

**Obstructive Sleep Apnoea and Driver Performance:
Prevalence, Correlates, and Implications for Driver Fatigue**

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Statement

The work described in this thesis was carried out in the Woolcock Institute of Medical Research and Royal Prince Alfred Hospital under the supervision of A/Professors R. Grunstein and G. Marks. Unless otherwise stated, it is the original work of the author and has neither been presented nor is it currently being presented for any other degree.

Anup Desai

Acknowledgements and Dedication

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Dedication

I would like to dedicate this thesis to my beautiful wife, Ankita

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Abbreviations and Definitions

General

- AI:** arousal index (see section 2.1.4.5.2)
- AHI:** apnoea hypopnoea index (see section 1.2.3.1)
- CI:** confidence interval
- CPAP:** continuous positive airway pressure (see section 1.2.3.7)
- EDS:** excessive daytime sleepiness
- ESS:** Epworth sleepiness scale (see section 2.1.4.1.2)
- Effect Size:** describes how many standard deviation units the experimental group was different from the control group; for reference, an effect size of 0.20 is considered small, 0.50 is considered medium, and 0.80 or greater is considered to be large (Hedges and Olkin 1985).
- MSLT:** multiple sleep latency test, a polysomnographic test of sleep tendency, that requires subjects to try to fall asleep during four or five daytime nap opportunities (see section 2.3.2). (Association of Sleep Disorders Centers Task Force on Daytime Sleepiness 1986)
- MVA:** motor vehicle accident
- MWT:** maintenance of wakefulness test, a polysomnographic test of sleep tendency, where subjects are asked to stay awake under soporific conditions several times during the day for 20 or 40 minutes at a time (see section 2.3.2) (Mitler *et al.* 1982)
- NAB:** neurobehavioural assessment battery (see section 2.2.4.4)

- OSA:** obstructive sleep apnoea (see section 1.2.3.1)
- OSLER:** Oxford sleep resistance test (see section 2.2.4.6)
- PLMs:** periodic limb movements, where subjects show repeated stereotyped movements, usually of the lower limbs, in certain stages of their sleep (O'Keefe 1996).
- PSG:** polysomnography (see section 2.1.4.5)
- PVT:** psychomotor vigilance task (see section 2.1.4.3)
- RDI:** respiratory disturbance index (see section 1.2.3.1)
- REM:** rapid eye movement sleep
- SAS:** sleep apnoea syndrome, clinical definition requiring the presence of both OSA on polysomnography, together with excessive daytime sleepiness (see section 1.2.3.1)
- SDB:** sleep disordered breathing
- SD:** sleep deprivation

AusEd™ - Australia Edinburgh Driving Simulator

Steering Variables:

- Median lane position (cm):** median lane position adopted on the road for the duration of the simulator drive
- Sd lane position median (cm):** standard deviation (sd) of lane position from the median lane position
- Area steer dev median (cm ms):** area of steering deviation (steer dev) from the median lane position

Av steer dev median (cm): average (av) steering deviation (steer dev) from the median lane position

Area dev steering centre (cm ms): area of steering deviation (dev) from the centre of the left hand lane

Av dev steering centre (cm): average (av) steering deviation (dev) from the centre of the left hand lane

Sd of lane position (cm): standard deviation (sd) of mean lane position

Reaction Time Variables:

RT mean (ms): mean reaction time (RT) for braking after the sudden appearance of trucks

RT sd mean (ms): standard deviation (sd) from the mean reaction time (RT) for braking

RT median (ms): median reaction time (RT) for braking

RT sd median (ms): standard deviation (sd) from the median reaction time (RT) for braking

RT 95% percentile (ms): ninety fifth percentile of reaction times (RT) for braking

Speed Variables:

Area speed dev zone (km/h ms): area of speed deviation (dev) outside the 60-80 km/hr zone

Av speed dev zone (km/h): average (av) speed deviation (dev) outside the 60-80 km/hr zone

Crash Variable:

Crashes: number of crashes of all types during the duration of the simulator drive

Psychomotor Vigilance Task (PVT)

PVT median (ms): median reaction time for the trial

Lapses: number of reaction times at least 500ms in duration. The lapse count can be **transformed** (square root (x) + square root (x+1)) for analysis to remove zero scores and normalise the distribution

Fast 10% (ms): mean optimum response domain for the trial (mean of fastest 10% of responses)

1/RT slow 10% (1/ms): this represents the worst (slowest) response domain for the trial (reciprocal of mean of slowest 10% of responses)

Errors: number of false-starts on depressing the button, the use of the 'wrong' button, or holding the button down for more than three seconds

Summary

Obstructive sleep apnoea (OSA) is characterised by repetitive reductions or pauses in breathing during sleep due to upper airway narrowing or closure. Due to disruption to normal sleep patterns, many patients with OSA suffer from increased daytime sleepiness. Epidemiological studies have established a link between OSA and driver fatigue and accidents, generally showing a two to seven times increased risk of road traffic accidents in non-commercial drivers with OSA. There is emerging evidence that commercial drivers have a higher prevalence of OSA than the general population, being predominately male, middle-aged and overweight, three important risk factors for OSA. However, little is known about the relationship between OSA and driver sleepiness in commercial drivers, whether road accidents are increased in commercial drivers with OSA, and whether OSA interacts with other fatigue promoting factors, such as sleep deprivation, to further escalate road accident risk.

One thousand randomly selected commercial drivers were surveyed in the field. In addition, 61 randomly selected NSW commercial drivers had in hospital sleep studies and daytime performance testing, including a PC based driving simulator task. The prevalence of OSA, defined as Respiratory Disturbance Index (RDI) > 10, was approximately 50% in NSW commercial drivers. Approximately one quarter of the drivers reported pathological daytime sleepiness, and 12-14% had both OSA and pathological daytime sleepiness. A diagnosis of OSA was the most important factor predicting excessive daytime sleepiness in these drivers: OSA was more important than

15 other work-related, lifestyle and medical factors that could be expected to promote, or be associated with, daytime sleepiness. Drivers with sleep apnoea syndrome (both OSA and pathological daytime sleepiness) had an increased driving accident risk, using driving simulator and daytime performance testing as proxy measures for accident risk. These results demonstrate the importance of OSA as a cause of driver fatigue in commercial drivers and suggest that all commercial drivers should be screened for the presence of sleep apnoea syndrome in order to potentially reduce road accident risk through treatment.

A separate, but related body of work examined the combined effects of mild OSA and other fatigue promoting factors (sleep deprivation and circadian influences) on driving performance. Twenty nine subjects, consisting of a group with mild OSA and a group of non-OSA controls, were tested on several occasions throughout the night and day using an intensive performance battery, under both baseline conditions and after a period of 36 hours of total sleep deprivation. The results suggest that drivers with mild OSA are not different to the control group in their response to sleep deprivation or time of day influences. However, the subjects with mild OSA were less aware of their impairment due to sleep deprivation, which is of concern if drivers with OSA are relying on their subjective awareness of fatigue to make decisions about when to stop driving.

A final perspective on OSA and driver fatigue is provided through a clinical case series of seven fall-asleep fatality associated MVA's associated with unrecognised or under-treated sleep disorders. As well as demonstrating the day to day potential for devastating

road accidents due, at least in part, to un-recognised or untreated sleep disorders, these cases also serve to highlight some of the current medico-legal controversies and difficulties in this area of driver fatigue.

In conclusion, this body of work has provided novel information about the epidemiology and implications of OSA in commercial drivers, and about how OSA interacts with other fatigue promoting factors. Finally, it has explored some of the medico-legal issues that relate to sleep disorders and driver fatigue. As well as providing much needed information in the area of driver fatigue, at the same time this work raises many more questions and suggests areas of future research. For instance, such research should examine the relationship between objective accident rates and OSA/sleep apnoea syndrome in commercial drivers, the interaction between mild sleep apnoea syndrome and other fatigue risk factors, and driver perception of sleepiness prior to sleep onset in drivers with sleep disorders.

Aims

Aims: Commercial Drivers Study

- To determine the prevalence of obstructive sleep apnoea and excessive daytime sleepiness in commercial drivers in NSW
- To examine the relationship between obstructive sleep apnoea and excessive daytime sleepiness in commercial drivers in NSW
- To examine the effect of obstructive sleep apnoea on driving and other neurobehavioural outcomes in commercial drivers in NSW
- To determine factors which predict obstructive sleep apnoea, excessive daytime sleepiness and driving impairment in commercial drivers in NSW

Aims: Mild Obstructive Sleep Apnoea Study

- To assess daytime driving performance and cognitive function in subjects with mild OSA, compared with subjects without OSA.
- To assess daytime diurnal variation in driving performance and cognitive function in subjects with mild OSA and subjects without OSA, and to compare the diurnal variation between these two groups.

- To assess the effect of sleep deprivation on daytime driving performance and cognitive function in subjects with mild OSA and subjects without OSA and to compare the effect of sleep deprivation between these two groups.
- To assess the effect of sleep deprivation on daytime diurnal variation in driving performance and cognitive function in subjects with mild OSA and subjects without OSA and to compare the effect of sleep deprivation on the diurnal variation between these two groups.
- To compare night time driving performance and cognitive function in subjects with mild OSA and subjects without OSA.
- To determine polysomnographic changes in subjects with mild OSA and subjects without OSA after one night's sleep deprivation.

Aims: Medico-Legal Case Series

- To identify a cohort of fatigue-related road fatalities on NSW roads, where the driver who caused the accident suffered from a sleep disorder
- To describe the medical, licensing and legal outcomes of these cases

Chapter 1: Background

1.1 Driver Fatigue

1.1.1 Importance of Driver Fatigue

Driver fatigue is an operational term, which includes within its meaning concepts such as drowsiness, sleepiness, impaired vigilance and inattention as well as falling asleep. Fatigue is a well recognised and common cause of motor vehicle accidents. Some of the evidence linking driver fatigue and motor vehicle accidents will be discussed later in this chapter.

Published statistics on driver fatigue include:

- In the four year period of 1996-2000, NSW Roads and Traffic Authority (RTA) statistics describe fatigue as a causal factor in 18% of all fatal crashes on NSW roads. Of all fatigue-related fatal crashes in NSW, 25% occurred on metropolitan roads in Sydney, Newcastle or Woollongong, 12% occurred on country urban roads, and 63% occurred on country non-urban roads (Roads and Traffic Authority of New South Wales 2001).
- Twenty five percent of all crashes in Victoria have been attributed to driver fatigue (Naughton M and Pierce R 1991).
- Fifteen to twenty five percent of all road accidents in England are believed to be sleep related (Horne and Reyner 1995).

Truck driver fatigue in particular is very important, as will be discussed later:

- Twenty to sixty percent of truck accidents in Australia are believed to be sleep related (Traffic Accident Commission 1994). In one Australian study, 28% of truck drivers reported feeling fatigued on most or every trip they made. Only 15% said it was a rare event. Further, 35% considered fatigue to be a major or substantial problem for themselves (Williamson *et al.* 1992).
- In 1999, NSW RTA figures indicated that of 1595 persons killed or injured on NSW roads in heavy truck crashes, truck driver speeding was seen to contribute to 170 casualties, truck driver fatigue to 98 casualties and insecure loads to 25 casualties (Quinlan 2001).
- Of 830 persons killed or injured in crashes involving articulated trucks, truck driver speeding contributed to 130 casualties, driver fatigue to 70 and insecure loads to 15 deaths or injuries (Quinlan 2001).
- In the USA, driver fatigue was recently judged to be the number one problem in commercial transportation (Department of Transportation 1995).

Driver fatigue is one of the three commonest causes of motor vehicle accidents and the effect of driver fatigue has been underestimated in the past due to difficulties in identifying fatigue as the cause of a crash. The problem of driver fatigue of course moves far beyond just road vehicles to all modes of transportation, being an important factor in rail, sea and air accidents as well. The Exxon Valdez oil spill and the destruction of the Space Shuttle Challenger are both examples of fatigue related disasters that have had devastating consequences (Coren 1996a; Mitler *et al.* 1988).

Driver fatigue commonly causes “fall asleep” motor vehicle accidents. These tend to be more severe or fatal compared with other road accidents. This is because they often involve a single vehicle running off the road at high speed, they tend to occur on higher speed roadways, and braking or other preventative measures may be absent (Horne and Reyner 1995). If truck drivers are involved, the potential to cause death or serious injury to other road users is greatly increased.

1.1.2 Economic Costs of Fatigue Related Accidents

1.1.2.1 All accidents

Recently the US National Highway Traffic Safety Administration published a technical report examining the economic impact of motor vehicle accidents (MVAs) in the USA in 1994 (NCDR/NHTSA Expert Panel on Driver Fatigue and Sleepiness 1998). The key findings are summarised below (all data in \$US):

- The cost of motor vehicle crashes that occurred in 1994 was \$150.5 billion. This total represented the present value of lifetime economic costs for 40,676 fatalities, 5.2 million non-fatal injuries, 3.7 million uninjured occupants and 27 million damaged vehicles. These incidents included both police-reported and unreported crashes. Property damage costs of \$52.1 billion accounted for the most significant portion of the total cost, followed by lifetime losses in marketplace production of \$42.4 billion.
- Economic cost components included productivity losses, property damage, medical costs, rehabilitation costs, travel delay, legal and court costs, emergency

service costs, insurance administration costs, premature funeral costs and costs to employers.

Significant findings on cost included:

- The cost of motor vehicle crashes that occurred in 1994 was \$150.5 billion, the equivalent of \$580 for every person living in the United States, or 2.2 percent of the US Gross Domestic Product.
- Each fatality resulted in lifetime economic costs to society of over \$830,000. Over 85% of this cost is due to lost workplace and household productivity.
- The average cost for each critically injured survivor was \$706,000 - nearly as high as for a fatality. Medical costs and lost productivity accounted for 84% of the cost for these Maximum Abbreviated Injury Scale (MAIS) level five injuries.
- Present and future medical costs due to injuries occurring in 1994 were \$17 billion, representing 11% of total costs. However, medical costs accounted for 22% of non-fatal injury crash costs.
- Lost market productivity totaled \$42.4 billion, accounting for 28% of total costs, and lost household productivity totaled \$12.3 billion, representing 8% of total costs.
- Because of their high incidence, crashes of vehicles that sustained only property damage were the most costly type of occurrence, totaling \$38.9 billion and accounting for 26% of total motor vehicle crash costs.
- Property damage in all crashes (fatal and injury) as well as property-damage-only crashes totaled \$52.1 billion and accounted for 35% of all costs, more than any

other cost category.

- About 24% of medical care costs resulting from motor vehicle crashes are paid from public revenues, with Federal revenues accounting for 14% and states and localities 10%.
- Roughly nine percent of all motor vehicle crash costs are paid from public revenues. Federal revenues account for six percent and states and localities paid for about three percent. Private insurers pick-up 55% while individual crash victims absorb about 29%. Overall, sources other than the individual crash victims pay about 70% of all motor vehicle crash costs, primarily through insurance premiums and taxes. Motor vehicle crash costs funded through public revenues cost taxpayers \$13.8 billion in 1994, the equivalent of \$144 in added taxes for each household in the United States.

Significant findings on incidence include:

- 5.2 million persons were injured in motor vehicle crashes in 1994; 1.1 million of these, or roughly 22%, were injured in crashes that were not reported to police.
- 27 million vehicles were damaged in motor vehicle crashes in 1994; 86% of these were damaged in property-damage-only impacts, with injuries occurring in, or pedestrian injuries caused by, the remaining 14%.
- Roughly half of all property-damage-only crashes and over a fifth of all non-fatal injuries are not reported to police.

An analysis was conducted of trends in motor vehicle crash costs since 1990:

- Inflation increased the cost of motor vehicle crashes by over 16% since 1990.
- A variety of factors including increased safety belt use, decreased driving under the influence of alcohol, safer vehicles, and improved roadways reduced the incidence of crashes, death and injury. This offset about half of the potential cost increases due to inflation, leaving costs 8.1% higher than in 1990.
- If fatality and injury rates had remained at 1990 levels, 1994 crash costs would have been \$29.7 billion (or 20%) higher than the \$150.5 billion measured in this study.

1.1.2.2 Fatigue Related MVA Costs

To derive the economic costs of fatigue related MVAs, one could multiply the total economic cost of MVAs by the proportion of MVAs believed to be due to sleepiness. If one used estimates of either 15 or 30% of accidents being fatigue related, then in the USA in 1994 the cost of fatigue related accidents ranged from \$US 22.6-45.2 billion (0.33-0.66 % of US GDP).

However, when performing an economic analysis for fatigue related motor vehicle accidents, it is important to consider several points generally established regarding fatigue related accidents. Fatigue related MVAs are more likely to be fatal, more likely to involve young drivers and more likely to involve heavy vehicles. This would suggest that the true economic cost of fatigue related MVAs in the USA is in fact greater than the \$US 22.6-45.2 billion estimate.

There is no recent analysis of MVA economic cost in Australia equivalent to the NHTSA report. If one simply assumes that economic cost is proportional to population, then the cost of fatigue related accidents in Australia would be in the range of \$A 2-4 billion.

1.1.2.3 Sleep Apnoea-MVA's Related Costs

It is possible to estimate the economic cost of sleep apnoea attributable MVAs. Approximately 28% of drivers are men aged 30-60, and in this age group the attributable risk expressed as a percentage varies from 12% to 46% (see section 1.2.3.6). This would suggest that sleep apnoea attributable MVAs would have an economic cost of \$70-600 million in Australia, depending on prevalence rates and relative risk values used in calculations.

There have also been other more recent economic analyses of OSA-related MVAs (Douglas N and George CF 2002; Findley and Suratt PM 2001). These have been centred around the cost-effectiveness of treating OSA patients with CPAP. Based on studies showing a reduction in accident rates with CPAP (Findley *et al.* 2000b; George 2001) (see section 1.2.3.7), Findley and Suratt estimated the economic savings from the reduction in serious motor vehicle crashes and personal injuries of treating 500 OSA patients for three years would exceed US\$1,000,000 (Findley and Suratt PM 2001). Similarly, Douglas and George have calculated the cost savings for the UK economy (Douglas N and George CF 2002). They estimate, that by treating 500 patients with CPAP for five years in the UK, the total accident related cost saving would be 5.335 million pounds compared with a treatment cost of 0.4 million pounds (500 CPAP units at 300 pounds and 100 pounds per

annum for consumables and follow up costs), giving a saving of 4.935 million pounds at a 12.3 fold return on pounds spent. Of course, these savings do not even take into account those from the marked improvements in work performance, quality of life, and blood pressure; and the decrease in hospitalisation costs resulting from CPAP treatment (Douglas N and George CF 2002).

