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## Simple Snoring: Not quite so simple after all?

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**Abstract:**

Simple snoring (SS), in the absence of obstructive sleep apnoea (OSA) is a common problem, yet our understanding of its causes and consequences is incomplete. Our understanding is blurred by the lack of consistency in the definition of snoring, methods of assessment, and degree of concomitant complaints. Further, it remains contentious whether SS is independently associated with daytime sleepiness, or adverse health outcomes including cardiovascular disease and metabolic syndrome. Regardless of this lack of clarity, it is likely that SS exists on one end of a continuum, with OSA at its polar end. This possibility highlights the necessity of considering an otherwise ‘annoying’ complaint, as a serious risk factor for the development and progression of sleep apnoea, and consequent poor health outcomes. In this review, we: 1) highlight variation in prevalence estimates of snoring; 2) review the literature surrounding the distinctions between SS, upper airway resistance syndrome (UARS) and OSA; 3) present the risk factors for SS, in as far as it is distinguishable from UARS and OSA; and 4) describe common correlates of snoring, including cardiovascular disease, metabolic syndrome, and daytime sleepiness.

**Keywords:** Breathing, Habitual snoring, Obstructive sleep apnoea, OSA, Primary snoring, Simple Snoring, Sleep, Upper airway resistance syndrome, UARS

Snoring is a common problem, yet prevalence estimates vary widely. The lack of clarity around snoring prevalence is in part a reflection of unresolved issues concerning its definition(s). Most authors agree on what snoring is: "...a fluttering sound created by the vibrations of pharyngeal tissues..." (1); or more generally "...a sound produced by the upper aerodigestive tract during sleep..." (2). There is less agreement as to what counts as clinically significant snoring, as well as the nature of the distinctions, qualitative or quantitative, between simple snoring (SS), upper airway resistance syndrome (UARS) and obstructive sleep apnoea (OSA). This picture is further confused by the variety of actual and proposed assessment methods for each of these disorders, and the variety of putative physiological and anatomical correlates within each snoring classification. Finally, the degree of associated daytime dysfunction is often, but not consistently, used as a distinguishing diagnostic marker and this in turn has (confusing) implications for clinicians and treatment decisions.

## **Prevalence**

In one of the largest prevalence studies to date, a Hungarian population survey of 12,643 people, 50% self-reported being loud snorers (3). The sample was subdivided into loud and habitual snorers, and further by gender. Thirty-seven percent of males self-identified as being loud snorers with breathing pauses and 23% habitual snorers; whereas in females 21% identified as loud snorers with breathing pauses and 21% as habitual snorers. Several factors may influence prevalence variation across studies, and between nations, including socio-demographic characteristics of study populations; health behaviours and variation in assessment methods and classification categories. For these reasons, the authors, like other researchers, concluded that cross-nation comparisons are not possible. Prior prevalence

estimates in other epidemiological studies varied between 2% and 85%, depending on measurements and population variables (4). A similar large population based study of 4533 Latin Americans, reported a prevalence of ~60% in four Latin American cities, with approximately 10% higher prevalence in males than females (4). There have been other recent international prevalence estimates. Adewole and colleagues estimate a 32% habitual snoring prevalence in a small sample of 370 adults in Nigeria (5). In one of the first studies in a Pakistani population, Hussain and colleagues surveyed 2497 adults and reported an average prevalence of self-reported snoring of 32%, yet in middle age (>35 years of age) prevalence was 46% (6). In a sample of 8583 Japanese adults (35-79 years of age) prevalence rates were 24% for men and 10% for women (7). This sex difference is perhaps not surprising given that being male is one of the risk factors for snoring (see section below). As well as there being prevalence variation between studies, there is also variation within studies which have looked at the ethnic mix of their populations. Among 1611 Malaysian adults with an overall habitual snoring prevalence of 47%, Indian and Chinese individuals were significantly more likely to report snoring than Malays (8). Further, in a survey of 2298 adults of Indian, Chinese and Malaysian origin, for Indian individuals the odds of reporting snoring were 1.5 times greater than in Chinese individuals (9). European estimates tend to be around 20-40% (1). Possible reasons for ethnic differences in snoring will be considered when we discuss risk factors below.

A major limitation of these studies is the definition of habitual snoring. Hussain and colleagues distinguished between habitual and occasional snoring (5.4% versus 26.9%) with the former being defined as “daily” (6). Other studies have defined habitual snoring as

"often"; or more than 3, 4 or 5 times per week. This is highlighted in one of the few meta-analyses in the epidemiology of snoring (10). This systemic review and meta-analysis of 63 studies reporting on gender differences in the prevalence of snoring identified significant methodological heterogeneity in population, age, sampling frames and assessment methods. Furthermore they found that ~62% of studies did not specify definitional criteria, and 81% did not ask about the loudness of snoring. As such estimates of snoring are somewhat piecemeal, and with continuing lack of internationally agreed definitions, classifications and measurement tools, are likely to remain so.

### **A continuum of snoring?**

Most authors support a continuum of snoring from SS through UARS up to and through degrees of OSA (for example, see 11, 12). OSA has the clearest definition and diagnostic criteria. Objectively it is marked by partial or complete collapse of the upper airway during sleep which leads to total (apnoea) or substantial (hypopnoea) decrease in inspiration which lasts for at least ten seconds (13). The number of these events per hour - the apnoea/hypopnea index (AHI) - is taken as a measure of the severity of the condition.

Conventionally people are classified as mild OSA if they have between 5-15 events an hour, moderate if they have between 15-30, and severe if they have >30 (14), as measured by Polysomnography (PSG). However, even within the relative objectivity of these criteria, there are still variations among researchers in diagnostic thresholds for airflow reduction, oxygen de-saturation and cortical arousal (15).

