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Supplement


# Sleep disorders:
## a practical guide for Australian health care practitioners

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An under-recognised individual and community problem

**Public health implications**
The community burden

**Circadian rhythm disorders**
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# Sleep disorders: a practical guide for Australian health care practitioners

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Darren R Mansfield and R Doug McEvoy

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Australasian Sleep Association and the Sleep Health Foundation.

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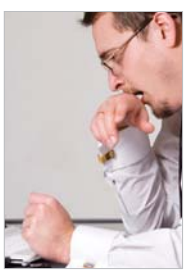


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# Sleep loss and sleep disorders

## Shedding light on common but under-recognised individual and community problems

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By the time the average person reaches his or her average life expectancy of around 80 years, they will have invested 28 years of their lives in sleep. It is remarkable that an activity of this scale is so taken for granted. Ironically, it is the defining characteristic of sleep — perceptual disengagement from the environment — that may provide the explanation for our disinclination to give our need for sleep its due attention. There is a natural tendency to invest effort in activities that provide conscious reward, and sleep risks being assigned a low priority compared with activities that occur during wakefulness. Importantly, these wakeful activities suffer where sleep is impaired.

While there are numerous hypotheses regarding the precise purpose of sleep, much of what we understand comes from experimental and naturalistic studies of individuals who are subjected to, or subject themselves to, inadequate sleep. Chronic sleep deficiency is believed to be widespread in Western societies.[1] Sleep deficiency adversely affects alertness, cognition, productivity, safety, learning and mood and is implicated in a raft of additional pathophysiological processes, leading to adverse metabolic, cardiovascular and mental health outcomes, and premature death. This demands programs to improve sleep habits of the community generally and to detect and treat sleep disorders where they exist.

Linking sleep loss to specific adverse physiological and psychological consequences has led to some important, although limited, instances of behavioural change at the community level. Useful examples can be found in safety-critical industries, where alertness failure can have significant and potentially catastrophic consequences. Transport, aviation and, to some extent, health care industries have attempted to improve rostering practices to allow adequate opportunity for sleep and to minimise disruption of endogenous circadian pacemaker sleep–wake cycles. The duty to provide a safe work environment through enlightened roster arrangements rests with the employer. Equally importantly, employees should act on opportunities for sleep afforded by these rostering systems to ensure that they are "fit for duty". Although as much as 16% of the Australian workforce is employed in shift work, optimal rostering systems and evidence-based countermeasures for workplace sleepiness are not always readily available or implemented. Despite some progress, the consequences of sleep loss remain under-recognised across the majority of workplaces and much of the community. The direct relationships between healthy sleep and a healthier, more productive and safer community needs to be better understood.

The previous Labor government in Australia identified productivity and population health and wellbeing as strategic research priorities, and as being among the most important challenges facing Australia (http://www.innovation.gov.au/research/Documents/SRP_fact_sheet_WEB.PDF). Good sleep health is a core consideration in both these domains. However, there remains insufficient awareness at leadership level of the importance of optimal sleep in achieving these national goals. The issue of sleep health is yet to be addressed in our national preventive health strategy. Diet and exercise are regarded as key components of a healthy lifestyle, yet despite compelling evidence, minimal attention has been given to healthy sleep. Sleep medicine and sleep science, which are relatively new fields, have much to do to deliver this message to community leaders.

As much as improvement is required in existing practices, sleep health is also confronted by new and emerging challenges. Communities are faced with a rate of technological advancement that is historically unprecedented. The extent to which technology intrudes on our sleep routines remains incompletely defined. However, current observational evidence implicates electronic entertainment and communication devices in sleep loss, academic underachievement and obesity among adolescents.[2] Further, late night exposure to the light that is emitted from these devices may disrupt the circadian pacemaker, compounding the sleep disturbance and potential health consequences. There is an urgent need to better educate adolescents and their parents about optimal sleep routines. Schools could be powerful allies in this effort.

As much as unhealthy sleep habits are pervasive in modern society, it is critical that the discipline of sleep medicine ensures that community efforts are focused on effective and cost-effective solutions. Sustainability of any health care program is best secured by establishing goals of care, defining desired outcomes and identifying high-risk groups requiring particular attention. Careful guidance is required to ensure that health care expenditure delivers on preset objectives. Such investment is likely to be richly rewarded through increases in productivity and improvements in safety alone.[3] However, blank cheques are never an option, and meeting the challenge of improving sleep health will need to be done within a tight, but not self-defeating, fiscal framework. For example, given that we recognise that continuous positive airway pressure (CPAP) is a cost-effective therapy for higher-risk and symptomatic obstructive sleep apnoea sufferers, strategies for better targeting care delivery to these groups may allow for much needed and consistent CPAP-funding models across the states and territories.

There is much information already in place to inform practice. For example, guidelines are available on appropriate use of therapeutic devices such as CPAP machines.[4] However, dissemination of this equipment is unregulated, with the Therapeutic Goods Administration yet to adopt the United States Food and Drug Administration principle of sale of CPAP devices by medical prescription. Guidelines have been recently updated for sleep studies in adults (http://www.sleep.org.au/information/sleep-documents)

**Sleep loss and sleep disorders: key points**

**Public health implications of sleep loss: the community burden (*page S7*)**

- An evaluation of the sleep habits of Australians demonstrates that disrupted sleep, inadequate sleep duration, daytime fatigue, excessive sleepiness and irritability are highly prevalent (20%–35%). While about half of these problems are attributable to specific sleep disorders, the balance appears largely due to poor sleep habits or choices to limit sleep opportunity.
- The economic impact of sleep disorders includes costs to Australia of $5.1 billion per year of which $800 million are direct health care costs of the disorders and of other medical conditions attributable to them, with the balance of $4.3 billion mainly attributable to productivity losses and non-health costs of sleep loss-related accidents.

**Common sleep disorders affecting individuals and communities**

Obstructive sleep apnoea:

- Obstructive sleep apnoea (OSA) is one of the most common sleep disorders. Population studies using sleep recordings show that OSA affects about 25% of adult males and 10% of adult females although most affected individuals do not complain of daytime sleepiness. Combining simple screening questionnaires with home sleep studies is helpful in identifying the severe and symptomatic cases that are likely to benefit most from treatment. Using simplified pathways in controlled studies has shown that patients with a high pretest probability of symptomatic OSA can be managed well in primary care, or by skilled nurses with appropriate specialist sleep service clinical support (*page S21*).
- Severe OSA is strongly associated with increased mortality, stroke and cardiovascular disease in middle-aged populations. The cardiovascular risk from moderate OSA is uncertain, although the data suggest an increased risk for stroke (particularly in men). There is no evidence of increased cardiovascular risk from mild OSA (*page S27*).

Shift work disorder (*page S11*):

- Nearly 1.5 million Australians are employed in shift work. Health, performance and safety are often degraded in shift workers due to the combined effects of circadian rhythm misalignment and inadequate and poor-quality sleep (resulting from disorders such as OSA, insomnia and shift work disorder).
- Optimal rostering, scheduled napping, appropriately timed light and melatonin treatment to promote circadian adaptation, and judicious use of pharmacotherapy are strategies that aim to mitigate the adverse effects of shift work, along with screening for sleep and mood disorders, and close monitoring of risk factors for cardiovascular disease.

Insomnia (*page S36*):

- Insomnia is a very common disorder, with Australian population surveys showing that 13%–33% of the adult population have regular difficulty either getting to sleep or staying asleep. Chronic insomnia is unlikely to spontaneously remit and, over time, will be characterised by cycles of relapse and remission or persistent symptoms.
- Chronic insomnia is best managed using non-drug strategies such as cognitive behaviour therapy, which can be highly effective. However, if patients have ongoing symptoms there may be a role for adjunctive use of medication such as hypnotics, observing recognised techniques that minimise tolerance and dependency.

Delayed sleep phase disorder (*page S16*):

- Delayed sleep phase disorder is a circadian rhythm sleep disorder most commonly seen in adolescents. It needs to be differentiated from insomnia — the use of sleep diaries illustrating delayed sleep onset and waking with normal sleep duration, without imposed restriction, confirms the distinction.
- Imposing conventional wake times fails to resolve the phase delay and risks sleep loss and the potential for adverse impact on academic performance and social functioning.
- Awareness and education are important components of the treatment plan. The effects of delayed sleep phase disorder may be minimised by a combination of behavioural and chronotherapeutic strategies. Bright light and melatonin can manipulate the circadian phase; however, their timing in relation to the natural sleep phase is critical to success and sometimes requires specialist input.

Sleep disorders in children (*page S31*):

- Sleep disorders are very common in childhood. They include insufficient sleep, frequent night awakenings and OSA.
- OSA in childhood has important implications for learning, behaviour and cardiovascular health.
- Adenotonsillectomy can be a highly efficacious therapy for paediatric OSA. However, in 20% of patients, the disease persists despite surgery, particularly among children with obesity, underlying syndromes or malformations. ◆

— an area of potential confusion with the increased availability of diagnostic tools of varying quality in the primary care setting. Accreditation standards among sleep health delivery services, including home and in-laboratory sleep-testing facilities, have led to the evolution an increasingly sophisticated array of benchmarks. These include a recent partnership between the National Association of Testing Authorities and the Australasian Sleep Association to ensure high standards in sleep medicine services (http://www.nata.com.au; http://www.sleep.org.au/information/sleep-documents). Balancing the principle of optimal standards against accessibility, affordability and viability of services is particularly challenging in Australia, with its unique regional and remote demographics.

The articles in this supplement summarise the current understanding of a range of highly prevalent sleep problems and their impact on individual and community wellbeing. Key learning points from the articles can be found in the Box. The articles outline the burden of common sleep problems and their substantial economic cost in the Australian community. Key bodies such as the Sleep Health Foundation and the Australasian Sleep Association play an important role in articulating these issues to the broader health profession, schools, industry, policymakers and society generally to ensure healthy sleep becomes more of an established community priority. This supplement is an expression of their intent to do so.

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# Public health implications of sleep loss: the community burden

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## Summary

- Poor sleep imparts a significant personal and societal burden. Therefore, it is important to have accurate estimates of its causes, prevalence and costs to inform health policy.
- A recent evaluation of the sleep habits of Australians demonstrates that frequent (daily or near daily) sleep difficulties (initiating and maintaining sleep, and experiencing inadequate sleep), daytime fatigue, sleepiness and irritability are highly prevalent (20%–35%). These difficulties are generally more prevalent among females, with the exception of snoring and related difficulties. While about half of these problems are likely to be attributable to specific sleep disorders, the balance appears attributable to poor sleep habits or choices to limit sleep opportunity.
- Study of the economic impact of sleep disorders demonstrates financial costs to Australia of $5.1 billion per year. This comprises $270 million for health care costs for the conditions themselves, $540 million for care of associated medical conditions attributable to sleep disorders, and about $4.3 billion largely attributable to associated productivity losses and non-medical costs resulting from sleep loss-related accidents. Loss of life quality added a substantial further non-financial cost.
- While large, these costs were for sleep disorders alone. Additional costs relating to inadequate sleep from poor sleep habits in people without sleep disorders were not considered. Based on the high prevalence of such problems and the known impacts of sleep loss in all its forms on health, productivity and safety, it is likely that these poor sleep habits would add substantially to the costs from sleep disorders alone.

Sleep is a basic and necessary biological process that demands to be satisfied as much as our need for food and drink. Inadequate sleep can occur if insufficient time is allowed for it or if a disorder is present that disturbs sleep quality. It is only recently that we have begun to understand the scale of the health and social consequences of insufficient sleep and sleep disorders. Sleep loss from these problems is associated with disturbances in cognitive and psychomotor function including mood, thinking, concentration, memory, learning, vigilance and reaction times.[1,2] These disturbances have adverse effects on wellbeing, productivity and safety. Insufficient sleep is a direct contributor to injury and death from motor vehicle and workplace accidents.[3] Further, relationships have been demonstrated between shortened sleep and a range of health problems including hypertension,[4] type 2 diabetes,[5] obesity,[6] cardiovascular disease[7,8] and total mortality risk.[9] Specific sleep disorders such as insomnia,[10] obstructive sleep apnoea (OSA)[11] and restless leg syndrome[12] have also been associated with increased morbidity and mortality. These sleep-related problems incur financial costs relating to health and other expenditures and non-financial costs relating to loss of quality of life. This article considers the prevalence and economic impacts of sleep problems in Australia.

## Prevalence of sleep problems

There have been very few studies of the prevalence of disturbed sleep in Australia. A small survey ($n = 216$) of sleeping difficulties, daytime sleepiness and hypnotic medication use was conducted in Adelaide more than 20 years ago.[13] A larger survey ($n = 535$) was conducted in Newcastle, New South Wales, in 1996 but was limited to a question about insomnia and hypnotic medications.[14] Another small survey ($n = 267$) in rural Victoria among Australian day workers was heavily weighted to men.[15] More recently, a large NSW mail survey ($n = 3300$) reported that 18.4% of participants slept less than 6.5 hours a night and 11.7% complained of chronic sleepiness.[16] A recent study of the insomnia burden suggested a prevalence of 5.6%, with increased use of health care.[17]

To further characterise sleep quality in a large representative sample of Australians, in 2010, the Sleep Health Foundation (www.sleephealthfoundation.org.au) commissioned a national survey of sleeping difficulties and negative daytime consequences of poor sleep. It was modelled on the Sleep in America surveys conducted by the National Sleep Foundation, in part to allow international comparisons. A national polling organisation (Roy Morgan Research) was commissioned to perform the work. It conducted a national landline telephone survey of adolescents and adults (14 to > 70 years of age) across successive weekend evenings. The survey contained 14 questions about sleep: five about sleeping difficulty, two about snoring and OSA, one about restless legs, one about sleeping medication, three about daytime impairments usually associated with sleep disturbance, and two about nocturnal sleep duration (weekdays and weekends) (Box 1). There were 1512 respondents from all states and territories, both urban and rural, with sampling proportionate to the populations of those areas, sex and age.

Box 1 shows the proportions of respondents reporting current sleep difficulties and daytime impairments at least a few times per week (indicative of significant problem), as well as average self-reported sleep duration for the population overall, for males and females, and for each age group. The results illustrate that a considerable proportion of Australians report frequent sleeping difficulties. Overall, 20% of respondents had frequent difficulty falling asleep, which was more prevalent among females and younger age groups. Frequent waking during the night was reported by 35% overall, again more commonly among females but increasing with age. Thirty-five per cent reported waking unrefreshed and 24% reported inadequate sleep. Daytime sleepiness, fatigue/exhaustion and irritability were common issues (19%–24%).

Symptoms were examined to determine likely prevalence of insomnia by selecting those with specific self-

**1 Proportions of survey respondents experiencing sleep difficulties, sleep disorder symptoms and daytime impairments a few times a week or more (often), overall and by sex and age group**

| Difficulty experienced often | Overall | Sex | | Age group | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Male | Female | 14–17 years | 18–24 years | 25–34 years | 35–49 years | 50–64 years | ⩾ 65 years |
| Weighted proportion of total | 100% | 49.4% | 50.6% | 6.4% | 11.7% | 17.4% | 26.0% | 21.9% | 16.5% |
| Sleeping difficulty | | | | | | | | | |
| Difficulty falling asleep | 19.6% | 16.9% | 22.4%* | 33.6%† | 32.2%† | 17.6% | 20.0% | 14.6% | 13.5% |
| Waking a lot during night | 34.9% | 30.4% | 39.3%† | 21.2% | 28.1% | 32.6% | 42.6%† | 31.8% | 39.5%† |
| Waking up too early | 25.3% | 22.9% | 27.7%* | 19.5% | 23.4% | 20.3% | 29.1%* | 25.5% | 27.9%* |
| Waking feeling unrefreshed | 34.7% | 31.8% | 37.6%* | 38.1%† | 44.0%† | 42.0%† | 39.8%† | 28.5% | 19.3% |
| Did not get adequate sleep | 23.7% | 17.9% | 29.4%† | 24.9%† | 29.3%† | 25.3%† | 24.5%† | 21.4% | 19.3% |
| Snoring, obstructed breathing | | | | | | | | | |
| Frequent or loud snoring‡ | 21.2% | 26.4%† | 12.1% | 8.4% | 8.6% | 21.7%† | 23.5%† | 20.0%† | 20.0%† |
| Pauses in breathing in sleep‡ | 6.6% | 6.2% | 5.1% | 2.9% | 4.4% | 3.8% | 4.6% | 7.8%* | 8.4%* |
| Restless legs | 9.4% | 8.6% | 10.3% | 4.0% | 5.3% | 11.2%† | 7.2% | 10.7%† | 14.5%† |
| Prescribed sleep medication use | 3.6% | 4.0% | 3.1% | 3.5% | 2.5% | 1.8% | 2.4% | 5.8%† | 5.4%† |
| Daytime symptoms | | | | | | | | | |
| Daytime sleepiness | 19.0% | 15.7% | 22.3%* | 24.6%† | 26.2%† | 21.1%† | 22.4%† | 13.6% | 11.4% |
| Fatigue or exhaustion | 23.5% | 20.0% | 27.0%† | 22.8% | 27.7%† | 27.7%† | 29.1%† | 18.8% | 14.2% |
| Irritable or moody | 18.8% | 18.2% | 19.3% | 18.8% | 19.2% | 27.9%† | 22.9%† | 12.9% | 9.8% |
| Sleep duration | | | | | | | | | |
| Weeknights (Sunday–Thursday), h | 7.16 | 7.15 | 7.17 | 8.24† | 7.49* | 7.18 | 6.86 | 7.01 | 7.14* |
| Weekend nights (Friday, Saturday), h | 7.37 | 7.37 | 7.37 | 8.45† | 7.37 | 7.54 | 7.19 | 7.29 | 7.14 |
| Overall, h | 7.22 | 7.21 | 7.23 | 8.30† | 7.46* | 7.28 | 6.95 | 7.09 | 7.14* |
| Sleep disorder estimates | | | | | | | | | |
| Severe clinical insomnia§ | 6.9% | 5.0% | 8.7%* | 2.0% | 11.3%* | 4.2% | 10.1%* | 6.9% | 3.8% |
| Sleep apnoea‡,¶ | 4.9% | 6.3%* | 3.6% | 0 | 2.2% | 2.1% | 4.7% | 7.7%* | 7.0%* |

* $P < 0.05$. † $P < 0.001$. ‡ Adjusted for the 10%–11% who "can't say". § Estimated Insomnia Severity Index > 14, derived from data for sleeping difficulty and daytime symptoms. ¶ Estimates derived from data for frequent breathing pauses and loud snoring. ◆

reported sleep difficulties plus daytime impairment[18] to derive a score that very closely simulates the Insomnia Severity Index, a highly reliable and valid tool to identify clinical insomnia.[19] This suggested an overall presence of severe insomnia (Insomnia Severity Index, >14) of 6.9%, 8.7% in women and 5% in men (Box 1).

