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Introduction

INSOMNIA is a distressing difficulty with sleep onset, sleep maintenance and/or early morning wakening, where the individual's sleep is insufficient for their needs.

These symptoms arise despite adequate time in bed to achieve sleep. Chronic insomnia is defined as sleep difficulties being present for at least one month and occurring three or more times a week.

Insomnia was previously defined as either primary (no other conditions deemed to be responsible for the poor sleep) or secondary (another disorder causally responsible for the poor sleep). In practice, determining cause and effect is very difficult. Bidirectional or interactive effects between insomnia and certain coexisting conditions, such as depression, are now widely accepted. The DSM-5 has now removed the primary and secondary causal attribution labels. 'Insomnia disorder' is now recognised as a condition requiring independent clinical attention, regardless of other medical problems that may be present.

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INSIDE

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A useful developmental model

THE 'three Ps' model is useful to help understand the development and persistence of insomnia. The three Ps stand for predisposing, precipitating and perpetuating factors.

Predisposing factors

A predisposing factor does not cause a problem, but may increase the likelihood of it occurring. Such factors could include a family history of poor sleep, being a 'worrier' or never being a 'good sleeper'.

Precipitating factors

These are triggers and may include acute stress/grief, lifestyle changes, the development of an illness or the birth of a baby. Many patients with insomnia can identify a trigger for their sleep disturbance. When insomnia becomes chronic, the insomnia persists despite the trigger resolving (see perpetuating factors).

Perpetuating factors

These are factors that maintain or even exacerbate the problem, for example, heightened anxiety/arousal levels or the development of depression. Other perpetuating factors include behaviours or coping strategies, such as napping during the day or spending excessive amounts of time in bed. With ongoing perpetuating factors, insomnia becomes learned over months and years, even though the initial stressor that may have been involved in its development has disappeared.

Prevalence

INSOMNIA is the most commonly reported sleep disorder. Prevalence rates range from 4-48%, depending on the criteria used.

In a review paper examining the epidemiology of insomnia, about 33% of the population reported experiencing at least one insomnia symptom, such as sleep-onset difficulties. Similar rates (32%) were found in a 2004 NSW survey.

The prevalence is reduced when reporting daytime dysfunction is included, dropping to between 9% and 15%, while the range broadens from 8% to 18% with the addition of sleep dissatisfaction.

Age and sex influence prevalence rates. Women are more likely to report all criteria — insomnia symptoms, frequency, daytime dysfunction and sleep dissatisfaction — compared with men. Insomnia increases in the peri- and postmenopausal phases, and prevalence rates are higher in older adults compared with younger adults.

Insomnia and psychiatric disorders

There is a strong comorbidity between chronic insomnia and both major depressive disorder and generalised anxiety disorder.[2,5] The highest attributable risk factor for first-episode depressive disorder is pre-existing insomnia.[6]

In one study, those with insomnia had 40% psychiatric comorbidity compared with those without, and were almost 40 times more likely to develop new major depression compared with non-insomniac subjects.[4]

The SA DRIVE study of young adult drivers found that short sleep duration had a linear relationship with level of psychological distress.[7] Those with less than five hours' sleep duration who were non-distressed at baseline were more likely to report experiencing psychological distress at follow-up.

History-taking

UNDERSTANDING the cycle of the patient's current sleep patterns, family history and factors associated with the onset and maintenance of insomnia gives the clinician a better idea of the problem and enhances rapport.

The following points may guide history-taking:

- The predominant problem for the patient and how they feel their lifestyle may have been compromised by poor sleep.
- The patient's normal bed routine, which might identify unhelpful behaviours or concerns, for example, lying in bed awake for long periods, watching television in bed or anxiety about sleeping.
- The patient's normal sleep routine, which will help to determine whether the patient suffers from sleep-onset or sleep-maintenance problems or both. Very variable sleep routines may be identified. A sleep diary over a two-week period is often useful to more objectively characterise the patient's bed and sleep routine.
- The impact of the sleeping problem on daytime function — fatigue, sleepiness, quality of life, for example. Typically, patients with primary insomnia experience more fatigue than sleepiness per se. If the patient is falling asleep frequently during the day, rather than just being tired of fatigued, look for sleep-breathing disorders, especially obstructive sleep apnoea.
- Whether the patient is undertaking behaviours known to interfere with sleep, such as using caffeine, alcohol, nicotine or recreational drugs; daytime napping; late-evening exercise; working late on the computer; and being available for work 24 hours a day.
- An evaluation for comorbid conditions, especially other sleep disorders, such as obstructive sleep apnoea, restless legs syndrome, shift work sleep disorder and sleep phase syndromes.
- An evaluation for other comorbid conditions, such as medical and psychiatric conditions and substance abuse. These conditions need to be optimally treated.
- An evaluation for medications that may cause insomnia.

Note: GPs are generally familiar with the clinical features of obstructive sleep apnoea. Patients with restless legs syndrome frequently experience at least one sleep-related symptom (one or more of an inability to fall asleep, inability to stay asleep, and disturbed sleep). Shift-work sleep disorder and advanced or delayed sleep-phase syndromes represent disorders of circadian rhythm, whereby the patient's physiological sleep time, as set by their circadian body clock, is at odds with their desired/required sleep time. If these sleep disorders are present, they may require treatment first or in parallel.

