

Sleep Research Review



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Issue 10 - 2018

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Abbreviations used in this issue:

AHI = apnoea-hypopnoea index; **BMI** = body mass index;
BP = blood pressure; **CPAP** = continuous positive airway pressure;
HF = heart failure; **OSA** = obstructive sleep apnoea;
PSG = polysomnography; **REM** = rapid eye movement.

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Welcome to the latest issue of Sleep Research Review.

In this issue we report the substantial economic costs associated with inadequate sleep in Australia, the use of portable sleep monitoring to diagnose sleep apnoea in hospitalised patients with HF, and the potential risk of AF in patients with insomnia and/or frequent nocturnal awakening. Swedish investigators report that severe OSA during REM sleep is independently associated with early signs of atherosclerosis in women, Brazilian investigators report the high prevalence of overweight and obesity in commercial airline pilots, and Korean investigators report an association between poor sleep quality and obesity. Comments for this issue have been provided by Dr Peter Solin (Melbourne).

We hope you find these and the other selected studies interesting, and look forward to receiving any feedback you may have.

Kind Regards,

Dr Janette Tenne

Medical Research Advisor

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The economic cost of inadequate sleep

Authors: Hillman D et al.

Summary: This study estimated the economic cost of inadequate sleep in Australia for the 2016–2017 financial year. Data were derived from national surveys and databases, and costs (financial and nonfinancial) were expressed in US dollars. The estimated overall cost of inadequate sleep in Australia in 2016–2017 was \$45.21 billion. The financial cost component (\$17.88 billion) comprised direct health costs of \$160 million for sleep disorders and \$1.08 billion for associated conditions; productivity losses of \$12.19 billion (\$5.22 billion reduced employment, \$0.61 billion premature death, \$1.73 billion absenteeism, and \$4.63 billion presenteeism); nonmedical accident costs of \$2.48 billion; informal care costs of \$0.41 billion; and deadweight loss of \$1.56 billion. The nonfinancial cost (reduced well-being) was \$27.33 billion.

Comment: The prolific inventor Thomas Edison felt that sleep was a regressive and wasteful habit! Slowly but surely, this view of sleep is ebbing from the popular view of health. But sleep deprivation in its various forms remains a huge public health issue, with Americans getting two hours less of sleep presently compared to 100 years ago. The obesity epidemic is one likely offshoot of sleep deprivation. From the Sleep Health Foundation, the authors including economists have put a value on disorders of sleep to the Australian economy. An estimate from a Boston consulting group 14 years ago put this value at around 5 billion. Four years later this was updated to around 8 billion. The present estimate over the 2016–2017 fiscal year is a staggering 17.88 billion, representing over 1.5% of Australia's total gross domestic product. This calculation was derived from direct health costs, indirect health costs, absenteeism, workplace accidents, performance inefficiency, and the concept of 'absent-presenteeism' (showing up to work, but not being fully capable). Perhaps if Thomas Edison achieved more sleep than the 4–5 hours he was purported to get, maybe he would have invented AC (the world standard power grid) instead of pushing for the DC current (an inefficient power grid and relegated to history!).

Reference: *Sleep* 2018;41(8):zsy083

[Abstract](#)

Portable sleep monitoring for diagnosing sleep apnea in hospitalized patients with heart failure

Authors: Aurora R et al.

Summary: This study examined whether portable sleep monitoring with respiratory polygraphy can accurately diagnose sleep apnoea in patients hospitalised with decompensated HF. 53 hospitalised patients with decompensated HF underwent concurrent respiratory polygraphy and PSG. Both recordings were scored for obstructive and central disordered breathing events, and AHIs were determined. The correlation coefficient for AHI from the two methods was 0.94. The average difference in AHI between the two methods was 3.6 events/h. Analyses of central and obstructive AHIs showed strong concordance between the two methods, with correlation coefficients of 0.98 and 0.91, respectively. 89% of patients had complete agreement in the classification of sleep apnoea severity between the two methods.

Comment: The treatment of sleep disordered breathing in HF has had the rug pulled from under its feet with the SERVE HF trial indicating an increased death rate in those with predominantly central sleep apnoea treated by adaptive servo ventilation (4 per patient-year) compared to those with usual treatment (3 per year). Significant OSA and mixed sleep apnoea remains a major concern in this patient group nevertheless. Patients in hospital may have acutely deteriorated sleep disordered breathing. It is therefore still worthwhile identifying sleep disordered breathing? Can this be done adequately in a hospital environment using limited channel monitoring? These well-known authors can readily and consistently identify and classify sleep disordered breathing using a limited channel device. This approach can be used on the ward, and not in the sleep laboratory, to identify individuals who should be followed and/or offered treatment. The results are similar to HF patients studied in a clinic and ambulatory environment.