Prevalence of sleep apnoea was derived by determining the proportion of respondents who snored loudly at least a few times a week and had observed breathing pauses during sleep at least a few times a month. An overall prevalence of 4.9% was noted, but in this case, prevalence was higher among males (6.4%) than females (3.6%).

While these prevalences of specific sleep disorders were derived from combinations of questionnaire responses, they are similar to the prevalences determined from other population-based studies.[10,20] These findings suggest that specific sleep disorders may account for about half of the complaints of daytime sleepiness and fatigue and exhaustion noted in our survey. While other health problems can disturb sleep, particularly in older patients, much of the balance may be due to insufficient sleep duration by choice or through circumstances that result in sleep being given a lower priority than work, social or family activities. Sleep duration estimates are significantly below the putative average adolescent sleep requirement of 9 hours a night and adult sleep requirement of 7.5–8 hours a night for both men and women, particularly among those between the ages of 35 and 65 years.[21] Insufficient sleep at least a few times a week was reported by 23.7% of the sample, more frequently by females, and more commonly in the younger to middle-aged groups. Perhaps relevant to this, a study of young adults has shown that those with shorter habitual sleep patterns carried the highest sleep debt, suggesting self-selected sleep restriction.[22]

The general point that emerges from these data is that inadequate sleep (duration or quality) and its daytime consequences are widely prevalent in Australians, either because of a specific sleep-related disorder or from voluntarily shortened sleep through choice or circumstance. Although there are limitations with telephone surveys (eg, low response rates to landline phone calls), the results are very comparable with those observed in similar surveys conducted elsewhere, such as the 2008 Centers for Disease Control and Prevention study, which reported that 28% of United States adults had insufficient sleep or rest (<7 h/night) on most nights over a 30-day survey period.[23]

## Economic impact

Poor sleep and its consequences result in significant costs to the community. Although there have been no detailed economic evaluations of the costs associated with insufficient sleep in otherwise healthy individuals, analyses have been undertaken for those with sleep disorders.[24,25] OSA provides an example of a widely prevalent sleep disorder with significant comorbidities, including impaired daytime alertness, increased accident risk, hypertension, vascular

**2 Summary of the annual costs of sleep disorders and associated conditions, 2010[21]**

| Variable | AUD (million) |
|---|---|
| **Direct health care cost** | |
| Sleep disorders | 274 |
| Associated conditions* | 544 |
| **Indirect financial cost** | |
| Productivity | 3132 |
| Informal care for accident victims | 129 |
| Other cost of motor vehicle accidents | 465 |
| Other cost of workplace accidents | 53 |
| Deadweight loss to taxation system | 472 |
| **Total financial cost** | 5069 |
| **Non-financial cost** | |
| Loss of disability-adjusted life-years | 31 350 |
| **Total economic cost** | 36 419 |

* Hypertension, vascular disease, depression, motor vehicle injuries and workplace injuries. ◆

disease and depression.[20] The associated costs include the direct care-related health costs of the sleep disorder itself and the costs of medical conditions occurring as a result of them. In addition, there are substantial indirect financial and non-financial costs. Other financial costs include the non-health costs of work-related injuries, motor vehicle accidents and productivity losses — all common consequences of insufficient sleep. Non-financial costs derive from loss of quality of life and premature death.[24]

In 2011, the Sleep Health Foundation commissioned Deloitte Access Economics, a national economics consultancy with a strong health economics background, to undertake an analysis of the direct and indirect costs associated with sleep disorders for the 2010 calendar year.[25] The methods used were similar to those that they had used in a previous evaluation.[24] Such an analysis requires robust data relating to the prevalence of the sleep disorder under consideration, the prevalences and costs associated with conditions with which it has a causal relationship, and the risk ratios describing the strength of these relationships. Using these data, the proportion of each condition attributable to the sleep disorder (the attributable fraction) can be derived. Specifying the prevalences and odds ratios used to calculate attributable fractions imparts transparency to the assumptions involved in calculating them. The fraction can then be used to derive the share of the costs associated with that condition that is attributable to the particular sleep disorder under consideration. Using these methods, Deloitte Access Economics examined costs associated with the three most common sleep disorders — OSA, primary insomnia and restless legs syndrome — as the robust data required for analysis were available.[25] It estimated total health care costs of $818 million per year for these conditions, comprising $274 million for the costs of caring for the disorders themselves and $544 million for conditions associated with them. Of these costs, $657 million per year related to OSA: $248 million for OSA itself and $409 million for the health costs of conditions attributable to OSA. These conditions include hypertension, vascular disease, depression, and motor vehicle and workplace accidents. The analysis suggested that 10.1% of depression, 5.3% of stroke, 4.5% of workplace injuries and 4.3% of motor vehicle accidents are attributable to a sleep disorder.

The indirect financial and non-financial costs associated with sleep disorders are much greater than the direct costs. The indirect financial costs were estimated to be $4.3 billion in 2010. These included $3.1 billion in lost productivity and $650 million in informal care and other indirect costs resulting from motor vehicle and workplace accidents. Of these indirect costs, OSA accounted for 61% ($2.6 billion), primary insomnia for 36% ($1.5 billion) and restless leg syndrome for 3% ($115 million).

The report also estimated the effect of sleep disorders on loss of quality of life in terms of disability-adjusted life-years. These costs were calculated using the proportion of total national health costs attributable to sleep disorders to proxy the proportionality of the total national disease burden attributable to these problems. A dollar cost was calculated from the product of these years lost (190 000) and the value of a statistical life-year ($165 000). This added a further non-financial cost of $31.4 billion to the total economic cost of sleep disorders (Box 2). The non-financial nature of this cost gave it less tangibility than financial costs, but the calculation does draw attention to the substantial burden associated with the loss of quality of life resulting from sleep disorders.

As large as they are, these costs are likely to significantly underestimate the total cost to the community of sleep-related problems. Deloitte Access Economics evaluated costs associated with common sleep disorders. The costs of accidents and illnesses associated with sleep loss resulting from poor sleep habits from personal choice and/or from conflicting priorities such as work, social or family activities were not considered as they are difficult to estimate. Further, the analysis used conservative estimates of the prevalence of sleep disorders. For example, the base prevalence of OSA used was 4.7%, which is below the proportion of moderate OSA observed in many contemporary studies, a proportion which is likely to increase further as the population ages and becomes more obese.[20] The prevalence of insomnia used in the analysis was also low at 3%, a figure based on primary insomnia estimates.[26] Secondary insomnias resulting from other causes were not considered. Our own estimate including all insomnia from a representative Australian sample (Box 1) was closer to 7%. Potential comorbidities of sleep disorders, even if reasonable evidence for an association existed (such as metabolic disorders in the case of OSA), were also excluded from consideration. Finally, the analysis did not cost some aspects of the known comorbidities of sleep disorders, such as the impact of presenteeism (being present at work but operating suboptimally) on productivity and safety. The reason for this omission was the difficulty in reliably quantifying its effects.

## Conclusion

Poor or inadequate sleep is very common among Australian adolescents and adults, affecting over 20% on a daily or near-daily basis. Epidemiological studies suggest about

half of this problem can be attributable to common sleep disorders such as OSA and insomnia, as together they affect about 10% of the community. The balance appears likely to be the result of inadequate sleep arising from other health problems or issues such as poor sleep habits or sleep loss because of competing demands on time from work, social or family activities. Economic estimates demonstrate that sleep disorders are associated with large financial and non-financial costs. Given that the greatest financial costs appear to be non-medical costs related to loss of productivity and accident risk, it is likely that inclusion of the effects of sleep restriction from poor sleep habits or choice could add considerably to these already substantial amounts.

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# Sleep loss and circadian disruption in shift work: health burden and management

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## Summary

- About 1.5 million Australians are shift workers. Shift work is associated with adverse health, safety and performance outcomes. Circadian rhythm misalignment, inadequate and poor-quality sleep, and sleep disorders such as sleep apnoea, insomnia and shift work disorder (excessive sleepiness and/or insomnia temporally associated with the work schedule) contribute to these associations.
- Falling asleep at work at least once a week occurs in 32%–36% of shift workers. Risk of occupational accidents is at least 60% higher for non-day shift workers. Shift workers also have higher rates of cardiometabolic diseases and mood disturbances.
- Road and workplace accidents related to excessive sleepiness, to which shift work is a significant contributor, are estimated to cost $71–$93 billion per annum in the United States.
- There is growing evidence that understanding the interindividual variability in sleep–wake responses to shift work will help detect and manage workers vulnerable to the health consequences of shift work.
- A range of approaches can be used to enhance alertness in shift workers, including screening and treating sleep disorders, melatonin treatment to promote sleep during the daytime, and avoidance of inappropriate use of sedatives and wakefulness-promoters such as modafinil and caffeine. Short naps, which minimise sleep inertia, are generally effective.
- Shifting the circadian pacemaker with appropriately timed melatonin and/or bright light may be used to facilitate adjustment to a shift work schedule in some situations, such as a long sequence of night work.
- It is important to manage the health risk of shift workers by minimising vascular risk factors through dietary and other lifestyle approaches.

Nearly 1.5 million Australians are employed in shift work, representing 16% of the working population. Shift work is associated with adverse health, safety and performance outcomes. Circadian rhythm misalignment, inadequate and poor-quality sleep, and sleep disorders are thought to contribute to these associations.

The most immediate consequence of shift work is impaired alertness, which has widespread effects on core brain functions — reaction time, decision making, information processing and the ability to maintain attention. This impairment leads to preventable errors, accidents and injuries, especially in high-risk environments. Long-term health consequences of shift work have been reported, including increased vascular events.[1]

This review evaluates the health burden associated with shift work and discusses strategies for the clinical management of sleep–wake disturbances in shift workers. Evidence-based management strategies require consideration of the key physiological sleep–wake determinants of alertness (Box 1).

## Circadian and sleep–wake disturbances

### Circadian timing

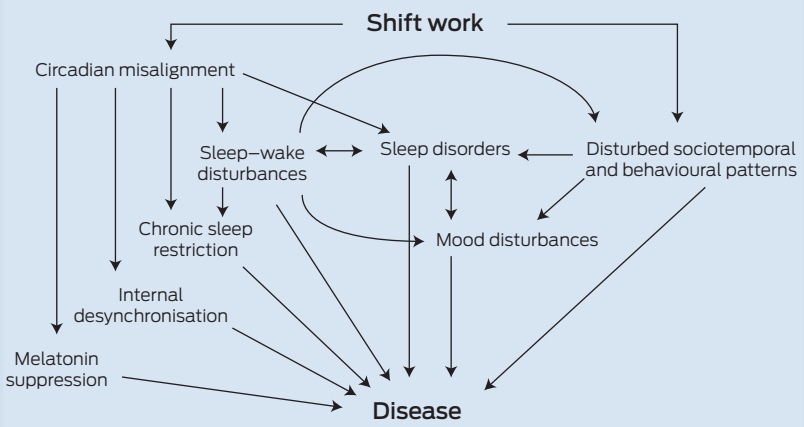
The endogenous circadian pacemaker located in the hypothalamic suprachiasmatic nuclei generates and maintains the timing of behavioural and physiological events according to a 24-hour rhythm. The pacemaker signals increased alertness during the day and high sleep propensity at night. Night shift and rotating or extended-duration shifts involve working at the time of the circadian nadir, when sleep propensity is maximal and consequently alertness is substantially impaired. Often complete circadian adaptation does not occur even in permanent night shift workers[2] and, as a result, many night workers experience misalignment of their circadian pacemaker and the imposed sleep–wake cycle. The effects of this misalignment are exacerbated by chronic sleep restriction (see below) due to insomnia and reduced sleep duration during the day.[2] Misalignment between the circadian pacemaker and the sleep–wake cycle may result in shift work disorder, defined as insomnia during daytime sleep and/or excessive sleepiness during wake episodes temporally associated with the shift schedule and occurring for at least 1 month.[3]

Circadian modulation of several cardiovascular risk markers (eg, circulating cortisol and catecholamines, blood pressure, cardiac vagal modulation) has been described, consistent with epidemiological studies showing a peak in adverse cardiovascular events in the morning.[4] Recent laboratory studies demonstrate that circadian misalignment (such that individuals sleep 12 hours out of phase with the circadian pacemaker) leads to impaired cardiovascular and metabolic function — for example, decreased leptin levels, increased glucose levels despite increased insulin levels, reversed daily cortisol rhythm and increased mean arterial pressure.[4]

### Duration of wakefulness

With increasing duration of wakefulness, the propensity for sleep increases and alertness becomes impaired. In an individual with a healthy sleep–wake cycle, alertness is maintained at a relatively stable level through interactions between the circadian pacemaker and the system that tracks how long the individual has been awake, referred to as the sleep homoeostat.[2] After about 16 hours, alertness will sharply decline such that the magnitude of impairment in neurobehavioural performance after 17 hours of wakefulness is comparable to that observed at a blood alcohol concentration of 0.05%.[5] After 24 hours of sleep deprivation, performance impairment is similar in magnitude to that observed at a blood alcohol concentration of 0.10%.

1 Multiple pathways potentially explaining the link between shift work and adverse health outcomes*




* Modified with permission from Knutsson A. Health disorders of shift workers. *Occup Med (Lond)* 2003; 53: 103-108. ◆

### Sleep duration

In laboratory studies, duration of the sleep episode shows a dose-dependent relationship with daytime neurobehavioural performance,[6] reflecting the adverse impact of chronic sleep restriction on alertness level. Adverse effects of chronic sleep restriction on cardiometabolic outcomes have also been demonstrated in both laboratory and epidemiological studies.[7] Although variations in intrinsic sleep need in the general population are well recognised, lifestyle factors appear to explain a substantial proportion of the variation in habitual sleep duration.[8] Poor sleep quality due to a sleep disorder, other medical conditions or misalignment of sleep in shift workers results in chronic sleep restriction, which causes an even greater degree of alertness impairment overnight in shift workers.[9]

### Sleep disorders

Alertness impairment is a hallmark symptom of many sleep disorders. Disorders such as obstructive sleep apnoea (OSA), insomnia and shift work disorder are associated with performance impairment or lost productivity, and increased risk of motor vehicle crashes and occupational injuries.[6,10] Sleep disorders are more common among shift workers, exacerbating the risk of adverse safety, performance and health outcomes. A recent large survey of a broad range of Australian workers found that 32% of night workers suffered from shift work disorder, including 9% with a severe problem.[11] Among United States police officers, 40.1% screened positive on a survey for at least one sleep disorder, with the most common being OSA (33.6%), followed by moderate to severe insomnia (6.5%), shift work disorder (5.4% of total, or 14.5% of those who work night shifts), restless legs syndrome (1.6%) and narcolepsy with cataplexy (0.4%).[6,10]

## Health and safety burden associated with shift work

The mismatch between the endogenous circadian pacemaker and the sleep–wake cycle results in immediate sleep–wake disturbances, chronic sleep restriction and possibly internal desynchronisation of the circadian system (Box 1). This results in deleterious effects on alertness, cognitive function, mood, social and work activities, and health. Sleepiness is common, increased by more than 50% in truck drivers working night shift and associated with brief sleep episodes.[12] Falling asleep during night shift occurred at least weekly in 36% of rotating shift workers, 32% of permanent night workers and 21% of day and evening nurses working an occasional night shift.[13]

Given this impairment in alertness and cognitive function, it is not surprising that, compared with day workers, the risk of accidents and near-miss events is significantly elevated in shift workers, including those involved in safety-critical industries such as health care, law enforcement and commercial driving.[14] Major catastrophes such as the industrial accidents at Three Mile Island, Chernobyl and Bhopal have been linked to human error related to shift work.[2] Shift workers have impaired driving performance and a two to four times increased risk of crashing during their commute to and from work.[6,13] Sleep-related accidents are most common during the night shift in transportation fields, peaking towards the end of the night shift, and the risk of occupational accidents is also increased when working outside regular daytime hours (relative risk, 1.6).[15] These findings are consistent with those from the general population showing increased risk of motor vehicle crash during the night and after sleep restriction.[16] In addition to personal and public safety risks, productivity is impaired, with frequent workplace errors and increased absenteeism.[17] Conversely, an intervention based on circadian principles significantly improved productivity in rotating shift workers.[18] There is a marked increase in preventable medical errors, including those resulting in fatalities, when medical residents work frequent extended-duration night shifts.[6] In police officers, poor sleep associated with shift work is also related to impaired function at work, including administrative and safety errors, falling asleep in meetings, uncontrolled anger and absenteeism.[10] Hence, shift work can impact on the safety of the worker and others, as well as reducing productivity.

Shift work is associated with a higher risk of several medical conditions, particularly metabolic syndrome, cardiovascular diseases and mood disorders.[6] Increased cancer risk has also been described, potentially through disruption of the circadian system from light exposure at night.[19] Circadian misalignment is related to cardiometabolic changes, and together with altered food choice and physical activity, leads to increases in obesity, dyslipidaemia and impaired glucose metabolism. Rotating shift workers are 20%–30% more likely to have impaired glucose metabolism (elevated $HbA_{1c}$ levels) with a 70% increase in metabolic syndrome among transport workers.[20] In large epidemiological studies, mortality from diabetes, cardiovascular disease and stroke is higher in long-term shift work, although all-cause mortality is not clearly increased.[21] Mood disturbance is common during rotating and night shifts, although the longer-term effects of shift work on mood are less clear. Doctors experience symptoms of anxiety, depressed mood and reduced motivation, in conjunction with impaired cognition, during prolonged

night shifts.[22] A recent US study of police found that anxiety and depression were more than twice as common in those who had symptoms of disordered sleep.[10] Depressive symptoms in shift workers are also linked to increased absenteeism and occupational errors.[23] Although impaired mood is common during shift cycles, it remains unclear as to whether shift work results in longer-term mood disturbance.

