Key points

- Sleep disordered breathing (SDB) is common and its prevalence increases with age. Despite this high prevalence, SDB is frequently unrecognised and undiagnosed in older people.

- There is accumulating evidence that SDB in older people is associated with worsening cardio-cerebrovascular, cognitive and functional outcomes.

- There is now good evidence to support the use of continuous positive airway pressure therapy in older patients with symptomatic SDB.

Educational aims

- To highlight the prevalence and presentation of sleep disordered breathing (SDB) in older people.

- To inform readers about the risk factors for SDB in older people.

- To explore the impact of SDB in older people.

- To introduce current evidence based treatment options for SDB in older people.

Alison McMillan[1], Mary J. Morrell[2,3]

alison.mcmillan1@nhs.net

[1]Sleep and Respiratory Dept, East and North Hertfordshire NHS Trust, Stevenage, UK.
[2]Academic Unit of Sleep and Ventilation, National Heart and Lung Institute, Imperial College, London, UK.
[3]Respiratory Disease Biomedical Research Unit at the Royal Brompton Hospital and Harefield NHS Foundation Trust, London, UK.

Sleep disordered breathing at the extremes of age: the elderly

Sleep disordered breathing (SBD) increases in prevalence as we age, most likely due to physiological and physical changes that occur with ageing. Additionally, SDB is associated with comorbidity and its subsequent polypharmacy, which may increase with increasing age. Finally, the increased prevalence of SDB is intrinsically linked to the obesity epidemic. SDB is associated with serious outcomes in younger people and, likewise, older people. Thus, identification, diagnosis and treatment of SDB is important irrelevant of age. This article reviews the age-related changes contributing to SDB, the epidemiology and the risk factors for SDB in older people, the association of SDB with adverse outcomes, and diagnostic and treatment options for this population.

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SDB is common in the elderly and treatment with CPAP therapy should be considered
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Introduction

The world's population is ageing, in almost every country; the proportion of people aged over 65 years is growing faster than any other age group, as a result of both longer life expectancy and declining fertility rates. According to the World Health Organization, the number of older people, defined as aged 65 years or older, is projected to grow from an estimated 524 million in 2010 to nearly 1.5 billion in 2050, with most of the increase in developing countries [1].

It is recognised older people have a diversity of health and functionality that may not be associated with their chronological age. For example, some individuals age well without serious disease and have preserved normal function; this would be considered healthy ageing [2]. At the other end of the spectrum, others may have significant comorbidities, leading to functional impairment, and would be considered frail. This is considered "pathological ageing", and there may be a wide spectrum and variation from person to person.

Sleep disordered breathing (SDB) is an umbrella term used to describe disorders of respiratory pattern or quantity of ventilation that occur periodically during sleep. The term is commonly associated with the condition obstructive sleep apnoea (OSA), upon which this review will concentrate, but can also include primary or secondary central sleep apnoea (CSA), Cheyne–Stokes respiration, high-altitude periodic breathing, nonobstructive hypoventilation, or hypoxaemia disorders secondary to pulmonary parenchymal, vascular, neuromuscular or chest wall disorders.

SDB is a common condition in older people, although estimates vary considerably due to the population studied, the diagnostic criteria applied and the heterogeneity of the older population. SDB is associated with significant morbidity in younger or middle-aged populations. However,

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Table 1 *The prevalence of SDB in older people*

First author [ref.]	Subjects n	Female %	Age years	Population	Prevalence of SDB %	
					AHI ≥5 events·h⁻¹	AHI ≥10 or ≥15 events·h⁻¹
CARSKADON [7]	40	55	62–86	Community	36	
COLEMAN [8]	83	28	66±5	Sleep clinic	39	
MCGINTY [9]	26	0	64.4±4.4	Community		62
ROEHRS [10]	97		61–81	Sleep clinic	27	
SMALLWOOD [11]	30	20	50–80	Community	37	
YESAVAGE [12]	41	0	69.5±6.5	Both	73	
HOCH [13]	56	52	69.3±5.4	Community	5	4
KNIGHT [14]	27	NG	75.8±5.9	Primary care	37	
MOSKO [15]	46	65	68.7±6.7	Community	28	16
ANCOLI-ISRAEL [16]	233	65	65–101	Nursing home	70	
HOCH [17]	105	53	60–91	Community	26	13
PHILLIPS [18]	92	52	64.2±8.6	Community	15	
ANCOLI-ISRAEL [3]	346	53	72.8±6.1	Community		30
BIXLER [6]	75	0	65–100	Community	31	24
YOUNG [4]	3448		60–99	Community	54	20
ENDESHAW [19]	58	76	77.7±6.7	Community	56	19
HAAS [20]	3643	52	70.2±6.9	Community	46	20
HADER [21]	80	50	74.1±6.3	General clinic	43	19

NG: not given. Reproduced and modified from [22].

it cannot be assumed that older people with SDB suffer from the same consequences as those in younger populations. We do not know what is considered physiological or pathological in terms of the severity of SDB in this population and it remains unclear how we should apply the current evidence for treatment to the extremes of age or a frail older population.

Epidemiology

The Prevalence of SDB in older people in the general population can vary from 20% to 40%; this is a large variation and a more conservative estimate would suggest that the prevalence is at least double that seen in younger age groups [3, 4]. Data also demonstrate the prevalence steadily increases with advancing age, with a plateau between 60 and 65 years of age [5]. In a classic study that defined SDB as an apnoea–hypopnea index (AHI) >10 events·h⁻¹ with the symptom of excessive daytime sleepiness (EDS), SDB was present at 3.2%, 11.3% and 18.1% in the 20–44, 45–64 and 61–100-year age groups, respectively [6]. This trend was also seen in women and, additionally, the sex difference is less apparent after menopause.

Although there is a clear consensus in the literature that the prevalence of SDB is significantly increased in older people, the estimates vary considerably, as demonstrated in table 1. Some of this wide variation can be explained by the differences in the definition of the SDB, the diagnostic threshold used and the heterogeneity of the population studied (*e.g.* healthy general population *versus* nursing home residents, where prevalence rates reach as high as 70% [16]). Furthermore, as the prevalence of obesity continues to increase [23], this will be intrinsically aligned to the increased prevalence of SDB within the general population as it ages.

This higher prevalence of SDB in older people has historically led to debate regarding the potential mechanisms, clinical significance and consequences in the older population [24].

Risk factors for the development of SDB in old people

There have been several physical and psychological mechanisms proposed for this age-related increase in SDB.

A reduction in pharyngeal muscle function

Functionally, the response of the genioglossus muscle to negative pressure applied during wakefulness [25] and sleep [26, 27] is reduced in older people. Additionally, the upper airway reflex sensitivity [28] and the genioglossus response to hypoxia [29], but not hypercapnia [30], are also reduced in older people. Overall, these changes result in reduced upper airway muscle function at sleep onset [31] and a more collapsible upper airway [32], with the mean ± SD critical closing pressure being -8.3 ± 2.3 cmH$_2$O in older people, compared to -16.0 ± 6.9 cmH$_2$O in younger people, independent of body mass index [27]. In healthy elderly people, pharyngeal resistance during sleep is increased compared to that in younger people, indicating a possible age-related predisposition to airway collapse [27, 31, 33].