1.2 Factors Influencing Driver Fatigue

Although driver fatigue can occur in any driver, research has shown that there are a number of clear risk factors that increase the propensity for driver fatigue. Often it is difficult to separate out the effects of fatigue and other potential causes. For example, inattention and sleepiness associated with fatigue may be additive to the accident risk associated with speeding. There may also be other indirect effects of these factors contributing to sleep related accidents. For example, both sleep deprivation and alcohol have been shown to increase risk-taking behaviour (Harrison and Horne 1998; Soderstrom *et al.* 2001).

Any one driver may be vulnerable to multiple fatigue promoting factors. These factors may be additive or perhaps even multiplicative to create a very dangerous sleep propensity. Many truck drivers, for example, are required to drive continuously for many hours at night, oftentimes with prior sleep deprivation, and are possibly further impaired by sleep disorders such as obstructive sleep apnoea.

Important risk factors for driver fatigue include –

1.2.1 Sleep Loss or Sleep Deprivation

Sleep deprivation is an important cause of driver fatigue that is perhaps underestimated in fatigue research compared with other causes, such as driving hours.

1.2.1.1 Sleep is as Essential as Eating and Drinking

Sleep is a basic homeostatic process, i.e. it is essential for normal organ function and life. As an individual deprives himself of sleep, there is an increase in the drive or “pressure” for sleep. Sleep drive is similar to other homeostatic processes, such as hunger or thirst e.g. if a person does not eat they become progressively more hungry and a similar pattern of function relates to sleep. In animal experiments, where rats have been totally and continuously deprived of sleep, the early response to sleep deprivation is debilitation and weight loss, but ultimately the animal dies in an average of 16 days (Horne 1985).

1.2.1.2 Types of Sleep Loss/Deprivation

Sleep loss can occur acutely if sleep is curtailed to commence an early drive. A common example would be waking early and starting a long drive in association with a family vacation or for work purposes (Kecklund *et al.* 1994). However, more commonly, sleep loss occurs on a chronic partial basis in many people who shorten their sleep hours to less than eight hours per day due to lifestyle, work or family commitments. Increasing 24 hour operation of industry and services, work hour deregulation and globalisation will also increasingly compromise sleep time for many individuals in the future.

Although there is a (probably genetic) inter-subject variability in the effects of sleep deprivation on performance, a progressive decrement in performance and increased likelihood of falling asleep with progressive hours of sleep deprivation exists in all individuals. Section 1.2.1.4 below describes important physiological and behavioural consequences of sleep deprivation that are particularly relevant to the driving task. Generally, the degree of sleep propensity and likelihood of falling asleep whilst driving is a combination of immediate sleep deprivation (past 24 hours) and accumulated sleep deprivation (over preceding week or weeks).

1.2.1.3 Prevalence of Sleep Deprivation

Sleep deprivation is very common in today's society at large, in many occupational settings, such as shift work, and in populations of drivers.

Available evidence suggests that society is becoming increasingly sleep deprived with the average sleep duration in the population now well below 8 hours: Four decades ago, the reported modal sleep duration was at least eight hours (Gallup 1979). In the mid-1980's, the US National Health Interview Survey found that middle-aged adults reported sleeping seven to eight hours at night (Schoenborn 1986). According to the 1995 Gallup survey, the modal sleep duration had decreased to seven hours (Gallup 1995). Then, in 1998, the "Sleep in America Poll" found an average reported sleep duration of 6.57 hours (Gallup 1998). These chronically reduced sleep hours have been confirmed in a contemporary population-based study of sleep patterns using actigraphy (a wrist watch like device that provides an objective measurement of sleep duration) (Jean-louis G *et al.* 2000a). A

recent article in Sleep Medicine Alert argued that society today may be sleeping 25% less than its forefathers 100 years ago (Jean-louis G *et al.* 2000b;Mahowald 1999).

On top of this background of chronic partial sleep deprivation, drivers frequently acutely curtail their sleep time, thereby further increasing their sleep propensity and accident risk. In a large European study, 2200 automobile drivers were randomly stopped on a major interstate motorway and asked to complete a questionnaire about sleep, wake and travel habits (Philip *et al.* 1999a). Fifty percent of the drivers had decreased their total sleep time in the 24 hours before the interview compared with their regular self-reported sleep time. Twelve and a half percent presented an acute sleep debt of greater than three hours and three percent presented a sleep debt of greater than five hours.

The problem of driving sleep deprived may be even worse for commercial drivers. A study on the working habits of Australian truck drivers found that 38% of on-duty truck drivers were exceeding 14 hours of driving per 24 hours at the time of the report, with a further 13% exceeding 14 hours of total work, including loading and paperwork (Arnold *et al.* 1997). Of these drivers, 12.5% reported at least one episode of less than four hours sleep whilst working. Mitler and co-workers, using round-the-clock electroencephalographic (EEG) monitoring of long haul truck drivers, showed that the average sleep time in this group on the job is only 4.8 hours per day, compared to a self-reported ideal of 7.1 hours (Mitler *et al.* 1997). Drivers on fixed 13 hour night shifts had the least sleep at an average of 3.8 hours per day. This group of drivers showed facial

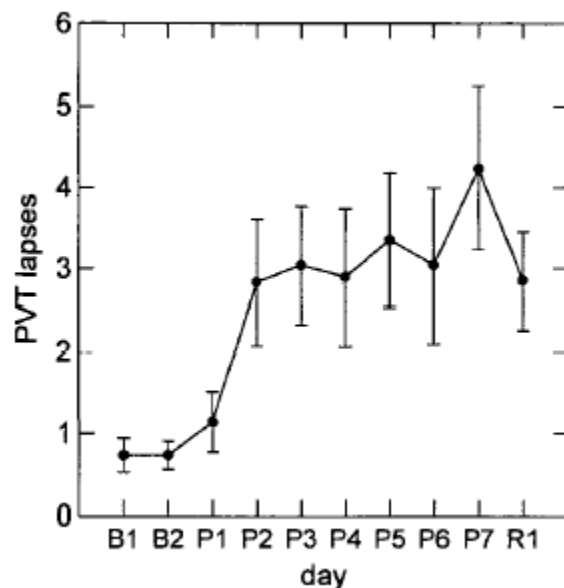
signs of drowsiness, as recorded on video tape, for 11.6% of their time on the road, by far the worst of all schedules.

1.2.1.4 Effects of Sleep Deprivation on Performance and Accident Risk

In experimental studies, sleep deprivation results in reduced alertness, mood changes, and poorer motor and cognitive performance (Dinges *et al.* 1997; Krueger 1989; Pilcher and Huffcutt 1996). Importantly, this has been shown even for chronic, partial sleep deprivation, suggesting that this seemingly mild sleep debt is harmful and that people do not adapt to it. In one study, 16 healthy young adults had their sleep restricted to an average of approximately five hours a night for seven consecutive nights (Dinges *et al.* 1997). Subjective alertness (measured with several sleepiness scales), objective alertness (measured polysomnographically with the multiple sleep latency test, MSLT) and mood all deteriorated with sleep restriction. Similarly, motor performance, measured with a reaction time/sustained attention task (psychomotor vigilance task, PVT (Dinges and Powell 1985) was worse with sleep restriction: figure 1 below shows that the mean number of lapses (reaction times greater than 500ms) on the PVT increased significantly on day two of sleep restriction, then appeared to level off at the higher level between the second and sixth day, finally to rise again quite markedly on the seventh day of partial sleep deprivation. Even one night of recovery sleep did not return the PVT performance to baseline levels. An increase in performance “unevenness” or variability (manifested here by increasing lapse frequency) is an important effect of sleep loss on reaction time tasks involving sustained attention (Dinges and Kribbs 1991). Performance unevenness can also be evident by slowing of response time, increased errors, reduction in the speed

of the fastest response times (optimal reaction time) and an increased number of false responses because of variability in response inhibition (false responses) (Dinges 1992; Weaver 2001).

Figure 1 Temporal profile of mean (standard error of mean) PVT lapses after baseline nights (B1, B2), after each of seven consecutive sleep restriction nights (P1-P7), and after a recovery night of sleep (R1) (Dinges *et al.* 1997)

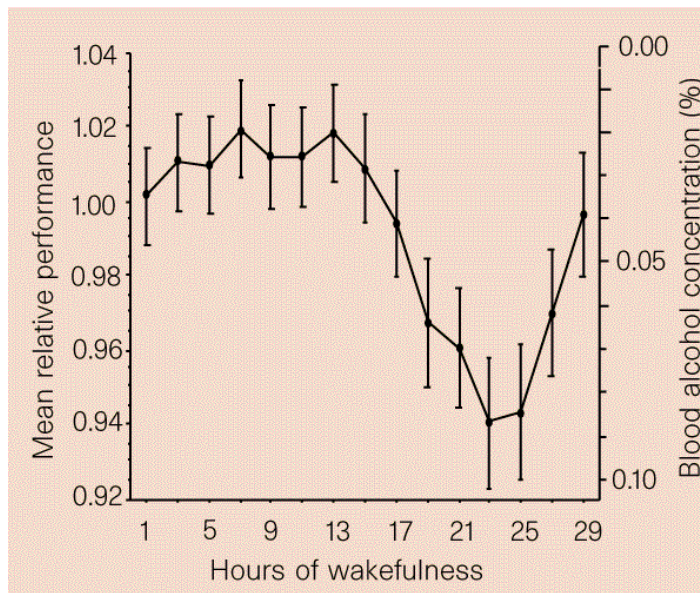


A recent meta-analysis (n = 2000) has further examined the effects of sleep deprivation on performance (Pilcher and Huffcutt 1996). Three main performance outcome measures were investigated: cognitive performance, motor performance and mood. Sleep deprivation strongly impaired human functioning in all three of these domains. The effect of sleep deprivation was greatest for mood (effect size = -3.16), followed by cognitive task performance (effect size = -1.55), and then motor task performance (effect size = -

0.87). Any effect size greater than 0.80 is generally considered a large experimental effect (Hedges and Olkin 1985). This study included papers that had examined the effects of short-term sleep deprivation (less than 45 hours), long-term sleep deprivation (greater than 45 hours) and partial sleep deprivation (less than five hours sleep in a 24 hour period) on human daytime function.

In order to illustrate the risks associated with sleep deprivation more simply, Dawson and co-workers have equated the performance impairment caused by sleep deprivation with that due to alcohol intoxication (Dawson and Reid 1997). They have shown that moderate levels of fatigue produce higher levels of impairment than the proscribed level of alcohol intoxication. To do this, they compared the performance on a computer administered test of hand-eye coordination between subjects kept awake for 28 hours and subjects who consumed 10 – 15 g of alcohol at 30 minute intervals until their mean blood alcohol concentration reached 0.10%. They found a very strong linear correlation between increasing performance impairment and increasing hours of sustained wakefulness ($r=0.96$). When this performance impairment was compared to the impairment seen in the subjects who consumed alcohol, they were able to show that after 17 hours of sustained wakefulness, performance impairment had decreased to a level equivalent to that observed at a blood alcohol concentration of 0.05%, which is the proscribed level of alcohol intoxication in many western countries. Further, after 24 hours without sleep, performance decreased to a level equivalent to that observed at a blood alcohol concentration of roughly 0.10% (see figure 2 below).

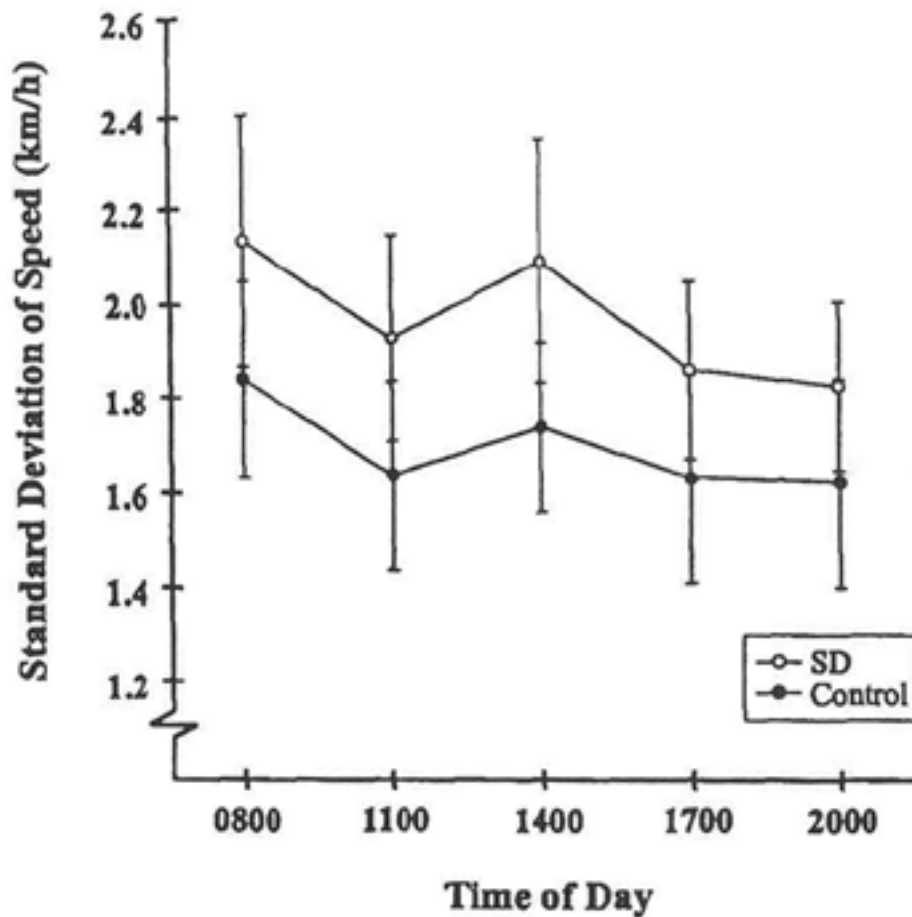
Figure 2 Performance in the sustained wakefulness condition expressed as mean relative performance and the percentage blood alcohol concentration equivalent (Dawson and Reid 1997)



Thus, from the above work, it is clear that sleep deprivation results in important daytime physiological and behavioural consequences. The effects of sleep deprivation have also been examined specifically in the context of driving. In a recent study which investigated the effects of acute total sleep deprivation on driving, subjects completed a driving simulator task for 20 minutes at five different times of day after a normal nights sleep and after one night without sleep (sleep deprivation condition) (Lenne *et al.* 1998). The driving task measured variables relating to speed, position on the road and reaction time to a secondary task (an indicator of the ability to cope with distracting stimuli while driving). Drivers were less able to maintain a steady position in the lane or a stable speed,

and showed a slower reaction time to the secondary reaction time task after 24 hours of sleep deprivation compared to their baseline testing conditions (see figure 3 below).

Figure 3 Standard deviation of speed across the day during control and sleep deprivation conditions (+/- SE) (Lenne *et al.* 1998)



Other studies have also shown impaired driving simulator performance after sleep deprivation (Fairclough and Graham 1999) (Roehrs *et al.* 1994). Similar to the work

described above by Dawson et al, impaired driving performance from sleep deprivation in these studies was at levels comparable to that seen with alcohol intoxication.

Following on from an article published in Science in the 1970s which showed that measurable changes in sleep pattern persist for up to five days after each time shift associated with daylight saving (Monk and Folkard 1976), Coren and co-workers have published an interesting article looking at the effect of daylight saving time zone changes on Canadian road accident rates (Coren 1996b). Using road accident data from the Canadian Ministry of Transport for the years 1991 and 1992 (in total approximately 20,000 reported accidents) they were able to show that the spring shift to daylight savings time, and the concomitant loss of one hour of sleep, resulted in an average increase in traffic accidents of approximately eight percent, whereas the fall shift resulted in a decrease in accidents of approximately the same magnitude immediately after the time shift. This suggested that even small changes in the amount of sleep people obtain can have major consequences on everyday activities, including the risk of traffic accidents. However, a similar study, reported more recently, did not show a measurable immediate effect on crash rates in Sweden associated with the shift to and from daylight savings time (Lambe and Cummings 2000).

Prior sleep deprivation is also reported to be an important factor in commercial driver fatigue related crashes. In a study conducted by the US National Transportation Safety Board in 1995, the duration of the driver's last sleep period, the total sleep obtained during the 24 hours preceding the crash, and fragmented sleep patterns were the most

important predictors of sleepiness-related single vehicle large truck crashes. This study also suggested that night driving after relatively little sleep was a better predictor of fatigue-related crashes than night driving alone (National Transport Safety Board 1995).

1.2.2 Circadian Timing of Drive

1.2.2.1 Circadian Periodicity of Biological Functions

Well over 100 human bodily functions and biochemical processes have been found to vary in accordance with a 24 hour schedule (Rhoades and Pflanzner 1989). This daily or *circadian* periodicity (*circa* – “approximately”, *dies* – “day”) of biological functions is most evident in the sleep-wake cycle. The suprachiasmatic nuclei of the hypothalamus act as the central neural pacemakers of the circadian timing system. The period and phase of the endogenous neural oscillators are normally synchronized to the 24 hour period of the environmental light-dark cycle. Entrainment of the human circadian rhythms by the light-dark cycle is mediated via a neural pathway linking the retina of the eye to the hypothalamus (retinohypothalamic tract).

The timing and internal architecture of sleep is directly coupled to the output of the endogenous pacemaker. Spontaneous sleep duration, sleepiness, rapid eye movement (REM) sleep propensity, and both the ability and the tendency to sleep vary with the circadian phase as marked by the endogenous circadian temperature cycle in humans. Sleep tendency, sleepiness, and REM sleep propensity all peak just after the nadir of the endogenous circadian temperature cycle (approximately two to three hours before

awakening). Eighty five percent of all spontaneous awakenings of subjects living in constant environmental conditions occur on the rising slope of the temperature cycle. Furthermore, there are certain times (wake maintenance zones) when it is very difficult to fall asleep, even for subjects who are sleep deprived. Misalignment of the output of the endogenous circadian pacemaker with the desired sleep-wake cycle is thought to be responsible for certain types of insomnia, as well as for some of the decrements of alertness and performance seen in certain settings, such as night shift work (Isselbacher *et al.* 1994).