The health and economic costs of shift work-related sleep–wake disturbances are high, taking into account the combined effects of impaired sleep, workplace and road accidents, mood disorders, lost productivity and cardiovascular health. Precise economic costs have not been quantified, although the economic impact of individual elements provides some idea. The average cost per year to a person suffering from regular insomnia, as occurs with shift work, is estimated at over $5000. Excessive sleepiness occurs in more than 30% of shift workers. The combined cost of road and workplace accidents caused by excessive sleepiness is estimated for 2009 at $71–$93 billion per annum in the US, with shift work a major contributor to this cost.[24]

## Clinical management of circadian and sleep–wake disturbances in shift workers

The key aims of managing sleep–wake problems in shift workers are to ensure sustained alertness during wake episodes when working and during social activities, and to facilitate restorative sleep when sleep is required. In part, this is achieved by prevention or minimisation of factors that worsen sleep–wake function and therefore impair alertness, such as long work hours or rotating shift schedules, an approach that has been shown to reduce adverse events related to shift work in the health sector. Forward rotation of shifts (from day to afternoon to night) is preferable. Second, given the interindividual variability in sleep–wake responses to shift work, it is also important to develop algorithms that predict whether a shift worker is fit for duty or potentially vulnerable to alertness failure. There have been major efforts to develop biomathematical models using information such as work and sleep–wake schedules to evaluate safety risk associated with particular shift rosters. The use of such approaches outside of the research setting is considered premature. In high-risk industries, such as transportation, companies should have systems in place to minimise the risk related to shift work.

With shift work, sleep–wake disorders are highly probable at some stage in all workers, and an approach to mitigate the consequences of shift work should be adopted in the workplace as occupational health policy; for example, through screening programs for sleep disorders and general health.

### Managing sleep complaints

It is important to identify and address any comorbid conditions that independently cause insomnia or sleepiness further compromising alertness in the shift worker. Examples are conditions such as OSA, or mood disorders such as depression. Treatment of acute or chronic insomnia is important to maintain sleep continuity, adequate sleep length and alertness during wakefulness. Psychological approaches such as cognitive behavioural therapy are important in managing chronic insomnia.[25] Limited but judicious use of sedative-hypnotic medication may help workers adapt to rotating sleep schedules but the data are controversial. Sedative-hypnotics should be used carefully owing to their potential side effects, including the carry-over of sedation to the night shift, which may negatively affect performance and safety.[26] Use of alcohol, cannabis and non-medically prescribed drugs to manage sleep complaints should be discouraged.

### Pharmacotherapy to improve alertness

The reality of shift work and long schedules during sustained operations, particularly in the transport industry, has resulted in even regulators considering use of medications to promote alertness under certain situations. This medicalisation of shift work to prevent human error and resulting consequences is controversial. Use of stimulants such as ephedrine or amphetamine is illegal and stigmatised. However, the availability of wakefulness-promoting agents modafinil and armodafinil (the R-enantiomer of modafinil), which improve alertness compared with placebo without much of the adverse effect profile of stimulants, has resulted in the possibility of managing alertness failure during shift work through pharmacotherapy. Based on evidence from large controlled clinical trials,[27] these agents are now specifically approved by the US Food and Drug Administration for the treatment of excessive sleepiness in workers with shift work disorder. Self-limiting headache is the most commonly reported adverse event with these drugs.

Caffeine is used universally as a stimulant to maintain alertness. Caffeine improves cognitive performance in shift workers.[28] A variety of doses, preparations and administration regimens are reported to be effective,[28] including a single dose of 200 mg and a low-dose, repeated caffeine administration protocol (0.3 mg/kg/h). Residual effects of higher doses of caffeine on daytime sleep have been reported,[29] which should be taken into consideration in caffeine administration guidelines, particularly for alertness management in night shift workers.

It should be noted that the above pharmacological strategies are aimed at managing sleepiness symptoms in shift workers. There is no evidence that these can facilitate circadian adaptation to a shift schedule or promote sleep.

### Napping

Scheduled napping for shift workers may be useful in relieving excessive sleepiness during work shifts.[6] However, the exact configuration of naps that maximises alertness on duty has yet to be clarified. Naps ranging from 20 to 40 minutes taken during night shifts (eg, between 2 am and 3 am)[30] are beneficial, as is prophylactic napping before a night shift.[6]

The potential for alertness impairment due to sleep inertia should be considered and sufficient time allowed for its dissipation, particularly for naps occurring during work shifts. Sleep inertia refers to the impairment that occurs immediately on awakening and can last from minutes up to several hours. The magnitude of impairment may even be worse than that after 24 hours of sleep deprivation.[31] The severity of sleep inertia varies according to the stage of sleep and circadian phase from which the

awakening occurred. There is insufficient evidence to recommend how long an individual in operational settings should wait after a nap for the effects of sleep inertia to dissipate. A recent laboratory-based, simulated night shift work study in healthy male volunteers suggests that a 15-minute interval should be allowed following nap opportunities of up to 60 minutes, and also that workplace education be provided that subjective feelings of sleepiness are not a reliable indicator of performance impairments due to sleep inertia.[32]

### Light and melatonin for circadian adaptation

Timed administration of melatonin can facilitate adaptation of the circadian pacemaker to a new sleep–wake schedule;[33] however, this is not recommended for rapidly rotating shift schedules. Melatonin can also be used to promote sleep during the daytime, thereby improving sleep quality and duration in night shift workers.[33] Although melatonin is safe for short-term use, long-term safety data are lacking.

For adaptation to a series of night shifts, the following is recommended: light exposure in the night and early morning hours to facilitate a circadian phase delay (ie, shift of the circadian pacemaker to a later time) and promote alertness; and shielding morning light exposure to minimise the competing circadian phase advance effect of light[34] and to reduce the residual impact of the alerting effect of light on daytime sleep. However, this regimen is only suitable for a limited range of shift types. There appears to be an increase in the frequency of certain types of shift schedule that expose individuals to higher safety risks, including slow rotating, long duration ($\geq$ 12 hours) and quick return (a break of only 8 hours when changing from one shift to another) shifts. Thus, the application of light treatment needs to be considered on a case-by-case basis, taking into account the specific characteristics of each schedule. Light is the most potent time cue for the circadian pacemaker, synchronising it to the 24-hour day. The magnitude and direction (ie, shift to an earlier or later time) of the effect critically depend on the timing of the exposure as well as the intensity, duration and wavelength. Here, timing relates to phase of the endogenous circadian pacemaker, which would ideally be measured through assessment of endogenous melatonin levels in saliva or core body temperature levels before an intervention. Timed light and darkness exposure can be used to facilitate adaptation of the circadian pacemaker to a new shift schedule.

### Reducing risk of cardiometabolic disease

Shift workers are at higher risk of cardiometabolic diseases and are therefore targets for closer monitoring of risk factors and avoiding unhealthy diets. High fat meals consumed during the night may produce more postprandial hypertriglyceridaemia than equivalent meals during the day.[2] Promoting physical activity in the workplace and home is another countermeasure to cardiometabolic risk. Laboratory studies have shown that exercise during the night phase shifts the circadian pacemaker,[35] thus potentially facilitating biological adaptation to shift work.

Shift work is commonly associated with adverse safety and health consequences (Box 2). Circadian misalignment, sleep loss and sleep disorders all contribute to these risks, and therefore should be the primary targets for clinical management approaches. Improved methods to detect those who are most vulnerable to the effects of shift work are needed. Diagnosis and management of shift work disorder is an important first step in tackling the significant health burden associated with shift work.

**2 Shift work summary**

- Misalignment between the circadian pacemaker and the timing of sleep, wake and work occurs in shift workers.
- Shift work disorder, with insomnia, reduced sleep and excessive sleepiness, is common.
- These abnormalities impair cognitive function, alertness and mood and increase accident risk.
- Metabolic syndrome is also common in shift workers, resulting in increased cardiovascular risk.

**Practical tips for the management of the chronically sleepy (night) shift worker**

- Optimal shift schedule is important, allowing adequate time for recovery sleep and minimising extended duration shifts.
- Have at least 7 hours of sleep per 24 hours.
- Initiate main sleep episode as soon as practicable after evening or night shift.
- Nap for 30 minutes to 2 hours before evening or night shifts to supplement main sleep episode.
- Nap for 20–30 minutes during night shift to help maintain wakefulness, particularly for high-risk occupations (eg, driving).
- Keep bedroom quiet and dark, use earplugs.
- Increase exposure to bright light during evening/first half of a night shift.
- After a night shift, avoid exposure to bright light; eg, use sunglasses or blue-light blocking glasses.
- Melatonin (1–2 mg) is effective in promoting daytime sleep.
- Caffeine can be used to promote alertness. High-frequency (eg, hourly) low-dose caffeine administration (eg, 30–40 mg — about one cup of tea or half a cup of instant coffee) is effective. High doses should be avoided close to daytime sleep.
- Novel alertness-enhancing agents may be beneficial in managing shift work disorder.
- Screen for sleep and mood disorders (eg, shift work disorder, sleep apnoea, insomnia, depression).
- Cardiovascular risk factors should also be addressed as a part of the clinical management plan. ◆

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# Circadian rhythm disorders among adolescents: assessment and treatment options

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> Lethargics are to be laid in the light, and exposed to the rays of the sun for the disease is gloom.
>
> Aretaeus of Cappadocia, celebrated Greek physician, 1st century CE

## Summary

- Delayed sleep phase disorder (DSPD) — a circadian rhythm sleep disorder — is most commonly seen in adolescents.
- The differential diagnosis between DSPD and conventional psychophysiological insomnia is important for correct therapeutic intervention.
- Adolescent DSPD sleep duration is commonly 9 hours or more.
- Depression may be comorbid with DSPD.
- DSPD has a negative impact on adolescent academic performance.
- DSPD treatments include bright light therapy, chronotherapeutic regimens, and administration of melatonin as a chronobiotic (as distinct from a soporific).
- Attention to non-photic and extrinsic factors including healthy sleep parameters is also important to enable better sleep and mood outcomes in adolescents.

## Circadian rhythm and the biological clock

Biologically, the timing and duration of sleep are regulated by two interacting systems — the homoeostatic sleep drive (process S) and the circadian system (process C).[1] Process S assumes that the longer one stays awake, the more pressure there is to fall asleep. Once asleep, this pressure dissipates until a homoeostatic equilibrium is achieved. Process C regulates the timing of sleep by controlling periods of biological activity and inactivity throughout the day. These peaks and troughs in biological functioning are known as circadian rhythms and run for slightly longer than 24 hours in humans.[2] Circadian rhythms are generated by the central nervous system pacemaker, the hypothalamic suprachiasmatic nucleus (SCN), sometimes called the body clock. The SCN regulates the rhythmicity of many biological processes, such as temperature and hormone release, and is responsible for synchronising these processes to each other and to the external environment.[3] For all terrestrial vertebrates, evening light phase delays and morning light phase advances the biological clock. This daily resetting is how the SCN is synchronised to the 24-hour light–dark cycle and to a multitude of internal rhythms at the level of organs, tissues, cells and genes. In regard to the sleep–wake cycle, the SCN uses external cues such as light, activity and food intake (in some species) to synchronise the timing of sleep to the 24-hour cycle of the social environment. Misalignment between the circadian system and the external environment, where sleep occurs outside societal norms, leads to a circadian rhythm sleep disorder. Only delayed sleep phase disorder (DSPD) and advanced sleep phase disorder are discussed in this article; other circadian rhythm sleep disorders are described elsewhere.[4]

## Common circadian rhythm sleep disorders

DSPD is commonly found in teenagers and young adults (average age of onset, 20 years), with the pattern developing in adolescence.[4,5] Sleep onset is delayed by 3–6 hours compared with conventional times (10–11 pm).[6] Once sleep is attained, it is normal in length and quality but is delayed, resulting in social and often psychological difficulties. DSPD develops due to an interaction of a delay in the intrinsic circadian rhythm and poor sleep hygiene (staying up increasingly late and often using social networking).

Non-24-hour sleep–wake syndrome (also known as free-running disorder) is where the circadian clock loses synchrony to the day–night cycle and free runs, with sleep onset and wake times occurring progressively later each day. Social and environmental time cues are essentially ineffective and the pattern temporarily moves in and out of phase with societal norms. Sleep onset times may be shifted by 7 hours or more across a week. DSPD is uncommon in the general population but is found in people who are visually impaired, former rotating shift workers and some chronic fatigue/fibromyalgia sufferers.

Advanced sleep phase disorder is uncommon in adolescence, although it may manifest secondary to anxiety and depression. Sleep onset occurs early in the evening (7–9 pm), despite efforts to achieve a later bedtime. Sleep quality is typically normal but duration is often curtailed as a result of early morning waking (2–5 am). Staying in bed until the desired waking time will fragment sleep and may be misdiagnosed as irregular sleep–wake pattern.

## Presentation of DSPD

DSPD is relatively common in adolescents and young adults, with a prevalence of 7%–16%, and represents 10% of individuals diagnosed with chronic insomnia disorder in sleep clinics.[4] Individuals with DSPD may have an extended circadian cycle of 24.75 hours or longer.[3] The major sleep period is therefore delayed, with wake times set intractably late, leading to a propensity to fall asleep later and get up later until there is relative pattern.

When forced to be out of bed at conventional wake-up times, adolescents with DSPD continually experience a short sleep duration and feel permanently jetlagged. This may mask the true nature of the problem, resulting in a

**1 Tips for assessing and treating delayed sleep phase disorder (DSPD) in adolescents presenting with severe sleep onset insomnia**

- Establish the patient's full family history — ask about sleep onset difficulties in other family members
- Establish whether there is a history of sleep onset difficulties as a child/adolescent. Is there a history of napping after school and difficulty getting up for school in the morning?
- Establish a DSPD diagnosis based on a 2-week diary in the form of a raster plot or actigraphy
- Refer the patient to a sleep clinic with circadian rhythm specialists where possible
- Refer to a good reference manual — eg, Wirz-Justice et al[15]
- Consider a chronotherapeutic regimen for school holidays if there is considerable family support
- Establish possible core temperature minimum (2–2.5 h before most usual getting up time)
- Encourage light exposure (outside or artificial light for at least 40 min) after the minimum core temperature time
- Consider carefully timed administration of a low dose of melatonin at 1 mg 4–6 hours before prescribed bedtimes
- Once desired sleep onset time is established, maintain a dose of 0.5 mg of melatonin 2 h before expected sleep onset
- Have realistic expectations — an individual successfully treated for DSPD is still likely to prefer a later sleep onset time ◆

diagnosis of psychophysiological insomnia (PPI; also known as sleep-onset insomnia) rather than a circadian rhythm sleep disorder. Adolescents may present to a general practitioner with a history of taking "hours" to get to sleep and being extremely difficult to wake in the morning for school, university or work. They are usually accompanied by a very frustrated parent who may also describe himself or herself as a "night owl". Exploring family history is important. Adolescents may be withdrawn, indicating an underlying depression often comorbid with DSPD.[7] Anxiety symptoms may also be present. The refusal to go to bed when the rest of the family do may be misinterpreted as an adolescent behavioural issue and not a genuine sleep problem. Misunderstandings from both perspectives will negatively impact on family dynamics.

An interaction between PPI and DSPD is not uncommon in adolescence, often stemming from unrealistic parental expectations. Expecting adolescents to fall asleep immediately after being mentally active with homework in the bedroom is unrealistic. The bed in that room has become a psychological reinforcement associated with heightened mental arousal and not sleeping. Time spent on the computer in the bedroom late in the evening playing video games and social messaging has a potentially similar outcome.[8]

Research indicates that mean optimal daytime alertness in adolescents requires a 9-hour sleep.[9] This is rarely achieved, with most students cumulatively sleep-deprived as school weekdays progress,[10] negatively impacting on academic performance and psychological health,[11] with the added potential of motor vehicle accidents in teenage drivers.[12] Restoring the correct timing, enabling sleep for daytime functioning and safety, is paramount.

## Treatment of DSPD

There is a paucity of studies examining treatment of DSPD. Few have examined combinations of treatments, and some have focused only on the effects of manipulating sleep timing in healthy sleepers.[13,14]

DSPD may be treated by:

- a chronotherapeutic regimen: changing the timing of sleep onset to progressively delay (send forward) sleep onset until it matches a more conventional time;
- photic factors: bright light therapy;
- chronobiotic administration: use of a phase-shifter such as melatonin;
- non-photic factors and healthy sleep parameters: timing of exercise; diet; limiting the use of social media; improving mood.

Tips for assessing and treating DSPD in adolescents are provided in Box 1.

### Chronotherapeutic regimen

A raster plot (a graphic representation of sleep–wake patterns) or actigraphy (using a device resembling a wristwatch, which measures movement via an accelerometer to infer sleep/wakefulness from rest/activity cycles) are essential for recording sleep patterns over time.[16] Once the current delayed sleep times are established, sleep/bedtime is progressively delayed (moved later and later), usually by 3 hours every 2 days or longer, until sleep onset time moves around the clock to reach the desired bedtime (around 10–11.30 pm).[6] Exposure to post-sleep morning light (natural or artificial or a combination) is used to anchor sleep phase to the new, desired time. Sleep and temperature need to be in tandem to maintain this new desired sleep time (Box 2). This is a difficult treatment to implement, as it requires considerable planning, time away from usual daytime activities, specialist input and considerable family support.

