Sleep apnoea in older people

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Educational Aims

- To provide a comprehensive, up-to-date review of the prevalence of obstructive sleep apnoea in older people
- To describe the mechanisms of central and obstructive sleep apnoea in older people
- To outline the symptoms of sleep apnoea in older people
- To discuss the evidence base for the treatment of obstructive sleep apnoea syndrome in older people.

Summary

Obstructive sleep apnoea is a common disorder in older people, with between 13 and 32% of people over 65 yrs old having some sleep apnoea. The variation in the estimated prevalence is likely to reflect the different health status of the older populations studied and the definitions of the disease. This review will address the prevalence and aetiology of sleep apnoea in older people; outlining the possible consequences and treatment options. Age-related changes in chemosensitivity, and sleep architecture may promote central sleep apnoea in older people; while obstructive sleep apnoea is likely to be the result of increased collapsibility of the upper airway; possibly due to changes in upper airway anatomy and muscle function. The consequences of sleep apnoea in older people are unclear, since both sleep apnoea and aging reduce sleep quality and cognitive function. Moreover, there may be a survival advantage of mild sleep apnoea on the cardiovascular system in older people. Therefore the therapeutic advantages of continuous positive airway pressure in older people require further investigation. If future studies demonstrate that continuous positive airway pressure therapy produces a therapeutic benefit in older people this could result improvements in care.

Competing interests
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The world's population is ageing and by 2045, the number of older people ($\geqslant$60 years of age) will be greater than the number of children ($<$15 years of age) [1]. In Europe, this historical crossover occurred in 1995 due to long-term reductions in fertility and mortality, and by 2050, the ratio of older people to children will be 2:1 (fig. 1). This situation poses major social and economic challenges across Europe. For example, in the UK, the additional cost of long-term care will be approximately £4 billion *per annum* by the year 2040, which is a 60% increase on current budgets [2]. Therefore, strategies to reduce age-related health care costs are vital. One approach could be to promote healthcare that maintains the independence of older people. Obstructive sleep apnoea (OSA) is a potential therapeutic target [3].

OSA occurs due to a loss of pharyngeal dilator muscle tone and increased extra luminal pressure during sleep, producing pharyngeal airway narrowing and occlusion that results in hypopnoeas and apnoeas in susceptible individuals [4]. Each respiratory event is associated with hypoxaemia, and is usually terminated by a brief arousal from sleep, which in turn leads to acute surges in blood pressure [5] and the cardinal symptom of sleep apnoea: excessive daytime sleepiness [6]. The longer term implications of severe OSA include an association with an increased risk of death [7, 8], specifically due to coronary heart disease [9], with severe OSA patients

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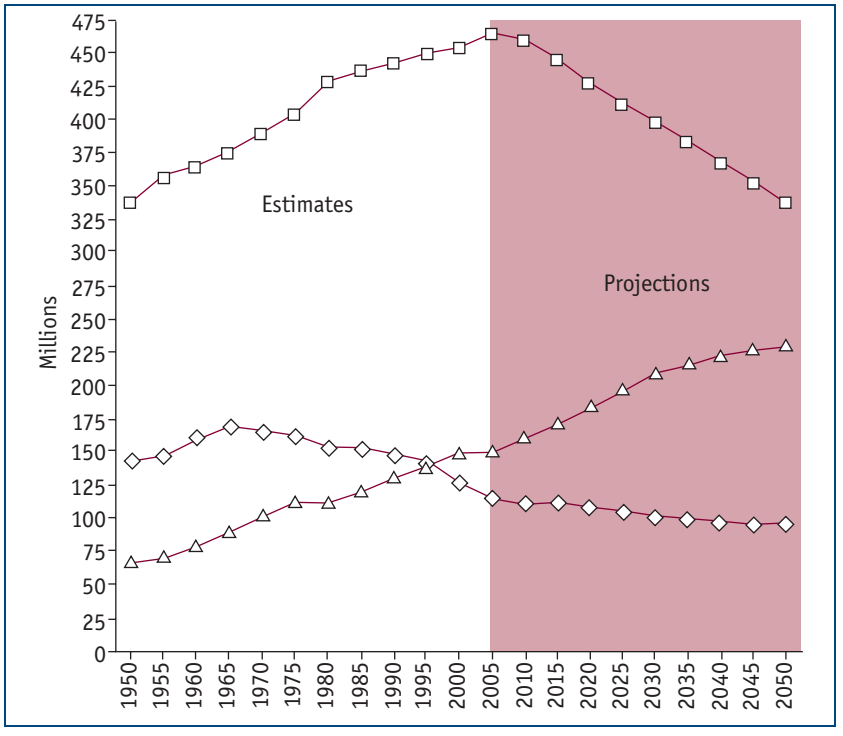

