1 ± 1.1	28,943	89 ± 10
>65 years						
Total	5,480	7.9 ± 1.1	8,195	7.0 ± 1.3	4,922	88 ± 13
Male	2,288	7.9 ± 1.1	3,504	7.2 ± 1.2	2,021	90 ± 11
Female	3,192	7.8 ± 1.1	4,691	6.8 ± 1.4	2,901	86 ± 14

[a]Studies are shown as number of studies and related time period. Prevalence was not calculated if <200 participants in a cell.

individual's sleep characteristics with that of men or women of the same age in the general population and quantify the prevalence of insufficient sleep at a population level.

The widely used sleep duration recommendations issued by the American National Sleep Foundation (NSF)[3,4], synthesize relevant empirical studies but partly rely on expert opinion, thus may differ from data-driven descriptions of sleep in the general population[5]. In addition, these recommendations were targeted for healthy populations, whereas the general population may represent a broader continuum between health and disease. It is also unclear how the three categories of sleep duration (recommended, acceptable and not recommended) relate to sleep quality or other sleep complaints. Ideally, recommendations for sleep duration in the general population should be described over multiple physiologically and clinically relevant aspects, including age, sex, demographics or lifestyle. We described variations in sleep duration and estimated the proportion that falls outside the recommendations and studied factors related to suboptimal sleep.

Few epidemiological studies have systematically summarized sleep characteristics in the general population. The studies conducted so far have either collected data via mobile devices[6] or online surveys[7,8], have focused on a particular age group such as children[9,10] or older adults[11,12], or studied a single sleep problem such as short sleep[13], long sleep or insomnia[14,15]. We summarized available information in the general population by jointly investigating multiple sleep variables across the lifespan. Importantly, as opposed to previous meta-analytical efforts[16–18], also of similar sample sizes[19], we assembled individual participant data (IPD) from 200,358 people aged 1 to 100 years, from 36 population-based studies from the Netherlands. This allowed us to explore sleep characteristics in various subgroups as well as interrelations between sleep indices. In addition, we compared the available estimates with those from two

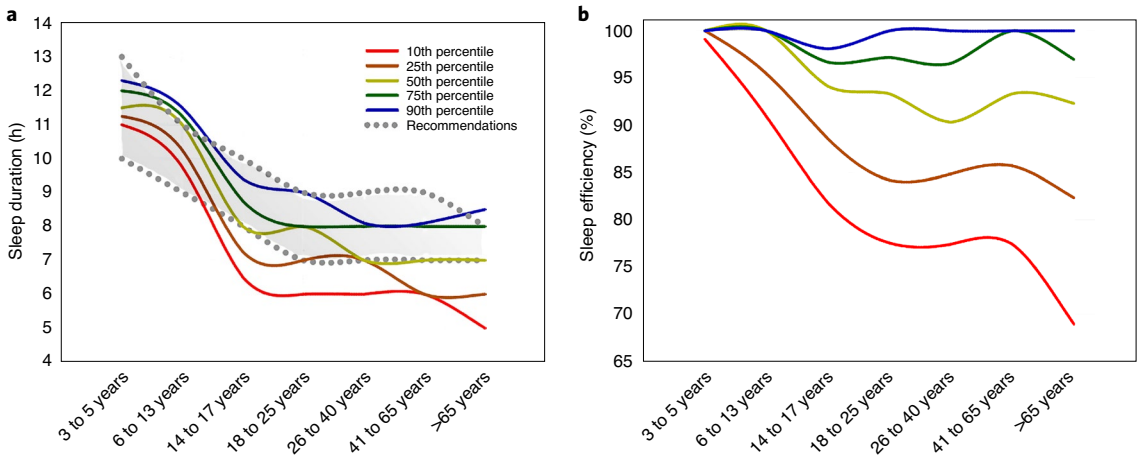

Fig. 1 | Age-specific percentile curves of TST ($n = 164,069$) and SE ($n = 76,746$). a, Percentiles of sleep duration per age group, where the grey area represents the NSF recommended sleep duration. **b**, Percentiles of SE (percentage of sleep within TIB: (TST/TIB) × 100) per age group.

large population-based adult samples from the United Kingdom ($n = 471,759$) and the United States ($n = 409,617$).

This study provides reliable estimates of self-reported sleep duration, sleep timing and sleep efficiency but also perceived sleep quality, insomnia symptoms and other sleep complaints (non-restorative sleep, sleepiness, snoring and use of sleep medication) in the general population. To obtain valuable population percentile curves and reference values we described sleep duration, time in bed and sleep efficiency across age and sex. We also explored educational level, ethnic origin, partnership and employment status, as well as body mass index (BMI) and smoking, as potential risk indicators associated with these sleep variables. Where data were available, we complemented subjective data with objectively estimated sleep variables. Moreover, we evaluated consistency and differences in sleep parameters across populations from the Netherlands, the United Kingdom and the United States.

Results

We included 34 studies, identified by systematic review, including 200,358 participants from the Netherlands between the ages of 1 and 100 years. Additionally, 471,759 people (40–69 years, 55.5% female) from the United Kingdom and 409,617 people (≥18 years, 55.8% female) from the United States were included. Population characteristics of the studies identified in the systematic review are presented in Supplementary Table 1. Compared to data of the 2011 Dutch Census[20], females in age groups between 10 and 80 years were slightly over-represented (ranging from a 1 to 9% difference). People in both the high ($\chi^2 = 60.1$ (1), $P < 0.001$, 0.9% difference, 95% confidence interval (CI) = 0.7; 1.1, 29.9% versus 29.0%) and the middle ($\chi^2 = 596.2$ (1), $P < 0.001$, 2.9% difference, 95% CI = 2.7; 3.1, 37.3% versus 34.4%) educational level were slightly over-represented in our sample, compared to the population in the Dutch Census of 2011. Study-specific sleep estimates are provided in Supplementary Table 2.

Time in bed, sleep duration and sleep efficiency. Adults (≥18 years) reported a mean ± s.d. time in bed (TIB) of 7.8 ± 0.9 h, a total sleep time (TST) of 7.1 ± 1.0 h and a sleep efficiency (SE) of 89 ± 9% (Table 1). Short sleep duration (TST < 6 h) was reported by 6.5% of this population, whereas 25.8% reported a TST of <7 h. Population percentile curves of TST and SE across age categories defined by NSF recommendations are shown in Fig. 1 and in Supplementary Fig. 2 for age (continuous). Although 24.5% of the population sleeps less than the recommended sleep duration for age, only 5.6% fall outside of the 'acceptable' ranges (Supplementary Table 3). More than half (51.5%) of those aged 14–17 years reported sleeping less than recommended 8–10 h per night. Teenagers in the 25th percentile sleep 54 min less, whereas those in the 10th percentile sleep 96 min less than recommended. In all other age groups, even the 5% and 95% percentile groups, sleep duration was in the 'acceptable range' as defined by the NSF (ref. [3]). SE decreases from mean ± s.d. = 97 ± 5% in childhood to 91 ± 8% in teenage years. This SE decline continues into adulthood; however, 25% of those aged >65 years reported sleeping over 95% of their TIB.

