

COMORBID INSOMNIA AND SLEEP APNOEA (COMISA)

CASE SCENARIO

Carmen, 54 years old, presents to the pharmacy reporting sleep difficulties. She reports poor sleep quality and daytime exhaustion that started about 6 months ago. She has no history of medicine use for sleep but would like information on the different medicines that are available. You ask Carmen about the specific sleep symptoms that she is experiencing, including her sleep patterns and symptoms of sleep disorders. She is not on any regular medicines.

Introduction

Insomnia and obstructive sleep apnoea (OSA) are the two most prevalent sleep disorders and frequently co-exist.¹ Comorbid insomnia and sleep apnoea (COMISA) is a prevalent and debilitating condition in Australia.² This article presents information on evidence-based assessment tools, pharmacological and

non-pharmacological management, and referral options for patients with COMISA.

Prevalence

Insomnia is defined as self-reported difficulties falling asleep, maintaining sleep, and/or early morning awakenings from sleep on at least 3 nights per week, with associated daytime impairment.^{1,3}

It is estimated that 10–15% of adults at any given time have chronic insomnia (≥ 3 month duration).^{4,5} Insomnia is associated with reduced quality of life and an increased risk of depression.⁶ When occurring in the presence of other mental and physical health conditions, insomnia should be viewed as a 'comorbid' disorder that requires targeted assessment and management.⁷ »

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SPONSORSHIP INFORMATION



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CONFLICTS OF INTEREST

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LEARNING OBJECTIVES

After reading this article, pharmacists should be able to:

- Describe the prevalence of comorbid insomnia and sleep apnoea
- Discuss management options for comorbid insomnia and sleep apnoea
- Explain how pharmacists can help identify and assist a patient with suspected comorbid insomnia and sleep apnoea.

Competency standards (2016) addressed:
1.1, 1.4, 1.5, 2.2, 3.1, 3.5

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OSA is characterised by frequent narrowing and/or closure of the upper airway during sleep, resulting in hypoxemia, hypercapnia and awakenings from sleep.^{1,3,8} Approximately 10% of the general population experience moderate-to-severe OSA at any given time.⁹ OSA is more prevalent in males than females, however some studies indicate that this equalises around the time of menopause.¹⁰ OSA is also associated with daytime impairments, risk of sleepiness-related accidents, and risk of cardiovascular disease, cognitive impairment and depression.^{8,10,11}

Both these disorders can occur separately, but if they co-occur, this is termed COMISA. Approximately 30–50% of people with OSA have comorbid insomnia, and 30–40% of people with chronic insomnia have comorbid OSA (see Figure 1).^{9,12} A recent population-based study reported that 11% of Australian adults report symptoms of COMISA.¹³



