Agenda for Asia-Pacific Economic Cooperation (APEC) 2017

Sleep Technology Agenda

by

Rayleigh Ping-Ying Chiang, M.D., M.M.S.
International Sleep Science & Technology Association (ISSTA), Berlin, Germany
Taiwan Institute of Economic Research (TIER), Taipei
Innovative Medical and Health Technology Center

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Part A. The contributions of Sleep Science and Technology to the industrial economy

Technoscientific developments could support the prime objectives of industrial reform and economic development, which is achievable provided that technology, professional talents and financial capital could complement each other in an orderly and efficacious dynamic. Such dynamism necessarily involves institutional innovation, an autonomous market, and coordinated utilization of scarce resources. The International Sleep Science and Technology Association (ISSTA) was established to promote a dynamic environment which could facilitate industrial reforms and economic developments. ISSTA was established with the following objectives.

1. To enrich the repertoire of talents in the field of sleep science and technology, and to promote cross-disciplinary applications of sleep science and technology through the recruitment of and collaboration between experts and researchers from disciplines other than medicine (e.g. engineering, industrial design, law, science & technology, business management, and leisure study and tourism).
2. To establish dialogues with major international organizations [e.g. Asia-Pacific Economic Cooperation (APEC), European Commission (EC), North American Free Trade Agreement (NAFTA), and World Health Organization (WHO)], and to advocate the importance of sleep science and technology as well as raising awareness about the hefty cost of ignoring the importance aforementioned.
3. To facilitate the cooperation between the industry, governments and the academia with the ultimate goal of promoting sustainable economic development and the common good of the world. This goal could be achieved through the means of improving workers' quality of sleep and their health in order to increase workers' day-time productivity so that economic and industrial developments can expand.

ISSTA has been synergizing the multidisciplinary domains of sleep technology. Experts and masters from 15 countries have consolidated their expertise and established a substantial multidisciplinary epistemic repertoire (i.e. documents) which can be coupled with effective analysis and control techniques (i.e. process) to show the advantageous domains of sleep technology as a promising industry. Currently, there is a lack of institutionalized platform and financial capital for ISSTA to industrialize sleep technology. However, Taiwan Institute of Economic Research (TIER) is able to create a niche for sleep science and technology among many industries in the global market. Here, we show an opportunity for countries in the Asia-Pacific region to pursue industrial reform which would place the industry, governments and the academia in a win-win situation.

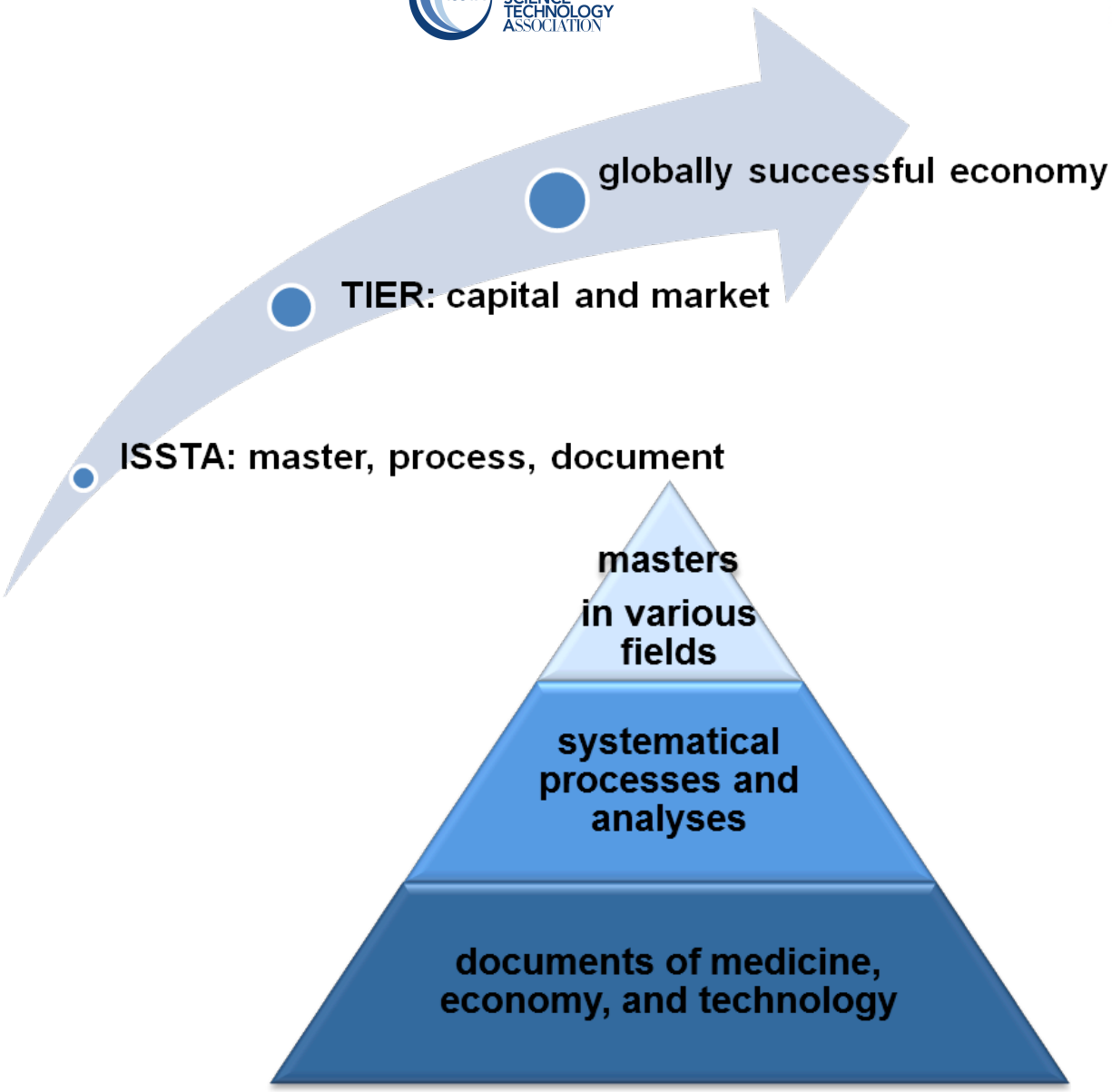


Figure 1. A blueprint for the global development of sleep science and technology: Integrating the resources of TIER and the ISSTA to promote and upgrade the industry

Part B. Conceptualizing the implications of sleep disorders in the context of preventive medicine

I. Sleep Disorder

In 2001, the International Mental Health and Neural Science Foundation launched the "World Sleep Day"; the goal is to promote the importance of sleep in populations worldwide. Sleep disorders have become a common health issue in modern societies, as much as 45% of the global population suffers from sleep disorders, according to the report being released by the World Association of Sleep Medicine (WASM) in 2011.

More than eighty types of sleep disorders have been recognized and categorized in the book "International Classification of Sleep Disorder, (2nd Ed.)" published by the American Academy of Sleep Medicine American Academy of Sleep Medicine (AASM) in 2005[1]. Sleep disorders include daytime sleepiness, apathy, and many other symptoms whose medical treatments involve various disciplines in medicine. For example, insomnia involves psychiatry; the restless leg syndrome involves neurology; the snoring problem involves otorhinolaryngology; the sleep apnea syndrome (SAS) involves cardiothoracic medicine; bed-wetting involves the pediatrics; bruxism involves dentistry. Sleep medicine is a special domain that concerns sleep disorders, which requires a multi/interdisciplinary managerial approach.