Sex difference were observed from adulthood onwards (Table 1). Adult women reported a longer TST ($t = 25.9$ (145,840), $B = 0.14$ h, $P < 0.001$, 95% CI = 0.13; 0.21) but a marginally lower SE ($t = -34.1$ (75,739), $P < 0.001$, $B = -0.02$%, 95% CI = −0.03; −0.02) than men (Supplementary Table 4). For example, women between 41 and 65 years of age sleep on average 7.1 ± 1.1 h, whereas at the same age men sleep on average 6.9 ± 1.0 h per night. However, the women sleep 89 ± 10% of the TIB, whereas men sleep 92 ± 9% of the TIB. From about 14 years onwards, the between-person variation in TIB increases substantially, more so for men than for women (Fig. 2). Sex-specific TIB percentiles using age (continuous) are shown in Supplementary Fig. 3. From 14 years onwards bedtime is gradually delayed, whereas wake time remains stable at around 7:00 across the lifespan (Fig. 3). Poor sleep quality is most prevalent in people (≥18 years) spending <6 h in bed, whereas difficulty initiating sleep is most commonly reported by those spending ≥9 h in bed (Fig. 4).

We found that TIB is longer on weekend days than on week days only for age groups that go to school or work. In young children and older adults, the TIB on week days and weekend days is roughly equal. The week day – weekend difference increases as children start going to school (median difference of 30 min), peaks in teenagers (median difference of 75 min) and is around 60 min in working adults.

Heterogeneity estimates were high: I^2 ranged between 97 and 99% for TIB, 90 and 99% for TST and 96 and 99% for SE (Supplementary Table 5). However, when meta-analyses were stratified by sex, heterogeneity estimates decreased to values as low as 0% for TIB (women, 26–40 years), 54% for TST (women, 18–25 years) and 0% for SE (both men and women, >65 years). For some age strata, however, sex and age stratification had minor effects on heterogeneity estimates, as I^2 remained high (up to 100%) (see forest plots in Supplementary Fig. 4a–c). Importantly, age- and sex-specific TIB, TST and SE estimates changed only marginally from the fixed-effect to the random-effects model (Supplementary Table 5).

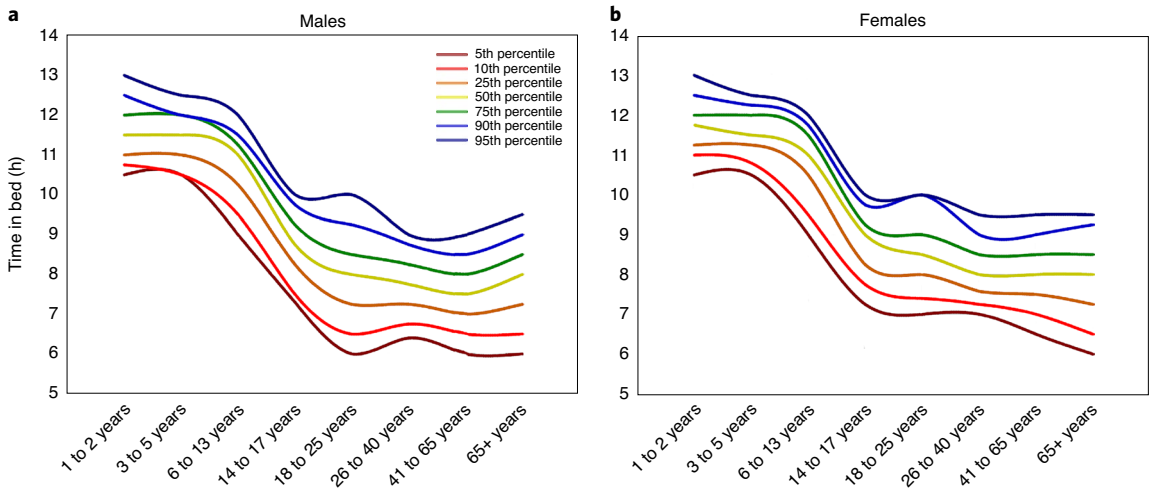

Fig. 2 | Age-specific percentile curves for TIB, stratified by sex ($n = 106,282$, 56% females). a,**b**, Percentiles of time in bed per age group in males (**a**) and in females (**b**).

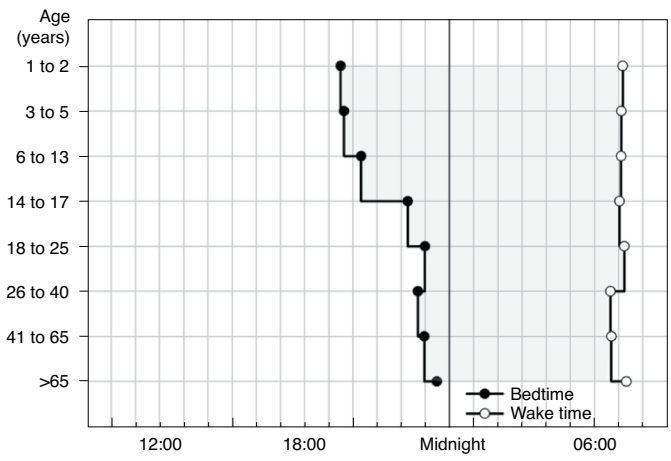

Fig. 3 | Sleep timing across lifespan. Night-time sleep timing across the lifespan (n=106,282).

Daytime napping. As expected, most children nap in the first 3 years (80% of 1–2-year-olds, 65% of 3-year-olds). Napping is less common during school age (12.7% of 6–13-year-olds nap) and adulthood (13.7% of people between 26 and 64 years nap regularly), than in people aged >65 years (27%).

Insomnia symptoms. Symptoms of insomnia (difficulty initiating sleep (DIS), difficulty maintaining sleep (DMS) and early morning awakening (EMA)) increase from childhood (3–5 years: 4% DIS, 6% DMS) into adolescence (6–13 years: 13% DIS, 9% DMS). In adulthood, insomnia symptoms are least frequent in those aged 26–40 years and most frequent in those >65 years (Table 2). DIS is most prevalent in those aged 18–25 years (22.6%), whereas DMS (23.2%) and EMA (23.5%) are most prevalent in those >65 years. Sex difference in insomnia symptoms become evident only in puberty (that is, for 14–17-year-olds, males versus females: 12% versus 19% DIS, 16% versus 28% DMS). In adults, women are at increased odds for DIS ($z = 34.8$ (108,447), $P < 0.001$, OR = 2.26, 95% CI = 2.16; 2.36), DMS (OR = 2.05, 95% CI 1.91; 2.19) or EMA ($z = 19.7$ (28,041), $P < 0.001$, OR = 1.49, 95% CI = 1.37; 1.62; Supplementary Table 6) compared to men, after adjusting for demographic factors.

Heterogeneity ranged from 0 to 99% for DIS, 0 to 97% for DMS and 17 to 97% for EMA, depending on age group (Supplementary Table 7). Heterogeneity of insomnia symptoms was low in paediatric cohorts aged 5 years or younger. When studies of adults were additionally stratified by sex, I^2 decreased to values as low as 48% for DIS in men aged >65 years, 54% for DMS in women aged 26–40 years and 0% for EMA in men aged 18–25 years. However, residual heterogeneity was substantial in most other strata (Supplementary Table 7 and Supplementary Fig. 5a–c). Pooled prevalence estimates (Supplementary Table 7) were comparable between fixed-effect and random-effect models, with the exception of DIS in the age groups 18–25 and 26–40 years (23.4–9.5%), DMA in ages 6–13 years (9–17%) and EMA in ages 26–40 years (14–11%) and 41–65 years (21–17%).