Patients who snore but have an AHI less than five tend to be classed as primary or habitual snorers (16). OSA is relatively rare compared to snoring, and is generally estimated to affect

2-4% of the population, though estimates suggest that at least 15% of snorers have an AHI >15 (17). This large excess of snorers to OSA patients suggests that the vast majority of snorers are simple or non-apnoeic snorers (also variously called primary, habitual and socially disruptive snorers). One of the main concomitants of snoring is daytime sleepiness, which has been used as a diagnostic proxy, in the absence of PSG, for distinguishing OSA from SS. The justifying hypothesis is that disordered breathing in OSA disturbs sleep. However, as Svensson and colleagues (18) note, linkage between OSA and daytime sleepiness is not clear-cut. Many people with apnoea do not report daytime sleepiness, while many non-apnoeic snorers do. Guilleminault and colleagues (19) attempted to address some of these inconsistencies by suggesting that there is a distinct, third clinical entity between SS and OSA, marked by non-apnoeic, non-hypopnoeic changes in respiratory effort and associated cortical arousal - respiratory effort-related arousals (RERAs) - which are associated with daytime sleepiness. This postulated clinical entity, Upper Airway Resistance Syndrome (UARS) is still disputed (17). The gold standard for objectively measuring increased upper airway resistance is a combination of pharyngo-oesophageal manometry (20) and PSG, with UARS being defined as an AHI <5, an oxygen saturation of 92%, and presence of RERAs (21). In practice the manometric diagnostic gold standard is rarely applied and the distinctions between UARS and OSA, and between UARS and SS are in part inferential, from subjective reports of daytime sleepiness. This reliance of disease classification upon subjective measures runs the risk of reifying clinical entities upon spurious criteria. For instance, patients who attract the UARS label tend to have more medically unexplained, or functional somatic, symptoms. As such, self-reports of daytime

sleepiness or fatigue may have little or no association with sleep quality (see 22), casting doubt on the reliability of the ontology of UARS.

Given the blurred and disputed boundaries between SS, UARS and OSA, it is worth reviewing what is done in practice to distinguish and define them. Several criteria have been proposed.

## **Definitions and Distinctions of Snoring**

### **Distinctions by anatomical and neurological markers**

Several authors have studied the structure and ultra-structure of the palate, following the hypothesis that snoring is a marker of pathology or abnormality of upper aerodigestive tract anatomy. The most popular version of this theory is the obstructive theory of snoring, which hypothesises that hypertrophy of uvular and palatal structures causes narrowing and collapse of airways. Karakoc and colleagues attempted to distinguish 133 SS and 131 OSA patients on an anatomical basis, although found no difference between groups in nasal obstruction (16). However, grouping patients according to their AHI category revealed significant differences in Fujita classification. The Fujita classification is a method of describing the location of any airway obstruction as seen by visual and endoscopic examination during sleep (23). SS patients were much more likely to be classified as type 1 (upper pharyngeal) and OSA as type 2 (hypopharyngeal) (80% and 61%, respectively). Differences in AHI based on Mallampati classification - which approximates to the tongue size relative to palate and pharynx (24) - were also significant: the greater the relative tongue size, the higher the AHI category. Finally a measure of collapsibility of the pharyngeal walls was also positively and significantly related to AHI. All of this would suggest that there



are at least quantitative differences between SS and OSA, although there was no normal control group for comparison. By contrast, in a battery of similar measures comparing 20 SS with 32 mild and 22 moderate OSA patients, Balsevičius and colleagues found only clinical assessment of tonsil size distinguished SS from the other two groups: SS had a higher Friedman's score of palatal tonsils (25). In a radiographic (CT scanning) comparison 34 SS patients had, predictably, less pharyngeal narrowing than did 33 OSA patients, but no useful quantitative metric emerged (13).

A cephalometric study compared posterior airway space (PAS), mandibular plane and hypoid distance (MPH), craniofacial angle (C3FI), and soft palate length in OSA, SS and normal controls. (26). Greater MPH (reflecting downward displacement by the tongue base), longer soft palate and narrower PAS distinguished OSA/SS from normal controls. As expected, the MPH and PAS values were higher in OSA than SS (26).

The clinical, endoscopic and radiographic anatomical literature suggests that whilst there are some markers that may be more pronounced in some OSA than SS patients, no single marker offers reliable clinical distinction. However the anatomical theory of snoring causation is not the only one to have been investigated.

Bassiouny and colleagues investigated an alternative, neurogenic hypothesis of OSA (27). This postulates neural degeneration of local nerves, whereby the vibratory effect of snoring causes nerve atrophy which in turn leads to muscle atrophy (as opposed to the proposed muscular hypertrophy of the obstructive theory). Despite the small sample, there was evidence of excess nerve fibre degeneration in 10 OSA patients compared with non-apnoeic snorers or controls. Interestingly however, another study by the same authors found

evidence for the obstructive theory. They note that this area of research is new and evolving, and that detailed histological and neurological studies are small (28).

Whilst often framed as mutually exclusive, there is no obvious reason why these two theories could not be complementary. Initial, subtle differences in the pharyngeal structure and ultra-structure could lead to snoring, which could cause neural and muscle atrophy of some muscles and compensatory hypertrophy of others, leading to more problem breathing, and further alterations in anatomy and further neural changes. Some theorists have attempted to chart the progression of SS to OSA by investigating a progressive sensory nerve degeneration hypothesis. Hagander and colleagues' comparison of vibration and cold sensation detection in 23 controls, 13 SS and 31 OSA participants found that controls were distinct from both snorers and OSA in their cold detection ability (higher) (29). The authors postulate that the vibratory impact of snoring may be a self-perpetuating cycle, causing progressive nerve lesions that impair the ability of the upper airway muscle to maintain upper airway patency. If nothing else, this gives us reason to take SS seriously, even in the absence of present pathology or impairment.