Sleep disorders may cause other diseases including:

1. Dysfunctional cognitive behaviors:
   Sleep disorders may cause attention deficits in children and affect their abilities in memory and long term learning. Studies have shown that 12.9% of teenagers (age 13~14) who performed worse academically also had the snoring problem during their childhood (age 2~6), which indicated a significantly higher percentage than those who performed well academically
2. Cardiovascular diseases:
   Obstructive sleep apnea syndrome (OSAS) may be the underlying mechanism of pathogenesis for cardiovascular diseases, such as stroke, and heart failure.
3. Stroke, and even death
4. Encephalopathy: degeneration of the cerebral cortex,
5. Metabolism diseases: such as diabetes
6. Sleep disorders in children:
   About 5% of the population in western countries suffered from OSA [2]; and in Taiwan, 4.5 million people shared the same health concern, according to the survey done by the Taiwan Society of Sleep Medicine (TSSM) in 2006. Sleep apnea can occur in any age group; studies have found the prevalence of OSA in: 1% of the pre-school children [3],[4], 2% and 3% of female and male middle-aged adults, respectively [5],[6],[7], and 11% of the elderly [8],[9]. The prevalence of OSA

increases dramatically with age. Sex difference constitutes another risk factor because the prevalence of OSA among teenage boys was found three times larger than the prevalence of teenage girls being diagnosed with OSA [10].

II. Sleep disorders can lead to chronic diseases (cardiovascular diseases, diabetes and metabolic syndrome):

Multiple and complex factors contribute to the onset of OSA, patients with OSA have poor sleep quality and OSA has been proven to be related to many diseases[11] :

Comorbidity of obstructive sleep apnea			
Comorbidity	Empirical support/evidence	Association ranking	Reference
Obesity	■ Consistent systematic meta-analyses	A	Young T, et al. [2] Young T, et al. [12]
Congestive heart failure	■ Consistent systematic meta-analyses'	A	Young T, et al. [12] Quan SF. el al. [13]
Hypertension	■ Consistent systematic meta-analyses ■ Cross-sectional analysis of prospective cohort studies	A	Nieto F, et al. [14] Richert A, et al. [15]
Congestive heart failure	■ Inconsistent systematic meta-analyses ■ Cross-sectional analysis of prospective cohort studies	B	Shahar E, et al. [16]
Coronary artery disease	■ Cross-sectional analysis of prospective cohort studies ■ Retrospective diagnostic cohort study	B	Shahar E, et al. [16]
Cerebral vascular incidents	■ Cross-sectional analysis of prospective cohort studies ■ Retrospective diagnostic cohort study	B	Shahar E, et al. [16]
Metabolic syndrome	■ Cross-sectional analysis of prospective cohort studies ■ Retrospective diagnostic cohort study	B	Punjabi NM, et al. [17] Vgontzas AN, et al. [18]
Cardiac arrhythmias	■ Case series	C	Punjabi NM, et al.

	■ Usual practice		[17] Vgontzas AN, et al. [18]
Diabetes	■ Retrospective cohort studies	C	Verrier Fi. et al. [19]

Reference：Hirshkowitz M, The clinical consequences of obstructive sleep apnea and associated excessive sleepiness, 2008.

Obesity is a high risk factor for cardiovascular diseases, and it is a proven comorbidity of OSA. The risk of obese middle-aged adults to have OSA is ten times greater than that of people with normal BMI [2],[12],[13],[20],[21],[22],[23] . There is a significant correlation between OSA and the cardiovascular diseases [14],[15],[16],[17],[18],[19],[24],[25],[26],[27],[28],[29],[30],[31].

	Cross-sectional (prevalence)		Prospective (incidence)	
	Unadjusted*	Adjusted†	Unadjusted*	Adjusted†
Hypertension	Yes[3,13,75]	Yes[3,13,75]	Yes[13]	Yes[13]
Dysglycaemia	Yes[76-78]	Yes[76-78]	Yes[78]	No[78]
Coronary artery disease	Yes[14]	Yes[14]	NA	NA
Heart failure	Yes[14]	Yes[14]	NA	NA
Cardiac arrhythmias				
Bradyarrhythmias	No[79,80]	No[79,80]	NA	NA
Atrial fibrillation	Yes[79]	Yes[79]	NA	NA
Ventricular ectopy	Yes[79]	Yes[79]	NA	NA
Cerebrovascular disease	Yes[11]	Yes[11]	Yes[11,12]	No[11,12]

Reference：Bradley TD, Floras JS. Obstructive sleep apnoea and its cardiovascular consequences. Lancet 2009;373:82–93

OSA involves the following pathophysiological mechanism: an increase in the ventricular load, hyperactivation of the sympathetic nervous system, and intermittent hypoxia, which increases the level of oxidative stress and inflammation leading to hypertension[14],[24],[25], coronary diseases[16], [26], the heart failure [6],[16], and the thoracic aortic dissection [27], [28] and other conditions. The chart below illustrates the mechanism in detail [31].

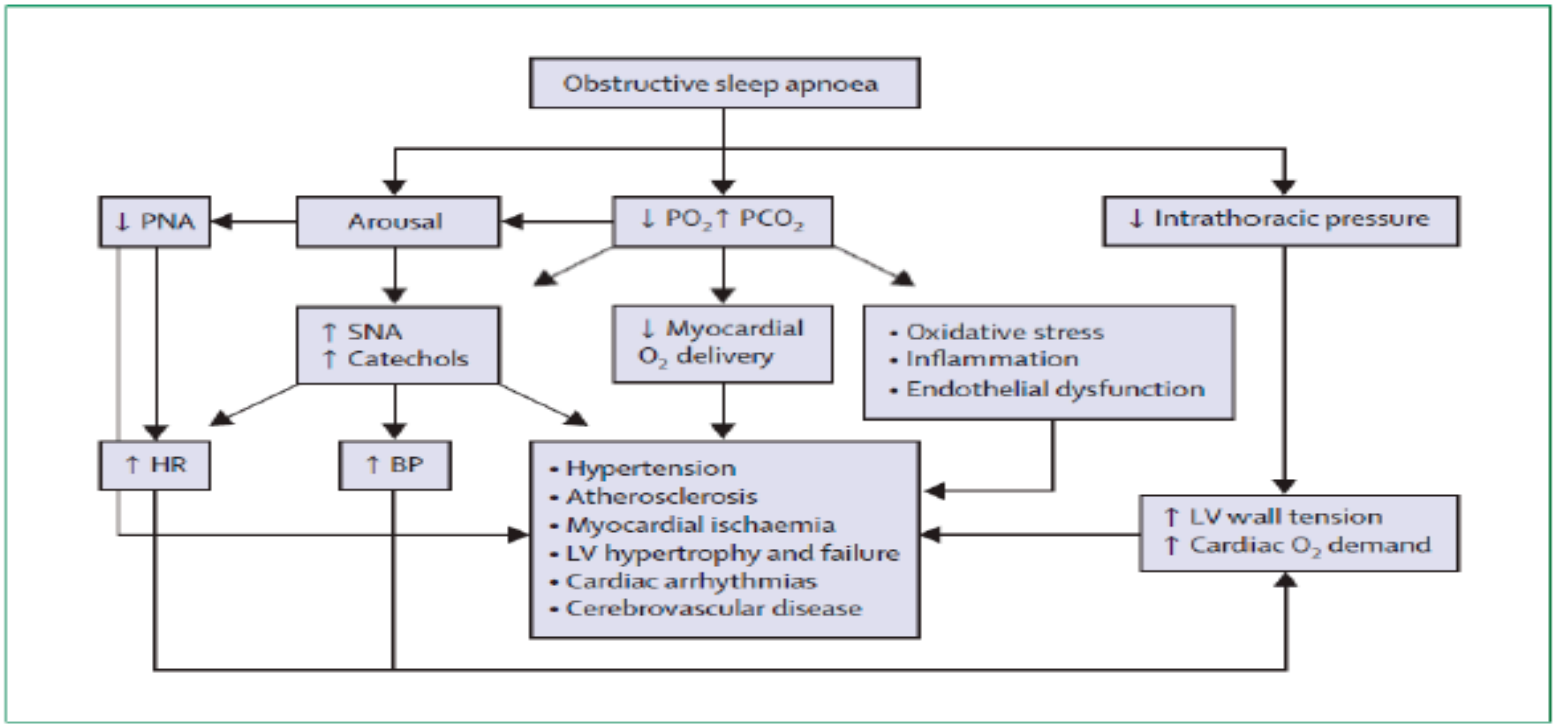


***Figure*: Pathophysiological effects of obstructive sleep apnoea on the cardiovascular system**
PNA=parasympathetic nervous system activity. PO_2=partial pressure of oxygen. PCO_2=partial pressure of carbon dioxide. SNA=sympathetic nervous system activity. HR=heart rate. BP=blood pressure. LV=left ventricular.

