Message from President, ISSR

Dear Members,

In the second issue of ISSR Literature updates I am happy to release “Best of Sleep Medicine Jan-June 2015”. The literature updates are based on the search in Pubmed.

ISSR is thankful to Dr. Teofilo L Lee Chiong Jr. who has agreed to contribute literature updates on Sleep Disordered Breathing on a regular basis. ISSR is also thankful to Dr. Ravi Gupta for providing the literature updates on Insomnia and Restless Leg Syndrome. Dr. Tripat put tremendous effort in compiling this issue including studies from India and neighboring countries.

I hope our members will be immensely benefitted from this initiative. We will appreciate your valuable feedback on this. We look forward to your continuous support. Next issue will be released in Jan 2016 summarizing literature updates from July-Dec 2015.

Sleep well, sleep on time.

Dr. Hrudananda Mallick, MD, PhD
Dr Teofilo L. Lee-Chiong Jr., MD, is Professor of Medicine at National Jewish Health in Denver and at the University of Colorado Denver School of Medicine. He is also currently the Chief Medical Liaison for Philips Respironics. He has authored or edited 16 textbooks in Sleep Medicine and Pulmonary Medicine and has authored and co-authored more than 170 publications. In addition, he developed and serves as the consulting editor for the *Sleep Medicine Clinics journal*, while also serving as an editorial board member and reviewer of several other medical journals and publications.

He has served as the Chair of the Nosology Committee of the American Academy of Sleep Medicine (AASM), vice-chair of the Associated Professional Sleep Societies LLC (APSS) Program Committee since 2009, and Chair of both the Sleep Medicine Network and Sleep Institute Steering Committees of the American College of Chest Medicine (ACCP). He also has served on the Council of Governors for the ACCP.

### A. SDB and Road traffic accidents

Prevalence of falling asleep at the wheel was high in many European countries, with a Pan European average prevalence of 17%


### B. SDB and PAP Therapy

APAP was better at reducing sleepiness and costs and improving QALYs vs. best supportive care among older persons with OSA.


Using clinical data alone to initiate CPAP therapy for suspected obstructive sleep apnea had a high specificity but low sensitivity.

*Can CPAP be indicated in adult patients with suspected obstructive sleep apnea only on the basis of clinical data?* Nigro CA, Dibur E, Aragone MR, Borsini E, Ernst G, Nogueria F. *Sleep Breath. 2015 Jun 4.*

A trend towards improved adherence was noted when patients intolerant of high CPAP settings were switched to a bilevel device.

Low span range APAP settings (8-12cmH2O) were as effective in correcting AHI as high span APAP (4-15cmH2O) but were associated with higher treatment compliance.


Unlike poor adherers to CPAP therapy, most good adherers did not remove their CPAP device during changes in body position.

One---third of poor CPAP adherers removed their CPAP device within 4 h from the start of recording

Among poor CPAP adherers, number of body position changes during the first 4---h recording was higher in those who removed vs. those did not remove their CPAP device

Frequency of body position changes and oxygen desaturations were higher within 15 min before removal of CPAP than during other periods of CPAP use


Providing financial incentives to OSA patients in the first week of starting PAP use did not increase adherence to therapy.

**Web based access to positive airway pressure usage with or without an initial financial incentive improves treatment use in patients with obstructive sleep apnea.** Kuna ST, ShuQleworth D, Chi L, SchuQe---Rodin S, Friedman E, Guo H, Dhand S, Yang L, Zhu J, Bellamy SL, Volpp KG, Asch DA. *Sleep.* 2015 Jan 12.

Improvements in ODI and percentage of deep sleep during CPAP titration predicted greater persistent CPAP use in patients with OSA.


Claustrophobic tendencies were highly prevalent among persons with OSA treated with CPAP, and they negatively impacted adherence to CPAP therapy.