### **Distinction of SS from UARS**

Other authors have attempted to establish a neurological distinction of SS from normal controls and from UARS. Gates and colleagues report one of the few studies of autonomic dysregulation in 11 normotensive non-apnoeic snorers without UARS or cortical arousal, and found evidence of increased sympathetic and decreased parasympathetic nervous activity in snorers compared to controls (30). As autonomic dysregulation and heart rate variability are both part of the hypothesised mechanism whereby snoring can lead to

cardiovascular events, this work indicates that non-apnoeic snorers, even in the absence of UARS, are on a continuum of disease vulnerability, ending in severe OSA. In another study the same authors found that baroreflex sensitivity was decreased in normotensive healthy non-UARS snorers (31). Again, baroreflex sensitivity, part of the regulatory system controlling blood pressure, has been implicated in the causal chain, leading from sleep disruption in OSA to hypertension.

The argument that simple snorers, rather than being a distinct group, are part of disease pathogenesis on a snoring continuum, is corroborated by a survey of all-cause mortality in 77,260 snorers which indicated that increasing levels of snoring were linked to mortality, particularly in non-obese, non-apnoeic snorers (OR = 1.16). This indicates that SS is in itself a risk factor for increased mortality (32). Non-palatal snoring was particularly linked to mortality, independent of either AHI or body mass index (BMI). The data do allow for objective measurement of the mechanistic links between snoring and mortality, however they propose two likely candidate mechanisms, both of which echo the research reported above. The first is the direct effect of vibrations on carotid artery atherosclerosis, leading to cardiovascular mortality; the second is a more indirect route, similar to that proposed by Gates and colleagues whereby hypoxia and/or respiratory effort has a long term physiological impact (31). These authors are also cautious of endorsing UARS as a distinct entity. This also fits with the findings of the two studies by Gate's team which seem to show that the effects of snoring on physiological functioning, as measured by autonomic dysregulation, occur independently of UARS or cortical arousal. Contrastingly, Pepin and colleague's review of UARS concludes that there is no extant convincing evidence of any link between UARS per se and cardiac morbidity (17).

The nature of the distinction between UARS, OSA and SS is the focus of a large study by Stoohs and colleagues (22). They performed a retrospective chart analysis of 2753 patients, 157 with SS, 424 with UARS, 562 with OSA and no sleepiness and 1610 with OSA and daytime sleepiness. Problematically, no formal analysis of RERAs was performed on the entire cohort to distinguish SS from UARS; rather they were distinguished according to self-reported daytime sleepiness. As mentioned above, this subjective means of classifying UARS may be confounded by the relationship between UARS and functional somatic symptoms. However, subsequent to this subjective classification, a post-hoc subset analysis was performed on 15 patients with SS and 15 with UARS. Within this subset UARS did exhibit more RERAs within non-REM sleep during 40 randomly selected epochs than SS. However, there were no differences in *objective* measures between SS and UARS cohorts. Yet the UARS subset reported more *subjective* impairment than both OSA groups in measures of joy for life, depressive mood, ability to concentrate, difficulty with daytime activities and quality of life in general. These measures of subjective impairment were independent of sleep-related breathing difficulties and BMI. Crucially, as the authors note, UARS perceived the quality of their sleep as worse than any other groups, but these subjective assessments bore no relationship to objective PSG findings.

So, in sum, the UARS group, whilst otherwise indistinguishable from the SS group, had the highest levels of distress and subjective perception of daytime dysfunction. As mentioned, several authors (see 17, for a review) have noted overlap between UARS and functional somatic syndromes, and this would inform one interpretation of the findings of Stoohs and colleagues' study. It could be argued that rather than being a distinct sleep disorder entity, UARS, certainly as measured here largely based on self-report, represents a sub-group of

people with snoring and low AHI who also have high general psychosomatic distress. Several other features of Stoohs' study support this interpretation. The UARS group had the lowest levels of objective illness markers, including hypertension, but higher rates of self-reported reflux and rhinitis, both suggestive of autonomic dysfunction. They also reported high levels of daytime sleepiness and daytime naps, and had the highest female to male ratio (3:1) of any of the groups. This combination of high self-reported distress, autonomic dysfunction, increased prevalence of daytime sleepiness and daytime napping, and the female to male ratio are all identical to findings in populations with functional somatic syndromes such as CFS and Fibromyalgia (33, 34).

Given this, the use of self-reported sleepiness should probably be considered with extreme caution in UARS. To their credit the authors do perform the 30 patient subset analysis, but this is both post-hoc and not necessarily representative of the cohort. Until more objectively classified, larger UARS cohort studies emerge, it remains unclear whether UARS is a distinct sleep disorder or merely a marker for people with mild sleep disordered breathing - SS in essence – who may also have functional somatic symptoms. Autonomic dysregulation may be an underlying mechanism involved in both. This merits further investigation.

### **Distinction by daytime impairment**

The fact that sleepiness may not, in and of itself, be the best criterion by which to classify sleep –related breathing disorders is confirmed by two large studies that show that sleepiness is related to habitual snoring, independent of AHI index (18, 35). These observations not only reinforce understanding that snoring is problematic but also further questions using daytime fatigue and sleepiness as a criteria for classifying sleep disorders.

Taken together these studies suggest that anatomically, neurologically, physiologically and functionally the distinctions between SS and OSA are quantitative rather than qualitative, and that SS may be problematic in and of itself not only because it can progress to OSA but because it is independently associated with mortality and daytime dysfunction. The latter is further reviewed below, but the continuum, rather than the distinction between SS and OSA can be seen in most studies of daytime functioning. However the blurred lines between SS and OSA have not stopped researchers attempting to identify other means to distinguish them, with the sound of the snore being the most often investigated.

