

# Sleep DownUnder 2024 Conference Review™

Making Education Easy

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### Abbreviations used in this review:

AHI = Apnoea-Hypopnea Index; CPAP = continuous positive airway pressure; OSA = obstructive sleep apnoea; PSG = polysomnography.



### Sleep DownUnder 2024 Conference Review™

#### Independent commentary by Dr Peter Solin

With 30 years in clinical sleep medicine, Peter Solin is a master clinician now dedicated to provision of clinical services, particularly to regional areas, while promoting easier access to sleep medicine for the under-resourced. After a cardiovascular research background, his PhD provided pivotal explanations for the cause of central sleep-disordered breathing in heart failure patients. Currently a medical director of two national and local sleep and respiratory clinical services, he enjoys the vibrancy of clinical medicine both at the individual level, and the broader sleep medicine community. This year Peter was energised by the breadth and depth of content at the ASA meeting.

## Welcome to our review of the 2024 Sleep DownUnder Conference held on the Gold Coast, Australia.

This year's conference showcased a rich programme dedicated to the full scope of sleep research, with a number of exciting updates that may substantially improve the sleep, health and lives of our patients. We begin with a comprehensive overview on the various treatments for restless legs syndrome, followed by a session which outlined the potential protective effects of intermittent hypoxaemia in OSA. The next presentation reveals the negative impacts of circadian rhythm disturbance on overall health, with higher mortality seen in those with irregular sleep cycles, and higher rates of diabetes among those frequently exposed to nightlight. We conclude with a presentation from this year's keynote speaker, with insights regarding the relationships between OSA, cardiovascular disease and diabetes.

I trust that this review will be interesting and clinically valuable. Your feedback is appreciated – we encourage you to send in your thoughts and comments.

Kind Regards,

**Dr Peter Solin**

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### Restless legs syndrome

**Speaker:** Prof Brendon Lee (Respiratory and sleep physician, Royal Prince Alfred Hospital)

**Summary/comment:** The 2024 AASM clinical practice guidelines were discussed and contrasted with the previous guidelines of 2012, where dopamine agonists (pramipexole and ropinirole) were classed as standard treatment. There has been a departure from the recommendation for the use of dopamine agonists, due to augmentation and tolerance. Augmentation refers to chronic use of dopamine agonists causing: 1) the earlier onset of RLS symptoms in a daily cycle, 2) a reduced latency to RLS onset when sedentary and 3) generalisation to the arms and body movements/trunk. Tolerance means that higher doses are required. In clinical practice, disinhibition and obsessive behaviour are further potential side effects in long-term users, and all patients should be warned of this potential (gambling behaviour, online engagement, sexual behaviour, etc). AASM guidelines recommend ensuring high-normal ferritin levels, with high-normal iron saturation. The primary treatment strongly recommended is alpha-2-delta ligands, which in Australia is gabapentin. Gabapentin does have potential adverse effects with dizziness, potential for weight gain and somnolence, and potentially respiratory suppression and sedation - particularly when combined with opioids. Therefore, care must be taken when respiratory suppression is at risk. Next in line are extended-release opioid formulations such as oxycodone, and this class does include methadone and buprenorphine. This clinician wonders whether American healthcare recommending a movement away from dopamine has more to do with individuals facing chronic use without sufficient monitoring, and lack of a drug holiday. It is acknowledged that dopamine agonists are in fact more effective than gabapentin. Therefore, physicians will need to be aware of these updated recommendations into the current Australian prescription environment. Our patients may already be aware through online forums.

**Symposium session: Year in review – sleep and neurology**

### Reflections by a pulmonologist on adaptive and maladaptive responses to intermittent hypoxia

**Speaker:** Prof Maria Bonsignore (Ospedale Riuniti, Villa Sofia-Cervello, Palermo, Italy)

**Summary/comment:** Hypoxaemia in obstructive sleep apnoea (OSA) is considered harmful, underpinning treatment for OSA by considering oxygen desaturation as a marker of poor health. However, recent discussions suggest that intermittent hypoxaemia, as seen in OSA, may have protective effects. Hypoxaemia activates the carotid body, reducing baroreceptor sensitivity and increasing sympathetic nerve activity, which triggers adaptive responses like hypoxic desensitisation at high altitudes. At sea level, repeated mild intermittent hypoxaemia has been shown to lower blood pressure in OSA patients. Interestingly, intermittent hypoxaemia may improve coronary collateral circulation, enhancing survival rates after coronary artery occlusion. Thus, hypoxaemia may not be a complete adversary, but could be seen as a conditioning factor, promoting adaptation and mitigating acute ischaemic events.