**Claustrophobic tendencies and continuous positive airway pressure therapy non--adherence in adults with obstructive sleep apnea.** Edmonds JC, Yang H, King TS, Sawyer DA, Rizzo A, Sawyer AM. *Heart Lung.* 2015 Mar--Apr;44(2):100---6.

CPAP therapy in persons with severe OSA improved job productivity and burnout symptoms, but had no effect on job stress.

OSA patients had similar total, higher night time and lower day time energy expenditure compared to controls; CPAP reversed the night--day time differences.


PAP device detected AHI agreed closely with data obtained from PSG and a PAP--AHI less than 10 supports good treatment efficacy.

Detection of upper airway status and respiratory events by a current generation positive airway pressure device. Li QY, Berry RB, Goecng MG, Staley B, Soto--Calderon H, Tsai SC, Jasko JG, Pack AI, Kuna ST. *Sleep*. 2015 Apr 1;38(4):597--605

### C. Obesity Hypoventilation Syndrome

42% of obese persons with OSA met criteria for OHS, and an elevated serum bicarbonate was a useful diagnostic feature.


Persons with obesity hypoventilation syndrome had a 2--fold increased risk of mortality and 1.86--fold increased risk of a cardiovascular event


### D. SDB and Respiratory diseases

Asthmatic had an increased likelihood of new onset OSA, with an adjusted relative risk of 1.39 compared to those without asthma.


Medical ward use of NIV improved ABGs in 82% of COPD patients with hypercapnic ARF who were all successfully discharged.


NIV with AVAPS was effective in improving day time and night time gas exchange in persons with
kyphoscoliosis and chronic respiratory failure


E. SDB and Patient Interface

Compared to conventional cushions, masks using customized cushions were associated with reduced force applied by the headgear and better fit

Clinical verification of patients with obstructive sleep apnea provided with a customized cushion for continuous positive airway pressure. Cheng YL, Hsu DY, Lee HC, Bien MY. J Prosthet Dent. 2015 Jan;113(1):29-34.e1

Switching from a full--face to nasal mask reduced residual RDI, arousal index, and required PAP settings in persons with OSA

Obstructive sleep apnoea and non--restorative sleep induced by the interface. Westhoff M, Lirerst P. Sleep Breath. 2015 Apr 16.

F. SDB and Prognosis

Persons with OSA had higher mortality, and incident coronary heart disease, strokes and chronic kidney disease compared to healthy controls.


A prospective cohort study demonstrated that CPAP therapy reduced mortality in older adults with moderate to severe obstructive sleep apnea.


Newly diagnosed obstructive and central sleep apnea in persons with acute heart failure was associated with higher mortality after hospitalization


OSA was associated with increased peak plasma troponin levels, more diseased vessels, and longer CCU stay among patients with ACS


CPAP therapy improved 5--year cardiovascular survival, but not cardiovascular event--free survival, in persons with first ever ischemic stroke and moderate to severe OSA.

Sleep disordered breathing increased mortality risk in chronic heart failure, and ASV significantly reduced all cause mortality, whereas CPAP did not.


G. SDB and Epidemiology

This study identified common comorbid disorders among hospitalized patients with OSA that provide potential targets for screening of this disorder.


Population based study reported a prevalence of moderate to severe sleep disordered breathing (≥ 15 per hour) of 23.4% in women and 49.7% in men.


H. SDB, Cardiovascular disease and Metabolic disorders

Intermittent hypoxia was associated with poorer glycemic control in patients with uncontrolled type 2 diabetes not treated for sleep apnea


In Japan, screening and treatment of obstructive sleep apnea was cost--effective for patients with diabetes mellitus or chronic kidney disease.


Risks for cardiopulmonary complications after general and vascular surgery were increased in OSA persons
who were untreated preoperatively with PAP.


Persons with type 2 diabetes had higher AHIs, more apneic events, and greater time with SaO2 <90% compared to controls.


I. SDB and Technology

Studies showed that analysis of snoring was accurate for diagnosing OSA, but the authors noted the need for more studies.