### **Distinction by sound**

In reviewing the literature on the acoustic assessment of snoring, both Pevernagie and colleagues (36) and Mesquita and colleagues (37) note that the holy grail of snoring research is to find a relatively cheap and reliable marker of OSA that is based on objective biomarkers without employing full PSG. The attempt to do this by the monitoring and analysis of snoring sound, with single or multiple microphones, has been intensively studied over the last two decades. The main conclusion of Pevernagie and colleagues' review is that current snoring sound technology and methodologies of sound analysis are highly variable, and conclusions regarding the relationship between sound quality and sleep disturbed breathing category unreliable. However, they assert that the ongoing attempt to assess acoustic information for the degree, or type, of sleep disordered breathing is a relevant research agenda. Below we point out significant studies omitted or subsequent to their review.

If we take AHI index as a reasonably accurate measure of where people lie on the snoring spectrum, there have been several attempts to capture this acoustically in terms of loudness, duration and/or pattern of snoring. A large study of 4860 home sleep studies investigated the acoustic characteristics of snoring as related to AHI and a number of common health complaints (35). Snoring was measured by placing a pair of microphones on the upper lip, one to measure snoring and the other to cancel ambient sound. This was a population mostly of overweight men who had been referred for home sleep studies where snoring was part of their presenting complaint. Average loudness of snoring, peak loudness and duration of snoring were all highly significantly related to AHI. Sustained loudness had a correlation of 0.62 with AHI, and both sustained loudness and AHI were significant independent predictors of sleepiness as measured by the ESS. Again this indicates, as noted above, that SS may be problematic in and of itself, if the snoring is loud enough. This is supported by a study of 850 French males, where loudness of partner reported snoring was related to daytime sleepiness (38). Furthermore, Azarbarzin and Moussavi (39) examined 42 OSA patients and 15 non-apnoeic snorers measured with a microphone over the suprasternal notch of the trachea. What distinguished the non-apnoeic snorers from the OSA patients was their lack of snoring sound variability. This parameter exhibited a high degree of accuracy and specificity in distinguishing the groups.

Intensity and frequency of snores are also common candidate parameters for distinguishing degrees of sleep disordered breathing. Investigation of 37 snorers with a range of AHI scores, demonstrated that an all-night recording with automated scoring of intensity and frequency could reliably distinguish AHI classifications (40). A large study of snoring volume intensity in 1634 snorers divided into non-OSA, mild, moderate and severe OSA found a

strong correlation between intensity and AHI (0.66) (41). However variability is still high within AHI classifications, precluding the use of intensity as the sole measure of OSA classification.

A contrasting approach is to analyse the segmental pattern of snoring sound generation (37). A cheap and reliable method based on analysis of the variability *within* a snoring segment and the time interval *between* the snoring segments showed intra-segment variability to be higher in OSA patients, whose time interval between snoring episodes was shorter. The analysis is novel in that the parameters studied were much fewer than in most acoustic analyses yet still provides reliable results. The study was relatively small (34 participants with a range of AHI) and needs further validation.

The main gist of this evolving field of research is that in problematic snoring, loudness, frequency and irregularity may be reliable markers of severity.

### **Distinguishing and evaluating types of snoring**

The above findings support the conclusion that there is a continuum of snoring from SS to severe OSA and that the putative intermediate entity - UARS - needs further validation. This continuum is not only one of abnormality of anatomical and neurological dysfunction, but also one of related autonomic dysfunction, disease vulnerability, daytime dysfunction and even mortality. There is a range of techniques for evaluating the snorer, and attempting to classify them: from objective monitoring such as PSG, through visual examination, auditory recording, partner or self-reported snoring and breathing, and subjective daytime dysfunction. However, apart from the rarely applied "gold standard" PSGs, none is a reliable marker of snoring status.



## Risk Factors

One of the few studies of the effect of early life events on adult snoring surveyed 16,190 randomly selected adults in Sweden, Norway, Iceland, Denmark and Estonia (42). The main significant predictors of habitual snoring, here defined as  $\geq 3$  times per week, were recurring respiratory infections as a young child, recurrent otitis as a child, being part of a large family and having a family dog in childhood. The questionnaire was retrospective, and causal pathways speculative, but the authors suggest that all the identified factors are associated with increased risk of upper airway infection/inflammation which may lead to hypertrophy of the tonsils and thus narrowing of the upper airway. However they had no data on tonsillectomy to further investigate this hypothesis. This latter factor was investigated in a study comparing a group of 460 adult volunteers, 227 with tonsillectomy and 233 without tonsillectomy (43). Having had a tonsillectomy significantly reduced the odds of being both a habitual and a severe snorer (odds ratio [OR] 1.81 and 2.61 for non-tonsillectomy vs. tonsillectomy for habitual vs. severe snorers, respectively). This was independent of age, BMI and gender. It is hypothesised that the absence of tonsils widens the upper airway making snoring less likely. They further suggest that the fibrosis of the pharyngeal wall associated with tonsillectomy may prevent both collapse and vibration of the pharynx. As such their findings suggest that tonsillectomy reduces risk factors associated with both anatomical and neurological theories of snoring described above. Another anatomical risk factor is pointed out by Hiraki and colleagues (44). In a population survey of 1459 Japanese adults, snoring was significantly more prevalent in individuals with nasal obstruction and nasal obstruction with allergic rhinitis. However as these features were self-reported rather than clinically assessed, the results must be interpreted with caution.