Other sleep complaints. Sleepiness is most prevalent in teenagers (20.4%; Supplementary Table 8). Although there are no clear sex difference in sleepiness, non-restorative sleep is more prevalent in women than in men. Women also use sleep medication more often (8.6% versus 5.2% in age group 26–40 years, to 17.5% versus 6.3% in >65 years). Snoring is more commonly reported in adult men than in women (40.2% versus 23.2%), although this difference becomes less pronounced at older ages (Supplementary Table 8).

Associations of sociodemographics with sleep characteristics in adults. Adults with a low educational level did not differ in TST ($t = -1.3$ (145,840), $P = 0.191$, $B = -0.01$ h, 95% CI = −0.02; 0.00) compared to highly educated adults but reported a marginally lower SE ($t = -5.2$ (75,739), $P < 0.001$, $B = -0.01$%, 95% CI = −0.03; −0.00). In addition, people living in the Netherlands with a non-European ethnic origin sleep shorter ($t = -21.4$ (145,840), $P < 0.001$, $B = -0.30$ h, 95% CI: −0.34; −0.30) and less efficiently ($t = -7.02$ (75,739), $P < 0.001$, $B = -0.03$%, 95% CI = −0.03; −0.02, $P < 0.001$) compared to people with Dutch ethnic origin. Similarly, both low education and non-European ethnic origin were risk indicators for insomnia symptoms in the Netherlands (Supplementary Table 6). Having paid employment and a partner were both associated with longer sleep duration and less insomnia symptoms, independent of demographics (Supplementary Tables 4 and 6). Unadjusted estimates stratified by ethnic origin, educational level, employment and presence of a partner are presented in Supplementary Table 9. Results were similar if participants >90 years ($n = 130$) were excluded (data not shown).

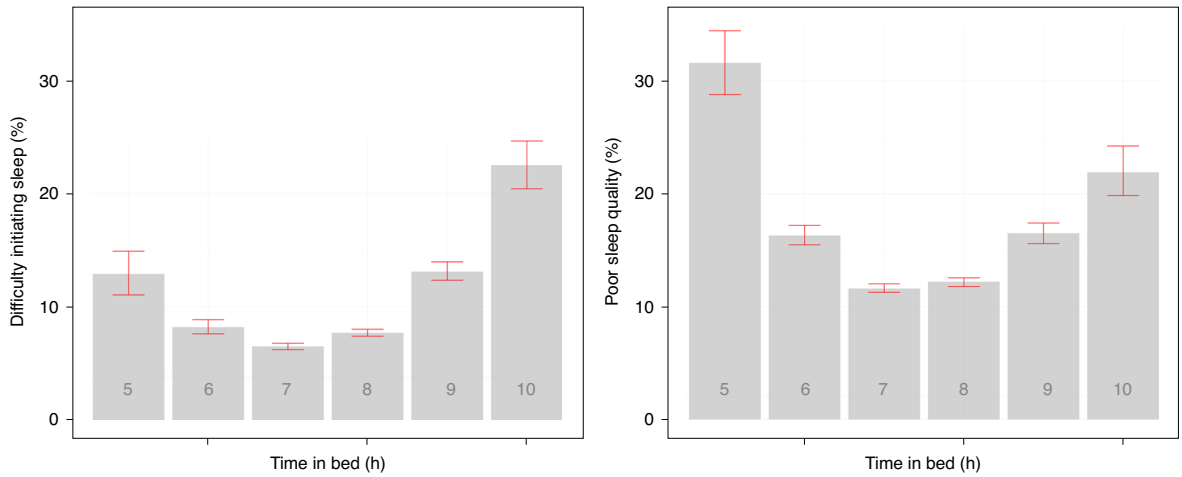

Fig. 4 | Prevalence of having difficulty initiating sleep ($n = 95{,}603$) and 'poor' sleep quality ($n = 77{,}854$), across different durations of time in bed. Data on DMS, EMA and TIB were not available.

Association of health risk indicators with sleep characteristics in adults. In adults, we observed 2.4 min (95% CI: −3.6; −1.8) shorter TST for overweight (BMI >25 kg/m²; $t = -6.8$ (145,832), $P < 0.001$, $B = -0.04$, 95% CI = −0.06; −0.03) and 6.6 min (95% CI: −7.2; −5.4) shorter sleep in people who are obese (BMI >30 kg/m²; $t = -12.7$ (145,832), $P < 0.001$, $B = -0.11$, 95% CI = −0.12; −0.09), compared to people with normal weight. People who are obese, but not those who are overweight, had a marginally lower SE ($t = -12.6$ (145,832), $P < 0.001$, $B = -0.004$%, 95% CI = −0.01; −0.00) and also experienced more DIS ($z = 5.3$ (108,444), $P < 0.001$, OR = 1.08, 95% CI = 1.02; 1.17; Supplementary Table 4). Both former and current smokers reported sleeping shorter relative to non-smokers and current smokers also reported a lower SE. Current smokers experienced more DIS but experienced less DMS (Supplementary Table 6). Estimates stratified by BMI and smoking status are presented in Supplementary Table 10.

Complementing subjective with objective sleep data. TIB and TST were between 0.4 and 1.9 h shorter when estimated with actigraphy as compared to sleep diary reports of the same nights (Supplementary Table 11). Similarly, actigraphic SE estimates were lower compared to diary estimates, averaging 9.7 ± 7% difference ($t_{paired} = -51.6$ (1,307), $P < 0.001$, $M = -0.097$, 95% CI = −0.10; −0.09) in the Generation R sample, and 9.6 ± 9% difference ($t_{paired} = -38.1$ (1,926), $P < 0.001$, $M = -0.095$, 95% CI = −0.09; 0.10) in the Rotterdam Study sample. The sleep diary SE estimates were also lower than those computed from the pooled IPD, except for the group of teenagers where SE based on pooled IPD was estimated to be 91 ± 8%, compared to 95.6 ± 4% estimated by sleep diary. According to actigraphic TST estimates, more than 80% of the population, sleeps less than the US recommendations (Supplementary Table 12). The proportion of people sleeping less than the 'acceptable' TST ranged between 16.3 and 38.7% in the paediatric cohort and between 9.4 and 47.3% in the older adults, as measured with actigraphy. Actigraphic sleep parameters of the adults from the Netherlands were compared with respective values from adults in the United Kingdom (Supplementary Table 13). Both TIB and TST were ≥1 h longer in the UK cohort regardless of age and sex, however SE differences were small between 1.6% ($t = 7.9$ (48,994), $P < 0.001$, $M = 1.6$, 95% CI = 1.2; 2.0) and 2.1% ($t = 7.7$ (38,439), $P < 0.001$, $M = 2.1$, 95% CI = 1.6; 2.6). Women (>41 years) reported sleeping slightly shorter times and/or less efficiently than men both in sleep diaries and sleep questionnaires, whereas actigraphy estimates indicate the opposite: women sleep longer and slightly more efficiently than men of similar age (Supplementary Table 11). This was also found in the UK Biobank (UKBB) cohort.

International comparisons. Average self-reported TST as well as sex difference in TST were similar in the adult Dutch, UK and US populations (Supplementary Table 14). The proportion of adults reporting TST shorter than recommended for age was the highest in the the United States (30.3%), compared to 24.5% in the Netherlands and 25.0% in the United Kingdom. The proportion of adults sleeping less than the 'acceptable' values was below 10% in all three countries. The prevalence of insomnia symptoms (Supplementary Table 15) was 1.5–2.9 times higher in the US sample (for DIS and DMS, across adult ages with the exception of those aged 18–25 years) than in the Netherlands. Sex and age differences in insomnia symptoms were similar across populations: DIS reduced and DMS increased with advanced age, whereas women reported insomnia symptoms more commonly irrespective of age.

