

SmarterSleep
INTERVENTIONS

THE SLEEP HANDBOOK

Educational Interventions in Sleep Medicine

Summary

1 in 3 people will report symptoms of insomnia at some point during their lifetime (Great British Sleep Survey 2012). Educating patients about 'normal sleep' helps manage unrealistic expectations and reduce sleep-related anxiety.

Medication to induce and maintain sleep (hypnotics) are available for insomnia, but these are only recommended where Cognitive Behavioural Therapy for Insomnia (CBT-I) is unavailable or has failed.

Practitioners should contribute to the identification and management of insomnia across care settings, and can easily embed CBT-I related interventions into their practice to spare hypnotic use and improve sleep.

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The Sleep Handbook: Educational Interventions in Sleep Medicine

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Before using this handbook

This educational handbook is accompanied by an overview video available here:

<https://www.youtube.com/watch?v=feBlrkX5fg8&t=4s>

All resources related to the SmarterSleep interventions can be found here:

www.cntw.nhs.uk/smartersleep

1. Introduction

Across healthcare systems, insomnia disorder (insomnia) is a neglected diagnosis.[1, 2] Defined as a difficulty initiating or maintaining sleep,[3] it can be highly subjective, and often seen as a condition of less importance or not a medical condition at all.[4] At least one in three people suffer from insomnia at some point in their lives[5] and this figure rising in industrialised nations.[6] Insomnia can cause sleeplessness or waking without feeling refreshed, ultimately impairing day time function causing tiredness, impaired concentration and mood disturbance.[7, 8]

Historical literature argues that physicians could do more to explore sleep disturbances with patients.[13] Many GPs recognise the risks of hypnotics and are willing to reduce prescribing, but feel they have a lack of resources and non-pharmacological alternatives to do so.[14] Greater awareness of CBT-I (Cognitive Behaviour Therapy for Insomnia) amongst practitioners will add an evidence-based,[15, 16] non-pharmacological alternative to the toolkit of these clinicians, and facilitate the reduction of unnecessary hypnotic use.[17]

This workbook aims to provide an overview of sleep and the disorders associated with it, particularly focusing on insomnia and how healthcare professionals can combat this disease state, with and without medication.

2. Sleep and health

Sleep effects all body systems, and deleterious effects on the immune, cardiovascular, endocrine and neuronal systems are clearly seen when sleep deprivation occurs.[9] Sleep deprivation has also been shown to impair cognitive and motor function to the same degree as alcohol intoxication.[10] One study showed that injury-involved car accidents were six times more likely to happen in drivers who had slept less than 6 hours the previous night.[11] The bi-directional relationship between sleep and health makes sleep disorders, both diagnosed and undiagnosed, a significant global health burden. Poor sleep is also a common predictor of cardiovascular, metabolic, neurological and psychiatric ill health.[12] This highlights the important role healthcare professionals have to explore sleep with their patients during routine consultations.

3. The SleepWell Project

The SleepWell project aims to improve sleep management across the NTW NHS Foundation Trust (NTW) by; adopting a more flexible approach to night time observations, identifying and managing sleep disorders, improving sleep health including through environmental changes and making CBTi available where needed. This is part of the “Positive and Safe” programme within NTW. So far, the SleepWell project has consisted of a hub and spoke model with staff representatives (either the ward manager or a designated “sleep champion”) from each of seven pilot wards, the Positive and Safe leads, an Associate Medical Director for inpatient services in NTW and the sleep expert from a neighbouring trust. The sleep management developments were labelled as the SleepWell project and the project was designed as a six-month intervention. The seven wards included one male (Collingwood Court) and two female (Lowry and Longview) adult acute admission wards, a high dependency unit (Newton), a neurorehabilitation ward (Ward 3, Walkergate Park) (WGP), an old age unit (Roker) and a rehabilitation unit (Kinnersley). Training was provided to staff to develop a greater understanding of the importance of sleep and its correlation with mental health.

4. Normal sleep

To understand insomnia, it is important to first understand sleep. Sleep is a restorative physiological process characterised by an alteration in brainwave activity, which can be measured on an electroencephalograph (EEG).

4.1. Clocks and Rhythms

According to Borbély's two process model of sleep,[18] sleep is governed by two distinctly separate rhythms: the circadian rhythm (intrinsic biological clock – circa: about, dian: day) and the homeostatic sleep drive, or sleep pressure.[20]

4.1.1. The Circadian Rhythm

The circadian rhythm (Figure 1) is an endogenous cycle of around 24 hours influenced by melatonin, and matched to environmental 'zeitgebers' (time givers) such as light, temperature and food. This clock can only adjust at a certain speed, which is why it can take a few days to adjust to jet lag when crossing time zones.

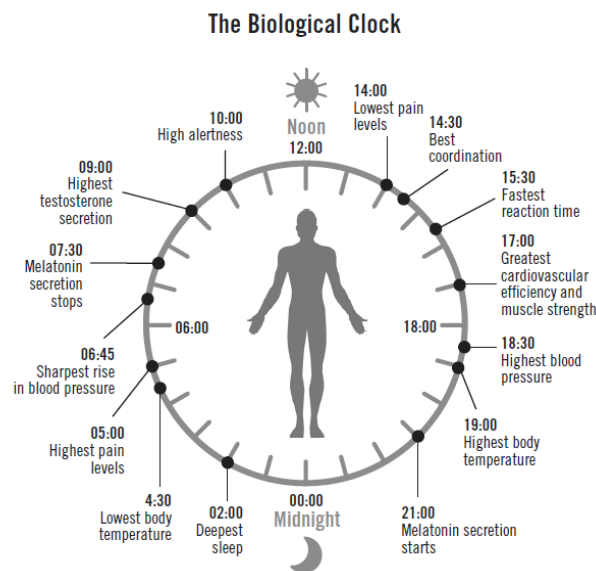


Figure 1: The circadian rhythm (Permission from Anderson [20])

Sleep pressure is determined by adenosine levels in the pre-frontal cortex of the brain: for every hour of waking, more adenosine accumulates and increases the urge to sleep. During sleep, this adenosine is anabolised back to adenosine triphosphate (ATP). Together, sleep pressure and the circadian rhythm form the sleep-wake cycle. External factors such as food, exercise, temperature, light and noise have been suggested as a third driver of this cycle. Optimising these factors improves the sleep-wake cycle and is known as 'sleep hygiene'. [21]

4.1.2. The Ultradian Rhythm

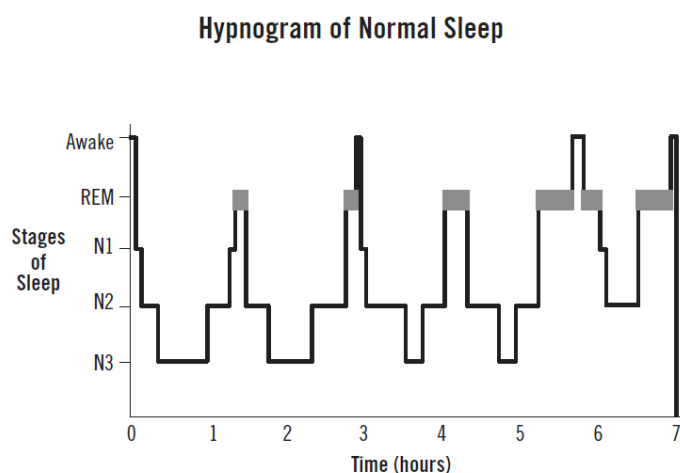


Figure 2 Hypnogram of normal adult sleep (Permission from Anderson [20])

Within the sleep-wake cycle there is another cycle: the ultradian rhythm (Figure 2). This rhythm is responsible for fluctuations in human consciousness both when awake and asleep. Each cycle lasts roughly 90 minutes, and in one full cycle the sleeper cycles between Rapid Eye Movement (REM) and non-REM (N1, N2 & N3) sleep stages. In REM sleep, the body enters a state of near paralysis, apart from breathing and rapid eye movements. In this stage dreams most frequently occur.[22]

4.2. Electroencephalography (EEG)

As the sleeper drifts from alertness into deep sleep, brainwave frequency slows, as measured by EEG.[19] Brain, eye, skeletal muscle and heart activity changes throughout differing phases of sleep, and this can be recorded through polysomnography (PSG).

