



CLINICAL REVIEW

Prevalence of obstructive sleep apnea in the general population: A systematic review



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SUMMARY

With this systematic review we aimed to determine the prevalence of obstructive sleep apnea (OSA) in adults in the general population and how it varied between population sub-groups. Twenty-four studies out of 3807 found by systematically searching PubMed and Embase databases were included in this review. Substantial methodological heterogeneity in population prevalence studies has caused a wide variation in the reported prevalence, which, in general, is high. At ≥ 5 events/h apnea-hypopnea index (AHI), the overall population prevalence ranged from 9% to 38% and was higher in men. It increased with increasing age and, in some elderly groups, was as high as 90% in men and 78% in women. At ≥ 15 events/h AHI, the prevalence in the general adult population ranged from 6% to 17%, being as high as 49% in the advanced ages. OSA prevalence was also greater in obese men and women. This systematic review of the overall body of evidence confirms that advancing age, male sex, and higher body-mass index increase OSA prevalence. The need to a) consider OSA as having a continuum in the general population and b) generate consensus on methodology and diagnostic threshold to define OSA so that the prevalence of OSA can be validly compared across regions and countries, and within age-/sex-specific subgroups, is highlighted.

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Introduction

Obstructive sleep apnea (OSA) is a condition characterized by repeated episodes of partial or complete obstruction of the respiratory passages during the sleep [1–3]. The body's response to obstructed breathing leads to arousal of the brain, sympathetic activation, and oxygen desaturation in the blood [12]. Repeated

episodes of upper airway obstruction during sleep may result in sleep fragmentation and non-restorative sleep. Those who have OSA may complain of tiredness, excessive day-time sleepiness, insomnia, or morning headaches, but many are asymptomatic [4–6]. The main metric for diagnosing OSA is the apnea hypopnea index (AHI). This reflects the average number of significant breathing disturbances per hour of sleep and is measured during some form of polysomnography (sleep study). While either laboratory-based, attended polysomnography (i.e., type 1 sleep study) or home based full polysomnography (type 2 sleep study) remains the 'gold-standard' of diagnosis, it has been suggested that other simpler diagnostic methods using measures such as nasal airflow, respiratory effort and/or events of oxygen desaturation in blood during sleep (type 3 or 4 sleep studies) also render reasonably accurate diagnostic results [7]. Screening questionnaires are sometimes used to detect those who are at high risk of OSA, who

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Abbreviations

AASM	American academy of sleep medicine
AHI	apnea-hypopnea index
AI	apnea index
BMI	body-mass index
CI	confidence interval
MeSH	medical subject headings
ODI	oxygen desaturation index
OSA	obstructive sleep apnea
OSAS	obstructive sleep apnea syndrome
RDI	respiratory disturbance index
SDB	sleep disordered breathing
SHHS	sleep heart health study
WCS	Wisconsin sleep cohort study

subsequently may undergo sleep studies [8,9]. OSA is emerging as a major health problem, particularly in high income countries. Its high disease burden is related to both the health care costs attributable to OSA alone and to its contribution as an independent risk factor for cardiovascular, metabolic, and psychiatric disorders such as hypertension, stroke, diabetes, and depression [3,7] which are global health priorities [10,11].

Many studies have demonstrated that OSA is a highly prevalent disorder, both in the general population and in specific disease-related and population sub-groups [6,12–16]. The reported prevalence of OSA has increased over time, in part due to increasing rates of obesity. Obesity is recognized as a major risk factor for OSA [17,18] and there has been an enormous increase in rates of obesity throughout the world over the past 25 y [19–23]. However, some of this increase in prevalence of OSA can be attributed to changes in measurement techniques and definitions for classifying respiratory events (predominantly hypopneas, the partial obstructions to breathing), which have changed over this same period [24,25]. Current measurement techniques and respiratory scoring rules are more sensitive at detecting respiratory disturbances than older measures and rules [12,26], leading to higher AHI [4,27,28]. Within this changing context, there are no published data available to date that are derived from systematically synthesizing evidence related to the population prevalence of OSA. Accurate determination of population prevalence is essential to estimate the true burden of OSA, which is vital when considering population-based health policies and intervention strategies.

The aim of this systematic review was to determine the prevalence of OSA in adults in the general population. Further aims were to determine how prevalence estimates: a) varied according to measurement criteria used for OSA b) were changing over time with rising obesity and; varied between populations and age- and sex- specific sub-groups.

Methodology

All authors discussed and agreed upon the protocol for the systematic review prior to commencement.

Search strategy

Our search strategy is given in Table S1. Using this pre-defined search strategy, we searched PubMed and Embase (on Ovid) from their inceptions to the 3rd March 2016. We searched the selected terms in the fields of Title/Abstract and medical sub-heading

(MeSH) terms in PubMed and Title/Abstract and Subject headings in Embase.

Screening of articles

We combined the articles found from both databases and removed the duplicates. One of us (CS) screened the titles and abstracts of the remaining articles to select those that were eligible for the full-paper review and subsequently assessed the selected full papers to determine their inclusion or exclusion. Another (BC) assessed the selected full papers for inclusion or exclusion independently. When there were doubts at either stage of screening, these were referred to another author (SD) for resolution.

Eligibility criteria

We included the cross-sectional studies and the cross-sectional components of longitudinal studies that objectively measured OSA in adults using laboratory instruments. The studies that reported OSA or sleep disordered breathing (SDB) in terms of the number of apneas and/or hypopneas, respiratory disturbance index, thermistor measurements or oxygen desaturation were included, even when the study population had been pre-selected using screening tools prior to administration of sleep studies. Only human studies and studies that were in English were eligible.

Studies based solely on questionnaires were excluded. We also excluded studies that were not based on the general population or the age- or sex-specific subgroups thereof, such as the studies on occupational sub-groups and clinical subgroups (see Table S2). Both these groups are not representative of the general population due to their morbidity profiles and other phenomena such as healthy worker effect [29], and comparing them with studies based on general population is challenging.

Quality assessment of the selected papers

To assess the papers we selected, we used a quality assessment tool [30] specifically designed to assess prevalence studies [31] and which has been widely used to assess the methodological quality of included articles in other systematic reviews on prevalence studies [32–39]. We rated the selected studies using this tool's eight components, namely, randomness of the sample, suitability of sampling frame, adequacy of sample size, use of standard measurement, use of unbiased assessors, adequacy of response rate and description of non-respondents, reporting of confidence intervals and prevalence for subgroups, and description of study subjects. Each component was given one point if the criterion was fulfilled and zero if not. When the relevant criterion was partially fulfilled, half-a-point was given. Thus the maximum score for any component was one (maximum score of eight points for a paper) [30]. Two of us (CS and BC) independently assessed and rated the articles, and referred to another (SD) when there were disputes.