Figure 1

The European population from 1950 to 2050, with estimated population before 2006 (light background) and projected population (dark background). The population is split into children (0–14 yrs; ◇), adult (15–59 yrs; □) and older people (⩾60 yrs; △). The older population is expected to increase in the future, whereas the population <60 years of age is expected to decrease. Reproduced and modified from [1] with the publisher's permission.

having a three-fold increased likelihood of developing hypertension over 4 years, independent of other risk factors [10]. OSA patients also have an increased risk of stroke [8, 11–12], with the 10-year predicted occurrence of stroke being 14% [13]. Patients with OSA syndrome (which is OSA plus symptoms of sleepiness) are two to four times more likely to have road traffic accidents as a result of reduced alertness while driving [14, 15], and possible neurological impairment [16]. This review will address the prevalence and aetiology of sleep apnoea in older people, outlining the possible consequences and treatment options.

Since older people do not always report sleepiness, we have used the term sleep apnoea, rather than obstructive sleep apnoea/hypopnoea syndrome in this article, unless stated otherwise.

The prevalence of sleep apnoea in older people

The prevalence of OSA, defined as an apnoea–hypopnoea index (AHI) >10 events per h, in a working population of people 30–39 years of age, is 5% in females and 12% in males [17]. In older people (>65 yrs), the prevalence of sleep apnoea is at least two-fold greater, with estimates ranging between 13 and 32% [18–23]. The wide variation in these estimates is likely to reflect the different health status of the older populations studied and the definitions of the disease. A detailed breakdown of the prevalence of sleep apnoea in older people is shown in table 1. Using similar study methods and disease criteria, BIXLER *et al.* [20] found the prevalence of sleep apnoea to be 24% in community-dwelling older men (65–100 years of age) compared with 3% in a younger population (20–44 years of age). The high prevalence of sleep apnoea in older people has led to a debate regarding its causes and consequences in the elderly [36, 37].

Aetiology of sleep apnoea in older people

In young healthy individuals, sleep onset is associated with a 10–15% reduction in ventilation [38, 39], due in part to a removal of the wakefulness drive to breath, a reduction in chemosensitivity [40]. The sleep-related reduction in ventilation enables arterial carbon dioxide tension to rise above the hypocapnic apnoeic threshold stabilising breathing during sleep [41]. Several factors can further augment the reduction in ventilation during sleep by increasing the amount of airway narrowing, such as obesity, craniofacial abnormalities and enlargement of upper airway soft tissue structure [42]. This section considers how aging may influence the pathophysiology of sleep apnoea.

Mechanisms of central sleep apnoea in older people

Age-related changes in the control of breathing at sleep onset could, in theory, increase the prevalence of sleep apnoea in older people [43]. However, careful studies of sleep-related changes in chemosensitvity, controlling for any age-related increase in pharyngeal resistance to airflow, indicate that aging *per se* does not promote central sleep apnoea [44]. Indeed, the central control of breathing is relatively stable in older people [45].

An alternative explanation for the increased prevalence of sleep apnoea in older people is that the prevalence of comorbidities associated

Table 1 A review of the literature describing the prevalence of sleep apnoea in older people