Changes in sleep patterns with calendar year. In the data from the Netherlands there was some evidence for a decrease in sleep duration from the 1990s to the 2000s; TST values between 1993 and 1997 averaged around 7.3 h per night. After 2004, values ranged between 6.7 and 7.1 h, with the exception of 2009 which is fully based on the LASA Study (Supplementary Fig. 6). In the United States, TST values between 2004 and 2017 were more stable, ranging between 7.07 h in 2017 and 7.19 h in 2007. There were no changes in the prevalence of insomnia symptoms across the years of the studies in the Netherlands and in United States (Supplementary Fig. 7).

Discussion

Our results suggest that: (1) the population of the Netherlands reported sleeping within 'acceptable' sleep duration range at all ages but more than half of teenagers slept almost an hour less than recommendations; (2) actigraphic sleep duration and efficiency are consistently lower than self-reported estimates, which limits the applicability of current recommendations to objective sleep variables; (3) insomnia symptoms were least frequent in 26–40-year-olds and most frequent in people aged >65 years, and those spending >9 h in bed; (4) self-reported TST did not differ substantially between adults from the Netherlands and from the United Kingdom and the United States but insomnia symptoms were 1.5–2.9 times more prevalent in the United States than in the Netherlands; (5) poor sleep quality and insomnia symptoms were more prevalent than short sleep duration; (6) women, people of

Table 2 | Prevalence of insomnia symptoms, stratified by age and sex

Strata by age and sex	Insomnia symptoms					
	Difficulty initiating sleep		Difficulty maintaining sleep		Early morning awakenings	
	Studies (22, 1997–2015)[a]		Studies (15, 1998–2015)		Studies (9, 1997–2015)	
	n	%	*n*	%	*n*	%
1–2 years						
Total	1,336	4.5	–	–	–	–
Male	655	4.9	–	–	–	–
Female	681	4.1	–	–	–	–
3–5 years						
Total	5,484	4.0	1,678	6.1	ND	ND
Male	2,778	4.2	834	6.6	ND	ND
Female	2,704	3.8	844	5.7	ND	ND
6–13 years						
Total	13,227	13.2	7,210	9.1	ND	ND
Male	6,697	12.3	3,601	7.9	ND	ND
Female	6,570	14.0	3,602	10.2	ND	ND
14–17 years						
Total	1,631	16.5	1,175	23.2	–	–
Male	719	12.9	501	16.8	–	–
Female	910	19.3	672	28.1	–	–
18–25 years						
Total	2,227	22.6	1,961	9.4	2,023	10.3
Male	969	19.4	856	8.6	892	9.2
Female	1,252	25.1	1,105	10.0	1,131	11.2
26–40 years						
Total	26,264	7.2	3,795	11.3	1,636	14.1
Male	10,850	5.5	1,550	7.4	722	12.0
Female	15,413	8.3	2,244	13.9	913	15.7
41–65 years						
Total	73,648	9.3	19,056	15.7	8,417	21.0
Male	31,637	5.4	8,640	10.5	3,904	17.5
Female	41,975	12.3	10,416	20.1	4,513	24.0
>65 years						
Total	8,869	14.9	3,255	20.2	3,376	23.5
Male	3,841	8.0	1,527	14.5	1,579	18.3
Female	5,028	20.2	1,728	25.3	1,797	28.0

[a]Studies are shown as number of studies and related time period. Prevalence rates were not calculated if <200 participants in a cell. ND, not defined if inapplicable for the age group.

non-European origin, people who are overweight and smokers were particularly prone to experiencing poor sleep.

In this large descriptive sleep study, pooling many individual studies inevitably results in high heterogeneity, thus absolute estimates should be interpreted with caution. Several methodological issues must be discussed. First, variables such as sleep timing and duration may be more objectively assessed with actigraphy or polysomnography[21,22]. However, subjective complaints are clinically relevant and highly related to daily functioning. Moreover, the implementation of measures such as polysomnography in large-scale population-based studies is currently limited. In this study we were able to complement subjective data with objective sleep parameters in teenagers and older adults. These are the two age groups with the highest prevalence of insufficient sleep duration. Sleep duration estimates differ by method of assessment but habitual sleep duration is reasonably stable within individuals[23,24]. Thus, the interindividual differences in sleep duration can reliably be compared when assessed with the same method only. Moreover, absolute numbers should be interpreted with caution because age or reporter could influence sleep estimates (for example, parents may under-report their children's sleep onset latency and wake time during the night, resulting in higher SE estimates). In addition, as SE is based on two self-reported measures, these variables might be particularly prone to error and should be interpreted with caution. Second, heterogeneity between studies may have introduced misclassification bias (for example, different definitions of bedtimes and wake times can influence TIB estimates). Analyses of sources of heterogeneity indicated that age and sex only partly account for the heterogeneity between the studies from the Netherlands and that most remaining heterogeneity probably originates from between-study differences in sampling, source population, regions or missing patterns. Other sociodemographic variables, within and beyond those assessed in this study, probably also influence sleep estimates and may account for residual heterogeneity. Although access to IPD improves data quality through standardization of definitions, this study was not sufficiently powered to tease out these influences on heterogeneity. Nevertheless, we provided crude estimates for sociodemographic strata, that could be valuable reference for future studies or clinical practice. Third, we could not assess potential confounding by underlying sleep disorders (for example, sleep apnoea), psychiatric disorders, substance abuse and other chronic medical conditions that could disturb sleep and the ability to go out of bed (for example, hypertension and diabetes mellitus), environmental (screen exposure and noise) or occupational factors (noise and shift work). In addition, differential recruitment strategies may have resulted in differential prevalence of disturbed sleep in the sample. These factors may have contributed to heterogeneity in the sleep estimates. Fourth, although we studied a representative large population sample of the Netherlands and compared sleep estimates to other populations from developed countries, findings may not be generalizable to populations with different sociodemographic or cultural characteristics. These international comparisons were possible for some sleep parameters only. However, all studies sampled participants from the general population, which reduces the chance of selection bias and increases the interpretability of the comparisons. Fifth, multivariable adjusted models indicated that the reported differences in sleep patterns across sociodemographic groups were small, thus their clinical implications may be limited.