A large population based survey of 15,555 adults examined the risks associated with active and passive smoking (45). Present smoking, past smoking and passive smoking all contributed to risk of snoring, independently of obesity, sex or age. Indeed, having ever smoked was associated with a much higher risk for developing snoring with the attributable risk being 17.1%, vs. 4.3% for obesity. Passive smoking had an attributable risk of 2.2%.

Whilst most studies point out the association between BMI and snoring, few have studied this longitudinally. One study investigated the development of snoring in a cohort of 8967 adults who had reported not snoring in a 1981 health survey and who were surveyed again in 1994-95 (46). Being male was associated with an odds ratio of 3.5 for developing habitual snoring. Baseline BMI was associated with a 1.4 odds ratio per  $3.4\text{kg/m}^2$  for developing snoring. Change in BMI over the 14 year period was an independent risk factor for snoring development (OR 1.55 per  $2.3\text{kg/m}^2$ ), as was development of asthma (OR 2.8) and starting smoking (OR 2.2). BMI was the focus of a study of 1890 obese adults in an Italian population (47). Whilst 56% of this population were snorers, snoring was positively and significantly associated with weight cycling and weight gain since the age of 20, echoing the longitudinal findings of Knuijman and colleagues (46). Further, in the Italian cohort, physical activity had a small but significant protective effect on snoring, independent of obesity.

However, the relationship between BMI and snoring, whilst strong, needs to be considered in the light of other factors. Svensson and colleagues (48) examined the relationship between BMI and snoring in a random selection of 6817 Swedish women. Whilst the prevalence of self-reported snoring increased with increasing BMI, the strength of the relationship was age dependent. Both being overweight (BMI  $25\text{-}30\text{kg/m}^2$ ) and being obese (BMI  $>30\text{kg/m}^2$ ) were strongly associated with snoring in the younger ( $<55$  years) group

whereas in the older group (55+) only obesity predicted being a habitual snorer. A clear dose-response relationship between smoking and snoring was present only in women of normal weight. Positive associations between alcohol dependence and snoring were present only in under-weight women. This change in the association of risk factors across BMI categories has also been found in mixed gender studies. Nagayoshi and colleagues looked cross-sectionally at the associations between BMI, age, smoking, gender and alcohol in 3138 men and 5345 women aged 35–79 years. BMI quartile (highest versus lowest) was associated with a 3.4 odds ratio of reporting everyday snoring (7). As in Svensson and colleague's survey, they found that the effect for smoking and drinking was stronger in the low BMI (<25) than in the high BMI (>25) group. Both of these large studies report ageing and snoring being linearly associated until the fifth decade, where the association peaks. It then declines from the late fifth decade onwards.

Whilst many studies have looked at health behaviours, lifestyle and early family environment, few have considered wider socio-demographic variables. In a large population survey of 12,270 adults, living in a rural area compared to an urban dwelling significantly increased odds of snoring, attributing this to exposure to bio-mass smoke (12).

Demographic differences, such as BMI, neck circumference, or cranio-facial differences, may be responsible for ethnic differences in snoring prevalence (8, 9).

In one of the largest snoring studies to date - a population based survey of 12,643 Hungarian adults - Torza and colleagues examined an extensive list of socio-demographic factors and their association with snoring (3). This study was notable both for the range of epidemiological and individual factors studied and for its categorisation of snoring severity -

non-snorers, habitual snorers and loud snorers. Loud snoring was associated with low social status, poor education, poor health behaviours (drinking and smoking) and the presence of 1 or more co-morbidities including diabetes, depression, musculoskeletal disorders and chronic pain. Across most of these variables, there was a graded difference between non-snorers, habitual snorers and heavy snorers. E.g. the self-reported prevalence of three or more co-morbid conditions rose significantly across the groups (28% vs. 35% vs. 43%, in non-snorers vs. habitual vs. loud snorers, respectively). A similar gradient was observed for the effects of snoring on daytime sleepiness and accidents. These large population based studies are rare and in some ways complicate our understanding of what causes snoring. For instance, is the association between education and snoring mediated by health behaviours? Their analysis would imply that it is not: lower levels of education predict snoring independently of BMI, smoking, drinking and age. However, this leaves the mechanism of association unclear. What this study does confirm is the fact that the distinctions between simple snoring and problematic snoring are a matter of degree rather than kind, and that simple snoring is in itself problematic.

The consistent findings of the association between snoring and other markers of ill health has led some authors to suggest that snoring is part of, or a marker of, a wider syndrome. A cross sectional survey of 1193 Chinese adults demonstrated that levels of pro-insulin, a strong predictor of cardiovascular risk, was also associated with snoring (OR=1.2) (49). Another study demonstrated that snoring is associated with hypertension independent of obesity in just under 10,000 Korean adults (50). Additionally, a clear dose-response relationship was found between markers of metabolic syndrome - such as

hypertriglyceridemia, low hdl-cholesterol and high fasting glucose - and the presence of snoring. Both studies were cross sectional, and therefore whether metabolic markers may be a cause or consequence of snoring is unclear, but both point to snoring as a marker of a more general illness vulnerability (discussed further below), and again that the degree of snoring associated pathology is related to the degree, rather than the type, of snoring.

Finally, the most consistent risk factor for snoring is being male. In one of the few meta-analyses in the snoring field, Chan and colleagues (10) analysed 63 studies including 104,337 males and 110,474 females. The combined M:F odds ratio was 1.89. In a useful discussion, they point out the usual reasons given for the relationship between gender and snoring: the differences in upper airway anatomy and in the degree and kind of obesity between men and women. However, they also highlight that there may be some sociological mediation at work. Women tend to report that snoring is more stigmatising than men, and there may be a tendency to over-report (male) partners' snoring and under report their own. Given the robustness of the observed gender disparity these less researched aspects deserve further study.