Lancet 2009; 373: 82–93

Reference：Bradley TD, Floras JS. Obstructive sleep apnoea and its cardiovascular consequences. Lancet 2009;373:82–93.

The National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure has listed OSA as

one of the ten major causes of the hypertension in 2003. Diabetes patients also have a higher chance of having OSA in comparison with non-diabetic people [11],[32],[33], [34],[35],[36],[37], therefore OSA is a common complication for patients with diabetes[38],[39],[40].

III. Sleep disorders and encephalopathy

OSA has also been regarded as a risk factor for stroke and even death [16],[24]. Patients with severe OSA and without proper treatments have a 3~4 times higher chance to suffer from lethal strokes than normal subjects [29].

ORIGINAL ARTICLE

Obstructive Sleep Apnea as a Risk Factor for Stroke and Death

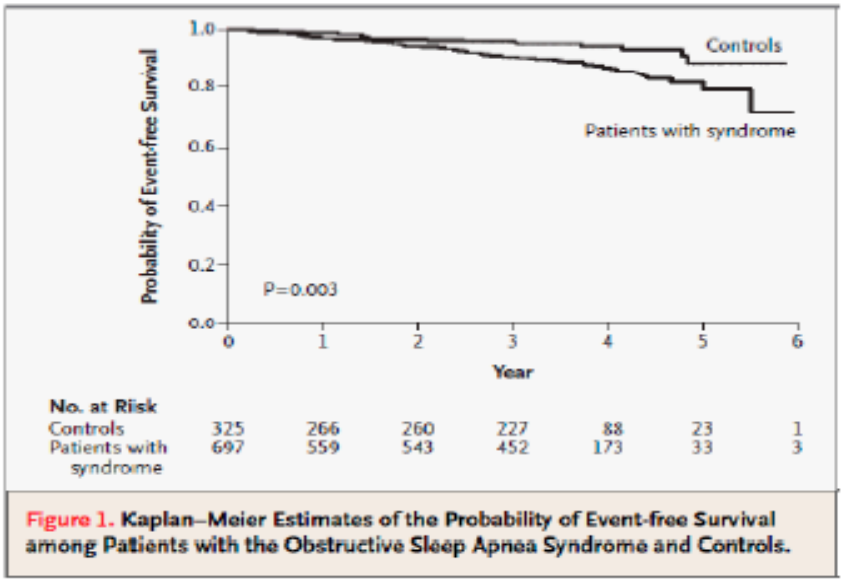


Figure 1. Kaplan–Meier Estimates of the Probability of Event-free Survival among Patients with the Obstructive Sleep Apnea Syndrome and Controls.

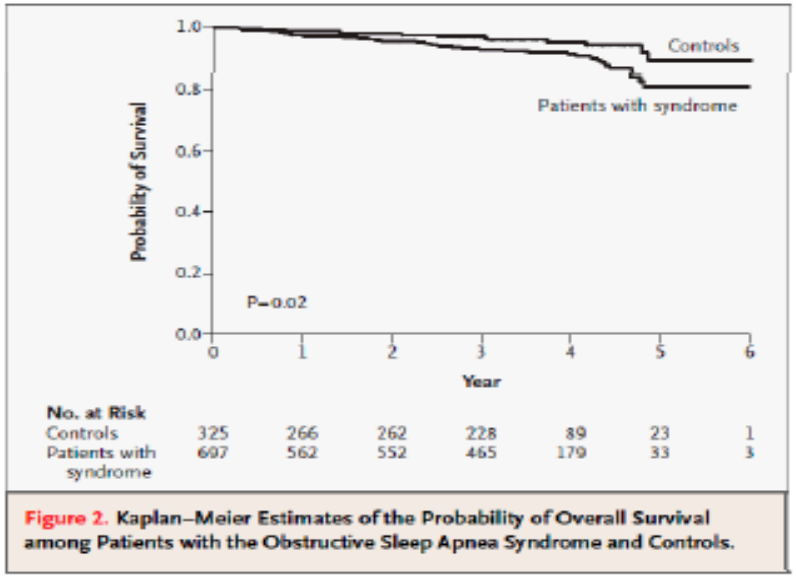


Figure 2. Kaplan–Meier Estimates of the Probability of Overall Survival among Patients with the Obstructive Sleep Apnea Syndrome and Controls.

N Engl J Med 2005;353:2034-41

Reference：Yaggi HK and K.W. Concato J, Lichtman JH, Brass LM, Mohsenin V., Obstructive Sleep Apnea as a Risk Factor for Stroke and Death. N Engl J Med, 2005.

OSA may result in damages of the nervous system [12],[13],[14],[16],[29]. The brains of OSA patients, according to studies that used magnetic resonance imaging (MRI), showed the loss of gray matter in multiple areas including the cortex area, the cerebellum, and the hippocampus. The cortex area is responsible for thinking, reasoning, language ability and perceptions. The cerebellum is in charge of coordinated movements and balance. The hippocampus is essential for the human faculties of memory and leaning ability. This indicates the correlation between the morphological change of the human brain and the degeneration of cognitive function in patients with OSA [41].

Consequences of obstructive sleep apnoea		
Effect	Magnitude(odds ratio)	Reference
Neurocognitive		
Motor vehicle accidents	7	Teran-Santos J, et al. [42]
Occupational accidents	2.2	Lindberg E, et al. [43]
Cardiovascular		
Prevalent hypertension	1.4	Neito F, et al. [14]
Incident hypertension	2.9	Peppard P, et al. [25]
Coronary disease	1.3~23	Shahar E, et al. [16] Hung J, et al. [26]
Stroke	1.6	Shahar E, et al. [16]
Congestive heart failure	2.4	Shahar E, et al. [16]

Reference: Atul Malhotra and David P. White, Obstructive sleep apnoea. Lancet, 2002.