In our study, 25% of the adult population reported sleeping less than the recommended 7–9 h, whereas the Centers for Disease Control and Prevention has estimated up to 44.1% of the US population aged ≥18 years slept less than 7–9 h (ref. [25]). We showed that the average self-reported sleep duration does not differ between the Netherlands, the United States and United Kingdom but the prevalence of sleeping below the recommended TST was higher in the US population (30%), than in the European populations (24–25%). In the Netherlands, there was some evidence for a 18–36 min decrease in the average sleep duration from the 1990s to the 2000s but this could also have resulted from between-study heterogeneity. We did not observe changes in average sleep duration in the United States, although one study[26] reported an increase in the prevalence of adults sleeping <6 h per night on the basis of the same data. We also showed that the recommendations are only applicable to subjective sleep reports. Specifically, 80% of participants >40 years, have an actigraphic TST less than the 'recommended' 7 h TST. It is important

to note that a portion of this population still falls within the 'acceptable' range of 6–11 h developed by the NSF expert panel[3,4]. The pooled IPD data show that 6.8% of the adult population report sleeping less than the 'acceptable' 6 h but this increased to 25% at an older age. Using actigraphic TST estimates up to 47% adults were estimated to sleep less than the 'acceptable' values. On the basis of an online questionnaire, Kerkhof has reported a higher percentage (30.4%) of <6 h of sleep in an adult population from the Netherlands[7]. Studies included in our meta-analysis have shown that participants aged 18–65 years sleeping both <6 h (ref. [27]) and <7 h (ref. [28]) per night have higher cardiovascular risk as compared to those sleeping 7–8 h per night, as confirmed by landmark meta-analyses on the associations between sleep and cardiometabolic health[29,30]. A Time Use Survey Panel in industrialized countries in Europe and North America[31] has also shown that older adults sleeping <7 h have lower self-reported health, although the 'acceptable' sleep duration for this age group can be as short as 5 h per night. It thus remains unclear what the appropriate amount of self-reported sleep duration is for preserving health and reference values for objective sleep duration are unknown. In teenagers, the prevalence of insufficient sleep and sleepiness was much higher than in any other age group. This could probably be explained by developmental bedtime delay (as evidenced by our analyses of sleep timing) but could also be influenced by adolescent lifestyle and environment such as social and peer pressure, screen exposure or social life.

Despite the premise that 'optimal' sleep duration probably differs per outcome, individual and circumstances, providing reference values for sleep length can be useful in clinical or prevention practice. This way it is possible to estimate the extent of the problem (that is, the proportion that falls outside of recommended values) which could guide public health policies for improving sleep in the general population. Therefore, we estimated sleep duration percentile curves, which so far have been estimated only in children and adolescents[9,10,32]. Healthcare professionals can easily assess sleep characteristics by interviews or questionnaires but with increased use of accelerometers in research and daily settings, reference curves for actigraphic sleep variables should also be estimated.

Several previous observational studies have estimated the prevalence of insomnia in European populations[7,11,14,15,33]. Our study estimates (7–23% depending on insomnia symptom and age group) largely correspond with those reported in telephone interviews by 25,579 people from seven European countries in the 1990s[14]. The prevalence of DIS and DMS in the Netherlands, however, was substantially lower than in the United States. Our study, adds age-specific information on the prevalence of insomnia symptoms across the lifespan and shows which insomnia symptoms are most common in each age group. We also show that these age-related changes in insomnia symptoms are similar in the United States. This information could be used to improve sleep on a population level; that is, young adults would probably benefit from interventions tackling difficulty initiating sleep, whereas older adults might need help with sleep maintenance or early morning awakenings. We also show that spending 7–8 h in bed is associated with better sleep quality and fewest insomnia symptoms, similar to a general-population study in Norwich, United Kingdom[11]. Importantly, our data also show that wake time is remarkably stable across the lifespan, thus any interventions targeting sleep duration but also those targeting sleep quality should primarily be aimed at adaptations of bedtime.

In line with previous reports based on smaller samples, we found using pooled IPD data that women report longer sleep duration but slightly lower sleep efficiency[7,11]. For example, a 28-year-old woman reporting to spend 9 h in bed is in the 90th percentile of the female population of similar age, whereas, a 28-year-old man with the same TIB, would be in the 95th percentile of the male population of similar age. When measured with actigraphy, however, women's sleep was slightly longer and more efficient than that of men in the Netherlands and in the United Kingdom. Women experience more insomnia problems than men in all three countries. This indicates that recommendations for appropriate sleep duration and quality should be sex-specific. This commonly reported difference[7,14,33,34] emerges during puberty, suggesting sex hormones, among other social factors such as stress or parenting, might play a role in the development of insomnia problems. Interestingly, women do not report daytime sleepiness more often, despite experiencing more insomnia problems and using more sleep medication than men.

The estimated population reference charts for sleep timing, sleep duration and efficiency across the lifespan, will help guide personalized advice on sleep. However, current recommendations are applicable only to self-reported average sleep duration and international differences point to the need for country-specific recommendations for adequate sleep. Given that poor sleep (low sleep quality or insomnia symptoms) is more common than short sleep (TST below 'acceptable' values) in Europe and in the United States, recommendations for improving sleep might need to focus more on sleep quality. Whereas most available guidelines address optimal sleep duration, our findings highlight the importance of also targeting sleep quality. Importantly, we identified subgroups that are prone to shorter or less efficient sleep, such as teenagers, women, people of non-European origin, those with obesity and smokers. These population strata could be used as sampling schemes when developing interventions to improve sleep at a population level. We also show that the lowest prevalence of poor sleep in the general population occurs in those spending 7–8 h in bed. This finding, together with the relatively high prevalence of poor sleep despite nearly appropriate sleep duration, warrants defining new targets for sleep hygiene advice. In other words, by recommending optimal sleep duration we are unlikely to accomplish better sleep at a population level.

Methods

Search strategy, eligibility and selection criteria. To chart sleep characteristics for the population of the Netherlands, we conducted a systematic literature search to identify population-based cohorts assessing sleep characteristics via questionnaires. We searched Embase, Medline Ovid and Web of Science Core Collection on 9 August 2019 with a search strategy developed by a biomedical information specialist (W.B.; Supplementary Text). Inclusion criteria were: (1) population-based sample from the Netherlands; (2) inclusion of at least 100 participants older than 1 year; (3) assessment of sleep with questionnaires; (4) publication in a peer-reviewed journal after the year 2000. Exclusion criteria and steps are outlined in a detailed flowchart (Supplementary Fig. 1a,b). All 5,750 identified abstracts were checked for eligibility by two independent reviewers (D.K. and either T.S.L., Y.X., M.E.K.V. or I.D.; references were split randomly), after which D.K. assessed 381 full-text articles for eligibility and T.S.L. again assessed the excluded articles. From 142 publications that met our inclusion criteria, we identified 43 non-overlapping study populations. We additionally added four studies identified by personal contacts but sought IPD from 44 studies (IPD was not requested from three studies that were published after data collection had been completed in early 2017), of which 36 agreed (response 81%). From studies with repeated measurements, the baseline measurement was used for this IPD as it comprised the largest sample size.

All studies included in the meta-analysis (Supplementary Table 1) were approved by the ethics committee of the local university, institute or organization. Written informed consent was obtained in the original studies from all participants or caregivers (see publications in Supplementary Table 1). The first and corresponding authors obtained legal rights for access to anonymized datasets. This article follows the preferred reporting items for systematic reviews and meta-analyses (PRISMA) statement for IPD reporting guidelines, Supplementary Text (ref. [35]).

To evaluate differences of sleep characteristics across countries, we included two large population-based datasets from adults in the UKBB (n = 498,320) and the National Health Interview Survey (NHIS) from the United States (n = 409,617). These samples were not meta-analytically pooled with the data from the Netherlands, as this would further increase heterogeneity, thereby resulting in estimates that cannot be better generalized to other populations.

Public involvement. This research is a response to public interest. In April 2015, residents of the Netherlands were asked to indicate which scientific questions should be addressed in the next decade. Requests of 11,700 people laid the

foundation for the National Science Agenda (https://wetenschapsagenda.nl/). Text analysis revealed that attention to sleep-related issues was requested 423 times; hence the current research question can be considered relevant by the general population. However, participants were not invited to comment on the study design or interpretation of the results. Participants did not contribute to the writing or editing of this document for readability or accuracy.