### **Daytime Dysfunction and Associated Difficulties**

The clinical significance of snoring in the absence of OSA, other respiratory disturbances during sleep, or other sleep complaints, is contentious. In this section we review research both supporting and refuting the existence of relationships between snoring and a number of health outcomes including cardiovascular disorder, metabolic syndrome, difficulties associated with daytime sleepiness, and its psychosocial impact on the bed-partner. Despite the wealth of both cross-sectional and longitudinal data on these associations, intricacies

and inconsistencies in the study designs hinder our ability to make an accurate judgement for or against the claim that snoring in the absence of OSA contributes to adverse health outcomes, although given the evidence presented above, its position on a continuum of OSA poses snoring itself as a risk factor for disease onset and progression.

**Cardiovascular and Cerebrovascular disease:** A number of studies have investigated the associations between snoring and cardiovascular difficulties including hypertension, myocardial infarction and atherosclerosis, and conclusions are mixed. Most studies investigating the association between snoring and cardiovascular disease risk have focused on middle-aged men, most likely due to the increased prevalence of both difficulties compared to women, although studies of older adults appear in the literature. Studies investigating these associations typically consider snoring on a continuum based on frequency of occurrence (e.g. never snored, snoring sometimes a month, sometimes a week, or everyday) or intensity (e.g. mild, or moderate vs. heavy, as indicated by either acoustic analysis or percentage of sleep time spent snoring). Cross-sectional studies have demonstrated an association between snoring frequency and cardiovascular risk factors, including hypertension, hyperglycemia, hypercholesterolemia, hypertriglyceridemia, BMI and visceral obesity (49). Likewise, a study of women with type 2 diabetes demonstrated that snoring frequency was associated with similar biomarkers of cardiovascular disorders (17). Snoring frequency has also been associated with increased carotid artery intima-media thickness and the presence of plaque (together an indicator of subclinical atherosclerosis) (51). Similarly, heavy snoring, as compared to mild or moderate snoring, has been associated with risk for carotid atherosclerosis, independent of other risk factors including OSA severity (52). However, other studies have failed to find an association between carotid

artery intima-media thickness and snoring frequency (53), or atherosclerotic manifestations and snoring habits (54).

Other studies have considered the confounding influence of age on the association between snoring and cardiovascular abnormalities. Male snorers <40 years of age in a Korean population survey showed a more pronounced prevalence of hypertension than did snorers aged 40-60 years; whereas in female snorers, both age groups showed comparable increased prevalence of hypertension compared with non-snorers (55). In a larger, Hungarian population survey quiet snoring in women, regardless of age, was also associated with hypertension (56). Likewise, both young and old adult loud snorers with breathing pauses (as opposed to quiet snorers) were more likely than non-snorers to experience hypertension or myocardial infarction. Interestingly, prevalence of stroke showed a dose-response relationship between snoring categories in younger adults only, whereas in older adults, stroke was equally common in non-snorers, quiet snorers and loud snorers with breathing pauses. This study is important as it suggests that informal, self-determined distinctions of different types of snoring may facilitate the identification of individuals at risk for severe cardiovascular disease, but also highlights that less severe snoring (quiet snoring without breathing pauses) has adverse cardiovascular concomitants.

Longitudinal studies have also provided mixed evidence for the role of snoring as an independent predictor of cardiovascular difficulties. For example, a recent US government funded, longitudinal study of post-menopausal women demonstrated a 40% increased risk of stroke and all cause cardiovascular disease in frequent snorers (compared to occasional- or non-snorers) over the course of a decade, after controlling for other cardiovascular risk factors such as obesity, hypertension and diabetes (57). Another US study examined the

predictive value of snoring as a risk factor for mortality in the 8 years following myocardial infarction, and demonstrated that both occasional (including some occasions per year or month) and regular heavy snorers (daily) were twice as likely to die within 28 days following infarction than non-snorers after correcting for age, gender, obesity, history of diabetes and hypertension, physical activity, smoking, and education (58). This study demonstrates that even occasional snoring influences short-term mortality post myocardial infarction. In a study of hypertension, Kim and colleagues demonstrated that snoring in the absence of hypertension at baseline was associated with a 1.5 fold increased risk for hypertension at 2 year follow-up (59). Others have focused on the role of daytime sleepiness in the prediction of adverse cardiovascular outcome. For example, Leineweber and colleagues demonstrated that snoring coupled with feelings of tiredness predicted increased progression of atherosclerosis over 3 years (60). A cross-sectional study demonstrated that the combination of snoring with EDS was a risk factor for hypertension, but not either symptoms in isolation (61). A recent longitudinal study of adults >70 years of age elegantly teased apart the effect of snoring and EDS on cardiovascular disease (including myocardial infarction, angina pectoris, or congestive heart failure) (62). Over a 9 year period, individuals exhibiting snoring with sleepiness at baseline were 40% more likely to have experienced a cardiovascular event at follow-up compared to those with only one of these symptoms. Similarly, another longitudinal study found that whilst snoring EDS was associated with increased mortality rate over a 10-year follow-up period in middle aged men, increased risk for mortality was not present in individuals exhibiting snoring without EDS (63). However, increased risk for mortality diminished in adults after 60 years of age, suggesting that snoring and EDS linked mortality decreases over the lifespan, perhaps as other factors pose



greater risk to mortality as one ages. In the context of OSA, some have suggested that moderate symptoms in older adults serve as a survival advantage (64). Thus, it is possible that the combination of snoring and daytime sleepiness, rather than snoring alone, predicts likelihood of cardiovascular complications. However, age effects are inconsistent.