Comorbid conditions and medications

Identify and treat other conditions that cause insomnia:

- Active psychosocial stressors
- Inadequate sleep hygiene due to lifestyle factors that impair sleep
- Active psychiatric disorder, such as anxiety or depression
- Medical conditions: breathing-related sleep disorder, restless legs syndrome, chronic pain, nocturnal cough, hot flushes
- Drug or substance use or abuse: consumption or discontinuation of medications, drugs of abuse, alcohol or caffeine (International Classification of Sleep Disorders, 2005)

Medications that can cause insomnia

- CNS stimulants: sympathomimetics, ephedrine, phenytoin
- Antidepressants: bupropion, SSRIs, venlafaxine
- Decongestants: pseudoephedrine
- Bronchodilators: theophylline
- Antihypertensives: beta-blockers, diuretics, clonidine, methyldopa
- Corticosteroids

Non-pharmacological treatments

CBT

CURRENTLY, the major non-pharmacological treatment for insomnia is CBT, which has the most broad, long-term and compelling evidence base. Mindfulness-based therapies and acceptance and commitment therapy are accumulating evidence for efficacy in insomnia treatment.[8]

CBT targets maladaptive behaviours and cognitions that maintain insomnia, and introduces healthy sleep behaviours in conjunction with raising the individual's awareness of unhelpful and unrealistic sleep thoughts.

Insomnia behavioural treatments

Two of the most effective behavioural methods of treating insomnia are stimulus control therapy and sleep or bed restriction (see box, 'Insomnia behavioural treatments'). These treatments can be instigated from the GP's surgery, along with a rationale of the benefits of changing present habits to improve sleep.

It is worth noting that some individuals may have defined themselves by their insomnia and may believe that change is not possible or wanted.

Stimulus control therapy

The rationale is to reassociate the bed and the bed environment with successful sleep. Broomfield and colleagues have called this the quarter-hour rule.

Sleep restriction

Most individuals try to make up for poor sleep by spending more time in bed, supposedly to increase

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sleep opportunity. The result is less consolidated sleep, more time in bed awake and more time spent worrying about not sleeping. Under these circumstances, individuals spend more time awake than asleep in bed. Restricting time in bed to the reported sleep time increases the homeostatic drive for sleep. Good sleepers will have a sleep efficiency of more than 85%, which means that sleep time and time in bed are closely matched.

Beyond CBT to metacognitive therapies

Mindfulness-based therapies and acceptance approaches — which are known as metacognitive frameworks for insomnia intervention — focus on building an awareness of mental and physical states, observing the shifting nature of mental processes, and defocusing from insomnia symptoms with an adaptive, values-based perspective that looks at building greater life quality, notwithstanding perceived insomnia symptoms.

Metacognitive (awareness of one's cognitive process) techniques differentiate insomnia-specific thought content and activity — for example, expectations about sleep, increase in mental activity in bed environment, fears regarding daytime consequences of sleep loss — from one's relationship to sleep beliefs, such as emotional salience of thought content, and attachment to, and meaning of, thoughts in relation to one's values.

For example, inflexible attachment to the thought, "Medications are the only way I can get sleep," disrupts genuine consideration of alternative ideas, and amplifies the emotional salience of the thought and associated negative effects. Unless there is cognitive flexibility allowing consideration of alternative thoughts ("Maybe I can use other alternatives to medication"), secondary arousal can become a mechanism for insomnia maintenance.

Mindfulness- and acceptance-based therapy models promote indirect, experiential change strategies (observing and describing thoughts and thinking shifts), and widen the focus of change to incorporate one's broader values.

The Buddhist tradition of accepting impermanence is key in recognising that attachment to desired outcomes causes suffering and distress, and promotes reactivity, rigidity and mood/emotional/physiological dysregulation. Instead of changing the triggering stressor, mindfulness works to change the relationship with stress, building non-judgemental awareness of the present moment, self-compassion and non-attachment to particular outcomes.

This promotes adaptivity, flexibility and pragmatism. The mindful reappraisal encourages a process-focus, from actions to reduce stress to simply observing the features of being stressed. With no further struggle to be rid of the stress, the attention is no longer selectively focused on a perceived threat, promoting an attenuated stress reaction.

Insomnia behavioural treatments

Stimulus control therapy

- Go to bed only when you are drowsy.
- Limit activities in bed to sleep and sex.
- Get up at the same time every morning.
- If unable to sleep within around 15 minutes, get up.
- Go to another room and do something non-stimulating — no surfing the net, watching television, catching up with work or household tasks. You need to feel less tense and more ready for sleep before going back to bed. Keep light levels low.
- Repeat the process as many times as necessary to facilitate faster sleep initiation.

Sleep restriction or bed restriction

- Slowly decrease time in bed by 30 minutes every 3-4 days, from either bedtime or getting-up time, until the time in bed matches the sleep time. Less than 5.5 hours in bed is usually not recommended. Then gradually increase time as sleep improves.