IPD coding. To maximize internal validity, we harmonized the datasets in a three-step procedure: (1) we agreed upon definitions for each sleep variable (described in the 'Coding steps and protocol' of the Supplementary Text), also sociodemographic variables were classified in line with Statistics Netherlands[36,37]; (2) two independent coders (D.K. and T.S.L.) coded all datasets according to the standardized protocol (reliability statistics reported in 'Coding steps and protocol', Supplementary Text); and (3) coding disagreements were resolved by consensus supervized by a senior sleep researcher (H.T.).

Sleep variables. We distinguished the following ten sleep variables:

1. Time in bed (TIB, h) was calculated as the difference between bedtime and wake time in hours, for week days and weekends separately. Bedtimes between 12:00 and 17:00 and wake up times between 17:00 and 02:00 were excluded ($n=97$).
2. Sleep duration (total sleep time, TST, h) was self- or caregiver-reported, values ≤2 h or ≥20 h were excluded ($n=81$).
3. Sleep efficiency (SE, %) was calculated as (TST/TIB) × 100. Note that TST and bedtimes/wake times were assessed separately, which may result in implausible values, for example TST of 7.5 and TIB between 23:00 and 07:00 results in implausible SE but probably represents high SE. To balance bias in estimates with loss of precision: values between 100 and 110% were recoded to 100% (mainly errors in reporting times, $n=7{,}630$, 8.8%), values above 110% were excluded ($n=2{,}597$, 2.9%, most from the largest cohort, Lifelines Study).
4. Daytime napping was defined as reporting 'regularly' or 'frequently' sleeping ≥30 min during the day (yes/no).
5. Insomnia symptoms (yes/no) included difficulty initiating sleep (DIS), defined as trouble falling asleep (≥30 min); difficulty maintaining sleep (DMS), defined as trouble falling asleep again after nocturnal awakening; and early morning awakening (EMA), defined as waking up earlier than desired and not being able to fall asleep anymore. Insomnia symptoms were present if symptoms were reported to occur often, frequently or ≥3 times per week[38].
6. Sleep medication was defined as the reported use of any medication to aid sleep at least once a week (yes/no).
7. Non-restorative sleep was defined as not feeling rested when waking up in the morning, reported at least 'often' or ≥3 times per week (yes/no).
8. Sleepiness was defined as 'feeling sleepy' during the day, reported at least 'often' or ≥3 times per week (yes/no).
9. Snoring was present if snoring was reported at least once a week (yes/no).
10. Poor sleep quality was present if any questions on how individuals perceived or judged their habitual sleep were answered with 'bad', 'unsatisfactory', 'insufficient' or similar qualifications (yes/no).

Sociodemographic variables. Ethnic origin for the samples from the Netherlands was based on self-report of the country of birth of the participant or his/her parent[39] and categorized into European origin—Dutch and European origin—other and non-European origin[37]. Educational level was based on self-reported highest education and categorized into low (lower vocational training or ≤3 years at general secondary), medium (>3 years general secondary school, intermediate vocational training or first year of higher vocational training) or high (university degree, higher vocational training)[36]. Having paid employment and having a partner (including non-cohabiting) were self-reported and classified as yes/no.

Health risk indicators and lifestyle variables. Smoking was self-reported and categorized into: never, former or current smoker. BMI (kg m^{-2}) was calculated on the basis of self-reported or measured weight and height. BMI of 18.5–25 kg m^{-2} was defined as normal weight. Underweight was defined as BMI <18.5 kg m^{-2}, overweight as BMI >25 kg m^{-2} and obese >30 kg m^{-2}. These variables were only defined for adults.

Complementary objective sleep estimates. In two cohorts from the Netherlands, subjective sleep reports were collected simultaneously with sleep diaries and actigraphy. In the Generation R Study, children aged 10–15 years ($n=1386$) wore Geneactiv watches for 9 d (ref. [40]). In the Rotterdam Study, participants aged 45–98 years ($n=1{,}940$) wore Actigraphy watches for 7 d (ref. [41]). Actigraphic sleep variables were estimated with validated algorithms. Actigraphy and diary sleep estimates were averaged across days. The actigraphic sleep variables were complemented by those of 85,499 participants from the UKBB (ref. [42]).

International comparisons. To evaluate consistency across countries, the IPD analyses were complemented by data from international cohorts. First, the UKBB (https://www.ukbiobank.ac.uk) is a large population-based cohort study aimed at improving prevention, diagnosis and treatments of various illnesses. Between 2006 and 2010, ~9.2 million people aged 40–69 years were invited to participate. Second, US data were obtained from the NHIS (https://www.cdc.gov/sleep), harmonized by Integrated Public Use Microdata Series (https://nhis.ipums.org/nhis/), a nationally representative survey of non-institutionalized American adults surveyed annually (2004–2017). We included adults aged 18–84 years with non-missing responses for the respective sleep measures.

In the UKBB, adults reported on TST by answering the question 'About how many hours sleep do you get in every 24 hours? (please include naps)'. We excluded participants reporting usual daytime napping from the UKBB ($n=26{,}561$). NHIS participants answered the question 'On average, how many hours of sleep do you get in a 24-hour period?', with responses in hour increments. Symptoms of insomnia in the UKBB were assessed by the question: 'Do you have trouble falling asleep at night or do you wake up in the middle of the night?', which did not map on any of our individual insomnia constructs, thus was not further analysed. NHIS participants reported DIS and DMS using two questions: 'In the past week, how many times did you have trouble falling asleep?' and 'In the past week, how many times did you have trouble staying asleep?', respectively. Participants who reported having these symptoms 'usually' in the UKBB and '≥3 times per week' in the NHIS were coded as 'yes'. These estimates were compared to the pooled IPD meta-analysis sample.

Statistical analyses. We explored whether the population in the meta-analysis was representative of the general population of the Netherlands by comparing the distributions of age, sex and education with the last Dutch Census in 2011[20]. For descriptive purposes, we pooled the data across studies, with different studies contributing data for different sleep variables, according to what data had been collected.

First, age- and sex-specific means and prevalences of sleep variables were computed on the basis of systematically coded variables to reduce between-study heterogeneity (Supplementary Text). Due to the pooling of multiple studies, no statistical tests were performed at this stage. Age categories were aligned to those of NSF: toddlers (1–2 years), preschoolers (3–5 years), school-aged children (6–13 years), teenagers (14–17 years), young adults (18–25 years), adults (26–40 years), middle-aged adults (41–64 years) and older adults (>65 years).

Second, variations in TST, SE and TIB were plotted using age-specific percentiles (10th, 25th, 50th, 75th and 90th). To facilitate comparison, TST was also plotted against the NSF sleep duration recommendations: 11–14 h for toddlers, 10–13 h for preschoolers, 9–11 h for school-aged children, 8–10 h for teenagers, 7–9 h for adults of 26–64 years and 7–8 h for older adults[3]. To explore detailed age-related changes in TST, SE and TIB we also estimated percentile curves against continuous age between 1 and 100 years using gamlss R package. To explore heterogeneity, the I^2 statistic was estimated (using two-step approach), which indicates the percentage of variance in a meta-analysis that is attributable to study heterogeneity. Also, we describe how the I^2 statistic changed with subgroup analyses (by age group, sex and cohort). In addition, we evaluated the differences between the pooled estimates of sleep duration and insomnia symptom as estimated by a fixed-effect versus random-effects meta-analysis.