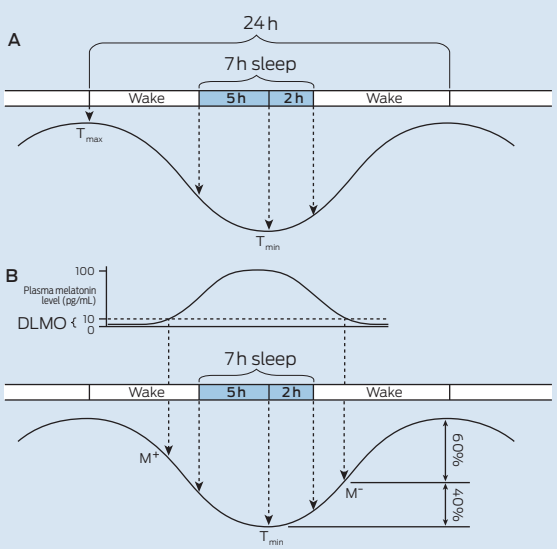
### Bright light therapy

For the whole of the animal kingdom, irrespective of whether the species is nocturnally or diurnally active, evening light exposure delays the clock while morning light phase advances it. Bright light therapy for DSPD must always be given after the core temperature minimum, which occurs 2–3 hours before wake-up time (Box 2). The body clock is then reset every day. At certain latitudes and seasons, natural exposure to dawn/dusk sunlight is not available and bright artificial light can be substituted to maintain a normal circadian phase. Bright light therapy at the appropriate post-sleep phase drives the sleeping times earlier, back to the desired bedtime (Box 3, B). Light intensity, spectrum, duration and distance from the source are crucial variables. Studies have shown the light intensity required to successfully advance the circadian phase is typically between 2500 and 10 000 lux.[17] However, when bright light therapy is used in combination with another therapy, such as cognitive behaviour therapy, as little as 1000 lux exposure is successful.[18] Retinal cells in the lower part of the eye sending information to the SCN are tuned to the blue-green end of the spectrum, and this wavelength appears more efficacious than full-spectrum lighting.[19]

### Melatonin

A chronobiotic is a chemical substance capable of therapeutically re-entraining short-term dissociated or long-term desynchronised circadian rhythms, or prophylactically preventing disruption following environmental insult.[20]

**2 Relationship between endogenous melatonin release, 24-hour sleep–wake cycle and core temperature**




DLMO = dim light melatonin onset. $M^+$ = melatonin onset. $M^-$ = melatonin off. $T_{max}$ = core temperature maximum. $T_{min}$ = core temperature minimum. **A.** Optimal sleep onset for 7 h total sleep time (TST) is well down the descending limb of the core temperature rhythm and wake up time about 2–2.5 h after $T_{min}$. **B.** For an 8 h TST, natural wake-up time would be about 3 h after $T_{min}$. DLMO occurs about 2 h before sleep onset and 40% of the fall in core temperature is due to melatonin release. From the perspective of a teenager with a "normal" melatonin profile, there is no reason to expect that exogenous melatonin administration can drop core temperature any lower and thereby increase TST (in contrast to older people with low melatonin, reduced circadian amplitude and often fragmented sleep). ◆

Melatonin is the most researched chronobiotic in terrestrial non-seasonal breeding vertebrates. Human endogenous melatonin levels start to rise about 2 hours before natural sleep onset and peak about 5 hours later (Box 2).

About 40% of overnight core temperature decline during natural sleep is caused by the endogenous release of melatonin, which increases peripheral temperature.[19,21] Time of day of melatonin administration is the critical variable with dose being second. Melatonin is administered at the reverse time of day to bright light therapy; ie, evening melatonin advances the sleep–wake cycle while evening light delays it (Box 3, A).

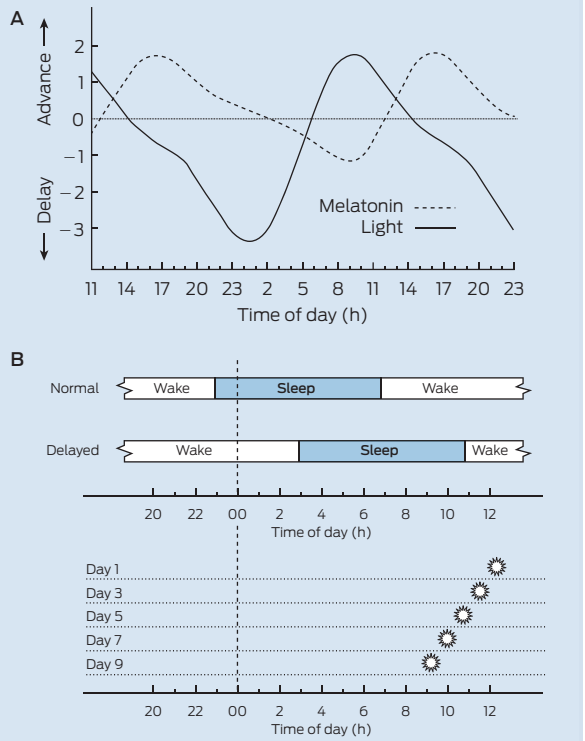
It is important to distinguish between the use of melatonin as a soporific (a weak hypnotic) for PPI[15] and its use as a chronobiotic for treating DSPD. In the treatment of PPI, exogenous melatonin administration works best when taken 2 hours before the desired bedtime. When taken for DSPD, it may need to be administered 4–6 hours before the current sleep onset time and be moved progressively earlier as sleep onset moves earlier.[22] A soporific effect may occur in the very early evening, with potential driving-safety consequences.

A combination of morning bright light therapy (after core temperature minimum) and evening melatonin can be an ideal treatment regimen. Compared with chronotherapy alone, this approach is more practical and manageable, owing to its shorter implementation period (10–20 days).[13]

### Melatonin: safety issues

Despite assurance from studies,[23] there are concerns recommending administration of high doses of melatonin.

**3 Phase–response curve in relation to melatonin administration and light exposure, along with how to instigate bright light therapy**

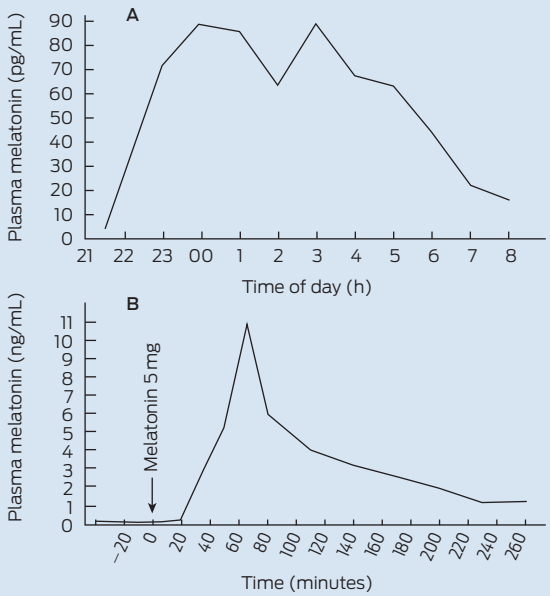



**A.** Phase–response curve in a normally entrained individual for melatonin (3 mg) administration over 3 consecutive days compared with bright light. Evening light phase delays the human clock while morning light phase advances. Early evening melatonin phase advances the clock while morning administration modestly delays phase. Source: Barion and Zee;[13] redrawn with permission. Original data derived from Littner et al[16] and Gooley.[17] **B.** Schematic diagram of "morning" bright light therapy in a delayed sleep phase disorder patient with sleep onset at about 0300 h and natural wake-up time at 1100 h. Full-spectrum bright light exposure is moved earlier and earlier every 2 days (in this example) until the target bedtime is achieved. The decision on how often to advance light exposure is made from the advancing sleep onsets recorded daily in raster plots. If pre-sleep melatonin is administered to achieve a similar result, it would be taken earlier and earlier as sleep onset advances over successive days. ◆

Circulating endogenous melatonin levels are very high in childhood and decline precipitously at puberty, hence melatonin was speculated but not substantiated to be the pubertal hormone.[24] The importance of this rapid natural decline of endogenous levels in early adolescence is unknown, and supplementing high dosages of exogenous melatonin has not been systematically researched. Although the liver is very efficient in clearing circulating levels of melatonin, with a half-life of 45–60 minutes (Box 4), a small dose of 0.3–0.5 mg was found to be as effective as 3 mg for advancing sleep onset.[22,25] In the absence of data, the lowest effective dose of 1 mg is recommended (compounding pharmacies).

Where sleep onset is 2 am, we suggest that melatonin be given, for example, at 8.30 pm (ie, 5.5 hours before) for four to five nights, at 8 pm for four to five nights, then slowly working back (7.30 pm, 7 pm, 6.30 pm) until an earlier, desired sleep onset time of 11 pm–12 am is achieved. Once this sleep onset time is established, the individual can be maintained on 0.5 mg of melatonin 2 hours before expected sleep onset (eg, 9.30–10 pm), which will then

4 Natural and exogenous melatonin profiles




**A.** Endogenous plasma melatonin profile (pg/mL) of an adult male. Source: Norman TR, Armstrong SM; unpublished data, 1986; redrawn with permission. **B.** Plasma melatonin profile (ng/mL) of another adult male after ingestion of 5 mg melatonin capsule during daytime hours. Note the efficient clearing of circulating melatonin by the liver within a 40 min window, but despite this efficiency, the persistence of aphysiological levels (1300 pg) 4 hours postingestion. Source: Short and Armstrong;[20] redrawn with permission. ◆

enhance the natural rise in the melatonin curve. The current prescribing norm of 3 mg (effective for jet lag in adults) and 9 mg doses needs more research and is not recommended for adolescents. Parental supervision is needed to ensure adherence.

Prolonged-release melatonin is thought to mimic the natural endogenous release profile, phase-advance sleep and improve sleep-maintenance insomnia when used as treatment for primary insomnia in older people (> 55 years).[26] Research has found the 2 mg melatonin dose subjectively improved sleep quality and morning and evening alertness in that population.[26] Anecdotally, it has been used in children and adolescents; however, until there are more research data it would be prudent not to use this medication in adolescents.

Agomelatine, currently marketed as an antidepressant, is a melatonin analogue with phase-advancing properties in rodents (as S 20098)[27] and humans.[28] Theoretically, agomelatine may be beneficial in older adolescents who have DSPD plus depression, since circadian changes can be associated with major depression.[7] It is not the absolute delay in sleep but changes to the phase angle (timing) of sleep relative to other internal changes (onset of endogenous melatonin release relative to sleep phase) that appear crucial in the onset of depression.

## Non-photic and extrinsic factors

DSPD can be exacerbated by extrinsic factors, such as use of social media (ie, electronic devices), diet, timing of exercise, and depression and anxiety. Good sleep habits or sleep hygiene are behavioural practices that result in good sleep quality and sufficient sleep duration, and prevent daytime sleepiness.[29]

### Limiting use of technology in the bedroom, particularly in the hour before desired sleep time

The alerting effect of media is strongest when light is predominantly emitted within a blue spectrum.[30] Watching television, texting and using a computer or electronic tablet device are associated with delayed sleep onset and poorer sleep quality.[8,31,32]

### Establishing regular sleep patterns

Adolescents tend to sleep longer on weekends to compensate for sleep deprivation incurred over the week. If a catch-up sleep of 1–2 hours (9 am) is required, it is better for this to occur on a Saturday morning. Sunday morning get-up time needs to be 8 am, a mid point between Saturday sleep in time and the necessary Monday morning get-up time of 7 am. Some health professionals advocate adjusting the get-up time to include weekends but we believe a balance between resetting sleep and repaying sleep debt is important.

### Caffeine and energy-dense foods before desired sleep time

Caffeine is a stimulant. The standard measure of one cup of espresso coffee (85 mg caffeine) can last 4 hours after consumption and longer.[33] Energy-dense foods, such as those high in sugar content, stimulate the digestive and endocrine system, producing an alerting effect.

### Exercise too close to sleep time

In general, regular exercise is a good way to promote sleep and good health. Exercise can delay sleep in young adults if undertaken at usual sleep onset time, and prolonged aerobic exercise even a few hours earlier can maintain high body temperature, increasing alertness and interfering with evening "wind down".[34]

### Treatment for depression and anxiety

Depression is common in DSPD. If symptoms of depression are present or develop later, it is imperative to treat to reduce exacerbation or a reduction in treatment response to DSPD.[7] Sleep anxiety is commonly associated with long periods of lying in bed waiting for sleep onset in DSPD.

## Conclusion

DSPD is a circadian rhythm sleep disorder that is most commonly seen in adolescents and needs to be differentiated from insomnia. Sleep diaries or actigraphy illustrating consistently delayed sleep onset and waking with normal (when unrestricted) sleep duration confirm the diagnosis. Many individuals with DSPD feel permanently jetlagged, which impacts on academic performance and has safety ramifications. Awareness and education are important components of the treatment plan, with care being taken to identify the core body temperature minimum. Without this, the effects of DSPD will be exacerbated and the individual is unlikely to respond to treatment. A combination of chronotherapeutic strategies (bright light therapy

and melatonin) and behavioural management appears to be the most effective treatment.

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# How to assess, diagnose, refer and treat adult obstructive sleep apnoea: a commentary on the choices

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## Summary

- Obstructive sleep apnoea (OSA) determined by polysomnography is highly prevalent, affecting about 25% of men and 10% of women in the United States, although most have few or no symptoms.
- Symptomatic moderate to severe OSA has major health implications related to daytime sleepiness, such as increased accidents, altered mood and loss of productivity in the workplace. Severe OSA may increase the risk of cardiovascular disease independent of daytime sleepiness.
- A major challenge is to correctly identify, from the large community pool of disease, people with symptoms and those at risk of long-term complications.
- For treatment plans to achieve quality patient outcomes, clinicians must have a clear understanding of patients' symptoms and their motivations for presentation, and be knowledgeable about the evidence surrounding the health risks of OSA and the relative merits of the various diagnostic and treatment options available.
- The diagnosis of OSA represents a teachable moment to target adverse lifestyle factors such as excessive weight, excessive alcohol consumption and smoking, which may be contributing to OSA and long-term cardiometabolic risk.
- OSA assessment and management has traditionally involved specialist referral and in-laboratory polysomnography. However, these services may not always be easy to access.
- Controlled studies have shown that patients with a high pretest probability of symptomatic, moderate to severe OSA can be managed well in primary care, or by skilled nurses with appropriate medical backup, using simplified ambulatory models of care.
- The future of sleep apnoea assessment and management will likely include models of care that involve early referral to specialists of patients with complex or atypical presentations, and an upskilled and supported primary care workforce to manage symptomatic, uncomplicated, high pretest probability disease.

Obstructive sleep apnoea (OSA) is a condition characterised by repetitive occlusions of the upper airway during sleep, resulting in arousals and sleep fragmentation. It impacts on daytime vigilance[1] and contributes to cognitive dysfunction[2] and mood disorders.[3] It is a source of lost productivity in the workplace[4] and increases motor vehicle accident risk.[5] OSA has also been implicated as a cause of hypertension,[6] with studies showing small but consistent falls in blood pressure following continuous positive airway pressure (CPAP) treatment.[7] Epidemiological studies have also shown OSA to be independently associated with an increased risk of diabetes[8] and cardiovascular disease,[9,10] although definitive evidence for a causal link with these diseases awaits the results of large-scale randomised controlled trials of OSA treatment. In the early 1990s, the prevalence of OSA in the community in the United States, determined by polysomnography (PSG), was shown to be 24% of adult men and 9% of women,[11] with recent evidence suggesting a further increase due to the obesity epidemic and an ageing population.[12] OSA is now recognised as a major public health and economic burden, with an estimated cost to the Australian community of more than $5.1 billion a year in health care and indirect costs.[4]

The purpose of this article is to describe the key issues in evaluation and management of OSA, to assist health care professionals to better engage in OSA management. We outline several evidence-based models of care that could be scaled up to allow the primary care physician to have a greater role in addressing the high burden of OSA in the community. To do this, primary care health professionals must be skilled in identifying those at high risk of OSA who are likely to benefit from treatment and must know which investigation to order, what treatments to recommend, and when specialist referral is needed.

## Polysomnographically determined versus clinically important OSA: telling the difference

Despite the high prevalence of OSA, most patients are minimally symptomatic. About 15% of patients have moderate to severe sleep apnoea.[13] The vital issue in clinical practice is to identify those with OSA who have clinically important disease. Lack of clarity around goals of treatment can lead to excessive investigation, inappropriate treatment and patient disengagement. We believe the major goals of management of OSA should be:

- to identify and offer treatment to symptomatic patients, regardless of disease severity, whose safety and quality of life is affected;
- to identify and offer treatment to patients with severe OSA determined by PSG, regardless of symptoms, who may be at risk of adverse health outcomes; and
- to modify adverse lifestyle factors that contribute to OSA pathogenesis and other poor health outcomes. This may include advice on diet and exercise to lose weight, and encouragement to reduce alcohol intake and stop smoking.