Involve your patient in the process

- Help your patient to estimate their sleep efficiency by using the following formula. Work out usual sleep time divided by time in bed: (Total sleep time/ total time in bed) x 100 = sleep efficiency; For example, (6/8) x 100 = 75%

Education about good sleep habits or sleep hygiene

Education about sleep is a very important component of understanding how present behaviours can be changed to improve sleep. There are many myths about sleep and challenging these beliefs allows individuals to be more aware of their current responses. Learning about behaviours known to interfere with sleep — such as caffeine, alcohol, nicotine, recreational drug use, daytime napping, timing of exercise and what not to do in bed — helps to maintain good sleep behaviours.

The bed and bedroom needs to be somewhere that is comfortable, quiet, dark and allows the individual to look forward to sleep time. Setting aside some wind-down time prior to sleep is an important component of relearning sleep. Not being available for work 24 hours a day is another important issue to address.

Exercise, light and relaxation therapy: A good combination

Anxiety is very common in individuals with insomnia, with 50% reporting they are kept awake at night by mental overactivity. Anxiety, worry and the ensuing heightened arousal response are detrimental to sleep.

Exercise reduces muscle tension and physiological arousal, promoting better sleep. It also improves mood, and allows the individual to get out and do something. It is a positive active behaviour compared with lying awake waiting for more sleep. However, exercising in the evening artificially raises core body temperature and must be completed at least 3-4 hours prior to expected bedtime to allow the body to cool down, which is necessary for sleep onset.

A constant waking time is a crucial component of setting sleep boundaries. Getting up at the same time means there is a definite end to the sleep time, regardless of the quality of the night-time sleep. Getting-up time is more important than a regular bedtime, which does not necessarily guarantee sleep onset. Early-morning light also resets the brain's sleep clock.

Relaxation reduces high levels of both physical and mental arousal. However, relaxation alone is not as effective as a standalone treatment compared with a combination of the other treatments. Relaxation techniques need to be seen in the context of reducing tension and the arousal response as opposed to being a means of getting to sleep, which puts pressure and effort onto sleep.

Relaxation techniques include progressive muscle relaxation, focused breathing strategies, imagery training, meditation and hypnosis. Relaxation needs to become part of the individual's usual lifestyle — a means of having time out, where the patient first learns to recognise increased stress responses and, second, becomes more confident in reducing those stress responses that result from day-to-day living.

Pharmacotherapy

PHARMACOTHERAPY is currently indicated in Australia for the short-term (2-4 weeks) management of insomnia in adults. There are many hypnotic agents available in Australia, each with different pharmacokinetic profiles and differing adverse effects. There is greater evidence for the efficacy of prescription agents rather than over-the-counter or natural products that are promoted to improve sleep.

Research into sleep mechanisms has identified multiple target areas for hypnotic agents. As a result, several new drugs have been developed to treat insomnia — some of which are only available overseas at present, while others are being tested in late-phase clinical drug trials around the world. Recent research has also examined the real-world issue of long-term hypnotic use in studies of 6-12 months' duration. As a result of this, some drugs currently have US Food and Drug Administration approval for the long-term management of insomnia in adults in North America.

Benzodiazepines

Benzodiazepines target the GABA type A receptor and non-selectively stimulate $GABA_A$ subunits, leading to a hypnotic effect, as well as anxiolytic, myorelaxant and anticonvulsant effects. In short-term, randomised, double-blind, placebo-controlled trials, they have been shown to reduce sleep latency, increase total sleep duration and improve sleep continuity. Different benzodiazepines will affect these sleep parameters to different extents, depending on their individual pharmacokinetics. Studies also show that benzodiazepines decrease

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slow-wave sleep and REM sleep, with an increase in stage 2 sleep — a light stage of sleep.

Some of the commonly used benzodiazepines and their half-lives are shown in table 1. Temazepam and oxazepam are commonly used in Australia for insomnia because of their relatively short half-lives. This minimises residual daytime drowsiness and psychomotor impairment, which can be a problem with the longer-acting agents and in the elderly. Common adverse effects of benzodiazepines include over-sedation, light-headedness, memory loss and slurred speech. Over-sedation and respiratory depression are possible with concurrent use of other CNS depressants, such as alcohol and antidepressants.

Tolerance, dependence and rebound insomnia may occur in patients taking benzodiazepines. No tolerance has been demonstrated with temazepam in studies of 4-8 weeks' duration. However, tolerance is a potential problem with longer-term administration of this class of drugs, reinforcing the recommendation for short-term use only.

Dependence is rare in patients taking normal therapeutic doses of benzodiazepine for short periods. However, it is thought about one-third of patients on long-term treatment have difficulty reducing or stopping their medication because of this adverse effect.

Rebound insomnia is characterised by a worsening of sleep relative to baseline after stopping a hypnotic. It has mainly been demonstrated with the shorter-acting benzodiazepines, such as triazolam, and may be more marked when the drug has been taken regularly for long periods. When discontinuing a long-term benzodiazepine, therapy should be withdrawn slowly over several weeks or months, with small dose reductions each week.