Age-related differences in pharyngeal morphology

A decrease in the size of the upper airway lumen in older people [34, 35] associated with an age-related lengthening of the pharyngeal airway in both men [36] and women [37], and a descent of the hyoid bone [38], particularly in individuals with long faces [39], which leads to increased airway resistance and a predisposition to airway collapse.

The central control of breathing

The central control of breathing is relatively stable in older people [40], although arousal frequency increases with age [41–43]. Arousal from sleep leads to hyperventilation and relative hypocapnia, which can promote respiratory instability and periodic breathing during the subsequent period of sleep onset. A tight correlation between fluctuation in the electroencephalogram frequency and breathing patterns in older people appears to support this notion [44].

The presence of comorbidities

The prevalence of comorbidities increases with age. It is estimated that up to 50% of patients with mild symptomatic chronic heart failure will have SDB [45]. Likewise, SDB is commonly associated with cognitive impairment [46]. COHEN et al. [47] demonstrated in a longitudinal cohort that declining cognitive function, as measured by the mini-Mental State Examination, was associated with both the increasing severity of SDB (measured by the respiratory disturbance index) and self-reported increasing daytime sleepiness. Moving through the spectrum of cognitive impairment to those patients with a diagnosis of dementia but still living in the community, reports suggest between 19% and 44% of these patients complain of sleep disturbance, the wide range in prevalence probably reflecting the lack of clear diagnosis. Finally, patients institutionalised with dementia have been studied by ANCOLI-ISRAEL et al. [48], who reported 70% had an AHI ⩾5 events·h^{-1}, and up to 48% had an AHI ⩾20 events·h^{-1}. This high prevalence of SDB in patients diagnosed with dementia was also reflected in a study by ROSE et al. [49]: 59 patients with geriatrician-diagnosed dementia with nocturnal agitation behaviour underwent two nights of in-home attended polysomnography, 49% had SDB defined as AHI >15 events·h^{-1}.

The most common cause of dementia is Alzheimer's disease, representing 60–70% of the dementias. The apolipoprotein E (APOE) gene is a common genetic risk factor for the development of Alzheimer's disease. APOE has been associated with an increased risk of developing SDB. Analysis of data from the Wisconsin Sleep Cohort Study showed a significantly higher probability of moderate to severe SDB (AHI ⩾15 events·h^{-1}) with APOE independent of age, sex, body mass index (BMI) and ethnicity than in subjects with an AHI <15 events·h^{-1} [50]. The Sleep Heart Health study (SHHS) also showed the same gene was associated with an increased odds ratio for SDB [51], although a meta-analysis suggested the association was weak [52]. In summary, the prevalence of SDB in patients with cognitive impairment may be as high 50%.

Taken together, these factors suggest there is an anatomical and physiological predisposition for developing SDB with increasing age and comorbidity.

Symptoms of SDB in older people

In the early 1990s, there was an emerging expert opinion that SDB was a distinct condition in older people [9]. This was fuelled by the increased prevalence of objectively measured SDB in this population but with an apparent mismatch in symptomology. This view has largely been superseded [53], although it is recognised the presentation of SDB may be more variable in older people.

Older people report different levels of sleepiness and rate their health differently for the same level of SDB severity compared to younger populations [54]. In older people, the association with obesity is less clear [55]: older SDB patients typically have a lower BMI and neck circumference, compared to younger patients with similar disease severity [56].

Additionally, clinical prediction models used in the diagnosis of SDB are mostly based on BMI and male sex, and have been shown to be inaccurate in groups such as women, the nonobese and older people [57].

Alternatively, increased daytime sleepiness may be less debilitating in older people. Normal sleep patterns vary greatly with age. Older people report that they experience difficulty falling asleep and maintaining sleep, with frequent nocturnal awakenings, as well as early morning awakening [58]. Sleep becomes more fragmented with age, independent of SDB [41, 43]. The number of spontaneous arousals per hour of sleep in older people (60 years and older) can be almost double that which occurs in younger people [42].

Age also influences diurnal preference. Morning preference appears to increase with age [59], which may be due to changing work schedules or variation in social activities, as well as changes in the circadian and physiological requirements for sleep [60]. Sleep architecture also deteriorates with age, with a loss of deep sleep, which may be a consequence of cortical degeneration, disrupting synchronisation of neuronal activation and reducing the amplitude of delta waves detected on the electro-encephalograpy (EEG) recordings [61]. An increase in lighter sleep partially compensates for the loss of deep sleep [62], although there is a reduction in the number of sleep spindles and K complexes within the EEG. In contrast, the duration of rapid eye movement (REM) sleep tends to remain constant throughout adulthood [63]. A reduction in the proportion of REM sleep has been reported by others [62]. These contrasting results may reflect the increased interindividual variability in sleep characteristics in older people.

Additionally, with increasing age, the prevalence of sleep disturbing comorbidities and subsequent polypharmacy increases [64], and loss of physical activity and iatrogenic sleep disruption may contribute to excessive sleepiness. For example, nocturia is a common symptom causing sleep disruption in older people with multiple causes, which also include SDB [65].

In summary, many factors contribute to sleep disruption in older people, and the symptom of EDS may be multifactorial in older people and obscure the interpretation of possible symptoms related to SDB. Additionally, the clinical presentation of SDB in older people may often be atypical. These factors may contribute to the lack of recognition and underdiagnosis of SDB in older adults. Therefore, although excessive sleepiness, regardless of its cause, is associated with increased all-cause mortality in older people [66], the proportion of sleepiness that is due to SDB in older people, and hence could be modified by treatment, is unknown.

Consequences of SDB in older people

Despite this high prevalence of SDB in older people, the consequences are less clear in this population. In middle-aged populations, SDB is associated with serious cardio- and cerebrovascular, metabolic, cognitive, and functional outcomes, including increased mortality. Additional outcomes of particular interest in older people may include glaucoma [67], falls with fractures [68], impaired quality of life [69], decreased pain tolerance [70], frailty [71] and mortality [72–74].

Cardiovascular disease

The significant cardiovascular impact of SDB on middle-aged populations has been established since community-based epidemiological studies have shown that people with untreated severe SDB have an increased incidence of coronary heart disease, myocardial infarction, heart failure, stroke and mortality after adjusting for established cardiovascular risk factors [75]. In older people, the data were less clear. There are limited studies on the long-term consequences, and epidemiological studies have shown inconsistent associations of SDB with cardiovascular risk across age and sex groups.