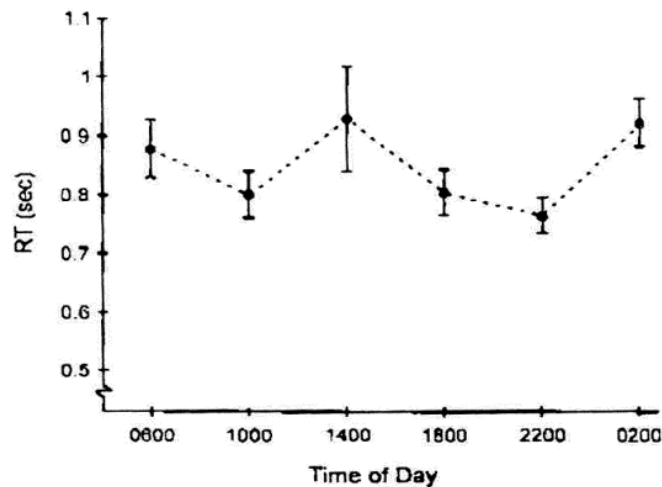
1.2.2.2 Circadian Variability in Performance Testing

From the very earliest studies of sleep loss that involved repeated measurements within a day, it was clear that there was a circadian pattern modulating the course of performance during each 24 hour period of wakefulness (Dinges and Kribbs 1991). The circadian patterns of sleepiness, temperature and performance seem to be closely related and have important effects on daytime physiological function and road accident risk. The time of day pattern of performance tends to show a maximum in the late afternoon and a trough in the early morning around 0500 hours (Akerstedt 1995), correlating closely with circadian changes in sleepiness.

In order to assess whether driving performance varied across the day, Lenne and co-workers tested 11 male subjects on a driving simulator for 30 minutes at six times of day (Lenne *et al.* 1997). Subjects were instructed to maintain a stable position in the left hand lane and to drive at a constant speed of 80km/hr. In addition, subjects performed a

secondary reaction time task. This study showed that the mean and standard deviation of speed, together with driver reaction time, varied significantly across the day. Performance was more impaired at 0600 and 0200, with improvements in driving performance between 1000 and 2200 hours and an early afternoon dip (see figure 4 below). The impairments in driving performance in the early afternoon were of similar magnitude to those occurring in the late evening and early morning. Such ‘post-lunch dips’ in performance have also been identified previously for a range of other performance measures (Smith and Miles 1986) (Blake 1971).

Figure 4 Driving simulator reaction time (RT) across time of day (Lenne *et al.* 1997)



In another study by Lenne and co-workers, discussed previously, there was a significant and similar variation in driving simulator performance across the time of day (Figure 3 above) (Lenne *et al.* 1998). In addition, this study showed no significant interaction between the sleep condition (normal sleep hours or sleep deprivation) and time of day. In

other words, the variability in performance across the day was similar after a night of normal sleep and after a night of sleep deprivation. This emphasizes the strong effect of circadian influences on performance, showing that they persist unaltered even after total sleep deprivation.

One study has compared daytime and night time performance of professional drivers on a simulated truck driving task (Gillberg *et al.* 1996). This study found that night driving was slower and was associated with greater variability of speed and lane position. Subjective and objective measures of sleepiness (measured by electroencephalogram (EEG), which measures brain activity) were also clearly higher during the nighttime. However, reaction time performance was not different between day and night driving, and neither a 30 minute nap nor a 30 minute rest period during the night time drive had any effect on sleepiness or driving performance.

The circadian effects on performance are additive to those performance changes seen with sleep deprivation. This becomes particularly important at night time, when there is both a circadian nadir in performance and the accumulating effects on performance from sleep deprivation due to extended wakefulness.

1.2.2.3 Circadian Variability in Accident Rates

Circadian effects are clearly evident in road accident data, with accident risk being highest in the early morning hours and in the mid-afternoon, corresponding with time of day influences.

In a study that investigated the characteristics of crashes attributed to the driver being asleep, crash statistics for all police reported crashes in North Carolina from 1990-1992 inclusive were analysed (Pack *et al.* 1995). By state law in North Carolina, police officers must fill out a crash report for any accident on a public road where there is personal injury or property damage greater than US\$500. During the years 1990-1992, there were 4333 crash reports in which the driver was judged to be asleep, but not intoxicated. The temporal distribution of these crashes followed that anticipated from what is known about circadian influences on performance: they occurred predominantly at night (midnight to seven am) and there was a secondary, albeit smaller peak, at the mid-afternoon period (around three pm). Fall-asleep crashes were also primarily of the drive-off-the-road type and took place at higher speeds.

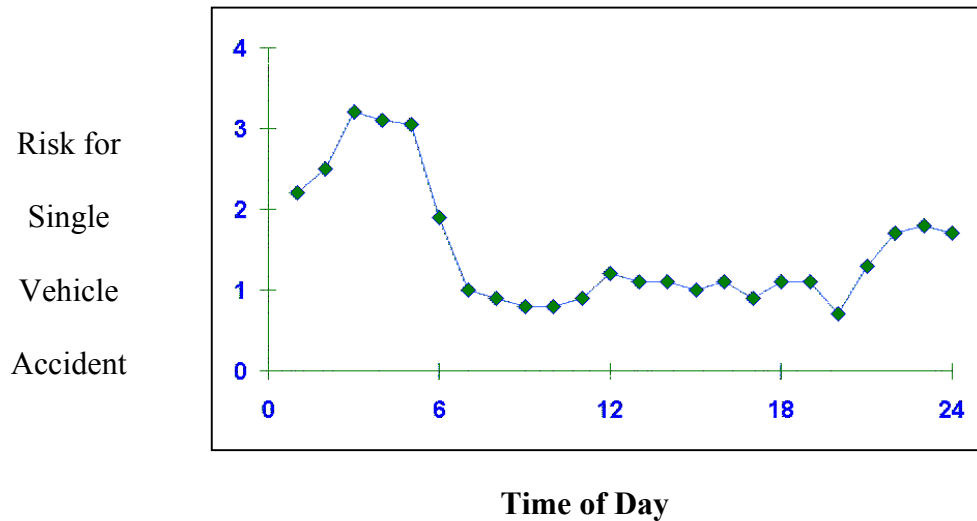
In a recent European study, Swedish highway accident data were used to compute the relative risk of being injured or killed in a traffic accident at different times of day (Akerstedt *et al.* 2001). Traffic density data was used to control for driving exposure. After removing accidents due to alcohol, approximately 10,000 accidents remained for analysis. The highest total accident risk was seen at 0400 (OR=5.7, CI 5.6-5.8), with an OR of 11.4 (CI=10.3-12.5) for fatal accidents at the same point. Further, in order to investigate whether darkness may be involved in the higher accident rate at night, accident patterns around the winter and summer solstices were analysed, since these two times of year differ greatly in daylight patterns at 58 – 61 degrees North, from which latitudes most of the data was obtained. This later analysis showed that, during the winter, the peak of total accidents occurred at 0300, five hours before sunrise, whereas

the summer peak occurred at 0400 hours, shortly after the summer sunrise and with consistently higher night time risk than for winter driving. It was concluded that the night time accident risk seemed related to sleepiness, but not to darkness.

Local NSW data also demonstrate the importance of time of day in accident rates. They show that at the circadian periods of increased sleepiness, the proportion of fatal accidents due to fatigue increases: for the four year period of 1996 – 2000, fatigue was identified as a factor in 32% of all fatal crashes between 4 - 8 am and 21% of all fatal crashes between 12 noon – 2 pm (Roads and Traffic Authority of New South Wales 2001).

For commercial drivers, circadian influences on accident rates appear similar. Several researchers have shown an association between driver fatigue and time of day (Harris 1972; Mackie and Miller 1978; Wylie *et al.* 1996). Some have clearly demonstrated that night time driving is associated with a higher crash risk (see figure 5 below) (Hertz 1988; Jovanis *et al.* 1991; Kecklund and Akerstedt 1993; Kecklund and Akerstedt 1994).

Figure 5 The risk of heavy lorry accidents in Sweden (Kecklund and Akerstedt 1994)



1.2.3 Sleep Disorders: Obstructive Sleep Apnoea

Sleep disorders, particularly obstructive sleep apnoea (OSA), are common, can be easily diagnosed, and readily treated, and as such, their identification and treatment, especially in high risk groups (such as transport drivers), has the potential to reduce driver fatigue and its associated costs, which are both economic and personal.

1.2.3.1 Obstructive Sleep Apnoea: Definition and Prevalence

OSA is the most common medical disorder to cause driver fatigue. Common symptoms of OSA include snoring, observed pauses in breathing during sleep and daytime sleepiness. OSA is a breathing disorder that occurs during sleep, with important night time and daytime consequences. Specifically, OSA is characterised by repetitive

reductions (hypopnoeas) or pauses (apnoeas) in breathing during sleep due to upper airway narrowing or closure. These respiratory events can last from a few seconds to minutes in duration, depending on severity. Clinicians use a definition of at least five events per hour to define OSA, but in severe cases these respiratory events can occur 100 times per hour. Most of these events are terminated by a brief awakening, which restores normal breathing, until the next event develops. This in turn is terminated by another arousal, which restores normal breathing again. This repetitive cycling between sleep and awakening in OSA causes the sleep to become very fragmented. As a consequence of the broken sleep and the repetitive falling of blood oxygen levels with respiratory events, patients with OSA usually suffer from excessive daytime sleepiness (Guilleminault C. 1989). The term “sleep apnoea syndrome” is frequently used to describe people who have both OSA on an overnight sleep study and are excessively sleepy (Lawrence 1990).

Most patients with OSA are overweight. Increased fatty tissue in the neck region and upper airway may contribute to the airway closure during sleep by structurally compromising airway lumen space. However, other factors are also felt to be important in the development of OSA in overweight individuals (McNamara S *et al.* 1993). OSA shows a male predominance (Bearpark *et al.* 1995; Young *et al.* 1993), with the highest prevalence in the middle-aged group (Bixler *et al.* 1998).

It is currently standard in clinical practice and epidemiological studies to assess the severity of OSA by combining the number of apnoeas and hypopnoeas per hour of sleep in an index called the apnoea-hypopnoea index (AHI) or the respiratory disturbance index

(RDI). A common grading of severity is shown below (American Academy of Sleep Medicine Task force 1999):

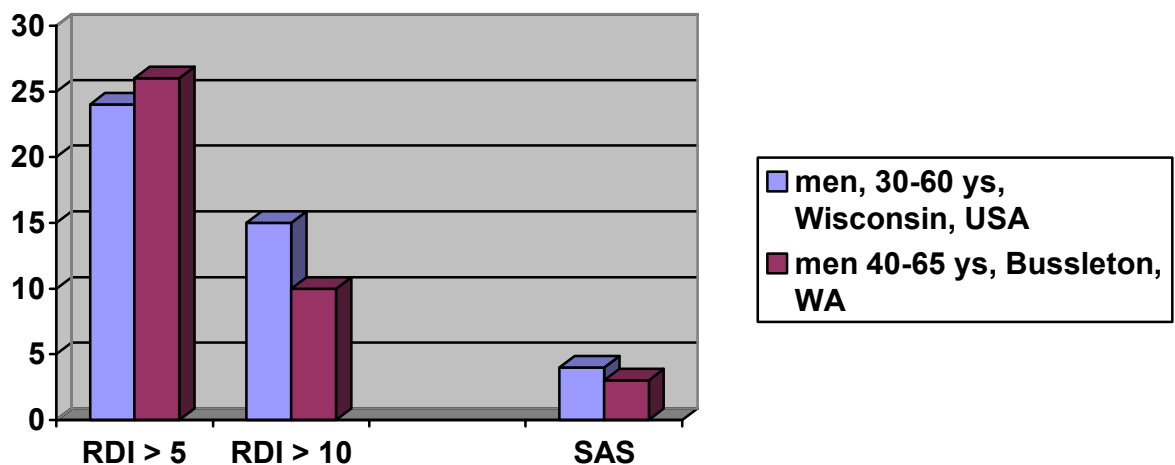
- Normal: less than 5 events per hour
- Mild OSA: 5 – 15 events per hour
- Moderate OSA: 15 – 30 events per hour
- Severe OSA: greater than 30 events per hour

Numerous studies have looked at the prevalence of OSA in the general population. Some have used questionnaire data alone to define OSA prevalence, others have used questionnaires initially which have then been then validated by full polysomnography or nocturnal respiratory monitoring in a random or selected subpopulation, while in other studies, all or most patients have undergone full sleep studies or nocturnal respiratory monitoring (McNamara S *et al.* 1993). When only those studies with in-laboratory polysomnography conducted on large samples are compared, the prevalence estimates for OSA in predominantly white men and women show that roughly 1 of every 5 adults has at least mild OSA and 1 of every 15 has at least moderate OSA (Young T *et al.* 2002)

In a large American study, Young et al studied a random sample of 602 employed men and women from 30 to 60 years old with overnight polysomnography (Young *et al.* 1993). They found 24% of men and 9% of women had OSA (defined by an RDI \geq 5/hr). Fifty seven percent of the men and sixty one percent of the women who were diagnosed with OSA had mild OSA (RDI 5 – 14). The prevalence of “sleep apnoea syndrome” (RDI

≥ 5 /hr, together with excessive daytime sleepiness) was four percent for men and two percent for women. However, in interpreting the prevalence of sleep apnoea syndrome in this study, the authors noted that the subjective measures of sleepiness they used to define excessive daytime sleepiness probably underestimated the true physiological state of sleepiness, and thus the actual prevalence of daytime hypersomnolence and sleep apnoea syndrome may be higher than these data indicate. Bearpark et al studied the prevalence of OSA in Busselton, Western Australia using home monitoring to measure sleep apnoea (Bearpark *et al.* 1995). In total they studied 294 men aged 40-65 years. Twenty six percent had an RDI of at least five per hour, and most of these had mild OSA (62% of OSA patients had an RDI between 5 and 9/ hr). Three percent met the diagnostic criteria for “sleep apnoea syndrome”.

Figure 6 Prevalence of OSA and sleep apnoea syndrome in middle-aged men (Bearpark *et al.* 1995;Young *et al.* 1993)



Much of OSA remains undiagnosed and untreated. However, little is known about the progression of untreated OSA. Preliminary data suggest that substantial progression can occur over relatively short time periods. In an eight year follow up study of 282 participants in the Wisconsin Sleep Cohort, there was a significant increase in RDI over this time period. The overall mean RDI increased by 2.6 events/hr, from 2.5 at baseline to 5.1 at follow up (Young T *et al.* 2002). Similarly, Redline and co-workers monitored 232 participants from the Cleveland Family Study with AHI less than five at baseline and reported a five year increase from a baseline mean (SD) RDI of 2.0 (1.4) to a follow-up AHI of 6.2 (7.9) (Redline *et al.* 2001). In two studies of patients with mild to moderate OSA who have refused treatment and were later restudied, significant progression was found (Pendlebury *et al.* 1997) (Svanborg and Larsson 1993).

1.2.3.2 Obstructive Sleep Apnoea: Consequences

OSA has many important medical and psychosocial consequences. The next section (1.2.3.4) will describe the association between OSA and motor vehicle accidents. However, it is important to first note other major effects and associations of OSA.

Excessive daytime sleepiness is a common symptom in patients with OSA. It is frequently used as part of the diagnostic criteria as discussed above. This excessive sleepiness is readily apparent both on subjective questionnaires and on objective tests, such as the maintenance of wakefulness test (MWT), a polysomnographic test of sleep tendency in which subjects are asked to stay awake under soporific conditions several times during the day for 20 or 40 minutes at a time. In one study, which used the MWT to

measure daytime sleepiness, OSA patients fell asleep considerably more readily than healthy controls, averaging 16 minutes, compared with 27 minutes for the healthy controls (Sforza and Kreiger J 1997). Similarly, OSA patients show a marked increase in their sleep tendency on the Oxford sleep resistance test (OSLER), a recently developed tool which objectively measures daytime sleepiness (Bennett *et al.* 1997).

Instead of sleepiness, subjects with OSA may alternatively report fatigue, tiredness or lack of energy. One study has found that these complaints may be even more common than subjective reports of sleepiness in OSA patients (Chervin 2000). This appears to be especially true for women.

OSA is associated with impaired cognitive performance. Studies have demonstrated mild and moderate decrements across a broad range of psychophysiological, attentional, perceptual and executive cognitive functions, including response speed and manual dexterity; attention and vigilance; verbal and visual memory; constructional skills; verbal fluency and planning (Engleman H and Joffe D 1999). In one case-control study, a comprehensive cognitive battery was administered to 10 patients with moderate OSA, 10 patients with severe OSA and 10 controls who were matched for age, education and intellect (Bedard *et al.* 1991). The moderate OSA patients showed poorer performance in the order of one to two standard deviations on tests of manual dexterity, visual memory and executive function, compared to the controls. This performance impairment was even more marked for the severe group (up to three standard deviations). In addition, the severe group showed other significant deficits - in response latency, general intellectual

performance, attention, verbal fluency, constructional skills, mental flexibility, planning and sequential thinking.

There appears to be an association between the severity of OSA and the degree of cognitive impairment (Engleman H and Joffe D 1999). Mild OSA patients show fewer cognitive deficits, but they are still apparent (Redline *et al.* 1997) (Engleman H *et al.* 1999) (Engleman H *et al.* 1997b) (Kim *et al.* 1997). In one case-control study of 32 mild OSA patients (mean RDI 17), scores for attention and immediate verbal memory were reduced by up to one standard deviation in subjects with mild OSA and a trend for increased perseverative errors on a frontal lobe sorting test was observed (Redline *et al.* 1997). The mild OSA patients in this study did not differ from the controls (RDI < 5) in terms of objective or subjective sleepiness, suggesting that sleepiness was not a factor in explaining the difference observed between the groups. The importance of mild OSA has been most reliably demonstrated in a large scale, population based sample of over 800 subjects who were tested with a cognitive battery (Kim *et al.* 1997). This study showed a significant negative association between RDI and psychomotor efficiency, independent of age, gender, and educational status ($p=0.017$). This relationship was not explained by self-reported sleepiness. Expressing the decrement associated with mild OSA in a more simple way, the authors estimated that an RDI of 15 was equivalent to a decrement in psychomotor efficiency associated with five additional years of age, or to 50% of the decrement associated with hypnosedative use.

