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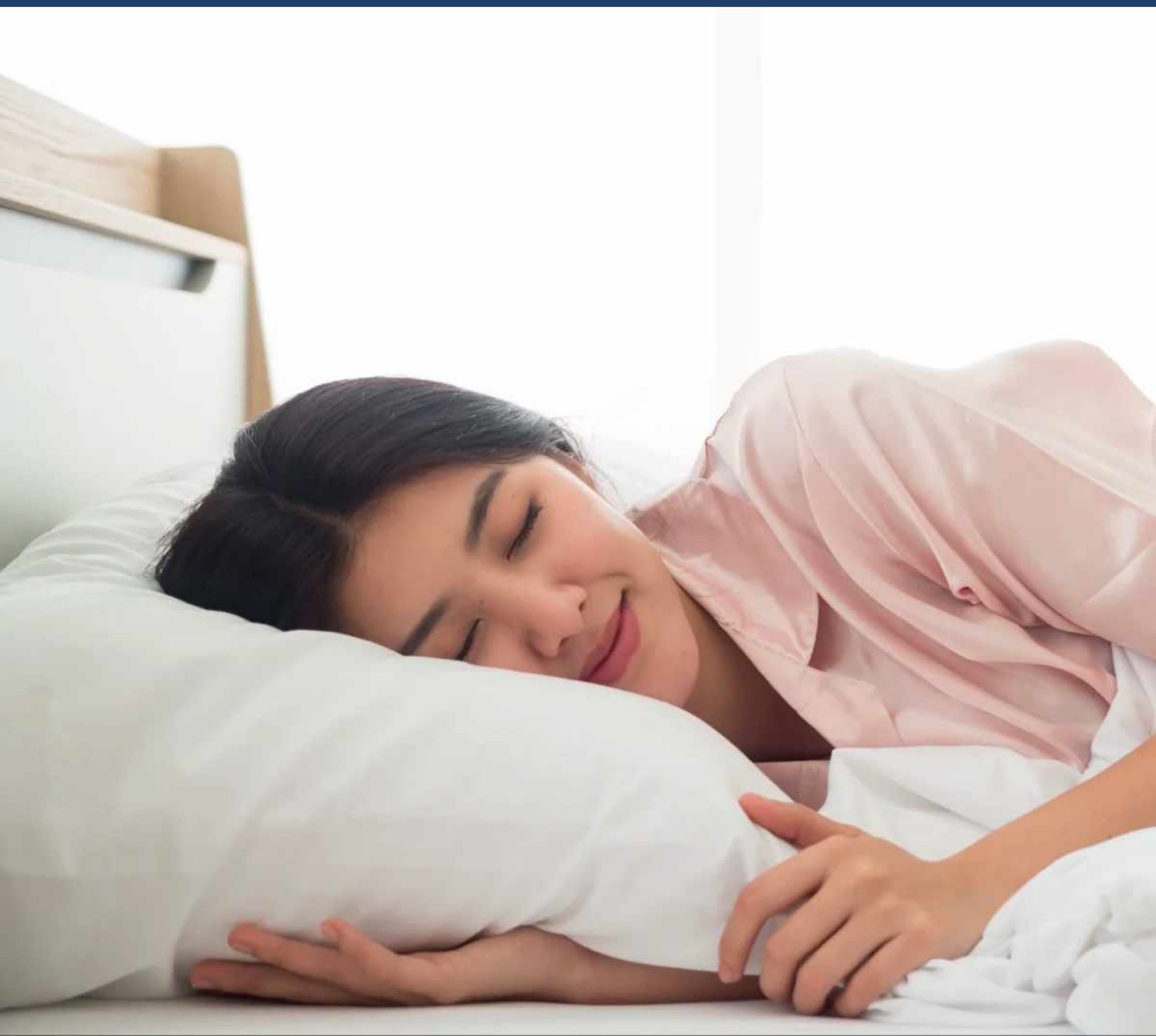
DO NOT SLEEP ON IT

An Experts' Consensus on the Impact and Management of Sleep Deprivation



EXECUTIVE SUMMARY

Sleep plays a crucial role in good health and overall well-being. Unfortunately, sleep problems constitute a global epidemic that threatens the health and quality of life for up to 45% of the world's population[1]. A multitude of factors, including biological and lifestyle factors, are associated with suboptimal sleep. Specifically, shift workers, females, individuals facing mental health issues and older adults are some of the groups identified to be at higher risk for sleep deprivation. Sleep deprivation refers to insufficient sleep or poor sleep quality due to sleep disorders or other sleep problems.

Past research highlights that poor sleep health puts individuals at serious risk of long-term health consequences such as neurodegenerative and metabolic diseases. Hence, early intervention of poor sleep health is vital. Non-pharmacotherapy such as cognitive behavioural therapy (CBT-I) is recommended as first line treatment, but its implementation may be challenging. Among pharmacological treatments, prescription medicines have been associated with negative side effects, while non-prescription supplements such as melatonin have more compelling safety profiles and should be considered.