J. SDB and Alternative therapies

Transvenous phrenic nerve stimulation was effective in treating central sleep apnea and improved oxygenation, arousals, quality of life and sleepiness.


K. Central Sleep Apnea

ASV significantly lowered AHI, CAI, and OAI in patients taking high doses of opioids for chronic pain in prospective study.


ASV was better at improving AHI than CPAP at baseline and at 3 months in persons taking high-dose opioids for pain.


L. SDB and Role of Primary care

Primary--care follow--up management of OSA was less costly and had similar CPAP compliance compared to care provided by sleep units.

Role of primary care in the follow--up of patients with obstructive sleep apnoea undergoing CPAP treatment: a randomised controlled trial. Sánchez--de--la--Torre M, Nadal N, Cortjo A, Masa JF, Duran-
Home sleep testing was a reliable method, with high sensitivity and specificity compared to PSG, to diagnose OSA in children.


In malpractice suits involving adverse perioperative outcomes in patients with known or suspected OSA, 58% of verdicts favored the plaintiffs.


Out of 106 patients with chronic Insomnia coming to a multidisciplinary sleep lab, 42.5% suffered from OSA and 4.7% suffered from PLMD


Patients with STOP-BANG scores ≥ 5 had a fivefold increased risk and STOP-BANG scores ≥ 3 had a 'one in four' chance of having an unexpected intraoperative and early postoperative adverse events.


In patients intolerant to CPAP, palatopharyngeal reconstructive surgery is a cost-effective alternative.


Berlin and STOP-BANG Questionnaire are of limited value to screen OSA during the first trimester but of acceptable value during the second trimester.

Screening of obstructive sleep apnea during pregnancy: differences in predictive values of questionnaires across trimesters. Tantrakul V, Sirijanchune P, Panburana P, Pengjam J, Suwansathit
Duchenne Muscular Dystrophy patient’s treated with steroids have severe REM OSA which is influenced by BMI.


**Literature update on SDB from India 2015**

In 58 OSA patients, Severity of OSA as assessed by AHI scores does not correlate with retro palatal collapse as assessed by Muller’s maneuver

Correlation Between Retropalatal Collapse as Observed During Muller’s Maneuver to Severity of OSA. Suresh RK¹, Nair AB², Sreenivas V¹, Shilpa C¹, Abraham S¹, Nayar RC¹. Indian J Otolaryngol Head Neck Surg. 2015 Jun;67(2):135-7.

In 20 OSA patients one night of CPAP therapy reduced oxidative stress, improved anti-oxidant levels and decreased the severity of different components of metabolic syndrome


In 209 pregnant ladies, snoring and high risk on modified Berlin questionnaire are strong risk factors for gestational hypertension and cesarean delivery


In 100 patients with nonalcoholic fatty liver disease (NAFLD) prevalence of symptomatic OSA was low and OSA predicted fibrosis in NAFLD independent of obesity and metabolic syndrome

Obstructive sleep apnea is an important predictor of hepatic fibrosis in patients with nonalcoholic fatty liver disease in a tertiary care center. Agrawal S¹, Duseja A, Aggarwal A, Das A, Mehta M, Dhiman RK, Chawla Y. Hepatol Int. 2015 Apr;9(2):283-91.

The prevalence and incidence of OSA was found to be 28% and 88% in non-dialysis CKD patients respectively and the risk and severity of OSA increased with the progression of CKD stages


**Parasomnia**

A. REM Sleep Behavior Disorder

A case series of 3 patients with Insulinoma presenting with REM Sleep Behavior disorder. The authors suggest to monitor blood glucose levels during night and early morning in patients presenting with
abnormal night behavior


A study reported that patients with RBD who progressed to neurodegenerative disease reported family history of dementia and more autonomic and motor symptoms.


A study reported that Advanced age (hazard ratio [HR] = 1.07), olfactory loss (HR = 2.8), abnormal color vision (HR = 3.1), subtle motor dysfunction (HR = 3.9), and nonuse of antidepressants (HR = 3.5) identified higher risk of RBD progressing to Parkinson disease.