The SHHS [76] observational cohort showed that cardiovascular risk was more likely to be elevated in the younger (aged <65 years) than older participants. A further study by HAAS et al. [20] in older people with SDB showed the risk of having hypertension was no greater than for older people without the disorder; this may be in part explained by the finding that older people have a reduced acute cardiovascular response to arousal from sleep compared to young people [77]. Thus, the poorer cardiovascular reactivity of older adults may paradoxically reduce the impact of arousal from sleep, which may be a protective response. Although a more recent prospective cohort [78] followed 939 older patients (≥65 years of age) for 69 months, they found patients with untreated severe SDB had increased all-cause and cardiovascular mortality. The cohort was further divided into groups by severity and whether they did or did not use continuous positive airway pressure (CPAP) therapy. Patients with severe SDB (AHI >30 events·h^{-1}) who were not treated with CPAP had the highest risk of mortality, while patients with severe SDB who were treated with CPAP had a risk of mortality similar to the group with an AHI <15 events·h^{-1}. It must be remembered that those who did not use treatment were self-selected as they had refused or were noncompliant with CPAP therapy, and the increased cardiovascular risk may be related to other factors that are associated with noncompliance, such as noncompliance with medication or advice, or adverse risk behaviour.

In summary, although the vascular risk benefits from treating SDB may be larger in older people, since the higher cardiovascular event rate in the older people implies that more events could be prevented per unit change in risk, the actual magnitude risk reduction may be less.

Cerebrovascular disease

Observational cohort studies in the general population, as discussed earlier, have also shown an increased risk of stroke [79], although it has been difficult to determine whether SDB preceded the stroke or was independent of the confounding risk factors of age, sex, smoking, BMI, diabetes mellitus and cardiovascular disease. ARZT et al. [80] performed a longitudinal analysis of SDB and stroke risk and found moderate to severe OSA (AHI ⩾20 events·h^{-1}) was associated with increased risk of stroke, whereas no increased risk was observed in patients with mild SDB. In this study, the increased risk of stroke appeared to be partially independent of hypertension but confounded by obesity. YAGGI et al. [81] also reported an increased incidence of stroke, including transient ischaemic attacks, or death from any cause in patients with pre-existing OSA and showed a relationship between OSA severity and risk, independent of confounding factors.

There has been one population-based cohort study in older patients (mean age 77 years). This study suggested that severe OSA (AHI ⩾30 events·h^{-1}) increased the risk of ischaemic stroke, independently of known risk factors [82].

Quality of life and driving

Symptomatic SDB patients are more likely to experience mood changes [83] and reduced quality of life [84], which is often attributed to reduced social functioning and vitality [85].

Daytime sleepiness also increases accident risk [86], with OSA syndrome patients being two to four times more likely to have road traffic accidents as a result of reduced alertness while driving [87–89]. There have been four systematic reviews of observational studies examining the risk of road traffic accidents in OSA patients [90–93]. All of the studies included in these reviews evaluated the risk of road traffic accidents in patients whose average age was below 60 years. Additionally, randomised controlled trials (RCTs) specifically in older people are unlikely to capture reductions in the rate of road traffic accidents, given their infrequency. For example, the rate of road traffic accidents in drivers aged 60–69 years within the UK is 96 per 100000 [94].

Cognition

Both the ageing process [95] and SDB are associated with cognitive dysfunction [96], although the pathogenesis, sequelae and clinical presentation remain unclear [97, 98]. SDB is characterised by chronically fragmented sleep and daytime somnolence, both of which are thought to contribute to cognitive dysfunction, although the relative contribution of each remains poorly understood [46]. More recently, chronic intermittent hypoxia (the hallmark of OSA) has been proposed as a third factor contributing to hypoxia-induced neural injury and, increasingly, the research in this field has concentrated on this area.

Few studies have investigated the impact of SDB on cognitive function in older people. In those studies that have measured cognitive function in older people, cognitive impairment appears to be independently related to both SDB severity and increasing age, but the coexistence of these factors does not further increase dysfunction [99–101]. One explanation for the preservation of cognitive function in SDB patients is that neural compensation can overcome the cognitive deficits that are associated with the effects of intermittent hypoxia and/or sleep deprivation on the brain. Whether or not the capacity for neural compensation is decreased in older people, who have less neural reserve, is unknown. Recent data have shown that poorer sleep quality is associated with factors that may accelerate cognitive decline in older people and this finding requires further investigation [102].

Diagnosis

The diagnosis of SDB has traditionally been based on nocturnal polysomnography (NPSG). This technique is expensive and requires the availability of specialised facilities and expertise, which are often not available or indeed easily accessible to frail, older, dependent adults. Pulse oximetry has been shown to be reliable in the diagnosis of moderate-to-severe SDB but of less use in mild SDB [103]. Several groups have validated the utility of limited-channel home-based testing (respiratory polygraphy) against NPSG in the diagnosis of SDB [104]. The level of agreement was moderate: 79%, rising to >90% in patients with AHI >30 events·h^{-1}. Domiciliary respiratory polygraphy typically measuring airflow, respiratory effort and pulse oximetry is now widely used in the diagnosis of SDB. Currently, there is no clear guidance on what would be considered the best test to complete in older patients. NPSG, which may be the helpful in excluding other codiagnoses or other primary sleep disorders such as insomnia, REM sleep behaviour disorder, restless leg syndrome and periodic limb movements, may be practically challenging in frail, comorbid populations.

Treatments for SDB

Treatments for SDB depend on disease severity, patient symptoms, and the presence of cardiovascular or metabolic disease. Treatments include advice on modifying lifestyle, including weight loss, stopping smoking and increasing cardiovascular exercise, improving sleep opportunity and environment, optimising medical management of

comorbidities, and reducing the use of stimulants such as caffeine, and substances such as alcohol, sedatives and recreational drugs.

Positional measures and oral mandibular advancement splints are recommended in mild-to-moderate SDB, with upper airway and bariatric surgery also being considered in some patients. However, positive airway therapy or CPAP is the mainstay treatment for symptomatic younger patients with moderate to severe SDB, and the therapeutic and economic benefits have been established [105].

Until recently, there had been a paucity of evidence for treatment of SDB in older people, with few RCTs specifically in older people, albeit that many CPAP RCTs did include older people, and their associated comorbidities including cardiovascular and cerebral vascular disease. Here, we review the evidence for CPAP therapy in older people, with a focus on RCTs.

Cardiovascular disease including heart failure

Although there is a large observational cohort study from the Spanish Sleep and Breathing Network, discussed earlier [78], demonstrating increased cardiovascular mortality in those patients with severe SDB not using CPAP therapy, there are only four recent RCTs [93–96], three of which focus on predominantly CSA [106–108] and a particular type of positive airway pressure known as assisted servoventilation (ASV).

Further reading

Continous positive airway pressure in older people with obstructive sleep apnoea syndrome (PREDICT): a 12 month multicenter randomized trial [115]
This article reports the first and longest randomised control treatment trial of CPAP therapy in older people in the UK. It is also the first comprehensive economic analysis of CPAP therapy specifically in this population.

Current treatment trials results awaited

Although these trials are not specifically in older people, they do not have upper age limits and will hopefully add to the current evidence base particular in cardio and cerebrovascular disease.