It is vital to raise awareness on the importance of sleep health, especially given the inadequate knowledge among the general population. This experts' consensus aims to discuss the impact of sleep deprivation across regions and populations and the role of sleep supplements in human care.

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March 17, 2023
World Sleep Day
Sleep is Essential for Health

1. What is sleep health?

When it comes to sleep health, both sleep quantity and quality are important for a restful sleep.

Attributes of sleep health include[2]:

- **Sleep efficiency:** percentage of time spent asleep while in bed. (Target: 85% or more)
- **Sleep disturbances:** problems initiating and maintaining sleep.
- **Sleep latency:** time taken for a person to fall asleep. (Target: within 30 mins)
- **Sleep duration:** total amount of time asleep. (Target: 7 to 9 hours for young and middle-aged adults and 7 to 8 hours for older adults)
- **Wake after sleep onset:** total amount of wake time after sleep onset.

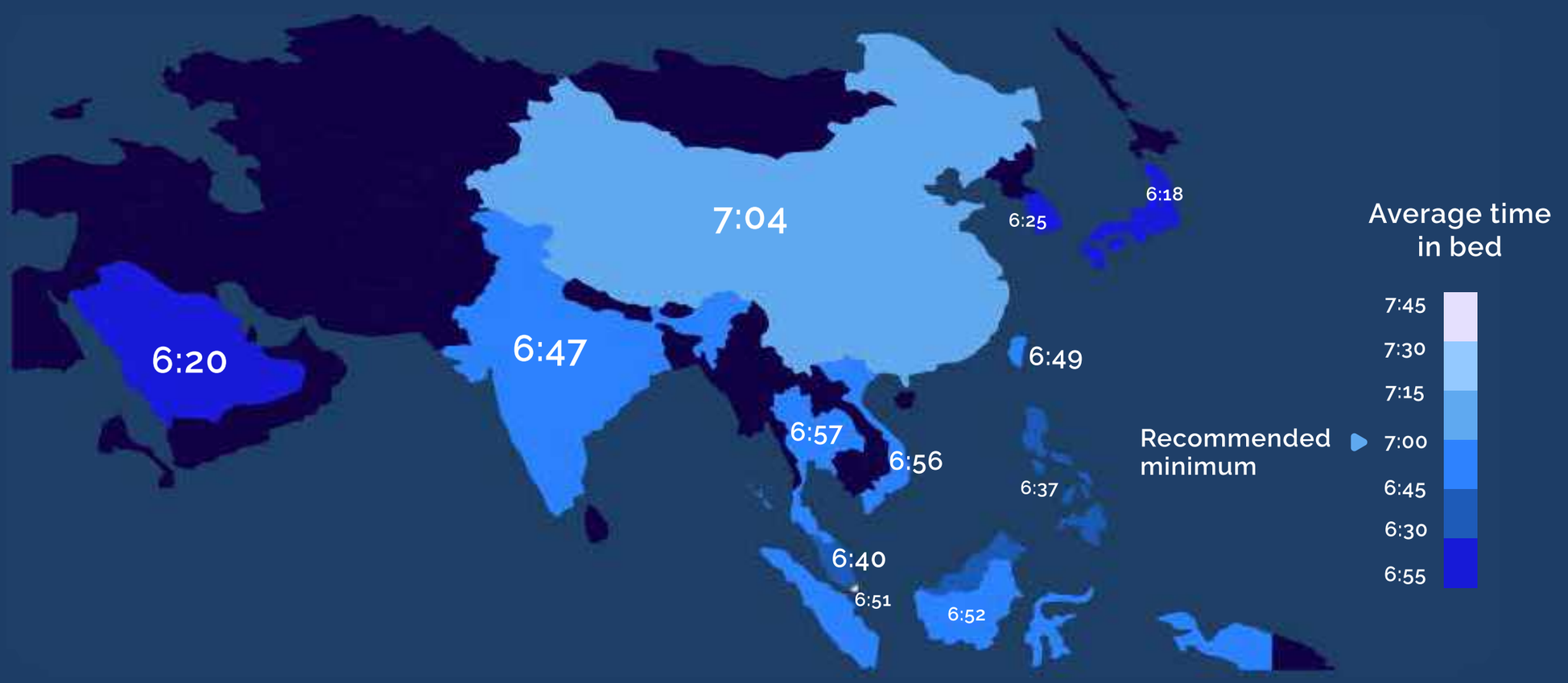
There is a multitude of domains associated with the measurement of sleep quality. Poor sleep consistency in sleep habits and circadian asynchrony (ie. not sleeping in rhythm with day night cycle for four hours from sunset and waking with sunrise) may also lead to poor sleep health. In clinical settings, the Pittsburgh Sleep Quality Index (PSQI)[3] is used to evaluate these components and assess sleep quality.