RBD was more common in Parkinson disease patients with longer disease duration and more severe motor and non-motor symptoms.


The study included 34 patients with PSG confirmed idiopathic RBD. It suggests that assessment of olfactory function particularly odor may predict development of Lewy body disease in idiopathic RBD over a short period of time.


This study suggest the possibility that development of RBD like symptoms in patients with Major Depressive disorder on antidepressant medications may be an early phase of alpha-synuclein neurodegeneration and not side effect of antidepressant medication.


This study is the first report of autonomic dysfunction as measured by Heart Rate Variability in isolated
Rapid eye movement sleep without atonia.


RBD in Parkinson disease is associated with increased risk of developing Impulse Control Disorders like pathological gambling, compulsive sexual behavior, compulsive eating and compulsive shopping.


The study reports that onset of sleepiness in idiopathic RBD predicts more rapid conversion to Parkinsonism and dementia.


Density of sleep spindles is altered in patients with RBD and should therefore be investigated as a potential marker of future neurodegeneration in these patients.

**REM sleep behaviour disorder is associated with lower fast and higher slow sleep spindle densities.** O’Reilly C, Godin I, Montplaisir J, Nielsen T. J Sleep Res. 2015 Jun 4. doi: 10.1111/jsr.12309. [Epub ahead of print]

This study reports developing a sensitive and quantitative, automatic algorithm to evaluate loss of atonia in RBD patients.


The study reported that PSG confirmed RBD is present in 88% of patients with MSA and more than half of the MSA patients reported symptoms of RBD before onset of motor deficit.


There are significant gender differences in demographics, associated comorbidities, and dream-related behaviors in patients with RBD. Female RBD patients reported significantly less behavior during dreams, but there was no significant gender difference in EMG activity during REM sleep.

The RBDSQ was administered to two independent samples of 52 and 75 consecutive PD patients investigated with video-polysomnography (vPSG). Main differences between both groups were that patients of sample A underwent a sleep history including RBD assessment prior to administration of the RBDSQ, whereas in sample B the RBDSQ was administered during routine work-up. In sample A, the RBDSQ identified 46/52 (88.5%) patients correctly. In sample B, 50/75 (66.7%) patients were identified correctly. Authors suggested that diagnostic value of the RBDSQ strongly depends on the clinical setting and may be influenced by the individual's awareness on RBD.


In 38 patients with Parkinsonism REM atonia index demonstrated low variability across two consecutive nights of PSG.


This study assessed diagnostic cutoff for the proportion of rapid eye movement (REM) sleep with tonic and phasic activities of the submentalis muscle activity that can be used to diagnose REM sleep behavior disorder (RBD). Cutoff value with the optimal sensitivity and specificity was 6.5% for the proportion of REMslee with tonic activity (sensitivity, 94.1%; specificity, 93.3%; area under the ROC curve, 0.976) and 9.5% for the proportion of REM sleep with phasic activity (sensitivity, 94.1%; specificity, 93.3%; area under the ROC curve, 0.992).


B. Sleep Related Eating Disorder

First-line treatment of idiopathic SRED includes selective serotonin reuptake inhibitors (SSRIs) at mean dosages of 20 to 30 mg/day. Topiramate at 100-300 mg/day and clonazepam at 0.5-2.0 mg/day can be alternative options.


C. NREM Parasomnia

I. Sleep Walking

In a prospective longitudinal study involving 1940 children, the authors reported strong familial aggregation for sleepwalking and sleep terrors. The author’s also reported that the prevalence of sleepwalking in parents predicted the incidence of sleep terrors in children.
This study reports that the alteration of slow-wave sleep during sleepwalking/sleep terror does not noticeably impact on sleep-related verbal memory consolidation.