Reference: *Chest* 2018;154(1):91-98

[Abstract](#)



Associations of sleep quality with incident atrial fibrillation

Authors: Chokesuwattanaskul R et al.

Summary: This meta-analysis evaluated the association between sleep quality and atrial fibrillation (AF). A search of MEDLINE, EMBASE and Cochrane databases identified 10 observational studies (n=14,296,314) that evaluated the risk of AF in adults with short sleep duration, long sleep duration, insomnia and/or frequent awakening. Meta-analysis of the data found that neither short sleep (<6h) nor long sleep (>8h) was associated with an increased risk of AF. However, insomnia (pooled odds ratio, 1.30) and frequent awakening (1.36) were both associated with incident AF.

Comment: In patients with AF, the presence of symptomatic OSA makes it fairly easy for physicians to endorse treatment. The question is raised as to whether poor sleep on its own can influence the development of or presence of AF. In this meta-analysis of 10 observational studies there was a significant correlation between AF and insomnia and frequent awakenings. This study is largely in agreement with a similar review in Californian Americans observed over a 5-year period (including adjusting for OSA), and a similar study from China (adjusted for multiple variables but not specifically sleep apnoea). The proposed mechanism is that autonomic disturbance at night, with either broken sleep or insufficient sleep, is causing cardiac rhythm dysregulation. The implication for physicians is that we should engage individuals with poor sleep and AF, and time or further study will tell whether improving sleep quality can have an impact on occurrence of AF.

Reference: *Intern Med J 2018;48(8):964-72*

[Abstract](#)

Obstructive sleep apnea during rapid eye movement sleep is associated with early signs of atherosclerosis in women

Authors: Ljunggren M et al.

Summary: This Swedish population study investigated whether OSA during REM sleep is associated with early signs of atherosclerosis in women. In the community-based Sleep and Health in Women cohort study, 400 women underwent PSG, anthropometric measurements, blood sampling and BP measurement. Ten years later, 201 of them (who were free of known atherosclerosis at baseline and not using CPAP for OSA) underwent a high-frequency ultrasound of the common carotid artery to assess the individual thickness of the layers of the artery wall. Severe OSA during REM sleep (REM AHI ≥ 30) was associated with a thicker intima. This association remained significant after adjustment for age, BMI, alcohol, smoking, systolic BP, low-density lipoprotein cholesterol, C-reactive protein, and diabetes.

Comment: Scrutinising the polysomnogram, OSA in REM may show further drops in baseline oxygen, longer apnoeas and deeper desaturations. Compared to non-REM sleep, respiratory drive is further reduced in REM, with shallower breathing, further reduction in upper respiratory tract muscle tone, greater oxygen desaturations from a lower baseline, and reduced arousal leading to longer apnoea events. Is this worse-in-REM sleep apnoea type more deleterious? This Swedish group, with a well-known interest in female health and cardiovascular disease with respect to sleep disorders, has suggested that this phenotype indeed is more dangerous for cardiovascular deterioration. Previously they determined that intima media thickness correlated better with severe sleep apnoea during REM but not with sleep apnoea or oxygen desaturations on their own. This more focused evaluation in half of the original 400 women showed significant thickness in the intima of the common carotid artery, 10 years later. The message here is that more severe OSA in REM may be more harmful.

Reference: *Sleep 2018;41(7):zsy099*

[Abstract](#)

Excess weight in regular aviation pilots associated with work and sleep characteristics

Authors: de Souza Palmeira M & Marqueze E

Summary: This study identified the prevalence of (and factors associated with) overweight and obesity in Brazilian commercial airline pilots. 1198 pilots completed an online questionnaire that collected data on sociodemographics, work, health, lifestyle and sleep. Poisson regression analysis was used to determine the factors associated with excess weight. 53.7% of the pilots were found to be overweight and 14.6% were obese. Risk factors for obesity included working night-shifts for 6–10 years, having difficulty relaxing after work, sleeping <6h on days off, having other diagnosed diseases, and participating in <150 min of physical exercise per week.

Comment: The association between shift work, broken sleep, and reduced sleep time, and its effect on weight, is well established. One group of individuals that may not be seeing regular sleep physicians is the commercial pilot group. They have their own medical officers. There is a push in aviation for tighter scheduling and increased flying hours. Some shifts don't include the time it takes to get to the airport and into the cockpit! With our love of cheap airfares there is going to be continued if not greater pressure on pilots. Long haul pilots are particularly at risk of shift work follow-on effects, particularly if rest times and downtimes are not guaranteed. With this background, almost 1200 Brazilian commercial pilots were interviewed by questionnaire. Nearly 54% were overweight and over 14% were obese. The BMI results are not surprising. Being overweight was associated with working night shifts for 6 or more years, difficulty in relaxing after work, and sleeping less than 6h on days off. Thus questionnaire data again associates shift work and relative lack of sleep with obesity, this time in commercial pilots.