Data extraction

CS and BC independently extracted and tabulated the data. Any unresolved differences were referred to SD for resolution. The extracted data included name/s of author/s, year of publication, study setting and country, sample size, sampling method/s, source population, methods used to measure OSA (including type of instrument), type of scorer/s, response rate and non-respondents, definition of OSA, and reported prevalence (including in sub-groups).

When the required information had not been directly reported in the article but could be derived using the reported data (e.g.,

deriving proportions using the reported values in the numerator and the denominator) we did this to obtain the necessary information.

We presented the prevalence from the selected studies categorized based on the diagnostic criteria (sleep study type and the definitions of the indices used) and the age and/or sex of the study participants. We also presented the prevalence reported for OSA syndrome (OSAS), which incorporates positive symptoms with the sleep study results, and for body-mass index (BMI) categories (when available) separately.

As we needed prevalence data pertaining to specific age- and sex-subgroups in the studies with matching diagnostic criteria to perform a meta-analysis, we contacted the authors of all papers requesting these additional data. When the email addresses of the corresponding authors were not given or the email addresses given in the articles were non-functional, we used the names of the corresponding authors to trace online for their current listed email addresses. When the corresponding author 1) did not have an email address or had a non-functional email, and 2) could not be traced to obtain their current email address, we traced one or more of the other authors and requested the data from them.

Results

Our systematic search (last run on 3rd March 2016) on PubMed and Embase identified 2318 and 3807 articles, respectively. After removing the duplicates, we screened the title and abstract of the remaining 3560 articles. A total of 59 articles were selected for full paper review, of which 21 articles were found to meet the inclusion criteria (the excluded studies and reasons for their exclusion are shown in Table S2). Searching reference lists of these articles yielded a further three eligible articles, resulting in a total of 24 articles. The flow diagram of the searching process is shown in Fig. 1.

Over half of these 24 studies had been conducted in Europe and five in North America (see Table 1). Except for three studies that had been conducted in 1980's [40–42], the others had been uniformly spread across the next three decades.

Study quality [30]

The quality scores received by the 24 studies varied from three [43] to eight [12] out of a possible eight (see Tables S3–S6). Although the majority of studies had relatively high quality ratings (7–8 (n = 5) or 5–6 (n = 13)), six studies were rated low (scores of 3–4). Almost all studies selected either the whole study population or a random sample, used standard sleep measurements, and described study subjects adequately. The components in which most studies performed poorly were the response rate [41,44–46], usage of unbiased assessors to determine outcome [40,43,44,47–50], and reporting of confidence intervals for the estimates and on sub-group analyses [42,47,51–53].

Assessment of the source population and sample

Only one study [54] included all adults aged >18 y (without an upper limit for age) in its sample while others had been limited to age- and/or sex-specific subgroups of the general population (see Tables 1 and 2 and S3–S6). Study populations of six [16,46,54–57] of the 24 studies included the elderly, the middle-aged, and those younger than 30 y, while five [40,44,52,53,58] included only the elderly. The others had the elderly and the middle-aged [12,41–43,45,47–51,59,60] in their study populations. Three studies included only women [51,55,59] and four studies only men [41,47,52,56].

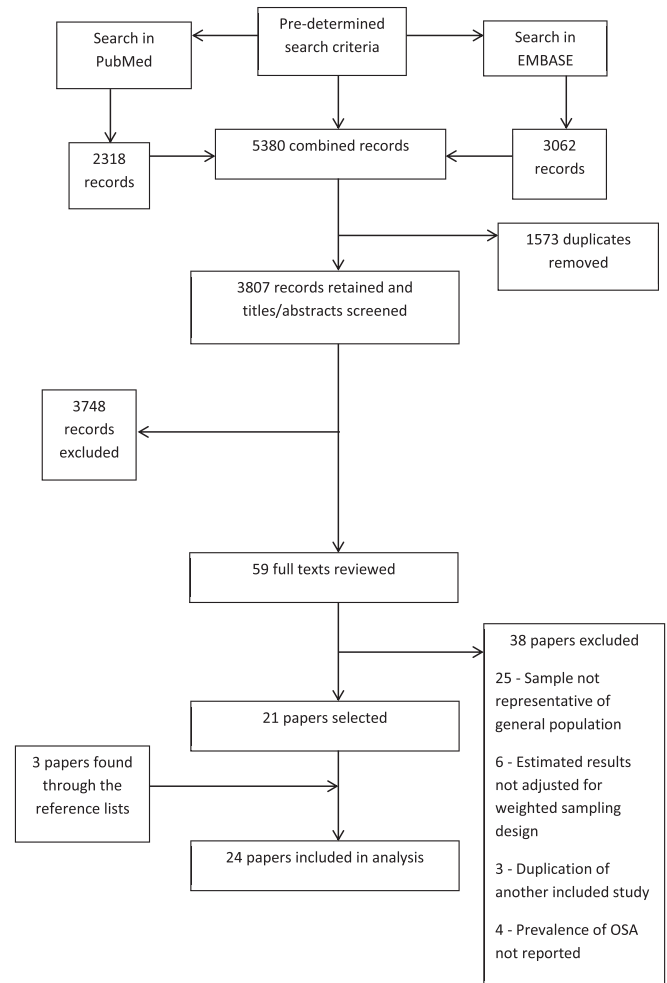


Fig. 1. Screening process of the papers included in the analysis. OSA = Obstructive sleep apnea.

Assessment of the sampling methods

A variety of sampling frames were used, the commonest being electoral registers (see Tables S3–S6) used in five studies [45,46,50,53,60] and census data or population registers used in another five studies [12,41,44,57,61]. Telephone directory lists were used in three [40,55,56]. Cluster randomized sampling was used in two studies [16,48]. Two studies [54,59] did not report their sampling frame.

Johansson et al. [58] and Neven et al. [42] included the total study population in their respective studies. Twenty one of the remaining studies used a random method to obtain their samples. Mehra et al. [52] did not report the randomness of their sample selection.

Samples were selected using equal probability, weighted probability, or mixed designs (when sampling had been done in multiple stages) (see Tables S3–S6). Those studies with weighted or clustered samples used one of two methods when reporting the prevalence of OSA a) accounted for the sampling design in the analysis and reported an adjusted prevalence, or b) reported an estimated minimum prevalence based on the sampling design [42,50,54].