Table 1: Brainwave activity and processes occurring throughout sleep stages

	Sleep stage	Brainwaves	Processes
	Awake	Beta (12-30 Hz)	-
	Drowsy	Alpha (8-12 Hz)	-
Non-REM	N1	Theta (4-10 Hz)	Easily roused by external stimuli. Some sleepers may not 'feel' asleep.
	N2	Theta (4-10 Hz)	Characterised by 'K-complexes' and 'sleep spindles' thought to be the brain's response to external stimuli to prevent itself from waking, and associated with memory.
	N3	Delta (0-4 Hz)	Slow wave sleep (SWS) occurs in this stage. This is the most restorative sleep stage. Blood pressure, breathing rate and temperature drop. Greatest sleep inertia (drowsiness) when woken from this stage.
REM	REM	Mixed	This stage is strongly associated with dreaming, learning and mood regulation. Skeletal muscles are paralysed but brain activity is similar to wakefulness in intensity. Heart rate and blood pressure increase again. A lack of REM sleep one night will cause 'REM rebound' the following night.

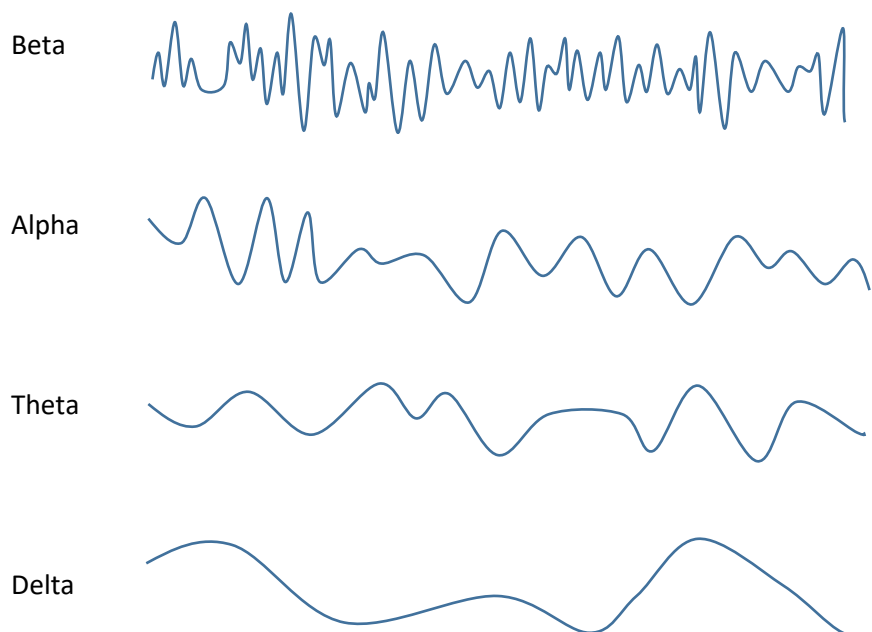


Figure 3: An illustration of EEG activity changes (Adapted from

4.3. Managing expectations of normal sleep

Even in healthy adults, as age advances the need for sleep decreases (Figure 4). The time spent asleep and the structure of this sleep, or 'sleep architecture', changes.[23] Sleep latency (the time taken to fall asleep) increases, more time is spent in stages 1 and 2 of non-REM sleep and less time is spent in REM sleep stages.[23]

Managing patient expectations around normal sleep length and quality through ageing is important. No matter the measures taken, it is unlikely that a 65+ year old will be able to routinely sleep like an adolescent again.

It is possible that in advanced age, those requiring less sleep are unnecessarily prescribed hypnotics to try to reach overzealous sleep targets, leading to over-sedation and increasing the risk of falls.

Cognitive impairment as a side effect of hypnotics or other sedative drugs can also lead to false dementia diagnoses.[24] Comorbidity and polypharmacy is more common in advanced age, and the impact of additional disease states and medicines can further disturb sleep.[25]

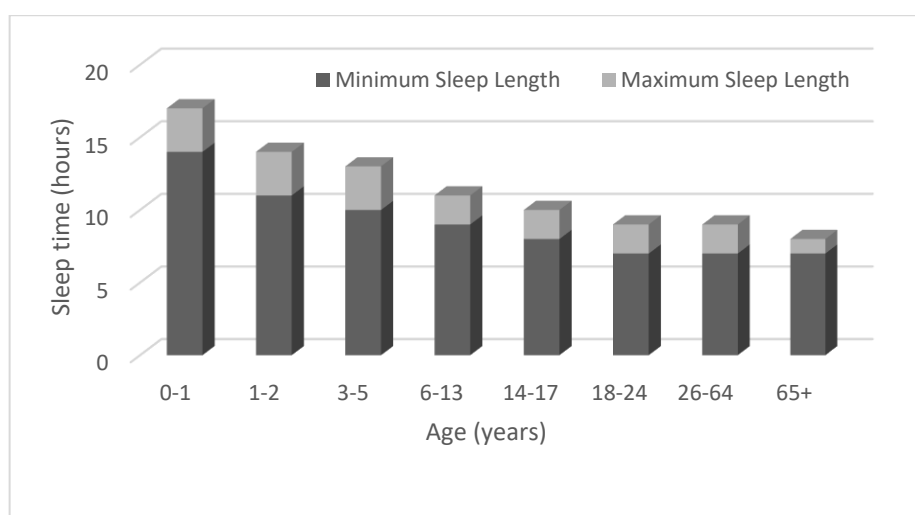


Figure 4: Sleep variation with age in healthy patients (Figures from Hirshkowitz, Whiton [26])

5. Insomnia disorder

5.1. Definition

Historically, multiple definitions of insomnia disorder have led to ambiguity over diagnosis and treatment. The International Classification of Diseases (ICD-10) manual and Diagnostic and Statistical Manual of Mental Disorders (DSM-V) definitions differ slightly, but commonly refer to insomnia as a 'difficulty initiating and maintaining sleep.' [3, 27]

The diagnostic criteria of the International Classification for Sleep Disorders (ICSD-3) neatly defines insomnia in three steps [7]:

1. A report of sleep initiation and/or maintenance problems, despite
2. Adequate opportunity and circumstances to sleep, resulting in
3. Daytime consequences

Additionally, the ICSD-3 differentiates chronic insomnia as the above lasting for more than 3 months, and occurring on 3 or more nights of the week. [7]

Alternatively, the National Institute for Health and Care Excellence (NICE) differentiates acute or short-term insomnia from long-term insomnia at the four week time point. [8] This figure is in relation to the maximum length stipulated on the product license of many hypnotics, whereas the ICSD-3 definition aims to differentiate persistent insomnia from self-limiting insomnia, which may not require specialist input. Regardless of the duration of symptoms, insomnia is a clinical predictor of depression, [28] and if distressing to the patient, should be treated.

5.2. Spielman's Model of Insomnia

Spielman's model (Figure 5) provides a useful lens through which to view insomnia.[29]

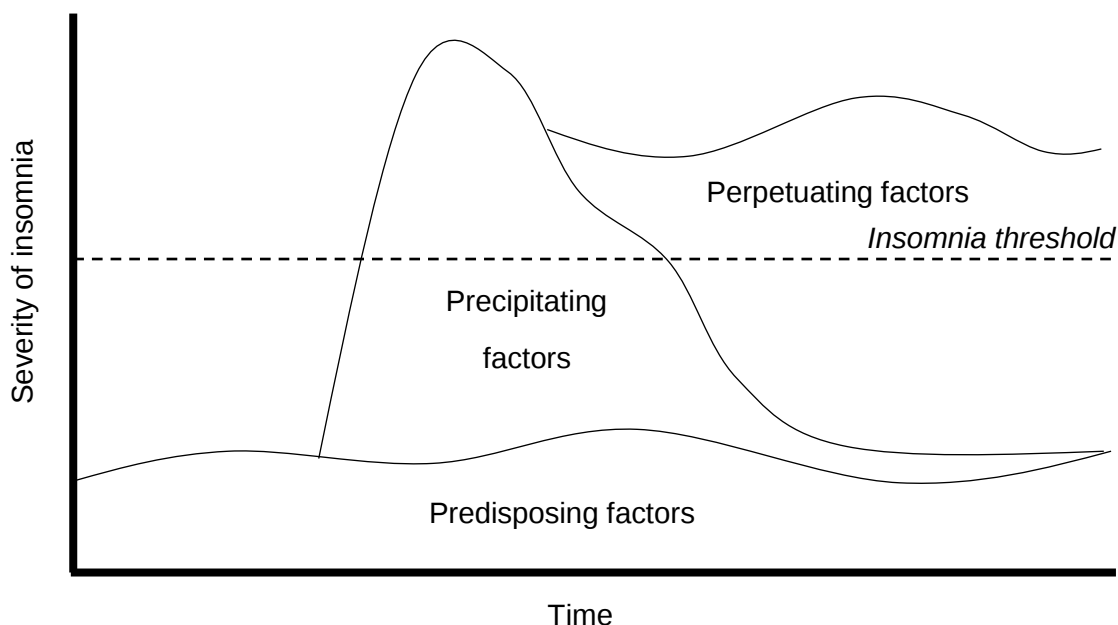


Figure 5: Spielman's Model of Insomnia (Re-created from Spielman, Caruso [29])

Factors such as age, disease state, and lifestyle factors can *predispose* people to insomnia. *Precipitating* factors such as a bereavement or exacerbation of a disease state can trigger insomnia. *Perpetuating* insomnia continues long-term once the original precipitating factor has been resolved. This type of insomnia is difficult to treat, as its perpetuating nature can be a result of cognitive and behavioural factors, rather than external causes.