> It is not only sleep duration but the timing, depth and quality of sleep that also matters. This synchrony is the most important thing.
>
> *- Dr Joy Desai*

> It is important to set consistent bedtimes and wake times on both weekdays and weekends to allow for sufficient sleep.
>
> *- Prof June Lo*

2. The Epidemic of Insufficient Sleep

Average sleep duration in various countries in Asia



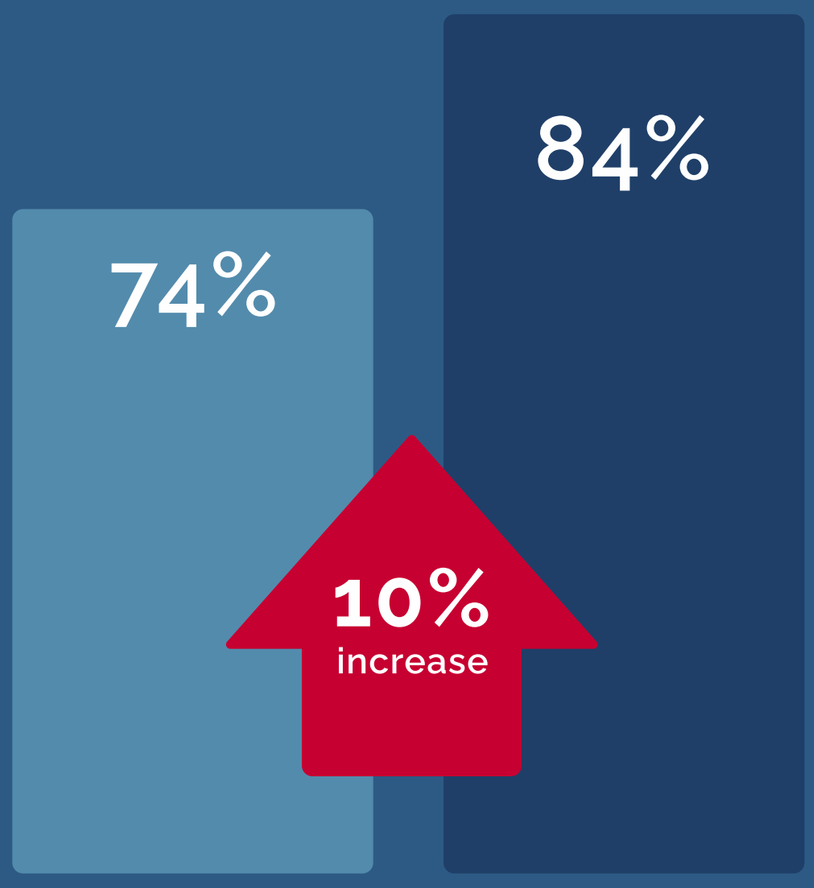
Individuals in Asia reported a shorter sleep duration as compared to individuals in Europe and Oceania[4] which could be a result of societal factors such as longer working hours, changes in work patterns or lifestyles. Sleep duration is also likely to be underreported due to the deep-rooted cultural stigmas against reporting illnesses in the Asian context.

Factors leading to shorter sleep duration include:

- Metropolitans versus rural areas[5,6]
- Weekday versus weekend
- COVID-19 pandemic[7]
- Electronic device usages

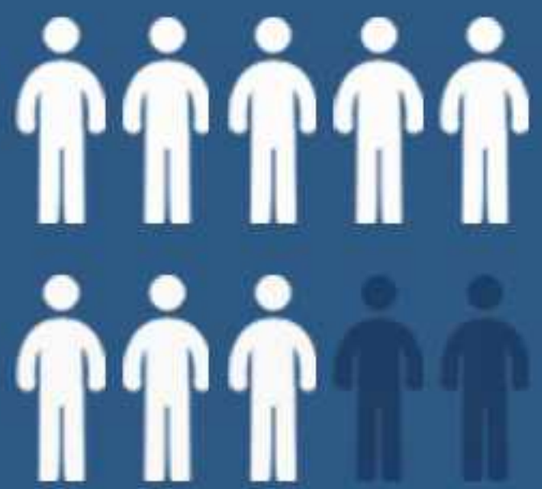
In fact, just two hours of exposure to blue light emitting devices before bedtime would result in a measurable reduction in melatonin production[8,9] and reduces sleep quality.