In some studies the participants were investigated initially with sleep studies, while in others they were screened at one or more stages (to detect those who were at higher risk of OSA) before

Table 1
Summary general characteristics of the selected studies.

Characteristic	Number of studies (n = 24)
The region in the world	
Europe	14
North America	5
Australia & New Zealand	2
Latin America	1
East Asia	1
South Asia	1
Year of publication	
1980's	3
1990's	7
2000's	7
2010's	7
Type of source population	
Total adult population	1
Age-specific subgroups of general population	15
Sex-specific subgroups of general population	1
Age- and sex-specific subgroups of general population	7

Table 2
Summary methodological characteristics of the selected studies.

Characteristic	Number of studies (n = 24)
Effective sample size for sleep studies	
<50	3
50–100	1
101–200	1
201–400	5
401–1000	9
>1000	5
Sampling process	
Unscreened, equal probability sampling	15
Unscreened, weighted sampling	1
Screened ^a , equal probability sampling	4
Screened ^a , weighted sampling ^b	4
Indices used to report OSA	
Apnea Index or Apnea-Hypopnea Index	19
Respiratory Distress/Disturbance Index	4
Oxygen desaturation Index	1
Reporting available by groups/sub-groups^c	
Entire source population	16
Age-specific subgroups	10
Sex-specific subgroups	20
Rating given for the quality of the study^d	
3–4 out of 8	6
5–6 out of 8	13
7–8 out of 8	5

OSA, obstructive sleep apnea.

^a Study population screened and screen positives subjected to sleep studies.

^b Sample weighted based on levels of screening scores or screening categories.

^c The total exceeds 24 as many studies have reported the prevalence for more than one group or sub-group.

^d As per Loney et al., 2000 [30].

selecting the final sample for sleep studies (see Tables S3–S6). The latter included eight [41,42,46–48,55,56,59] of the 24 studies. Of these, one [48] used only laboratory methods for screening whilst two [42,59] used both laboratory methods and questionnaires or clinical-based assessments for screening. The remaining five had only used questionnaires or clinical-based assessments.

The effective sample size, i.e., the number of sleep records used in the analysis varied across the studies. While some studies had over two thousand [12,52] (sometimes as high as over 14,000 [57]) sleep records analyzed, the number of records analyzed in others was very low (e.g., 25 in Neven et al. [42], 22 in Gislason et al. [59]). The number of sleep records analyzed was not reported in two studies [54,55].

Assessment of the type of sleep studies and the definitions of the measurement outcomes

Sleep studies were categorized into four types: type 1 studies using full polysomnography at laboratories, type 2 studies using full polysomnography at home, type 3 studies using three or four channels to record variables other than the ones used to determine sleep stages or sleep disruption, and type 4 studies continuously recording one or two variables [62,63].

All studies that screened their study population prior to sleep studies (n = 8) as well as two others [16,41,42,44,46–48,55,56,59] used type 1 sleep studies. Heinzer et al. [12] used type 2 sleep studies. Ten other studies [40,43,49–53,57,58,60] used type 3 and one study [54] used type 4 (see Tables S3–S6). Combinations of different types of sleep studies were used in three of the 24 studies; types 1 and 2 in Piwaczewski et al. [45] (participants randomly allocated to each type), types 1 and 3 in Durán et al. [48] (outcome reported using Type 1), and types 1 and 4 in Neven et al. [42] (outcome reported using type 1).

Depending on the sleep study type, either the apnea index (AI), the apnea hypopnea index (AHI), the respiratory disturbance index (RDI), or the oxygen desaturation index (ODI) were used to measure outcome of sleep studies; one study used ODI [54], four studies used RDI [49,50,52,60], and the other nineteen studies used AI or AHI (see Tables S3–S6).

Various criteria are available to define apnea, hypopnea, respiratory disturbance and oxygen desaturation and these have changed over the time. The 24 studies we included used several varying definitions (see Table S7). Seven used one of the successive American academy of sleep medicine (AASM) criteria to define these indices [12,16,44,46,52,53,58] while thirteen used various other definitions. Four of the studies [40,43,49,54] had not defined the indices used.

Assessment of the reporting of prevalence

Using one of the four indices (AI/AHI/RDI/ODI) to determine sleep apnea, 22 of the 24 studies reported their outcome of interest as OSA, OSAS, or SDB. The remaining two only reported the prevalence of various frequencies of AHI [48] or RDI [51] (at different standard cut-off levels). Similar reporting of prevalence based on one or more clinically acceptable AHI/RDI/ODI cut-off levels was also done by some of the studies that defined a disease outcome of OSA, OSAS, or SDB.

Prevalence of OSA

Prevalence reported in the 24 studies varied widely. These are categorized and shown in Table 3 (OSA prevalence reported for overall study population), Table 4 (age-specific OSA prevalence), Table S8 (sex-specific OSA prevalence), Table S9 (OSAS prevalence by age and sex), and Table S10 (OSA and OSAS prevalence by BMI subgroups).

Overall, OSA in the general adult population (aged >18 y) measured as ≥ 5 events/h AHI/RDI ranged from 9% [46] to 38% [16]. In men this varied from 13% [46] to 33% [57], and in women from 6% [46] to 19% [57]. In some advanced age groups, however, the prevalence was as high as 84% overall, and as high as 90% in men [12]. At the clinically important ≥ 15 events/h AHI level, the prevalence in the overall adult population (aged >18 y) ranged from 6% [46] to 17% [16] although much higher (36%) in the older groups [12,44].

Due to methodological heterogeneity of the studies from different timeframes, their reported prevalence estimates could not be compared with each other to investigate how prevalence has changed overtime. Only one study provided adequate information to determine how the reported prevalence varied according to measurement criteria used for OSA [12]. This study showed that when hypopnea was defined as 3% oxygen desaturation, it detected substantially more events per hour than when hypopnea was defined as 4% oxygen desaturation. Similarly, the use of AASM 1999 and AASM 2012 criteria generated nearly

similar prevalence estimates, which were higher than the prevalence estimate generated using AASM 2007 criteria [12]. Similar disparity due to different combinations of percentage airflow reduction and percentage oxygen desaturation used in these successive criteria has also been shown before [25]. As shown in Tables S7, 3, 4, and S8–S10, each selected study had a unique combination of four factors, namely, the sleep study type used, definition of indices used, age-/sex-specific prevalence reported, and the cut-off levels of the indices for which the prevalence was reported. Importantly, there were no two studies that had the same combination of the above four factors, which also makes it difficult to analyse and describe trends across time, geographical regions, sleep study types, or age groups. Due to this inadequacy of age-sex-specific prevalence reported in the reviewed papers, we could not perform a meta-analysis. Although we requested from authors of all articles the additional data that would have enabled us to perform a meta-analysis, no usable data could be obtained due to several reasons (e.g., not having access to data, data retrieval and analysis taking very long time, data not being available in the requested format or data not being homogeneous with other available data, etc.).