## Personalised care plans on a public health scale — the challenges of meeting the burden of disease

Optimal outcomes are usually achieved through an initial identification of the presenting clinical triggers, an evaluation of the symptom profile, and an exploration of the patient's treatment preferences and capacity to afford or comply with the range of treatment options. The workup for OSA must start with a careful clinical assessment to

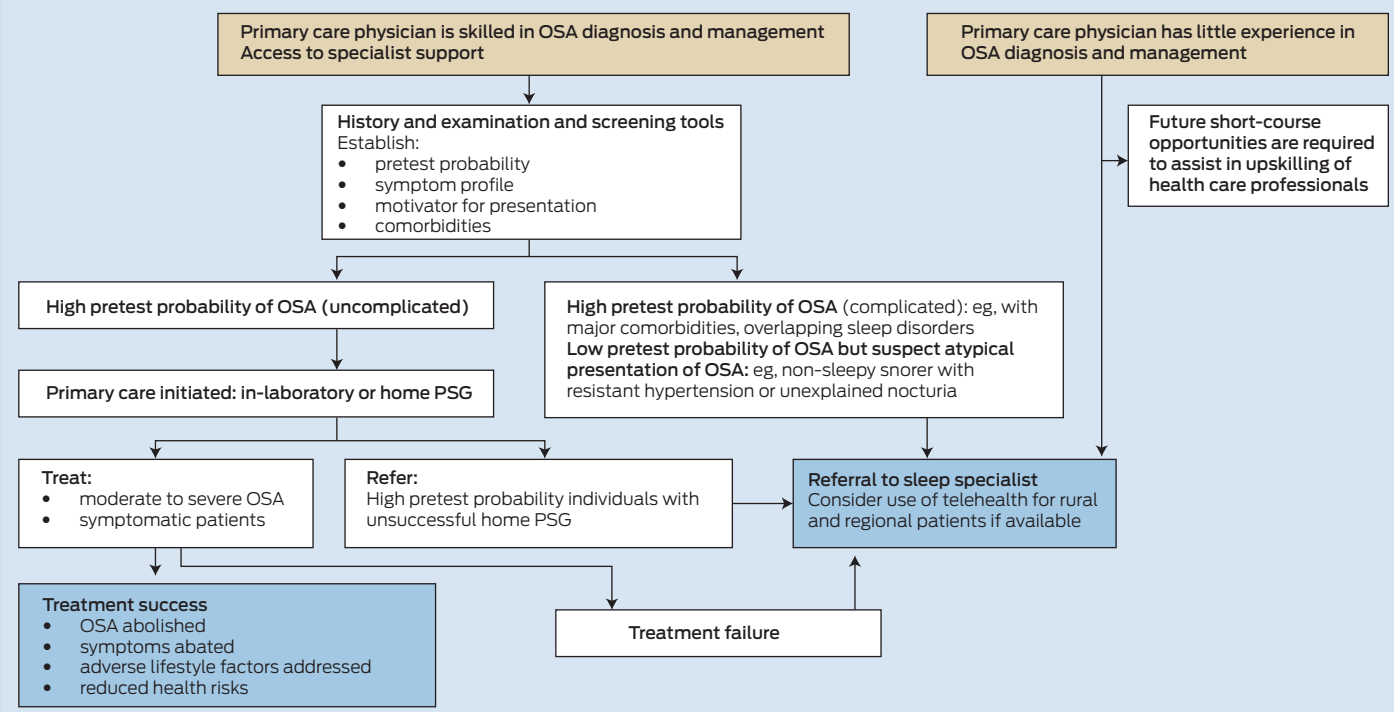
identify patients who are likely to benefit from treatment. Clinicians must then select an investigation: either in-laboratory PSG, home-based PSG or simplified limited channel sleep testing. The test result must then be coupled closely with the clinical assessment to inform a personalised treatment plan. This plan should identify adverse lifestyle factors, overlapping sleep disorders and medical comorbidities (eg, hypertension, diabetes, depression, dyslipidaemia), and consider these when advising on OSA-specific treatments.[14] Box 1 depicts an algorithm that may assist the primary care practitioner with this process. There is no one preferred treatment for OSA but rather a range of options of proven effectiveness that can be applied individually or in combination, depending on patient preference, symptoms, OSA severity, comorbidities and other health risk factors (Box 2). Development of a personalised treatment plan requires the active involvement of the patient, partner and family in goal-setting.[14] For the health professional, it requires that they be sufficiently familiar with the field and the practical application of each of the available OSA investigations and treatment options. The complexity of this process has meant that OSA has been traditionally managed by a relatively small specialised workforce using the gold standard, in-laboratory PSG. However, patient access to specialist sleep services has been limited and alone will not be able to cope with the evidently large burden of disease.[12]

## The emerging landscape

Given these service barriers, various simplified, lower-cost clinical models have been developed for OSA. These have incorporated screening questionnaires to identify patients at high risk of OSA,[15-19] simplified testing with home-based PSG or limited channel sleep studies (typically without sleep electroencephalography) and selected use of automatically titrating CPAP devices that lessen the need for supervised in-laboratory CPAP titrations. If patients are identified as having a high pretest probability of OSA and if major comorbidities and overlapping sleep disorders are excluded (Box 3), the use of home-based PSG or limited channel sleep testing and automatically titrating CPAP has been shown to produce similar or non-inferior patient outcomes to more traditional specialist referral and in-laboratory PSG approaches.[20-23] Further, it has been shown that with suitable training and support from a specialist sleep centre, these management approaches can be applied effectively to uncomplicated OSA patients by nurses and primary care physicians.[24]

A major challenge is how to translate and upscale these research findings from controlled settings to the "real world" to meet the demonstrably high community burden of disease while ensuring high-quality, holistic patient care. The current availability of open-access PSG has enabled primary care practitioners to become more involved in the care of OSA patients. However, few of these services currently select for high pretest probability of disease, nor do they train or adequately support the referring health care professional to ensure that they are sufficiently knowledgeable in assessment and personalised treatment of OSA. Some patients accessing this service model who are found to have uncomplicated moderate to severe symptomatic OSA may adhere to CPAP treatment and be successfully managed in primary care. However, there are no data available on the overall adequacy of CPAP treatment for patients with milder or

**1 Algorithm for management of obstructive sleep apnoea (OSA) in the community**




PSG = polysomnography.

**2 Obstructive sleep apnoea: treatment options***

| Option | Optimal group | Cost | Trial option | Comfort | Comment |
|---|---|---|---|---|---|
| Nasal CPAP | Moderate to severe OSA; selected mild cases; prominent symptoms; high cardiovascular risk | $1000–$2400 | Yes — rental | Variable — can be uncomfortable | Gold standard — most efficacious; adherence variable |
| MAS (custom fit) | Primary snorers; mild to moderate OSA; supine dominant OSA; some severe cases; OSA and bruxism | $1200–$2000 | No, but temporary devices emerging | Variable — can be uncomfortable | |
| Nasal EPAP (single-night use) | Mild to moderate OSA; some severe OSA | $3.50/night | Yes | Variable — can be uncomfortable | Recent innovation — role emerging |
| Weight loss (stand-alone therapy) | Goal, 10% body weight; mild to moderate OSA | Low | na | na | Low achievement rate |
| Bariatric surgery | BMI > 35 kg/m$^2$ | High | No | Medium | Variable reduction in OSA; often limited availability in public system |
| Supine avoidance device | Supine OSA | Low | Yes | Comfortable | Limited data on efficacy and adherence |
| Upper airway surgery | All ranges of OSA | High | na | Uncomfortable | Salvage treatment for failed CPAP or MAS |
| Tonsillectomy | Gross tonsillar hypertrophy; all severities of OSA | High | na | Uncomfortable | May have high cure rate if BMI 18.50–24.99 kg/m$^2$ |

CPAP = continuous positive airway pressure. EPAP = expiratory positive airway pressure. MAS = mandibular advancement splint. na = not available. OSA = obstructive sleep apnoea. * All patients should receive advice about weight loss and/or prevention of weight gain; this may include advice to reduce alcohol consumption. ◆

complex OSA, or overlapping sleep disorders and adverse lifestyle issues. There is also a lack of such data for patients who refuse CPAP treatment or for whom the treatment is unsuccessful.

## Clinical assessment

If sleep service delivery at the primary care level is to be upscaled and the recently validated simplified models of care for OSA translated into routine care, there will need to be greater awareness around clinical assessment, goals of OSA treatment and the various available treatment options. Objectives of the clinical assessment are to determine the motivating factor(s) for presentation and the patient's symptom profile and pretest probability of disease, and to identify modifiable adverse lifestyle factors and co-occurring sleep problems. Collectively, these factors will have an important influence on the investigation and management pathway.

### Why does a patient seek evaluation?

Identifying the patient's motivations for seeking help will influence the treatment recommendation and likely adherence to therapy.

Patients present for three fundamental reasons:

- snoring causing social disruption or embarrassment;
- symptoms of unrefreshing sleep, daytime fatigue and sleepiness and its social or professional consequences;
- concerns that untreated sleep apnoea may contribute to adverse health outcomes.

### Pretest probability of disease

The patient's and bed partner's reports combined with patient characteristics such as age, sex and body habitus help determine the pretest probability of OSA (Box 3). The initial assessment by the general practitioner or practice nurse can be assisted by the use of a simple 3–5 minute screening tool such as the OSA50[16] (Box 3) or Berlin[17] questionnaires, which have been validated in the primary care setting, and can be followed by the 8-item Epworth Sleepiness Scale questionnaire[25] to further screen for excessive sleepiness and thus identify those most likely to benefit from treatment.

In general, straightforward, high pretest probability symptomatic OSA (Box 3) may be suited to clinical assessment, home-based PSG and treatment in primary care. A high pretest probability of OSA will improve accuracy for limited channel sleep testing and home-based PSG and reduce equivocal results that need repeating in the laboratory. Robust testing of this model of care has demonstrated favourable outcomes;[24] however, it is predicated on primary care physicians and nurses having the necessary training to manage sleep disorders, being willing to engage in patients' management, and in having ready access to specialist backup when required.[23] Unless the primary care physician has acquired considerable expertise, less clear-cut cases are best referred to a specialist early in the clinical pathway, as are patients with high pretest probability, and patients with overlapping sleep pathologies and serious medical comorbidities such as heart failure and chronic obstructive pulmonary disease.

### Clinical features of OSA

There are nuances to sleep history-taking that, if appreciated, will further enhance the clinical assessment and improve the chances of identifying the high-risk patient and increase the likelihood of a favourable treatment outcome.

*Snoring:* impression of snoring severity can be obtained from its reported frequency (variable or habitual) positional nature, or association with alcohol. A collateral history from a bed partner, if available, can assist although the description will be influenced by their tolerance levels. More severe snoring is associated with a dry or even painful throat in the morning. While chronic loud snoring is one of the most reliable pointers to OSA, the absence of a snoring history does not rule it out. Bed partners may be absent or unreliable, and silent forms of OSA exist.

*Witnessed apnoeas:* partner reports of breathing pauses during sleep, when available, are a useful guide to the presence of OSA. OSA patients are rarely aware themselves of apnoeic events, but when this occurs the patient may describe that snoring woke them, sometimes with a brief palpitation or sense of transient breathlessness. More prolonged choking to full wakefulness should prompt consideration of other causes such as nocturnal laryngospasm, an alarming but non-fatal symptom often triggered by gastro-oesophageal reflux. Reflux is more prevalent in OSA,[26] so both forms of nocturnal choking may coexist.

*Unrefreshing sleep and daytime sleepiness*: contrary to conventional wisdom, excessive daytime sleepiness has been shown to have low discriminatory power for predicting OSA.[16] Community studies of OSA have generally found low rates of associated sleepiness and, when OSA is present, other causes including depression, sedative medication and inadequate sleep duration need to be considered.[27] Nonetheless, sleepiness in someone with proven OSA is a key consideration in determining the need for treatment.

OSA-related sleepiness is classically unrelated to sleep duration and should be distinguished from fatigue, an overlapping but less specific symptom. It is most pronounced in passive situations and enquiry should target these, including lunch breaks, meetings, seminars, watching television and driving (particularly long-distance driving or travelling as a passenger). Some patients avoid situations that induce sleepiness and thus do not spontaneously volunteer this symptom. Others are reluctant to self-report sleepiness because of perceived negative consequences for their driver's licence or occupation. The Epworth Sleepiness Scale (Box 3) is a validated and useful clinical guide for quantifying subjective sleepiness,[25] which assists but does not replace history-taking.

## Investigation: home-based versus in-laboratory PSG

In Australia, Medicare reimbursement is provided for full PSG, conducted in either supervised (in-laboratory) or unsupervised (home) settings. For home-based PSG, patients are connected to the electrodes and sensors at the facility on the afternoon of the test and return home, or self-connect in their own home before bed, according to written, verbal or audiovisual instructions. Patients may perceive an increased level of convenience and comfort with testing in their own home, sensing a more sleep-conducive environment. When directly compared, one study showed 50% of patients preferred home-based testing, 25% preferred laboratory-based testing and 25% had no preference.[28] Comparison of home-based versus in-laboratory PSG showed reduced total cost for home testing[28] and high overall satisfaction rates for both forms of testing.[28] However, home-based PSG is associated with higher test-failure rates, partial signal loss producing equivocal results,[28,29] and a tendency to underestimate sleep apnoea severity.[29] More severe sleep apnoea (high pretest probability) may overcome the shortfalls of partial signal loss and any tendency to underestimate severity, and this will improve diagnostic accuracy.

### Limited channel ambulatory sleep testing

Limited channel devices dispense with electroencephalographic measurements of sleep and rely on one to four channels of respiratory data to assess the frequency and severity of disordered breathing events. The signals may include finger pulse oximetry and thoracic and abdominal impedance bands to assess respiratory efforts and oronasal airflow. One concern is that dispensing with direct measurements of sleep will underestimate OSA severity for patients with short sleep duration. However, there is reasonably good agreement between these simplified devices and in-laboratory PSG in measuring the frequency of disordered breathing events, and professional guidelines have given qualified support to their use.[30] As with home-based full PSG testing, their successful application requires careful screening to first establish a high pretest probability of disease, followed by test interpretation and treatment advice by suitably trained professionals with specialist backup, including further in-laboratory testing if required.

In Australia, there is no Medicare reimbursement for limited channel sleep testing, restricting its availability. Currently, this type of testing tends to be offered directly to the patient at various outlets and pharmacies linked to the potential sale of CPAP and other therapeutic devices, sometimes bypassing the medical profession entirely.

**3 Obstructive sleep apnoea: simple questionnaire determinants of pretest probability and symptom profile**

**OSA50**[15]

| Determinant | Question | If yes, score* |
|---|---|---|
| Obesity | Is your waist circumference† > 102 cm (men), > 88 cm (women)? | 3 |
| Snoring | Has your snoring ever bothered other people? | 3 |
| Apnoea | Has anyone noticed that you stopped breathing during sleep? | 2 |
| 50 | Are you aged 50 years or over? | 2 |
| Maximum total score | | 10 |

* In Chai-Coetzer et al,[16] an OSA50 score ⩾ 5 was 100% sensitive (95% CI, 86%–100%) for moderate to severe OSA (ie, detected all cases) and an OSA50 score < 5 had high negative predictive value (100% [95% CI, 73%–100%]). However, the positive predictive value of the test was relatively modest (48% [95% CI, 35%–63%]), indicating that while it can be used to increase the pretest probability of OSA, patients who have a positive score (> 5) need to have a sleep study to definitively establish the diagnosis. † Measured at the level of the umbilicus.

**Epworth Sleepiness Scale (ESS)**[25]

How likely are you to doze off or fall asleep in the following situations, in contrast to feeling just tired? This refers to your usual way of life in recent times. Even if you have not done some of these things recently, try to work out how they would have affected you. Use the following scale to choose the most appropriate number for each situation:

| Situation | Chance of dozing (score)* |
|---|---|
| Sitting and reading | |
| Watching television | |
| Sitting inactive in a public place (eg, a theatre or meeting) | |
| As a passenger in a car for an hour without a break | |
| Lying down to rest in the afternoon when circumstances permit | |
| Sitting and talking to somebody | |
| Sitting quietly after a lunch without alcohol | |
| In a car, while stopped for a few minutes in traffic | |

* 0 = no chance of dozing; 1 = slight chance of dozing; 2 = moderate chance of dozing; 3 = high chance of dozing. The ESS is a guide only. An ESS score > 10 is indicative of pathological daytime sleepiness. It is not a strong independent predictor of the presence of OSA; however, in established OSA, it is a predictor of response to treatment. Patients with lower scores (eg, 8–10) may also have mild impairment of vigilance in the day and should be evaluated. ◆

The evidence suggests that most modes of testing for OSA have a role when supported by a validated model of care. Currently in Australia, the extent to which sleep testing is coupled to an evidence-based model of care that ensures good patient outcomes varies widely. This situation is in part determined by the reimbursement scheme for testing and the regulatory framework.

## Treatment, treatment failures and the disengaged patient

A comprehensive overview of all treatment options is beyond the scope of this manuscript, and international guidelines are available.[31] Options are summarised in Box 2. Identification of sleep apnoea is a teachable moment for the health care professional to guide the patient and suggest interventions to modify lifestyle and reduce weight. Thereafter, treatment considerations ought to extend beyond CPAP. Studies have shown large variation (17%–71%) in adherence to optimal CPAP (defined as average of ⩾ 4 hours per night).[32] More recent randomised controlled trial evidence suggests that mandibular advancement splints may be as effective as CPAP across a range of OSA severity,[33] although there is limited information on longer-term compliance. Newer surgical techniques are emerging for OSA and the combination of uvulopalatopharyngoplasty, tonsillectomy where appropriate, and a low-morbidity technique to reduce tissue volume at the tongue base shows promise in highly selected patients for whom conventional therapies such as CPAP or a mandibular advancement splint have been unsuccessful.[34] Adults with gross tonsillar hypertrophy and sleep apnoea are uncommon but often do very well following tonsillectomy. Some preliminary success is reported with nasal positive expiratory pressure devices,[35] although long-term adherence to treatment is unknown and patient selection needs more evaluation.

Overall, treatment for OSA includes a range of options, all of which have their unique challenges. Cost is a consideration and commitment is required to achieve long-term adherence. There is a risk that patients may not persevere with the treatment plan if the clinical assessment was not patient-focused and did not address key presenting symptoms or motivators. A negative experience has consequences in terms of lost opportunity if the patient withdraws from the therapeutic process. All patients should be clinically reassessed after a treatment option is tried, to ensure the treatment has been effective in controlling both OSA and its symptoms.

## The future

The specialty of sleep medicine now has a robust curriculum, encompassing both respiratory and non-respiratory sleep disorders, and requires a full year of dedicated training. This will see larger numbers of specialists with sufficient skills to assist with managing the public health burden of OSA. Telehealth will also enable sleep specialists to assist health care practitioners and patients in rural and regional communities.

However, the large burden of disease is likely to be best served in the long term by an expanded trained pool of primary care and other health care providers working alongside sleep and respiratory specialists. In this model of care, sleep specialists working in a multidisciplinary environment would have as their major clinical focus complex or atypical OSA cases (eg, those with comorbidities or overlapping sleep disorders) or treatment failures. All modalities of sleep testing will be used in accordance with existing validated algorithms. These models of care will take time to evolve and will require changes to clinical guidelines and accreditation standards, the upskilling of the health care workforce, and government and private sector policy changes with respect to reimbursement.