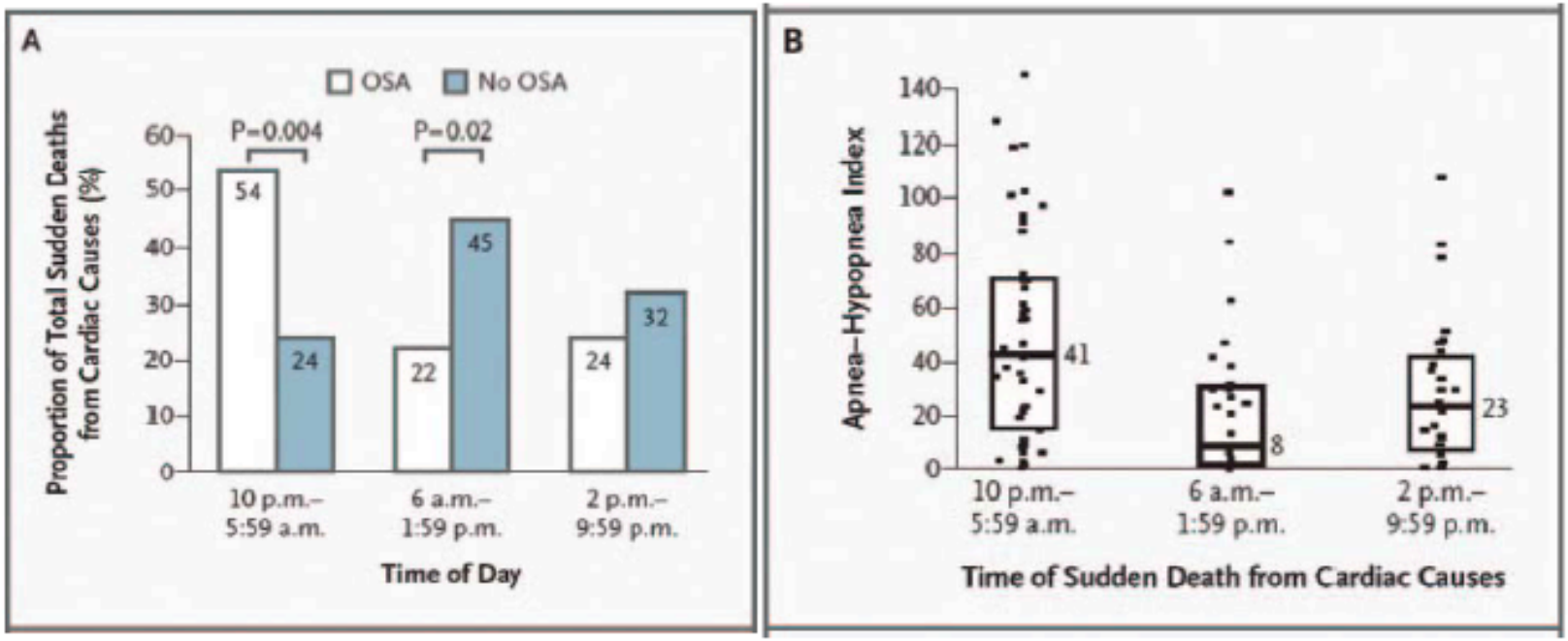
Patients with OSA have a reported lower quality of life [41], [44]~[48], and psychological problems, such as depression, anger, hostility and emotional disorders[49], [50].

Psychological variable	Sleep variable	Without covariates		With covariates of Age, BMI, HTN	
		Apnea	Nonapnea	Apnea	Nonapnea
Depression					
CESD	Deep sleep	+			
CESD	REM	+			
Anger					
BD experience	REM	+			
BD experience	RDI				+
BD expression	Hypoxemia	+			
BD expression	TST		−		−
BD total anger	Hypoxemia	+			
POMS anger	REM	+		+	
Mood disturbance					
POMS total	REM	+			
Vigor					
POMS vigor	TST		+	+	+
POMS vigor	Hypoxemia		−		

+, Positive correlation; −, negative correlation.

Reference：Bardwell WA, Berry CC, Ancoli-Israel S, Dimsdale JE: Psychological correlates of sleep apnea. Journal of Psychosomatic Research. 1999,

Sudden Death from Cardiac Causes According to Usual Sleep-wake Cycles



N Engl J Med 2005; 352:1206 –1214,

Reference：Gami AS, Howard DE, Olson EJ, Somers VK. Day-night pattern of sudden death in obstructive sleep apnea N Engl J Med 2005;352:1206-1214

IV. Waste of medical resources:

According to a study that compared the consumptions of medical resources by 181 patients with OSA over a ten-year period, patients with the OSA paid for medical rsources with an average of $3,972 US dollars per person whereas the control group paid an average $1,969 US dollars per person. Patients with OSA also required a longer period of hospitalization (an average of 6.2 nights per person) than those without OSA (an average of 3.7 nights per person). The study showed extensive and serious impacts of OSA: compromising personal quality of life and putting a heavy burden on families, society and the economy [51].

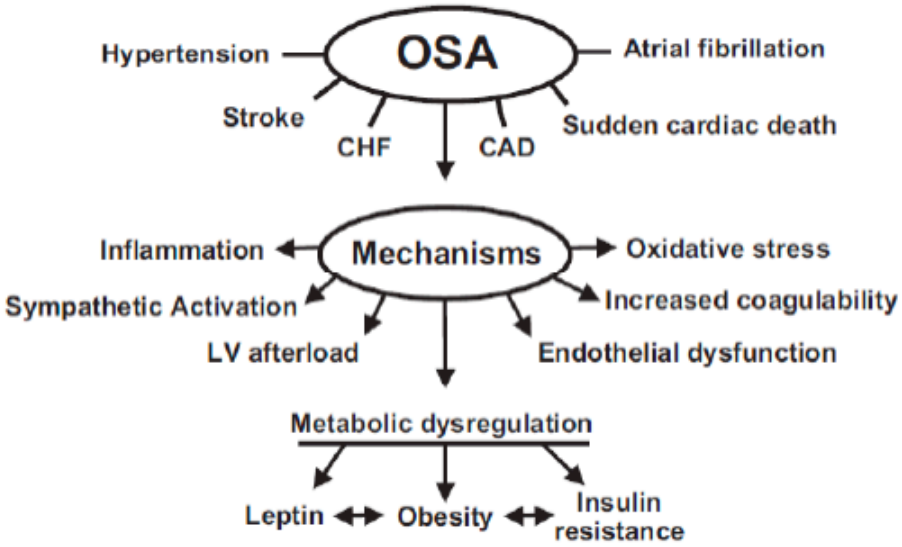


FIGURE 2. Association between OSA and cardiovascular disease; partial list of the disease mechanisms associated with OSA considered as possible links to several cardiovascular diseases and metabolic dysregulation. CHF = congestive heart failure; CAD = coronary artery disease; LV = left ventricular.

Reference：Lopez-Jimenez F, Sert Kuniyoshi FH, Gami A, Somers VK. Obstructive sleep apnea: implications for cardiac and vascular disease Chest 2008

The impact of insomnia

Sleep survey in Taiwan was performed every 3 year by Taiwan Society of Sleep Medicine since 2000. The prevalence of

chronic insomnia was 11.5% in 2006 and was elevated to 21.8 % in 2009. According to Taiwan Society of Sleep Medicine, the people who have sleep disorders constitute approximately a quarter of the total population in Taiwan (6 million people). The number of patients whose chronic insomnia involved more than 30 minutes to fall asleep and whose consecutive insomnia exceeded 1 month have reached 2.5 million. Mood disorder such as depression or bipolar disease has been the most common cause of insomnia. Primary insomnia without definite causes accounts for 20 percent of all insomnia cases. Insomnia due to psychological problems accounts for 40 percent of all insomnia cases. Other causes of insomnia are Circadian Rhythm disturbance, leg restless syndrome and obstructive sleep apnea syndrome. Women are 1.5 times more susceptible to chronic insomnia than men. This is because women's sleep architecture tends to be more susceptible to the influence of the sleep environment.

Insomnia is a very common problem in the elderly population. The surveys found that 42% to 47% of the elderly people in Taiwan suffered from various sleep disorders. Usually, people who experienced insomnia were also affected by the so called 'Three H diseases' (i.e. hypertension, hyperglycemia and hyperlipidemia). One in four insomniacs was affected by at least one of the 'Three H diseases'. Director Liang-wen Hang of Taiwan Society of Sleep Medicine said that the economic downturn and high unemployment rate have formed the main cause of the proliferation of the insomnia epidemiology. The surveys identified the problems that triggered insomnia: economy, work, family and health problems. The surveys showed that number of people who were affected by chronic insomnia and in poor health were 3.5 times greater than that of the people without insomnia. Insomnia patients ignored the relationship between sleep and health. Only 25% of patients indicated their intention to seek medical advice and treatment from physicians.