Significantly more people reported use of cell phone in bed compared to the previous year[7]



78%

of respondents in APAC reported that phone usage[7]



results in shorter sleep durations and falling asleep later than they would like to

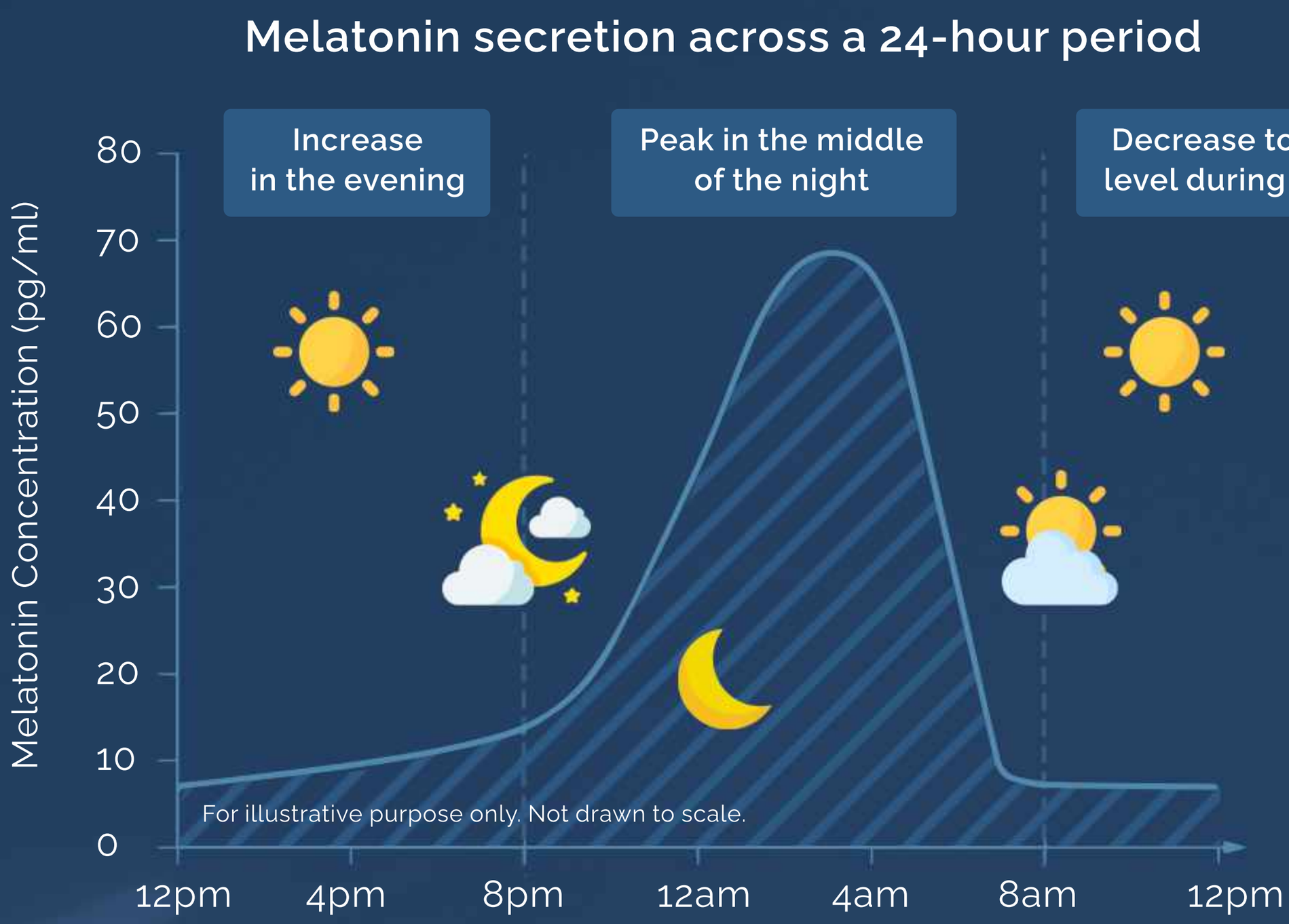
> There are obvious gaps among the population for achieving good sleep. Many individuals tend to perceive less than 6 hours of sleep to be sufficient, highlighting that there is a concerning degree of normalisation, or worse, 'glorification' of low sleep duration. - *Dr Harish Shetty*

Sleep issues are often grouped into categories, each with varying symptoms and behaviors. Some common types of sleep issues and their profiles are summarized in the table below:

	Sleep cycle disruption/ occasional sleeplessness	Insomnia	Para-somnias	Hyper-somnia	Sleep-related breathing disorders	Sleep-related movement disorders
Prevalence in population (global estimates)	30-36% [10,11]	15-18% [11-13]	17% (children) 3-4% (adults)[14]	4-6%[15]	18.1% (sleep apnea) 30.5% (all types)[16]	1.5-3% [17]
Symptoms	✓ = less common ✓ = very common					
Sleeplessness	✓	✓	✓	✓	✓	✓
Tired/drowsy	✓	✓		✓	✓	
Irritability	✓	✓		✓		
Snoring					✓	
Gasping/choking throughout the night					✓	
Headaches	✓	✓		✓		
Involuntary muscle movement			✓			✓
Hallucinations		✓				
Subtypes	Shift work, jet lag, irregular sleep-wake timing	Inability to fall asleep or stay asleep	Night terrors, teeth grinding, sleep walking	Long sleep, excesssive sleepiness	Snoring, sleep apnea	Sleep leg, cramps, restless, syndrome