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# Impact of obstructive sleep apnoea on diabetes and cardiovascular disease

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## Summary

- Obstructive sleep apnoea (OSA) is a potential cause of systemic hypertension in young and middle-aged people, and treatment helps reduce blood pressure in some patients.
- Severe OSA (apnoea–hypopnoea index [AHI] > 30/h) is strongly associated with increased mortality, stroke and cardiovascular disease in middle-aged populations.
- The cardiovascular risk from moderate OSA (AHI, 15–30/h) is uncertain, particularly if the oxygen desaturation index is low, although the data suggest an increased risk for stroke (particularly in men). There is no evidence of increased cardiovascular risk from mild OSA (AHI < 15/h). In the elderly, the cardiovascular risks of OSA are uncertain, although there is a likelihood of increased risk of stroke. Current, ongoing randomised controlled trials will inform whether OSA is a reversible cardiovascular risk factor within the next 5 years.
- Patients with cardiovascular disease, stroke, diabetes, obesity or poorly controlled hypertension are at high risk of OSA and should be questioned for symptoms of OSA, which, if present, may warrant further investigation and treatment.
- Weight loss has an unpredictable effect on OSA severity, but is independently beneficial for symptoms and metabolic health in OSA patients and is recommended for all overweight and obese OSA patients.

Patients with obstructive sleep apnoea (OSA) have a high prevalence of insulin resistance (IR), type 2 diabetes mellitus and cardiovascular disease (CVD), indicating a strong association among the conditions. Intermittent hypoxia with fragmentation of normal sleep contributes to significant autonomic dysfunction plus proinflammatory and procoagulopathy states,[1] leading to IR and CVD (Box 1). Although obesity is a common risk factor for OSA, IR and particularly CVD, current evidence suggests that OSA itself is an independent risk factor for both IR and CVD. Clinical data suggest that this effect is most likely mediated via intermittent oxygen desaturation. However, teasing out the precise role that OSA plays in IR and CVD, independent of obesity, is difficult given the confounding effects of inactivity, sleep deprivation, diet and OSA variability in terms of age of onset, duration and severity. With this in mind, this paper attempts to review the epidemiological and interventional evidence connecting OSA with IR and CVD (Box 2).

## Obesity

Obesity is the major risk factor for OSA, particularly central adiposity with visceral fat. Large epidemiological studies have reported a dose–response association between OSA prevalence and increased body mass index (BMI) plus neck and waist circumferences. One large prospective epidemiological study reported that a 10% weight gain led to a sixfold increase in the odds of developing moderate to severe OSA, independent of confounding factors.[22]

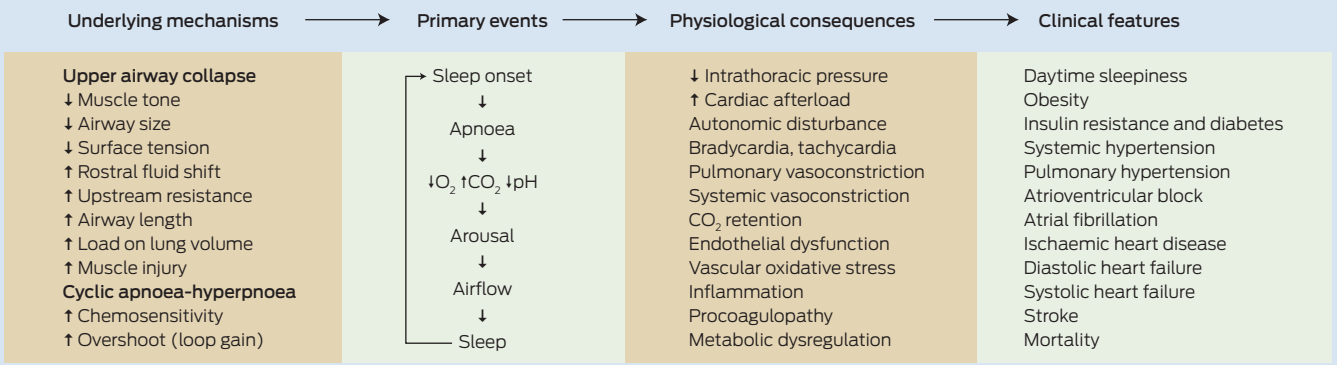
Conversely, weight loss improved OSA, but to a lesser extent than weight gain worsened it (10% weight loss predicted a 26% decrease in the apnoea–hypopnoea index [AHI]). The latter observation underscores the potential for weight loss as a treatment for OSA. Observational data suggest an improvement in OSA with weight loss, although results from randomised controlled trials (RCTs) have been available only more recently. Trial data indicate that patients with mild OSA substantially improve their OSA with weight loss, although only 22% achieved a "cure" (AHI < 5/h).[23] However, among obese patients with severe OSA, results from weight loss studies are more unpredictable. Data from lifestyle interventions show an improvement in OSA, with weight loss of at least 10 kg, but only a minority of patients achieved an AHI < 5/h.[24,25]

A recent Australian RCT assessing the effect of laparoscopic gastric banding surgery in morbidly obese patients with moderate to severe OSA showed that although surgical patients lost more weight, there was no significantly greater reduction in AHI in the surgical group compared with the control group who undertook lifestyle measures.[26] In both groups, there were significant improvements in symptoms of sleepiness and mood, despite only about a 50% reduction in the group AHI, suggesting that weight loss per se, rather than OSA reversal, contributed to improved quality of life. Metabolic parameters also improved with weight loss and were greatest in the surgical group, who lost more weight. This trial underlines two important points. First, obese patients with mild OSA may be "cured" by weight loss, but those with moderate to severe OSA are rarely "cured" by either surgical or medical weight loss strategies. Second, many significant health benefits (relating to quality of life, depression and diabetes control) can be achieved by weight loss in obese OSA patients, even if OSA persists.

## Systemic hypertension

OSA and systemic hypertension commonly coexist — the prevalence of OSA in populations with systemic hypertension has been reported to vary from 30% to 83%.[27] Several large epidemiological cross-sectional studies of community dwellers indicate that the presence of untreated OSA is associated with a greater prevalence of hypertension when controlled for known confounding factors,[2] although the association is weaker in prospective incidence studies.[3] Although some prospective incidence studies of middle-aged adults have found untreated OSA to be associated with a two- to threefold risk of developing hypertension over a 4–8-year period,[4] not all studies have found a positive association between OSA and hypertension.[3] In addition, the relationship between OSA and hypertension

1 Schematic summary of precipitating factors towards obstructive sleep apnoea, with physiological consequences and downstream cardiovascular consequences




has not been confirmed in patients aged >65 years,[5] probably because of additional accumulating risk factors.

Treatment of OSA with continuous positive airway pressure (CPAP) has been shown to lead to reductions in mean systemic blood pressure measured over 24 hours, although these falls are small (about 2–3 mmHg), with the greatest benefit seen in patients with more severe OSA.[6] There is also evidence that treatment with mandibular advancement splints leads to an improvement in hypertension,[7] suggesting that the benefit of OSA treatment with respect to blood pressure is independent of the treatment modality.

Despite this, pharmacological antihypertensive therapy (valsartan) is more effective than CPAP (9 mmHg v 2 mmHg fall in mean 24-hour blood pressure) over 8 weeks, according to one RCT of 23 patients with hypertension and OSA.[28]

Four important messages need consideration regarding OSA and hypertension. First, clinicians should assess for OSA symptoms and consider a sleep study in patients with resistant hypertension.[29] Second, OSA treatment in hypertensive OSA patients may improve blood pressure control but without large reductions, while snoring and quality of life should improve. Third, CPAP is not a substitute for pharmacological treatments. Fourth, obesity is a unifying factor and, accordingly, assistance with weight loss should be the primary objective for clinicians.

## Insulin resistance and diabetes

Metabolic disorders of glucose control and OSA share the same major risk factor of central obesity with excess visceral fat and, unsurprisingly, the disorders commonly coexist. Mechanistically, OSA may aggravate IR and type 2 diabetes via intermittent hypoxia, fragmented sleep and elevated sympathetic activity. Diabetes may contribute to OSA via neuropathy and weight gain related to insulin use. The prevalence of OSA in patients with type 2 diabetes has been reported to vary between 23%[8] and 86%,[9] with differences in study populations and OSA definitions explaining the marked variation in results.[10] Most cross-sectional studies have demonstrated that OSA is independently associated with IR and type 2 diabetes in adult sleep clinic populations and in unselected communities, independent of age and BMI, but prospective incidence studies have been less convincing.

The effect of OSA treatment with CPAP on insulin sensitivity and glucose control (ie, $HbA_{1c}$ levels) is unclear. A recent meta-analysis[11] of five RCTs (four with crossover design) suggested that reversal of OSA with CPAP for 1–12 weeks has a beneficial effect on IR, as measured by homoeostatic model assessment in OSA patients without diabetes, although the effect size was small (– 0.44) in contrast to pharmacological effects (– 0.9). The only RCT of CPAP treatment of OSA among adults with type 2 diabetes indicated that CPAP did not improve homoeostatic model assessment scores, $HbA_{1c}$ levels or BMI in 42 patients with moderate to severe OSA and type 2 diabetes, although patients were symptomatically and objectively less sleepy.[30] A larger and longer international trial is nearing completion (NCT00509223). Some authors suggest the variable effects of CPAP on glucose control may relate to duration of CPAP treatment (potentially >3 months) and that the effects may be greatest in patients who are less obese.[31]

The observations above indicate that factors for developing IR other than obesity, sedentary lifestyle and age, such as OSA and loss of normal sleep, should be considered, especially among patients with difficult-to-control diabetes. Moreover, it is important to realise that the OSA and IR pathophysiological association may be bidirectional.

## Stroke

Patients with untreated OSA have an elevated risk of developing stroke, and the data are more consistently positive than for cardiac disease,[18] including in the elderly.[32] Mechanisms include large swings in systemic blood pressure, local vibrational damage to the carotid artery bifurcation, increased coagulopathy, surreptitious development of atrial fibrillation during sleep with thrombus formation and paradoxical emboli through asymptomatic patent foramen ovale opening during transient sleep-related hypoxaemia with pulmonary hypertension.[33]

Prospective observational studies show increasing risk for ischaemic stroke with increasing OSA severity.[19] A large epidemiological study in the United States found that the risk for stroke in men increased almost three times

**2 Summary of cross-sectional prevalence and prospective incidence epidemiological trials that show an independent link between severe obstructive sleep apnoea and cardiovascular risk***

| | Cross-sectional prevalence | Prospective incidence | Interventional |
|---|---|---|---|
| Hypertension | Yes[2] | Yes (not in elderly)[3-5] | Yes, but small[6,7] |
| Insulin resistance | Yes[8-10] | Conflicting data | Yes, non-diabetic[11] |
| Ischaemic heart disease | Yes[12,13] | Yes[12] | Not available |
| Atrial fibrillation | Yes[14] | Not available | Not available |
| Heart failure | Yes[15] | Yes[16] | Yes[17] |
| Stroke | Yes[18] | Yes[19] | Not available |
| Mortality | Yes[20] | Yes (uncertain in elderly)[21] | Not available |

*Adjusted for all known confounding factors and obstructive sleep apnoea-treatment randomised controlled trials (interventional). ◆

once the AHI was > 19/h, but that the risk in women was much smaller and did not become significant until AHI was > 25/h.[19]

CPAP treatment may reduce stroke risk; however, large RCTs are lacking. Observational studies have shown that treatment of OSA reduces stroke risk. The only RCT assessing the effect of CPAP on risk of mortality and subsequent stroke did not show a benefit, but had only small numbers and was not adequately powered to address the issue.[34]

## Ischaemic heart disease

The prevalence of OSA is high (estimated to be 30%–58%) in patients with ischaemic heart disease (IHD).[12] In the general community, cross-sectional epidemiological evidence supports a link between OSA and IHD. OSA is associated with a greater risk for acute myocardial infarction than are smoking or hypertension.[13] Further, the presence of OSA in patients with established IHD is associated with greater 7-year mortality compared with patients without OSA.[12] Whether underlying OSA contributes to the well described circadian distribution of myocardial infarction (peak incidence around 8 am) remains to be determined. RCTs of OSA treatment on the development or outcomes of IHD are presently lacking.

## Cardiac arrhythmias

Benign cardiac arrhythmias are commonly present in OSA. Examples include cyclic tachycardia–bradycardia, atrial and ventricular ectopics, bigeminy, heart block and atrial fibrillation.[35] In a large study, subjects with severe OSA (AHI > 30/h) were found to be more likely to have atrial fibrillation (fourfold risk), non-sustained ventricular tachycardia (4.4-fold risk) and quadrigeminy (twofold risk) compared with subjects without OSA.[14] The clinical significance of this is unknown. Similar data were provided for Australians with moderate OSA (AHI > 15/h), with an odds ratio of 3 for having atrial fibrillation.[35]

Some data suggest that all arrhythmias improve with CPAP treatment,[36] whereas other data are not as supportive.[37] One study suggested the 12-month recurrence of atrial fibrillation after cardioversion was significantly lower if coexistent OSA was treated with CPAP compared with untreated OSA.[38]

Although the risk of fatal arrhythmias from OSA is unknown, an increased risk is suggested from data showing that subjects with OSA who die of sudden cardiac death are more likely to do so at night compared with those without OSA.[39]

Although RCTs of the effect of OSA treatment on cardiac arrhythmia frequency and severity are lacking, it does appear prudent to question for OSA symptoms in patients with difficult-to-control arrhythmias, such as cyclic tachycardia–bradycardia or atrial fibrillation, especially when they occur during sleep.

## Heart failure

Both diastolic and systolic heart failure (HF) are common in OSA populations. In addition to the proposed effect of OSA on CVD, large swings in negative intrathoracic and positive intravascular pressures that result from OSA are thought to contribute to the development of cardiomyopathy as well as hypertension, hypoxia, hypoxic pulmonary hypertension and oxidative stress.[1] Epidemiological data indicate a threefold greater prevalence of diastolic and systolic HF in community dwellers with severe OSA (AHI > 30/h) compared with those without OSA.[15] Further, the risk of developing incident HF due to untreated OSA is estimated to be 1.6 times greater, based on 4422 community dwellers (controlled for age, sex, race, diabetes and hypertension) followed for a mean of 8.7 years.[16]

OSA and central sleep apnoea (defined by about 30 seconds of hyperventilation followed by about 30 seconds of apnoea with no respiratory effort and usually absence of snoring) are also commonly seen within HF populations. A study demonstrated that 55%–85% of HF patients have sleep apnoea (either obstructive or central) when patients were tested several times over a 12-month period.[40] In general, central sleep apnoea is seen in the more advanced severe spectrum of HF and can be explained by additional pathophysiology to that seen in pure OSA. The high prevalence of each type of apnoea does not appear to have been affected by the introduction of β-blockers or spironolactone.[41]

Evidence suggests that coexistent OSA worsens HF and is improved by CPAP therapy. An RCT found that treatment of patients with OSA (AHI > 20/h) and systolic HF with fixed pressure CPAP over 3 months was associated with improvements in systolic function, quality of life, exercise capacity and autonomic control.[17] Nevertheless, the data are not universally positive. The study was not large enough to assess mortality; however, an observational study suggests an improvement in survival with long-term CPAP treatment, compared with untreated OSA.[42]

## Mortality

Several large, longitudinal epidemiological studies have consistently indicated that in middle-aged populations, severe untreated OSA (AHI > 30/h) is associated with greater mortality compared with treated OSA, mild to moderate OSA or no OSA.[20] These data suggest that severe OSA confers a mortality risk, which is prevented by CPAP treatment. Nevertheless, these studies were not

RCTs and, given that unrecognised bias may confound the results, whether OSA is a reversible risk factor for mortality remains inconclusive.

The mortality effects of untreated OSA are less certain in the elderly. In a large cohort of 14 589 Israeli patients, severe OSA led to increased mortality only for those aged < 50 years.[21] Similarly, a large US study also failed to show increased mortality in patients aged > 70 years.[20] However, a recent Spanish observational trial reported that elderly patients (> 65 years of age) with severe untreated OSA (AHI > 30/h) had 2.25 times increased mortality — due largely to stroke and HF, but not to IHD.[21] No excess mortality was seen in severe OSA treated with CPAP, or in less severe OSA.

## Role of CPAP in CVD: the future

Observational studies suggest that CPAP improves survival in severe OSA, although formal long-term RCTs are needed. The SAVE trial (ANZCTR 12608000409370; NCT00738179), instigated by the Adelaide Institute for Sleep Health, is currently underway. The trial aims to randomly allocate 2500 high CVD-risk patients with OSA to either CPAP or no CPAP, with a primary end point of time to cardiovascular event or death (results are expected in 2016). Several other large outcome-based trials are also underway, including a Spanish trial (NCT01335087) of CPAP treatment of OSA in patients with acute coronary artery syndromes. These and other studies will provide valuable clarification about whether OSA is a reversible cardiovascular risk factor. In addition, newer variants of positive airway pressure, such as adaptive servoventilation, are being tested in patients with sleep-disordered breathing and HF (NCT01164592 and NCT01128816), and we also await the results of these large multinational trials.

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# Sleep disorders in children

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Sleep problems, including problems at bedtime and frequent night waking, affect 30%–40% of infants and children before school age.[1] Effects of sleep disorders on the health of the child may include poor growth, adverse behavioural and learning effects and, for the child and family, worsened mental health, and poor quality of life.[2] The likelihood that important and treatable sleep disorders go unrecognised is increased because many parents do not mention their concerns to their general practitioner, or the doctor does not ask about or identify the issues.[3,4] Simple management strategies can be effective at a primary care level. An important role of the GP or general paediatrician is to identify children's sleep problems and to differentiate those who would benefit from referral to specialty services.