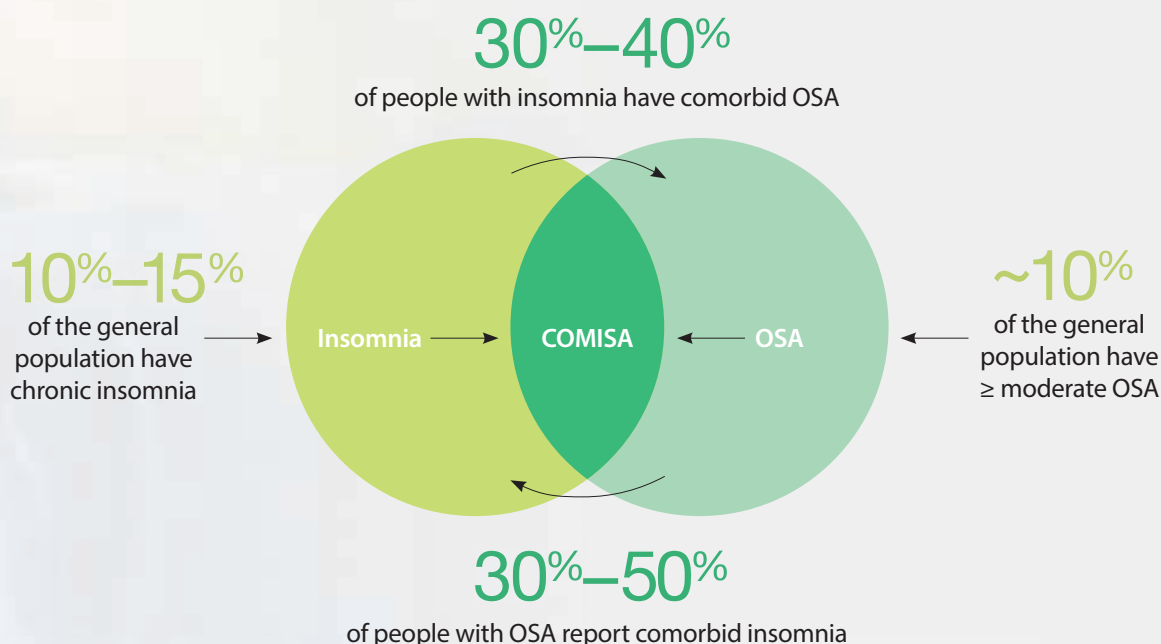
Aetiology and pathophysiology

Some models of insomnia suggest that insomnia results from¹⁴:

- predisposing factors that increase the risk of disturbed sleep
- precipitating factors that trigger the initial sleep disturbance
- perpetuating factors such as psycho-behavioural factors that maintain insomnia over time.

In people with chronic insomnia, a state of 'conditioned insomnia' can develop, whereby the bed or bedroom environment becomes a conditioned stimuli for a state of alertness/worry/wakefulness.¹⁵ Short-term insomnia can initially result from different mental and physical stressors (i.e. the precipitant), however insomnia can rapidly develop functional independence of these precipitating triggers and become maintained by specific psycho-behavioural processes (perpetuating factors and a state

Figure 1 – Venn diagram of insomnia, OSA and COMISA prevalence



Reference: Sweetman et al⁹

of conditioned insomnia).¹⁶ The most consistent risk factors for OSA are increasing age, overweight/obesity, male sex,¹¹ cranio-facial abnormality and adenotonsillar hypertrophy.

Pharmacists should avoid viewing insomnia as a 'secondary symptom' of other mental and physical health conditions.¹ In the context of COMISA, insomnia symptoms may initially result from untreated OSA, however insomnia can quickly develop functional independence of the OSA and become maintained by insomnia-specific perpetuating factors.¹

Clinical features

People with COMISA experience impaired sleep, daytime functioning, mental health, physical health and quality of life, compared to people with neither condition. COMISA is often associated with greater impairment across these domains,

compared to people with either disorder alone.^{1,17,18} COMISA is associated with a 50–70% increased risk of all-cause mortality compared over 10–20 years of follow-up, potentially due to mental and physical health consequences or misdiagnosis and reduced treatment acceptance.^{2,18–21}

People with COMISA may present with a general complaint of sleep dissatisfaction, specific insomnia symptoms, obvious manifestations of OSA (e.g. witnessed breathing pauses, choking awakenings, loud snoring), or daytime impairment (e.g. fatigue, lethargy, irritability).

Many people with insomnia symptoms attempt self-management approaches before presenting to health professionals (e.g. simple 'sleep hygiene' recommendations; complementary/alternative medicines; consuming different foods/beverages promoted on social media to improve sleep; relaxation breathing exercises).^{22,23} A state of learned

helplessness can develop in people that experience persistent insomnia despite using a large range of remedies that are not effective over the long term.

Many people with long-term insomnia may present with a history of sedative-hypnotic medicine use, and many people with OSA and COMISA may present with a history of previous/current use of continuous positive airway pressure (CPAP) therapy.