**Plenary: International keynote presentations**

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## Higher central circadian temperature amplitude is associated with greater metabolite rhythmicity in humans

**Speaker:** Dr Daniel Windred (Research Associate, Flinders University)

**Summary/comment:** Big data and wearable devices provide new insights into health, revealing the negative impact of circadian rhythm disturbances. Two important studies highlighted the importance of sleep regularity and a dark sleep environment for overall health. A prospective cohort study published in *Sleep* found that irregular sleep cycles significantly increase mortality risk. Irregular cycles mechanistically suppress circadian rhythm amplitude, with the most disturbed individuals experiencing the highest mortality rates, as tracked through wearables over a 3-year period and a 7-year follow up in UK national health registries. Similarly, a study in *The Lancet* found that exposure to nightlight increases the risk of type 2 diabetes. People with higher light exposure (below the 50th percentile) had a relative risk of approximately 2.0, compared to approximately 3.0 for those with the lowest exposure. This suggests a 50% increased risk of developing diabetes for those frequently exposed to nightlight over the next decade.

**Plenary: New investigator award presentations**

## Turning technological advancements into diagnostic advantages and introducing precision into sleep diagnostics

**Speaker:** Danny Eckert (Flinders University, Australia)

**Summary/comment:** In recent years, the focus on targeted therapy for OSA has grown, with the PALM scale emerging as a diagnostic-treatment tool. This composite measure includes four parameters:

P: Critical closing pressure of the upper airway

A: Arousal threshold (a destabilising factor)

L: Loop gain (reactivity to disturbances)

M: Muscle response (effectiveness of airway musculature)

New AI and auto-analysis algorithms are enabling better interpretation of traditional 'old' markers like slow wave morphology, K complexes and sleep spindles, alongside PALM data, to refine treatment strategies. With advanced computing and diagnostic algorithms, these measures may now be integrated into clinical decision-making. Therefore, these new candidate factors, combined with hypoxic burden and the above PALM measures, provide further nuance to specific 'tailored' treatments. Only now with powerful computing and diagnostic algorithms can they begin to be integrated into the decision pathway. It's feasible that with these newer measures, the traditional sleep study report (in 5 to 10 years' time) will look quite different, and have better predictive value for potential treatments, if not suggest treatment pathways.

**Industry lunch symposium: Temple Medical and Scientific**

## A global perspective on weekly and seasonal variability in sleep timing and duration

**Speaker:** Dr Bastien Lechat (Flinders University, Australia)

**Summary/comment:** Single-night sleep studies often misrepresent a patient's condition. The research has shown that a single abnormal study can misclassify disease severity. Repeated measurements from the sleep laboratory or wearable devices show that there is often an adjustment downwards in the amount of abnormality with repeated measures. Over successive nights, data often regress to the mean, revealing that what appears severe at one timepoint may be moderate or mild over time. This highlights the importance of clinical judgment and caution in interpreting one-time results.

**Symposium session: Rhythms disrupted - sleep irregularity characteristics, consequences and clinical implications**

## Symposium session: The orexin/hypocretin system: implications for sleep, wake and the ageing brain

**Chair:** Prof Ronald Grunstein (Head, Sleep and Circadian Group, Woolcock Institute of Medical Research)

**Summary/comment:** Despite the effectiveness of cognitive behavioural therapy, mindfulness and sleep restriction for insomnia, medication remains necessary for some patients. This session reviewed two orexin antagonists available in Australia: suvorexant (approved in 2014) and lemborexant (approved in 2019). Both show moderate evidence of effectiveness over 4 weeks and have favourable safety profiles, though side effects like morning somnolence, abnormal dreams and dry mouth are reported. Compared to benzodiazepines and Z-drugs, which remain the most effective for short-term insomnia, the orexin antagonists offer improved safety, though with somewhat reduced efficacy. The challenge with benzodiazepines and Z-drugs is their side effects (sedation, hangover and coordination issues), making their long-term use problematic. Therefore, orexin antagonists now occupy the space of reasonable effectiveness, with a better side effect profile.