Sleep Apnoea in TIA/Stroke: Reducing Cardiovascular Risk with Positive Airway Pressure (Sleep Tight)
This 12-month RCT was designed to evaluate whether a diagnosis and treatment intervention strategy for sleep apnoea results in a reduction in the five domains of cardiovascular risk markers among patients at high risk of both sleep apnoea and cardiovascular events.

Sleep Apnoea Cardiovascular Endpoints Study (SAVE)
This is a multicentre RCT to determine the effects of nasal CPAP in preventing cardiovascular disease in high-risk patients with moderate-to-severe OSA.

The results from the largest and most recent trial, SERVE HF [108], which studied the effect of ASV on SDB, predominantly CSA, in patients with chronic heart failure across a large age range suggest that ASV may have detrimental effects, so the value of this particular type of positive airway pressure in older patients with heart failure remains uncertain.

Cerebrovascular disease

There are three studies that included stroke patients or had stroke as the primary outcome [109–111] or mortality due to stroke as a secondary outcome [110]. Two were RCTs of CPAP *versus* best supportive care as the control groups [110, 111]. All showed fewer stroke or vascular events in the CPAP group. The one study examining the effect of CPAP on OSA symptoms in stroke patients found no improvement [111].

Cognition

There have been a few small, short-duration studies of CPAP treatment in older patients with cognitive impairment [112, 113]. The study by Ancoli-Israel *et al.* [113] randomised 78 patients with mild-to-moderate Alzheimer's disease to CPAP treatment *versus* sham CPAP, and concluded it was well tolerated, and reduced daytime sleepiness and some objective sleep parameters. Later, the same group completed a smaller follow-up study in the original study group and studied 10 of the original patients, five of whom continued CPAP treatment and five who discontinued CPAP [114]. This preliminary study raised the possibility that CPAP treatment may slow cognitive deterioration, although the patients were highly selected, and assessments were subjective and provided by the caregivers. Interestingly, good adherence with CPAP treatment was noted. It is generally accepted larger RCTs are still required in this population.

Symptom-related outcomes including quality of life and cost-effectiveness

There have been two recent large RCTs exclusively in older people: he PREDICT trial [115] and a study from the Spanish Sleep and Breathing Network [116], who also completed the prospective observational cohort discussed earlier [78]. The PREDICT trial demonstrated that CPAP therapy in older people with symptomatic SDB reduced subjective and objective sleepiness while improving quality of life. The magnitude of the improvements was similar to that seen in middle-aged patients and was cost-effective. The study by Martinez-Garcia *et al.* [116] further reinforced these findings, with additional improvements in behavioural, cognitive and quality of life outcomes.

Adherence to CPAP treatment in older people

SDB can be treated effectively with CPAP therapy, but it is often a lifelong condition. Furthermore, the minimum and optimal hours of use required to improve various outcomes has not been established.

There is limited information on the adherence to CPAP therapy in older people. The last systematic review on adherence to CPAP prior to the recent RCTs discussed above [117] identified three studies evaluating adherence to CPAP therapy in patients with an average age of 65 years and over: one by Russo-Magno et al. [118] in patients with an average age of 73 years and one by Bravata et al. [119] in patients with an average age of 66 years, and Woehrle et al. [120] presented a subgroup analysis in patients 60–70 years and patients 70 years of age and older. Although none of the three studies reported the proportion of patients using CPAP at specified time-points from treatment initiation, they suggested that CPAP compliance is similar in older and middle-aged populations.

In the recent large RCTs [115, 116], the compliance was lower, which reflects the intention-to-treat statistical analysis and may not reflect clinical practice. Certainly, age has not been identified as a risk factor for lower adherence to CPAP therapy [117]. Moreover, the observational studies in frail, older patients with Alzheimer's disease [121] demonstrated good adherence.

Although there have been systematic reviews of additional measures to support and enhance CPAP adherence, such as educational and behavioural modification, there is no work specifically in older people, but likewise, nothing to suggest any apparent disadvantage [122].

Additionally, new technologies that enable remote titration and follow-up of CPAP therapy may need special adaption for older patients or may indeed be advantageous in frail elderly populations who may not be able to attend traditional hospital-based appointments. This technology will require detailed assessment in selected patient groups to identify how we can use it optimally and cost-effectively.

Overall summary

SDB is a common condition in older people and with an ageing population, increasingly, clinicians will be asked to assess older patients with SDB. There is increasing evidence to suggest older patients with SDB have at least similar consequences to younger populations. Until recently, there were few RCTs examining the treatment of SDB in older adults; there is now good evidence to support treatment in the form of CPAP therapy.

Case study

A 73-year-old male is referred to your sleep clinic for investigation of EDS. His self-reported Epworth Sleepiness Scale score is 10 out of 24, yet his wife reports that he has been increasingly sleepy over the last couple of years, and falls asleep shortly after waking and while he is having his breakfast. He is known to snore and has done for many years, but due to his disability, he and his wife sleep in separate rooms, and there have been no witnessed apnoeas and he is not aware of any choking or gasping episodes.

He goes to bed at approximately 23:00 and wakes at 08:00. He wakes two to three times during the night to go to the toilet. He is an ex-smoker, having quit 22 years ago, and drinks up to 9 units of alcohol a week. He drinks up to two cups of coffee a day. He is retired but he and his wife live independently, and he uses a mobility scooter or wheelchair when out. He also continues to drive, which is important for his independence.

His past medical includes secondary progressive multiple sclerosis and recurrent urinary tract infections. His medication includes tolterodine 4 mg modified release once daily, calcium and vitamin D supplements, lansoprazole 15 mg once daily, and tizanidine 4 mg three times daily.

His blood pressure is 154/66 mmHg with a heart rate of 60 beat·min^{-1}. He weighs 82 kg with a BMI of 23.9 kg·m^{-2} and a collar size of 38 cm. On examination, his oropharynx is normal and his chest is clear. His oxygen saturation is 98% on air.

His restless leg score is 11 out of 40, and his Hospital Anxiety and Depression Scale scores are anxiety 0 and depression 4, which are all within the normal range.

1. **What factors could contribute to the symptom of EDS in this patient?**

2. **What further investigations if any would you request?**

   An overnight pulse oximetry study is performed. The patient completes the study successfully. His average overnight oxygen saturation is 92.7% with a 4% oxygen desaturation index of 43 events·h^{-1}. His mean heart rate is 53 beat·min^{-1} (figure 1).