Third, we examined associations of sleep duration, sleep efficiency and insomnia symptoms with sociodemographic and health indicators using one-step approach. After testing assumptions, we used linear mixed models, with a random intercept for each study to account for between-study heterogeneity. The random effects for study were significant in all models. In these analyses, we only included participants aged 18 years and older as sleep characteristics change rapidly during childhood and adolescence[9]. Three models were constructed: a 'demographic determinants model' where we studied the association of mutually adjusted age (continuous), sex, educational level and ethnic origin with sleep variables, a 'social determinants model' where we studied the association of employment status and partnership on sleep variables adjusted for demographic determinants, and a 'health indicators model' where we studied the association of smoking and BMI with sleep variables adjusted for demographic determinants.

Fourth, since sleep may change due to social changes like economic crisis or increasing use of blue-light emitting screens, we assessed whether changes in average sleep duration (TST), as well as in the prevalence of DIS and DMS, occurred in the Netherlands and the United States during the years of study.

As more sophisticated imputation methods cannot account for within-study clustering, missing values on age (0.3%) were imputed with the study-specific mean and a missing category was used to account for missing values in categorical variables (education = 0.6%, ethnic origin = 26.6%, employment = 7.4%, partner = 62.2%, smoking = 15.0% and BMI = 13.3%). Ethnicity was not assessed in eight studies, whereas of the studies in adult populations five did not assess employment and three did not assess smoking. Missing or implausible values on sleep variables were not imputed. The distribution of missing data across age and sex is shown in Supplementary Table 16. Data were analysed using SPSS Statistics v.21 (IBM Corp.) and R v.3.4.1.

Reporting Summary. Further information on research design is available in the Nature Research Reporting Summary linked to this article.

Data availability

Our data protection agreements with the participating cohort studies do not allow us to share individual-level data from these studies to third parties.

Code availability

The coding protocol for data analysis is provided in the Supplementary Text. Scripts of the statistical analyses are available upon request.

Received: 14 January 2020; Accepted: 7 September 2020;
Published online: 16 November 2020

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Acknowledgements

This research has been conducted using the UK Biobank Resource (UKBB application nos. 6818 and 9072). We would like to thank the participants and researchers from the UKBB who contributed or collected data. This work was supported by a grant financed by the Dutch Brain Foundation (Hersenstichting, grant no. GH2015.4.01). The work of D.K. was supported by an NWA Startimuls KNAW 2017 grant no. AZ/3137. E.J.W.V.S. was supported by European Research Council grant no. ERC-2014-AdG-671084 INSOMNIA. The work of H.T. was supported by a Netherlands Organization for Scientific Research grant no. 017.VICI.106.370. The funders had no role in study design, data collection and analysis, decision to publish or preparation of the manuscript.

Author contributions

D.K., H.T. and E.J.W.V.S. designed the study and, together with T.S.L. and A.I.L., worked on establishing definitions, and obtaining contact with the included cohorts and drafting the manuscript. O.H.F. provided expertise in systematic reviewing and meta-analysis. W.M.B. provided systematic literature reviewing of online databases expertise. D.K., T.S.L., I.P.M.D., M.E.K.-V. and Y.X. independently screened abstracts identified by systematic review. D.K., T.S.L., M.P.C.M.L. and A.I.L. closely monitored data coding and ensured reliability. D.K. and T.S.L. independently coded all individual datasets and D.K. analysed the data. A.D., N.A., N.R.B., A.B., J.B., W.J.B., H.C.C., E.C., H.S.D., E.J.d.B., R.d.G., J.F.D.-K., P.J.M.E., R.J.B.J.G., L.G., L.H., C.A.H., C.J.H., M.H., A.H., M.A.I., S.E.J., M.K.V., M.K., A.M.M., K.M., R.M., A.J.O., J.O.G., B.W.J.H.P., H.S.J.P., S.P., S.A.R., E.R., C.M.R., G.R., F.R., M.C.S., A.S.S., M.B.S., K.S., M.t.H., J.W.R.T., D.v.d.M., J.v.d.E., K.B.v.d.H., P.G.v.d.V., F.J.v.L., R.R.L.v.L., S.H.v.O., F.J.v.S., C.M.S., R.A.V., F.C.V., M.C.M.V., R.C.H.V., W.M.M.V., T.G.M.V., A.H.W., A.M.W., M.t.W. and A.R.W. were involved in the design, data collection or management of the individual studies and provided important insight into the respective datasets and their coding, cleaning and usage. All authors critically evaluated the manuscript and approved the last version.

Competing interests

All authors have completed the International Committee of Medical Journal Editors (ICMJE) uniform disclosure form and declare: no financial relationships with any organizations that might have an interest in the submitted work in the previous 3 years; no other relationships or activities that could appear to have influenced the submitted work.

Additional information

Supplementary information is available for this paper at https://doi.org/10.1038/s41562-020-00965-x.

Correspondence and requests for materials should be addressed to H.T.

Peer review information Peer reviewer reports are available. Primary Handling Editor: Jamie Horder.

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nature research

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Last updated by author(s): Aug 18, 2020

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n/a	Confirmed	
☐	☒	The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement
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☒	☐	For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
☒	☐	For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
☒	☐	Estimates of effect sizes (e.g. Cohen's *d*, Pearson's *r*), indicating how they were calculated

Our web collection on statistics for biologists contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection	Data were collected in SPSS version 21 (IBM Corp., Armonk, NY), and Microsoft Excel version 16.16.20.
Data analysis	Data were analyzed using SPSS Statistics, version 21 (IBM Corp., Armonk, NY), SigmaPlot version 14.0 and R version 3.4.1.

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research guidelines for submitting code & software for further information.

Data

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All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A list of figures that have associated raw data
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Datasets including individual participant data cannot be shared due to data protection policies of individual studies. Summary data and code will be made availbale upon request to the first author.

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☐ Life sciences ☒ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

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Behavioural & social sciences study design

All studies must disclose on these points even when the disclosure is negative.

Study description	Quantitative, observational study
Research sample	Individual participant data from 34 individual studies from the general population of the Netherlands, and two general population surveys from the UK and USA were analyzed.
Sampling strategy	Studies to be included were identified through a systematic Literature search. All studies used random sampling strategies.
Data collection	Datasets were securely shared with the first author (DK) bu the first corresponding authors of each identified study. All datasets were systematically recoded by the first and second author (TSL), according to a standardized protocol reported in the Supplement.
Timing	Studies published between 2000 and 2019 were included. The last search was conducted in August 2019.
Data exclusions	No studies that met the inclusion criteria were excluded.
Non-participation	Studies that could not contribute individual participant data, or did not respond (in time) are described in the Supplement (Flowchart)
Randomization	N/A

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
☐	☐ Antibodies
☐	☐ Eukaryotic cell lines
☐	☐ Palaeontology and archaeology
☐	☐ Animals and other organisms
☐	☐ Human research participants
☐	☐ Clinical data
☐	☐ Dual use research of concern

Methods

n/a	Involved in the study
☐	☐ ChIP-seq
☐	☐ Flow cytometry
☐	☐ MRI-based neuroimaging

Antibodies

Antibodies used	*Describe all antibodies used in the study; as applicable, provide supplier name, catalog number, clone name, and lot number.*
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Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	*State the source of each cell line used.*
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Mycoplasma contamination	*mycoplasma contamination OR declare that the cell lines were not tested for mycoplasma contamination.*
Commonly misidentified lines (See ICLAC register)	*Name any commonly misidentified cell lines used in the study and provide a rationale for their use.*