There are other broad psychosocial consequences of OSA. In a large epidemiological study of 1300 overweight subjects, those with nocturnal and daytime symptoms of OSA were 15 times as likely to report impaired work performance, four times as likely to have experienced multiple divorce, and three times as likely to have had psychiatric care (Grunstein *et al.* 1995). Studies which have measured general health-related quality of life in OSA patients have concluded that OSA affects quality of life on a par with other chronic disorders of moderate severity (Baldwin *et al.* 2001;Finn *et al.* 1998). One study that assessed quality of life in a sample of older black volunteers with self-reported sleepiness and snoring found that OSA was related to general physical and mental function over the range of RDI 1 to 15 events per hour (Stepnowsky *et al.* 2000).

Occupational accidents are a major social problem. There is evidence that OSA is associated with increased occupational accidents outside of driving (see section 1.2.3.4). In a recently published large Swedish study, men with a history of both snoring and excessive daytime sleepiness had a greater than two fold increased risk of occupational accidents during 10 years of follow up (Lindberg *et al.* 2001). In this study, data on occupational accidents was obtained from a government maintained national register of occupational accidents and accidents occurring during travel to or from work were excluded.

There is a growing consensus that OSA is an important risk factor for hypertension, independent of excess weight and other potentially confounding factors (Peppard P *et al.* 2000;Young T *et al.* 2002). An association appears to be present even at the mild end of

the OSA severity spectrum. One prospective population-based study showed that a minimally elevated RDI at baseline ($0 < \text{RDI} < 5$) was associated with a 42% (95% CI, 13 to 5.6) increased odds of developing hypertension over a four year follow up period. A dose response relationship was observed for more severe categories of OSA, with an odds ratio of 2.9 (95% CI, 1.5 to 5.6) for an RDI of 15 or greater versus an RDI of zero events per hour (Peppard P *et al.* 2000;Peppard P and Young T 2000). Although the magnitude of the association between OSA and hypertension in studies to date has generally been modest, the high prevalence of OSA suggests that it may be responsible for a substantial portion of the population burden for hypertension. Many researchers now view OSA as a cause of secondary hypertension (Young T *et al.* 2002). Further, myocardial infarction, stroke, cardiovascular morbidity and mortality have all been linked to OSA in various studies. However, strong empirical evidence for these associations and precise estimates of the magnitude of the associations will have to await the outcomes of further studies, many of which are currently ongoing.

1.2.3.3 Obstructive Sleep Apnoea: Effect on Driving (Simulator Studies)

Driving simulators have been used widely in motor accident research to assess driving impairment associated with recognised risk factors. They have been shown to detect performance deficits due to alcohol and drug consumption as reliably as on-road studies (Moskowitz H and Robinson CD 1990;Smiley A 1986;Smiley A 1987). In fatigue research, they have been used to describe driving performance deficits in association with sleep deprivation (Fairclough and Graham 1999;Lenne *et al.* 1998), circadian variability

(Lenne *et al.* 1997), long driving hours (Philip *et al.* 1999b), and sleep apnoea (Findley *et al.* 1989; George CF *et al.* 1996; Juniper *et al.* 2000).

Early studies demonstrated that severe apnoeics ($RDI \geq 50$) performed significantly worse in all parameters of a film driving simulator than controls (Findley *et al.* 1989). Furthermore, on a simple reaction-time test in which subjects avoid obstacles on the road ('Steer Clear'), apnoeics hit over four times as many obstacles as controls. In another study using a more advanced PC based driving simulator, which incorporated two essential features of driving, tracking and visual search, George *et al.* showed that OSA patients ($AHI 73 \pm 29$) as a group performed much worse than control subjects in a test of steering ability ("tracking error"). In fact, half of the OSA patients were worse than any control subject, with some showing performance worse than control subjects impaired by alcohol (George CF *et al.* 1996).

Recently, Juniper and co-workers reported that drivers with sleep apnoea syndrome ($RDI \geq 10$, together with daytime sleepiness) performed significantly worse than controls on their PC based driving simulator (Juniper *et al.* 2000). The driving simulator that was used in this study allowed the separate assessment of two visual tasks required for steering a car, immediate positioning on the road with reference to the road edges, and assessment of the curve of the oncoming road which allows faster driving. The sleep apnoea syndrome patients appeared to be particularly impaired on the two drives when only part of the road ahead was available to guide steering, suggesting that they may be

more disadvantaged compared to normal subjects when the view of the road ahead is limited (such as in fog).

1.2.3.4 Obstructive Sleep Apnoea: Accident Risk in Non-Commercial Drivers

The presence of sleepiness and/or cognitive dysfunction associated with OSA is likely to interact in the substantially increased risk of road traffic accidents seen in non-commercial drivers with OSA. Epidemiological studies have established a link between OSA and motor vehicle accidents (MVAs), generally showing a two to seven times increased risk of road traffic accidents in non-commercial drivers with OSA (Barbe *et al.* 1998a; Findley *et al.* 1988; Findley *et al.* 1992; Teran-Santos *et al.* 1999b; Wu and Yan-Go 1996a; Young *et al.* 1997a).

The evidence linking OSA and MVAs in the general population comes from several sources. Firstly, early questionnaire studies reported that about a third of sleep apnoea patients had a MVA in the past five years (Gonzalez-Roth R *et al.* 1988), 19-27% had a MVA due to falling asleep (Bearpark 1990; Guilleminault C. *et al.* 1978) and 22-57% had habitual sleepy spells whilst driving their motor vehicle (Bearpark 1990; Haraldsson PO *et al.* 1990). Studies that have compared self-reported accident rates in sleep apnoea patients to those of controls have consistently shown OSA patients to have higher accident rates (Haraldsson PO *et al.* 1990; Horstmann S *et al.* 200; Masa J *et al.* 2000; Wu and Yan-Go 1996b). Wu *et al.* reported that sleep apnoea patients (RDI > 5) were three times as likely to have been involved in an MVA as non-OSA patients (Wu and Yan-Go 1996b). One Swedish questionnaire study found a seven-fold increase in the number of

single MVAs in sleep apnoea sufferers (defined as the habitual occurrence of the clinical triad of snoring, awakenings and/or history of sleep apnoeas, and daytime somnolence) when compared with controls (Haraldsson PO *et al.* 1990).

However, because of the limitation of questionnaire studies, which rely on subject participation, honesty and memory (in other words, they are subject to 'recall bias'), other researchers have confirmed the increased accident risk of sleep apnoea sufferers using objective government records or insurance accident data. However, it is important to realise that even this objective data may underestimate the frequency of road traffic accidents in this population because OSA patients are prone to single vehicle accidents, which may sometimes go unreported. Similarly, more trivial accidents, which do not require mandatory government or insurance reporting, would not be included in these figures. In one study, Findley et al compared the number of reported MVAs in proven OSA patients (RDI > 5) with that in age and sex matched controls with negative sleep studies and with the total 3.7 million licensed drivers of Virginia (Findley *et al.* 1988). They found that the number of accidents per driver per five years was 0.41, 0.06, and 0.16 in the three groups respectively, indicating that drivers in the OSA group were seven times more likely to be involved in a MVA compared with controls and almost three times more likely compared with the general population. The general population may have had a higher incidence of accidents than the control group due to hidden medical conditions such as stroke, epilepsy, sleep apnoea, etc (Naughton M and Pierce R 1991). Barbe et al obtained objective accident data from insurance companies and compared 60 consecutive patients with sleep apnoea (RDI > 20) and 60 aged and sex matched controls

(Barbe *et al.* 1998b). They demonstrated that sleep apnoea patients had a 2.3 times greater risk of accidents and a 5.2 times greater risk of multiple accidents, compared with controls.

Recently, Teran-Santos and co-workers conducted a case-control study of the relationship between sleep apnoea and the risk of traffic accidents (Teran-Santos *et al.* 1999a). They performed sleep studies on patients presenting to hospital after a highway vehicle crash and on a control group of primary care patients. They found a seven-fold increase of OSA (RDI \geq 10) in the highway accident victims. This relation remained significant after adjustment for potential confounders, such as alcohol consumption, visual refraction disorders, body mass index, years of driving, age, history with respect to traffic accidents, use of medications causing drowsiness, and sleep schedule. When the presence of OSA was combined with having consumed alcohol on the day of the accident, the odds ratio was 11 for accident victims compared with controls.

In arguably the best study to date that has examined the risk of having a MVA associated with undiagnosed OSA, Young *et al.* reported on 913 employed public servants in Wisconsin (Young *et al.* 1997b). This was a population based sample, and hence free from clinic selection bias. All subjects underwent full sleep studies. Motor vehicle accident history was obtained from a state wide database of all traffic violations and accidents from 1988 to 1993. Overall, men with sleep disordered breathing (SDB - habitual snorers, RDI $>$ 5) had three times the odds of having at least one motor vehicle accident in five years compared to those without SDB ($p < 0.001$). Men with only mild

OSA (5–15 apnoeas per hour of sleep) were 4.2 times more likely to have had a motor vehicle accident compared to those without SDB. Observed odds ratios did not increase with OSA severity, and there were no associations for women. In contrast, the odds ratios for SDB and multiple reported crashes were positive for both men and women – men and women combined with more than 15 apnoeas per hour of sleep were 7.3 times more likely to have multiple motor vehicle accidents in five years than those with no SDB.

In the study by Young et al above, there was no association between OSA severity and MVA risk. This lack of a dose-response relationship between OSA severity and accident risk has been discussed by several authors (Barbe *et al.* 1998b;Engleman H and Joffe D 1999;George 2001). It suggests mild OSA patients may share the same MVA risk as severe apnoeics. Given the relative frequency of mild OSA, its individual contribution to road accidents is therefore potentially very large. The significance of mild OSA to driver fatigue will be discussed in more detail in section 1.3 of this chapter.

1.2.3.5 Obstructive Sleep Apnoea: Prevalence & Accident Risk in Commercial Drivers

Specific and robust data on the prevalence and accident risk with respect to OSA in commercial drivers is generally lacking. Commercial drivers are thought to constitute a high risk group for OSA, being predominantly male, and often middle aged and overweight - 3 important risk factors for OSA (Dealberto *et al.* 1994;Diaz *et al.* 2001;Redline *et al.* 1994).

In a Finnish study, the frequency of sleep apnoea syndrome and its contribution to driver sleepiness was assessed by questionnaires in a sample of both long haul (n=184) and short haul (n=133) drivers (Hakkanen and Summala 2000). This study found that only four percent of the long haul drivers and two short haul drivers reported the clinical syndrome of snoring heavily and loudly at least three nights per week, respiratory disturbances at least one night per week, and excessive daytime sleepiness (Epworth Sleepiness Score above 10). Sleep apnoea syndrome contributed only slightly ($R^2 < 5\%$) to predicting driver sleepiness-related problems (difficulty in staying alert during work driving, microsleeps, or near misses). This study was limited by a non random selection of Finnish truck drivers (all the drivers surveyed were from the one trucking company), a variable and inadequate response rate (from 10% to 95% for different sub groups of drivers), and the need to rely on symptoms alone to define sleep apnoea syndrome; age and body mass index were measured, but not incorporated into a multivariate prediction formula for OSA (Rowley *et al.* 2000), and there was no driver polysomnography.

Stoohs *et al.* used portable screening devices to investigate the prevalence of OSA in a group of long haul truck drivers from a single US trucking company (Stoohs *et al.* 1995a). They performed limited sleep studies on 41% of all the drivers who presented to a truck loading hub over the study period. Different prevalence rates were reported for different degrees of severity of OSA. They found that 78% of the drivers had an oxygen desaturation index (ODI, a measure of nocturnal breathing disturbance, like the 'RDI') of at least 5, 46% had an ODI at least 10, and 10% had severe OSA (ODI at least 30). These high prevalence figures for OSA in commercial drivers are similar to those obtained in a

recent study of commercial bus drivers from one bus company in Hong Kong (Hui *et al.* 2002). This study also used limited sleep studies to measure OSA (MESAM IV device). They found that 61% of drivers had an RDI of at least 5 per hour of sleep, 41% had an RDI of at least 10 per hour of sleep, and 10% had an RDI of at least 5 per hour together with excessive daytime sleepiness (ESS > 10).

Stoohs' alarmingly high prevalence rates for OSA led the US Department of Transportation to fund a further study of sleep apnoea prevalence in commercial drivers. Pack *et al* from the University Of Pennsylvania have recently completed and presented their results in abstract form (Pack *et al.* 2000b). In this study, commercial drivers were first sent a survey which contained questions that stratified the drivers into high and low risk groups for OSA. However, the response rate from this survey was only 31%. Then, approximately one half from the higher risk strata and one fifth from the lower risk strata had full in laboratory polysomnography (n=408). The weighted prevalence for OSA was found to be 25% (RDI \geq 5/hr) and 5% of the drivers had severe OSA (RDI \geq 30/hr). Shortfalls of this study include a limited response rate and a low percentage of long distance drivers (approximately 11%). A similar prevalence figure has been reported in abstract form for Spanish long-haul professional drivers (Diaz *et al.* 2001). These authors found that the prevalence of OSA (AHI > 5) was 25% amongst a cohort of 188 drivers who had full polysomnography. However, the prevalence of sleep apnoea syndrome was disproportionately high in this Spanish study (8.6%). The studies by Pack *et al* and Diaz *et al* report much lower prevalence figures for OSA in commercial drivers than those by

Stoohs et al and Hui et al, but these lower figures are in line with estimates from prevalence studies in other populations.

It is clear that adequate data on the prevalence of OSA in commercial drivers is lacking; much of the existing data is of poor quality (diagnosis of OSA by symptoms or limited sleep studies), lacks generalisability (select populations, poor response rates), or is only reported in abstract form. However, there is even less data on the accident risk associated with OSA in this occupational group.

In one study which investigated factors associated with falling asleep at the wheel in a sample of 600 truck drivers, symptoms and signs of a sleep disorder (higher body weight, snoring, breathing stopping during sleep, and self-reported poor sleep at home) were one of 6 variables found to be significant predictors of a driver ever having fallen asleep at the wheel (McCartt *et al.* 2000). Other predictors included more arduous work schedules; shorter, poorer sleep on the road; and a greater tendency to night time drowsy driving. Another study has reported that heavy goods vehicle drivers who report regular snoring or who are obese or who have a noticeably large collar size have higher accident rates than those not exhibiting these characteristics (Maycock 1997). Other information on accident risk due to OSA in commercial drivers comes from a recently published abstract. This has shown greater sleepiness and driving impairment (based on MSLT, driving simulator, and PVT tests) with increasing RDI in commercial drivers, especially among those with an RDI > 30 (Dinges *et al.* 1998).

Finally, in an extension of the study by Stoohs et al. discussed above, the authors have reported on self-reported and company recorded accident rates in their long haul truck driver cohort (Stoohs *et al.* 1994b). They found that truck drivers with sleep disordered breathing had a two-fold higher accident rate per mile than drivers without sleep disordered breathing. Accident frequency was not dependent on the severity of the sleep disordered breathing. Obese drivers with a body mass index of at least 30kg/m² also presented a two-fold higher accident rate than non-obese drivers.

1.2.3.6 How many MVAs are caused by sleep apnoea?

In a recent submission to the Australian Commonwealth Parliamentary Enquiry into Fatigue and Transport, the population attributable risk for sleep apnoea was estimated as between 12% and 46% depending on which sleep apnoea prevalence figure and which relative risk value is used in the calculation (Neville 2000). Using this measurement and NSW RTA figures for 1997, between 5164 and 19794 accidents involving male drivers aged 30-60 are estimated to be attributable to sleep apnoea in NSW annually. In other words, completely eliminating the risk of sleep apnoea in the NSW population would reduce the number of annual road accidents by this figure (for more detailed discussion, see Attachment 1).

1.2.3.7 Reduction of Fatigue Accidents with OSA Treatment

OSA can be effectively treated with nasal continuous positive airway pressure (CPAP). This device, placed by the patient's bedside, generates air pressure and delivers it through a sealed face mask, thus splinting open the upper airway during sleep (Sullivan *et al.*

1981). In this way CPAP prevents recurrent upper airway obstruction during sleep and treats OSA on a night-to-night basis whenever it is used.

Regular use of CPAP improves self-reported MVA rates (Cassel *et al.* 1996a;Engleman *et al.* 1996b;Krieger *et al.* 1997;Yamamoto *et al.* 2000) and objective MVA rates (Findley *et al.* 2000a;George 2001). In a self-report study of 59 drivers, Cassel and co-workers found a decrease from 0.8 accidents per 100,000 km driven to 0.15 after treatment (Cassel *et al.* 1996b). Recently, Findley et al showed a marked reduction in objective reports of motor vehicle crashes over two years in 36 subjects with sleep apnoea (mean RDI 37/hr) treated with CPAP (0.07 versus 0 crashes per driver per year) while, in contrast, the crash rate did not fall in 14 subjects with sleep apnoea who did not accept treatment (0.07 crashes per driver before and after diagnosis) (Findley *et al.* 2000b). This study found that successful treatment of sleep apnoea prevented five motor vehicle crashes in 36 patients during two years of treatment. The state reported crashes analysed in this study were serious “at fault crashes”, where the driver was given a traffic citation and caused property damage and/or personal injury (Findley and Suratt PM 2001). In a larger group of patients with sleep apnoea (mean AHI 54/hr), George confirms that those who are treated with nasal CPAP have a decrease in objectively measured crashes (George 2001). His study found that successful treatment of sleep apnoea with CPAP prevented 75 motor vehicle crashes in 210 patients during three years of treatment (a decrease of 0.12 crashes/driver per year) (Findley and Suratt PM 2001). These were also serious crashes resulting in property damage and/or personal injury (see figures below).