There is a lack of long-term studies evaluating benzodiazepine safety and efficacy. For this reason, and given the adverse events detailed above, benzodiazepines should be used for the shortest time possible, with a definite duration of use agreed with the patient at the outset.

Non-benzodiazepine benzodiazepine receptor agonists

There are three marketed drugs in this class: zolpidem, zopiclone and zaleplon. In North America, zopiclone is sold as eszopiclone (the active (s)-isomer). A long-acting form of zolpidem has also been introduced in Australia (Stilnox CR). Zaleplon is not currently available in Australia.

Non-benzodiazepine benzodiazepine receptor agonists more selectively stimulate the $GABA_A$ receptor compared with benzodiazepines, which non-selectively stimulate this receptor. As a result, these drugs have a marked hypnotic effect but fewer anxiolytic, myorelaxant and anticonvulsant effects, contributing to a more favourable side-effect profile.

Table 1. Benzodiazepines and their half-lives

Benzodiazepine	Half-life in hours (active metabolite)
Diazepam	20-100 (36-200)
Clonazepam	18-50
Nitrazepam	15-38
Flunitrazepam	18-26 (36-200)
Clobazam	12-60
Lorazepam	10-20
Temazepam	8-22
Alprazolam	6-12
Oxazepam	4-15
Triazolam	2

Zopiclone and zolpidem have comparable efficacy to benzodiazepines in reducing sleep latency, decreasing nocturnal awakenings and increasing total sleep time. Oral zopiclone has a rapid onset (15-30 minutes), and its elimination half-life is around five hours, increasing with age. Zolpidem has a similar onset of action (30 minutes), although its elimination half-life is shorter (2.4 hours). For patients who wake up in the middle of the night and cannot go back to sleep after taking zolpidem, Stilnox CR may be more suitable because of its longer duration of action. Common adverse effects of non-benzodiazepine receptor agonists include bitter taste, dry mouth, nausea and sleepiness (zopiclone); nausea, dizziness, headache and drowsiness (zolpidem CR); and headache (zaleplon).

Compared with benzodiazepines, non-benzodiazepine receptor agonists cause less residual morning sedation and psychomotor impairment, and do not affect normal sleep patterns. There are also fewer reports of dependency and misuse. Rebound is less frequent and milder than that seen after the discontinuation of benzodiazepines. No tolerance to non-benzodiazepine receptor agonists has been demonstrated in double-blind trials of up to five weeks' duration.

Eszopiclone was shown to maintain effectiveness in a six-month, double-blind, placebo-controlled study of 788 subjects. Improvements in sleep and daytime function were also maintained during a six-month open-label extension. During the 12 months of the study, few adverse effects and no tolerance was reported. After this trial, eszopiclone was approved by the US FDA for the long-term treatment of sleep-onset and sleep-maintenance insomnia.

Zolpidem has also been shown to maintain effectiveness for 6-12 months, although these studies were not double-blinded.

In past years, there has been much media interest and some concern regarding possible neuropsychiatric adverse reactions with zolpidem. Australian Adverse Drug Reactions Advisory Committee bulletins, released in 2002 and February 2007 (Zolpidem and bizarre sleep-related effects), detail several possible adverse effects that have been reported with zolpidem since it has been marketed in Australia. These include hallucinations, confusion, amnesia and episodes of sleepwalking, sleep eating and other parasomnia behaviour.

After the February 2007 bulletin, the Australian product information was revised for Stilnox and Stilnox CR. In particular, warnings were added regarding the possibility of sleep-related side effects with zolpidem (sleepwalking, 'sleep driving', preparing and eating food). It has been emphasised that the use of alcohol and other CNS depressants with zolpidem appears to increase the risk of such behaviours, as does the use of zolpidem at doses exceeding the maximum recommended dose.

Taking zolpidem too early before sleep time appears to be a further risk factor for hallucinations and confusion. Despite the recent warnings, it is important to note that a causal relationship between zolpidem and parasomnia behaviour has not been definitively established in the literature. The associations to date are through case reports and small case series.

Melatonin receptor agonists

The suprachiasmatic nucleus in the hypothalamus of the brain is responsible for the regulation of our circadian or diurnal rhythms. The sleep–wake cycle in humans, one such circadian rhythm, causes increased sleepiness overnight (from around 2-6am) and in the mid-afternoon hours. Melatonin helps to regulate this circadian rhythm through its action on melatonin receptors (MT1 and MT2 receptors) in the suprachiasmatic nucleus.

Agonism or stimulation of the MT1 receptor has a sleep-promoting effect, and stimulation of the MT2 receptor helps to synchronise the circadian clock and adjust the timing of sleep. This pathway of sleep regulation has been explored for therapeutic potential in insomnia using drugs that stimulate the MT1 and MT2 receptors.

Circadin is a prolonged-release formulation of melatonin available in Australia. It attempts to mimic the physiological release of melatonin, with peak concentrations occurring 1.6-2.6 hours after a dose. It is indicated in Australia for the short-term treatment of primary insomnia in patients who are 55 or over.

Circadin should be taken 1-2 hours before bed because it has a gradual onset of action. Side effects include headache, nasopharyngitis, back pain and arthralgia. Circadin does not appear to cause impaired daytime alertness, dependence, withdrawal effects or rebound insomnia.