Average sleep times vary with age, and community surveys indicate considerable variability in sleep requirements, to the extent that normative values are sometimes debated. However, systematic review of the literature can guide general recommendations for sleep duration at different ages.[5] Newborn infants sleep 16–18 hours per day in cycles of 3–4 hours (day and night). After 6 months of age, healthy infants can sleep for more than 6 hours at night without a feed. By 18 months of age, sleep patterns usually mature to overnight sleep plus one daytime nap. By school age, sleep consolidates into a single night sleep of 11–12 hours. Sleep duration continues to slowly reduce from about 10 hours in prepubescent children to 8 hours by 16 years of age. Individual children and adolescents may benefit from longer sleep times than these average figures, and enquiry about daytime functioning is an important part of assessing adequacy of sleep.[5,6]

Initial screening is an important aspect of identifying sleep issues in children and the first step in providing timely advice and intervention. An example of a mnemonic to remind physicians of important aspects of history-taking regarding sleep quality in children is BEARS: B = bedtime (settling) problems; E = excessive daytime sleepiness; A = night awakenings; R = regularity and duration of sleep; S = snoring.[7] Parents define the presence of children's sleep problems, so evaluation of the validity of parental expectations is also important. Age-specific common non-respiratory sleep problems are tabulated in Box 1.[8]

## Non-respiratory disorders

### Sleep phenomena or parasomnias in children

Parasomnias are undesirable motor, autonomic or experiential phenomena that occur exclusively or predominantly during sleep.[9] Parasomnias are common in childhood — examples include bruxism (teeth grinding, 6%–10%), sleep terrors (0.7%–2%) and somnambulism (sleep walking, up to 7%).[10] A simplified summary of parasomnias with their prevalence rates is provided in Box 2.[8] Benign parasomnias may run in families, increase in frequency with any condition that causes sleep deprivation or sleep fragmentation such as fever, and tend to improve with age (Box 2).[8]

## Summary

- Sleep disorders are very common in childhood and are often amenable to simple advice and parental education.
- Questions about sleep should be an integral part of every paediatric consultation.
- Children with underlying syndromes or complex medical conditions often have multiple sleep issues.
- Excessive sleepiness in children requires careful history-taking and consideration of specialised investigation.
- Obstructive sleep apnoea (OSA) is a common condition in childhood with important health implications.
- The high prevalence of OSA warrants rigorous attempts to identify children at higher risk and manage them appropriately.
- Adenotonsillectomy is a highly efficacious therapy for paediatric OSA.
- A current major issue is to improve ways of distinguishing mild from severe OSA before a child undergoes adenotonsillectomy, as those with more severe disease are at increased risk of postoperative complications and should undergo adenotonsillectomy in a tertiary centre.
- Children with obesity and other comorbid conditions are at increased risk of persisting OSA despite adenotonsillectomy.
- Topical (nasal) steroids and/or anti-inflammatory agents have a role in the non-surgical treatment of mild OSA.
- Continuous positive airway pressure and orthodontic interventions are treatment options for treatment of persisting OSA in children.

### Behavioural sleep disorders

Extremely common sleep problems in children include a child not getting into bed, having difficulty or requiring undue help to settle to sleep, frequent waking in the night and/or getting out of bed, and very early morning awakenings. They are often grouped as behavioural sleep disorders because of the perception that the problem lies with how the child behaves. These problems may lead to insufficient sleep and considerable family disruption. Children with developmental disorders, attention deficit hyperactivity disorder, depression and anxiety have higher incidence of these types of sleep disturbances than other children.[11]

### Management of behavioural sleep disorders and parasomnias

Key to reducing the frequency and severity of behavioural sleep disorders is the provision to parents of preventive information, best provided opportunistically in primary care and by maternal child health nurses. Treatment interventions should then be evidence-based and developmentally appropriate. Parasomnias are usually benign and most decrease in frequency in later childhood. Education and reassurance of parents may be all that is required in less severe cases. Behavioural strategies for management of parasomnias include anxiety-relaxation techniques for poor sleep initiation, and sleep hygiene measures.[11] These

1 Examples of non-respiratory sleep disorders in childhood, by most common age at presentation[8]

| Age group | Non-respiratory sleep disorder |
|---|---|
| Infant/toddler (0–2 years) | Behavioural insomnia of childhood: eg, excessive night waking, sleep associations (aids to sleep onset, such as rocking, dummy, milk) |
| | Rhythmic movement disorders: eg, body rocking |
| Preschool (3–5 years) | Behavioural insomnia of childhood: eg, excessive night waking, bedtime refusal |
| | Rhythmic movement disorders: eg, head banging |
| | Night terrors |
| Primary school (6–12 years) | Inadequate sleep: eg, due to social pressures such as evening activities and/or poor sleep habits such as watching television in bed |
| | Sleep walking |
| Adolescent (13–18 years) | Inadequate sleep: eg, due to delayed sleep phase syndrome |
| | Narcolepsy |
| | Periodic limb movements |

include limit-setting — for example, gradually removing parents' attendance at the child's bedside, so they are not present at the time of sleep onset — and moving bedtime closer to the usual time of sleep onset, to avoid periods of lying in bed awake before sleep onset. These measures help to eliminate the need for parents to attend to the child at each night-time awakening, and encourage a pattern of prompt sleep onset after going to bed. Together, they avoid prolonged periods of wakefulness during the night.

The core principle of preventing and managing bedtime (settling) issues and frequent night waking is to promote independence in settling to sleep. Infants and children who depend on a parent or other sleep association (music, dummy, rocking) at the start of the night are likely to require the same attention to resume sleep after what are otherwise normal, brief awakenings during the night. Consistency is the most important factor, but the rate of possible change is family-specific and sometimes needs to occur in slow, small steps to be sustained. Maternal mental health is an important factor in managing paediatric sleep disorders; children's sleep problems and poor maternal sleep can contribute to mental health disorders, as well as being an aetiological factor for the inconsistent maintenance of the infant's sleep routines. In a small group of toddlers with difficulty initiating or maintaining sleep, melatonin could be used to entrain their sleep routine. The interventions are also safe, with no negative long-term outcomes and many benefits to child and family health and functioning.[12]

Parasomnias can occur very frequently, cause distress and/or disrupt family life. Management strategies should ensure the safety of the child; for example, by placing the mattress on the floor rather than on a bed frame, and by adding locks to doors to prevent the child opening simple latches while sleep walking. Simple strategies to minimise the frequency of events are often effective for managing parasomnias in otherwise normal children and include:

*Extending sleep:* insufficient sleep increases the frequency of parasomnias. As little as 30 minutes of additional sleep can reduce the frequency of parasomnias. Work towards earlier bedtime and/or later rise times. Making bedtime earlier should occur in small steps of 10–15 minutes, to avoid increasing bedtime struggles.

*Reducing bedtime anxiety and struggles/conflict:* going to bed in an aroused state (anxious, angry or upset) can intensify parasomnias. Aim for a gentle and predictable bedtime routine. Avoid stimulating activities like television or computer games for an hour before bed. If necessary, match bedtime to the usual sleep onset time (even if this is late), then slowly bring bedtime earlier, as above. Medication is rarely indicated.[11,13] If the problem is very severe, very frequent or atypical, raising the possibility of a seizure disorder, then referral to a sleep specialist is indicated, with polysomnography and/or electroencephalography indicated depending on the clinical scenario.

*Investigating excessive daytime sleepiness and circadian rhythm disorders:* excessive sleepiness requires systematic evaluation. Possible causes include inadequate sleep, sleep disruption from conditions such as restless leg syndrome and obstructive sleep apnoea (OSA), and circadian rhythm disorders. In children with an apparently sufficient duration of sleep, marked daytime sleepiness may be the only manifestation of narcolepsy, which has an estimated prevalence of 1 in 4000 to 1 in 2000, and a peak of onset at 14 years of age.[14] Recognition of narcolepsy onset in childhood and appropriate treatment is likely to improve learning and daytime functioning.

Disruption to normal circadian rhythmicity, such as very late bed and rise times, can have substantial effects on the ability of a child to participate in school and other activities. Circadian sleep problems are especially common in children with pervasive developmental disorders such as autism spectrum disorder, and also occur in adolescents, where many factors impact on a tendency for the sleep phase to be delayed into the night, making socially imperative morning rise times difficult to achieve. The main focus of therapy is to establish and maintain good sleep hygiene including settling strategies (eg, avoiding screen time and caffeine-containing drinks before bedtime) and consistent timing of sleep throughout the 7-day week. Specialist referral is advised if there is concern about accuracy of diagnosis, or need for additional medical therapy including use of medications such as melatonin. Use of such medications may be indicated but must be in the context of awareness of the high need for ongoing surveillance of short- and long-term side effects.

## Respiratory disorders

### Snoring and OSA

Snoring and OSA are common, affecting 3%–15% of children, with peak prevalence in the preschool years when lymphoid tissue size in the upper airway is largest relative to the size of the facial skeleton.[15] OSA affects up to 5.7% of children,[16] and so potentially affects one child in every classroom in the country. Although the highest incidence of OSA is in preschoolers (3–5 years of age) with large tonsils, 9% prevalence of snoring has been documented in infants aged 0–3 months.[15,17]

Identification of severe OSA is important because it is linked to increased risk for postoperative respiratory com-

**2 Sleep-state distribution of sleep-related symptoms and parasomnias in childhood that do not require treatment unless they are very frequent or severe***

| Sleep state | Diagnosis | Prevalence | Presentation |
|---|---|---|---|
| Non-rapid eye movement-related | Hypnogogic imagery (awake or lucid dreaming) | 51% | Vivid visual dreams while in transition to sleep |
| | Sleep starts | 33% | Sudden involuntary "jumps" at sleep onset |
| | Confusional arousals | 17% | Child appears to wake, often distressed, but does not respond normally |
| | Night terrors | 17% | Out of slow-wave sleep, so most often in first third of the night. Child appears to wake and be terrified, but remains unaware of surroundings; attempts to comfort can prolong the event |
| | Sleep walking | 14% | Out of slow-wave sleep, so most often in first third of the night. Child performs apparently coordinated activity (walking, opening doors) but electroencephalography and behaviour retain some characteristics of sleep |
| Rapid eye movement-related | Dreams | na | Semi-coherent images and sensations recalled after sleep |
| | Sleep paralysis | 7.6%, general population | Seconds to minutes of being unable to perform voluntary movement at sleep onset or awakening |
| | Nightmare | 5.2%, one per week; 10%–50%, 3–5 year olds | Dreams with frightening content |
| Sleep-state independent | Bruxism | 28% | Sounds of grinding and/or evidence of tooth wear |
| | Rhythmic movement disorder | 17% | Body rocking or head banging mainly at sleep onset and/or following night awakenings |
| | Sleep talking | 55% | Semi-coherent speech while apparently asleep |
| | Periodic limb movements | 8.4%–11.9% | Repetitive, brief limb movements during sleep that can cause sleep disturbance, daytime sleepiness and leg discomfort. Associated with reduced iron stores |

* The major differential diagnosis of parasomnias, which needs to be excluded in frequent or severe cases, is frontal lobe epilepsy. ◆

promise, including emergency reintubation and unplanned admissions to intensive care. It is a major challenge to identify the children who require perioperative management in tertiary paediatric centres. Box 3 highlights cases where referral for polysomnography is warranted, rather than direct referral for adenotonsillectomy.

OSA is associated with sleep fragmentation and repeated episodes of hypoxia. Polysomnography is superior to other testing methods for determining disease severity and also permits diagnosis of comorbid disorders (eg, periodic limb movements). The thresholds for severity of OSA are lower than in adults, with OSA defined as $\geq 1$ obstructive event per hour of sleep on polysomnography. Treatment is generally recommended if the frequency of obstructive respiratory events is $>1.5$ per hour. Severity is usually defined as mild for 1–5 events per hour, moderate for 5–10 events per hour and severe for $\geq 10$ events per hour. However, no threshold has been established for disease severity with regard to the development of complications. Even mild disease is associated with adverse neurocognitive, behavioural and cardiovascular outcomes, such that even chronic partial obstruction causing snoring without gas exchange abnormalities or evident sleep disruption is associated with adverse effects.

Despite the fact that no clinical assessment method other than polysomnography has proven discriminatory for OSA in children who snore, the number of paediatric sleep units in Australia is inadequate to provide polysomnography to screen all snoring children. The presence of snoring and large tonsils is a sensitive but not specific marker. Helpful clinical indicators include increased work of breathing, parental concern, and frequent daytime mouth breathing.[18] Markers that are specific but not sensitive (helpful when positive, but unable to rule out disease) include excessive daytime somnolence and observed OSA.[19] Almost all screening tools are also specific but not sensitive, including overnight oximetry (most useful if positive, but most children have a negative study that does not rule out OSA[20]), video recordings and nap studies, so the search for an ideal screening tool continues. Overnight oximetry is helpful in identifying cases with marked hypoxia, but those using it need to be familiar with the technical aspects and diagnostic limitations of the tool.[21] All screening tools, including oximetry, are best used in combination with clinical indicators such as young age (under 3 years) and comorbidities (syndromes, obesity, etc), to help evaluate the likelihood of postoperative respiratory complications.[21]

Among the major sequelae of untreated OSA, cardiovascular risks include systemic hypertension, increased sympathetic activation and ventricular hypertrophy, while pulmonary hypertension and right heart failure still occur occasionally in infants and children with severe OSA.[22] Even mild OSA is linked to daytime neurocognitive dysfunction that translates into decrements of intelligence quotient, and a randomised controlled study has now been published regarding assessment of neuropsychological development in school-age children with OSA after tonsillectomy.[23] Plausible mechanisms for this association include sleep fragmentation, repetitive hypoxia, and reduced cerebral blood flow and oxygenation. Behavioural improvements follow adenotonsillectomy,[24-26] but responses in neurocognitive function are variable.[27] A review of 25 studies investigating behavioural and neurocognitive outcomes following adenotonsillectomy found that all studies reported improvement in one or more measures including quality of life, behavioural problems including hyperactivity and aggression, and neurocognitive skills including memory, attention and school performance.[26] Improvement or resolution of OSA has also been linked to concomitant improvements in systemic and pulmonary blood pressures, heart rate and pulse variability, cardiac morphology and cardiac function.[22]

**3 Indications for polysomnography in a child suspected to have obstructive sleep apnoea (OSA)**

| Indications | |
|---|---|
| Conditions with increased surgical risk that should have documentation of disease severity | Complex medical conditions such as Down syndrome, neuromuscular disorders and craniofacial syndromes<br>Age < 3 years |
| Discordance between history and examination | For example, strong history of OSA with small tonsils and no apparent nasal obstruction |
| Potential alternative explanations for sleep disturbance | Possible combination of central apnoea/hypoventilation (eg, spina bifida)<br>Need to differentiate nocturnal epilepsy (eg, from parasomnias) |
| Persistence of symptoms after adenotonsillectomy | High-risk groups for persisting OSA: severe initial disease; history of prematurity; congenital syndrome/malformation; obesity; atopy; age > 7 years |

The natural history of symptoms of OSA (eg, snoring, mouth breathing and apnoea) is for around 50% of preschool children to move (bidirectionally) among severity groups over a 2-year follow-up period.[28] In a cohort of 12 447 children studied across seven time points between ages 6 months and 6.75 years, the prevalence of OSA symptoms was highest between 3.5 and 4.8 years of age.[29] The highest peak of new symptoms occurred between the ages of 1.5 and 2.5 years.[29] Another study undertook polysomnography on 45 children with mild OSA at baseline; at follow-up 4 years later, disease had worsened in 37% and resolved in 26%.[30]

Preschool children generally respond to adenotonsillectomy; meta-analysis shows cure rates of 82% in otherwise normal children.[31] Success rates for adenotonsillectomy are lower in obese[32] and older[33] children, and adenoidectomy and/or tonsillectomy is usually not appropriate for infants. Although adenotonsillectomy reduces the severity of OSA in obese children, such children have more severe initial disease, and obesity increases the risk for persisting disease.[32,34] Nasal corticosteroid sprays[35-37]and leukotriene-receptor antagonists (eg, monteleukast)[38] are helpful in children with mild OSA and for some with persistent disease after adenotonsillectomy, and a treatment trial is appropriate before pursuing other interventions.[39] Specific airway problems, especially infants with Pierre Robin sequence, may respond to mandibular distraction, continuous positive airway pressure, nasopharyngeal tube, and/or oral tongue positioning devices, but may necessitate tracheostomy.

Factors that indicate a higher risk for persisting OSA despite adenotonsillectomy include more severe initial disease (respiratory disturbance index > 10/h or minimum $SaO_2$ < 80%), obesity with body mass index > 95th percentile for age and sex, and children aged > 7 years at the time of surgery (whether obese or non-obese).[33] There is interplay between obesity and atopy, in that for non-obese children, comorbid asthma increases the risk of persisting disease whereas allergic rhinitis is only significant when both obese and non-obese groups are considered together.[40] These groups need follow-up after surgery to establish whether snoring has or has not resolved.

Older children and adolescents may respond to adenotonsillectomy or require other treatments including continuous positive airway pressure, orthodontic and other surgical or dental procedures (rapid maxillary expansion, or mid-face advancement). Evidence of efficacy and safety in children is limited for orthodontic options such as mandibular advancement splints.[41-44] These interventions aim to affect growth of the face and oropharyngeal airway to produce long-term structural changes, irrespective of whether the initial airway problem is primary, or secondary to OSA.

### Children with underlying medical disorders

Underlying medical disorders work to both increase risk for OSA and to reduce the effectiveness of surgical treatment (Box 3). In particular, congenital abnormalities that affect craniofacial or thoracic growth, such as achondroplasia and Down syndrome, will predispose to sleep-disordered breathing. In Down syndrome, there appears to be particular risk for hypertrophy of the lingual tonsils.[33] It is also known that children with multiple disabilities have increased risk for other sleep disturbances such as difficulties with sleep initiation and maintenance, insomnia and other sleep pattern abnormalities.[45]

Children with neuromuscular diseases have increased incidence of OSA in the first decade.[46] Congenital cardiothoracic abnormalities or restrictive lung disorders, often linked to neuromuscular disorders or neurodevelopmental disability such as cerebral palsy, also predispose to nocturnal respiratory failure. Symptoms suggestive of nocturnal hypoventilation include increased frequency or severity of lower respiratory tract infections, and progression of scoliosis. Screening should include pulmonary function testing, with sleep studies for children with vital capacity < 60% of that predicted and for non-ambulant children before scoliosis surgery, and pragmatic consideration of screening versus full polysomnographic studies.[47] Early identification and treatment of impaired pulmonary function can prevent or reduce the frequency and duration of admissions to intensive care units, as well as improving quality and duration of life.[48]

Congenital central hypoventilation syndrome is a rare but highly treatable condition (incidence, 1 in 50 000 live births).[49] This usually presents during the neonatal period with frequent apnoeas or colour change during sleep, but milder forms can present in older children.[50]

## Conclusion

Sleep disorders are common in childhood and are associated with significant consequences for children and parents. Behavioural disorders include sleep onset delay, sleep interruptions, early morning waking and combinations of these elements. Parasomnias are very common and can be frequent and severe enough to warrant specialist referral. Access to tertiary and specialist assessment services is limited, so good triage of sleep disorders by primary care services and general paediatricians is essential. Identification and treatment of OSA is important in children. Immediate risk for respiratory compromise can be identified before adenotonsillectomy, and there are high rates of cure after surgery. Untreated, OSA is associated with risk of cardiovascular, neurodevelopmental and ongoing respiratory health problems. For triage purposes, Box 3 highlights situations where referral for specialist services with access to polysomnography is suggested in cases of sus-

pected OSA. Finally, children with persisting symptoms despite surgery will often benefit from polysomnography and specialist evaluation to determine the severity of ongoing disease, identification of cause, and need (or not) for ongoing treatment. Childhood presents an opportunity for effective, early intervention in sleep disorders.