Figure 7 Effect of CPAP treatment on accidents (George 2001)

Mean (SD) accident rates for -

**(A) patients with OSA during the 3 years before and after treatment with CPAP and
(B) control subjects during the same time frame**

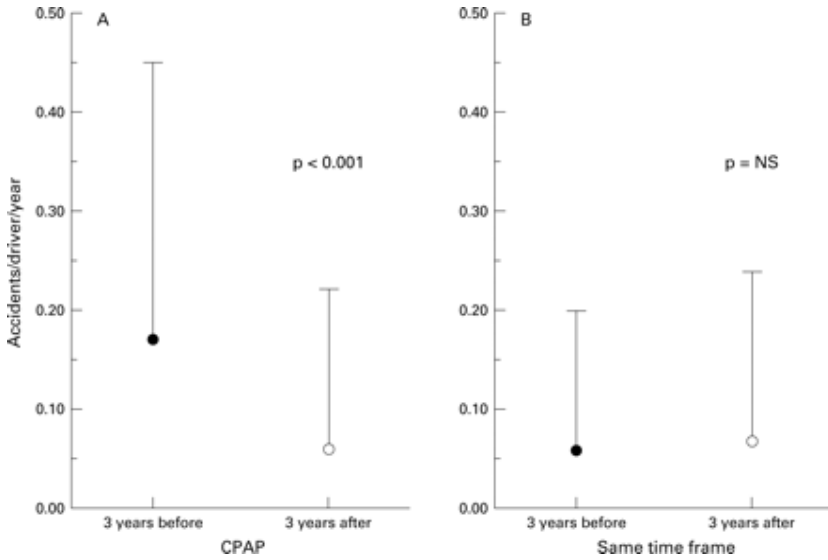
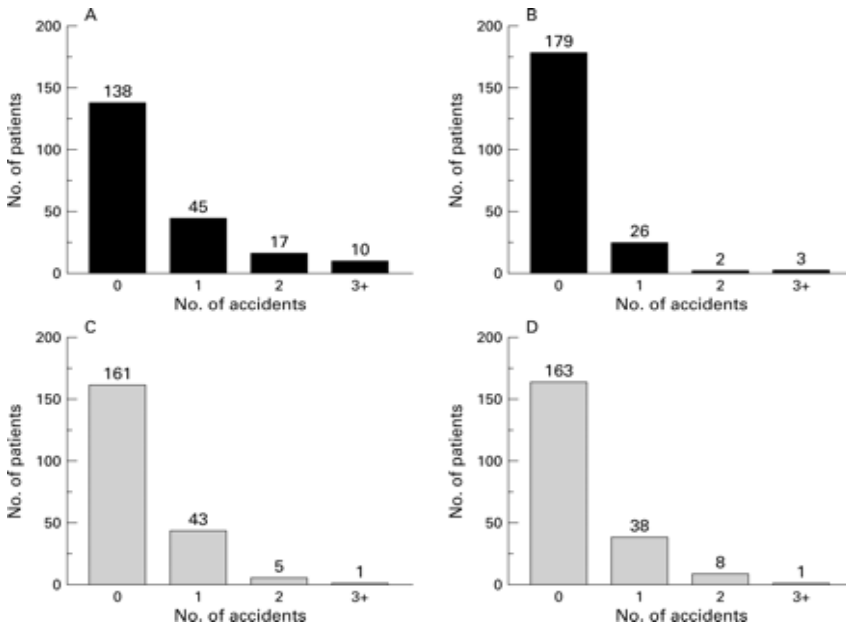


Figure 8 Distribution of accidents in patients with OSA (George 2001)

**(A) during the 3 years before and
(B) during the 3 years after treatment with CPAP
and in controls during the same time frame (C, D)**



Both of the above studies show an improvement in objectively measured accident rates after commencing CPAP treatment (Findley *et al.* 2000b;George 2001). These findings extend the data that show improvements in self-reported accident rates in OSA patients who are treated with CPAP. However, a placebo controlled, randomized prospective trial is lacking to more definitively show this important effect of CPAP on MVA rates.

A recent study has reported on the ability of a driving simulator test (C.A.R.) to demonstrate an improvement in accident risk in OSA patients on CPAP treatment (Ortho *et al.* 2002). In this study, driving simulator performance was measured in 31 patients with OSA (RDI 24.8 +/- 21.5/h) before, 2 and 42 days after initiation of CPAP, and was compared to 10 healthy controls in whom OSA was excluded by polysomnography. Driving simulator performance before treatment was significantly worse in OSA patients as compared to healthy controls, especially in terms of accident frequency and concentration faults. However, on CPAP, accident frequency and the frequency of concentration faults were lowered significantly for both the short and medium terms of therapy. Others have also demonstrated significant improvements in driving simulator performance in OSA patients on CPAP therapy (Findley *et al.* 1989;George CF *et al.* 1997;Munoz *et al.* 2000), including one study in which patients who had been randomized to therapeutic CPAP showed improved steering performance and reaction times, compared to OSA patients randomized to subtherapeutic nasal CPAP (control group) (Juniper *et al.* 2000).

1.2.3.8 Legal Discussion of OSA and Road Safety in Commercial Drivers

Ian Callinan, Q.C., currently a Justice of the High Court of Australia, addressed some of the legal issues relating to OSA and commercial driving in Australia in a discussion paper in 1993 (Attachment 2). The framework for his discussion of the issue of OSA in commercial drivers was that of hypothetical situations which could in the future confront an employee, employer or an insurance company in this area.

In his opening remarks, he likened the current thinking about sleep apnoea to early thinking about Asbestosis and AIDS, commenting on the inevitable greater public awareness of both sleep apnoea and “its very serious implications”.

1.2.3.8.1 Driver Issues

When discussing sleep apnoea in the context of employee drivers, Justice Callinan briefly explored some legal aspects of fall asleep road accidents, where the driver who caused the accident thinks he might suffer from OSA. He explained that if the accident was caused by a sudden and unpredictable event without any warning (e.g., falling asleep *suddenly*), then it does not constitute criminal conduct. The key to this defence is the “suddenness and unexpected nature” of the precipitating event. However, he went on to state that:

“a driver who suspects that he might suffer Sleep Apnoea can hardly claim that if he is overtaken by sleep at the wheel he has been overtaken by a sudden and unpredictable

event. Such a driver runs the serious risk of being charged in respect of the accident caused by his falling asleep.”

This important issue of whether falling asleep at the wheel can occur without warning is very controversial. In 1992, in *Jiminez v the Queen* (Commonwealth Law Reports 1992), the High Court of Australia set an important precedent in their judgement on a case of a fall-asleep road accident. In this judgement, they said that just because an accident is caused by a driver falling asleep, this does not necessarily mean that the driver has had sufficient warning to allow himself or herself to stop driving. In other words, they believed that a driver can fall asleep without warning or remembering. Since sleep is an involuntary state, and people cannot be charged for involuntary acts, a “*Jiminez-defence*” potentially provides many drivers with the legal ability to escape any blame in the case of fall-asleep road accidents. A significant number of other cases in NSW which may have been charged under section 52A of the *Crimes Act* (NSW 1900) have been the subject of successful application that there be no further proceedings because of sleep or blackouts (Gray 1998). Since the Jiminez findings, there have also been a series of unsuccessful prosecutions or successful appeals (1995) based on the defence that the driver fell asleep without warning or did not remember falling asleep.

The premise that sleep can occur without warning, however, is at odds with legal opinion in other countries and current medical evidence (Ellis and Grunstein 2001). The Canadian and English courts maintain that, regardless of the circumstances, the ordinary person who allows themselves to fall asleep at the wheel is liable for their actions. These

judgements are predicated on the “prior fault” principle (McCutcheon JP 1997) that there was a period of time prior to being asleep, of voluntary conduct when a person chose to take the risk of continuing to drive. This way of thinking was recently used in the United Kingdom to convict a driver who had fallen asleep at the wheel after driving sleep-deprived, and subsequently caused an extensive rail crash involving two trains and killing 10 people (Leeds Crown Court 2002). This rail disaster, occurring in February, 2001, attracted extensive world-wide press at the time.

Although the view of the Australian High Court allows for the possibility of pathological conditions such as narcolepsy or sleep apnoea to suddenly be expressed, this view is difficult to justify in patients who do not have these conditions and does not agree with medical evidence. A recently published study (Reyner and Horne 1998) has shown that healthy people do not fall asleep without significant symptoms of sleepiness for some period of time. In this study, 28 healthy drivers had their sleep restricted to five hours on the night before they were required to drive an (immobile) car for two hours under realistic simulation. In the twelve subjects who had accidents that were related to sleepiness, in each case these incidents were preceded by periods where the subjects had forewarning of moderately severe sleepiness for an average of 43.5 minutes. This would certainly amount to sufficient warning to allow an individual to stop driving and take some remedial action. Similar evidence has been reported by Lisper and co-workers, using drivers in real cars on a closed track (Lisper HO *et al.* 1986). Further, in another study where subjects were acutely sleep deprived and then underwent serial performance testing, subjects reported a systematic increase in subjective sleepiness in the period

leading up to their first sleep episodes (Atzram *et al.* 2001). All of these studies have used healthy volunteers. Similar evidence looking at an individual's perception of sleepiness prior to sleep onset is now needed for other groups, especially for those with OSA. It is important to note that, in order to be aware that one has fallen asleep, a person has to be asleep for at least a minute or so (Bonnet and Moore 1982). People who are woken in less than that time, genuinely disbelieve that they have been asleep. A driver who dozes momentarily at the wheel of a vehicle is likely to be woken spontaneously or crash before waking and is unlikely to remember being asleep. However, this "amnesia" would not be expected to extend to a period of drowsiness prior to actually falling asleep.

1.2.3.8.2 Employer Issues

When discussing OSA in the context of employer obligations, Justice Callinan felt that a driver with obvious signs of sleep apnoea can certainly be legally removed from duties until he has been tested and treated: "Indeed, in my opinion, he must be". Furthermore, he writes that if a driver was found to have sleep apnoea after a fall asleep road accident, even if his symptoms prior to the accident were not apparent: "I still think that an employer, today (1993), if not today, certainly tomorrow, runs the risk of being found to be negligent, by failing to have a system which keeps susceptible drivers off the road".

1.2.3.8.3 Insurance Issues

When discussing sleep apnoea in the context of driver insurance, Justice Callinan felt that there was a clear obligation for a driver to inform his insurer of sleep apnoea, as it might affect his capacity to drive, in a similar way that epilepsy or partial blindness might be

reported. Furthermore, he felt that “it would be perfectly reasonable for any insurer of fleet owners to request that they screen their drivers (for sleep apnoea) as a condition of the obtaining of a policy”.

1.2.3.9 The Licensing Issue of OSA

One area Justice Callinan did not address in his paper is the responsibility of licensing authorities to have appropriate policies in place to deal with OSA and driver fatigue. Indeed, recent licensing decisions in NSW concerning fall asleep road accidents in the setting of undiagnosed or under treated sleep disorders have been very variable (Desai *et al.* 2002). As part of a strategy to deal with this, on August 17, 2001, the NSW government introduced new regulations giving the NSW RTA explicit power to suspend a license immediately where there has been loss of consciousness and death or injury, modifying the Road Transport (Driver Licensing) Regulation of 1999. This has effectively removed some of the legal constraints on license suspension which had previously handicapped the RTA in managing fall asleep MVAs. Similarly, Austroads has recently updated the 1998 “Assessing Fitness To Drive” Guidelines for Medical Practitioners in the area of sleep disorders to more accurately reflect current knowledge about the dangers of sleep apnoea and driving for both private and commercial drivers (Australian Sleep Association 2002). These new guidelines will increase the pressure for all types of drivers with OSA to be effectively treated and followed up medically in order to remain licensed to drive.

1.2.3.10 Difficulties in Identifying Drivers with OSA at Most Accident Risk

Parts of the preceding sections of this chapter have shown that as a group non-commercial drivers with OSA have increased road accident rates and poorer driving simulator performance. In fact, George et al. have demonstrated that many subjects with OSA show driving impairment equal to or greater than that due to alcohol, strengthening the argument that many patients with untreated OSA should not drive (George CF *et al.* 1996). However, in the study by George et al., it is important to also note that some drivers with OSA were as good as, if not better than, the control subjects in terms of their driving performance. This is consistent with the clinical impression that not all patients with OSA are poor drivers or have accidents.

No studies have yet been able to determine which individuals with OSA have the greatest risk of road accidents. Importantly, there does not appear to be a clear dose-dependent relationship between RDI and either real-world or laboratory-assessed driving ability (Engleman H and Joffe D 1999; Engleman *et al.* 1996a; Flemons *et al.* 1993; George 2001; Stoohs *et al.* 1994a; Young *et al.* 1997b). Young et al, in their important paper describing the positive relationship between sleep-disordered breathing and motor vehicle accidents in a large population based sample, found that the odds ratios for having an MVA did not increase with RDI severity of OSA (Young *et al.* 1997b); in fact, the group of men with only mild OSA (AHI 5 to 15) showed the greatest odds ratio for having a single vehicle accident in the five year study period (OR 4.2, 95% CI 1.6 to 11.3), compared to private drivers without sleep disordered breathing. The frequency of self-reported actual accidents (Stoohs *et al.* 1994a) and near misses (Engleman *et al.* 1996a)

has also been shown to have no significant correlations with RDI, either in a clinical series (Engleman *et al.* 1996a) or in a community sample of transport drivers (Stoohs *et al.* 1994a). Finally, in 180 consecutive OSA patients, Flemons and co-workers found no significant correlation between RDI and obstacles hit during Steer Clear (Flemons *et al.* 1993). Hence, OSA severity, as measured by the RDI, does not seem to predict road accident risk.

Other clinical or physiological markers commonly used to describe OSA disease severity (e.g., degree of daytime sleepiness, nocturnal hypoxaemia) do not appear to be able to clearly differentiate those OSA patients at higher risk of having an automobile accident. The MSLT has not been shown to predict accident risk in OSA patients in two studies (Aldrich M 1989;Young *et al.* 1997b). Two studies have shown that the degree of nocturnal hypoxaemia on a sleep study does help to predict accident risk in OSA patients (Aldrich M 1989;Noda *et al.* 1998), whereas one has reported that it does not (Barbe *et al.* 1998b). Several researchers have investigated whether hypersomnolence on the Epworth Sleepiness Scale (ESS) might identify those drivers with OSA at most risk of road accidents (Barbe *et al.* 1998b;Masa J *et al.* 2000;Maycock 1996;Noda *et al.* 1998;Teran-Santos *et al.* 1999a;Young *et al.* 1997b). These studies have for the most part been negative in this respect (Barbe *et al.* 1998b;Masa J *et al.* 2000;Teran-Santos *et al.* 1999a;Young *et al.* 1997b). In the study by Young *et al.*, the addition of ESS scores into their analyses did not substantially change the magnitude or the statistical significance of any of the odds ratios for SDB and accident history. Also, the combination of both sleepiness and SDB did not significantly predict accident history in their sample (Young

et al. 1997b). Similarly, Teran-Santos and co-workers, in their case-control study of highway accident victims, did not find that self-reported sleepiness using the ESS explained the association of OSA and motor vehicle crash history (Teran-Santos *et al.* 1999a).

While studies have generally not shown that sleepiness as measured by the ESS can predict road accident risk in those drivers with OSA, there is a small amount of encouraging data which suggests that other questions asking specifically about *driver sleepiness* may help to identify those with OSA at greatest accident risk (Lloberes *et al.* 2000;Masa J *et al.* 2000). One reason for this may be that the ESS lacks adequate sensitivity and specificity with regard to driving performance. Alternatively, the lack of finding sleepiness as a clear explanatory factor in the OSA-motor vehicle crash association is concerning because it may indicate that drivers with OSA do not perceive performance impairment, and thus may not be likely to take extra precautions when driving.

There is still therefore an urgent need to identify those subgroups of drivers with OSA who are most at risk of MVAs. From a road safety point of view, however, it is comforting that CPAP treatment of drivers with OSA significantly reduces, and possibly even eliminates, their accident risk from OSA (see section 1.2.3.7).

1.2.4 Length of Driving without Rest

A fourth cause of driver fatigue will be discussed briefly in this section. This factor is targeted extensively in local road safety advertising e.g. the ‘Stop, Revive, Survive’ campaign of the NSW RTA.

The effects of prolonged driving on fatigue are well documented. Common findings are that driving performance deteriorates steadily within a four to six hour driving session, and that these deteriorations are apparent much sooner during night time driving (Dureman and Boden 1982; Haworth *et al.* 1987; Kecklund and Akerstedt 1993; Riemersma *et al.* 1977).

In a recent European study, 300 drivers who had driven into a highway rest stop were interviewed about their drive and previous sleep/wake patterns, and tested with a reaction time test (Philip *et al.* 1999b). Time of day of testing was controlled for in the analysis. These authors found that the duration of driving, the absence of rest stops, and the driver’s age were significant predictors of poor reaction time performance.

In an ambulatory EEG study of night driving in long distance truck drivers, Kecklund and co-workers reported an increase in drivers’ subjective sleepiness and objective sleepiness (as measured by greater alpha and theta EEG burst activity) during the last three hours of a night drive (Kecklund and Akerstedt 1993). Regression analyses showed that total work hours and total break time predicted 66% of the variance of the alpha burst activity

during the end of the drive, suggesting that extended work hours, together with reduced break time, were the major factors causing the drivers' sleepiness.

Similar to the other fatigue promoting factors discussed in previous sections, prolonged driving without rest has been shown to be associated with increased MVA rates. Much of the evidence for this comes from studies of commercial drivers (Hamerlin 1987; Harris 1977; Hertz 1988; Jones and Stein 1987; Lin *et al.* 1994). In one study, using operational data from a US national motor carrier, researchers reported that total driving time had a greater effect on crash risk among truck drivers than either time of day or driving experience (Lin *et al.* 1994). In another study, Jones and Stein observed that tractor-trailer drivers who violated logbook regulations (OR=2.6) or who drove more than eight hours at a stretch (OR=1.8) were at increased risk of being involved in crashes (Jones and Stein 1987). Finally, Hertz found a significantly increased risk of fatal crash involvement associated with splitting the required eight hours of rest into two consecutive sessions in a sleeper berth (OR=3.0) (Hertz 1988).

1.2.5 Alcohol Consumption

Alcohol has well known effects on vigilance and attention and there is also strong evidence indicating that the vigilance impairing effects of alcohol are exacerbated by sleepiness & fatigue.

Studies have shown that during periods of increased circadian propensity to sleep, alcohol produces greater impairment in performance than corresponding alcohol levels

tested at other times (Horne and Baumber 1991;Koelega 1995). In a study by Horne et al, young women with blood alcohol concentrations within the United Kingdom legal limits underwent a 40 minute monotonous motorway driving task in the early afternoon (increased sleep propensity time) and these results were compared with a six pm drive (low sleep propensity time) (Horne and Baumber 1991). Alcohol significantly affected performance on this task, especially during the early afternoon.