Ramelteon is a highly selective and potent MT1 and MT2 agonist. It is available in North America and has been tested in clinical trials in Australia. In North America, it has been approved for the long-term treatment of sleep-onset insomnia. Unlike benzodiazepines and non-benzodiazepine receptor agonists, this drug is not classified as a scheduled or controlled drug by the US Drug Enforcement Administration, as trial data so far have not demonstrated dependence or abuse potential.

The melatonergic antidepressant agomelatine, a potent MT1/MT2 agonist, has also been shown to be effective in the treatment of depression-associated insomnia.

Sedating antidepressants and atypical antipsychotics

Antidepressants with sedative effects are occasionally prescribed for insomnia. The doses used tend to be lower than those used for depression. Caution should be used when prescribing these drugs to treat primary insomnia because there are few studies that examine their efficacy and safety in non-depressed patients with insomnia, and they can cause significant side effects, particularly in the elderly.

Amitriptyline and doxepin are most commonly used in Australia, causing sedative effects primarily via their anticholinergic properties. Side effects of these tricyclic antidepressants include anticholinergic effects — such as dry mouth, blurred vision, constipation, urinary retention and delirium — and alpha-adrenergic effects, including orthostatic hypotension and dizziness. In addition, many antidepressants can exacerbate periodic limb movements during sleep.

Mirtazapine — a selective alpha-2, serotonin and histamine receptor blocker — is another antidepressant associated with sedation and increased total sleep time. Weight gain, restless legs symptoms and residual morning sleepiness (due to its long half-life) are potential limiting side effects.

Most SSRIs will also exacerbate insomnia in the first few weeks of use through increased sleep fragmentation. This side effect tends to diminish with continued use.

Newer sedating antipsychotics, such as quetiapine and olanzapine, are increasingly used in the treatment of insomnia, especially comorbid insomnia, but have not been studied extensively for this purpose.

Antihistamines

There is little published data on the efficacy of first-generation histamine antagonists in insomnia, and adverse effects can be high. Promethazine, diphenhydramine and other H1 antagonists are the usual sleep-promoting agents in over-the-counter preparations. These agents extend sleep duration, but are associated with rapid tolerance to the hypnotic effect, residual daytime sedation due to long half-lives and anticholinergic side effects.

Over-the-counter therapies

Valerian is commonly used as a sleep aid and is available over the counter. However, evidence for its efficacy in insomnia is inconclusive. Melatonin can be obtained over the counter as part of health supplements or as a compounded product by some pharmacists. The dose of melatonin can vary among these products, and there is no TGA regulation of the compounding process.

In contrast to Circadin, it is not feasible to produce a compounded prolonged-release melatonin product. Good-quality efficacy

studies are not available for over-the-counter melatonin, although available evidence would suggest a mild hypnotic effect.

Which hypnotic to use?

There are many factors that need to be taken into account when prescribing a particular hypnotic for a patient. Consider the following:

- The drug's side effects
- The potential for the drug or its adverse effects to interact with other medications, including CNS active agents
- Concurrent alcohol use
- The patient's comorbid conditions, for example, benzodiazepines should be avoided in patients with significant respiratory disease
- The patient's prior experience with hypnotics
- The patient's own preferences and expectations
- The cost of the drug
- The intended duration of use

In addition, hypnotics should be appropriate for the type of insomnia symptoms the patient is experiencing.

For sleep onset or initiation problems only, drugs with rapid onset and short or ultra-short half-lives should be considered, for example, triazolam, zaleplon, ramelteon and zolpidem.

For sleep onset and maintenance problems, drugs with rapid onset and longer half-lives should be considered, for example, zolpidem CR and zopiclone.

For sleep maintenance problems only, a delayed onset and long half-life are preferable, for example, temazepam, estazolam and Circadin.

Hypnotics: duration of use

All prescribed hypnotics in Australia are currently indicated for short-term use (less than a month). Therefore, these drugs should be prescribed for the shortest time possible, with a definite duration of use agreed at the outset. However, as noted previously, eszopiclone is now indicated for long-term use in North America for sleep-onset and sleep-maintenance insomnia. In addition, the FDA has approved ramelteon for the long-term treatment of sleep-onset insomnia and zolpidem extended-release for the treatment of insomnia without limitation in length of use.

Despite this, the author feels that more long-term efficacy and safety data are required before these medications are routinely prescribed for long-term use. In addition, it is important to remember that CBT has been shown to be superior in the long term for the management of insomnia in research studies to date.

Intermittent use of hypnotic therapy: Does it work or cause harm?

A double-blind, placebo-controlled trial has investigated the intermittent use of zolpidem over eight weeks. Subjects were instructed to, "Take the medication when you think you need it, at bedtime, between three and five nights a week," simulating usual use for many patients.

The study showed that patient and investigator rating of sleep was better in the zolpidem arm, but not all sleep parameters were consistently improved with zolpidem when the two arms were compared. For example, overall patient-reported sleep latency and total sleep time, after five weeks, were not different between the groups. However, importantly, there were no rebound effects from the drug on the nights the active drug was not taken, and no tolerance to zolpidem was demonstrated over the eight weeks.