> Individuals may be unaware that they have an underlying sleep disorder such as sleep apnea, and instead report great sleep based on incorrect parameters (ie. ability to sleep anywhere or loud snoring as an indication of good deep sleep) - *Dr Joy Desai*

3. Melatonin helps to regulate sleep/ wake cycle



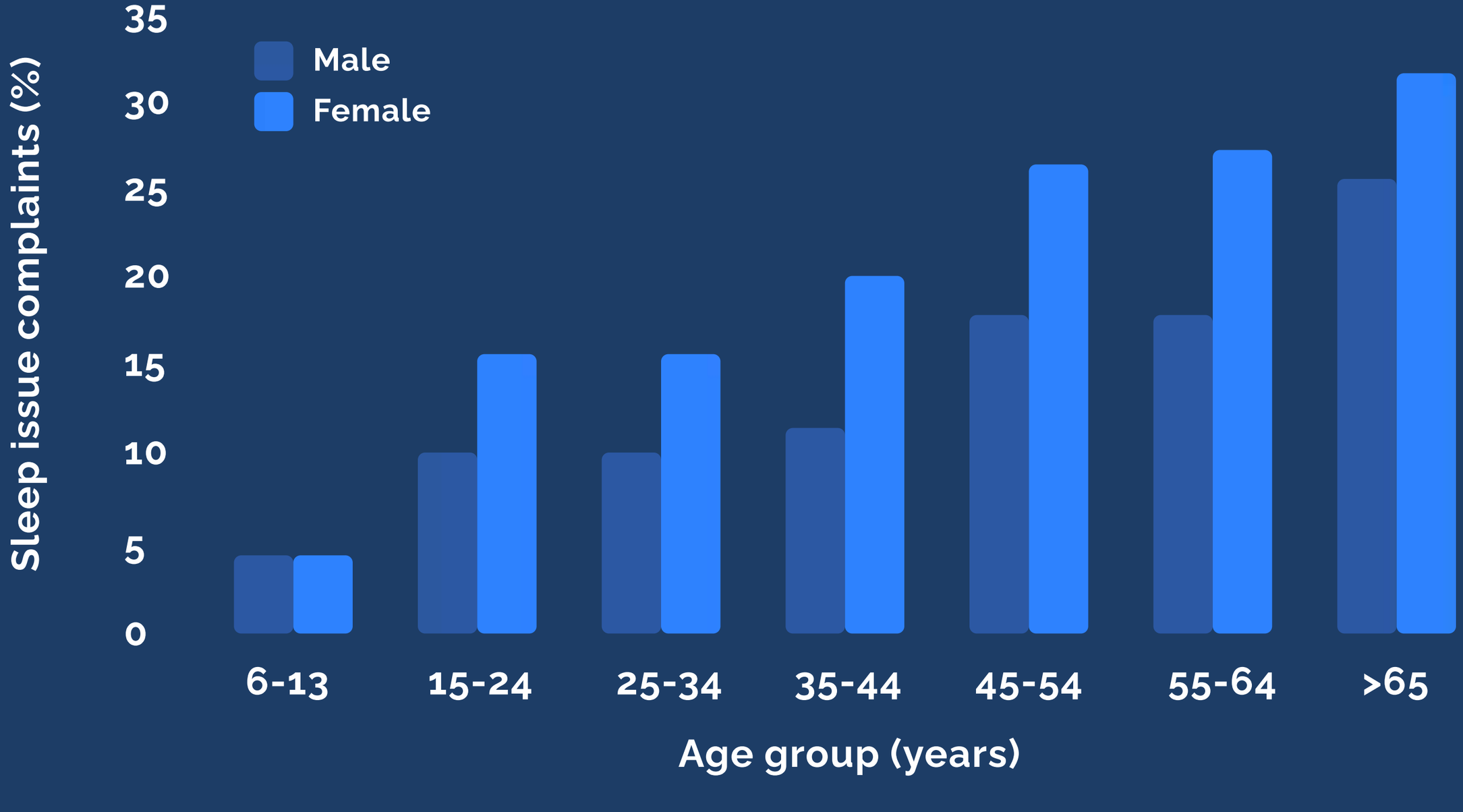
Melatonin is a natural sleep hormone that is released at night and increases feelings of sleepiness[18]. Its secretion is regulated by the suprachiasmatic nucleus in the hypothalamus, which receives information about light exposure and adjust the secretion of melatonin accordingly[18]. Melatonin secretion decreases in the morning and peaks at night when we sleep.

These changes in melatonin levels follow a roughly 24-hour cycle and play a key role in regulating our sleep-wake cycles[19]. Therefore, individuals with suboptimal or disrupted melatonin secretion may be at higher risk for poor sleep health.