In another study, subjects who had been sleep restricted (to four hours time in bed the night before) and had blood alcohol concentrations of around 0.01, performed significantly worse on a driving simulator task in the afternoon than a control group who had been similarly sleep restricted, but whom had taken oral placebo drinks (Roehrs *et al.* 1994). In other words, in the setting of sleepiness or fatigue, blood alcohol levels well below the accepted legal limits are associated with important impairments of driving skills.

In a major review of the effects of alcohol on vigilance, Koelega et al extensively reviewed the literature in this area, examining 38 studies which compared the effects of alcohol and placebo on vigilance tasks (Koelega 1995). These studies showed that the main effect of moderate doses of alcohol is on attention and information processing. The capacity to divide and sustain attention is already impaired at blood alcohol levels of 0.02 to 0.03%. The effects of alcohol appeared to some extent time dependant and were greatest during periods of sleepiness (the early afternoon and after midnight). This author stated that on the evidence from the literature, the blood alcohol standard for driving

should be lowered to 0.02% for driving after midnight and for special risk groups (young and less experienced drivers).

1.3 Additive Fatigue Effects

It is clear that many of the above factors that promote driver fatigue are unlikely to operate in isolation. Any one driver may be vulnerable to multiple fatigue promoting factors, creating an enhanced sleep propensity and road accident risk. For instance –

- both acute and chronic sleep deprivation are very frequent in society and likely to co-exist in a driver
- driving at night may be coupled with driving acutely sleep deprived if an individual starts the night drive without sleeping during the preceding day. In this situation, the individual's driver fatigue may be even further increased by prolonged driving, if insufficient breaks are made during the night drive
- driving under the effects of alcohol may be coupled with night time or early afternoon (post lunch) driving

Commercial drivers, in particular, are vulnerable to compounded fatigue promoting factors. Their schedules usually require them to work long hours, frequently at times which conflict with natural circadian rhythms, both acute and chronic sleep debt are common (section 1.2.1.3), and there is evidence that they have a very high prevalence of sleep disorders (section 1.2.3.5). As an occupational group with a high level of driving

exposure, and who operate heavy and dangerous motor vehicles, driver fatigue and the additive factors promoting it clearly represent important safety issues.

1.3.1 Additive Effects of Mild OSA and Other Fatigue Promoting Factors

Just as fatigue associated with prolonged driving or alcohol is enhanced by circadian factors (sections 1.2.4, 1.2.5), it is intuitive that OSA should show additive fatigue effects when combined with other fatigue promoting factors, such as time of day or sleep deprivation. There has been some limited work on the additive effect of sleep deprivation and OSA. This has shown that the coincidence of OSA and sleep deprivation may have a multiplicative adverse effect on OSA outcomes (section 1.3.2 below). However, the interaction of OSA and other fatigue promoting factors has never been studied specifically in the context of driving. This issue is very important, particularly for the large group of drivers with only mild OSA, who may not be aware of their diagnosis or who may not accept treatment. Should patients with mild sleep apnoea avoid driving if they have been unable to sleep more than seven hours per night over the preceding nights? Should mild sleep apnoea patients avoid night driving all together?

Most patients with mild OSA are undiagnosed and untreated. Since many of these people experience few daytime symptoms, they often do not present to doctors and, if they do, they may not necessarily be treated; in the medical community, there is debate about the importance of treating patients with mild OSA (Engleman H 2002). Most clinicians would agree that patients with moderate to severe OSA require treatment, usually with nasal CPAP. However, mild OSA patients, who typically have between 5 to 15

respiratory events per hour of sleep, have a less disrupted sleep pattern than those patients with more severe disease. Advocates of CPAP treatment for mild OSA point to the neurocognitive deficits (including sleepiness), the risk of hypertension and the risk of MVAs associated with mild OSA (sections 1.2.3.4, 1.2.3.5), while those against CPAP treatment for this group are concerned with the difficulties patients have complying to nasal CPAP, especially if reported symptoms are minimal, and the huge numbers of individuals that would need CPAP treatment if all patients with mild OSA were treated.

Trying to ascertain the added effect of other fatigue promoting factors on driving in mild OSA patients will have important implications for advice about driving habits and accident risk for this large group of drivers, but will also aid in decisions about therapy for mild OSA, especially in the setting of high risk occupational groups such as commercial drivers.

1.3.2 The Effect of Sleep Deprivation on Obstructive Sleep Apnoea

There is a small amount of published work, which shows that sleep deprivation (acute and chronic partial) worsens OSA. There are several physiological reasons why this might occur. Firstly, breathing responses to hypoxia may be decreased after sleep deprivation (White *et al.* 1983); second, sleep deprivation has been shown to have a depressant effect on upper airway dilator muscle activity, which is important in maintaining upper airway patency during sleep (Leitter *et al.* 1985); and finally, sleep deprivation subsequently increases REM sleep, where apnoeas are more likely to occur.

Some of the earliest published work on sleep disordered breathing noted the deleterious effect of sleep deprivation on nocturnal breathing (Guilleminault C. 1980;Lugaresi *et al.* 1978;Sullivan C *et al.* 1984). Sleep deprivation was reported to exacerbate snoring (Lugaresi *et al.* 1978) and increase the frequency and severity of sleep-related obstructive breathing disorders in both snorers (Sullivan C *et al.* 1984) and patients with mild-moderate OSA (Guilleminault C. 1980).

More recent work has shown that the loss of one night's sleep results in an increase in the RDI of OSA patients of over 200% (Persson and Svanborg 1996). Haraldsson and co-workers have also reported similar results (Haraldsson PO *et al.* 1992). Furthermore, a small pilot study investigating the effect of chronic partial sleep deprivation (reduced sleep below normal levels for multiple nights) on OSA revealed an increase in RDI of over 50% after six nights of only four hours sleep per night (Stoohs and Dement 1993). In addition, this study reported that the minimum oxygen saturation was significantly reduced following sleep deprivation. Guilleminault and co-workers have also shown a general trend towards longer apnoeic events during sleep and a lowering of blood oxygen saturation secondary to apnoeic events following acute sleep deprivation of a small number of mild-moderate OSA subjects (Guilleminault C. and Rosekind 1981).

Given the interaction between sleep deprivation and OSA described above, one could easily imagine a “self-feedback loop”, in which sleep deprivation would worsen OSA, which would, in turn, have a negative impact on nocturnal sleep quality and sleep hours, worsening sleep deprivation even further. Hence, the coincidence of OSA and sleep

deprivation may even have a multiplicative, rather than an additive, adverse effect on daytime function, e.g. with respect to driving.

Chapter 2: Methods

The data for the “Commercial Drivers Study” were collected over a 21 month period from June 2000 to February 2002 in two groups of NSW transport drivers. One group consisted of 1000 transport drivers who were surveyed at their workplace. The other group consisted of 61 transport drivers who had detailed testing in a hospital sleep laboratory. Data for the “Mild Obstructive Sleep Apnoea Study” were collected over a 10 month period from February to November 2001 from a sample of 29 subjects. The third study consisted of a “Medico-Legal Case Series”. These clinical cases were identified by an audit of consecutive referrals to the Sleep Disorders Centres at Royal Prince Alfred Hospital (n = 6) and Westmead Hospital (n=1), Sydney, for medico-legal opinions in fall asleep road accidents, where the driver who caused the accident survived. This chapter describes the research protocols, subjects, data collection instruments, and statistical analyses for these studies.

2.1 Commercial Drivers Study

2.1.1 Project Design

One group of drivers were asked to complete an anonymous questionnaire at their workplaces (truck yards and truck stops) by researchers who traveled out to these locations. The second group of drivers, who had more comprehensive testing, were tested in a hospital sleep laboratory. By testing this second, smaller group of drivers in a more detailed fashion, the prevalence of OSA and its effect on driving performance could be

determined more accurately for commercial drivers. The administration of the same survey to both groups enabled some direct comparisons between the groups to be made. In this later cohort, participant anonymity was not possible, but all results were kept strictly confidential. These drivers were also compensated for their time and the inconvenience of participating in the study.

The full protocol was approved by the Central Sydney Area Health Service Ethics Committee (RPA zone), Royal North Shore Hospital Ethics Committee and the University of Sydney Ethics Committee.

2.1.2 Subjects

2.1.2.1 Target Population

Transport drivers operating in NSW were targeted for this study. Transport drivers could include truck drivers, bus drivers and forklift drivers.

2.1.2.2 Eligibility

Subjects were eligible if they were current drivers, i.e. not retired. Subjects needed to be able to understand the study requirements and had to agree to participate.

As the field study was anonymous, there was no record of drivers who had completed the questionnaire in the field. Hence, avoidance of multiple questionnaires from individual drivers relied on the subjects themselves, when approached, indicating that they had previously completed the questionnaire. Drivers with an established diagnosis of OSA

were not excluded from the study. However, when studied in the sleep laboratory, they were asked to not use any prescribed sleep apnoea treatment (e.g., CPAP or dental splints) for several nights prior to presenting to the hospital and on the night of the sleep study, so that their OSA severity could be recorded off treatment.

2.1.2.3 Recruitment

2.1.2.3.1 Field Questionnaire Collection

The subjects for the field questionnaire were recruited from three sources. Firstly, truck yard sites in and around Sydney, which had been selected at random by the NSW Transport Workers Union (TWU). Secondly, truck stops in and around NSW, which were initially selected at random from a list of major NSW truck stops provided by the NSW TWU. After this list was exhausted, additional truck stops that were on major freeways and that had a large daily throughput of transport drivers were surveyed. All transport drivers who were spending at least 10 minutes at the truck stop (time taken to complete the questionnaire) were asked if they would like to participate. Thirdly, drivers were surveyed at several large meetings, which occurred periodically throughout the recruitment period. One was a yearly delegates meeting of the NSW TWU, where drivers from all over the state were represented. Another was a fundraising event in Orange. And the third was a fatigue workshop for a large transport driving company within Sydney.

It was initially expected that all the survey data would be obtained from drivers at the truck yard sites within NSW, with access to the yards obtained with the help of the NSW TWU. Unfortunately, partly due to limited resources within the NSW TWU, it proved

very difficult to obtain adequate and frequent access to these yard sites. Rather than considerably compromising progress of the study, other drivers were surveyed in the broader way outlined above.

2.1.2.3.2 Sleep Study & Driving Impairment Investigation

The subjects for the sleep laboratory investigations were recruited from a list of transport drivers provided by the NSW TWU. This list was generated by them at random from their database of members. Specifically, the TWU selected all member drivers that were born on a particular day of the year and supplied their names and contact details. In batches of twenty, drivers on the list were mailed a letter to their home address, which detailed the laboratory testing and asked if they would like to participate. These drivers were then telephoned one to two weeks later to discuss the study more fully and gauge their interest. However, on some occasions, if the TWU contact details did not include a current telephone number, and the driver could not be found through work or a telephone directory search, the driver was not contactable; drivers who were not contactable were removed from the recruitment list. There could be many reasons for a driver to have not been contactable; for instance, the driver may have given insufficient contact details to the TWU, moved house, or died. Alternatively, some drivers considered uncontactable may merely have been non-responders, choosing not to respond to both the mail out and telephone enquiries.

2.1.3 Protocol

2.1.3.1 Field Questionnaire Collection

Eligible drivers were informed about the study, and if they agreed to participate, written informed consent was obtained. Drivers then completed the questionnaire, which generally took 10 to 20 minutes. Participants were supervised while completing the questionnaire, and were free to ask questions to clarify any parts of the survey that they did not understand. After completing the surveys, their height, weight and neck circumferences were recorded using portable measuring equipment. Drivers then placed their completed surveys and signed consent forms into separate sealed collection boxes. By separating the driver information at this point, driver anonymity and confidentiality were assured.

2.1.3.2 Sleep Study and Driving Impairment Investigation

Enrolled subjects used a sleep diary for the week preceding their arrival in the sleep laboratory. Subjects were permitted to maintain their usual caffeine intake in the days prior to attending the sleep laboratory. This usual level was recorded in questionnaire responses.

On arrival in the sleep laboratory on the Friday evening (seven pm) subjects were familiarized with the laboratory and the testing schedule, and their consent was obtained. Caffeine products and cigarette smoking were not allowed for the duration of the laboratory testing. The drivers then practised the driving simulator test and the psychomotor vigilance task (PVT), parts of the subsequent performance testing battery.

At 8 pm, the first performance testing battery commenced. This consisted of a 10 minute PVT test and then a 30 minute driving simulator test. Upon completion, the drivers were set up for their diagnostic sleep study, with lights out at approximately 10.15pm. Experienced sleep technologists monitored the patient's sleep study and saved the data for subsequent scoring and reporting. The drivers were allowed to sleep until approximately 5.30 am the next day. All leads were then removed, following which they showered and had breakfast. After breakfast, subjects were asked to fill out the same questionnaire that had been administered to the drivers surveyed in the field.

At seven am, the performance testing battery was administered for a second time. Following this, the subjects' height, weight, neck circumference, and blood pressure were measured and recorded. A urine sample was also taken for a biochemical drug screen. Finally, a brief battery of neuropsychological tests was performed prior to the last performance testing battery, which commenced between 9-10 am. Generally, all testing was finished by 10.30 am.

After the drivers' diagnostic sleep studies were scored and reported in the following week, each driver was contacted by telephone and their results discussed. A follow up thank you letter, together with a cheque to compensate for their time and inconvenience, was then sent to the driver's home address. This letter again detailed their sleep study results, and recommended that they be discussed with the driver's GP, who could obtain further specialist opinion if necessary. Contact details for specialists trained in Sleep Medicine were provided.

2.1.4 Data Collection Instruments

The following questionnaires, tests and other instruments were used to collect the data for this study. The field questionnaire is first described, as it was common to both parts of the study. The rest of the data collection instruments were used only for the drivers studied in the sleep laboratory. They are discussed in the approximate order that they were administered.

2.1.4.1 Participant Questionnaires

The participant questionnaire (Attachment 4) collected information about demographic and physical measures, daytime sleepiness, obstructive sleep apnoea, and lifestyle/driving details.

2.1.4.1.1 Demographic and Physical measures

Subjects' age and postcode were recorded and their height, weight and neck circumference were measured.

2.1.4.1.2 Epworth Sleepiness Scale

To assess the extent to which subjects felt “sleepy” during the day, the Epworth Sleepiness Scale (ESS) was used (Johns 1991). This self-reporting scale provides a measurement of a subject's general level of daytime sleepiness. It asks about the chance of dozing off or falling asleep in eight different low stimulation situations commonly encountered in daily life, e.g. sitting and reading, watching TV, sitting inactive in a public place. The subject is asked to rate (from 0 – 3) the likelihood of falling asleep in

each circumstance. A total from 0 to 24 is then calculated, with greater scores correlating with increased reported somnolence.

The ESS has been validated against objective sleepiness measures, in particular the Multiple Sleep Latency Test (MSLT), in both normal sleepers and those with a range of sleep disorders (Johns 1991). It has also been demonstrated to be an effective tool for measuring persistent daytime somnolence in adults (Johns 1992). In a community sample of 510 Australian workers, normal sleepers (no evidence of a sleep disorder) were found to have an mean ESS score of 4.6, with a range from 0 to 10; all subjects with an ESS score greater than 10 had evidence of a sleep disorder (Johns and Hocking 1997). The ESS is now used extensively throughout the world in sleep medicine research and a score of > 10 is generally accepted to represent excessive daytime sleepiness, i.e. the tendency to doze in situations that seldom facilitate dozing in normal subjects (Johns and Hocking 1997).

2.1.4.1.3 Maislin Questionnaire

The Maislin Questionnaire and equation were used to identify the presence of OSA in the questionnaire survey (Maislin *et al.* 1995). In the Maislin questionnaire, subjects report on the frequency of three symptoms of sleep apnoea – loud snoring, snorting or gasping, and breathing cessation. For each symptom, they mark a score from 0 to 4, with a higher score representing a higher reported frequency of the symptom. The probability that the subject has OSA is assessed by a formula that incorporates questionnaire responses together with data on the subject's age, BMI and gender. In a sleep clinic population, this

formula has positive and negative predictive values (definition: see Attachment 3) for an RDI ≥ 10 of 75% and 74% respectively (Maislin *et al.* 1995). The Maislin equation has been shown to perform similarly to other clinical prediction formulas used in sleep medicine research (Rowley *et al.* 2000). It is more accurate when used in a male population, compared with a female population (Rowley *et al.* 2000). The Maislin questionnaire has also been recently used in a large US prevalence study of OSA in commercial drivers, where it was used to stratify drivers into high and low risk groups for OSA, prior to polysomnography (Pack *et al.* 2000a).

2.1.4.1.4 Lifestyle and Driving Details

Questions were asked about usual sleep and work routine, type of driving (e.g., interstate or metropolitan, rotating shifts or otherwise), alcohol/caffeine intake and motor vehicle accident history. Participants were also asked to list any medical illnesses they suffer from, any medications they were taking (including those taken to improve alertness while driving) and whether they had had any treatment for OSA.

2.1.4.2 Sleep Diary

A sleep diary was sent to all subjects studied in the sleep laboratory prior to their hospital testing. Subjects were asked to complete the sleep diary for seven days before their hospital attendance. The sleep diary sought subjective information about each day's work and sleep hours. Any daytime naps could also be recorded on the sleep diary. Sleep diaries have been shown to correlate well with objective sleep measures (Lacks 1988).

2.1.4.3 Psychomotor Vigilance Task

The Psychomotor Vigilance Task (PVT) measures vigilance (sustained, focused attention) in terms of the time taken to react to a stimulus. The test is a 10 minute reaction time test, which is paced (outside the control of the subject), non stimulating, repetitive, measurable, standardised, and relatively lengthy. It provides data on various reaction time (RT) outcomes (e.g. mean RT, median RT, standard deviation of RT) and records errors (occurrences of false-starts on depressing the button, the use of the 'wrong' button, or holding the button down for more than three sec) and lapses (reaction times at least 500ms in duration). The lapse count is transformed (square root (x) + square root (x+1)) for analysis to remove zero scores and normalise the distribution. Previous studies have shown that PVT performance deteriorates with increasing sleepiness, and it can therefore be used as a means of gauging the effects of sleep deprivation or impaired sleep quality on performance (Chugh *et al.* 1998;Dinges *et al.* 1997).