Assessment and diagnostic measures

It is important for pharmacists to be aware of presenting symptoms of insomnia and OSA, and evidence-based screening, assessment and diagnostic tools for each condition (Table 1). OSA symptoms should be assessed in people with insomnia symptoms, and insomnia symptoms should be assessed in people with suspected or confirmed OSA.²⁴ »

Table 1 – Examples of assessment tools to identify people with insomnia and obstructive sleep apnoea

QUESTIONNAIRE	DESCRIPTION
Insomnia screening questionnaires	
Insomnia Severity Index	7-item self-report measure of global insomnia severity. Scores range from 0–28, with scores ≥ 8 indicating mild insomnia and scores ≥ 15 indicating moderate to severe insomnia.
Sleep Condition Indicator	8-item self-report measure of insomnia presence and severity that maps to formal diagnostic criteria. Scores range from 0–32, with scores of ≤ 16 indicating insomnia is likely.
Sleep studies	
An overnight polysomnography sleep study (laboratory or home-based) interpreted by a sleep and respiratory physician is the gold-standard measure of OSA presence and severity. Information about sleep studies can be found at: www.sleepprimarycareresources.org.au/osa/investigations-and-referral	
Obstructive sleep apnoea screening questionnaires	
OSA50	4-item self-report tool to identify patients with a high risk of OSA who are suitable for overnight sleep study assessment. Scores ≥ 5 indicate a high risk of OSA.
STOP-Bang	8-item self-report tool to identify patients with a high risk of OSA who are suitable for overnight sleep study assessment. Scores ≥ 3 indicate a high risk of OSA.
Daytime impairment	
Epworth Sleepiness Scale	8-item self-report measure of likelihood of falling asleep in different daytime situations. Higher scores represent increased daytime sleepiness. Patients with scores ≥ 16 suggests pathological daytime sleepiness.
Flinders Fatigue Scale	7-item self-report measure of symptoms of daytime fatigue.
Sleep quality questionnaire	
Pittsburgh Sleep Quality Index	May be useful in screening for overall sleep quality and can highlight areas for further clinical investigation to identify potential comorbid sleep disorders.

References: Australasian Sleep Association²⁵, Buysse²⁷

The 'gold standard' measure of OSA presence and severity is an overnight sleep study (Table 1).²⁵ The most common single metric to determine OSA presence and severity is the apnoea-hypopnoea index (AHI), representing the average number of airway narrowing and closure events occurring per hour of sleep.²⁴ Identifying the most appropriate management approaches for OSA also requires consideration of lifestyle factors, symptoms and consequences, occupation, chronic conditions, and other sleep conditions. Self-report questionnaires may be used to screen for a high-risk of OSA and identify patients suitable for referral and consideration of overnight sleep study assessment (Table 1).²⁴

Insomnia, sleep apnoea and COMISA may co-occur with other sleep disorders such as restless legs syndrome and shift work sleep disorder. Circadian misalignment may be a factor in some patients with COMISA.²⁶

Management of COMISA

Successful management of COMISA can be more difficult than management of either disorder alone, and requires a tailored treatment approach.²⁰





Pharmacological management

Sedative and hypnotic medicines (e.g. benzodiazepines, non-benzodiazepine hypnotics, off-label antidepressant medicines) are often used in the management of insomnia.²⁸ Although hypnotics provide rapid therapeutic relief from insomnia via increasing sleep duration, they are not the recommended first-line insomnia treatment, and are not recommended for long-term use.²⁹ This is because hypnotics do not target or treat the underlying psycho-behavioural factors that maintain insomnia. Most medicines used for insomnia are associated with adverse effects and risks of adverse events, including psychomotor impairment, falls/fractures, and next-day sedation.^{29–31} Over time, patterns of short-term therapeutic benefit are often replaced by patterns such as tolerance, long-term dependence and withdrawal symptoms in attempts to reduce use.³² Upon discontinuation of hypnotics, patients may experience insomnia relapse.³² Some sedatives that are used in the management of insomnia may also exacerbate apnoea events in specific patients with OSA.³⁰