						Prevalence of SDB %	
First author [ref.]	Subjects n	Females %	Age yrs	Population	BMI kg per m^2	AHI $\geqslant$5	AHI $\geqslant$10/ $\geqslant$15
Carskadon [24]	40	55	62–86	Community		36	
Coleman [25]	83	28	66±5	Sleep clinic		39	
McGinty [26]	26	0	64.4±4.4	Community			62
Roehrs [27]	97		61–81	Sleep clinic		27	
Smallwood [28]	30	20	50–80	Community	±15%	37	
Yesavage [29]	41	0	69.5±6.5	18 community and 23 clinic		73	
Hoch [30]	56	52	69.3±5.4	Community	±20%	5	4
Knight [31]	27	NG	75.8±5.9	Primary care	25	37	
Mosko [32]	46	65	68.7±6.7	Community		28	16
Ancoli-Israel [33]	233	65	65–101	Nursing home	30.6±6.0	70	
Hoch [18]	105	53	60–91	Community	25.4±3.8	26	13
Philips [34]	92	52	64.2±8.6	Community	25.6±4.3	15	
Ancoli-Israel [19]	346	53	72.8±6.1	Community	24.4±4.2		30
	54	57	70.8±6.2	Community	27.2±5.4		32
Bixler [20]	75	0	65–100	Community		31	24
Young [21]	3448		60–99	Community		54	20
Endeshaw [35]	58	76	77.7±6.7	Community		56	19
Haas [22]	3643	52	70.2±6.9	Community	28.2±5.0	46	20
Hader [23]	80	50	74.1±6.3	General medical clinic	26.8±4.6	43	19

BMI: body mass index; SDB: sleep-disordered breathing; AHI: apnoea–hypopnoea index.

with sleep apnoea is higher in older people; for example, chronic heart failure [46]. Indeed it is estimated that $\leqslant$50% of heart failure patients will have sleep-related breathing disorders [47], but other disorders, such as diabetes and renal failure, also have high prevalence of sleep apnoea and are increased in older people.

Another factor that may predispose older people to sleep apnoea is the age-related increase in arousal frequency [48–50]. 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 fluctuations in the electroencephalogram frequency and breathing patterns in older people appears to support this notion [51].

Mechanisms of obstructive sleep apnoea in older people

Although the prevalence of central sleep apnoea is increased in older people, the majority of sleep-disordered events are obstructive. The increase in OSA may be due to a generalised age-related decrease in the size of the upper airway lumen in older people, specifically in males [52]. Structural changes to the dimensions of the upper airway include a lengthening of the pharyngeal airway in both males [53] and females [54], and the descent of the hyoid bone [55], particularly in individuals with long faces [56], leading to an increase in pharyngeal resistance. It is interesting that, even in healthy elderly people, pharyngeal resistance is increased compared with that in younger people, indicating a predisposition to airway collapse (fig. 2) [43].

The collapsibility of the pharyngeal airway is determined by the transmural pressure across the airway, which is, in turn, influenced by the extraluminal pressure. Fat tissue around the airway is a key factor in the development of OSA in middle-aged people [42, 57], and neck circumference has been shown to be a significant risk factor [58], although older people with OSA typically have a lower body mass index (BMI) and neck circumference, compared with younger patients with similar disease severity [59].

Functionally, the response of the genioglossus muscle to negative pressure applied during wakefulness [54] and sleep [60] is reduced in