2.1.4.4 AusEdTM Driving Simulator

The Australia Edinburgh (AusEdTM) driving simulator measures several cognitive skills important for driving; it is a test of tracking ability (through steering accuracy), a vigilance task (requiring sustained attention over 30 minutes), a divided attention task (through speedometer placement – see below), and a reaction time test.

A standardised 30 minute run on the AusEdTM Driving Simulator was performed subsequent to each PVT test. The AusEdTM driving simulator is designed to simulate a monotonous night time drive on a rural road. In this way the driving environment of the

simulator is very conducive to driver fatigue. Most other simulator programmes have used more stimulating protocols to assess driving performance and associated sleepiness.

The AusEd™ driving simulator evolved as a joint research project between the Sleep Units of St Vincents' Sleep Disorders Service and Royal North Shore Hospital in Sydney, Australia, and the Respiratory and Sleep Research Unit at the Royal Infirmary in Edinburgh, Scotland. Research and development of the AusEd driving simulator began in 1998 and a multi-centre validation study is presently underway.

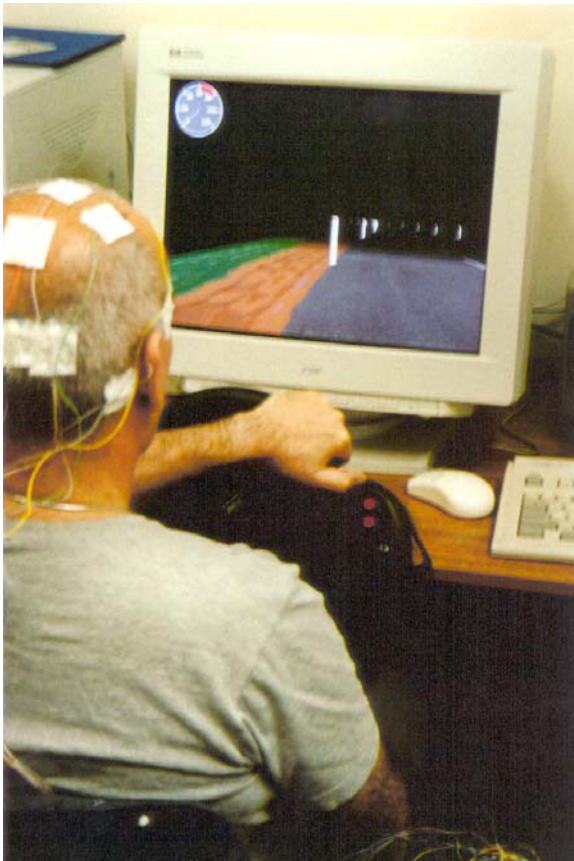
The driving simulator was installed on a Windows NT workstation in a sound-insulated room in the Sleep Laboratory, with a 21" computer screen, a Thrustmaster T2 steering wheel and pedals (Hillsboro, Oregon, USA) and dual stereo computer speakers. A full screen projection of the view from the driver's seat of a truck is provided, along with a small speedometer in the upper left hand corner of the screen (see figure below). The simulator is controlled using acceleration and brake pedals and the steering wheel. The drive takes place on a dual carriageway highway at night, with forward vision limited to "low beam" lights. During practice sessions the lights in the room remained on, whereas during the 30 minute tests, the lights were switched off. There are no other motor vehicles on the road, apart from ten slowly moving trucks, which appear during each 30 minute drive, traveling in the same direction as the subject. There are no traffic signs or markers apart from regularly placed reflective markers on both edges of the road, similar to rural roads in NSW. A continuous, low frequency, approx. 60 dB simulated engine noise is played through the computer speakers for the length of the drive. For the

purpose of this study, 5/7 of the road was straight while 2/7 of the road consisted of chicanes. The layout of the road and time of presentation of the trucks was identical for each drive.

Figure 9 AusEd™ driving simulator view

This figure shows the subject's view of the road using the AusEd™ driving simulator. In the top left hand corner is the speedometer. The background on the screen is black (to simulate night time). The markers at the side of the road and line markers in the centre of the road are white and easily visible.

NB: subjects in the present study did not have EEG monitoring whilst using the simulator



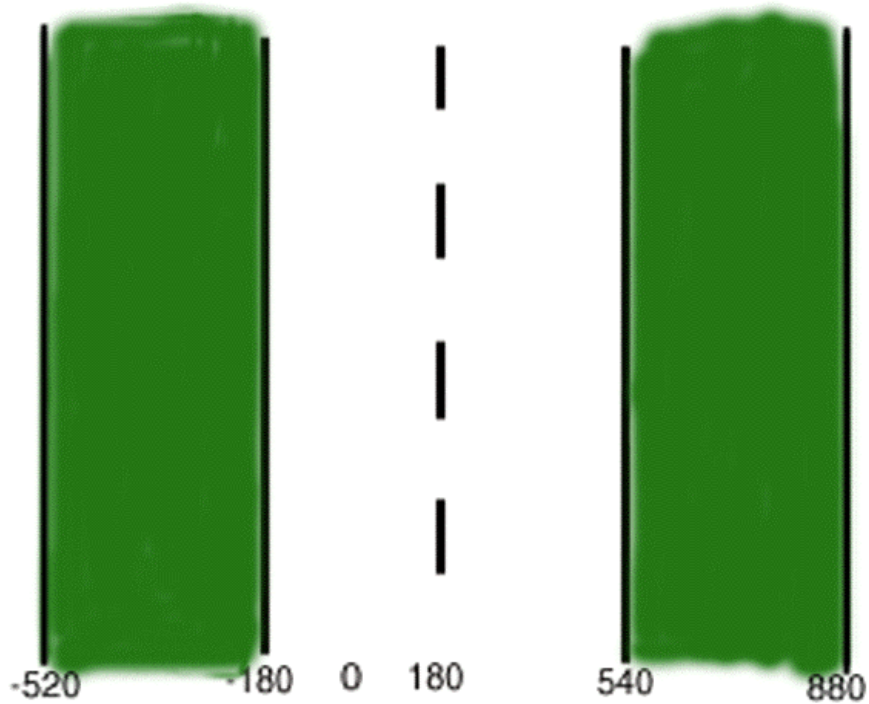
The AusEd™ driving simulator assesses driving ability using four separate measures: velocity deviation, steering deviation, crashes and reaction time.

- velocity deviation: subjects are instructed to keep their speed between 60 to 80 kilometres per hour, using the speedometer as a guide. As the speedometer lies outside of the line of sight for the road, this also represents a divided attention task.
- steering deviation: subjects are instructed to stay as close to the middle of the left hand lane as possible for the duration of the drive. In accordance with standard road width in New South Wales, each lane on the simulated road is 360 centimetres wide. An additional shoulder of 340 cm is provided on either side of the road (see figure below).
- crashes: crashes were registered under three conditions: (1) driving off the 340 cm limit of either shoulder of the road, (2) hitting the back of a truck and (3) remaining stationary for more than 10 seconds.
- reaction time: subjects were instructed to press the brake pedal towards the floor as quickly and firmly as possible whenever a truck appeared in the distance. The time to do this was automatically recorded by the computer as the reaction time, with 10 truck presentations (reaction times) in total for each 30 minute drive. Computer scored reaction times were later manually checked and any necessary

corrections made using customized software, prior to calculating final reaction time outcomes.

To minimize practice effects, all subjects underwent a five minute practice run on the Friday evening prior to their first driving simulator test bout. In addition, the first six minutes of every 30 minute drive was not included in the analysis of driving simulator outcomes.

Figure 10 The road layout of AusEd™



2.1.4.5 Polysomnography

A supervised overnight sleep study in a sleep laboratory is the gold standard test to measure obstructive sleep apnoea and other sleep disorders accurately. It is a time consuming and expensive test, which requires very specialised equipment and highly trained staff. Over 15 recording leads are attached to each subject and channeled through

overhead cabling to a nearby monitoring room, where night staff supervise the collection and recording of multiple physiological variables while the subject sleeps.

2.1.4.5.1 Polysomnography Setup

A standard sleep study (polysomnography) setup was used for all subjects. The EEG placement was according to the 10-20 system with four electrodes attached to the scalp (C₃, O₂, A₁ and A₂), two eye electrodes (EOGL & EOGR), and two chin or submental leads (EMG). There were also two ECG leads, one near the right shoulder and a second ECG lead in the sixth intercostal space on the left hand side of the chest. Sensor leads were placed on each leg over the anterior tibialis for recording any leg movements. Breathing was monitored by a nasal pressure transducer in all studies and in some studies an oral-nasal thermistor (triple thermistor) was additionally added. Inductive Respiratory Effort Bands were placed around the chest and abdomen to monitor thoracic and abdominal wall movement. A position sensor was attached to monitor body position during sleep. A finger probe oximeter recorded the subject's oxygen saturation continuously. Specialised computer software (Compumedics, Melbourne) was used to acquire, store and analyse the sleep study data collected.

2.1.4.5.2 Polysomnography Scoring

One experienced sleep technician scored all sleep studies.

Sleep stages were scored according to Rechtschaffen & Kales criteria (Rechtschaffen and Kales 1968), defined as:

1: Low voltage mixed frequency with or without slow rolling eye movements.

2: Presence of spindles or K-complexes.

The absence of the above excluded epochs from Stage 2.

3: Presence of > 20% and <50% delta waves per epoch.

4: Presence of > 50% delta waves per epoch.

REM: Low voltage mixed frequency, reduction in chin EMG signal, and fast eye movements on the EOG

Arousals were scored according to the Atlas Task Force of the American Sleep Disorders Association (Atlas Task Force of the American Sleep Disorders Association (ASDA).Guilleminault C 1992); arousals were defined as a > 3 second change in EEG sleep state with an increase in chin EMG.

For scoring of respiratory events, thoracic and abdominal bands and nasal pressure/thermistor were used as measures of breathing. Apnoeas and hypopnoeas were defined as:

- Apnoea - cessation of airflow for ≥ 10 seconds (with or without a three percent oxygen desaturation or arousal)
- Hypopnoea – clear reduction (>20%, compared with the baseline over the preceding two minutes) in one of the measures of breathing during sleep for ≥ 10

seconds in association with a $\geq 3\%$ oxygen desaturation or an EEG arousal (or both).

In addition, snoring or flattening in the nasal pressure trace terminating in an arousal was scored as a sub-criterion respiratory event. These were not included in the total RDI, but formed part of the total arousal index (AI) score.

2.1.4.6 Urine Drug Screen

In order to assess whether subjects studied in the sleep laboratory had taken any substances that might influence their performance in the testing battery, they had a urine screen for a wide range of prescription and illicit drugs including benzodiazepines, barbiturates, anti-depressants, anti-psychotics, amphetamines, opiates and ephedrine.

2.1.4.7 Neuropsychological Measures

Several neuropsychological tests were administered to determine the effect of OSA on cognitive outcomes in transport drivers. Each test is discussed below and presented in the order that it was administered. This whole sequence of neuropsychological tests took approximately 40 minutes to complete. Test administration was limited to two researchers in order to minimise variation attributable to the multiple examiners.

The neuropsychological tests were used to specifically assess language skills (Word Fluency Test), psychomotor speed (Trail Making Test), executive function (Stroop Test), short term memory (Digits Forward), working memory (Digits Backward), and general

intellectual ability/IQ (Shipley Institute of Living Scale). Each of these tests has been used previously to demonstrate cognitive deficits in sleep apnoea patients (Decary *et al.* 2000;Greenberg *et al.* 1987;Weaver 2001).

2.1.4.7.1 Word Fluency/Controlled Oral Word Association (COWAT)

The controlled oral word association test (COWAT) is predominately a test of verbal knowledge. It is a timed test requiring reasonable verbal agility. The subject is presented in turn with three consonants: F, A & S. They are given 60 seconds to call out as many words as possible starting with the given letter. Proper nouns, perseveration and words of like structure (e.g. run and ran, eat and eating) are scored correctly for the initial word only.

A normative value is derived from age-matched totals for the sum of the three trials. The test has been demonstrated by Axelrod et al to be unrelated to intellectual competence, educational experience or general health status of the subject, although there is age related decline (Axelrod and Henry 1992).

2.1.4.7.2 Trail Making Test

Trail making tests part A and B are timed tests of visual tracking and sequencing.

- Part A: the subject is instructed to join numbered circles in ascending order e.g. 1 to 2, 2 to 3, 3 to 4, etc. The circles are spread across the page in random order, but in such a manner that no lines are ever crossed. Time from start to completion

is recorded and normal values are derived from controls matched for age and level of education.

- Part B: Follows a similar paradigm to the first part to the test but incorporates an added task of mental dexterity. The subject is required to join the circles in sequence. However, they must simultaneously progress through a concurrent alphabetic process i.e. 1 to A, A to 2, 2 to B, B to 3, etc. Normal values are derived for age and level of education from tabular data (Smith 1982).

Trails B is deemed harder since it demands greater levels of motor speed and visual search (Gaudino *et al.* 1995). Furthermore, it is more closely associated with visual non-verbal intelligence than with attention information processing. For subjects of average or higher intelligence, test performance is independent of intellectual ability (Waldmann *et al.* 1992) and demonstrates good inter-rater variability (Fals-Stewart 1992).

2.1.4.7.3 Stroop

The Stroop test measures the ease with which a person can shift his or her perceptual set to conform to changing demands and suppress a habitual response in favour of an unusual one. In other words, it measures cognitive flexibility, a component of cerebral executive function. Stroop originally developed this test in 1935 (Stroop 1935), but since then others have made minor modifications.

The Stroop test consisted of three white sheets of paper (A4 size), each containing 20 rows of five items. There were three parts to the test:

- In part 1, the subject was instructed to read colour names (blue, green, red, yellow) printed in coloured ink (blue, green, red, yellow), ignoring the colour of the print (the print colour never corresponded to the colour name).
- In part 2, the subject was instructed to name the colour of the ink (blue, green, red, yellow) that was used to print “XXXX” on the page.
- In part 3, subjects were presented with a sheet similar to that used in part 1. In this part, however, they were asked to name the colour of the ink the words were printed in, ignoring the word that was actually printed.

Of major interest in the Stroop test is the subject’s behaviour when presented with coloured words printed in non-matching colours. Stroop reported that normal people can read coloured words printed in coloured ink as fast as when the words are presented in black ink. However, the time to complete the task increases significantly when the subject is asked to name the colour of the ink rather than read the coloured word. This decrease in colour-naming speed is called the “colour-word interference effect” (Stroop 1935).

For each part, the subject was asked to stop after 45 seconds, or when they had completed the page, whichever took longer. Their scores for each page were then age corrected (Das 1970), and a predicted colour word score was subtracted from the raw age corrected colour word score to determine the colour-word interference effect.

The Stroop test has been studied in psychiatric and brain damaged patients. The test is fairly effective in distinguishing between normal controls and brain damaged patients and between psychiatric and brain damaged samples (Golden 1976). Impairment on the Stroop may relate specifically to frontal lobe damage (Perret 1974).

2.1.4.7.4 Digits Forward and Digits Backward

Digitspan forward is a test of immediate numerical recall (Wechsler 1981b). The subject is given a series of numbers of increasing length (3 - 8 digits). They are required to retain the sequence and repeat it in exactly the same order. Two different sequences are presented at each length. The score is derived by the total correct (out of 12) and the test terminated once an incorrect sequence has been given at both presentations of a given digit length. Normative scoring for age is then calculated (Wechsler 1981b).

The reverse presentation of digitspan is a test of numerical short term memory and attention (Wechsler 1981b). The subject is presented with a series of single digit numbers of progressively increasing length, ranging from two to seven digits. They are required to remember the numbers as presented and call them back to the instructor in exactly the opposite order. For each digit length they are given two trials. The test is

terminated when an incorrect answer is given for both trials of a given length. A total out of 12 is calculated and normal values derived from age-matched tables (Wechsler 1981b).

The test has been demonstrated to be age sensitive in patients over 60 years, possibly due to a decreased flexibility in processing changes (Dobbs and Rule 1989). This needs to be considered when using the test in older patients.

2.1.4.7.5 Shipley Institute of Living Scale

The Shipley Institute of Living Scale (SILS) is a test of general intellectual ability / IQ. There are three components.

- Vocabulary component of the Shipley Institute of Living Scale
- Abstraction component of SILS
- Estimated WAIS full scale IQ from SILS

The vocabulary component of the SILS is an untimed word matching test. The subject is given a key word and asked to find the appropriate synonym from four given choices. Forty words are presented and a score calculated from the total of correct answers. A t-score is then derived from the accompanying text manual (Zachary 1991) as corrected for age. Vocabulary as a fixed measure of intellectual ability is generally recognised to be unimpaired by cognitive insult, thus the derived Vt was used as a regression covariable to control for general intellectual ability across all other cognitive measures.

The abstraction component of the SILS is a 10 minute timed test of problem solving. The subject is given a series of words, letters or numbers followed by blank spaces. They are instructed to examine the pattern of the preceding series in order to complete the solution. A total of 20 puzzles are given with an instruction to attempt all problems in the time allocated. The total of correct answers is used to derive a t-score from normal tables for age-matched controls. A further sub-analysis is possible using predicted values for the test based on the level of education and the Vt. This is used to derive the abstraction quotient again from the normed tabular data.

The WAIS full-scale IQ is calculated from the sum of the t-scores for vocabulary and abstraction using normal tables published with the manual for the test. The use of this test as a comparable measure of IQ has been validated by Dalton particularly for grouped data (Dalton *et al.* 1987).

2.1.5 Statistical Analysis

Maislin score, Epworth Sleepiness Scale, and number of accidents were analysed as both continuous variables and dichotomized (binary) variables. For the binary analysis of Maislin scores, a threshold of 0.5 was used as recommended by the authors of this instrument (Maislin *et al.* 1995) for a diagnosis of OSA. An ESS score > 10 was used to define pathological daytime sleepiness (Johns 1991). Two thresholds were used for the analysis of number of accidents: 1, as an indicator of any accidents, and 2, as an indicator of multiple accidents. RDI was analysed as a continuous, dichotomised or categorical variable in separate models. Two alternative RDI thresholds were used to identify the presence of OSA: $RDI \geq 5$ and $RDI \geq 10$ (American Academy of Sleep Medicine Task force 1999). In further analysis, the RDI was categorised as absent, mild, moderate and severe with cut-points at values of 5, 15, and 30 (American Academy of Sleep Medicine Task force 1999). Lifestyle and work variables that were measured on a continuous scale were dichotomised at cut-points selected to represent clinically relevant risk factors for driver fatigue. Some risk factors (such as night driving or interstate driving) were naturally dichotomous. BMI and age were analysed as continuous variables. Two alternative criteria were used to define sleep apnoea syndrome: $RDI \geq 5$ with Epworth > 10 , and $RDI \geq 10$ with Epworth > 10 .