Using this model it is easier to take steps to reduce factors predisposing patients to insomnia, discern between disease states which are not insomnia (but may precipitate it, such as restless leg syndrome and sleep apnoea) and identify perpetuating insomnia, which tends to be largely psychological in nature and caused by behaviours developed in response to the original precipitating insomnia.

5.3. Risk factors for insomnia

Up to 50% of older individuals experience sleep disturbance, although this may be due to a decline in sleep efficiency and unrealistic expectations of sleep at this stage of life.[7, 30-34] With older age comes an increased prevalence of co-morbidities which also increase the likelihood of developing insomnia.[35]

Women are more likely to suffer from insomnia than men, [30-32, 35] as are individuals who are unemployed, or have low levels of education or financial income.[7, 36] Despite low income, unemployment and low level of education, students are often considered to have a low risk of developing insomnia, whereas retirees and homemakers are at highest risk.[32]

Epidemiological studies have demonstrated that individuals who are separated, divorced or widowed also have a higher likelihood of developing insomnia than those who are coupled or single, although the association was more commonly observed for women than men.[32] This evidence highlights the complex social context of sleep disturbances.

The bi-directional relationship between insomnia and other health conditions is well-established,[30] with the prevalence of insomnia in adults with two or more illnesses being greater than 50%.[37]

Insomnia is a risk factor for the development or exacerbation of chronic health conditions, which in turn can worsen insomnia. Cardiovascular, gastrointestinal and pulmonary diseases are more prevalent in patients with insomnia than those without.[7, 31, 38] Often multiple underlying pathologies can lead to symptoms that disrupt sleep, for example nocturnal polyuria, can be present in several disease states, including diabetes and prostate enlargement.[8, 39] Other examples include restless leg syndrome (RLS) and obstructive sleep apnoea (OSA).[33]

A historical study of male participants illustrated an increased prevalence of sleep disturbance in subjects with untreated hypertension, chronic obstructive pulmonary disease, rheumatism, diabetes and obesity, with similar relationships in women reported in literature that is more recent.[38, 40]

Insomnia is also a risk factor for anxiety, depression and increased perception of pain.[34] Insomnia and mental health conditions are frequently concurrent in the general population,[32, 38] epidemiological evidence suggests that one third of patients who were diagnosed with a mental health disorder and also showed symptoms of insomnia or expressed dissatisfaction with sleep, did not have their insomnia diagnosed as a condition in its own right.[32]

In practice, the opportunity to treat patients holistically may be being missed and conversations around sleep may be an appropriate segue into more guarded topics, such as mental health.

5.4. Diagnosis

Insomnia presents a variance of physical and mental symptoms during the day and night. Typical daytime symptoms include fatigue, irritability and poor concentration. Some patients develop increased anxiety around bedtime rituals.[41] This can lead to an underlying state of hyperarousal, intrusive thoughts and a racing mind, creating a vicious cycle of maladaptive, compensatory sleep behaviours, which may perpetuate insomnia.

Like pain, there is a large psychological component to insomnia. Whilst there are objective parameters that can be measured, such as sleep efficiency, patient reported symptoms are largely subjective and therefore the account of a bed partner, if present, can be useful. Keeping a sleep diary for a minimum of two weeks is another common diagnostic tool.[7, 8]

A sleep study, either at home or measured via polysomnography, requires a referral to secondary care but is not required in the diagnosis of insomnia.[38] It remains important if other sleep disorders are suspected such as obstructive sleep apnoea or restless legs, or if there is believed to be a discrepancy between the subjective symptoms the patient reports and the reality of their sleep pattern.

Table 2: Sleep history example questions (Adapted from Anderson [20])

An example of sleep history questions:
• Do you find it difficult to get to sleep or stay asleep? • Does this occur most nights? • Does this effect your daytime activities? <i>Does it fit the diagnostic criteria of insomnia or is another sleep disorder possible?</i> • Are there any patterns or triggers? How long has this occurred for? • Do you snore heavily? <i>Screen for Obstructive Sleep Apnoea – if ‘yes’, complete STOPBang questionnaire (tool used to identify those at high risk of sleep apnoea)</i> • Do you feel an uncomfortable feeling in your legs that is relieved when moving them, especially when in bed? <i>Screening question for Restless Leg Syndrome (very specific set of symptoms)</i> • What medication do you take? What about alcohol, caffeine, nicotine? • Talk me through your average day, hour by hour • Do you nap at all during the day? • Can we start a sleep diary?

Table 1 provides examples of tools to assess sleep quality and aid diagnosis. These tools can be useful to record changes over time to sleep quality.[42] Table 2 provides an overview of common sleep disorders, and Figure 6 outlines a flowchart for diagnosis of insomnia as per the *British Association for Psychopharmacology consensus statement on evidence-based treatment of insomnia, parasomnias and circadian rhythm disorders: an update* (2019).[36]

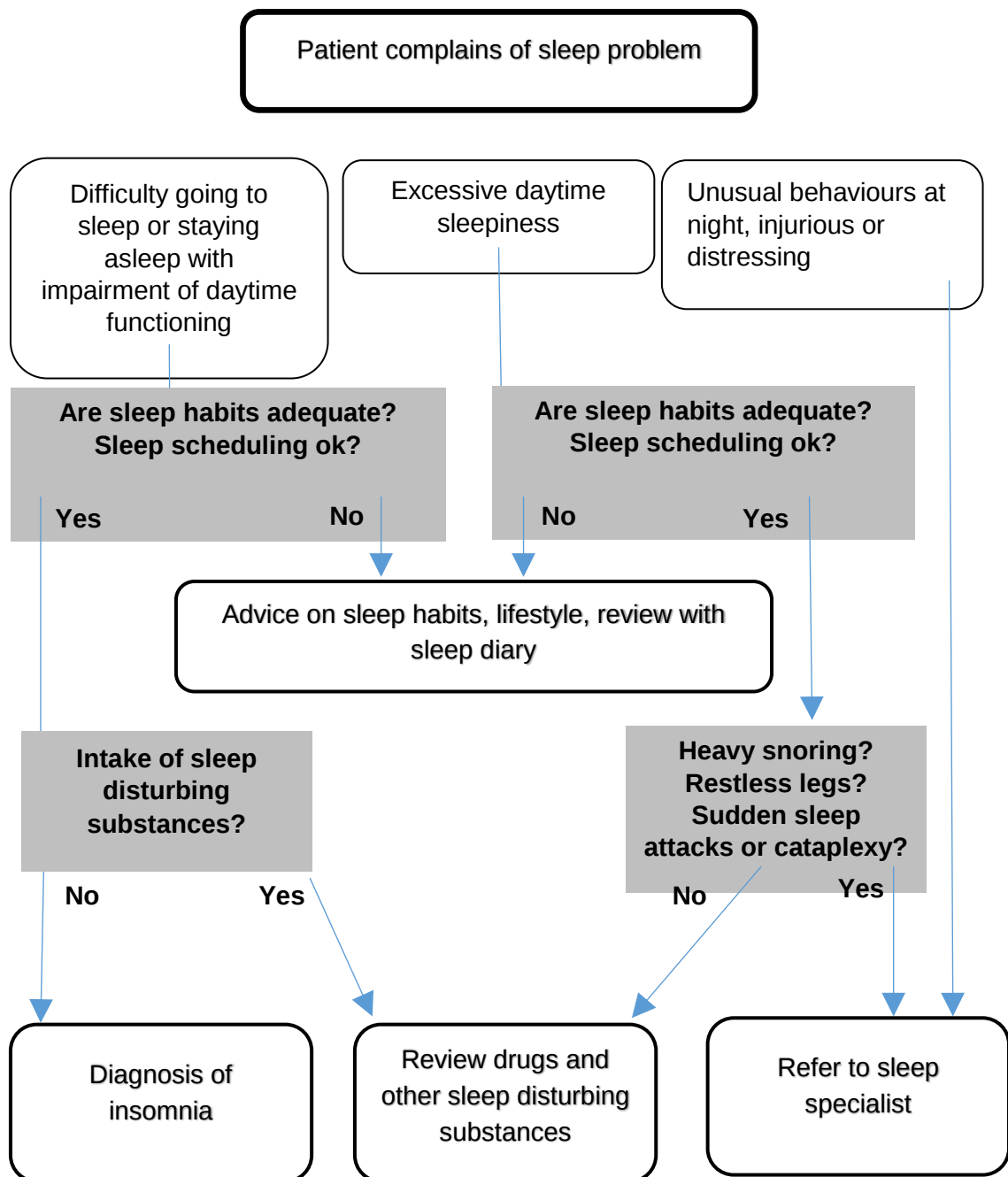


Figure 6: Diagnosis of insomnia (Recreated from Wilson, Anderson [36])