3. **What treatment would you recommend for this patient?**

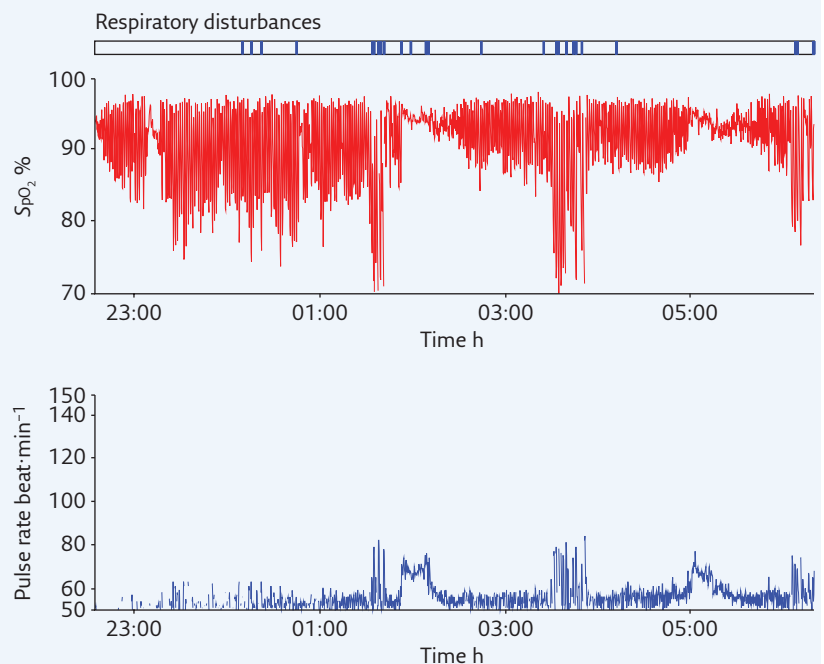4. **What advice would you give to this patient about driving?**

Figure 1 *Overnight pulse oximetry. SpO$_2$: oxygen saturation measured by pulse oximetry.*

1. Other factors that could contribute to the symptoms of EDS would be sleep disruption secondary to urinary frequency and the medication tizanidine used for spasticity associated with multiple sclerosis.
2. Ideally, a limited multichannel respiratory polygraphy or nocturnal polysomnogram.
3. The patient was offered CPAP therapy, which he accepted and is using successfully.
4. The patient was advised to inform the UK Driver and Vehicle Licensing Agency and his car insurance provider of the diagnosis, and must cease driving until satisfactory control of his symptoms has been attained.

As yet, there remains little evidence for treatment in frail older populations, and challenges remain in how to stratify frail older patients with comorbidities and how best to assess the effectiveness of CPAP therapy; further patient-centred outcomes may be required in this specialised population. It has been recognised there is an inequality of research in older people [123] and although clinical guidelines play an important role in improving healthcare for people with long-term conditions, it is well recognised they often fail to address the effect of comorbidity and polypharmacy [124]. Age should not be considered a barrier to assessment and treatment of SDB in older patients.

Conflict of interest

None declared.

References

1. US Department of Health and Human Services, World Health Organization. Global Health and Aging. NIH publication no. 11-7737. Bethesda, National Institutes of Health, 2011.
2. Rowe JW, Kahn RL. Successful aging. *Gerontologist* 1999; 37: 433–440.
3. Ancoli-Israel S, Klauber MR, Stepnowsky C, *et al*. Sleep-disordered breathing in African-American elderly. *Am J Respir Crit Care Med* 1995; 152: 1946–1949.
4. Young T, Peppard PE, Gottlieb DJ. Epidemiology of obstructive sleep apnea: a population health perspective. *Am J Respir Crit Care Med* 2002; 165: 1217–1239.
5. Ancoli-Israel S, Gehrman P, Kripke DF, *et al*. Long-term follow-up of sleep disordered breathing in older adults. *Sleep Med* 2001; 2: 511–516.
6. Bixler E. Effects of age on sleep apnea in men. *Am J Respir Crit Care Med* 1998; 157: 144–148.
7. Carskadon MA, Dement WC. Respiration during sleep in the aged human. *J Gerontol* 1981; 36: 420–423.
8. Coleman RM, Miles LE, Guilleminault CC, *et al*. Sleep–wake disorders in the elderly: polysomnographic analyses. *J Am Geriatr Soc* 1981; 73: 773–778.
9. McGinty D, Littner M, Beahm E, *et al*. Sleep related breathing disorders in older men: a search for underlying mechanisms. *Neurobiol Aging* 1982; 3: 337–350.
10. Roehrs T, Zorick F, Sicklesteel J, *et al*. Age-related sleep–wake disorders at a sleep disorder center. *J Am Geriatr Soc* 1983; 31: 364–370.
11. Smallwood RG, Vitiello MV, Giblin EC, *et al*. Sleep apnea: relationship to age, sex, and Alzheimer's dementia. *Sleep* 1983; 6: 16–22.
12. Yesavage J, Bliwise D, Guilleminault C, *et al*. Prelminary communication: intellectual deficit and sleep-related respiratory disturbance in the elderly. *Sleep* 1985; 8: 30–33.
13. Hoch CC, Reynolds CF 3rd, Kupfer DJ, *et al*. Sleep-disordered breathing in normal and pathologic aging. *Sleep* 1985; 8: 30–33.
14. Knight H, Millman RP, Gur RC, *et al*. Clinical significance of sleep apnea in the elderly. *Am Rev Respir Dis* 1987; 136: 845–850.
15. Mosko SS, Dickel MJ, Paul T, *et al*. Sleep apnea and sleep-related periodic leg movements in community resident seniors. *J Am Geriatr Soc* 1988; 36: 502–508.
16. Ancoli-Israel S, Klauber MR, Kripke DF, *et al*. Sleep apnea in female patients in a nursing home. Increased risk of mortality. *Chest* 1989; 96: 1054–1058.
17. Hoch CC, Reynolds CF 3rd, Monk TH, *et al*. Comparison of sleep-disordered breathing among healthy elderly in the seventh, eighth, and ninth decades of life. *Sleep* 1990; 13: 502–511.
18. Phillips BA, Berry DT, Schmitt FA, *et al*. Sleep-disordered breathing in the healthy elderly. Clinically significant? *Chest* 1992; 101: 345–349.
19. Endeshaw YW, Johnson TM, Kutner MH, *et al*. Sleep-disordered breathing and nocturia in older adults. *J Am Geriatr Soc* 2004; 52: 957–960.
20. Haas DC, Foster GL, Nieto FJ, *et al*. Age-dependent associations between sleep-disordered breathing and hypertension: importance of discriminating between systolic/diastolic hypertension and isolated systolic hypertension in the Sleep Heart Health Study. *Circulation* 2005; 111: 614–621.
21. Hader C, Schroeder A, Hinz M, *et al*. Sleep disordered breathing in the elderly: comparison of men and women. *J Physiol Pharmacol* 2005; 56: Suppl. 4, 85–91.
22. Glasser M, Bailey N, McMillan A, *et al*. Sleep apnoea in older people. *Breathe* 2011; 7: 248–256.
23. Flegal KM, Carroll MD, Ogden CL, *et al*. Prevalence and trends in obesity among US adults; 1999-2008. *JAMA* 2010; 303: 235–241.
24. Levy P, Pepin JL, Malauzat D, *et al*. Is sleep apnea syndrome in the elderly a specific entity? *Sleep* 1996; 19: Suppl., S29–S38.
25. Horner RL, Innes JA, Murphy K, *et al*. Evidence for reflex upper airway dilator muscle activation by sudden negative airway pressure in man. *J Physiol* 1991; 436: 15–29.
26. Horner RL, Innes JA, Morrell MJ, *et al*. The effect of sleep on reflex genioglossus muscle activation by stimuli of negative airway pressure in humans. *J Physiol* 1994; 476: 141–151.
27. Eikermann M, Jordan AS, Chamberlin NL, *et al*. The influence of aging on pharyngeal collapsibility during sleep. *Chest* 2007; 131: 1702–1709.
28. Erskine RJ, Murphy PJ, Langton JA, *et al*. Effect of age on the sensitivity of upper airway reflexes. *Br J Anaesth* 1993; 70: 574–575.
29. Klawe JJ, Tafil-Klawe M. Age-related response of the genioglossus muscle EMG-activity to hypoxia in humans. *J Physiol Pharmacol* 2003; 54: Suppl. 1, 14–19.
30. Browne HA, Adams L, Simonds AK, *et al*. Ageing does not influence the sleep-related decrease in the hypercapnic ventilatory response. *Eur Respir J* 2003; 21: 523–529.
31. Worsnop C, Kay A, Kim Y, *et al*. Effect of age on sleep onset-related changes in respiratory pump and upper airway muscle function. *J Appl Physiol (1985)* 2000; 88: 1831–1839.
32. Kirkness JP, Schwartz AR, Schneider H, *et al*. Contribution of male sex, age, and obesity to mechanical instability of the upper airway during sleep. *J Appl Physiol (1985)* 2008; 104: 1618–1624.
33. Browne HA, Adams L, Simonds AK, *et al*. Impact of age on breathing and resistive pressure in people with and without sleep apnea. *J Appl Physiol* 2001; 90: 1074–1082.
34. Martin SE, Mathur R, Marshall I, *et al*. The effect of age, sex, obesity and posture on upper airway size. *Eur Respir J* 1997; 10: 2087–2090.
35. Carlisle T, Carthy ER, Glasser M, *et al*. Upper airway factors that protect against obstructive sleep apnoea in healthy older males. *Eur Respir J* 2014; 44: 685–693.
36. Shigeta Y, Ogawa T, Venturin J, *et al*. Gender- and age-based differences in computerized tomographic measurements of the orophaynx. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2014; 106: 563–570.
37. Malhotra A, Huang Y, Fogel R, *et al*. Aging influences on pharyngeal anatomy and physiology: the predisposition to pharyngeal collapse. *Am J Med* 2006; 119: 72 e79-14.