However, we selected studies that reported the age- and sex-specific prevalence at the conventional clinical cut-off levels of ≥ 5 events/h AHI/RDI, ≥ 15 events/h AHI/RDI, or ≥ 30 events/h AHI/RDI, and plotted the prevalence reported for various age-groups in the selected studies against the median age of the reported age-

Table 3
Reported prevalence of OSA for overall study populations.

Type of sleep study used to diagnose OSA	Criteria used to diagnose OSA ^a	Study reference	Target age group (y)	Directly reported or estimated OSA prevalence (%) ^b
Type 1 or type 2				
	AASM 2012	Heinzer et al., 2015 [12] (Personal communication)	40–85	≥ 5 AHI 71.9%; ≥ 15 AHI 36.1%; ≥ 30 AHI 14.5%
	AASM 2007 alternate or similar	Tufik et al., 2010 [16]	20–80	AHI ≥ 5 : 38%; AHI ≥ 5 to <15: 21.2%; AHI ≥ 15 : 16.7%
	AASM 1999 or similar	Johansson et al., 2009 [58] Reddy et al., 2009 [46]	65–82 30–65	≥ 5 AHI: 32%; ≥ 15 AHI: 16%; ≥ 30 AHI: 7% AHI ≥ 5 : 9.3% (8.2–10.5); ≥ 10 AHI: 7.9%; ≥ 15 AHI: 6.1%
	Other	Plywaczewski et al., 2008 [45] Lee et al., 2014 [44]	>30 ≥ 60	>5 AHI: 27.8%; >10 AHI: 14.3% ≥ 5 AHI: 71.8%; ≥ 15 AHI: 36.5%; ≥ 30 AHI: 15.5%
Type 3				
		Ancoli-Israel et al., 1987 [40] Olson et al., 1995 [50]	≥ 65 35–69	17% Reported prevalence ≥ 5 RDI: 68.7%; ≥ 10 RDI: 35.4%; ≥ 15 RDI: 17.9%; ≥ 20 RDI: 11.3%; ≥ 25 RDI: 8.6%; ; Estimated minimum prevalence ≥ 5 RDI: 13.7%; ≥ 10 RDI: 7.1%; ≥ 15 RDI: 3.6%; ≥ 20 RDI: 2.3%; ≥ 25 RDI: 1.7%
		Mihaere et al., 2009 [60]	30–59	≥ 5 AHI: Not reported numerically (only a graph available – difficult to obtain the actual value); ≥ 10 AHI: Māori = 10.9%; Non-Māori = 3.3%; ≥ 15 AHI: Māori = 6.5%; Non-Māori = 1.5%
		Soriano et al., 2010 [43]	30–80	≥ 10 AHI: 35.9% (95% CI 25.3–47.6); Mild ^c : 14.1%; Moderate ^c : 7.7%; Severe ^c : 7.7%; Very severe ^c : 6.4%
		Sforza et al., 2011 [53] Redline et al., 2014 [57] Arnardottir et al., 2016 ^d [6]	65 18–74 42–66	AHI >15: 57%; AHI >15 & <30: 34%; AHI >30: 24% ≥ 5 AHI: 25.8%; ≥ 15 AHI: 9.8%; ≥ 30 AHI: 3.9% ≥ 5 AHI: 43.1%; AHI ≥ 5 to <15: 24.6%; AHI ≥ 15 to <30: 13.7%; ≥ 30 AHI: 4.8%
Type 4				
		Marin et al., 1997 [54]	>18	≥ 10 ODI: 11%

OSA = Obstructive sleep apnea; AASM = American academy of sleep medicine; AHI = Apnea hypopnea index; RDI = Respiratory disturbance index; CI = Confidence interval.

^a See Table S7 for details.

^b % is the reported direct or estimated prevalence.

^c These categories are not defined in the article.

^d Almost equal numbers of men and women selected for cohort. Prevalence estimates may not be accurate if population male: female ratio differs from 1:1.

Table 4

Reported prevalence of OSA for the specific age-groups.