5.5. Scales and Indexes for Insomnia

There are a number of scales and indexes which are useful for diagnosing sleep disorders and differentiating between them. They can also be used to track the effectiveness of interventions done on these patient groups. Table 3 outlines those useful in screening for and measuring insomnia. Scales not included are: Pittsburgh Sleep Quality Index (PSQI), useful for diagnosing a sleep disorder in general; Epworth Sleepiness Scale (ESS), more useful in diagnosing non-sleep conditions which disturb sleep, e.g. Obstructive Sleep Apnoea; and the Beck Depression Inventory, which can be useful for monitoring the effect of improved sleep on depression. The two tools below have been validated against the DSM-V criteria for insomnia.[43]

Table 3: Assessment tools for insomnia disorder (Adapted from Omachi [42])

Tool	Purpose
Insomnia Severity Index (ISI)	A self-reporting index relating to patient concerns and perception of symptoms of insomnia over the past 2 weeks. 7 item questionnaire linked to DSM-IV items.[44] Used to assess severity of insomnia once diagnosis has been made.
Sleep Condition Indicator (SCI)	A two-item version of this questionnaire is available which comprises of a 0-4 Likert rating scale. This simple tool is useful for screening for insomnia in primary care. [43]

5.6. Sleep Diaries

Sleep diaries consist of a chart on which the sleeper records their time into bed, time out of bed, time asleep and time they woke, as well as any night-time awakenings. Anything else that may affect sleep such as caffeine, alcohol, meals and smoking should also be recorded too. Over a minimum of two weeks, these diaries can give a good insight into the nature of the patient's experience of sleep disorder. Insomnia may typically look as shown in Figure 7 below, characterised by long sleep latency (downwards arrow indicates the patient went to bed to sleep but did not fall asleep until 01:00) and frequent night-time awakenings (gap recorded between 02:30 until 04:30 and 05:30 and 06:30).

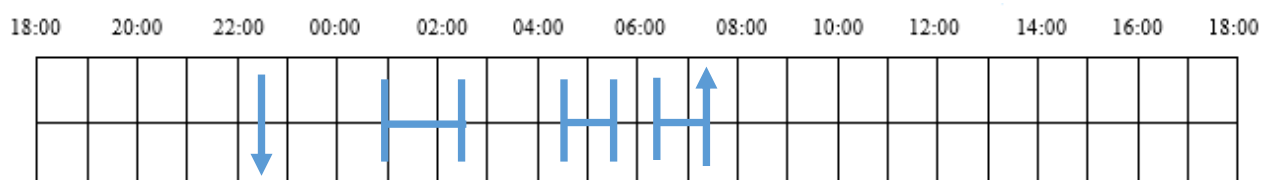


Figure 7: One night's sleep diary characteristic of insomnia disorder

5.7. Sleep Efficiency

Sleep efficiency is a useful parameter calculated from sleep diaries:

$$\text{Sleep Efficiency} = \frac{\text{time asleep}}{\text{total time in bed}} \times 100$$

A sleep efficiency >85% is consistent with normal sleep. A sleep efficiency of <50% indicates severe insomnia. Using the sleep diary shown in Figure 6 where the patient went to be at 22:30 and woke up at 07:30, the total time in bed can be identified as 9 hours, with the total time asleep as 3.5 hours. Using the Sleep Efficiency formula of 'time asleep' divided by 'total time in bed' multiplied by 100 would indicate a sleep efficiency of 38%. Sleep efficiencies can vary largely night on night, so it is best practice to average these findings over a period of at least two weeks. This data can also be used to track patient response to pharmaceutical care interventions (summarised below in Table 4) by observing sleep efficiency over time.

5.8. Prevalence

The prevalence of insomnia varies across literature due to disparities in definitions and diagnostic criteria.[45] Approximately one third of the general population report symptoms of insomnia, at some point in their life.[34, 46] with up to ten percent of the adult population report persistent insomnia.[46, 47] However, a large European epidemiological study of over 25,000 participants showed that only 25% of patients who met the criteria for insomnia diagnosis actually requested a medical consultation about their condition, suggesting prevalence may be underestimated.[38]

Table 4: An overview of common sleep disorders

Disorder	Nature	Treatment
Sleep Disorders		
Insomnia	Difficulty initiating or maintaining sleep	Cognitive Behavioural Therapy for Insomnia (CBT-I) Hypnotics
Hypersomnia	Disorder of excessive daytime sleepiness	Refer to specialist
Parasomnia	An umbrella term for: sleepwalking, confusional arousals, sleep eating disorder, REM sleep behaviour disorder, sleep paralysis, sleep hallucinations	Refer to specialist if causing injury
Circadian rhythm disorders	Disorder of the sleep-wake cycle (e.g. advanced/delayed sleep phase syndrome, free running circadian rhythm disorder)	Refer to specialist
Restless leg syndrome (RLS)	Characterised by an unpleasant aching/creeping/crawling sensation in the legs resulting in the irresistible urge to move. Often worse at night or at rest. May cause limb twitching. Precipitating factor for insomnia.	GP management initially RLS-UK for patient support Lifestyle: avoid stimulants in the evening, quit smoking, exercise, good sleep habits. Medicines: dopamine antagonists (pramipexole, ropnirole, rotigotine with supervision given risk of impulse control disorder).
Obstructive sleep apnoea (OSA)	A respiratory condition where an interruption in breathing during sleep causes the person to wake. More prevalent in men over 40 who are overweight, particularly in those with fat distribution around neck. Alcohol and sedative medications also risk factors. Consider in those who have daytime sleepiness.	Refer to specialist for sleep study Continuous Positive Airway Pressure (CPAP) device first line Mandibular Advancement Device (MAD) second line for mild to moderate disease only

5.9. Protecting people from poor sleep

Poor sleep can be improved by modifying intrinsic and extrinsic factors such as stress, excitement, anticipation, pain, illness, changes in sleep schedule, day time napping, change of time zone or altitude, medication noise and light.[7] Many causes of sleep disruption are preventable, therefore issues with sleep can be prevented before insomnia precipitates. As discussed earlier, modifying this hypothesised ‘third driver’ of the circadian cycle protects sleep.

There are three simple steps every clinician can take to protect a patient’s sleep:

1. Ask the question “how are you sleeping?” Especially in patients with chronic disease.
2. Review medication - are any stimulating or sedating at the wrong times?
3. Educate patients about normal sleep and how it can be improved.

Although patient-directed information about this may be limited, some examples are shown below in Table 5, which outline the effect of lifestyle and medication factors on sleep, and highlight some key points where changes can be made to create ‘quick wins’.

Table 5: Lifestyle and medication factors affecting sleep.

Substance	Impact on sleep
Food	Eating a high calorie meal within one hour of bedtime slows down the onset of sleep due to increased gastric volume causing discomfort[49]. For patients experiencing dyspepsia that keeps them awake, a proton pump inhibitor at night may aid with sleep.
Exercise	Exercise during the day improves sleep, however exercise just before bedtime can be stimulating.[50, 51]
Inactivity	Inactivity can cause insomnia, particularly for those remaining indoors. This can create negative cycles, as day time fatigue due to insomnia can create a lack of motivation to do things.[50, 52-54]
Nicotine	Nicotine can cause insomnia through its stimulant action, and overnight withdrawal symptoms which decrease N3 sleep.[55] Smoking cessation can precipitate or exacerbate insomnia.[56]
Caffeine	Caffeine temporarily reduces homeostatic sleep pressure.[36] It increases sleep latency and decreases N3 sleep.[57] Drinking 5-6 cups of coffee a day creates a constant level of caffeine in the bloodstream.[57]
Alcohol	Alcohol helps induce sleep due to its initial sedative action.[58, 59] However later in the night causes a dose-dependent disruption to sleep by delaying the onset of, and fragmenting REM sleep. This results in frequent awakening and a greater proportion of N1 sleep, which is not as restorative.[54] The following night a ‘REM rebound’ occurs, to restore the REM deficit. This suggests there is a homeostatic control mechanism associated with REM sleep.[59] This REM rebound causes more restorative sleep, but increases the risk of parasomnias occurring.
Medication	Stimulating medicines late at night, or sedative medications during the day can disturb the sleep-wake (see Table 4 for further information)

6. Treatment of insomnia disorder

Before initiating treatment in insomnia, it is crucial to determine the nature of the insomnia. Mild insomnia may be effectively treated with simple advice, but if good sleep habits have been tried and yet significant distress and daytime symptoms persist, treatment should be considered. If the insomnia is due to a short-term stressor and is resolved quickly, a short course of z-drugs for 3-7 days should be considered. If more long-term, a bifurcated strategy is recommended. Licensed only for short-term use, hypnotics are effective in the treatment of short-term insomnia but provide symptomatic relief only. In practice, these drugs are continued beyond the course of their license without thorough review, and on cessation patients can return to troubled sleep states. Evidence shows behavioural treatment (CBT-I) is equally effective compared to hypnotics in short-term treatment of insomnia symptoms and this approach is preferred over hypnotics for maintaining sleep improvement. There is some evidence that the best treatment option is a course of CBT-I in combination with a course of hypnotics.[60]

For treating long-term insomnia, CBT-I should be offered first-line.[36] If this is ineffective or unavailable, or the patient urgently requires immediate improvement in their sleep, hypnotics should be offered alongside CBT-I. The patient should be reviewed after CBT-I is complete, or every four weeks if using hypnotics.