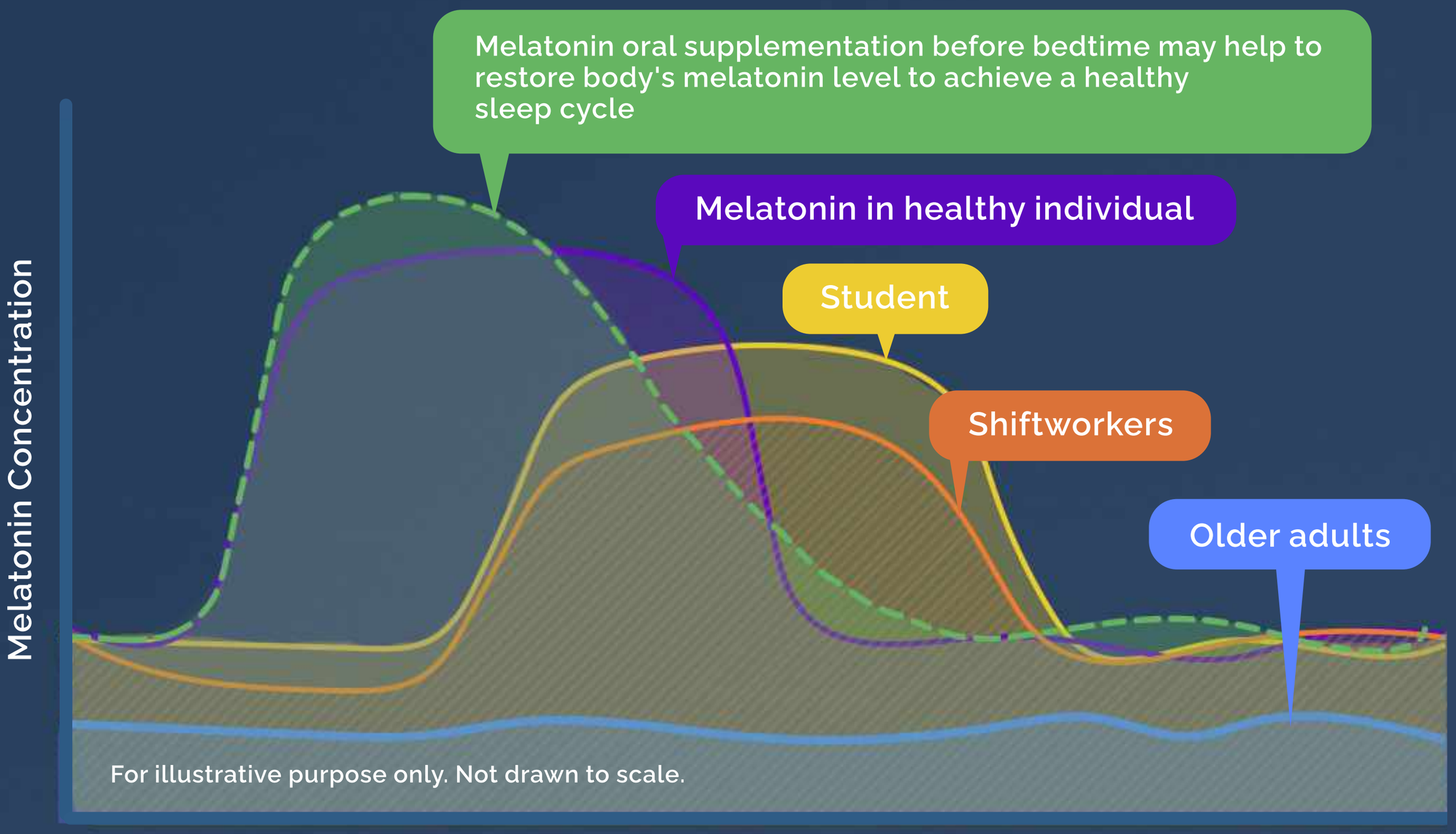
4. Who are at higher risk of sleep issues?

Certain groups of individuals are at higher risk for the development of sleep issues. While some risk factors are biological, others may be related to lifestyle choices. Some of these groups are typically associated with lower levels of melatonin secretion and/or dysregulation in their sleep cycle (ie. older adults). Insomnia prevalance is also significantly higher among females as compared to males as they are more likely to report sleep problems.

Prevalence of sleep issue complaints by age and gender[20]



Some population groups identified to be at higher risk of sleep deprivation are summarized below.



Older adults

An average adult, at age 30 years old, would have less than half melatonin levels as they did in childhood[20, 21]. Age-related decline in melatonin secretion is associated with insomnia prevalence.

Shift work workers

Night-shift work is associated with decreased melatonin secretion[22-24]. Shift workers who routinely change their shift schedule for consecutive days may have different sleep issues.

Students

Students may have poor sleep due to several factors, including stress, anxiety and/ or late nights[25].

Individuals with mental disorder

Individuals with depression and other mental disorders have abnormal melatonin secretion pattern, which may disrupt their sleep leading to worsening symptoms[26].

Individuals in abusive environments

Individuals who live in abusive households often experience chronic stress, which can interfere with sleep quality[27, 28].

Females

Higher rates of insomnia are reported among females. Attributing factors include biological differences and social and cultural disparities[11, 29, 30].