Type of sleep study used to diagnose OSA	Criteria used to diagnose OSA ^a	Study reference	Age (y)	AHI/RDI level (events/h)	Directly reported or estimated prevalence ^b		
					Unclassified	Among males	Among females
Type 1 or type 2							
	AASM 2012						
		Heinzer et al., 2015 [12] (Personal communication)	40–60	≥5	63.2%	79.6%	46.7%
				≥15	26.8%	39.6%	13.9%
				≥30	8.9%	15.2%	2.6%
			60–85	≥5	83.6%	90.0%	78.2%
				≥15	48.7%	64.7%	35.2%
				≥30	22.1%	32.1%	13.6%
	AASM 2007 alternate						
		Tufik et al., 2010 [16]	20–29	≥5 to <15		12.4% (8.7–17.5)	1.4% (0.6–3.1)
				≥15		3.8% (1.3–10.4)	0%
			30–39	≥5 to <15		22.3% (16.8–29)	16.9% (10.4–26.4)
				≥15		16% (11.2–22.4)	2.9% (1.4–6.1)
			40–49	≥5 to <15		29.4% (22.7–37.2)	21.5% (15.6–28.8)
				≥15		35.2% (27.1–44.4)	6.3% (3.8–10.1)
			50–59	≥5 to <15		30.4% (21.1–41.7)	29.9% (24.4–36.2)
				≥15		30.2% (19.8–43.1)	18.6% (12.5–26.7)
			60–69	≥5 to <15		19.3% (8.7–37.5)	35.9% (23.1–51.1)
				≥15		52.3% (37.4–66.8)	36.2% (22.3–52.9)
			70–80	≥5 to <15		11.1% (5.2–41.7)	71.3% (51.8–85.2)
				≥15		84.7% (70.7–92.7)	22.8% (11.3–40.6)
	AASM 1999						
		Reddy et al., 2009 [46]	30–39	≥5		9.7% (7.5–12.6)	6.4% (4.7–8.6)
			40–49	≥5		13.5% (10.4–17.4)	5.0% (2.9–7.9)
			50–65	≥5		17.6% (13.8–22.7)	6.9% (4.2–11.2)
		Lee et al., 2014 [44]	60–64	≥5		69.4% (54.4–84.5)	62.5% (50.6–74.4)
				≥15		38.9% (23.0–54.8)	25.0% (14.4–35.6)
				≥30		19.4% (6.5–32.4)	4.7% (0.5–9.9)
			65–69	≥5		87.8% (80.4–95.3)	65.6% (57.1–74.0)
				≥15		59.5% (48.3–70.7)	25.4% (17.7–33.1)
				≥30		25.7% (15.7–35.6)	9.0% (3.9–14.1)
			75–89	≥5		80.0% (64.3–95.7)	74.1% (57.5–90.6)
				≥15		52.0% (32.4–71.6)	33.3% (15.6–51.1)
				≥30		36.0% (17.2–54.8)	18.5% (3.9–33.2)
	Other						
		Bixler et al., 1998 [56]	20–44	≥5		7.9% (5.0, 12.1)	
				≥10		3.2% (1.6, 6.4)	
				≥20		1.7% (0.6, 4.4)	
			45–64	≥5		18.8% (15.4, 22.8)	
				≥10		11.3% (8.5, 14.5)	
				≥20		6.3% (4.2, 8.8)	
			65–100	≥5		24.8% (16.3, 35.7)	
				≥10		18.1% (10.9, 28.4)	
				≥20		5.1% (1.9, 13.0)	
		Bixler et al., 2001 [55]	20–44	≥15			0.6% (0.2, 2.0)
			45–64	≥15			2.0% (1.0, 4.0)
			65–100	≥15			7.0% (4.0, 11.9)
		Durán et al., 2001 [48]	30–39	≥5		9.0% (2–16)	3.4% (0–7)
				≥10		7.6% (0–15)	1.7% (0–4)
				≥15		2.7% (1–5)	0.9% (0–2)
				≥20		2.1% (0–4)	0%
				≥30		2.1% (0–4)	0%
			40–49	≥5		25.6% (14–37)	14.5% (3–25)
				≥10		18.2% (9–27)	9.7% (0–19)
				≥15		15.5% (7–24)	0%
				≥20		10.1% (5–15)	0%
				≥30		7.0% (3–11)	0%
			50–59	≥5		27.9% (17–38)	35.0% (20–50)
				≥10		24.1% (15–34)	16.2% (5–27)
				≥15		19.4% (11–27)	8.6% (1–17)
				≥20		14.7% (8–21)	8.3% (0–16)
				≥30		11.4% (6–17)	4.3% (0–10)
			60–70	≥5		52.1% (33–71)	46.9% (31–63)
				≥10		32.2% (17–48)	25.6% (13–38)
				≥15		24.2% (12–37)	15.9% (6–26)
				≥20		15.0% (8–22)	13.0% (3–22)
				≥30		8.6% (4–14)	5.9% (0–13)
		Ptywaczewski et al., 2008 [45]	41–49	>5		25.3%	6.9%
				>10		12.0%	1.1%
			50–59	>5		31.5%	13.5%
				>10		21.5%	6.3%

(continued on next page)

Table 4 (continued)

Type of sleep study used to diagnose OSA	Criteria used to diagnose OSA ^a	Study reference	Age (y)	AHI/RDI level (events/h)	Directly reported or estimated prevalence ^b		
					Unclassified	Among males	Among females
Type 3		Olson et al., 1995 [50]	60–69	>5		44.8%	29.9%
				>10		22.4%	14.0%
			≥70	>5		73.3%	46.1%
				>10		26.7%	30.8%
			35–39	≥15		7.5%	
			40–44	≥15		10.7%	
			45–49	≥15		11.6%	
			50–54	≥15		15.6%	
			55–59	≥15		19.1%	
			60–64	≥15		15.4%	
Type 4		Jennum & Sjøel, 1992 [49]	30	≥5		3.2%	5.3%
			40	≥5		12.0%	5.1%
			50	≥5		10.2%	7.7%
			60	≥5		18.3%	7.6%
			35–39	≥15		40.9%	
			40–44	≥15			
			45–49	≥15			

OSA = Obstructive sleep apnea; AASM = American academy of sleep medicine; AHI = Apnea hypopnea index; RDI = Respiratory disturbance index.

^a See Table S7 for details.

^b % is the reported direct or estimated prevalence. When available, the 95% confidence interval is given within parenthesis.

group (see Fig. 2), for males and females separately. These graphs indicate that, within a given study, and within each AHI/RDI category, the prevalence of OSA increased with increasing age. They also show that within the same study and within each AHI/RDI category, men have a higher prevalence compared with women. Both these trends are also true for OSAS (see Table S9).

We then extended this analysis to examine how the use of 3% vs 4% oxygen desaturation to define hypopnea affects the prevalence estimates (see Fig. 3). Although, in general, it appears that the studies using 3% oxygen desaturation to define hypopnea reported higher prevalence for a given age and sex sub-group compared with the studies that used 4% oxygen desaturation to define hypopnea, the number of studies in each sub-group is

inadequate to draw meaningful conclusions. We used a similar method to examine how the use of thermistor/thermocouple or nasal pressure measurements changed the OSA prevalence estimates (see Fig. 4). Although the other methodological heterogeneity and the small number of studies in each sub-group prevents direct comparison between the included studies, in general, it appears that the use of nasal pressure measurement leads to reporting of higher prevalence for the same age and sex sub-group compared with when thermistor or thermocouple was used to record the airflow.

Only Tufik et al [16] reported data for men and women in separate age groups using AHI categories that are mutually exclusive (>5 to <15 and ≥15 events/h). When the ratio of the