This study reported 27 cases of "abnormal sleep related events" often associated with abnormal dreams, nightmares, or somnambulism with Varenicline drug. The authors suggest that Varenicline drug information should include sleep related harmful and potentially harmful events.


This study reported that in parkinson's disease and multiple system atrophy there is an amplitude reduction in the EEG 5-6 Hz band 40 seconds before NREM Parasomnia Behavior’s (NPB) arousal as compared to no-NPB arousals at F4 and C4 derivations (p<0.01).


**D. Enuresis**

This study reported that T&A significantly improved HRQoL in all children with SDB and NE, regardless of NE outcomes.


The study found increased PLMI and arousals in children with nocturnal enuresis and polyuria. The authors hypothesized for sympathetic and dopaminergic systems to cause both the disorders.


**E. Nightmares**

This study found strong correlation between nightmares at age 12 and psychosis at age 18. The authors suggest that presence of nightmares may be an early indicator of psychosis.
Circadian rhythm disorders of Sleep and Wakefulness

A. Delayed Sleep Phase Syndrome

This study included 9338 adolescents in the age group of 16-19yrs. It highlighted adolescents with DSP reported higher levels of depression, anxiety and ADHD symptoms and also exhibited significantly lower levels of resilience.


This study suggests 30 min bright light exposure in the morning along with afternoon melatonin an efficient way of phase advancing the circadian rhythm

Phase advancing human circadian rhythms with morning bright light, afternoon melatonin, and gradually shifted sleep: can we reduce morning bright-light duration? Crowley SJ1, Eastman CI2. Sleep Med. 2015 Feb;16(2):288-97.

Evening type chronotype, when compared with morning type chronotype, was significantly associated with diabetes (odds ratio [OR], 1.73; 95% confidence interval [CI], 1.01-2.95), metabolic syndrome (OR, 1.74; 95% CI, 1.05-2.87), and sarcopenia (OR, 3.16; 95% CI, 1.36-7.33) after adjusting for confounding factors


B. Free Running Circadian rhythm disorder

This study highlights that alcohol and lithium have opposing effects on behavioral circadian rhythms and individuals with bipolar disorder who are prescribed lithium and who drink alcohol might be inadvertently altering their sleep and circadian cycles, which may exacerbate their symptoms.

Alcohol and lithium have opposing effects on the period and phase of the behavioral free-running activity rhythm. Nascimento NF1, Carlson KN1, Amaral DN1, Logan RW2, Saggio JA3. Alcohol. 2015 Jun;49(4):367-76.

This case report highlights the combined use of light therapy in morning, melatonin at bed time and modafinil during day time to correct a free running circadian rhythm disorder in a sighted individual over a period of 3-4 weeks.

C. Jet Lag

Jet lag symptoms improved after transcranial bright light exposure for 3-4 days after reaching the destination.


D. Shift Work Disorder

This review focuses on health risks of night work and the underlying mechanisms for this relationship which can help us to devise strategies to minimize health risk with night work.


Insomnia and not excessive sleepiness is the cause for functional and cognitive impairments in shift work disorder patients.


The study reported that shift work without nights was associated with hypertension and the association was mediated by behavioral factors.


Five-repeat variant of the Period 3 gene show elevated levels of nocturnal sleepiness and earlier circadian phase compared with homozygotes for the four-repeat allele.

Length polymorphism in the Period 3 gene is associated with sleepiness and maladaptive circadian phase in night-shift workers. Drake CL1, Belcher R1,2, Howard R1,3, Roth T1, Levin AM4, Gumenyuk V1,5. J Sleep Res. 2015 Jun;24(3):254-61.

Dr Ravi Gupta joined the Department of Psychiatry, SMS Medical College, Jaipur as postgraduate trainee in 2000. During his residency program, he developed an inclination towards Sleep Medicine. However, its clinical transformation remained limited to the sleep disorders associated with Psychiatric disorders. In 2008, he left the academic position to pursue his interest in Sleep Medicine and started his own clinic in Jaipur with one Sleep-laboratory. In 2010, he was awarded the mini-fellowship from American Academy of Sleep Medicine.