> It is especially important to note the significant role of external environmental factors on poor sleep. For example, if an insomnia patient is sitting in front of blue light emitting screen for an entire workday, and return home to abusive environments, it is essential to first seek help in resolving these underlying negative external factors in the environment as a main priority. - *Prof Keith Aguilera*

Intervention for sleep issues should be prioritised for those with high-stake professions (e.g. nurses, long-distance drivers) as a lack of concentration may unintentionally result in harm towards others.

Similarly, individuals with mental health issues also remain a priority as insomnia can exacerbate depression[31] and even increases suicide risk[32]. For these individuals, a multidisciplinary approach including sleep experts and mental health professionals should be considered.

5. The impact of sleep deprivation

Insufficient sleep is associated with a range of long and short-term consequences.

Poor sleep health is associated with:

- Slower and less accurate responses, poorer attention, and reduced inhibition[33,34]
- Impaired learning, and the encoding, consolidation, and retrieval of memory[35-37]
- Significant economic impact, due to poor work performances and absenteeism[38]

3x to 10x

the number of attention lapses [34,39,40]

2x

the odds of making placekeeping errors [34,39,40]

Consequences for the general population:

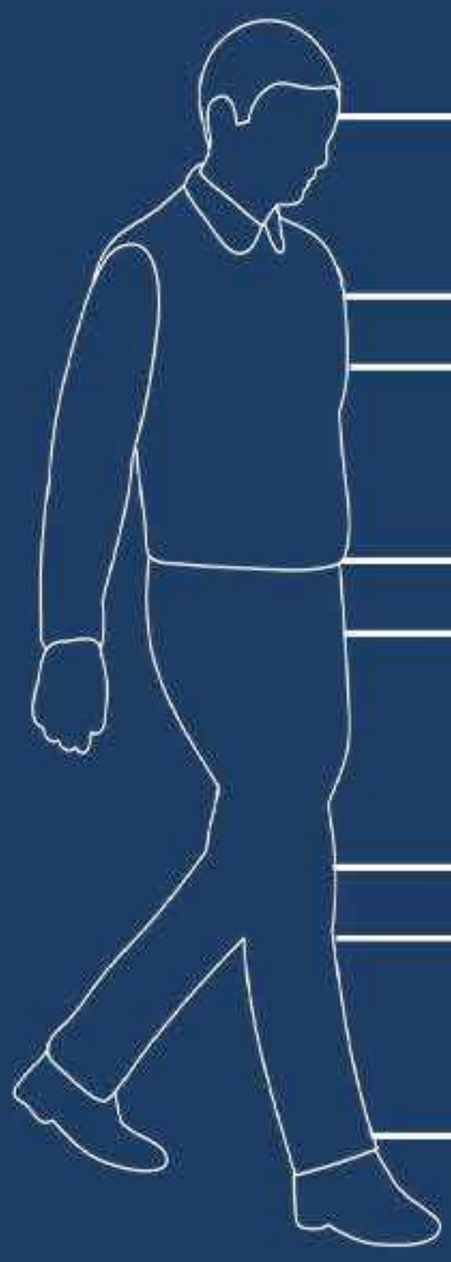
~20% of car accidents[41]

Healthcare professionals with moderate, high, very high sleep-related impairment:

Moderate	High	Very High
53%	96%	97%

...more likely to commit a clinically significant medical error[42]

Short sleep duration is also associated with several chronic health conditions:



Depression and anxiety
Perpetuates mental health issues namely depression and anxiety

Neurodegenerative diseases
Increased risk of Alzheimer's disease or dementia later in life[43]

Metabolic diseases
People with short sleep consume more calories particularly after dinner leading to obesity and diabetes[44-46]

Other chronic diseases
Such as cancer and cardiovascular morbidity and mortality[47]

> Raising awareness of the co-morbidities associated with poor sleep to the general public is important, as there are people with sleep issues who do not seek help. - *Prof Nevin Zaki*

6. Healthy lifestyle for healthy sleep: The science behind diet and exercise on sleep

Diet

Diet and nutrition may affect quality of sleep. Generally, a balanced diet consisting of a variety of fruits (ie. berries) and vegetables can provide the recommended daily intake of nutrients required for improved sleep[48].

Nutrients linked to improved sleep quality

- Mediterranean Diet[49]
- Dietary Approaches to Stop Hypertension Diet (DASH Diet)[50]
- Vitamin B6[51]
- Tryptophan[51,52]

Nutrients linked to reduced sleep quality

- High-carbohydrate meals with high glycaemic indexes[52]
- Energy drinks and sugar-sweetened beverages[25]
- High caffeine drinks e.g. coffee[53]
- Alcohol[54]

Exercise

Exercise has also been suggested to have beneficial impact on sleep quality[55,56]. This may be due to the release of neurotransmitters like endorphins, serotonin, dopamine, and norepinephrine which promote feeling of well-being. However, the timing of physical activity is important, it is recommended that exercise should be done at the latest, 4 hours before bedtime[48].