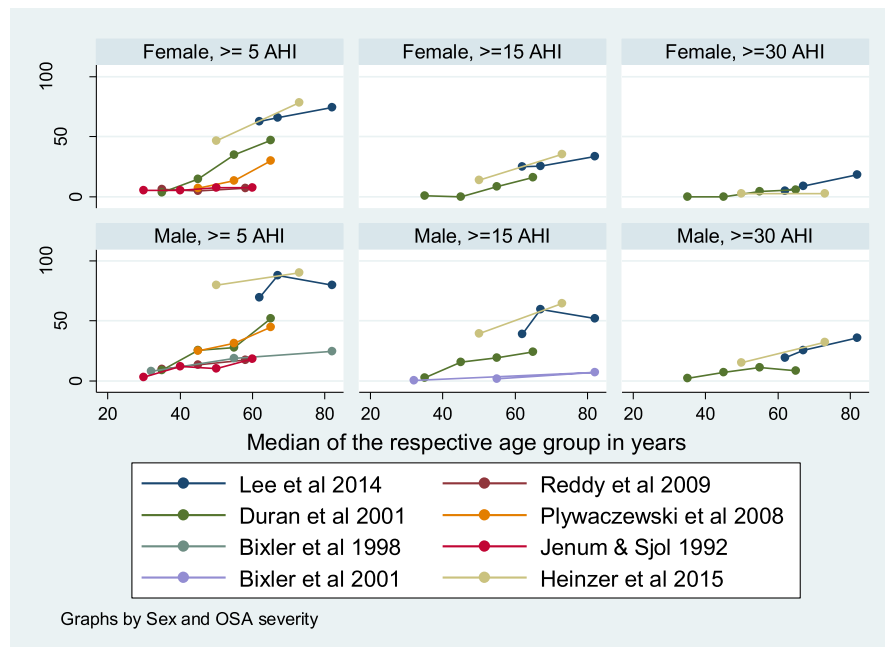


Fig. 2. Distribution of the OSA prevalence by age, sex, and severity of disease (AHI in the graphs represents either AHI or RDI); OSA = Obstructive sleep apnea; AHI = Apnea hypopnea index; RDI = Respiratory disturbance index.

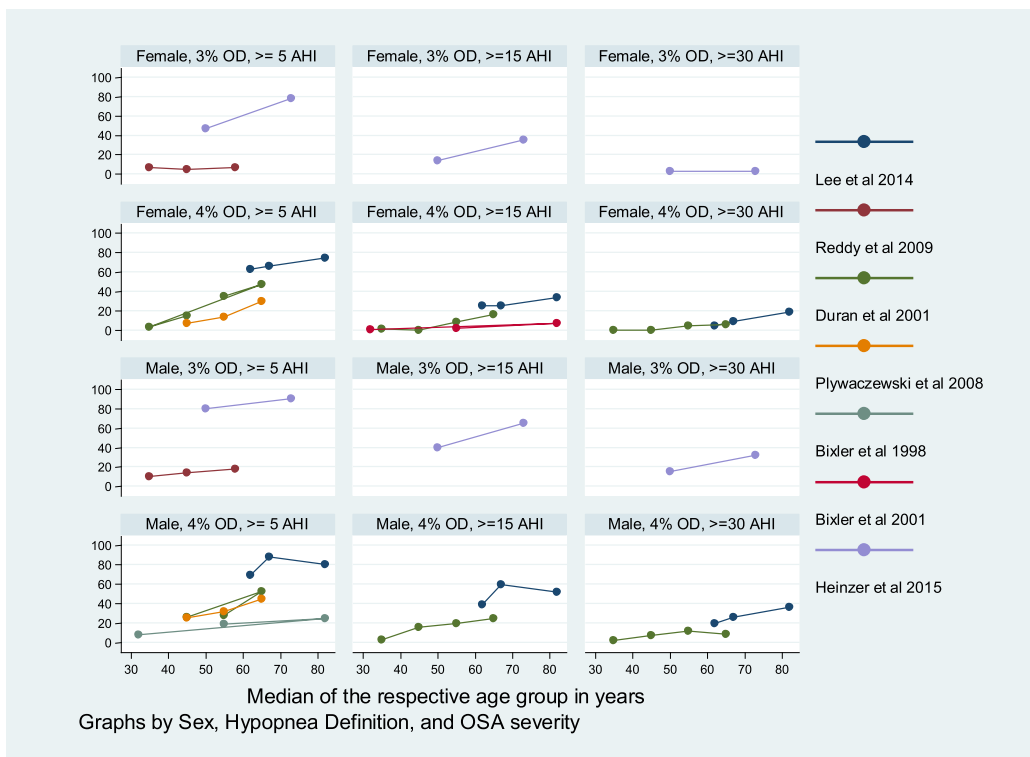


Fig. 3. Distribution of the OSA prevalence by age, sex, definition of hypopnea used, and severity of disease (AHI in the graphs represents either AHI or RDI); OSA = Obstructive sleep apnea; AHI = Apnea hypopnea index; RDI = Respiratory disturbance index; OD = Oxygen desaturation from baseline.

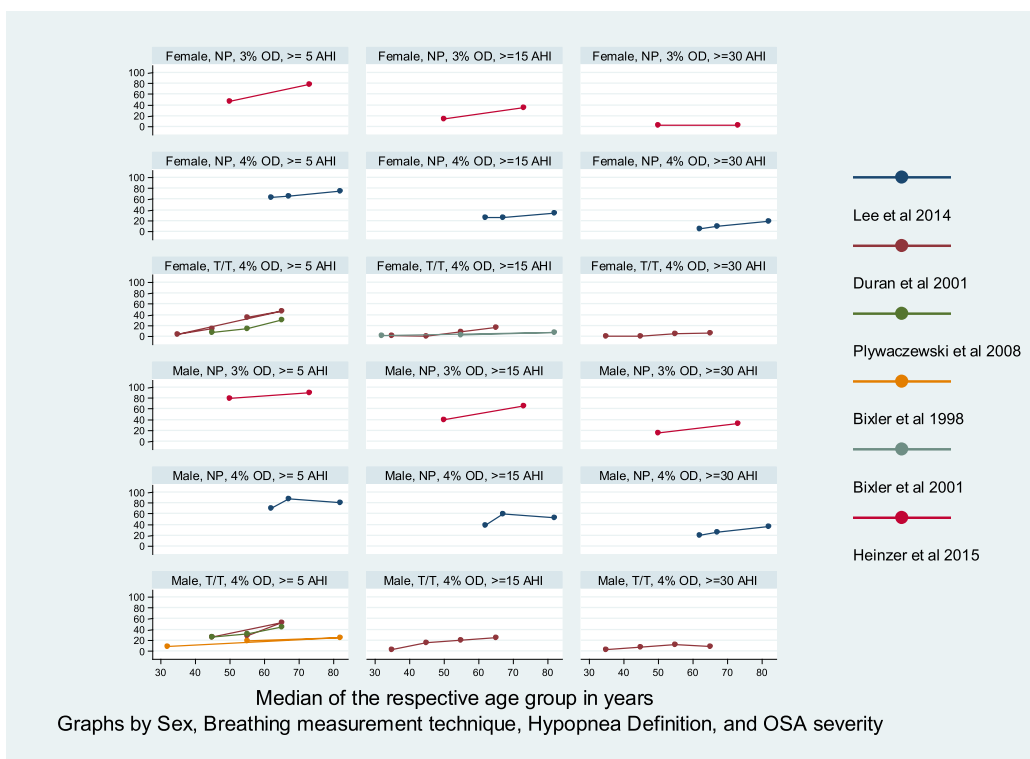


Fig. 4. Distribution of the OSA prevalence by age, sex, definition of hypopnea used, method used to measure airflow, and severity of disease (AHI in the graphs represents either AHI or RDI); OSA = Obstructive sleep apnea; AHI = Apnea hypopnea index; RDI = Respiratory disturbance index; OD = Oxygen desaturation from baseline; NP = Nasal pressure used to measure airflow; T/T = Thermistor or thermocouple used to detect airflow.

proportions reported in this study were analyzed it shows that, in both men and women, as age increases the ratio of less severe disease to more severe disease decreases (i.e., there is an overall increase in severity of OSA with age in both sexes) (see Fig. S1). Fig. S2, which uses the same data, indicates that moderate or severe OSA predominates in men whereas mild OSA predominates in women.