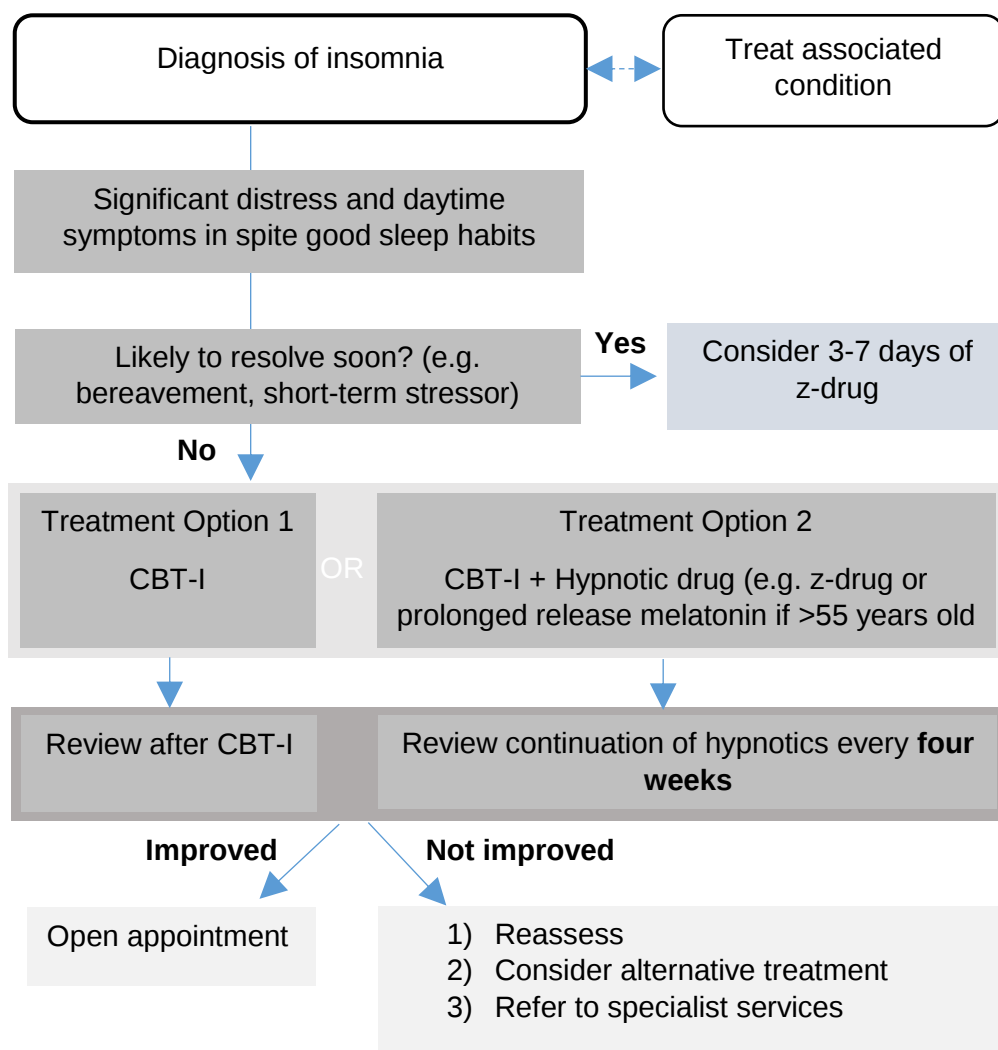


Figure 8: Treatment of insomnia (Adapted from Wilson, Anderson [36])

Hypnotics can be extremely useful for patients struggling from severe insomnia who cannot engage in talking therapies, for example those with an acute episode of mania or psychosis. Preliminary work has linked insomnia with cardiovascular health indicating that hypnotics could promote health in other ways.[61]

All patients suffering from insomnia should be offered CBT-I related advice about sleep. A clinical judgement should be made in parallel regarding the need for hypnotics (see Figure 6). For patients already on hypnotics, CBT-I should be added in alongside the existing hypnotic prescription, and not used to replace it. As sleep efficiency increases past the normal sleep threshold of 85%, the hypnotic dose can be reduced. This can be repeated until the hypnotic has been completely withdrawn.

6.1. Cognitive Behavioural Therapy for Insomnia (CBT-I)

First line treatment for chronic insomnia as recommended by NICE in England and the European Insomnia Guideline is cognitive behavioural therapy for insomnia (CBT-I).[8, 62, 63] Specifically developed to support patients with insomnia, CBT-I involves a collection of techniques outlined below. The effectiveness of CBT-I alone in treating long-term insomnia is superior to that of hypnotics alone, but the best treatment outcomes are seen when both are used in combination.[64, 65]

CBT-I usually consists of between 4-8 sessions,[66] face-to-face, over the telephone or online using website or mobile phone applications.[66] These can be delivered individually or in group settings. The aim is for the patient to practice these techniques at home to provide long-term relief, with high success rates reported in the literature.[67] CBT-I is increasingly accessible, although referral pathways can limit availability in some areas[59]. Restrictions to access CBT-I appear to be based on unfamiliarity of CBT-I by healthcare professionals such as GPs or community mental health teams, who may not readily offer it to patients in preference of traditional therapies, such as a pharmaceuticals.[68]

Healthcare professionals practicing CBT-I has historically not been a broad church, although this is changing and a range of health professionals have effectively delivered CBT-I in recent times as well as online and self help versions of the therapy now available.[69] It is not unrealistic for practitioners to deliver CBT-I interventions within their practice, and the intent of this article is to show that a change of practice is possible. Although not pharmaceutical-related advice, this advice can be pharmaceutical-sparing and has the potential to prevent a range of disease states. Whilst CBT-I may not necessarily be in the format of structured sessions as above, interventions containing CBT-I concepts delivered at opportunistic moments has potential to affect the care of patients with insomnia.

6.1.1. Sleep Education and Hygiene

Managing expectations of normal sleep (night-time waking, decreased sleep need with increased age). Advice on potential sleep disruptors such as diet, exercise, daily routine, substance use (including caffeine, alcohol and nicotine) and light, noise and temperature in the bedroom.

6.1.2. Stimulus control

Techniques used to reinforce psychological associations between the bed and sleep, and break psychological associations between the bed and wakefulness. For example, only get into bed when sleepy, get out of bed if unable to sleep, only use the bedroom for sleep, sex and getting dressed.

6.1.3. Psychoeducation and relaxation strategies

Routines such as progressive muscle relaxation and meditation, which create a wind-down period before bed, relieve body tension and thoughts that may interfere with sleep.

6.1.4. Sleep Scheduling

Setting times for waking and, getting out of bed. Go to bed when feeling tired, not at a set time. 'Sleep restriction therapy', which aims to slightly sleep-deprive the patient in a controlled manner, such that they sleep more effectively during their time in bed.[64] This works by setting an anchor point to wake up slightly earlier than their normal time. Then the time the patient goes to bed is made later in the night to when the patient feels tired, around midnight

or 01:00, for instance. Over the first few weeks the patient will feel worse, but sleep efficiency will increase (showing patients this using a sleep diary can be a motivating factor), and nighttime waking will be reduced. As sleep efficiency increases, bedtime can gradually be moved back in stages of 15-30 minutes until a normal night's sleep is restored. Sleep should not be restricted below 5 hours, and sleep restriction is contraindicated in patients who must drive in their line of work, have a history of mental illness, seizures, or other sleep disorders such as sleep apnoea. In these patients, sleep compression can be used instead, with caution. Where sleep is restricted, supervision is recommended, and this should be reviewed after 1-2 weeks.