This study suggests some efficacy and safety with this approach over an eight-week period. More research is needed to determine whether the approach is useful and safe for a longer term.

Investigational drugs

Research into sleep mechanisms has identified multiple target areas for hypnotic agents. As a result, several drugs are being investigated as treatments for primary insomnia. These include drugs that act on the serotonergic system, others that act on the orexin neurotransmitter pathway (important in the pathogenesis of narcolepsy), and those that selectively work on the GABA and histaminergic pathways.

With intense research and interest in this area of sleep medicine, many new drugs are likely to be available on the market in future years, with the hope that some of these drugs will prove safer and superior to existing agents.

References

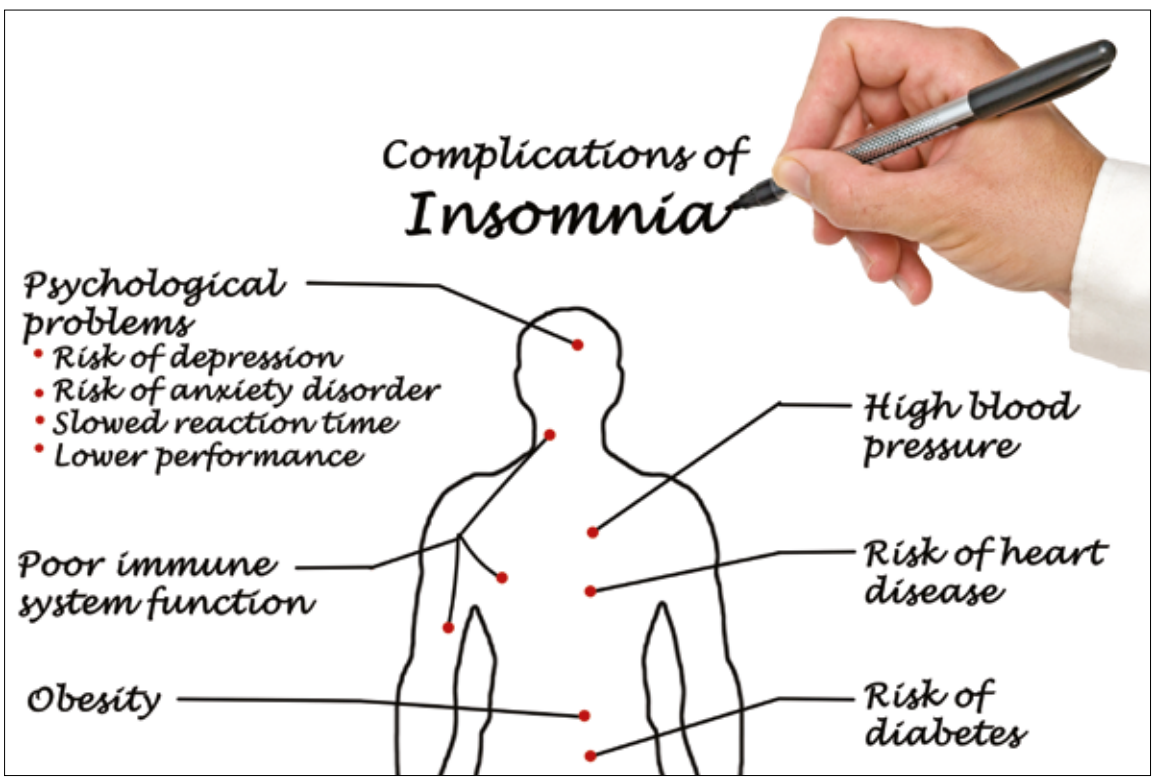
1. Frances A, (editor). *Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR). 4th edn.* American Psychiatric Association, Washington DC, 2000.
2. Breslau N, et al. Sleep disturbance and psychiatric disorders: A longitudinal epidemiological study of young adults. *Biological Psychiatry* 1996; 39:411-18.
3. Chorney et al. The interplay of sleep disturbance, anxiety and depression in children. *Journal of Pediatric Psychology* 2008; 33:339-48.
4. Ford DE, Kamerow DB. Epidemiological study of sleep disturbance and psychiatric disorders. An opportunity for prevention? *Journal of the American Medical Association* 1989; 262:1479-84.
5. Buysse DJ, et al. Diagnostic concordance for DSM-IV sleep disorders: A report from the APA/NIMH DSM-IV. *American Journal of Psychiatry* 1994; 151:1351-60.
6. Cole M and Dendukuri N. Risk factors for depression among elderly community subjects: A systematic review and meta-analysis. *American Journal of Psychiatry* 2003; 160:1147-56.
7. Glozier N, et al. Short sleep duration in prevalent and persistent psychological distress in young adults: The DRIVE study. *Sleep* 2010; 33:09.
8. Ong J, et al. Improving sleep with mindfulness and acceptance: A metacognitive model of insomnia. *Behaviour Research and Therapy* 2012; 50:651-60.
9. Ansfield M, et al. Ironic effects of sleep urgency. *Behaviour Research and Therapy* 1996; 34:523-31.
10. Espie C. Insomnia: Conceptual issues in the development, persistence and treatment of sleep disorder in adults. *Annual Review of Psychology* 2002; 53:215-43.
11. Harvey AG. A cognitive model of insomnia. *Behaviour Research Therapy* 2002; 40:869-93.