It is possible to posit several likely mechanisms through which snoring may influence cardiovascular difficulties. One study investigated chemoreceptor response during voluntary apnoea and demonstrated increased mean arterial blood pressure in snorers compared to non-snorers (65). Increased arterial blood pressure may be triggered by an increase in sympathetic activity following hypoxia, leading to an exaggerated cardiac response. It has been suggested that the efficiency of the baroreflex may be disrupted by continuously heightened sympathetic output in snorers (66). Although it is possible that intermittent hypoxia, repetitive desaturations and resultant increased sympathetic activity may contribute to cardiovascular complications, it has been suggested that snoring vibrations themselves have the potential to damage carotid arterial walls and contribute to plaque rupture as observed in atherosclerosis (67). A further possibility is that the association between snoring and cardiovascular events is mediated by obesity. Nagayoshi and colleagues demonstrated an increased risk of cardiovascular events including myocardial infarction, angina pectoris, sudden cardiac death and stroke in female snorers, but that these associations were attenuated after adjusting for BMI (68).

However, it should be noted that the majority of studies reviewed above did not explicitly exclude apnoea symptoms (such as breathing pauses) from their snoring groups. It is likely that at least some of the individuals categorised as habitual snorers within these studies may have also had apnoea (of which snoring is a primary symptom). Indeed, Joo and

colleagues, investigating snoring frequency highlighted that nearly half of their 'snoring' sample also exhibited OSA (69). Kamil and colleague's cross-sectional study differentiated habitual snorers from clinically diagnosed OSA cases yet demonstrated increased risk for hypertension and ischemic heart disease in snorers, and albeit to a greater degree, in individuals with OSA (8). Contrastingly, one of the only longitudinal studies to differentiate habitual snorers from individuals with diagnosed OSA found that habitual snorers exhibited comparable risk of cardiovascular events as non-snorers, and that only individuals with OSA were at risk of cardiovascular events over a 7 year follow-up period (70). Likewise, a study which objectively measured snoring and its association with mortality, cardiovascular disease and stroke over the course of 17 years showed no effects of snoring after controlling for OSA (71). Thus, based on the current data, it is not possible to determine whether snoring in the absence of other apnoea-related symptoms (such as upper airway resistance) increases risk for cardiovascular disease. However, because snoring is considered a precursor to the development of apnoea, early identification and treatment could prevent disease progression. Further, self-reported snoring frequency could be used as a screening tool to aid in the detection and prevention of premature cardiovascular disease.

**Metabolic syndrome:** Contrary to investigations of cardiovascular disease, recent studies of risk for metabolic syndrome in snorers have largely been cross-sectional. Leineweber and colleagues demonstrated a five-fold increased risk of snorers compared to non-snorers to experience metabolic syndrome defined using a combination of fasting serum glucose level, arterial blood pressure, fasting serum triglycerides, cholesterol, and obesity in a sample of healthy middle-aged women after controlling for age, menopause, smoking, activity level and education (72). Interestingly, this effect was independent of poor sleep quality,

suggesting that the mechanism of action is purely related to the respiratory difficulty, possibly through increasing micro-arousals and sleep fragmentation and disrupting the restorative value of sleep rather than its psychological effects on sleep. In a sample of middle-aged non-obese males habitual snorers compared to non-snorers had a 2-fold increased risk of elevated haemoglobin – an independent indicator of long-term glycaemic control, and thus, a potential risk factor for metabolic syndrome and cardiovascular disease (69). Shin and colleagues demonstrated that, whilst habitual snorers' and non-snorers' levels of fasting blood glucose and insulin were comparable, habitual snoring was associated with elevated glucose and insulin levels 2 hours following ingestion of glucose even after controlling for diabetes and hypertension in non-obese individuals (73). This study suggests that snoring may contribute to insulin resistance and impaired glucose homeostasis. Indeed this has been shown to be the case for OSA (74). Further, snoring has been linked to microalbuminuria – a persistent increase in urinary albumin – an early indicator of diabetes nephropathy (75). Interestingly, one study showed increased prevalence of diabetes in habitual snorers compared to non-snorers in women but not in men, after controlling for BMI and waist circumference (76). Note that increased risk of diabetes in snoring women has been noted previously (77). Although these studies were cross-sectional, it is possible to postulate that snoring may precede the development of metabolic syndrome. It has been suggested that the sleep-disordered breathing as in snoring may influence sympathetic nervous system hyperactivity (78), which may consequently impair glucose homeostasis and induce insulin resistance by increasing glycogenolysis and gluconeogenesis (79, 80). Additionally, hypoxia may promote the release of proinflammatory cytokines, including tumour necrosis factor- $\alpha$  and interleukin-6, which may result in impaired glucose tolerance

and insulin resistance (81, 82). One study demonstrated that regular snoring was associated with inflammatory markers, adipokines, and risk for metabolic syndrome, but that these effects were either attenuated or abolished after controlling for BMI or waist circumference (83). However, an alternative explanation is that risk for metabolic derangement is influenced by the severity of EDS accompanying snoring. Indeed, one study demonstrated that EDS in the absence of snoring was associated with increased risk for diabetes of a similar magnitude as EDS in the presence of snoring (61). Thus, from this study it is not possible to determine whether snoring, per se, exhibited effects on diabetes risk over and above effects due to associated EDS. A further mechanism is also likely. For example it has been suggested that diabetes may act as a risk factor for the development of OSA (75), possibly mediated by obesity and resultant obstruction to the upper airways. However, all of these studies suffer from the problem that apnoea was not ruled out. Prospective studies are required in order to determine causal relationships between snoring and metabolic abnormalities.