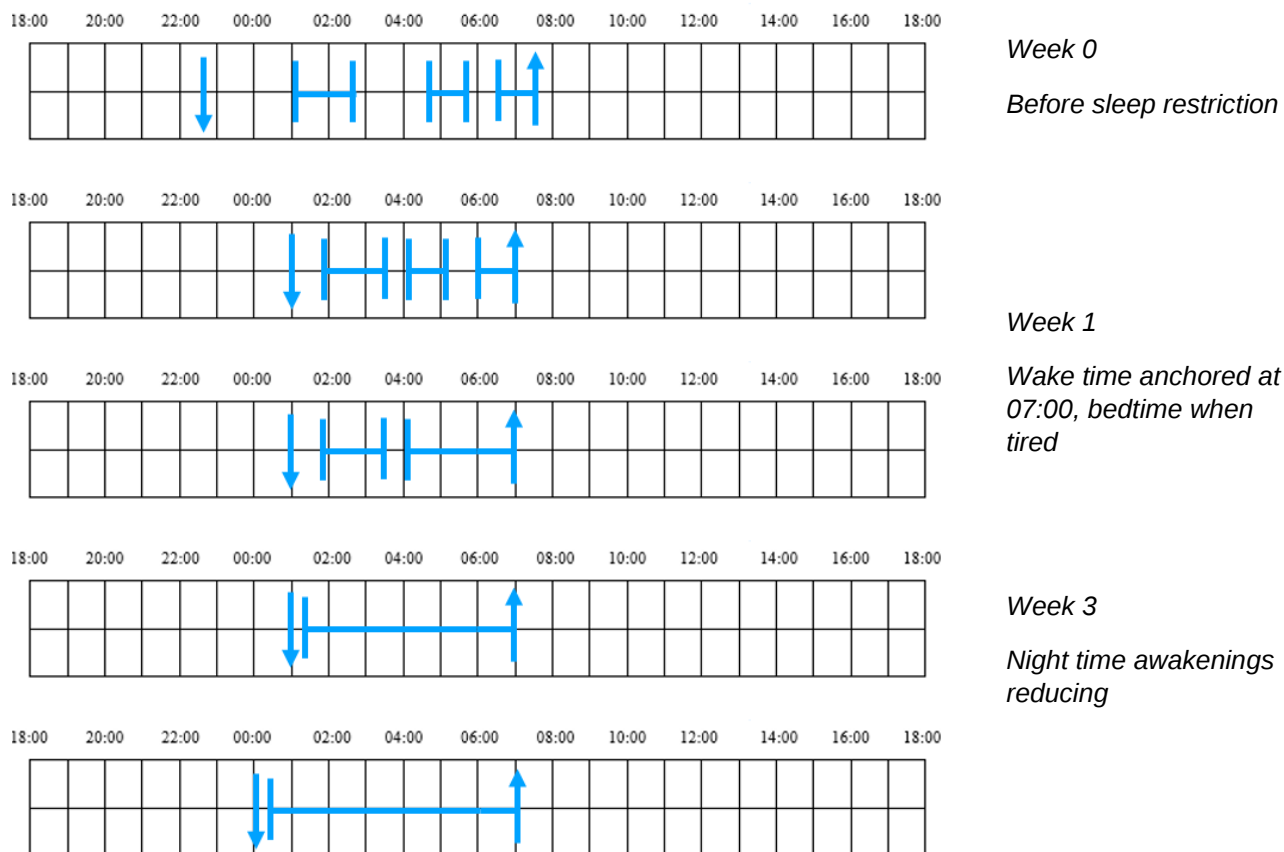


Figure 9: An example of sleep diary extracts over an 3-week treatment period.

Sleep Compression Therapy is a milder form of sleep restriction, the only difference being instead of immediately restricting sleep to a certain time, the time allowed in bed is gradually moved forwards in 30 minute intervals until 85% sleep efficiency is reached. The minimum sleep should be compressed to is 6.5 hours.[16, 64]

6.1.5. Cognitive Therapy

Addressing factors perpetuating insomnia, such as irrational routines before bedtime and discussing paradoxical intention – the harder you try to fall asleep the more difficult it becomes can also be effective methods to improve sleep. Patients should be encouraged not to 'try' and sleep, to destigmatise and manage expectations at bedtime.

6.2. Medication

The brain's arousal system is governed by activating neurotransmitters (norepinephrine, serotonin, acetylcholine, dopamine, histamine and orexin) which promote wakefulness, and sedating or inhibitory neurotransmitters (GABA, adenosine) which promote sleep. These two teams of neurotransmitters form the basis underpinning hypnotic medication.

6.2.1. Benzodiazepines and Z-drugs (GABA-PAMs)

Both benzodiazepines and z-drugs increase the effect of neurotransmitter gamma-aminobutyric acid (GABA) at GABAA receptors, making them GABA-positive allosteric modulators (GABA-PAMs). This gives rise to their hypnotic, anxiolytic, muscle relaxant and anticonvulsant properties. Temazepam, a benzodiazepine, is useful for acute episodes of insomnia, however in bereavement benzodiazepines can cause emotional blunting, preventing the grieving process. Zopiclone and zolpidem (z-drugs) are similarly useful for short-term treatment. Zolpidem has a shorter half-life than zopiclone, making it less effective in insomnias where sleep maintenance is problematic, but less likely to cause a 'hangover effect' the next day. Z-drugs generally have a more acceptable side effect profile than benzodiazepines.

Long-term use of GABA-PAMs has been known to increase anxiety, worsen sleep, increase falls risk and worsen depression.[70] The hypnotic effect of these drugs comes from their ability to enhance the sleep-inducing effect of gamma-aminobutyric acid (GABA) at GABAA receptor sites in the brain.[36] Agents with longer half-lives such as flurazepam, nitrazepam and diazepam are more likely to cause this, making them inappropriate for treatment of insomnia disorder.[71]

NICE recommends that GABA-PAMs are used for the shortest time possible due to potential abuse.[72] However there is an emerging body of evidence showing that the dependence potential of GABA-PAMs may have been overestimated, particularly for z-drugs.[36] which can also be abused. An increase in sleep latency that resolves over a matter of days during GABA-PAM withdrawal has also been reported which may reduce patient experience of these products.[73] The addictive nature of these products supports the use of CBT-I during withdrawal.[36]

Epidemiological data shows an increased risk of road traffic accidents, fractures and falls when using benzodiazepines, further work is needed to identify risks relating to the development of other illness such as dementia.[75] It is important that clinicians counsel patients regarding driving legislation in relation to sedating drugs, especially considering the frequent use of these products outside of licensed indications.[76]

6.2.2. Melatonin

The suprachiasmatic nucleus (SCN) receives signals from the optic nerve as it passes to the visual cortex at the back of the brain. As light levels diminish, the SCN ceases its inhibitory control of the pineal gland, giving rise to endogenous melatonin release in response to darkness. In the hypothalamus, melatonin binds to MT1 and MT2 receptors, creating the feeling of sleepiness and resynchronizing the circadian clock.[36] Decreases in endogenous melatonin production during ageing can precipitate sleep problems. Endogenous melatonin secretion has been found to become dysregulated in intensive care patients and there is some evidence that exogenous melatonin can be useful in correcting the 'abolished circadian rhythm' to reinstate a normal sleep-wake cycle, although a Cochrane review states that the evidence is of very low quality.[77]

Both immediate and sustained release exogenous melatonin formulations act by increasing the levels of endogenous melatonin in circulation to regulate circadian rhythm and sleep-wake cycles.[8] The use of melatonin for insomnia is licensed for short-term treatment of insomnia in patients over 55 years old.[72] Beta-blockers and non-steroidal anti-inflammatory drugs inhibit the secretion of endogenous melatonin, which can sometimes lead to sleep disturbances and may benefit from the use of melatonin. Melatonin has a short half-life and so is useful in initiating sleep rather than maintaining it. It has a favourable side effect profile, but evidence for its benefit is limited when compared to more traditional hypnotics.

6.2.3. Antidepressants

Antidepressants have a range of receptor binding profiles, and those currently licensed in the UK are rooted in the science of the monoamine hypothesis of depression.[36] SSRIs and SNRIs, selectively inhibit the reuptake of serotonin and norepinephrine respectively, can be stimulating and consequently worsen insomnia. These antidepressants should therefore be administered in the morning. Other antidepressants such as amitriptyline and low dose mirtazapine (15mg) have an antihistamine effect and can create a feeling of drowsiness.[78] In practice, these are often given at night to assist with sleep onset, although at higher doses (30mg, 45mg), mirtazapine becomes less sedating. Amitriptyline is not licensed for insomnia and a recent Cochrane review found there to be no evidence to support its use.[79] Despite all this, and a considerable side effect profile, it is regularly prescribed by general practitioners.[13] These drugs are more likely to be lethal in overdose than GABA-PAMs,[80] therefore this practice is not founded in evidence and may be dangerous.