Palaeontology and Archaeology

Specimen provenance	*Provide provenance information for specimens and describe permits that were obtained for the work (including the name of the issuing authority, the date of issue, and any identifying information).*
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Ethics oversight	*Identify the organization(s) that approved or provided guidance on the study protocol, OR state that no ethical approval or guidance was required and explain why not.*

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Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research

Laboratory animals	*For laboratory animals, report species, strain, sex and age OR state that the study did not involve laboratory animals.*
Wild animals	*Provide details on animals observed in or captured in the field; report species, sex and age where possible. Describe how animals were caught and transported and what happened to captive animals after the study (if killed, explain why and describe method; if released, say where and when) OR state that the study did not involve wild animals.*
Field-collected samples	*For laboratory work with field-collected samples, describe all relevant parameters such as housing, maintenance, temperature, photoperiod and end-of-experiment protocol OR state that the study did not involve samples collected from the field.*
Ethics oversight	*Identify the organization(s) that approved or provided guidance on the study protocol, OR state that no ethical approval or guidance was required and explain why not.*

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Human research participants

Policy information about studies involving human research participants

Population characteristics	We included 1081734 participants aged 1-100, 55% women.
Recruitment	All studies used random sampling from the general population.
Ethics oversight	Local Universities provided ethics approval.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Clinical data

Policy information about clinical studies

All manuscripts should comply with the ICMJE guidelines for publication of clinical research and a completed CONSORT checklist must be included with all submissions.

Clinical trial registration	*Provide the trial registration number from ClinicalTrials.gov or an equivalent agency.*
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Outcomes	*Describe how you pre-defined primary and secondary outcome measures and how you assessed these measures.*

Dual use research of concern

Policy information about dual use research of concern

Hazards

Could the accidental, deliberate or reckless misuse of agents or technologies generated in the work, or the application of information presented in the manuscript, pose a threat to:

No	Yes	
☒	☐	Public health
☒	☐	National security
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☒	☐	Ecosystems
☒	☐	Any other significant area

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Does the work involve any of these experiments of concern:

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☒	☐	Demonstrate how to render a vaccine ineffective
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☒	☐	Increase transmissibility of a pathogen
☒	☐	Alter the host range of a pathogen
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ChIP-seq

Data deposition

☐ Confirm that both raw and final processed data have been deposited in a public database such as GEO.

☐ Confirm that you have deposited or provided access to graph files (e.g. BED files) for the called peaks.

Data access links *May remain private before publication.*	*For "Initial submission" or "Revised version" documents, provide reviewer access links. For your "Final submission" document, provide a link to the deposited data.*
Files in database submission	*Provide a list of all files available in the database submission.*
Genome browser session (e.g. UCSC)	*Provide a link to an anonymized genome browser session for "Initial submission" and "Revised version" documents only, to enable peer review. Write "no longer applicable" for "Final submission" documents.*

Methodology

Replicates	*Describe the experimental replicates, specifying number, type and replicate agreement.*
Sequencing depth	*Describe the sequencing depth for each experiment, providing the total number of reads, uniquely mapped reads, length of reads and whether they were paired- or single-end.*
Antibodies	*Describe the antibodies used for the ChIP-seq experiments; as applicable, provide supplier name, catalog number, clone name, and lot number.*
Peak calling parameters	*Specify the command line program and parameters used for read mapping and peak calling, including the ChIP, control and index files used.*
Data quality	*Describe the methods used to ensure data quality in full detail, including how many peaks are at FDR 5% and above 5-fold enrichment.*
Software	*Describe the software used to collect and analyze the ChIP-seq data. For custom code that has been deposited into a community repository, provide accession details.*

Flow Cytometry

Plots

Confirm that:

☐ The axis labels state the marker and fluorochrome used (e.g. CD4-FITC).

☐ The axis scales are clearly visible. Include numbers along axes only for bottom left plot of group (a 'group' is an analysis of identical markers).

☐ All plots are contour plots with outliers or pseudocolor plots.

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Methodology

Sample preparation	*Describe the sample preparation, detailing the biological source of the cells and any tissue processing steps used.*
Instrument	*Identify the instrument used for data collection, specifying make and model number.*
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Magnetic resonance imaging

Experimental design

Design type	*Indicate task or resting state; event-related or block design.*
Design specifications	*Specify the number of blocks, trials or experimental units per session and/or subject, and specify the length of each trial or block (if trials are blocked) and interval between trials.*
Behavioral performance measures	*State number and/or type of variables recorded (e.g. correct button press, response time) and what statistics were used to establish that the subjects were performing the task as expected (e.g. mean, range, and/or standard deviation across subjects).*

Acquisition

Imaging type(s)	*Specify: functional, structural, diffusion, perfusion.*
Field strength	*Specify in Tesla*
Sequence & imaging parameters	*Specify the pulse sequence type (gradient echo, spin echo, etc.), imaging type (EPI, spiral, etc.), field of view, matrix size, slice thickness, orientation and TE/TR/flip angle.*
Area of acquisition	*State whether a whole brain scan was used OR define the area of acquisition, describing how the region was determined.*

Diffusion MRI ☐ Used ☐ Not used

Preprocessing

Preprocessing software	*Provide detail on software version and revision number and on specific parameters (model/functions, brain extraction, segmentation, smoothing kernel size, etc.).*
Normalization	*If data were normalized/standardized, describe the approach(es): specify linear or non-linear and define image types used for transformation OR indicate that data were not normalized and explain rationale for lack of normalization.*
Normalization template	*Describe the template used for normalization/transformation, specifying subject space or group standardized space (e.g. original Talairach, MNI305, ICBM152) OR indicate that the data were not normalized.*
Noise and artifact removal	*Describe your procedure(s) for artifact and structured noise removal, specifying motion parameters, tissue signals and physiological signals (heart rate, respiration).*

Volume censoring

Define your software and/or method and criteria for volume censoring, and state the extent of such censoring.

Statistical modeling & inference

Model type and settings

Specify type (mass univariate, multivariate, RSA, predictive, etc.) and describe essential details of the model at the first and second levels (e.g. fixed, random or mixed effects; drift or auto-correlation).

Effect(s) tested

Define precise effect in terms of the task or stimulus conditions instead of psychological concepts and indicate whether ANOVA or factorial designs were used.

Specify type of analysis: ☐ Whole brain ☐ ROI-based ☐ Both

Statistic type for inference
(See Eklund et al. 2016)

Specify voxel-wise or cluster-wise and report all relevant parameters for cluster-wise methods.

Correction

Describe the type of correction and how it is obtained for multiple comparisons (e.g. FWE, FDR, permutation or Monte Carlo).

Models & analysis

n/a	Involved in the study
☐	☐ Functional and/or effective connectivity
☐	☐ Graph analysis
☐	☐ Multivariate modeling or predictive analysis

Functional and/or effective connectivity

Report the measures of dependence used and the model details (e.g. Pearson correlation, partial correlation, mutual information).

Graph analysis

Report the dependent variable and connectivity measure, specifying weighted graph or binarized graph, subject- or group-level, and the global and/or node summaries used (e.g. clustering coefficient, efficiency, etc.).

Multivariate modeling and predictive analysis

Specify independent variables, features extraction and dimension reduction, model, training and evaluation metrics.