When to refer

GPs are well placed to identify insomnia, characterise it and start treatment. Non-pharmacological treatment for insomnia should be initiated by GPs, depending on interest and expertise.

This therapy might include education regarding good sleep habits, addressing active psychosocial stressors and the initiation of cognitive behavioural approaches.

Patients with suspected obstructive sleep apnoea, restless legs syndrome or difficult-to-control psychiatric problems should be referred to specialists for further investigation and management of their comorbid conditions. Pharmacotherapy, if required, should only be used in the short term, in conjunction with the initiation of non-pharmacological strategies to treat insomnia. Referral to experienced sleep psychologists or sleep physicians is important if the insomnia does not improve.



Case study: Non-drug management of insomnia

GINA, aged 42, has a generalised anxiety disorder. Her 20-year history of intermittent insomnia episodes has worsened into a near-constant difficulty maintaining sleep for the past two years. She generally experiences sleep maintenance difficulties, with waking periods from 2am to 4am after about four hours of sleep for 11-12 days out of 14.

She reports that her insufficient sleep worsens her worrying, leading to behaviours specifically employed to bring about sleep, which then lessens her sleep likelihood. She strongly believes eight hours of sleep nightly is crucial to preventing physiological and psychological damage.

Gina believes this sleep must be made to happen using a range of over-the-counter aids and prescription medications if sleep hygiene measures do not work. She constantly monitors her fatigue levels during the day and believes she has only a finite amount of energy daily, which must be conserved, leading her to frequently curtail or cancel her social and work activities during the day.

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CBT treatment choices for Gina include education about good sleep habits, sleep hygiene and stimulus control measures, specifically focusing on behaviour change around standard rising time, getting early-morning sunlight, eschewing naps during the day and restricting time in bed if unable to sleep. These behaviours will ensure greater sleep efficiency, greater build-up in homeostatic drive to sleep and a strengthened association with bed as a conditioned signal for sleep rather than waking.

There will also be a focus on reducing her CNS reactivity with daily practice of progressive muscle relaxation and controlled breathing strategies. To reduce her worry about sleeplessness, a daily 'worry session' could be introduced, conditioning her to attend to her worries to a specific time and place daily to reduce vulnerability to worry-driven sleep disruption at night.

Then behavioural experiments could be used to gather evidence to challenge her fears. For example, a trial set over several days that contrasts a half-day conserving energy with only mundane tasks done at a slow pace with a half-day generating energy with more activity — then rating her fatigue, mood and coping after each experimental session.

Evidence for catastrophic thoughts — such as "I won't function at all tomorrow; I will get fired" — and probability overestimations — "It is 95% likely I will get fired if I function badly" — can be addressed, along with a discussion on selective attention to negative sleep-related evidence, and ignoring neutral or positive evidence.

A metacognitive perspective, on the other hand, will promote mindful awareness and indirect, experiential change strategies of observing and describing the experience of insomnia. A primary focus for Gina and the therapist will be her struggle to control sleep and her use of aids (safety-seeking behaviours, medications) to make sleep happen, which ultimately generates more focus on sleeplessness, more intense distress and further ineffectual efforts to control sleep.

This accords with findings of longer sleep-onset latency found in normal sleepers with a high mental load, when attempting to fall asleep quickly.[9]

The metacognitive framework of mindful acceptance can help Gina to broaden her focus from a narrow preoccupation with insomnia and its negative consequences. Such an approach will promote an understanding of shifts in her mental activity, her strong attachment to certain beliefs, insights about selective biases, a broader assessment of her values and building a quality of life around more compelling factors than the vagaries of her sleep.

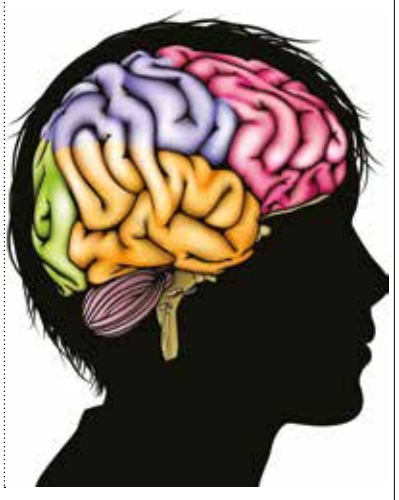
Through this broader focus, the therapist encourages a non-judgemental and present-focused acceptance of her sleep experience, with acceptance of a range of cognitive and emotional phenomena in the moment and non-attachment to sleep outcomes. This promotes balance, flexibility and improved coping when confronting inadequate sleep and fatigue.

The acceptance and commitment therapy component targets identification of Gina's values under various life domains (family, close relationships, friendships, career, etc), which can then help her perceive the cost of an included or omitted behaviour in reference to a relevant value. This includes absenteeism from work due to morning tiredness when a core value is 'investing in career'. In this manner, Gina's behaviour change is more likely to follow from commitment to her personal values, rather than safety-seeking behaviours driven by her hour-by-hour mood, feelings or threat appraisals.