Antidepressants could be considered for insomnia where there is a comorbidity with depression or anxiety, however should not be used solely for the treatment of insomnia.[78] In order to achieve the greatest clinical outcome for patients, both the mental health disorder and the insomnia diagnosis should be targeted for treatment.[47]

6.2.4. Sedating antihistamines

The 2019 British Association for Psychopharmacology (BAP) guidance on insomnia management states that sedating antihistamines such as diphenhydramine and promethazine have a 'limited role in psychiatric and primary care practice for the management of insomnia'. Promethazine brings about drowsiness by opposing the action of histamine in the body, an activating neurotransmitter. Promethazine is non-selective for its target receptor, and so produces many unwanted anticholinergic side effects, such as; dry mouth, urinary retention, blurred vision, dizziness, confusion, hallucinations, and increased heart rate. These side effects contribute to a patient's falls risk, particularly when used in the elderly.

Practitioners have a good understanding of the risks associated with benzodiazepines, and as a consequence Z-drugs (zopiclone, zolpidem), as these share a common mechanism of action (GABA positive allosteric modulator). As a result, it is likely that there is an overestimation of risks associated with z-drugs, and underestimation of risks associated with sedating antihistamines. They are often considered to be 'weaker' or 'safer' hypnotics. In reality, the risks of promethazine appear to outweigh the benefits of its use, and its continued use in practice should be reviewed.

Over-the-counter options for the treatment of insomnia are limited to sedating antihistamines, and their use can mask symptoms of an underlying sleep disorder. Some over-the-counter preparations are only licensed for symptomatic relief of colds, chills and influenza and are not indicated for the treatment of insomnia.[8, 20, 63] Clinicians should counsel patients to ensure the safe use of these products and to rule out other diagnoses. Using the model outlined in

Figure 8 these products should only be offered for insomnia that is 'likely to resolve soon', and patients seeking these medicines for prolonged periods warrant further investigation of symptoms. This may culminate in referral to a GP for a formal diagnosis of insomnia.[81]

Table 6: Comparison of side effects of commonly used hypnotics

Benzodiazepines	Z-drugs	Melatonin	Promethazine
Depression Paradoxical reaction (increased anxiety, irritability, hyperactive or aggressive behaviour)		Headache Nasopharyngitis Back pain Arthralgia	Dizziness Dry mouth Headache Hypotension Urinary retention Drowsiness Confusion Delirium Hallucinations Tachycardia Blurred vision Constipation Elevated body temperature Increased falls risk
Cognitive and psychomotor impairment Emotional blunting	Nausea and vomiting Diarrhoea Dizziness Dry mouth Headache Amnesia Confusion Hallucinations Nightmares		

Table 7: Comparison of hypnotics

Mechanism of action	Drug	Elimination half-life (hours)	Comments
GABA positive allosteric modulator	Benzodiazepines Diazepam ^F Nitrazepam ^{NF} Temazepam ^F Lormetazepam ^{NF} Loprazolam ^{NF}	20-100* 15-38* 8-15* 10-12* 6-12*	Useful for acute episodes of insomnia. Temazepam is best formulary choice. Diazepam can be useful where insomnia is associated with daytime anxiety.
	Non-benzodiazepines Zopiclone ^F Zolpidem ^{NF} Zaleplon ^{NF}	5-6 2 1	Z-drugs have lower side effect profile compared to benzodiazepines. Zopiclone best for insomnia where sleep maintenance is also an issue.
Histamine (H1) receptor	Antihistamines Promethazine ^F	5-14*	Likely to be overprescribed as side effect profile underestimated.
Melatonin receptor agonist	Pineal hormone Melatonin (MR) ^{F/NF}	20-50 minutes	Licensed for patients over 55 due to decline in endogenous melatonin secretion with age, children due to low melatonin secretion in early years, and .

*Drugs with a half life longer than 6 hours are more likely to cause hangover effect the next day.

^F = Formulary, ^{NF} = Non-formulary (As per North of Tyne and Gateshead Area Prescribing Committee Formulary [Accessed: 19/08/19])

7. Summary

In clinical practice there is an over-reliance on hypnotics in the treatment of chronic insomnia. Too often these agents are started without holistic consideration of alternatives. The continuation of hypnotic agents without thorough and timely review is common. This can be to avoid patient confrontation and to satisfy patient expectations of the medical model. The appropriate use of hypnotics is crucial, as when necessitated these drugs are of therapeutic value. Care needs to be taken not to stigmatise patients who use these drugs, as it can be easy to label people as drug-seeking, when in fact these patients are just seeking a good night's sleep. A careful assessment of sleep will often detect secondary causes of poor sleep which requires different treatment.

In the treatment of insomnia, a culture shift away from hypnotics and towards CBT-I as a first-line intervention needs to be made. This culture shift starts with recognition from all practitioners, regardless of background, that providing non-pharmacological therapeutic interventions can be just as good practice as providing pharmacological interventions. By providing CBT-I advice as a first-line treatment option, clinicians may negate the need for a hypnotic prescription, reducing drug spend, risk of side effects, and improving treatment outcomes.

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82. Lindam, A., et al., Gastroesophageal Reflux and Sleep Disturbances: A Bidirectional Association in a Population-Based Cohort Study, The HUNT Study. *Sleep*, 2016. 39(7): p. 1421-7.
<https://doi.org/10.5665/sleep.5976>

9. Appendices

Appendix 1: Pharmaceutical Care Interventions to minimise sleep disruptions

Table 8: Pharmaceutical Care Interventions to minimise sleep disruption

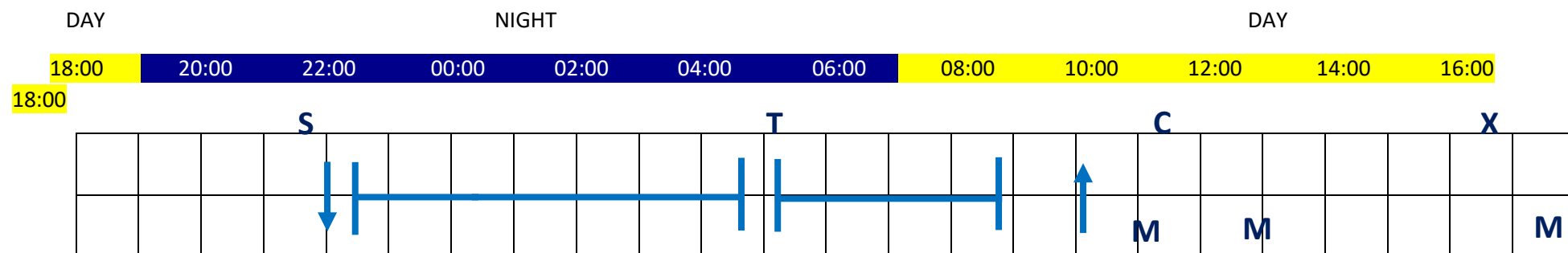
Therapeutic class	Example	Impact on sleep	Pharmaceutical Care Intervention
Short acting beta agonists	Salbutamol	Adrenergic stimulation.	Check inhaler technique. Consider increasing preventer inhaler dose to reduce the requirement of reliever inhaler.
Sympathomimetics	Pseudoephedrine	Central nervous system (CNS) stimulant effects.	Avoid at least 2 hours before bedtime, limit use to when required only, consider switching to steam inhalation for decongestant action.
Beta Blockers	Bisoprolol	Lipid soluble so can enter the brain, causing nightmares.	Switch to a water soluble beta blocker if clinically appropriate, e.g. Atenolol.
Systemic corticosteroids	Prednisolone	Nightmares can occur particularly in high doses or longer term use.	Reduce dose to minimum effective dose (avoid abrupt withdrawal, refer to BNF treatment cessation guidelines)
Monoamine oxidase inhibitors	Phenelzine	CNS stimulation due to inhibition of monoamine neurotransmitter breakdown.	Seek advice from patient's psychiatric team. Dose timing change may be appropriate.
Antiepileptics	Lamotrigine	Increases REM sleep duration, decreases proportion of slow wave sleep. Some may find it alerting.	Seek advice from patient's neurologist to explore scope of dose reduction, dose timing change, or change of medication.
Calcium channel blockers	Amlodipine	Reports of abnormal dreams and insomnia. Causal relation not yet established.	Consider switching to lercanidipine if clinically appropriate as no listed side effects of sleep disturbance, abnormal dreams or insomnia.
Centrally acting antihypertensives	Moxonidine	CNS stimulation due to inhibition of monoamine neurotransmitter breakdown.	Consider switching to methyldopa if clinically appropriate as no listed side effect of sleep disturbance or insomnia, although can cause nightmares so limit dose to <1g daily to minimise risk
Tricyclic antidepressants	Amitriptyline	Sedative effect – on cessation may cause rebound insomnia	Withdraw gradually.
Centrally acting sympathomimetics	Atomoxetine	CNS stimulation; particular effects during the first few months of treatment on dose change	Take last dose before 6pm. Discuss alternative treatment or dose reduction with ADHD specialist as these medications are prescribed in primary care under a shared care agreement with specialist