Although evidence-based guidelines unanimously recommend avoiding long-term use of hypnotics, they are indicated for a minority of patients that present with severe acute insomnia that is causing significant psychological distress or functional impairment.²⁹ Most people who experience short-term insomnia symptoms (1–2 weeks) can be reassured that sleep will return to 'normal' after the underlying precipitant has subsided, without targeted treatment (i.e. hypnotic medicines).^{29,33} For those who experience persistent insomnia, cognitive behavioural therapy for insomnia (CBTi) is the first-line treatment. Pharmacotherapy may be considered in patients with severe insomnia that is causing significant impairment or distress (e.g. times of acute work/exam stress, bereavement).³⁴

Non-pharmacological management

CBTi is the recommended first-line treatment for insomnia.³⁵ It is effective in people with both acute and chronic insomnia.^{29,36} CBTi is a multi-component treatment that aims to identify and gradually treat the underlying

precipitating triggers and perpetuating factors of long-term insomnia. For this reason, CBTi is often associated with moderate-to-large improvements in insomnia, daytime function and mental health that are sustained long after treatment cessation.³⁷ A recent systematic review and meta-analysis reported that CBTi is an effective treatment for insomnia in the presence of comorbid OSA.³⁸ CBTi is associated with increased daytime sleepiness during the initial stages of bedtime restriction therapy (a core therapeutic component of CBTi), and patients should be warned of feelings of sleepiness while driving or performing other tasks that require sustained attention, and monitored closely.^{39,40}

Although CBTi improves insomnia symptoms in the presence of comorbid OSA,³⁸ depression, anxiety and pain, it is only accessed by approximately 1% of Australian adults with insomnia.²⁸ Access to CBTi may be further reduced in people with COMISA if the OSA is viewed as the 'primary disorder' that should be managed before treatment of insomnia, or if there is reservation about referring patients with »

untreated OSA for sleep restriction therapy (one component of CBTi that aims to temporarily reduce time spent in bed).⁴¹

CBTi delivered by a suitably trained and experienced 'sleep' psychologist is the 'gold standard' form of this treatment.²⁴ Insomnia is an eligible condition for a GP referral to a psychologist, with a mental health treatment plan.⁴² Evidence-based self-guided digital CBTi programs may also be appropriate for patients with COMISA that are receiving treatment for OSA (e.g. well-controlled on CPAP therapy), with close oversight from a specialist sleep/respiratory clinician.^{41,43}

CPAP therapy is the most effective treatment for OSA.^{24,44} In a minority of patients with COMISA, CPAP therapy is accepted and improves symptoms of both the insomnia and OSA.⁹ However, on average, patients with comorbid insomnia are less likely to initially accept a trial of CPAP therapy, and use CPAP therapy for fewer hours per night compared to patients with OSA alone.^{2,45} Some randomised trials indicate that initial management with CBTi may improve CPAP acceptance and use in patients with COMISA, however this finding is not consistent across all studies.¹⁷

Tailored recommendations for non-CPAP therapies may also be provided to patients with different levels of OSA severity and presenting features.¹⁷ For example, weight management advice where indicated, positional devices (in the presence of supine-predominant OSA), mandibular advancement splints (in patients with mild-to-moderate OSA), and upper airway surgery are effective treatments that may be tailored to each individual patient.²⁴

Reasons for referral

Patients with suspected COMISA should be referred to a medical practitioner for

further assessment and management.³⁴

After initial assessment, some patients may be initially managed in the primary care setting. The GP may also refer the patient to a specialist sleep and respiratory physician and/or 'sleep' psychologist. The Australasian Sleep Association's Primary Care Sleep Health Resources website lists criteria a GP may use for specialist referral for insomnia (www.sleepprimarycareresources.org.au/insomnia/referral-to-psychologist) and OSA (www.sleepprimarycareresources.org.au/osa/investigations-and-referral).

Knowledge to practice

Pharmacists should be aware that insomnia and obstructive sleep apnoea (OSA) are the two most prevalent sleep disorders and frequently co-occur.

Pharmacists can use brief evidence-based self-report screening tools to support the identification and referral of patients with suspected insomnia and/or OSA.