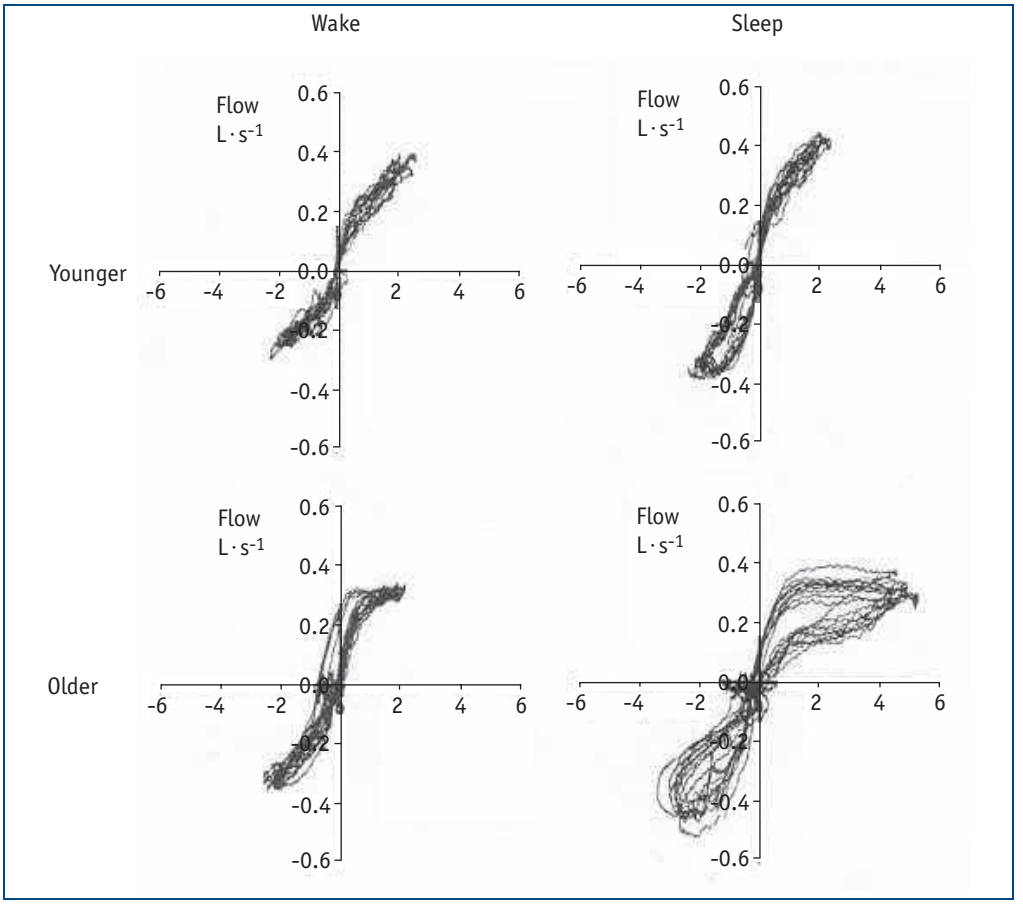

Figure 2

Traces of breathing in a young (top) and older (bottom) person during wakefukness (left) and sleep (right). Each trace shows airflow (measured using a phenunotachograph) plotted against resistive pressure (measured using an oesophageal catheter) for several breaths. Breathing during sleep results in marked airflow limitation, due to upper airway collapse in the the older person. Modifed from [44] with permission from the publisher.

older people compared with younger people [61]. The response to hypoxia is also reduced [62]. Overall, these changes result in reduced respiratory pump and upper airway muscle function at sleep onset [63], and a more collapsible upper airway [64], with the critical closing pressure being -8.3±2.3 cmH_2O in older people, compared with -16.0±6.9 cmH_2O younger people, independent of BMI [58]. This increased collapsibility of the pharyngeal airway in older people may be the explanation for the reduced continuous positive airway pressure (CPAP) requirements recorded in one study of in older patients presenting at a sleep clinic with obstructive sleep apnoea syndrome. The therapeutic level of CPAP being, on average, 2.5 cmH_2O less than in younger OSA patients with matched disease severity (mean±SD CPAP level: older patients 6.9±1.9 cmH_2O; younger patients 9.4±3.5 cmH_2O) [65].

The symptoms of sleep apnoea in older people

The symptoms of OSA in older people are similar to and could be confused with some of the functional impairments of ageing. Both OSA and ageing led to poor sleep, cognitive dysfunction and increased cardiovascular morbidity.

Sleepiness

Sleep becomes more fragmented with age, independent of sleep apnoea [48–50], and there is a well documented age-related reduction in sleep quality [66, 67]. These features of sleep in older people have led to the suggestion that older OSA patients may be habituated to the added disease-related sleep disruption of OSA and, therefore, do not suffer symptoms of

daytime sleepiness in the same way as younger patients. In the large epidemiological study (Sleep Heart Health Study; n=5,407) of community-dwelling adults (mean age 63 years, range 45–99 years) showed that age was associated with a reduction in subjective sleepiness, measured using the Epworth Sleepiness Scale (ESS) in females, but not in males (ESS in young (39–40 years of age) *versus* older ($\geqslant$80 years of age) subjects: females 7.4±4.4 *versus* 6.5±4.0; males 7.3±4.3 *versus* 7.7±4.7 [68]). Assuming age was associated with an increased prevalence of OSA, these data could be interpreted as support for the notion that older OSA patients are less sleepy than younger patients. Although in another study comparing older people with and without OSA (defined as an AHI $>$ 10–15 events per h), patients with OSA were more sleepy than those without OSA [69]. In older OSA patients recruited from sleep clinics, subjective daytime sleepiness was found to be similar to that experienced by younger patients matched for disease severity and BMI in one study [44] and less in another [59]. Thus, the current information on the symptoms of sleepiness in older people with OSA is unclear.