Reference: *Sleep Sci 2016;9(4):266-71*

[Abstract](#)

Association between sleep duration, quality and body mass index in the Korean population

Authors: Park S et al.

Summary: This Korean population study examined the association between sleep quality and BMI. 107,718 Korean individuals (63,421 men and 44,297 women) were assessed for sleep duration and sleep quality using the Pittsburgh Sleep Quality Index (PSQI). Compared to normal sleep and good sleep quality, adjusted odds ratios of short sleep, long sleep and poor sleep for BMI categories (underweight, overweight, obesity and severe obesity) were calculated. Short sleep duration (<7h) had a dose-dependent relationship with BMI categories from overweight to severe obesity, and an inverse relationship with underweight (adjusted odds ratios for underweight, overweight, obesity, and severe obesity versus normal weight were 0.88, 1.15, 1.31 and 1.70, respectively). Poor sleep quality was significantly associated with severe obesity in men, and with obesity and severe obesity in women.

Comment: Another study, although this time very large, through questionnaire of almost 108,000 Korean individuals, roughly 58% men, looking at sleep times correlating with bodyweight. Again there was a major dose-dependent relationship between duration of sleep and markers of BMI and obesity. There was a relationship between poor sleep quality with severe obesity in males. There was a relationship between poor sleep quality and obesity and severe obesity in the female group. It should be noted that in Asian populations BMI of 23 is regarded as the cut-off for normal weight. Therefore the classification of these groups is different from standard Caucasian delineations. BMI of 23 up to 25 is regarded as overweight, 25 up to 30 is obese, and greater than 30 is severe obesity.

Reference: *J Clin Sleep Med 2018;14(8):1353-60*

[Abstract](#)



Independent commentary by Dr Peter Solin, MBBS FRACP PhD

Dr Peter Solin is the medical director of the Sleep & Respiratory Group and a highly trained authority in sleep and respiratory medicine. Covering all facets of sleep medicine, he has a particular interest in the effects of cardiovascular and cerebrovascular diseases on sleep and performance, the impact of ill-health and infirmity on sleep, how medications interfere with sleep and rest, as well as unusual causes of fatigue and sleepiness, particularly in young adults. Dr Solin is also a dedicated teacher, educating medical students, GPs, as well as public and professional audiences. In recent years, he has delivered expert healthcare and sleep diagnostic services in more regional and remote centres, such as his program of home sleep testing through National Sleep Diagnostics.

RESEARCH REVIEW

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References: **1.** CIRCADIN® Product Information, 9 June 2016. **2.** Zisapel N. Sleep and sleep disturbances: biological basis and clinical implications *Cell Mol Life Sci* 2007;64:1174-1186. **3.** http://search.tga.gov.au/s/search.html?collection=tga-artg&profile=record&meta_i=153959 (Accessed 30th April 2018) **4.** EPAR. Assessment report for Circadin. *Procedure No EMEA/H/C/695* 2014.

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Effect of supplemental oxygen on blood pressure in obstructive sleep apnea (SOX)

Authors: Turnbull C et al.

Summary: This randomised, double-blind trial assessed the effects of overnight supplemental oxygen versus air (sham) on morning BP after CPAP withdrawal in patients with moderate to severe OSA. The primary outcome was the change in home morning BP after CPAP withdrawal for 14 nights. Supplemental oxygen virtually abolished the BP rise following CPAP withdrawal and, compared with air, significantly reduced the rise in mean systolic BP, mean diastolic BP, and median oxygen desaturation index after CPAP withdrawal. There were no between-group differences in subjective or objective sleepiness.

Comment: The physiological explanation for hypertension in OSA has been put forward as either hypoxaemia or intermittent hypoxaemia, or recurrent arousability. Although they may come down to common eventual pathways (raised sympathetic nerve activity), is one more important than the other? In this interesting study, oxygen supplementation reduced hypoxaemia, but left sleep disordered breathing largely intact. Patients were taken off CPAP, but one group had supplemental oxygen to abolish oxygen variability, the other was left breathing air (control). The study lasted 14 days. Patients still described similar subjective and objective sleepiness, and there was minimal effect on change in arousability by these two protocols. As the authors stated, supplemental oxygen largely abolished the morning rise in BP in individuals who had their CPAP withdrawn. This points the blame at intermittent hypoxaemia, and not recurrent arousals as the dominant injurious factor in morning hypertension.