If a patient has COMISA, it is important to consider assessment and management/referral options for both conditions.

Treatment approaches for OSA can be tailored to each individual's presenting features. The most effective and recommended 'first-line' treatment for insomnia is cognitive behavioural therapy for insomnia (CBTi).

RESOURCES

Resources for patients:

- Sleep Health Foundation
www.sleephealthfoundation.org.au

Resources for healthcare professionals:

- Sleep Health Primary Care Resources
www.sleepprimarycareresources.org.au
- Australasian Sleep Association
www.sleep.org.au
- Australian Pharmaceutical Formulary and Handbook: Insomnia: <https://apf.psa.org.au>
- Therapeutic guidelines: Insomnia in adults: <https://tgldcdp.tg.org.au/viewTopic?etgAccess=true&guidelinePage=Psychotropic&topicfile=insomnia-adults>

Conclusion

Comorbid insomnia and sleep apnoea (COMISA) is a prevalent and debilitating condition in the Australian population that requires nuanced assessment and management approaches. Pharmacists can play an important role in supporting the identification, assessment, initial management and referral of patients with COMISA, by using brief screening tools and providing information about evidence-based treatment options.

CASE SCENARIO CONTINUED


You discuss Carmen's symptoms further and offer her a 7-item Insomnia Severity Index and the 4-item OSA50 questionnaire to fill in. The results indicate likely long-term symptoms of insomnia and a high risk of undiagnosed OSA. Carmen reports daytime fatigue but no daytime sleepiness. You refer her to a GP for further assessment and explain that the GP may provide a further referral for an overnight sleep study, consultation with a sleep and respiratory physician and a psychologist for CBTi. You explain that CBTi is most effective for treatment of insomnia. Carmen is encouraged that there are non-pharmacological options available and is looking forward to discussing this with her GP.

UP TO

1.5
CPD
CREDITS

GROUP 2

KEY POINTS

- Comorbid insomnia and obstructive sleep apnoea (COMISA) is a prevalent and debilitating sleep disorder in the Australian population.
- Brief evidence-based assessment tools can be used to identify insomnia and OSA.
- Cognitive behavioural therapy for insomnia (CBTi) is the recommended first-line treatment for insomnia and is effective in patients with COMISA.
- Evidence-based therapies for OSA should be guided by patients' presenting symptoms and the characteristics of their condition. 



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ASSESSMENT
QUESTIONS

Each question has only one correct answer.

1 What percentage of people with insomnia have comorbid obstructive sleep apnoea?

- A 1–2%.
- B 5–10%.
- C 30–40%.
- D 70–80%.

2 Which ONE of the following options is **MOST** accurate?

- A In a patient with sleep apnoea and insomnia symptoms, the insomnia is almost always caused by the sleep apnoea and will resolve when the sleep apnoea is treated.
- B In a patient with sleep apnoea and insomnia symptoms, it is important that they are assessed and managed for both sleep conditions.
- C In a patient with sleep apnoea and insomnia symptoms, the sleep apnoea must always be treated first.
- D In a patient with chronic sleep apnoea and insomnia symptoms, the use of sedatives is considered 'gold standard' treatment.

3 Which ONE of the following questionnaires can a pharmacist recommend to be used as a self-report measure to help assess for symptoms of insomnia?

- A OSA50.
- B STOP-Bang.
- C Insomnia Severity Index.
- D Sleep study.

4 Which ONE of the following is the **MOST** suitable treatment recommendation for insomnia for a patient with comorbid insomnia and sleep apnoea (COMISA)?

- A Sedative-hypnotic medicines are recommended first-line to help insomnia for patients with COMISA using continuous positive airways pressure.
- B Sedative-hypnotic medicines should be recommended to all patients with insomnia.
- C In patients with insomnia and sleep apnoea, it is important to treat the sleep apnoea first so the insomnia will improve.
- D Cognitive behavioural therapy for insomnia (CBTi) from a psychologist with training in insomnia management.