In the study by Tufik et al. [16] (see Table S10 and Fig. S3) moderate to severe OSA was markedly increased in obese men and women when compared with overweight men and women. Prevalence of mild OSA also increased in the same manner in women, but not in men. Similar increases were also reported in Bixler et al. [55].

Discussion

OSA in the general adult population ranged from 9% [46] to 38% [16], and was higher in men compared with women. Prevalence of OSA increased with increasing age. It was also greater in obese men and women compared with overweight men and women. However, diagnostic criteria and the age groups and cut-off levels of the indices used in reporting sleep apnea varied widely between studies. Reported prevalence of OSA/OSAS also varied considerably depending on the diagnostic criteria used and the age and sex of the study population.

The prevalence in the elderly population is strikingly high; at ≥ 5 events/h AHI, this was 88% in men aged 65–69 y [44] and 90% in men aged 60–85 y [12], the corresponding figures in women being 66% [44] and 78% [12]. Even at the clinically important ≥ 15 AHI level, the prevalence in the overall adult population ranged from 6% [46] to 17% [16] whereas in the advanced age-groups this was as high as 49% [12]. However, the reporting of prevalence based on the traditionally accepted cut-off levels of AHI ≥ 5 , ≥ 15 , and ≥ 30 events/h is arbitrary and is not evidence-based. Heinzer et al. [12] suggested a shift in the ≥ 5 events/h AHI cut-off as it measures a high prevalence of OSA at this threshold given the sensitivity of current recording techniques and scoring criteria. As our review shows that apnea-hypopnea events occur in a large proportion of the general population, and the variability in the reported prevalence depends on the technicalities of measurement, it may be justified to attempt to reach consensus to consider OSA as a disease with a continuum in the population and revise the diagnostic criteria through an evidence-based process to determine an AHI cut-off point that is diagnostic of “need-to-treat” OSA. As in the case of hypertension, hyperlipidemia, and diabetes mellitus, this diagnostic AHI level where the treatment needs to begin can be determined based on the related morbidity/mortality profile. Although only one study included in our review used ODI to describe OSA [54], it may be important to determine similar cut-off points for ODI as well, given the recent evidence of independent association between intermittent hypoxia and diabetes mellitus (type 2), dyslipidemia, and hypertension [64–66]. It is also timely to establish a treatment protocol where treatment becomes increasingly aggressive as AHI/ODI increases further from this cut-off point. A similar argument has also been stated by Heinzer et al. [12] previously. It is important that these processes be primarily based on evidence generated through prospective studies rather than expert opinion. Although the preparations of past and present clinical guidelines have been based on available evidence, this evidence has been constrained by several methodological issues including those mentioned in this review.

This is the first systematic review of the literature on the prevalence of OSA in adults in all regions of the world. A previous systematic review limited to the Asian region [4] also differed in a

number of important areas. It included: studies that had not measured sleep apnea objectively; studies on population groups that did not represent the true general population or the age-sex-specific subgroups thereof; and, studies with weighted sampling, the effects of which had not been adjusted for when reporting prevalence. These key differences may explain why their reported prevalence (ranging from 3.7% to 97.3%) [4] differed markedly from our findings.

The most significant strengths of our systematic review are that we included all studies from around the world, but only those that measured the prevalence of OSA in the true general population (or age-/sex-specific subgroups thereof) and measured sleep apnea using standard objective instrumental measurements. However, due to the strict selection criteria we used, we excluded some well-known sleep cohort studies such as the Wisconsin sleep cohort study (WSCS) [5,67] and the sleep heart health study (SHHS) [68,69] (see Table S11). Although these studies have contributed greatly to the evidence on epidemiology of OSA, they were deemed ineligible for our review due to following reasons. Our main objective was to determine the general population prevalence of OSA, so our inclusion criteria required general-population-based samples. The WSCS was excluded as its sample was selected from an employed population, and the SHHS sample was assembled from existing cohorts (not directly from the general population) and excluded a proportion of existing OSA patients [69]. Due to differences in diagnostic criteria used, the prevalence reported in the studies included in our review cannot be compared directly with the prevalence reported in these two studies. Nevertheless, the prevalence reported in some of the included studies [16,45,48] were also similar to those in the WSCS [5] and SHHS [68].

To examine if the language criterion we used was a threat to the validity of our systematic review, we duplicated the search strategy to search for non-English language articles in PubMed and Embase databases. This resulted in 407 articles, the screening of titles and abstracts of which suggested that six of those (one each from Poland and Switzerland, and four from China) would be eligible for full-paper screen (see Fig. S4) if they were in English. This proportion of 1.5% of screened abstracts being eligible for full-paper screening (six out of 407) is comparable with 1.6% of screened abstracts being eligible for full-paper screen (59 out of 3807) in our review. In our review, 24 out of the 59 articles we screened fully were eligible for inclusion in the review; if this eligibility fraction of 40.7% was applied to the above six studies only two of them would become eligible for inclusion. This suggests that, at most, only a handful of studies have been excluded on the basis of being non-English. Furthermore, estimates from Poland and Switzerland are already available in our review as they are covered in other English language articles [12,45].

The fact that almost all the included studies found an increasing prevalence of OSA with increasing age is of significance to countries with older or ageing populations. The male predominance, especially with the more severe disease, needs to be given due regard, especially in planning risk-reduction interventions. Although only one study reported OSA prevalence by BMI categories [16], the finding of higher prevalence in obese men and women has been recognized clinically and in other literature [17,18,70]. It is notable that the WSCS found that 10% weight gain led to a 6-fold increase in the odds of developing moderate-severe OSA, independent of confounding factors such as age and baseline body habitus measures [18].