38. Pae E-K, Quas C, Quas J, et al. Can facial type be used to predict changes in hyoid bone position with age? A perspective based on longitudinal data. *Am J Orthod Dentofacial Orthop* 2008; 134: 792–797.

39. Kollias I, Krogstad O. Adult craniocervical and pharyngeal changes – a longitudinal cephalometric study between 22 and 42 years of age. Part I: morphological craniocervical and hyoid bone changes. *Eur J Orthod* 1999; 21: 333–344.

40. Wellman A, Malhotra A, Jordan AS, et al. Chemical control stability in the elderly. *J Physiol* 2007; 581: 291–298.

41. Mathur R, Douglas NJ. Frequency of EEG arousals from nocturnal sleep in normal subjects. *Sleep* 1995; 18: 330–333.

42. Boselli M, Parrino L, Smerieri A, et al. Effect of age on EEG arousals in normal sleep. *Sleep* 1998; 21: 351–357.

43. Browne HA, Adams L, Simonds AK, et al. Sleep apnoea and daytime function in the elderly – what is the impact of arousal frequency? *Respir Med* 2003; 97: 1102–1108.

44. Pack AI, Millman RP. Changes in control of ventilation, awake and asleep, in the elderly. *J Am Geriatr Soc* 1986; 34: 533–544.

45. Vazir A, Hastings PC, Dayer M, et al. A high prevalence of sleep disordered breathing in men with mild symptomatic chronic heart failure due to left ventricular systolic dysfunction. *Eur J Heart Fail* 2007; 9: 243–250.

46. Rosenzweig I, Glasser M, Polsek D, et al. Sleep apnoea and the brain: a complex relationship. *Lancet Respir Med* 2015; 3: 404–414.

47. Cohen-Zion M, Stepnowsky C, Marler, et al. Changes in cognitive function associated with sleep disordered breathing in older people. *J Am Geriatr Soc* 2001; 49: 1622–1627.

48. Ancoli-Israel S, Klauber MR, Butters N, et al. Dementia in institutionalized elderly: relation to sleep apnea. *J Am Geriatr Soc* 1991; 39: 258–263.

49. Rose KM. Sleep disturbances and nocturnal agitation behaviors in older adults with dementia. *Sleep Breath* 2011; 34: 779–786.

50. Kadotani H, Kadotani T, Young T, et al. Association between apolipoprotein E ε4 and sleep-disordered breathing in adults. *JAMA* 2001; 285: 2888–2890.

51. Gottlieb DJ, DeStefano AL, Foley DJ, et al. APOE ε4 is associated with obstructive sleep apnea/hypopnea: the Sleep Heart Health Study. *Neurology* 2004; 63: 664–668.

52. Thakre TP, Mamtani MR, Kulkarni H. Lack of association of the APOE epsilon 4 allele with the risk of obstructive sleep apnea: meta-analysis and meta-regression. *Sleep* 2009; 32: 1507–1511.

53. Launois SH, Pepin JL, Levy P. Sleep apnea in the elderly: a specific entity? *Sleep Med Rev* 2007; 11: 87–97.

54. Morrell MJ, Finn L, McMillan A, et al. The impact of ageing and sex on the association between sleepiness and sleep disordered breathing. *Eur Respir J* 2012; 40: 386–393.

55. Young T, Shahar E, Nieto FJ, et al. Predictors of sleep-disordered breathing in community-dwelling adults: the Sleep Heart Health Study. *Arch Intern Med* 2002; 162: 893–900.

56. Chung S, Yoon IY, Lee CH, et al. Effects of age on the clinical features of men with obstructive sleep apnea syndrome. *Respiration* 2009; 78: 23–29.

57. Rowley JA, Aboussouan LS, Badr MS. The use of clinical prediction formulas in the evaluation of obstructive sleep apnea. *Sleep* 2000; 23: 929–938.

58. Cajochen C, Munch M, Knoblauch V, et al. Age-related changes in the circadian and homeostatic regulation of human sleep. *Chronobiol Int* 2006; 23: 461–474.

59. Taillard J, Philip P, Chastang JF, et al. Validation of Horne and Ostberg morningness-eveningness questionnaire in a middle-aged population of French workers. *J Biol Rhythms* 2004; 19: 76–86.