Cognitive dysfunction

A decline in cognitive function is considered part of the aging process; particularly affected is the ability to encode new memories [70]. OSA has also been shown to be associated with cognitive dysfunction [71–76]; however, few studies have included older OSA patients. MATHIEU *et al.* [77] found cognitive dysfunction was independently related to both OSA severity and increasing age, but the coexistence of both factors did not result in increased cognitive dysfunction. AYALON *et al.* [78] showed cognitive dysfunction, on performance of the Go-No-Go cognitive task, in older OSA subjects, but no significant impairment when OSA and increasing age were considered separately. Finally, COHEN-ZION *et al.* [79, 80] used the mini-mental state examination to study the effects of OSA on cognitive function in older patients and found a significant association between the severity of OSA and the self-reported severity of daytime somnolence but, again, once other variables (including total sleep time) were included in the model, only the relationship between cognitive impairment and excessive somnolence remained significant.

When cognitive function is preserved in OSA patients, functional brain imaging has revealed that brain activation is increased, compared with the activation that occurs in healthy controls performing the same task. The association between preserved cognitive function, and greater activation in OSA patients suggests that increased cerebral recruitment is required to maintain cognitive performance [81]. Similar preservation of cognitive function, with compensatory increased cerebral activation, has been found in older subjects; however, older patients with coexistent OSA show decreased cerebral activation and cognitive dysfunction [78]. This suggests that age and OSA could have synergistic effects on cerebral activation and consequently cognitive function.

Acute cardiovascular consequences of sleep apnoea in older people

Acute surges in blood pressure and heart rate associated with arousal at the termination of an apnoeic event have been implicated in the increased prevalence of hypertension in patients with sleep apnoea [10, 82]. In older people with sleep apnoea, the risk of having hypertension is no greater than for older people without the disorder [22]. This may be a consequence of the age-related shift in sleep apnoea characteristics described earlier. For example, a recent study has shown that older people have a reduced acute cardiovascular response to arousal from sleep, compared with younger people [83]. Thus, the poorer cardiovascular reactivity of older adults may, paradoxically, reduce the impact of arousals from sleep and protect against cardiovascular morbidity and mortality. However, it is important to remember that the cardiovascular consequences of sleep apnoea in older people may also be influenced by survival bias, as middle-aged, hypertensive OSA patients may not survive into old age.

Treatment of sleep apnoea in older people

OSA syndrome can be effectively treated with CPAP. The recent National Institute of Clinical Excellence (NICE) Health Technology Appraisal reviewing the use of CPAP concluded that it was an effective and cost-efficient treatment for middle-aged people with OSA syndrome [84].

The large therapeutic benefit of CPAP therapy is typically measured as an improvement in sleepiness. Using the ESS as a measure of

subjective sleepiness, the mean difference between patients treated with CPAP *versus* conservative (or placebo) treatment was a reduction of 2.7 points (95% CI -3.45– -1.96 points); in patients with severe symptoms, the treatment effect was greater (mean difference in ESS -5.0, 95% CI -3.0– -1.6) [84]. In older people who may be less sleepy, the CPAP treatment benefits may differ.

The specific cost of CPAP therapy is less than £4,000 per quality-adjusted life-year (QALY) gained, allowing for changes in sleepiness, quality of life, vascular risk, driving performance and CPAP costs [84]. However, in older people with reduced symptoms of sleepiness, vascular risk, and a shorter life expectancy, the cost per QALY gained with CPAP may fall. Therefore the benefits of CPAP treatment cannot be presumed to be replicated in older people without an evidence base.

Systematic literature searches show that the available trial evidence for the efficacy of CPAP therapy is almost entirely from the middle-aged [84], with few trials in older people [85]. Likewise, there is limited information on CPAP treatment adherence in older people. Retrospective data suggest that CPAP compliance is similar in older and younger OSA patients, with 64% of older people being able to tolerate CPAP [86].