General Insomnia Statistics

•People today sleep 20% less than their predecessors did 100 years ago.
•More than 30% of the population suffers from insomnia.
•One in three people suffer from some form of insomnia during their lifetime.
•More than half of Americans lose sleep due to stress and/or anxiety.
•Between 40% and 60% of people over the age of 60 suffer from insomnia.
•Women are up to twice as likely to suffer from insomnia than men.
•Approximately 35% of insomniacs have a family history of insomnia.
•90% of people who suffer from depression also experience insomnia.
•Approximately 10 million people in the U.S. use prescription sleep aids.

Part C. Economic implications of sleep disorders

V. Issues on shift workers

Impacts on health, family relationships, vocational safety and work performance
(Rayleigh Ping-Ying Chiang & Jing Jun Liu, Economic Daily News 2012/03/21)

More than 30% of the working population in Taiwan is comprised of shift workers. Shift work can have profound impacts on workers in terms of personal health, family relationships, vocational safety and work performance. The establishment of organizations and protocols for sleep medicine is essential and we hope the authority could attach importance to this issue.

According to Dr. Rayleigh Ping-Ying Chiang (Attending Physician, ENT and sleep center, Hsin-Kong Memorial Hospital), 17.7% to 25.9% of the American population is comprised of second shift to third shift workers (from 2 pm to 6:30 am). There are a lot of shift workers in Taiwan as well. The prolonged night life results in an increase in the number shift workers in the service industry. Therefore, the prevalence of circadian rhythm sleep disorder will continue to expand in the population.

Shift workers can be classified into three major groups. Group I workers work the overnight (the third shift) over a long period of time, and they may initially suffer from insomnia. Workers in this group may feel sleepy during the night shift, but they tend to have difficulty in falling asleep during the day. There is a good chance that they would cause accidents at work. However, the problem is less prominent as it gets improved over time. Group II workers work the rotating shifts. Workers in this group can be further classified according to two types of shift work: clockwise shift and anti-clockwise shift. The clockwise shift begins during the day and followed by the evening hours and continues overnight. Hence, the health effect of the clockwise shift is relatively small. In contrast, the health repercussion of undertaking the anti-clockwise shift is more serious because of the drastic change from the first shift (day shift) to the third shift (overnight shift) in the absence of a transition. According to the results of surveys done in the US, people who worked the anti-clockwise shift got a 50% increase in the chance of causing a traffic accident when commuting for work. Anti-clockwise shift workers are more susceptible to strokes and other cardiovascular diseases due to the elevation of blood pressure caused by sympathetic and parasympathetic nervous disorders. Group III workers are those who work the second shift (night shift). They are prone to psychological problems in the long run. They tend to feel being isolated because they usually wouldn't have the opportunity to form adequate bonding with their families after they arrive home from work after the midnight. According to American studies, workers in this group have a 57% greater chance of ending up their marriage with a divorce.

Shift workers not only need to overcome sleep problems, but they also have to deal with the health repercussions of sleep disorders. This problem is particularly serious to the people who work the second shift and the third shift. The health issue at stake is concerned with the problem of oncogenesis that results from the inhibition of the free radical scavenging function in the human body due to the light-induced suppression of the secretion of melatonin in a well-lit environment. According to the US studies, female shift workers are 36% to 60% more susceptible to the risk of getting breast cancer in comparison with the susceptibility of the ordinary people. Female shift workers are four times more likely to develop duodenal ulcers than the ordinary people, and this group of workers also has a higher probability of having endometrial cancers. Male shift workers are more prone to prostate cancer and lymphomas (other than the Hodgkin's disease). These health issues need the attentions from government authorities, and the countermeasures to the aforementioned health concerns should be put in place as soon as possible.

Here, we present three examples of issues on the shift workers in different professions: nursing staff, workers in the manufacturing industry, and workers of a chemical plant. Taking a teaching hospital in southern Taiwan as an example [52], the participants of the study are a group of female nurses, aged from 20 to 45 years old; they have been working in hospital wards for more than a year. The result of the study shows that the third shift nurse's "workload" is significantly higher than that of the first shift staff. The third shift nurses have a higher fatigue index, and the proportion of workers who had experienced sleep problems is higher in comparison with the proportions of other groups. No significant difference was found between the three groups (the first shift, the second shift, and the third shift). However, there is a positive correlation between long-term sleep problems, stress and fatigue across the three groups. The positive correlation between fatigue and workload is present only among the first shift group. The night shift workers (inclusive of the second shift and the third shift) have a greater potential to be affected by sleep and fatigue problems because of physiological change and heavier workload that they have to endure. Therefore, it is necessary to promote the health of nightshift workers through the provision of health check-ups and activities for promoting workplace health.

The survey research on shift workers in the manufacturing industry [53] incorporated a sample of respondents being enlisted in the business directory of Directorate-General of Budget, Accounting and Statistics (Taiwan). In total, 8710 workers from 1255 institutions participated in this investigation. The results show that the workers who were under the age of 30 had low work autonomy, but the workload and the amount of fatigue that this group of participants had received were high. The workers who worked more than 60 hours per week had the highest autonomy and the heaviest workload. The workers who had less than

5 years of professional experience had the lowest autonomy, but the workload for this group was second to that of the workers whose professional experience was more than 20 years. Overall, shift workers tended to have heavy workload, low autonomy, high level of fatigue, high correlation with sleep disorders and other health problems. The employees of large companies (>300 employees) and laborers were found to have the heaviest workload and the highest level of fatigue. The workers who regularly performed highly stressful jobs, in comparison with the workers who regularly perform low-stress activities, suffered from sleep problems and physical discomforts (e.g. menstrual irregularity, gastric ulcer, psychosomatic disorders, and dysautonomia) in a significantly larger proportion ($p<0.0001$).

A questionnaire survey [54] has provided insights into the causal factors of sleep disorders among shift workers in a chemical plant in Taiwan. The study was based on 1701 effective questionnaires with an effective response rate of 99%. The average age of the respondents was 45.7 ± 7.5 years old, and the percentage of male respondents was 96.1%. The study found that the percentage of workers who suffered from severe snoring was 12.1%, and the percentage for those who suffered from severe sleepiness was 11.9%. A further exploration of the correlations between the consumption of energy/caffeine drinks among different groups of participants has found that most shift workers relied on caffeine drinks to maintain stamina ($p<0.05$). In comparison with the ordinary workers, the shift workers consistently underperformed in the scores of sleep fitness and the tests on drowsiness and snoring ($p<0.05$). The study concluded that shift work could be a major risk factor for sleep disorders, drowsiness and snoring. It suggested that the companies should pay attention to the issue of shift rostering in order to improve the health of employees.
(Reference：http:// /hospital.kingnet.com.tw/essay/essay.html?category=%C2%E5%C3%C4%AF e%AFf&pid=20501)

VI. Sleepy drivers

There are about 100,000 cases of traffic accidents reported each year. According to the estimate of the National Highway Traffic Safety Administration (NHTSA), the cases of traffic accidents were related to fatigue, with 71,000 people injured, 1,550 people killed, which led to a total financial loss of $ 1.25 billion US dollars. Nevertheless, this knowledge may be just the tip of

an ice berg because the complex factors of traffic accidents associated with fatigue driving remains illusive.

Fatigue is a common problem for patients with OSA, and this affects their daytime cognitive and behavioral abilities [15], [16], which results in decreased alertness/acuity, and in turn, increases the probabilities of accidents [4], [15]. Many studies have shown the strong link between OSA and traffic accidences [28], [29], and the relevant laws have been established.