60. Dijk DJ, Duffy JF, Riel E, et al. Ageing and the circadian and homeostatic regulation of human sleep during forced desynchrony of rest, melatonin and temperature rhythms. *J Physiol* 1999; 516: 611–627.

61. Dijk DJ, Beersma DG, van den Hoofdakker RH. All night spectral analysis of EEG sleep in young adult and middle-aged male subjects. *Neurobiol Aging* 1989; 10: 677–682.

62. Van Cauter E, Leproult R, Plat L. Age-related changes in slow wave sleep and REM sleep and relationship with growth hormone and cortisol levels in healthy men. *JAMA* 2000; 284: 861–868.

63. Landolt HP, Dijk DJ, Achermann P, et al. Effect of age on the sleep EEG: slow-wave activity and spindle frequency activity in young and middle-aged men. *Brain Res* 1996; 738: 205–212.

64. Willcox SM, Himmelstein DU, Woolhandler S. Inappropriate drug prescribing for the community-dwelling elderly. *JAMA* 1994; 272: 292–296.

65. Bing MH, Jennum P, Moller LA, et al. Obstructive sleep apnea in a Danish population of men and women aged 60-80 years with nocturia. *J Clin Sleep Med* 2012; 8: 515–520.

66. Empana JP, Dauvilliers Y, Dartigues JF, et al. Excessive daytime sleepiness is an independent risk indicator for cardiovascular mortality in community-dwelling elderly: the three city study. *Stroke* 2009; 40: 1219–1224.

67. Onen SH, Mouriaux F, Berramdane L, et al. High prevalence of sleep-disordered breathing in patients with primary open-angle glaucoma. *Acta Ophthalmol Scand* 2000; 78: 638–641.

68. Onen F, Higgins S, Onen SH. Falling-asleep-related injured falls in the elderly. *J Am Med Dir Assoc* 2009; 10: 207–210.

69. Onen F, Onen SH. Fundamentals of quality of life and daytime sleepiness measurements in older sleep apnea patients. *Sleep Med* 2010; 11: 332.

70. Onen SH, Onen F, Albrand G, et al. Pain tolerance and obstructive sleep apnea in the elderly. *J Am Med Dir Assoc* 2010; 11: 612–616.

71. Cochen V, Arbus C, Soto ME, et al. Sleep disorders and their impacts on healthy, dependent, and frail older adults. *J Nutr Health Aging* 2009; 13: 322–329.

72. Gooneratne NS, Richards KC, Joffe M, et al. Sleep disordered breathing with excessive daytime sleepiness is a risk factor for mortality in older adults. *Sleep* 2011; 34: 435–442.

73. Onen SH, Dauphinot V, Gooneratne NS, et al. Morbidity and predicted mortality in older adults with central sleep apnea. *J Sleep Disorders Ther* 2013; 2: 146.

74. Tarasiuk A, Greenberg-Dotan S, Simon-Tuval T, et al. The effect of obstructive sleep apnea on morbidity and health care utilization of middle-aged and older adults. *J Am Geriatr Soc* 2008; 56: 247–254.

75. Marin JM, Carrizo SJ, Vicente E, et al. Long-term cardiovascular outcomes in men with obstructive sleep apnoea-hypopnoea with or without treatment with continuous positive airway pressure: an observational study. *Lancet* 2005; 365: 1046–1053.

76. Newman AB, Nieto FJ, Guidry U, et al. Relation of sleep-disordered breathing to cardiovascular disease risk factors: the Sleep Heart Health Study. *Am J Epidemiol* 2001; 154: 50–59.

77. Goff EA, O'Driscoll DM, Simonds AK, et al. The cardiovascular response to arousal from sleep decreases with age in healthy adults. *Sleep* 2008; 31: 1009–1017.

78. Martinez-Garcia MA, Campos-Rodriguez F, Catalan-Serra P, et al. Cardiovascular mortality in obstructive sleep apnea in the elderly: role of long-term continuous positive airway pressure treatment: a prospective observational study. *Am J Respir Crit Care Med* 2012; 186: 909–916.

79. Redline S. Obstructive sleep apnea–hypopnea and incident stroke: the Sleep Heart Health Study. *Am J Respir Crit Care Med* 2010; 182: 1332–1333.

80. Arzt M, Young T, Finn L, et al. Association of sleep-disordered breathing and the occurrence of stroke. *Am J Respir Crit Care Med* 2005; 172: 1447–1451.

81. Yaggi HK, Concato J, Kernan WN, et al. Obstructive sleep apnea as a risk factor for stroke and death. *N Engl J Med* 2005; 353: 2034–2041.

82. Munoz R, Duran-Cantolla J, Martinez-Vila E, et al. Severe sleep apnea and risk of ischemic stroke in the elderly. *Stroke* 2006; 37: 2317–2321.

83. McCall WV, Harding D, O'Donovan C. Correlates of depressive symptoms in patients with obstructive sleep apnea. *J Clin Sleep Med* 2006; 2: 424–426.

84. Baldwin CM, Griffith KA, Nieto FJ, *et al*. The association of sleep-disordered breathing and sleep symptoms with quality of life in the Sleep Heart Health Study. *Sleep* 2001; 24: 96–105.

85. Jenkinson C, Stradling J, Petersen S. Comparison of three measures of quality of life outcome in the evaluation of continuous positive airways pressure therapy for sleep apnoea. *J Sleep Res* 1997; 6: 199–204.

86. Teran-Santos J, Jimenez-Gomez A, Cordero-Guevara J. The association between sleep apnea and the risk of traffic accidents. Cooperative Group Burgos-Santander. *N Engl J Med* 1999; 340: 847–851.

87. George CF. Reduction in motor vehicle collisions following treatment of sleep apnoea with nasal CPAP. *Thorax* 2001; 56: 508–512.

88. George CF. Sleepiness, sleep apnea, and driving: still miles to go before we safely sleep. *Am J Respir Crit Care Med* 2004; 170: 927–928.

89. George CF, Findley LJ, Hack MA, *et al*. Across-country viewpoints on sleepiness during driving. *Am J Respir Crit Care Med* 2002; 165: 746–749.

90. Ellen RLB, Marshall SC, Palayew M, *et al*. Systematic review of motor vehicle crash risk in persons with sleep apnea. *J Clin Sleep Med* 2006; 2: 193–200.

91. Tregear S, Reston J, Schoelles K, *et al*. Obstructive sleep apnea and risk of motor vehicle crash: systematic review and meta-analysis. *J Clin Sleep Med* 2009; 5: 573–581.

92. Tregear S, Reston J, Schoelles K, *et al*. Continuous positive airway pressure reduces risk of motor vehicle crash among drivers with obstructive sleep apnea: systematic review and meta-analysis. *Sleep* 2010; 33: 1373–1380.

93. Antonopoulos CN, Sergentanis TN, Daskalopoulou SS, *et al*. Nasal continuous positive airway pressure (nCPAP) treatment for obstructive sleep apnea, road traffic accidents and driving simulator performance: A meta-analysis. *Sleep Med Rev* 2011; 15: 301–310.