Conclusion

Our review has revealed a paucity of data in older patients with sleep apnoea. Since the European population is aging, this represents a research challenge for the field. If future studies demonstrate that CPAP therapy produces a therapeutic benefit at the level of the individual patient, this could result in significant changes in the care of older people with OSA.

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References

1. United Nations DESA. Population Division, Population Estimates and Projections Section. Fact Sheet, Series A, 7 March 2007. New York, UN DESA, 2007.
2. Karlsson M, Mayhew L, Plumb R, *et al*. Future costs for long-term care: cost projections for long-term care for older people in the United Kingdom. *Health Policy* 2006; 75: 187–213.
3. 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.
4. Remmers J, deGroot WJ, Sauerland EK, *et al*. Pathogenesis of upper airway occlusion during sleep. *J Appl Physiol* 1978; 44: 931–938.
5. O'Driscoll DM, Meadows GE, Corfield DR, *et al*. Cardiovascular response to arousal from sleep under controlled conditions of central and peripheral chemoreceptor stimulation in humans. *J Appl Physiol* 2004; 96: 865–870.
6. Stradling JR, Davies RJ. Sleep. 1: Obstructive sleep apnoea/hypopnoea syndrome: definitions, epidemiology, and natural history. *Thorax* 2004; 59: 73–78.
7. Marin J, Carrizo S, 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.
8. Yaggi H, Concato J, Kernan W, *et al*. Obstructive sleep apnea as a risk factor for stroke and death. *N Engl J Med* 2005; 353: 2070–2073.
9. Punjabi NM, Caffo BS, Goodwin JL, *et al*. Sleep-disordered breathing and mortality: a prospective cohort study. *PLoS Med* 2009; 6: e1000132.
10. Peppard P, Young T, Palta M, *et al*. Prospective study of the association between sleep-disordered breathing and hypertension. *N Engl J Med* 2000; 342: 1378–1384.
11. 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.
12. Redline S, Yenokyan G, Gottlieb DJ, *et al*. Obstructive sleep apnea–hypopnea and incident stroke: the sleep heart health study. *Am J Respir Crit Care Med* 2010; 182: 269–277.
13. Kiely J, McNicholas W. Cardiovascular risk factors in patients with obsctuctive sleep apnoea syndrome. *Eur Respir J* 2000; 16: 128–133.
14. George CF. Sleep. 5: Driving and automobile crashes in patients with obstructive sleep apnoea/hypopnoea syndrome. *Thorax* 2004; 59: 804–807.
15. 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.
16. Morrell MJ, Jackson ML, Twigg GL, *et al*. Changes in brain morphology in patients with obstructive sleep apnoea. *Thorax* 2010; 65: 908–914.
17. Young TD, Palta M, Dempsey J, *et al*. The occurence of sleep-disordered breathing among middle-aged adults. *N Engl J Med* 1993; 328: 1230–1235.