The bill of "Maggie's Law" was passed in the US in 2003; those who cause fetal traffic accidents due to self-inflicted sleep deprivation in a consecutive period of twenty-four hours or more are liable to be charged for a 100,000 fine in US dollars and ten years in jail.

- Edinburg, England : Nearly 10% of the bus drivers have OSA
- Canada: Even more dangerous than the drunken driver? [52]
  OSA patients v.s. 21 normal people with age and gender matched
  Divided attention driving test, (DADT): higher score means more steering errors with poor performance:
  OSA group (average AHI = 73 +/- 29) poor performance than the control group
  More than 50% in OSA group performed worse than the control group, even worse than the drunken group. (Blood alcohol concentration = 95 +/- 25 mg/dl, far above the upper limit of regulation, 52.5mg/dl)
- Canada: Traffic accident rates can be lowered by treating patients with OSA.
- Canada, England: Treating OSA patients can actually lower government expenditure.
- US: Drivers aged between 18 and 29: 70% of these drivers had been feeling drowsy when driving in the past year, 30% of them admitted that they fell asleep while driving.
- Canada: Physicians need to report patients with diagnosed OSA to the ministry of traffic by law.
- A survey done by the institute of roads and transportation in Sweden in 2008 has shown that, more than 40% of the traffic accidents were caused by fatigue drivers; this was higher than previous estimations.

Studies in Australia, Britain and other European countries also show that 10% to 20% of the traffic accidents are caused by sleepy/fatigue drivers. Sleepiness/fatigue cannot be easily measured like a simple alcohol test; therefore it is hard for authorities to have enough knowledge and information to analyze the causes of traffic accidents in connection with fatigue driving. Many traffic accidents that were ruled as "bizarre" and/or other reasons may actually have been caused by sleepiness/fatigue drivers.

Many people understand the danger of drunk driving, but very few know that sleepiness/fatigue driving can be as deadly. Drunk driving and sleepiness/fatigue both affect drivers in a similar way that lead to the following consequences: reduced

reaction to the environment, reduced alertness, poor judgment, or frustration and reckless driving. Studies show that the level of danger associated with driving after being awake for 24 hours is equal to drunk driving. A simulation study in Canada has shown that more than half of the OSA patients actually performed worse than those being drunk and driving [52]. The individual subjects who were awake for more than 18 hours reacted/responded poorly to the simulated driving test at a level that is equivalent to the test score of a person with a blood alcohol concentration greater than 0.05%. The risk of fatigue driving is no less than drunk driving. Also, accidents caused by fatigue driving usually occur in the absence of break marks resulting in more serious casualties..

In 2005, the National Sleep Foundation of the US conducted the "national survey for sleep". The survey shows that more than 60% of the drivers who took the survey admitted feeling sleepy while driving in the past year, and 37% of the drivers admitted falling asleep when driving. The same study showed the result of the 2002 survey: 50% of the drivers who took the survey admitted feeling sleepy while driving in the past year; 17% of the drivers admitted falling asleep when driving.

A joint investigation conducted by Stanford University and the ISSTA was performed to study the danger of sleepy near-misses. Dr. Rayleigh Ping-Ying Chiang, one of the founders of ISSTA, had collected more than 35,217 cases in five years. The study entitled "Sleepy Driver Near-Misses May Predict Accident Risks" was published in the peered reviewed journal "Sleep" in March, 2007. It is too late to make a difference after accidents already happened; hence the study was done on drivers with "near-misses" cases. The result showed that the actual rate of accidents happened was 23.2% when drivers were aware of near misses without being self-aware of sleepiness. For those who were self-conscious of sleepiness for more than 4 times, the actually rate of accidents was 44.5%. There is a 1.87-fold difference between the rates of accidents associated with the test groups. [53]

In 2009, the Taiwan Society of Sleep Medicine (TSSM) did a survey to demonstrate the positive correlation between the seriousness of traffic accident and sleep disorders. The study found that the people who experienced insomnia and drowsiness were three times more likely to get injured in a traffic accident and causing damages to their vehicles in comparison with the people without sleep problems. In 2006, a Taiwanese bus driver with diagnosed OSA drove into a civilian's house and left six persons severely injured. There was another case in which a truck driver fell asleep at the wheel causing a chain accident which resulted in ten casualties. The driver in the second case was later diagnosed with OSA as well. Sleep disorders not only result in day time drowsiness, but also trigger other diseases. Most of the patients are not self-aware of the danger of and the relationship between fatigue driving and sleep disorders, and this ignorance is the most dangerous thing. Hence, sleep disorders should be regarded as a silent killer. "Fatigue driving" is an important issue for the general public and the government.

According to the result of the "Ten Great Visions for Transportation" Year 2011 network voting (organized by the Consumers's Foundation, Chinese Taipei and published by Epoch Times on July 19, 2011), the internet users were most concerned with the topic of "Regulatory reinforcement on fatigue driving and the undertaking of consecutive shift work by drivers of public transportations". The topic was ranked on the top of the list with the rating of 96%. The next two highly ranked topics were "road maintenance" and "the construction of a convenient transportation network", respectively. Chairperson Jinxia Su of the Consumers' Foundation, Chinese Taipei pointed out that six fatal traffic accidents took place between 2005 and 2009 due to coach drivers' drowsiness and fatigue driving. The accidents took 22 lives and injured 60 people. In the light of this event, the Control Yuan (Taiwan) has demanded the Ministry of Transportation and Communications and the Council of Labor Affairs (now called Ministry of Labor) to standardize and regulate the working hours of drivers and to implement a way of tracking the working hours of truck drivers.

Despite the publicity of the agenda on fatigue driving, suspected cases of fatigue driving and driver's drowsiness have been linked to recent traffic accidents since 2010. Although the recent traffic accidents did not cause heavy casualties, the lives and safety of passengers are apparently being threatened. Moreover, there was a recent incident in which a driver of the Taiwan High Speed Rail fell asleep and left the control system of the train unmonitored for 13 minutes which undermined the safety of passengers. To this point, the Consumers' Foundation, Chinese Taipei shows that working overtime and fatigue driving of public transport drivers are age-old problems. It urges the government to take actions in order to protect the lives and safety of people as well as the health of drivers.

Economic implications of insomnia:

•Insomnia statistics aren't confined to the relationship between insomnia and health. This sleep disorder costs the government and the industry billions of dollars a year.

•The Institute of Medicine estimates that hundreds of billions of dollars are spent annually on medical costs that are directly

related to sleep disorders.
•The National Highway Traffic Safety Administration statistics show that 100,000 vehicle accidents occur annually due to drowsy driving. An estimated 1,500 people die each year in these collisions.

VIII. Sleep deprivation

•Population: According to the analysis of Centers for Disease Control and Prevention of American in 2012, about 41 million people sleep less than 6 hours and it accounts one third of the total work force. 42% of the workers in the mining industry have long-term sleep deprivation while 27 % of the workers in the finance and insurance industries have the same problem.
•People who suffer from sleep deprivation are 27% more likely to become overweight or obese. There is also a link between weight gain and sleep apnea.
•A National Sleep Foundation Poll shows that 60% of people have driven while feeling sleepy (and 37% admitted fallen asleep at the wheel) in the past year.
•Statistics also show that the US industry loses about $150 billion each year because of sleep deprived workers. This takes absenteeism and lost productivity into account.
•A recent Consumer Reports survey showed the top reason that couples gave for avoiding sex was "too tired or need sleep."
•Employers spend approximately $3,200 more in healthcare on employees with sleep problems than for those who sleep well.
•According to the US Surgeon General, insomnia costs the U.S. Government more than $15 billion per year in healthcare costs

These sobering insomnia statistics underscore the importance of enhancing sleep disorder awareness and why individuals need to seek immediate treatment for the health and the well-being of others.