94. Department for Transport. Drivers in reported accidents by gender, number injured, road user type and age, Great Britain, 2012. London, DfT, 2013.

95. Hedden T, Gabrieli JD. Insights into the ageing mind: a view from cognitive neuroscience. *Nat Rev Neurosci* 2004; 5: 87–96.

96. Wallace A, Bucks RS. Memory and obstructive sleep apnea: a meta-analysis. *Sleep* 2013; 36: 203–220.

97. Gozal D. CrossTalk proposal: the intermittent hypoxia attending severe obstructive sleep apnoea does lead to alterations in brain structure and function. *J Physiol* 2013; 591: 379–381.

98. Rosenzweig I, Williams SC, Morrell MJ. CrossTalk opposing view: the intermittent hypoxia attending severe obstructive sleep apnoea does not lead to alterations in brain structure and function. *J Physiol* 2013; 591: 383–385.

99. Ayalon L, Ancoli-Israel S, Drummond SP. Obstructive sleep apnea and age: a double insult to brain function? *Am J Respir Crit Care Med* 2010; 182: 413–419.

100. Mathieu A, Mazza S, Decary A, *et al*. Effects of obstructive sleep apnea on cognitive function: a comparison between younger and older OSAS patients. *Sleep Med* 2008; 9: 112–120.

101. Cohen-Zion M, Stepnowsky C, Marler, *et al*. Changes in cognitive function associated with sleep disordered breathing in older people. *J Am Geriatr Soc* 2001; 49: 1622–1627.

102. Spira AP, Gamaldo AA, An Y, *et al*. Self-reported sleep and beta-amyloid deposition in community-dwelling older adults. *JAMA Neurol* 2013; 70: 1537–1543.

103. Ryan PJ, Hilton MF, Boldy DA, *et al*. Validation of British Thoracic Society guidelines for the diagnosis of the sleep apnoea/hypopnoea syndrome: can polysomnography be avoided? *Thorax* 1995; 50: 972–975.

104. Kuna ST, Gurubhagavatula I, Maislin G, *et al*. Noninferiority of functional outcome in ambulatory management of obstructive sleep apnea. *Am J Respir Crit Care Med* 2011; 183: 1238–1244.

105. McDaid C, Griffin S, Weatherly H, *et al*. Continuous positive airway pressure devices for the treatment of obstructive sleep apnoea-hypopnoea syndrome: a systematic review and economic analysis. *Health Technol Assess* 2009; 13: 143–274.

106. Randerath WJ, Nothofer G, Priegnitz C, *et al*. Long-term auto-servoventilation or constant positive pressure in heart failure and coexisting central with obstructive sleep apnea. *Chest* 2012; 142: 440–447.

107. Arzt M, Floras JS, Logan AG, *et al*. Suppression of central sleep apnea by continuous positive airway pressure and transplant-free survival in heart failure: a post hoc analysis of the Canadian Continuous Positive Airway Pressure for Patients with Central Sleep Apnea and Heart Failure Trial (CANPAP). *Circulation* 2007; 115: 3173–3180.

108. Cowie MR, Woehrle H, Wegscheider K, *et al*. Adaptive Servo-Ventilation for Central Sleep Apnea in Systolic Heart Failure. *N Engl J Med* 2015; 373: 1095–1105.

109. Bravata DM, Concato J, Fried T, *et al*. Continuous positive airway pressure: evaluation of a novel therapy for patients with acute ischemic stroke. *Sleep* 2011; 34: 1271–1127.

110. Martínez-García MA, Galiano-Blancart R, Román-Sánchez P, *et al*. Continuous positive airway pressure treatment in sleep apnea prevents new vascular events after ischemic stroke. *Chest* 2005; 128: 2123–2129.

111. Hsu CY, Vennelle M, Li HY, *et al*. Sleep-disordered breathing after stroke: a randomised controlled trial of continuous positive airway pressure. *J Neurol Neurosurg Psychiatry* 2006; 77: 1143–1149.

112. Chong MS, Ayalon L, Marler M, *et al*. Continuous positive airway pressure improves subjective daytime sleepiness in mild-moderate Alzheimer's disease patients with sleep disordered breathing. *J Am Geriatr Soc* 2006; 54: 777–781.

113. Ancoli-Israel S, Palmer BW, Cooke JR, *et al*. Effect of treating sleep disordered breathing on cognitive functioning in patients with Alzheimer's disease: a randomized controlled trial. *J Am Geriatr Soc* 2008; 56: 2076–2081.

114. Cooke JR, Palmer BW, Loredo JS, *et al*. Sustained use of continuous positive airway pressure slows deterioration of cognition, sleep, and mood in patients with Alzheimer's disease and obstructive sleep apnea: an exploratory study. *J Clin Sleep Med* 2009; 5: 305–310.

115. McMillan A, Bratton DJ, Faria R, *et al*. Continous positive airway pressure in older people with obstructive sleep apnoea syndrome (PREDICT): a 12 month multicenter randomized trial. *Lancet Respir Med* 2014; 2: 804–812.

116. Martínez-García MA, Chiner E, Hernandez L, *et al*. Obstructive sleep apnea in the elderly. Role of continuous positive airway pressure treatment. *Eur Respir J* 2015; 46: 142–151.

117. Sawyer AM, Gooneratne NS, Marcus CL, *et al*. A systematic review of CPAP adherence across age groups: clinical and empiric insights for developing CPAP adherence interventions. *Sleep Med Rev* 2011; 15: 343–356.

118. Russo-Magno P, O'Brien A, Panciera T, *et al*. Compliance with CPAP therapy in older men with obstructive sleep apnea. *J Am Geriatr Soc* 2001; 49: 1205–1211.

119. Bravata DM, Concato J, Fried T, *et al*. Auto-titrating continuous positive airway pressure for patients with acute transient ischemic attack: a randomized feasibility trial. *Stroke* 2010; 41: 1464–1470.

120. Woehrle H, Graml A, Weinreich G. Age- and gender-dependent adherence with continuous positive airway pressure therapy. *Sleep Med* 2011; 12: 1034–1036.

121. Ayalon L, Ancoli-Israel S, Stepnowsky C, *et al*. Adherence in patients with Alzheimer's disease and obstructive sleep apnea. *Am J Geriatr Psychiatry* 2006; 14: 176–180.

122. Wozniak DR, Lasserson TJ, Smith I. Educational, supportive and behavioral interventions to improve usage of continuous positive airway pressure machines in adults with obstructive sleep apnoea. *Cochrane Database Syst Rev* 2014; 1: CD007736.

123. McMurdo MET, Roberts H, Parker S, *et al*. Improving recruitment of older people to research through good practice. *Age Ageing* 2011; 40: 659–665.

124. Hughes LD, McMurdo MET, Guthrie B. Guidelines for people not for diseases: the challenges of applying UK clinical guidelines to people with multimorbidity. *Age Ageing* 2013; 42: 62–69.