18. Hoch CC, Reynolds CF. Comparison of sleep-disordered breathing among healthy elderly in the seventh, eighth, and ninth decades of life. *Sleep* 1990; 6: 502–511.
19. Ancoli-Israel S, Klauber M, Stepnowsky C, *et al.* Sleep-disordered breathing in African-American elderly. *Am J Respir Crit Care Med* 1995; 152: 1946–1949.
20. Bixler EO, Vgontzas AN, Ten Have T, *et al.* Effects of age on sleep apnea in men: I. Prevalence and severity. *Am J Respir Crit Care Med* 1998; 157: 144–148.
21. Young T, Shahar E, Nieto F, *et al.* Predictors of sleep-disordered breathing in community-dwelling adults: the Sleep Heart Health Study. *Arch Intern Med* 2002; 162: 893–900.
22. Hass D, Foster G, Nieto J, *et al.* Age-dependent associations between sleep disordered breathing and hypertension. *Circulation* 2005; 111: 614–621.
23. Hader C, Schroeder A, Hinz M, *et al.* Sleep disordered breathing in the elderly: comparison of women and men. *J Physiol Pharmacol* 2005; 56: 85–91.
24. Carskadon M, Dement W. Respiration during sleep in the aged human. *J Gerontol* 1981; 36: 420–430.
25. Coleman RM, Miles LE, Guilleminault CC, *et al.* Sleep–wake disorders in the elderly: polysomnographic analysis. *J Am Geriatr Soc* 1981; 29: 289–296.
26. 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.
27. 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.
28. Smallwood RG, Vitiello MV, Giblin EC, *et al.* Sleep apnea: relationship to age, sex, and Alzheimer's dementia. *Sleep* 1983; 6: 16–22.
29. Yesavage J, Bliwise D, Guilleminault C, *et al.* Preliminary communication: intellectual deficit and sleep-related respiratory disturbance in the elderly. *Sleep* 1985; 8: 30–33.
30. Hoch CC, Reynolds CF 3rd, Kupfer DJ, *et al.* Sleep-disordered breathing in normal and pathologic aging. *J Clin Psychiatry* 1986; 47: 499–503.
31. Knight H, Millman R, Gur R, *et al.* Clinical significance of sleep apnea in the elderly. *Am Rev Respir Dis* 1987; 136: 845–850.
32. Mosko S, Dickel M, Ashurst J. Night-to-night variability in sleep apnea and sleep-related periodic leg movements in the elderly. *Sleep* 1988; 11: 340–348.
33. Ancoli-Israel S, Parker L, Sinaee R, *et al.* Sleep fragmentation in patients from a nursing home. *J Gerontol* 1989; 44: 18–21.
34. Phillips B, Berry D, Schmitt F, *et al.* Sleep-disordered breathing in the healthy elderly. Clinically significant? *Chest* 1992; 101: 345–349.
35. Endeshaw YW, Johnson TM, Kutner MH, *et al.* Sleep-disordered breathing and nocturia in older adults. *J Am Geriatr Soc* 2004; 52: 957–960.
36. Lévy P, Pépin JL, Malauzat D, *et al.* Is sleep apnea syndrome in the elderly a specific entity? *Sleep* 1996; 19: S29–S38.
37. Lavie P, Lavie L, Herer P. All-cause mortality in males with sleep apnoea syndrome: declining mortality rates with age. *Eur Respir J* 2005; 25: 514–520.
38. Douglas NJ, White DP, Pickett CK, *et al.* Respiration during sleep in normal man. *Thorax* 1982; 37: 840–844.
39. Stradling JR, Chadwick GA, Frew AJ. Changes in ventilation and its components in normal subjects during sleep. *Thorax* 1985; 40: 364–370.
40. McKay LC, Atalla A, Morrell MR. Physiology and neural control of breathing during sleep. *Eur Respir Mon* 2010; 50: 1–16.
41. Dempsey JA, Veasey SC, Morgan BJ, *et al.* Pathophysiology of sleep apnea. *Physiol Rev* 2010; 90: 47–112.
42. Schwab RJ, Pasirstein M, Pierson R, *et al.* Identification of upper airway anatomic risk factors for obstructive sleep apnea with volumetric magnetic resonance imaging. *Am J Respir Crit Care Med* 2003; 168: 522–530.
43. Browne HAK, 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.
44. 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.
45. Wellman A, Malhotra A, Jordan AS, *et al.* Chemical control stability in the elderly. *J Physiol* 2007; 581: 291–298.
46. Cowie M, Wood D, Coats A, *et al.* Incidence and aetiology of heart failure; a population-based study. *Eur Heart J* 1999; 20: 421–428.
47. 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.
48. 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.
49. Mathur R, Douglas NJ. Frequency of EEG arousals from nocturnal sleep in normal subjects. *Sleep* 1995; 18: 330–333.
50. Boselli M, Parrino L, Smerieri A, *et al.* Effect of age on EEG arousals in normal sleep. *Sleep* 1998; 21: 351–357.
51. Pack AI, Silage DA, Millman RP, *et al.* Spectral analysis of ventilation in elderly subjects awake and asleep. *J Appl Physiol* 1986; 64: 533–544.
52. 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.
53. Shigeta Y, Enciso R, Ogawa T, *et al.* Changes in three dimensional simulation models of the airway which are due to increases in age or body mass index. *Stud Health Technol Inform* 2008; 132: 460–462.
54. 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: e9–e14.
55. 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.
56. Pae EK, 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.
57. Horner RL, Shea SA, McIvor J, *et al.* Pharyngeal size and shape during wakefulness and sleep in patients with obstructive sleep apnoea. *Q J Med* 1989; 72: 719–735.