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# Insomnia: prevalence, consequences and effective treatment

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## Summary

- Insomnia is common and can have serious consequences, such as increased risk of depression and hypertension.
- Acute and chronic insomnia require different management approaches.
- Chronic insomnia is unlikely to spontaneously remit, and over time will be characterised by cycles of relapse and remission or persistent symptoms.
- Chronic insomnia is best managed using non-drug strategies such as cognitive behaviour therapy.
- For patients with ongoing symptoms, there may be a role for adjunctive use of medications such as hypnotics.

Insomnia is a very common disorder that has significant long-term health consequences. Australian population surveys have shown that 13%–33% of the adult population have regular difficulty either getting to sleep or staying asleep.[1,2] Insomnia can occur as a primary disorder or, more commonly, it can be comorbid with other physical or mental disorders. Around 50% of patients with depression have comorbid insomnia, and depression and sleep disturbance are, respectively, the first and third most common psychological reasons for patient encounters in general practice.[3] Insomnia doubles the risk of future development of depression, and insomnia symptoms together with shortened sleep are associated with hypertension.[4,5]

Insomnia is defined in the fifth edition of the *Diagnostic and statistical manual of mental disorders* (DSM-5) as difficulty getting to sleep, staying asleep or having non-restorative sleep despite having adequate opportunity for sleep, together with associated impairment of daytime functioning, with symptoms being present for at least 4 weeks.[6] Having a sleep experience that does not meet our expectation, such as with some transient awakenings but with good daytime functioning, does not constitute insomnia.

## Acute versus chronic insomnia

Acute insomnia is defined as sleep disturbance meeting the DSM-5 definition of insomnia, but with symptoms occurring for less than 4 weeks.[6] Generally, acute insomnia is triggered by precipitating events such as ill health, change of medication or circumstances, or stress. Once the precipitating event passes, sleep settles back to its usual pattern. Hence, treatment for acute insomnia is focused on avoiding or withdrawing the precipitant, if possible, and supporting the acute distress of not sleeping with short-term use of hypnotics if symptoms are significant. This is the usual approach in primary care, with 95% of general practitioner consultations for insomnia resulting in the prescription of a hypnotic, usually a benzodiazepine.[7]

However, if patients have repeated episodes of acute insomnia or ongoing comorbidities, insomnia symptoms can persist and evolve into chronic insomnia, which requires a different treatment approach. Once people have had difficulty sleeping for over 4 weeks, they have usually begun to behave and think about sleep differently, in ways that are maladaptive and perpetuate their sleep difficulties.[8] The long-term course is then generally one of relapse and remission rather than resolution,[9] which continues well after the acute precipitating circumstances have passed. Therefore, the treatment approach needs to match this, with a chronic disease management model educating and upskilling patients on how best to manage their insomnia symptoms over time. Health care providers need to see insomnia as a chronic illness and emphasise the role of strategies to prevent relapses, rather than focusing on treatment of acute episodes or crises.

## Assessment and diagnosis of insomnia

The assessment and diagnosis of insomnia is formulated mainly from a systematic sleep history. To assist in establishing premorbid baseline sleeping patterns and formulating treatment goals, clinicians must ask patients about their typical sleeping pattern before they developed insomnia.

Insomnia assessment involves understanding the patient's typical sleep pattern at night and over a time frame of weeks to months. Therefore, part of the sleep assessment is asking for the patient's narrative of typical bedtime, time taken to fall asleep after lights out (sleep latency), frequency and rough duration of awakenings in the middle of the night, and what time the patient gets out of bed. Are there times when sleep returns to normal? Was there an initial trigger or did the symptom arise spontaneously? Was it related to a period of stress, anxiety or depression? Did it start during childhood and continue thereafter? Are there lifestyle factors contributing to insomnia, such as too much caffeine or exercise late in the day, television or pets in the bedroom, or use of alcohol or nicotine? Knowing the patient's cognitions, beliefs and worries about sleep, which are often apparent in the language and emotion used when they describe their sleep, can assist in the formulation of specific behavioural and calming approaches to assist with sleep.

It is important to assess the effects of poor sleep on the patient. Common daytime consequences include mood lowering, irritability, poor memory, fatigue, lack of energy and general malaise. These can manifest as work absenteeism, with insomnia being one of its leading medical causes.[10] It is also imperative to ask for risky consequences of insomnia, including accidents and sleepiness while driving.

Identifying the body clock type of the patient is crucial in excluding circadian rhythm disorders. A commonly undiagnosed condition, delayed sleep phase disorder is a body clock variation where the patient is biologically inclined to go to sleep much later than usual (typically after midnight), yet generally sleeps well after sleep onset, with a natural wake time that is much later than for most people and is often incompatible with normal school or work start times.

It is also important to look for comorbid conditions that can present with insomnia, such as depression and anxiety, chronic medical conditions, and other sleep disorders. Comorbid conditions have a bidirectional relationship with insomnia, with each influencing or exacerbating the other and requiring concurrent assessment and management. The Auckland Sleep Questionnaire, a validated sleep screening questionnaire in primary care, is one tool that can assist in identifying these disorders.[11] Other validated questionnaires such as the Insomnia Severity Index can help to document the severity of patients' symptoms and assess their response to treatment.[12]

Since many people with insomnia overestimate their sleep disruption and underestimate actual sleep time, a 2-week sleep diary is a very helpful assessment tool as it assists the sleep clinician to get a more accurate snapshot of sleep compared with a pure verbal account.[13] For some, a sleep diary is revealing in that they realise that they do get some sleep, albeit fragmented or superficial. This can provide the basis for discussion. There are several downloadable sleep diaries online — for example, http://yoursleep.aasmnet.org/pdf/sleepdiary.pdf. If patients have difficulty completing a sleep diary, or there is significant misperception of sleep suspected, actigraphy (using a device worn on the wrist to monitor sleep–wake cycles) can be used to objectively measure sleep.

Although an overnight sleep study or polysomnography is not routinely indicated in diagnosing insomnia, it can be helpful in diagnosing several conditions, including obstructive sleep apnoea, sleep-related movement disorders, parasomnias, or insomnias that are treatment-resistant.[13] A routine physical and mental status examination can give clues regarding comorbid medical and or mental health conditions. Other tests including laboratory and radiographic procedures are not routinely indicated in chronic insomnia.[13]

## Non-pharmacological treatment of insomnia

Cognitive behaviour therapy aimed at treating insomnia (CBT-i) targets maladaptive behaviour and thoughts that may have developed during insomnia or have contributed to its development. CBT-i is considered to be the gold standard in treating insomnia, with effect sizes similar to or greater than those seen with hypnotic drugs and, unlike with hypnotics, maintenance of effect after cessation of therapy.[14,15] These effects are seen in both primary and comorbid insomnia.[16]

The implementation of individual face-to-face CBT-i is typically delivered by a trained health professional, which makes it expensive, labour intensive and therefore beyond the reach of many. Patients with insomnia are eligible for Medicare rebates for psychological treatment if they are referred under the Chronic Disease Management or Better Access to Mental Health Care initiatives. Telephone and online delivery of CBT-i have been shown in clinical trials to be as effective as face-to-face CBT-i.[17,18] While these different treatment delivery models have the potential to markedly improve access to CBT-i, they need to be investigated further with respect to their long-term reliability and effectiveness. They might be best used as part of a stepped-care approach.[19] Some patients may need little guidance, while others may need more personal treatment and guidance.

CBT-i consists of five major components: stimulus control, sleep restriction (also known as sleep consolidation or bed restriction), relaxation techniques, cognitive therapy and sleep hygiene education (Box). Typically, CBT-i is delivered in four to 10 sessions, either individually or in a group setting, ideally involving four to eight participants.

Stimulus control is a reconditioning treatment forcing discrimination between daytime and sleeping environments.[20] For the poor sleeper, the bedroom triggers associations with being awake and aroused. Treatment involves removing all stimuli that are potentially sleep-incompatible (reading, watching television and use of computers) and excluding sleep from living areas. The individual is instructed to get up if he or she is not asleep within 15–20 minutes, or when wakeful during the night or experiencing increasing distress, and not return to bed until feeling sleepy.

Sleep restriction relates to better matching the time spent in bed to the average nightly sleep duration.[21] Patients keep a sleep diary to determine average sleep duration. They are then allowed a period of time in bed equal to this plus 30 minutes, and set a regular arising time. As some patients can underperceive the amount of sleep, the time in bed should never be set at less than 5 hours. As sleep becomes more consolidated, the length of time in bed can be gradually increased in 15–30 minute increments. This effective intervention induces natural sleepiness (reduced time in bed) and gives the individual a sense of assurance that bed is now a safe place to sleep. Bed restriction has recently been shown to be an effective intervention in primary care.[22]

Relaxation techniques include progressive relaxation, imagery training, biofeedback, meditation, hypnosis and autogenic training, with little evidence to indicate superiority for any one approach. Patients are encouraged to practice relaxation techniques throughout the day and early evening. Even a few minutes two to four times a day is useful. A last-minute relaxation attempt minutes before sleep will not work miracles. Muscular tension and cognitive arousal (eg, a "chattering" mind) are incompatible with sleep. At the cognitive level, these techniques may act by distraction. Relaxation reduces physical and mental arousal but is less effective as a stand-alone treatment and is better used in combination with other treatment interventions.

**Cognitive behaviour therapy for insomnia**

| Intervention | General description | Specific instructions |
|---|---|---|
| Stimulus control | BED = SLEEP. Set of instructions aimed at conditioning the patient to expect that bed is for sleeping and not other stimulating activities. Only exception is sexual activity. Aim is to promote a positive association between bedroom environment and sleepiness | Go to bed only when sleepy/comfortable and intending to fall asleep. If unable to sleep within what feels like 15–20 minutes (without watching the clock), leave the bed and bedroom and go to another room and do non-stimulating activity. Return to bed only when comfortable enough to sleep again. Do not read, watch television, talk on phone, pay bills, use electronic social media, worry or plan activities in bed |
| Sleep-restriction therapy | Increases sleep drive and reduces time in bed lying awake. Limits the time in bed to match the patient's average reported actual sleep time. Slowly allows more time in bed as sleep improves | Set strict bedtime and rising schedule, limited to average expected hours of sleep reported in the average night. Increase time in bed by 15–30 minutes when the time spent asleep is at least 85% of the allowed time in bed. Keep a fixed wake time, regardless of actual sleep duration |
| Relaxation techniques | Various breathing techniques, visual imagery, meditation | Practise progressive muscle relaxation (at least daily). Take shorter relaxation periods (2 minutes) a number of times per day. Use breathing and self-hypnosis techniques |
| Cognitive therapy | Identifies and targets beliefs that may be interfering with adherence to stimulus control and sleep restriction. Uses mindfulness to alter approach to sleep | Unhelpful beliefs can include overestimation of hours of sleep required each night to maintain health; overestimation of the power of sleeping tablets; underestimation of actual sleep obtained; fear of stimulus control or sleep restriction for fear of missing the time when sleep will come |
| Sleep hygiene education | Emphasises environmental factors, physiological factors, behaviour, habits that promote sound sleep | Avoid long naps in daytime — short naps (less than half an hour) are acceptable. Exercise regularly. Maintain regular sleep–wake schedule 7 days per week (particularly wake times). Avoid stimulants (caffeine and nicotine). Limit alcohol intake, especially before bed. Avoid visual access to clock when in bed. Keep bedroom dark, quiet, clean and comfortable |

Cognitive therapy involves enabling the patient to recognise how unhelpful and negative thinking about sleep increases physiological and psychological arousal levels. Setting aside 15–20 minutes in the early part of the evening to write down any worries, make plans for the following day and address any concerns that might arise during the night allows the day to be put to rest. It is helpful to challenge thoughts that arise at night with "I have already addressed this and now I can let go of it!". "Time out" — some form of soothing activity before bed — can be useful in reducing arousal levels. Thought-stopping attempts or blocking techniques, such as repeating the word "the" every 3 seconds, occupy the short-term memory store (used in processing information), potentially allowing sleep to happen. Cognitive restructuring challenges unhelpful beliefs, such as "if I don't get enough sleep tonight, tomorrow is going to be a disaster", which maintain both wakefulness and helplessness. Another cognitive and behavioural technique is paradoxical intention. Clients are encouraged to put the effort into remaining wakeful rather than trying to fall asleep (decatastrophising), thereby strengthening the sleep drive and reducing performance effort.[14]

There is limited evidence to suggest that, on its own, sleep hygiene is efficacious.[14] However, it is an essential component of CBT-i and involves "cleaning up" or improving an individual's sleep environment and behaviour to promote better sleep quality and duration.[23]

### Mindfulness and insomnia

In recent years, the technique of mindfulness has become increasingly popular and is likely to be efficacious in helping to promote sleep by reducing cognitive and physiological arousal. Mindfulness treatment interventions have demonstrated statistically and clinically significant improvements in several night-time symptoms of insomnia, as well as reductions in presleep arousal, sleep effort and dysfunctional sleep-related cognitions.[24] In many cases, mindfulness is combined with CBT-i.[24,25] As an adjunct to CBT-i, it can be used for psychoeducation to help the client develop a more functional schematic model of sleep and for dealing with sleeplessness, including the detrimental role of hyperarousal. Typically, the chattering mind is focused on past or future events, whereas mindfulness emphasises being non-judgemental in the present, which potentially can reduce mind activation.

### Bright light exposure (natural or artificial)

Educating the patient about sleep and the importance of bright light is an important aspect of treating insomnia. Good objective information about sleep, sleep loss and the body clock are helpful starting points for self-management. Bright light is a potent synchroniser for human circadian rhythm. In particular, morning light, which can be combined with exercise such as walking, can be helpful in consolidating night-time sleep and reducing morning sleep inertia.[26]

## Pharmacological treatment of insomnia

Although psychological and behavioural interventions are indispensable and effective for most insomnia sufferers, some will still need the extra help from pharmacological agents. Current medications and natural products used for insomnia include benzodiazepine-receptor agonists, melatonin and variants, antidepressants, antipsychotics and antihistamines.

Hypnotic drugs that act on the γ-aminobutyric acid receptor include benzodiazepines, such as temazepam, as well as the benzodiazepine-receptor agonists, such as zopiclone and zolpidem. Medications of this group have been studied in randomised controlled trials, with efficacy over 6 months[27] and longer in open-label exten-

sions.[28] Many doctors avoid prescribing medications from this family, mainly because of concern regarding dependence and tolerance. However, long-term trials of eszopiclone (not available in Australia) and extended-release zolpidem have shown sustained response with no tolerance and dependence after 6 months of daily use.[27-29] Despite these findings, the concern remains that there are vulnerable patients who may become dependent on hypnotic drugs. To limit the risk of tolerance and dependence, the prescriber can instruct the patient to use the medication on a scheduled basis; for example, only on alternating nights, or three times a week and at the lowest effective dose possible for a limited time (ie, a month).[27] Zolpidem has been associated with parasomnias, so clinicians need to warn patients about unusual sleep behaviours as a side effect. Sudden discontinuation of this class of medications can result in a rebound insomnia that can be mitigated by a gradual taper.

Despite the similarity in the mode of action and pharmacokinetics of these agents, patients react differently to each product. Lack of response to one agent does not mean that others of the same group will not work. Similarly, an adverse effect of one does not mean that others will cause the same reaction. The decision whether or not to prescribe hypnotics should rely on a careful risk–benefit analysis by both the doctor and the patient. In addition to the perceived risk of dependence and tolerance, clinicians should consider the risks of untreated insomnia.

Melatonin has been shown to be effective in treating insomnia, particularly among people aged over 55 years.[30] However, melatonin is more effective as a chronobiotic for treating body clock conditions like jetlag and delayed sleep phase disorder than as a treatment for chronic insomnia.[31]

Sedating antidepressants (eg, doxepin, amitriptyline, mirtazapine, trimipramine), sedating antipsychotics (eg, quetiapine, olanzapine) and antihistamines are used off-label as sleep medications, despite insufficient evidence.[13,32,33] Many clinicians prefer prescribing these medications over hypnotics, because of perceived concerns regarding the risks of dependence and tolerance associated with hypnotics, and despite antidepressants, antipsychotics and antihistamines also having serious side effects including weight gain, anticholinergic side effects and diabetes. The decision to prescribe this group of medications for insomnia should be based on a careful risk–benefit analysis, not solely on concerns regarding the risks associated with hypnotics.

Among herbal and alternative medication choices for treating insomnia, valerian has the most evidence showing possible mild improvements in sleep latency, with inconsistent effects on the rest of the objective sleep parameters.[13] Although valerian shows some promise in improving sleep latency without side effects, the clinical trials are poorly designed and generally of short duration.[34]

## Conclusion

Insomnia is complex and usually chronic by the time the individual consults a health practitioner, with cognitive, behavioural and social factors involved in its maintenance. Simple instructions, such as avoiding stress, or short-term use of hypnotics are usually not effective. CBT-i is an effective intervention with long-term efficacy that enables patients to better manage and live with their insomnia symptoms. The development of online delivery of CBT-i markedly improves access to treatment and can be readily used in primary care as first-line treatment for most patients, with specialised sleep services managing more complex cases, those with ongoing symptoms and those who require person-to-person care.

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