He joined his present institute in 2010 and started the Sleep Clinic and Sleep-laboratory.

Presently, he is working as Associate Professor in Department of Psychiatry, Himalayan Institute of Medical Sciences, Dehradun and also the in-charge of Sleep Clinic and sleep laboratory.

Restless Leg Syndrome (RLS)

Acute stroke is associated with restless legs syndrome. However, the causative relationship between the two is unknown and requires further exploration.

One fourth of the patients with RLS suffer from peripheral neuropathy. They are older and have symmetrical symptoms as compared to RLS without neuropathy. Both respond to dopamine agonists.


Primary RLS does not increase the risk for cardiovascular or cerebrovascular events. However, secondary RLS does.


One fourth of the patients on maintenance hemodialysis have RLS. It is associated with oxidative stress. Serum 8-OHdG level predicts its severity.

**Association of restless legs syndrome with oxidative stress and inflammation in patients undergoing hemodialysis.** Higuchi T1, Abe M2, Mizuno M3, Yamazaki T1, Suzuki H4, Moriuchi M4, Oikawa O4, Okawa E1, Ando H5, Okada K4. Sleep Med. 2015. pii: S1389-9457(15)00746-7.

RLS is an early clinical manifestation of altitude related hypoxia.


One third of the RLS patients have daytime symptoms. Rotigotine may be a promising therapy in these patients.


Occult OSA is seen in patients with RLS and chronic insomnia.


RLS patients with painful symptoms have clinically more severe illness but lesser score on PLMS index.


**Insomnia**

Mindfulness aware practices intervention is better than sleep hygiene education in improving insomnia among elderly.

Mindfulness meditation and improvement in sleep quality and daytime impairment among older adults
with sleep disturbances: a randomized clinical trial. Black DS1, O'Reilly GA1, Olmstead R2, Breen EC2, Irwin MR2. JAMA Intern Med. 2015 Apr;175(4):494-501

CBT-I is efficacious in sleep maintenance insomnia in patients with osteoarthritis.


CBT-I helps in improving the subjective-objective sleep discrepancy and improving sleep.


Good sleep is a default state that can be manipulated by stress.

The development of insomnia or the plasticity of good sleep? A preliminary study of acute changes in sleep and insomnia resulting from an analogue trauma. Richardson C1, Gradisar M, Pulford A. Behav Sleep Med. 2015;13(1):19-35.

Integration of partner in CBT-I makes it more efficacious.

The role of perceived partner alliance on the efficacy of CBT-I: preliminary findings from the Partner Alliance in Insomnia Research Study (PAIRS). Ellis JG1, Deary V, Troxel WM. Behav Sleep Med. 2015;13(1):64-72.
The Indian Society of Sleep Research (ISSR) works to protect sleep health and promote high quality patient care. These goals are dependent on the support of the professionals working in the field. Membership with the ISSR funds the activities executed for the benefit of all who practice sleep medicine or conduct sleep research.

The ISSR works to improve sleep health through advocacy, education, strategic research and practice standards. Issue 1 of the *ISSR Newsletter* describes some of the new initiatives that are helping to achieve this goal.

The Society will have Life members, Regular members and Corresponding members. In addition to membership the members will receive subscription to-

1. Journal of Sleep and Biological Rhythm
2. ISSR Newsletter

We encourage you to become member of ISSR and members to renew their membership so that we have your support in continuation of the field of Sleep Medicine.

For more details on membership please visit [www.issr.in](http://www.issr.in)

### Professional Sleep Societies and Web links

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### Letter to the Editor:

**Dr. Tripat Deep Singh**  
MBBS, MD(Physiology), RPSGT, RST  
International Sleep Specialist  
(World Sleep Federation Program)

Our readers are invited to write to the editor regarding their views on the published material and also to contribute interesting content or updates in the field.

Email us on sleepwatching@yahoo.com.sg