7. Intervention for sleep issues

There are various intervention options available for sleep issues. These include Cognitive Behavioural Therapy for Insomnia (CBT-I), mindfulness-based programs that can be in a in-person session or through a digital application platform, food supplements such as melatonin and prescription medications such as benzodiazepines or antidepressants. There are several advantages and disadvantages to each approach, and these are summarised below.

Summary of various interventions for sleep issue

Cognitive Behavioral Therapy for Insomnia (CBT-I)

Review of clinical practice guidelines for insomnia globally stated CBT-I as 1st line treatment

- Evidence suggested to be effective
- High barriers to access including limited trained personnel delivering CBT-I, time-consuming, expensive and low awareness
- A combination of sleep hygiene + pharmacological treatment (non-prescription and prescription) is typically used in actual clinical practice

Mindfulness-based Practices and Programs

Increasing use of mindfulness group sessions and digital app-based programs

- Potentially cost saving due to group sessions and incorporate elements of CBT-I
- App-based program, when paired with a wearable, may generate data on nature of poor sleep and tailor a solution based on individual needs
- Some evidence on effectiveness in addressing sleep issues
- Technology may not be accessible especially for the elderly and in rural area

Food Supplements (Non-prescription)

2nd line treatment when 1st line is not available, ineffective or declined by the patient

- Consumers prefer to have a quick fix
- Generally high preference among consumers to self-treat with non-prescription drugs or supplements first
- Examples: Melatonin, Valerian

Pharmacological Treatment (Prescription medicine)

- Prescription medicine may be associated with rebound insomnia
- Induces sedation or drowsiness by acting nervous system to make brain less excited
- May have undesirable side effects such as drowsiness, confusion, light-headedness, confusion, dizziness, and blurred vision
- May develop dependence
- Examples: Benzodiazepines, antidepressants

There is a general preference to self-treat with non-prescription sleep aids first[57] and melatonin can be an appropriate consideration due to its tolerable safety and efficacy profile.

Scientific evidence of melatonin supplements for sleep

Melatonin is a substance naturally produced in the body and the safety profile is well-established. A range of meta-analyses and systematic reviews of studies involving a wide range on population indicated that melatonin has a low toxicity, side effects and has no serious adverse events[57-59].

No difference in side effects [57-60]

The differences in the reports (headaches, dizziness, nausea, and drowsiness) were not significant.

Melatonin has a tolerable safety profile in various individuals

No serious adverse events[60,61]

There was no evidence related to the appearance of adverse effects.

Melatonin has no dependency[62,63]

No studies have reported any dependency or tolerance build to the supplementation of Melatonin.

Melatonin is effective at reducing sleep latency and increasing total sleep duration

2.5-34 mins

Reduction in sleep latency[63,64]

12.8-50 mins

Increase in sleep duration[63,64]

The efficacy of melatonin in reducing sleep latency and improving sleep efficiency has also been well-studied in different groups of population. The European Food Safety Authority scientific opinion on melatonin recommended that for the general population, 1 mg of melatonin should be consumed close to bedtime to reduce the time to fall asleep[62].

Use of prescription medication as sleep aids

The use of prescription medication as a sleep aid like benzodiazepines should be considered if non-pharmacological interventions and other non-prescription sleep aids are not helpful. One should however consider side effects like habit-forming and associated rebound insomnia[65].

It is also important for physicians to manage individual's expectations of sleep supplements as it may not be suitable for all of them. For example, due to its tolerable safety profile, melatonin may be recommended to older individuals, those with chronic diseases, or healthy individuals with occasional sleeplessness. However, those with concomitant mental health illnesses should seek help from mental health professionals. This highlights the importance for physicians to understand their patient's sleep physiology and the different biological factors and aetiology which contribute to the sleep issue and identifying right interventions in addressing all of them.

> Managing expectation is important when it comes to melatonin. Sleep issues might be different between patients so you will have to level with the patient when it comes to the treatment, and you have to make them understand what the issues there are at hand.
>
> *- Prof Keith Aguilera*

8. Conclusion

Poor sleep has multiple domains and is related to the duration, depth, and quality of sleep. There is a need for awareness in the community of what constitutes good sleep and the importance of the synchrony of duration, depth, and quality. Poor sleep has varying aetiology depending on the patient and affects a substantial proportion of people, leading to a significant burden individually and to the society. It is important to set consistent bedtimes and wake times on both weekdays and weekends to allow for sufficient sleep. Intervention for people with sleep issues should include a stepwise holistic approach starting with non-pharmacological intervention, non-prescription sleep supplements and then prescription medication. It is also important to manage individual's expectations of the intervention and multiple approaches may be required to provide holistic treatment for people with sleep issues.

This paper is intended for Healthcare Professional educational purposes only. The information provided reflects only the perspectives and opinions of the authors following an expert round-table discussion. The development of this paper was supported by P&G Health and Ipsos.

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