Thyroid hormones	Levothyroxine	Stimulatory effect due to increased thyroid function.	Blood test for thyroid function to check if prescribed correct dose, dose reduction if necessary. Administer in the morning.
Antimetabolites	Methotrexate	Associated with insomnia, potentially due to neurological effects of drug.	Discuss with secondary care specialist as these medications are prescribed in primary care under a shared care agreement with specialist.
Opioids	Morphine, Oxycodone, Codeine	Insomnia can occur on withdrawal. Side effect of drowsiness could lead to day time napping, altering the patients sleep schedule and reducing the desire to sleep at bedtime. Can cause analgesic overuse headache.	Gradually reduce dose to minimum effective licensed dose in line with NHS policy: opioids in non-malignant chronic pain. Change dosing times to evening where possible, swap for longer acting opioids overnight.
Neuropathic agents	Pregabalin, Gabapentin	Insomnia can occur on withdrawal. Side effect of drowsiness could lead to day time napping, altering the patients sleep schedule and reducing the desire to sleep at bedtime.	Gradually reduce dose to minimum effective licensed dose, or move dose timing to evening.
Sedating antihistamines	Chlorphenamine	Side effect of sleep disturbance and insomnia due to paradoxical CNS stimulation which usually occurs with high doses.	Switch to a non-sedating antihistamine or limit use to only when required. Change dosing time to evening.
Diuretic	Furosemide	Potential for causing nocturnal polyuria if taken in the afternoon or evening which in turn can cause sleep disturbance.	Check timing of dose and change to morning if necessary.
Proton pump inhibitor	Lansoprazole	Patient may complain of worsening reflux symptoms at bedtime that impacts the ability to fall asleep. CNS effects of abnormal dreams and insomnia.	Change timing of dose to a night time or consider twice daily dose. Considering trialling a different proton pump inhibitor or histamine type 2-receptor antagonist although they also carry the risk of these side effects.

Appendix 2: A 2-week sleep diary

Patient name: _____ Date started: _____

EXAMPLE



Comments: Slept well with one period of waking at 4:30am to go to the toilet

Arrow down = into bed

Solid vertical line = start/end of sleep

Sleeping pill = S

M = Meal

T = Use of toilet during sleep time

Arrow up = out of bed

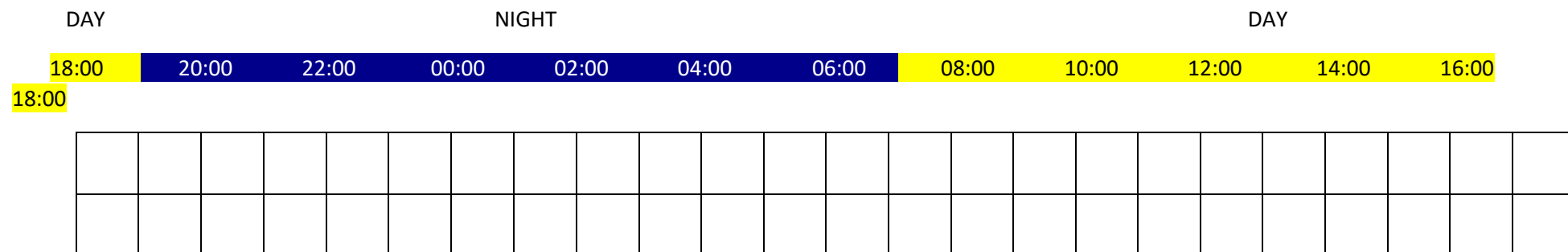
Solid horizontal line = time asleep

Caffeinated drink = C

X = Exercise

N = Noise waking patient from sleep

NIGHT 1



Comments: _____

NIGHT 2

DAY

NIGHT

DAY

18:00	20:00	22:00	00:00	02:00	04:00	06:00	08:00	10:00	12:00	14:00	16:00
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18:00

Comments:

NIGHT 3

DAY

NIGHT

DAY

18:00	20:00	22:00	00:00	02:00	04:00	06:00	08:00	10:00	12:00	14:00	16:00
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18:00

Comments:

NIGHT 4

DAY	NIGHT												DAY										
18:00	20:00	22:00	00:00	02:00	04:00	06:00	08:00	10:00	12:00	14:00	16:00												
18:00																							

Comments: _____

NIGHT 5

DAY	NIGHT												DAY										
18:00	20:00	22:00	00:00	02:00	04:00	06:00	08:00	10:00	12:00	14:00	16:00												
18:00																							

Comments: _____

NIGHT 6

DAY

NIGHT

DAY

18:00	20:00	22:00	00:00	02:00	04:00	06:00	08:00	10:00	12:00	14:00	16:00
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18:00

Comments:

NIGHT 7

DAY

NIGHT

DAY

18:00	20:00	22:00	00:00	02:00	04:00	06:00	08:00	10:00	12:00	14:00	16:00
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18:00

Comments:

NIGHT 8

DAY

NIGHT

DAY

18:00	20:00	22:00	00:00	02:00	04:00	06:00	08:00	10:00	12:00	14:00	16:00
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18:00

Comments:

NIGHT 9

DAY

NIGHT

DAY

18:00	20:00	22:00	00:00	02:00	04:00	06:00	08:00	10:00	12:00	14:00	16:00
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18:00

Comments:

NIGHT 10

DAY		NIGHT										DAY											
18:00	20:00	22:00	00:00	02:00	04:00	06:00	08:00	10:00	12:00	14:00	16:00												
18:00																							

Comments: _____

NIGHT 11

DAY		NIGHT										DAY											
18:00	20:00	22:00	00:00	02:00	04:00	06:00	08:00	10:00	12:00	14:00	16:00												
18:00																							

Comments: _____

NIGHT 12

DAY		NIGHT										DAY											
18:00	20:00	22:00	00:00	02:00	04:00	06:00	08:00	10:00	12:00	14:00	16:00												
18:00																							

Comments: _____

NIGHT 13

DAY		NIGHT										DAY											
18:00	20:00	22:00	00:00	02:00	04:00	06:00	08:00	10:00	12:00	14:00	16:00												
18:00																							

Comments: _____

NIGHT 14

DAY

NIGHT

DAY

18:00	20:00	22:00	00:00	02:00	04:00	06:00	08:00	10:00	12:00	14:00	16:00
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18:00

Comments:

Appendix 3: Sleep Hygiene tips

Box 1 Sleep Hygiene and healthy lifestyle measures to prevent insomnia

- Regular moderate aerobic exercise helps to reduce pre-sleep anxiety and overall sleep quality evidence varies for duration and frequency of exercise sessions- three to four times per week, from 10 through to 50 minutes per session[50, 52, 53];
- Avoid exercise within four hours before going to bed[51];
- Smoking cessation, or less preferably-avoid nicotine within six hours of bedtime if unable to abstain completely[55, 56];
- Drink alcohol only within recommended limits: maximum 14 units per week, spread over three or more days, avoid within six hours of bedtime[58];
- Increase daytime natural light exposure[20];
- Avoid large meals near bedtime[82];
- Reduce the number of caffeine containing drinks consumed throughout the day, consider complete elimination and switch to decaffeinated products or no caffeine after midday[57];
- Avoid day time napping and have a wind-down hour prior to bedtime.[5] Practice relaxation techniques before bed such as deep breathing, progressive muscle relaxation, relaxation tapes or yoga;
- Only use the bedroom for sleep, sex and getting dressed[21];
- Create a sleep environment in the bedroom- dark, quiet, no TV, phones or clock, set a comfortable temperature[21];
- Set a regular wake time 7 days a week, only go to bed when you feel sleepy[21];
- If unable to sleep for what feels like more than 20 minutes get out of the bedroom. Find a comfortable place in the house and try reading, having a light snack or do some quiet activity. Do not attempt alerting activities such as household chores, office work, watching television, using your mobile phone or work/play on the computer, but try to find something relaxing you can enjoy. Only return to bed when you feel sleepy. If you are still not sleeping after 20 minutes, get up again until you feel sleepy;
- Avoid clock-watching to see how long you have been awake. Turn it to face the other way.