**Morning headache:** Morning headache is a frequent accompanying symptom of OSA, but whether it occurs in snorers in the absence of sleep apnoea is a contentious claim. Ekici and colleagues demonstrated an increased prevalence of morning headaches as a function of snoring intensity, from ~30% in non-snorers to ~43% in extremely loud snorers (12). Similarly, another study demonstrated a prevalence of around 23% of morning headache in habitual snorers (84). However, 69% of these snorers also had OSA, so it is difficult to determine the effect of snoring directly on morning headache. A prospective diary-based study indicated a prevalence of around 60% of snorers and their bed-partners to experience at least one morning headache over the course of 90 days (85). The latter study suggests

that the influence of snoring on morning headache may be mediated by sleep fragmentation, given its occurrence in bed-partners.

**Fragmented Sleep and Daytime Sleepiness:** As outlined above, snoring is a risk factor for daytime sleepiness, even in the absence of apnoea (86). One study showed associations between snoring intensity, awakenings from sleep, daytime sleepiness and psychological distress (12). Snoring intensity also predicted likelihood of falling asleep at the wheel and traffic accidents, suggesting that sleepiness-related outcomes may lead to impairments in daytime performance, increasing the risk of detrimental consequences on the road.

Although some studies use the criteria of habitual snoring and EDS to determine OSA, one study which examined habitual snorers who did not experience breathing pauses demonstrated that this group were 5 times more likely to exhibit daytime sleepiness (a score on the ESS  $\geq 11$ ) than non-snorers (8). In support another study demonstrated that the association between snoring and daytime sleepiness was independent of respiratory disturbance (87).

**Psychosocial Difficulties:** Whilst it may be a matter of debate whether snoring in its own right has adverse health consequences, it is incontrovertible that for bed-partners, snoring is a serious annoyance that can impair sleep quality. In most cases, snorers are unaware of their snoring, and it is their bedpartner who urges them to seek help due to the disruption to their own sleep and their relationship. Indeed one study showed that female partners of male snorers had objectively poorer sleep quality and increased sleep fragmentation on a night with their partner compared to a night sleeping alone (88). Further, around one half of bed-partners reported that snoring contributed to their own constant sleep disturbances on

almost a nightly basis, around 40% had to sleep in another bedroom weekly, and a third reported that snoring contributed to disharmony in the relationship at least from time to time in one study (89). In addition to annoyance and disturbed sleep, snoring has also been shown to contribute to unilateral high-frequency hearing loss in bed-partners (90). Although little research has focused on simple snoring, research from the OSA literature has shown that sleeping with a partner with apnoea contributes to poor sleep and poor quality of life in the bedpartner (91). Another study examining changes in bedpartner depression, anxiety and sleepiness following radiofrequency tissue ablation in their snoring/OSA bedpartner, revealed reductions in depression in bedpartners of snorers (92).

### **Conclusions:**

Despite the prevalence of snoring, we still know relatively little about its role as a predictor of serious health related outcomes independent of apnoea related phenomena. Likewise, the evidence surrounding the presence of daytime sleepiness in snoring is mixed, and it remains unclear whether non-apnoeic snoring contributes to daytime sleepiness in its own right. Part of this uncertainty is due to the variation across studies in their diagnosis of snoring in the absence of apnoeic symptoms, and the few studies that have clearly distinguished symptomology. Regardless of this, it is clear that snoring exists at one end of a continuum, with OSA at the polar end. This highlights the potential severity of an otherwise thought “annoying” problem – a problem which should be taken seriously in its own right. Treating snoring early in the natural history may prevent the development of more serious breathing related difficulties, consequently reducing risk for further complications such as cardiovascular disease and metabolic syndrome.

**Practice Points:**

1. Snoring is common worldwide, with prevalence rates ranging from 2% to 85% depending on diagnosis, age, gender and population.

2. Snoring exists on a continuum from simple snoring, through UARS, to degrees of OSA.

3. It is possible to distinguish snoring from UARS and OSA on several criteria, including anatomical and neurological markers, presence of daytime dysfunction, or acoustic analysis.

However, research studies often rely on self-reported or partner-reported snoring symptoms.

4. Risk factors for snoring include those associated with increased risk of upper airway infection/inflammation, nasal obstruction, BMI, smoking, alcohol dependence, rural dwelling and being male.

5. It is unclear whether snoring independently poses risk for the development of poor health outcomes in the absence of OSA, although its presence on a continuum with the likely development of subsequent OSA highlights the necessity of early treatment.

**Research Agenda:**

1. Studies focussing on snoring, be they examining prevalence, risk factors or concomitant complaints, should differentiate simple snoring from apnoea related symptoms rather than blurring the distinctions between these groups.
2. Longitudinal studies charting the time-course of development from snoring through to OSA are needed to provide support for the notion that snoring poses risk for OSA progression.
3. If evidence supports the notion that snoring proceeds to OSA, investigation of the mechanisms underlying disease progression is warranted.
4. Clearly phenotyped studies examining whether snoring does predict daytime sleepiness and consequent health complaints are necessary in order to determine whether such difficulties are a result of non-apnoeic snoring.
5. Studies identifying the mechanisms underlying the association between snoring and health related consequences are warranted to further our understanding of disease progression.



<b>Abbreviations</b>	
AHI	Apnoea-Hypopnea Index
BMI	Body Mass Index
CFI	Craniofacial Angle
CFS	Chronic Fatigue Syndrome
EDS	Excessive Daytime Sleepiness
MPH	Mandibular Plane and hyoid distance
OSA	Obstructive Sleep Apnoea
PAS	Posterior Airway Space
PSG	Polysomnography
REM	Rapid Eye Movement
RERAs	Respiratory Event Related Arousals
SS	Simple Snoring
UARS	Upper Airway Resistance Syndrome

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