Part D. The vision and strategic goals of ISSTA for the provision of multi/interdisciplinary talents

The International Sleep Science Technology Association (ISSTA) was established in 2012 in Berlin, Germany; it has five committees. ISSTA has been active in the promotion of sleep education and the sleep technology industry. Across 15 countries,

the vision and goals of the ISSTA have been held in esteem by government officials, academics and field experts.

The vision and goals of the ISSTA

The ISSTA functions as a point of nexus which supports communications and the multi/interdisciplinary integration of medical and scientific issues on sleep. This integrative function encourages the implementation of sleep science and technology in educational programs. Through education, the ISSTA aims to help people who are affected by sleep disorders and also to solve people's problems concerning sleep disturbances. As a strategic goal towards the advancement of sleep technology, the ISSTA aims to develop a novel and comprehensive diagnostic method which would eliminate the discomforts that patients often experience with the traditional polysomnographic tests. In terms of enforcement and implementation, the ISSTA will seek the support from the industry and governments over the world in order to complement professional experts in a collective effort to embark a globalized development of the sleep industry.

The task of globalizing the sleep industry in the immediate future will concentrate on the promotion of sleep agenda among the international organizations including the Asia-Pacific Economic Cooperation (APEC), European Commission (EC), North American Free Trade Agreement (NAFTA), Bill and Malinda Gates Foundation, and the World Health Organization (WHO). This strategic goal shall accelerate the globalization which would benefit more people. In the current stage of ISSTA's organizational development, five committees have been established to serve the purpose of providing professional talents, know-hows, and technology in a multi/interdisciplinary capacity. The organization of the ISSTA is depicted below.

International Committee

Chair: ***Mignonne Chan****, Ph.D. (APEC Study Center, TIER Taiwan)*

Co-Chair: ***Gino Yu,*** *Ph.D. (PolyU, Hong Kong, China)*
Co-Chair: [Pending]
Co-Chair: ***Mahadevan Murali,*** *MBchB, FRACS* ***(****Starship Children's Hospital, University of Auckland, New Zealand)*
Advisory Board: [Pending]

The mission of the International committee are:

A. To promote/facilitate international research collaboration within academia, between industry and governments
B. To propose agendas for international organizations/forums, such as APEC, WEF, EU, WHO...etc. to raise the awareness of the importance of modern sleep technology.

Popularizing Committee

Chair: ***Rita Carter*** *(Science Writer, Lecturer, Broadcaster, U.K.)*
Co-Chair: ***Emilia Hsieh,*** *M.S. (International Channel, Public Television Service Taiwan)*
Co-Chair: ***Lawrence Lee, J.D. (****Fair Trade Commission, Executive Yuan, Taiwan****)***
Co-Chair: ***Kannan Ramar, M.D. (Mayo Clinic, Rochester, MN, U.S.A.)***
Advisory Board: ***Arianna Huffington, M.A.*** *(President and editor-in-chief of the Huffington Post Media Group, U.S.)*

The mission of the Popularizing committee are:

To preach the importance and impact of sleep science and technology in the general population internationally via website, by publishing or exposure in media or public for laypersons, organizing awareness activities, and co-operate with the International Committee and R&D Committee. The mission includes writing up the bi-monthly official communicating letters of ISSTA for the members.

Research&Development Committee

Chair: ***Murat Özgören, M.D., Ph.D.*** *(Dokuz Eylul Universitesi, Turkey)*
Co-Chair: [Pending]
Co-Chair: ***Chih-Ting Tim Lin,*** *Ph.D. (Department of Electrical Engineering, National Taiwan University, Taipei)*
Co-Chair: ***Jose Haba-Rubio,*** *M.D. (Centre d'Investigation et de Recherche sur le Sommeil [CIRS], Centre Hospitalier Universitaire Vaudois [CHUV], Lausanne, Switzerland)*
Principal Investigators (P.I.s):

Sissel Tolaas *(Smell Research Lab, Berlin)*
Yi-Wen Jacob Liu, *Ph.D. (Department of Electrical Engineering, National Tsing Hua University, Hsinchu, Taiwan)*
Wen-Yang Lin, *MSc (Department of Biological Science and Technology, National Chaio-Tung University, HsingChu, Taiwan)*
Shao-Chin (William) Chang, *M.S. (CEO, Alchemy Technology Co. Ltd.)*
Bo-Han Chiu, *M.D. (Dept. of Otolaryngology, Shin Kong Wu Ho-Su Memorial Hospital, Taipei, Taiwan)*
Rita Carter *(Science Writer, Lecturer, Broadcaster, U.K.)*

Advisory Board:

William Lin, M.S. *(Greater Chinese GM of Underwriter Laboratory)*
Chii-Wann Lin, Ph.D. *(National Taiwan University, Taipei,Taiwan)*

The missions of R&D Committee are:

A. To review the proposals by the members and issue the grants together with the Board of the Directors.
B. To do the basic and cross-domain researches
C. To develop the techniques, devices and instruments based on these researches.
D. To establish the standards (such as UL, ISO) in this field and issue certificates for the members and the 3rd parties.

Industrialization Committee

Chair: ***Gow-Jiumn Huang, Ph.D.*** *(III, Taipei, Taiwan)*
Co-Chair: ***Xiangyu Wang, Ph.D.*** *(Curtin University, Perth, Austrália)*
Co-Chair: ***Chii---Wann Lin, Ph.D.*** *(Dept. Of Medical Engineering, National Taiwan University, Taipei,Taiwan)*
Co-Chair: [Pending]
Advisory Board: ***David White****, M.D. (CMO, Philips; Harvard Medical School)*
Shao-Chin (William) Chang, *M.S. (CEO, Alchemy Technology Co. Ltd.)*

IP platform:

Director: ***Louis Chen, J.D.*** *(National Taipei University of Technology, Taipei, Taiwan)*
Co-Director: ***Hung-Hsiang Chu, M.S. (****Tamkang University, Taipei, Taiwan)*
Co-Director: ***Shao-Chin (William) Chang,*** *M.S. (CEO, Alchemy Technology Co. td.)*
Co-Director: [Pending]

The missions Industrialization Committee are:

A. To be in charge of patents application based on the researches among our members.
B. To promote the collaboration between members with industry.
C. Establish the ***IP platform*** for technology transfer between global academia and industry.

Education Committee

Chair: Jennifer L. Martin, Ph.D. (David Geffen School of Medicine, UCLA, U.S.A.)
Vice-Chair: ***Sharon Keenan, Ph.D.*** *(Stanford, U.S.A.)*
Vice Chair: ***Sin-Chien Lee****, M.D., M.Ph. (Taipei Medical University, Taipei, Taiwan)*
Vice Chair: ***Su-Wan Kim, M.D., Ph.D. (****Kyun-Hee University Hospital, Seoul, South Korea)*
Global Ph.D./Master Program
Director: ***Rayleigh Ping-Ying Chiang, M.D., M.M.S.*** *(National Taiwan University, Taipei, Taiwan)*
Co-Director: ***Gino Yu, Ph.D.*** *(PolyU,Hong Kong,China)*
Murat Özgören, M.D., Ph.D. *(Dokuz Eylul Universitesi,Turkey)*
Thomas Penzel, Ph.D. *(Charite Medical University, Berlin, Germany)*
Maria-Cecilia Lopes, M.D., Ph.D. *(Universidade Federal de Sao Paulo, Sao Paulo, Brazil)*
JerryWang, Ph.D. *(Chung Hua University, Hsinchu, Taiwan)*
Potential Co-Directors: ***Chii-Wann Lin, Ph.D. (****National Taiwan University, Taipei,Taiwan)*
Xiangyu Wang, Ph.D. *(Curtin University, Perth, Austrália)*
Michael M Vitiello, Ph.D. *(University of Washington, Seattle, U.S.A.)*
Louis Chen, J.D. *(National Taipei University of Technology, Taipei, Taiwan)*