## Next steps for cardiovascular clinical trials in OSA

**Speaker:** Professor Bhajan Singh (Sir Charles Gairdner Hospital, Australia)

**Summary/comment:** At what point can the Apnoea-Hypopnea Index (AHI) be relegated to a second-class measure of sleep apnoea severity? The AHI may no longer be viewed as the 'best' measure of OSA severity. A higher AHI can sometimes indicate more frequent but less severe events, with shorter durations and less pronounced desaturations. A better marker of severity is hypoxic burden, which quantifies the total time spent with oxygen saturation below baseline. This measure has a clear correlation with cardiovascular events, mortality, and the risk of heart failure and stroke. With advances in electronic analysis, hypoxic burden is becoming a more reliable metric and should be prioritised over AHI in assessing OSA severity. The time has come for this metric to be on the front page of a sleep study as a marker/measure of severity. Given the AHI is a flawed marker, going forward, what other better markers are there to define disease in sleep medicine? This question was addressed at a few sessions, and a few candidates emerged. Hypoxic burden, as mentioned above, can be more readily measured through electronic PSG analysis, and is defined by the period of hypoxaemia after an event, from a baseline measure. Although now calculable, a definition of hypoxic burden can only arise after a clear definition of the baseline is determined: is the baseline movable e.g. lower in REM, higher in non-REM, and positional - lower when supine. Another proposed marker is ventilatory burden, defined by the suppression of ventilation, or overshoot in ventilation in response to a perturbation. Again, this can be measured through electronic PSG analysis. It is probably a weaker marker of abnormality than hypoxic burden. Lastly, it is known that cardiovascular event risks are higher in OSA patients who are excessively sleepy. Therefore, differentiation based on symptom burden scores (comprising upper airway symptoms, disturbed sleep, morning symptoms and daytime sleepiness) predicts for cardiovascular events. Higher symptom burden scores correlate with disease. These new metrics are particularly useful in younger patients involved in OSA trials, which are currently dominated by older age groups. Other identifiable abnormality markers were also discussed during this and other sessions, e.g. incorporating arousals of lesser duration, and change in amplitude/morphology of the EEG such as spindles, etc.. Measures beyond the AHI are required!

**Clinical stream: Sleep and cardiometabolic disease - from populations to clinical trials**

## Drive awake, arrive alive: navigating the dangers of sleepiness in driving

**Chairs:** Miss Alisha Guyett (PhD Candidate, Flinders Health and Medical Research Institute) and Assoc Prof Nicole Lovato (Associate Professor Sleep Health, Flinders University)

**Summary:** It should be noted that insomnia is a risk factor in motor vehicle accidents, with a 2-3-fold increase in motor vehicle accidents (Garbarino 2017, Smolensky 2011) and this propensity towards accidents is also evident in a younger population with insomnia (Lin 2021). Therefore, in the treatment pathway for an individual with significant insomnia, road safety becomes an important factor for those particularly spending more time on the roads. Additionally, the combination of insomnia and sleep restriction, such as that experienced by shift workers, has a substantial further increase on road accidents. Consequently, road safety in major insomnia, particularly in shift workers, shouldn't be ignored. Preventing the drowsy driver from road accidents has been an ongoing theme for the last 20 years given that untreated sleep apnoea patients have a 3-7-fold increased rate of car accidents. Given that driving in industrialised countries is ubiquitous, there is an opportunity for intervention to reduce sleep and fatigue-related road accidents. But how can this be done? From a systematic review and meta-analysis, two markers appear to be the most sensitive for alertness or lack thereof. The first is PERCLOS 80, defined as percentage of time that the eyes are 80% closed, and the second is a high Karolinska sleepiness scale score (this is a quick, self-rated sleepiness scale). In this session, an excellent review was presented on ocular alertness biomarkers, and how they can reduce harm. One version of eye closure and eye movement tracking already exists in commercial driving environments. Future advances may integrate wearable sensors, providing data on head nodding, combined with lane keeping and steering inputs, to enhance eye current closure technology. What about a roadside test for sleepiness? This current science suggests that vestibular ocular metrics, if measurable (e.g. roadside virtual reality goggles or similar headset) could be developed for a useful roadside fatigue and sleepiness test.



## Sleep disturbance in patients with long-term neurological sequelae of COVID-19

**Speaker:** Ms Kathy Lung (Research Assistant, Neuroscience Research Australia)

**Summary/comment:** Kathy Lung et al. looked at individuals with neurological sequelae of a major covert illness, and then looked at whether measurable abnormalities during sleep were present. In this pilot study, long COVID individuals had increased arousability and were sleepy on MSLT, with higher ESS self-rated sleepiness and fatigue scales. However, there was no clear increase in OSA, and no major abnormalities in sleep architecture were found. This pilot study indicates that occult OSA is not the cause of sleep disturbance in long COVID.