The heterogeneity in a) the sampling methods, b) the diagnostic criteria used, c) method used to measure airflow (nasal pressure measurement vs. thermistor or thermocouple measurement),

d) age-/sex-specific subgroups used to report prevalence, and e) the cut-off levels in indices used in reporting the prevalence in the studies we reviewed make comparison of these studies with each other difficult and preclude pooling of the data through meta-analysis. Due to the same reason, we could not sufficiently achieve our aims of determining how prevalence estimates varied over time and according to measurement criteria used to detect OSA. These variations are also likely responsible for the dissimilarity in the prevalence reported in these studies, even within similar age-/sex-specific subgroups. It would be useful, especially when tracking the trends in OSA prevalence, if the studies reported prevalence based on more than one OSA diagnostic criterion. This argument is strengthened by the fact that Heinzer et al [12] have shown that when AHI is analyzed using different criteria, the respective median AHIs differ drastically even within the same age- and sex-specific subgroup, especially between AASM 2007 and AASM 1999 or AASM 2012 criteria. The wide variation in the diagnostic criteria also raises the question as to what measure is best to determine the presence of OSA in a population, and more particularly, what thresholds should be used to define disease presence and severity. Even within the AASM criteria, successive versions have altered the ease by which hypopneas are able to be scored, but diagnostic thresholds for defining OSA and moderate – severe OSA have remained unchanged (see Table S7). The diagnostic threshold used has direct implications on the proportion of subjects given a diagnosis of OSA in any given population [26]. A consensus on OSA definition and a standardized measurement process is required to accurately quantify the global burden of this emerging public health problem.

Our attempt to compare estimates of prevalence based on the prevalence reported in the selected studies was also constrained by the time-related trends in the prevalence of OSA risk factors. For example, the changes in the global prevalence of obesity from 1980s to present [19–23] as well as that of population ageing [71] (both of which are risk factors for OSA [17,18,27,72]) are likely to have contributed to the variation seen in the reported prevalence in studies from different timeframes. In addition, the completeness of the sampling frames and the variation in the sampling processes are two conditions that would also have affected the reported prevalence. Most of the studies had not commented on the completeness of the records they used as sampling frames. Although it would be fair to assume that the social security codes, census data, or electoral registers would have provided relatively complete sampling frames, the same may not be true for the telephone directories and combinations of various records. Moreover, when the exact nature of the sampling frames was not stated clearly in studies [43,54,59], it limited the extrapolation of the reported prevalence data. When a study used weighted or unequal probability sampling, the methodology of the article contained some description of the adjustments made to correct for the sampling process [16,41,42,46–48,55–57,59]. However, often the details given were inadequate to decide to what extent these adjustments have adequately corrected the prevalence estimates for the sampling process used. Furthermore, several studies reported high non-response rates (e.g., Johansson et al., 2009 [58], Mihaere et al., 2009 [60], Lee et al., 2014 [44]), which will have affected the reported prevalence if these non-response rates were related to the OSA risk in the samples. Similar methodological issues also arise when questionnaires were used to screen the sample to detect groups at high risk of OSA prior to sleep studies. As the sensitivity and specificity of the study-specific questionnaires [41,42,46,47,55,56,59] are not reported, screening prior to sleep studies may have introduced errors that could not be accounted for. If the sensitivity of these questionnaires were <100% at the chosen threshold, some participants with OSA would be missed,

underestimating the prevalence. As most of these studies have used screening questionnaires that had been developed for each specific study rather than commonly used standard OSA screening questionnaires that have known sensitivity, it was not possible for us to quantitatively estimate to what extent the use of screening questions to filter-in the sample for sleep studies affected the reported prevalence. Any screening tool that has less than perfect sensitivity will have resulted in a bias towards lower measured OSA prevalence.

An important finding in this review is the very low number of OSA prevalence studies (based on the true general population and using sleep studies) in Latin American and Asian regions, and the total absence of such studies in Africa. More than half of the studies that measured prevalence of OSA using objective sleep measurements were conducted in Europe. Although there were several studies in Asian [4] and Latin American [73–76] regions that did not meet the strict criteria we used, we could not find any population prevalence study conducted in the African region. However, this can be a result of language criterion we used. As such, the results from this review represent the prevalence and major risk factors for OSA predominantly in westernized settings.

Conclusion

This systematic review has highlighted both the substantial methodological heterogeneity that exists in studies that investigated the population prevalence of OSA, and the resultant wide variation in the reported prevalence: the overall prevalence of any OSA ranged from 9% to 38% in the general adult population, from 13% to 33% in men and from 6% to 19% in women, although much higher in the elderly groups. The available data were primarily limited to Europe and North America. Despite these limitations, this systematic review confirms the positive effect of advancing age, male sex, and higher BMI on OSA prevalence. Furthermore, there is a current need to generate consensus on the methodology and diagnostic threshold to define OSA, so that the prevalence of OSA can be validly compared across regions and countries, and within age-/sex-specific subgroups. Further consideration is required to reach a consensus on guidelines for the treatment of clinically important OSA, considering its apparent continuum in the general population. Detailed information on population prevalence of OSA from the current evidence-sparse regions will help determine the global disease burden of OSA more accurately, and repeated measurements over time will enable us to draw conclusions on time trends.

Practice points

- 1) OSA prevalence is high in the general population.
- 2) OSA prevalence is higher in older ages, in males, and in those with higher BMI.
- 3) OSA prevalence and severity estimations depend significantly on the type of sleep study and definitions of the measurement indices used.
- 4) Given the high levels and wide variation in reported prevalence, as well as the effects of ageing, OSA must be considered as having a continuous range in the general population (where there is overlap between physiology and pathology), rather than a disease with dichotomised cut-off points.

Research agenda

1. This review highlights the need for consensus on methodology to study and report OSA prevalence.
2. Prevalence studies based on the true general population are limited. Future prevalence studies need to ensure that the samples included are representative of the true general population.
3. Most of the prevalence studies have been done in the western or westernized settings. Prevalence data from the general populations in many other parts of the world are limited. Data from these evidence-scarce regions are needed to determine the global epidemiology of OSA.
4. Some population prevalence studies have used very small sample sizes, which may not be sufficient to detect the true population prevalence. Future population prevalence studies need to ensure that their samples are adequate in size.
5. Given the continuum of OSA in the general population, future research needs to determine the point at which treatment should be started based on the possible morbidity profiles of patients. Research is also needed to determine how treatment should vary when disease severity increases. Furthermore, it is also important to determine through prospective studies the genetic, physiological, epidemiological, or sleep study-related parameters that allow better stratification of the risk for developing comorbidities associated with OSA.

Conflicts of interest

Prof Hamilton has received equipment for research from Resmed and Philips Respironics. None of the other authors declared conflicts of interest.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at <http://dx.doi.org/10.1016/j.smrv.2016.07.002>.

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