58. Davies RJ, Ali NJ, Stradling JR. Neck circumference and other clinical features in the diagnosis of the obstructive sleep apnoea syndrome. *Thorax* 1992; 47: 101–105.
59. 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.
60. Eikermann M, Jordan A, Chamberlin N, *et al.* The influence of aging on pharyngeal collapsibility during sleep. *Chest* 2007; 131: 1702–1709.
61. 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.
62. 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.
63. 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* 2000; 88: 1831–1839.
64. 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* 2008; 104: 1618–1624.
65. Kostikas K, Browne HA, Ghiassi R, *et al.* The determinants of therapeutic levels of continuous positive airway pressure in elderly sleep apnea patients. *Respir Med* 2006; 100: 1216–1625.
66. Bixler EO, Kales A, Jacoby JA, *et al.* Nocturnal sleep and wakefulness: effects of age and sex in normal sleepers. *Int J Neurosci* 1984; 23: 33–42.
67. Redline S, Kirchner HL, Quan SF, *et al.* The effects of age, sex, ethnicity and sleep disordered breathing on sleep architecture. *Arch Intern Med* 2004; 164: 406–418.
68. Unruh ML, Redline S, An MW, *et al.* Subjective and objective sleep quality and aging in the sleep heart health study. *J Am Geriatr Soc* 2008; 56: 1218–1227.
69. Endeshaw Y. Clinical characteristics of obstructive sleep apnoea in community-dwelling older adults. *J Am Geriatr Soc* 2006; 54: 1740–1744.
70. Hedden T, Gabrieli JD. Insights into the ageing mind: a view from cognitive neuroscience. *Nat Rev Neurosci* 2004; 5: 87–96.
71. Twigg GL, Papaioannou I, Jackson M, *et al.* Obstructive sleep apnea syndrome is associated with deficits in verbal but not visual memory. *Am J Respir Crit Care Med* 2010; 182: 98–103.
72. Naegele B, Launois SH, Mazza S, *et al.* Which memory processes are affected in patients with obstructive sleep apnea? An evaluation of 3 types of memory. *Sleep* 2006; 29: 533–544.
73. Quan SF, Wright R, Baldwin CM, *et al.* Obstructive sleep apnea–hypopnea and neurocognitive functioning in the Sleep Heart Health Study. *Sleep Med* 2006; 7: 498–507.
74. Ferini-Strambi L, Baietto C, Di Gioia MR, *et al.* Cognitive dysfunction in patients with obstructive sleep apnea (OSA): partial reversibility after continuous positive airway pressure (CPAP). *Brain Res Bull* 2003; 61: 87–92.
75. Adams N, Strauss M, Schluchter M, *et al.* Relation of measures of sleep-disordered breathing to neuropsychological functioning. *Am J Respir Crit Care Med* 2001; 163: 1626–1631.
76. Redline S, Strauss ME, Adams N, *et al.* Neuropsychological function in mild sleep-disordered breathing. *Sleep* 1997; 20: 160–167.
77. 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.
78. 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.
79. Cohen-Zion M, Stepnowsky C, Johnson S, *et al.* Cognitive changes and sleep disordered breathing in elderly: differences in race. *J Psychosom Res* 2004; 56: 549–553.
80. 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.
81. Ayalon L, Ancoli-Israel S, Klemfuss Z, *et al.* Increased brain activation during verbal learning in obstructive sleep apnea. *Neuroimage* 2006; 31: 1817–1825.
82. Nieto FJ, Young TB, Lind E, *et al.* Association of sleep-disordered breathing, sleep apnea, and hypertension in a large community-based study. *JAMA* 2000; 283: 1829–1836.
83. Goff EA, O'Driscoll DM, Simmonds AK, *et al.* The cardionvascular response to arousal from sleep decreases with age in healthy adults. *Sleep* 2008; 31: 1009–1017.
84. McDaid C, Griffin S, Weatherly H. 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: iii–iv, xi–xiv, 1–119, 143–274.
85. Chong MS, Ayalon L, Marler M, *et al.* Continuous positive airway pressure reduces subjective daytime sleepiness in patients with mild to moderate Alzheimer's disease with sleep disordered breathing. *J Am Geriatr Soc* 2006; 54: 777–781.
86. 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.