Reference: *Am J Respir Crit Care Med* 2018; published online Jul 20
[Abstract](#)

Fixed but not autoadjusting positive airway pressure attenuates the time-dependent decline in glomerular filtration rate in patients with OSA

Authors: Marrone O et al., for the ESADA Network

Summary: This study examined the impact of fixed vs autoadjusting CPAP modes on estimated glomerular filtration rate (eGFR) in a large sample of patients in the prospective European Sleep Apnea Database cohort. Three groups of patients were evaluated: 144 untreated patients, 1178 patients using fixed CPAP, and 485 patients using autoadjusting CPAP. In the overall cohort, eGFR decreased over time. The rate of eGFR decline was significantly faster in patients with eGFR above median (91.42 ml/min/1.73m²) at baseline. The decline was attenuated or absent in the subgroup of patients with OSA receiving fixed CPAP. A follow-up duration exceeding the median (541 days) was associated with eGFR decline in the untreated and autoadjusting CPAP groups but not in the fixed CPAP group. Multiple regression analysis showed that eGFR decline was accentuated by advanced age, female sex, cardiac failure, higher baseline eGFR, and longer follow-up duration, whereas fixed CPAP had a protective effect.

Comment: In my experience, in patients with OSA unrestrained by cost, 70% would prefer an automatic CPAP unit, and 30% would be content with a fixed pressure approach. Thus in well-to-do individuals, there seems to be little to dissuade individuals from saving money and pursuing fixed pressure. This alarming study suggests that fixed pressure is better at maintaining renal function through the ageing process. About 1800 patients from the European Sleep Apnea Database cohort were followed, with a group of untreated OSA, a fixed pressure CPAP group, and an automatic CPAP group. Over a median of 541 days of follow-up, both the untreated group and the automatic CPAP treatment group had deterioration in eGFR, but this deterioration was largely ameliorated in the fixed pressure CPAP group. This association increased for individuals studied for longer than the 541 days. What do we make of this? Is fixed pressure better at controlling hypertension, autonomic dysregulation of glomerular microcirculation? More evaluations of the physiological benefits of automatic versus fixed pressure are clearly welcome.

Reference: *Chest* 2018;154(2):326-34
[Abstract](#)

Visually detected non-rapid eye movement stage 2 sleep spindle density at age five years predicted prosocial behavior positively and hyperactivity scores negatively at age nine years

Authors: Mikoteit T et al.

Summary: This study examined whether stage II non-REM sleep spindle density (SSD) at age 5 years predicts emotional and behavioural traits at 6 and 9 years. 19 healthy children aged 5 years underwent in-home sleep electroencephalogram (EEG) recordings for visual scoring of stage II non-REM sleep spindles. Their emotional and behavioural characteristics were then rated by parents and teachers at ages 5, 6, and 9 years. Higher SSD at 5 years predicted higher prosocial behaviour scores and lower hyperactivity scores at 9 years, independently of earlier prosocial behaviour or hyperactivity.

Comment: Digging into the neurological signals from sleep has pointed to the presence of sleep spindles as an important marker of neurophysiological activity. There is even a whole conference (Budapest Hungary 2018) on sleep spindles and related phenomena! In this study the density of sleep spindles in stage II non-REM sleep at the age of 5 years predicted better behavioural and emotional traits 4 years later. Prosocial behaviour traits (determined by parents and teachers) positively correlated, and hyperactivity (determined by teachers) negatively correlated.

Reference: *Sleep Med* 2018;48:101-6
[Abstract](#)

Sleep timing is associated with diet and physical activity levels in 9–11-year-old children from Dunedin, New Zealand: the PEDALS study

Authors: Harrex H et al.

Summary: The PEDALS study investigated sleep timing in association with diet and exercise levels in children aged 9–11 years in NZ. Sleep and physical activity data were collected using accelerometry, and food choices were assessed using a short food-frequency questionnaire. Participants were classified into 4 sleep timing behaviour categories using the median split for sleep-onset and sleep-offset times. Differences between sleep timing groups for weekly consumption of selected food groups and minutes of moderate-to-vigorous physical activity were examined. Children in the late sleep/late wake category ate less fruit and vegetables, and drank more sweetened beverages than those in the early sleep/early wake category. Children in the late sleep/late wake category also had less daily moderate-to-vigorous exercise than those in the early sleep/early wake category.

Comment: The question in this investigation was whether timing of sleep, as opposed to amount of sleep, also correlated with excess bodyweight and food intake choices. As a parent of teenagers, delayed sleep phase may come with reduced sleep times, and the grumpy teenager. This begs the question whether a pattern where earlier versus later sleep times plays a role. Four categories were determined. The group in late sleep and late to wake category made poorer nutritional choices, and were less likely to engage in vigorous physical activity. The important conclusion here indicated that the timing of sleep, after controlling for sleep duration, has an effect on food choices including sweetened foods, and less physical activity. The obvious question for parents is whether they can shift behaviours and sleep patterns, and is this effort worthwhile?

Reference: *J Sleep Res* 2018;27(4):e12634
[Abstract](#)



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