The mission of the Educational committee are:

A. To establish the first global Sleep Science and Technology Master/Ph.D. Program, be co-directed with Charite Medical University in Berlin, Federal University of Rio de Janeiro in Brazil, Dokuz Eylul University, Balcova, Izmir in Turkey, PolyTech University, Hong-Kong, Chung-Hua University in Hsingchu, Taiwan, National Taipei University of Technology in Taipei, University of Kentucky in Lexington, U.S.A.. Mayo Clinic in Rochester, U.S.A., University of Washington, Seattle, U.S.A., University of Sydney, Australia, National Taiwan University, Taipei Medical University...etc. will be invited thereafter, plus University of Sydney if you agree.
B. To give regular training courses on Sleep Science and Technology
C. Host the board exams in the field of Sleep Science and Technology.

Global Policy & Regulation Committee

Co-chair: **Kenneth P. Wright Jr., Ph.D.** (Department of Integrative Physiology, University of Colorado, USA)

The mission of the Global Policy & Regulation Committee:

The Global Policy & Regulation Committee serves the purpose of policy and regulation developments concerning the health and safety consequences of insufficient sleep and circadian misalignment. The mission of the Committee is to improve public health and safety through the development of a global policy and regulatory standard for the prevention of the health and safety consequences of insufficient sleep due to sleep disorders.

Part E. The state-of-the-art in the global development of sleep technology

Energy Pod

Energy Pod provides an innovative and elegant way of addressing the need for a suitable place to rest in the workplace. This equipment ergonomically supports the human anatomy, and it helps the user of this equipment to maintain mental and physical wellbeing. Energy Pod has a streamline contour that helps the human body to relax the stressed muscles. Inside the hemispherical cover, the user could rest with privacy and enjoy the pleasure of listening to music. The in-built timer of Energy Pod enables the user to set the alarm which would wake up the user by the means of lighting and vibration. All of the design features of Energy Pod promote the quality of sleep which makes an efficient rest.

Cranial electrostimulation (CES) Device

This sleep therapy device produces and sends signals in a specific waveform (a registered patent) across the temporal lobe of the human brain towards the skull in order to stimulate the regions of the brain that control psychological and emotional activities. The signals act on the Hypothalamus, the Limbic System, and the Reticular Activating System which results in the secretion of various neurotransmitters being responsible for the regulation of a human individual's emotion and cognition. For instance, the endogenous morphine-like peptides produce sedative and euphoric results which the immunity of a human individual. Moreover, serotonin participates in the regulatory mechanism of multiple physiological functions and pathophysiological states. Therefore, the sleep therapy device corrects abnormal brainwaves through the regulation of the neuropharmacological mechanisms that occur in the brain. It can noticeably enhance the activity of the alpha wave (the relaxed

state of the brain) and reduce the activity of the delta wave (the fatigue state of the brain). In addition, the elevated secretion of gama-aminobutyric acid, GABA (another neurotransmitter) would lessen the occurrences of negative emotions such as anxiety and depression. Overall, this therapeutic approach leads to improved physiological signals such as the heart rate, blood pressure, muscle tone, skin potential and skin temperature.

Sleep improving wrist band

This type of treatment device for sleep disorders by releasing low frequency magnetic pulses which mimic the action of needles on the acupuncture points of the wrists. Based on the therapeutic principles of acupuncture, the treatment regulates the sleep-wakefulness cycle and thereby effectively reduces the episodes of chaotic dreaming, nightmares and wakefulness.

Continuous positive airway pressure (CPAP) ventilator

A traditional continuous positive airway pressure (CPAP) ventilator works on the principle of applying mild air pressure on a continuous basis which creates a positive air pressure being capable of keeping the patient's airway open. When a large air flow passes through the surface of the epithelium in the nostril, the capillaries in the tissue cause hyperemia (swelling congestion) so as to compensate the drying effect of the inhaled cold air. As such, the traditional CPAP treatment causes symptoms including nasal congestion, dry mouth and sore throat. According to the literature, 65% to 75% of the patients who undertook the CPAP treatment were bothered by the undesirable side effects of the treatment. Breathing becomes difficult when the nasal airway resistance increases as a consequence of hyperemia, and naturally, the human body would have to rely on buccal breathing as the alternative means of autonomous respiration. Many patients have discontinued or abandoned their CPAP treatment because of the undesirable side effects of the treatment.

New designs of CPAP ventilators have addressed the necessity to include temperature and humidity in the treatment without compromising the convenience of applying the treatment. This ensures that patients do inhale warm and moist air as they receive the initial CPAP treatment. Clinical studies have repeatedly shown the improved effectiveness of the CPAP plus heated humidifier treatment due to the reduction of patient's discomfort caused by the dehydration of the upper respiratory tract.

Sleep study equipment

Sleep study equipment is also known as polysomnography. The equipment monitors the patient's overnight physiological change which is reflected in: sleep architecture, the stability of sleep brainwaves, the concentration of oxygen in the blood, stream, apnea, the duration and frequency of inadequate respiration, sleep myocardiography, electrocardiography, and electrooculography. The polysomnographic approach is the gold standard for diagnosing sleep disorders. Innovative research and developments are successively producing new instruments to support the diagnosis and treatment of sleep disorders.

Part F. Conclusion

In the recent years, people have paid more attention to their health due to the global trend of personalized healthcare along with the advancements in science and medicine. The surge in the prevalence of chronic diseases has made people realized the importance of making a healthy life. The cardiovascular diseases caused by sleep disorders have increasingly made people understood the importance of sleep. Issues on shift workers, fatigue driving and sleep deprivation have arose from the fast-paced work place and the stressful lifestyle of the contemporary society. Sleep deprivation and compromised quality of sleep have affected people which, in turn, have noticeably influenced the development of the global economy. Amid this universal problem, the role of sleep technology as a potential solution to the universal problem is of crucial importance. In the light of this vision, the ISSTA is committed to the integration of sleep technology into people's everyday life. According to the ideal of synergized multi/interdisciplinary integration, the ISSTA has incorporated precision instrumentation and a variety of technology products in the making of a new generation of sleep technology products. Members of the ISSTA team are equipped with technical ability as well as strategic managerial talent. The principles and processes of project control have been adopted to carry out project management and to complement the organizational appraisal of information technology systems. The ISSTA synergizes the research and development of the market, business opportunities, and sleep technologies. In the synergized R&D approach, the research team of the ISSTA has advanced its academic standing, which gave the ISSTA an edge to create a niche in the commercial market.

The achievement of Taiwan's industrial development over the past decades has gained international recognitions. However, all trades and businesses are currently facing the challenges and impacts from the global economic reshuffling. In order to improve the situation and to promote Taiwan, the local entrepreneurs need to be familiarized with the marketing channels of medical equipment throughout the world, to be internationally competitive in the processes of product development and

marketing, and to become an important stakeholder in the supply chain of the medical equipment industry. With the assistance from the TIER, the entrepreneurs could understand the characteristics of the individual markets across the world, and they could perform comprehensive evaluation of the global business opportunities and legal requirements. Through the guidance of TIER, the power and dynamism of research activities in the fields of internet communication technology and electronic engineering could be directed at the facilitation and development of sleep technology. With a comprehensive marketing strategy plus constant innovations in the sleep technology industry, entrepreneurs could gain a foothold in the global market and find new business opportunities.

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