**Poster presentations - Sleep breathing disorders: predictive factors and cardiac comorbidities**

## No mythical effect of moon cycles on sleep

**Speaker:** Dr Phuc Nguyen (Research Fellow, Flinders Health and Medical Research Institute/Flinders University)

**Summary/comment:** Doc Nguyen et al. took the interesting question as to whether the lunar cycle influences sleep. Taking measurements from 98,000,000 sleep nights worldwide, but predominantly in Europe, using wristwatch active sensors or under mattress sensors, there was no clear change in total sleep time adjusted for confounding variables such as AHI, demographic variables, the seasons, and weekday alterations. Therefore, the lunar cycle did not demonstrate a change in human sleep using these wearable/wearables.

**Poster presentations - Good sleep is one for the ages and stages – children, teenagers, parents, and shift workers**

## Can extending the time between last meal of the day and bedtime improve sleep regularity? A pilot study in Australian adults

**Speaker:** Dr Charlotte Gupta (Research Fellow, CQ University / Appleton Institute)

**Summary/comment:** Charlotte Gupta and colleagues looked at the question of whether the timing of the last major meal of the day influences sleep regularity. Given our propensity to go to bed later, and eat later, a protocol was established for time-restricted eating - here 10 hours between the first and last meal, and the last meal by 8pm. Unfortunately, no significant improvements in sleep regularity were found, although participants often were more mindful of the negative effects from eating late just prior to sleep time.

**Poster presentations - Take a deep breath - improving treatments, services and education for patients and practitioners dealing with sleep disorders**

## Obstructive sleep apnoea severity varies markedly across seasons: An analysis of in-home, objective sleep apnoea assessments

**Speaker:** Dr Bastien Lechat (Research Fellow, Flinders University)

**Summary/comment:** Bastien Lechat and colleagues analysed 70,000 participants with mild OSA utilising an under-the-mattress sensor over 3 1/2 years, and found that there was a significant seasonal variation in AHI, i.e. less sleep apnoea in summer, and more in winter. How could this be so? Some of the variability was explained by 1) ambient temperature i.e. deeper sleep in colder environments with less restlessness, and more broken sleep with higher ambient temperature, and 2) variation in sleep duration (less sleep over summer and more sleep over winter months). This multiple-night big data approach across the world provides a taste as to what new associations in sleep medicine can be found through these globalised recording methods.

**Poster presentations - Sleep breathing disorders: From epidemiology to clinical translation**

## Relationships between daily step count and sleep in over 30 million person-days of real-world longitudinal monitoring data

**Speaker:** Dr Phuc Nguyen (Flinders University, Australia)

**Summary/comment:** Phuc Nguyen and colleagues looked at under-the-mattress sensors, and a wearable step counter in the 70,000 participant cohort from around the world. Are we doing what's best and healthy for us? The data showed that 83% of individuals could not attain the ideal 7-9 hours of sleep per night and more than 8000 steps per day!

**Poster presentations - Sweet dreams? The challenges for improving sleep health in our communities**

## What can clinical cohorts, in particular the ESDA cohort, teach us about cardiometabolic risk?

**Speaker:** Prof Maria Bonsignore (Ospedali Riuniti, Villa Sofia-Cervello, Palermo, Italy)

**Summary/comment:** Maria Bonsignore talked over a few sessions about the learnings from the European Sleep Apnoea Database. In particular, the relationship between OSA with cardiovascular disease and diabetes were highlighted. OSA clearly is a toxic metabolic stimulus. OSA independently predicts for lipid levels. Sleep apnoea severity independently predicts for glycaemic health in non-diabetic subjects, and oximetry measures such as mean SpO2 and nadir SpO2 are important biomarkers of this relationship. Derangement in oximetry correlates with hyperlipidaemia prevalence, even after for adjustment for regional factors. The most profound impact on HbA1c in diabetics is in the severe desaturation OSA groups. These large longitudinal large data cohorts demonstrate a clear benefit with CPAP on glycaemic control and insulin resistance, independent of body weight changes, and a positive shift in overall metabolic markers. Tantalisingly, CPAP improves early cardiovascular disease such as coronary artery calcification (plaque volume measurements). Lastly, CPAP reduces HbA1c further than just weight loss. We were left in no doubt that severe sleep apnoea deserves effective treatment.

**Clinical stream: Sleep and cardiometabolic disease - from populations to clinical trials**

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