Conclusion

NON-PHARMACOLOGICAL behavioural measures are the most efficacious treatments of insomnia, both in the short and long term. One of the ironies about insomnia management is that most GPs have considerable knowledge of CBT and insomnia strategies, but are not always sure how to instigate these treatments.

GPs also appear hampered by their perceptions that patients expect a script for hypnotics, which is often not the case. Improvement in communication from both sides of the consultation would be beneficial in relation to the management of insomnia.



How to Treat Quiz

Insomnia — 27 May 2016

INSTRUCTIONS

Complete this quiz online and fill in the GP evaluation form to earn 2 CPD or PDP points.
We no longer accept quizzes by post or fax.

The mark required to obtain points is 80%. Please note that some questions have more than one correct answer.

GO ONLINE TO COMPLETE THE QUIZ

www.australiandoctor.com.au/education/how-to-treat

1. Which THREE form part of the three Ps model for insomnia?
a) Predisposing
b) Prolonging
c) Perpetuating
d) Precipitating

2. Which TWO statements regarding the prevalence of insomnia are correct?
a) Insomnia is the most commonly reported sleep disorder.
b) In a review paper, about 55% of the population have reported experiencing at least one insomnia symptom.
c) Age and sex do not influence prevalence rates.
d) There is a strong comorbidity between chronic insomnia and major depressive disorder.

3. Which TWO give the clinician a better understanding of the patient's insomnia?
a) Understanding the cycle of the patient's current sleep patterns
b) How keen the patient is to have their insomnia treated
c) Factors associated with the onset and maintenance of insomnia
d) How the patient's family responds to their complaints of insomnia

4. Which THREE conditions may cause insomnia?
a) Hypertension
b) Restless legs syndrome
c) Anxiety
d) Chronic pain

5. Which TWO medications may cause insomnia?
a) Paracetamol
b) Theophylline
c) ACEIs
d) SSRIs

6. Which THREE statements regarding the non-pharmacological treatment of insomnia are correct?
a) CBT challenges maladaptive behaviours and cognitions that maintain insomnia and raises the individual's awareness of unhelpful and unrealistic sleep thoughts.
b) Mindfulness-based and acceptance approaches focus, among other things, on building an awareness of mental and physical states.
c) There is currently an equivalent evidence base for both CBT and mindfulness-based therapies for treating insomnia.
d) Two of the most effective behavioural methods of treating insomnia are stimulus control therapy and sleep restriction or bed restriction.

7. Which TWO statements regarding the non-pharmacological management of insomnia are correct?
a) Exercising immediately before going to bed is a useful technique because exercise tires one out, thus promoting falling asleep more rapidly.
b) Checking work emails in bed last thing at night will alleviate anxiety and promote sleep.
c) Anxiety is very common in individuals with insomnia, with 50% reporting they are being kept awake at night by mental overactivity.
d) A constant waking time is a crucial component of setting sleep boundaries.

8. Which THREE statements regarding the pharmacotherapy of insomnia are correct?
a) Pharmacotherapy is currently indicated in Australia for the short-term (2-4 weeks) management of insomnia in adults.
b) Benzodiazepines have hypnotic, anxiolytic, myorelaxant and anticonvulsant effects.
c) Over-the-counter and natural products for sleep have been shown to be as effective as prescription agents.
d) Common adverse effects of benzodiazepines include over-sedation, light-headedness, memory loss and slurred speech.

9. Which TWO statements regarding non-benzodiazepine benzodiazepine receptor agonists are correct?
a) There are three marketed drugs in this class, and all three are available in Australia.
b) Compared with benzodiazepines, these drugs have a marked hypnotic effect but fewer anxiolytic, myorelaxant and anticonvulsant effects, contributing to a more favourable side-effect profile.
c) Benzodiazepines and non-benzodiazepine receptor agonists cause the same amount of residual morning sedation and psychomotor impairment.
d) Common adverse effects of non-benzodiazepine receptor agonists include bitter taste, dry mouth, nausea, sleepiness, dizziness and headache.

10. Which THREE statements regarding the choice of hypnotics are correct?
a) For sleep-onset or initiation problems, drugs with rapid onset and longer half-lives should be considered.
b) Consider the drug's side effects.
c) Consider the patient's comorbid conditions.
d) Consider the cost of the drug.

CPD QUIZ UPDATE

The RACGP requires that a brief GP evaluation form be completed with every quiz to obtain category 2 CPD or PDP points for the 2014-16 triennium. You can complete this online along with the quiz at **www.australiandoctor.com.au.** Because this is a requirement, we are no longer able to accept the quiz by post or fax. However, we have included the quiz questions here for those who like to prepare the answers before completing the quiz online.

Australian Doctor Education

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NEXT WEEK

Next week's How to Treat explores the range of preventative health measures which can be employed to halt the transmission of HIV. The author is **Dr Catriona Ooi,** clinical services lead, Western Sydney Sexual Health Centre, Western Sydney Local Health District, Sydney, NSW; and senior lecturer, Sydney Medical School — Westmead, University of Sydney, NSW.