All neurocognitive outcomes were adjusted for age and level of education. Oral word fluency, Digits forward and backward, and Trails A and B were all transformed to a normal distribution, with results expressed as *Z* scores, representing the extent of deviation from expected values. The transformed interference score was used for Stroop

analysis. IQ was calculated using Shipley's Institute of Living Scale (SILS), and the SILS vocabulary T score (Vt) was used to control for the effect of general intellectual ability in the analysis of the neurocognitive tests.

The value of the Maislin score as a test for OSA was evaluated in this study population by constructing an ROC curve in which the sensitivity at various cut-points was plotted against the 1 - the specificity at those same cut-points (Sackett *et al.* 1991). Likelihood ratios were calculated for four ranges of the Maislin score as the ratio of the proportion of people with RDI ≥ 10 who had a Maislin score within the prescribed range to the proportion of people with RDI < 10 who had a Maislin score in this range. The likelihood ratio represents the extent to which the prior odds of an individual having RDI ≥ 10 are increased (if the LR is greater than one) or decreased (if the LR is less than one) by the given Maislin score (Sackett *et al.* 1991) (see Attachment 3).

Hypothesis testing was undertaken using generalised linear modeling with concurrent estimation of effects and their 95% confidence intervals. Effects were expressed as means, ratios, differences or odds ratios, as appropriate. Univariate tests and estimations of differences between groups were performed using analysis of variance. In cases where the measurements were made at different times of the day in the same individuals, a two way analysis of variance was implemented to test for diurnal variation in the effects. Age was introduced as a covariate in some of these analyses. The effects of multiple potential predictors, adjusted for each other, on the outcomes of interest were tested using multiple regression. Linear regression was used for outcomes measured on a continuous scale and

the logistic regression was used for outcomes measured on a binary scale. A stepwise selection procedure was used to identify the final best predictive model. This procedure was implemented with the threshold for variable entry set to 0.05 and the threshold for variable removal set to 0.10.

For the drivers studied in the sleep laboratory, sample size calculations were performed mid way through data collection. These suggested that 60 drivers needed to be studied to detect performance decrements due to sleep apnoea. For this reason and partly for convenience, data collection for this part of the study was terminated after the 61st participant.

The data analysis described above was undertaken using the SPSS statistical package 10.0.05 (SPSS Inc., Chicago).

2.2 Mild Obstructive Sleep Apnoea Study

This project involved intensive experimental work on 29 subjects, consisting of a group with mild OSA and a group of controls. Each subject was tested continuously for between 24 to 36 hours on two separate occasions.

2.2.1 Project Design

Every subject was tested over two weekends. The testing performed on one weekend was under normal sleeping conditions (“baseline testing”) while the testing on the other weekend was after 36 hours of acute total sleep deprivation (SD). The order of weekend testing was balanced with approximately half of the subjects of each group (mild OSA and controls) tested under baseline conditions as their first weekend of testing, and approximately half of the subjects tested under SD conditions as their first weekend of testing. Subject choice and convenience for the most part determined whether subjects did their baseline or SD weekend first. Generally, the second weekend of testing was within two to four weeks of the first weekend of testing. Subjects were instructed to obtain at least eight hours sleep per night for the four nights preceding each weekend of testing to minimize any pre-existing sleep debt at the start of a weekend’s testing. Sleep hours for these four nights preceding each weekend were also measured objectively using actigraphy and sleep diaries.

Given the nature of the testing, it was impossible to “blind” either the subjects or researchers to the order of weekend testing or testing conditions (baseline or SD).

However, all the sleep studies were scored by an experienced technician who was blinded to the patient's status.

Subjects were compensated for their time and the inconvenience of participating in the study. The protocol was approved by the Central Sydney Area Health Service Ethics Committee (RPA zone) and the University of Sydney Ethics Committee, and informed consent was obtained from each patient.

2.2.2 Subjects

2.2.2.1 Target Population

Subjects with mild OSA and control subjects with no OSA were sought. Men were studied exclusively for several reasons: mild OSA is much more common in men; there is very little evidence of increased driving accident risk in women with mild OSA; and finally, to avoid known gender differences in some aspects of performance.

2.2.2.2 Eligibility

Subjects were eligible if they were of driving age (18 to 70 years), held a current N.S.W. driver's license, and drove regularly. Subjects needed to be free of significant cardiorespiratory disease, or other medical conditions that might affect their ability to perform the experimental protocol adequately and safely (e.g. narcolepsy, epilepsy). Subjects were ineligible if they were taking any medications that might affect daytime alertness, such as antidepressants or benzodiazepines, or if they were currently being treated or had had previous treatment for OSA. Subjects were excluded if they were

taking any illicit substances, such as amphetamines or were heavy drinkers (regular alcohol consumption greater than 40 gm per day). Subjects needed to be able to understand the requirements of the study and had to agree to abide by the study conditions.

2.2.2.3 Recruitment

Subjects were recruited from three sources. Mild OSA patients were identified in specialist consulting rooms or outpatient departments and then invited to participate, or alternatively, they were identified through an audit of recent sleep study results from Royal Prince Alfred Hospital Sleep Investigation Unit. Controls were recruited from these same sources and also from advertising among university students. In this way, some of the controls, although not age-matched, would be free of clinic selection biases.

Although many of the subjects had had previous diagnostic sleep studies, classification of subjects as having mild OSA or no OSA (i.e. control status) for this study was made on the basis of their baseline weekend's sleep study result. Subjects were regarded as having mild OSA if their total RDI was ≥ 5 , but < 30 events/hr. Controls had a total RDI < 5 /hr.

2.2.3 Protocol

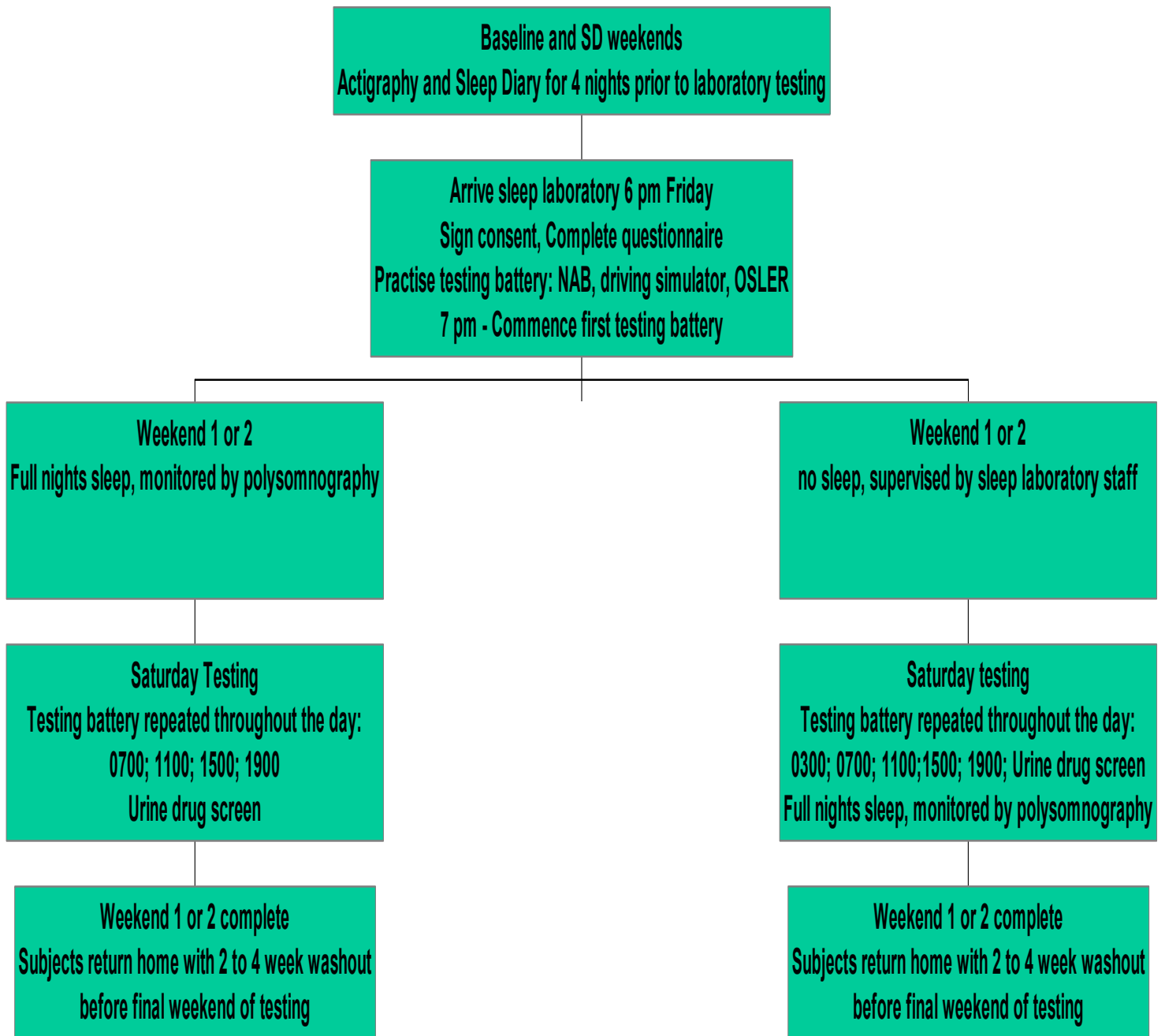
The protocol is described in the figure below. All testing was performed on weekends (Friday evening to Sunday morning), when the sleep laboratory was for the most part free, to create a stable testing environment and to minimize any distractions during the

testing procedures. Where possible, subjects were also tested in pairs in order to increase motivation and thereby decrease sleepiness and boredom.

Subjects used a sleep diary and an actigraph for the four nights preceding their arrival in the sleep laboratory. Subjects were permitted to continue their usual caffeine intake in the days prior to attending the sleep laboratory. This usual intake was recorded in responses to the questionnaire.

On arrival in the sleep laboratory on the Friday evening (six pm) subjects were briefed about the laboratory and the testing schedule, their consent was obtained and, while they had their evening meal, they completed a questionnaire. Caffeine products and cigarette smoking were not allowed for the duration of the weekend testing. Soon after completing dinner, the subjects were familiarized with and practiced the three main instruments of the testing battery (Neurobehavioural Assessment Battery (NAB), AusEDTM Driving Simulator, and Oxford Sleep Resistance Test (OSLER)), and then at seven pm they commenced their first run of the testing battery. The order within the testing battery was NAB, driving simulator, and finally OSLER. Each testing battery took approximately 1 hour and 45 minutes to complete.

Figure 11: Flow chart of study protocol



After the seven pm testing battery was complete, the subjects who were undergoing their baseline weekend of testing were then set up for overnight polysomnography. Lights out was at approximately 10.15 pm, and the subjects slept, while being monitored, until approximately six am. Subjects then showered, had breakfast (no caffeine), and commenced their next testing battery run at seven am. The testing battery was again repeated at 11 am, 3 pm, and finally at 7 pm. A urine sample was also obtained from the subjects on the Saturday for laboratory analysis. The baseline testing weekend concluded after the completion of the seven pm testing battery, at approximately nine pm.

Subjects who were being sleep deprived were not set up for polysomnography on the Friday night, but instead stayed up awake overnight. They were supervised by sleep laboratory staff at all times to ensure they did not sleep. The testing battery was repeated at 3 am, 7am, 11am, 3pm, and 7 pm. A urine drug screen was also collected. On Saturday evening, these subjects were set up for polysomnography, and a sleep study performed on their overnight sleep. There was no formal testing after the subjects awoke on Sunday morning, and they were then free to make their way home.

A television, computer, videocassette player, DVD player, and video game playstation were available for the subjects' entertainment for both testing weekends. Subjects were also free to bring in any other reasonable form of activity, such as reading material or academic work. They were not, however, permitted to exercise or drink alcohol. At all times subjects were under the close supervision of research staff to ensure they complied with the protocol conditions.

2.2.4 Data Collection Instruments

The following questionnaires, tests and other instruments were used to collect the data for this study. They are discussed in the approximate order that they were administered. Some of the tools used were common to the Commercial Drivers Study, and these have not been reviewed again.

2.2.4.1 Actigraphy

Actigraphs are small electrical devices that look similar to and are worn like conventional wrist watches on the non-dominant wrist. They sense and record limb movements over a selected threshold using an acceleration sensor (accelerometer). Analysis of actigraphy data for the assessment of sleep is based on the principle that fewer limb movements occur during sleep than during wakefulness.

Many researchers have substantiated the accuracy of estimating total sleep time using actigraphy (Cole *et al.* 1992;Mullaney *et al.* 1980;Shinkoda *et al.* 1998;Stanley *et al.* 2000). As early as 1980, Mullaney and co-workers demonstrated that actigraphic data could provide a reliable and valid differentiation between sleep and wakeful states (Mullaney *et al.* 1980). They reported a 94.5% agreement between actigraphic data and polysomnographic scoring. This is only slightly lower than the usual inter-rater reliability of polysomnographic scoring. More recent research in a sample of 41 subjects, including some with sleep disorders, found that, compared to overnight polysomnography, actigraphy correctly distinguished sleep from wakefulness approximately 88% of the time

(Cole *et al.* 1992). Another recent study has found an agreement of 97% with polysomnographic scoring (Shinkoda *et al.* 1998) .

Actigraphy has a number of advantages when compared with overnight polysomnography or sleep EEG. Most importantly, it is far less expensive, less technically demanding and can be used in the home. However, of course it does not give nearly as much information as conventional PSG, in particular it gives no information with respect to sleep disordered breathing.

Mini-Mitter Actiwatches (AW64 series) (Cambridge Neurotechnology Cambridge U.K/Mini-Mitter, Sunriver, Oregon, USA) were used in this study. The Actiwatch has a large memory capacity and can be worn for many days continuously. Subjects were asked to wear the Actiwatch on their non-dominant wrist for the four nights and days prior to their presentation to the sleep laboratory. In addition, they were asked to press the round event marker on the front of the watch at the time of significant sleep/wake events, such as getting into bed, attempting sleep, waking in the middle of the night, and waking in the morning. When the subjects presented to the sleep laboratory on the Friday evening, the actigraphs were collected and their data downloaded into a PC, where it was then manually scored for sleep with reference to the subjects's sleep diary.

2.2.4.2 Sleep Diary

A sleep diary was sent to all subjects prior to their weekend testing periods. Subjects were asked to complete the sleep diary each morning for the four mornings before their

sleep laboratory attendance. The sleep diary sought subjective information about the previous nights sleep, such as the estimated time of getting into bed, turning off the light and attempting sleep, any known wake periods during the night and final time of awakening and getting up in the morning. Any daytime naps could also be recorded on the sleep diary. Sleep diaries have been shown to correlate well with objective sleep measures (Lacks 1988).

The sleep/wake information from the sleep diary was compared with the recorded data obtained from the Actiwatch and using both this subjective and objective sleep data, the subjects previous nights' sleep hours were accurately estimated.

2.2.4.3 Participant Questionnaires

Two different questionnaires were used, depending on which weekend of testing the subjects were attending. The main questionnaire (Attachment 5) was given when the subjects presented for their first weekend of testing, regardless of whether this was under baseline or SD conditions, whereas the one page additional questionnaire (Attachment 6) was given when the subjects attended their second weekend of testing.

The main questionnaire collected basic physical and demographic information, information regarding caffeine intake, driving and lifestyle, and also included the Epworth Sleepiness Scale. The second questionnaire documented recent caffeine intake and any changes in weight.

2.2.4.3.1 Demographic and Physical Measures

Subjects' age was recorded and their height, weight and neck circumference were measured at the initial assessment. Weight was re-measured on the second testing occasion, to allow adjustment for any significant change in weight over the interval between tests.

2.2.4.3.2 Caffeine Intake

Questions were asked about the subject's usual caffeine intake (tea, coffee, cola) in the main questionnaire. Additional questions were asked about the amount of caffeine containing products the subject had had on each Friday of their testing weekends, to control for the possible influence of caffeine on alertness, which may in turn have affected their performance on the testing battery that Friday evening.

2.2.4.3.3 Epworth Sleepiness Scale

See discussion above

2.2.4.3.4 Lifestyle and Driving Details

In the main questionnaire, questions were asked about average sleep hours, occupation, alcohol intake and motor accident history. Subjects were also asked to list any medical illnesses they suffer from, any medications they were taking and whether they had had any treatment for OSA. These later questions were particularly important to re-confirm eligibility criteria.

2.2.4.4 Neurobehavioural Assessment Battery (NAB)

The computerized Neurobehavioural Assessment Battery (D. Dinges, U Penn, USA) was selected as it has been shown to be sensitive to performance and mood changes in studies of total (Dinges *et al.* 1994;Kribbs and Dinges 1994) and partial sleep deprivation (Dinges *et al.* 1997). Further, being a PC based battery, it is administered in a fixed and reproducible way, free from potential biases that are possible with human administration of cognitive tests.

The NAB includes the Stanford Sleepiness Score (SSS), Karolinska Sleepiness Score (KSS), Effort to Stay Awake (ESA) questionnaire, Profile of Mood States (POMS) questionnaire, Psychomotor Vigilance Task (PVT), Probed Recall Memory test (PRM), Serial Addition /Serial Subtraction test (SAST), Adjective Check List (ADCL), Digit Symbol Substitution Task (DSST), Time Estimation Task (TET), and visual analogue responses to questions on mental and physical exhaustion (VAS). At the start of the computerized battery, subjects are presented with subjective questionnaires of sleepiness, including the Effort to Stay Awake questionnaire, the SSS and the VAS. Performance testing then commences after these questionnaires and consists firstly of the SAST, which assesses the accuracy and speed of basic mathematical calculations, followed by the Word Presentation component of the PRM. This is separated from the Word Recall component of the PRM by a 10 minute run of the PVT. The PRM involves the memorisation of six pairs of unrelated words in a 30 second period and subsequent recall of word pairing 10 minutes later. The PVT is a basic reaction time test, which involves pressing a button when numbers begin counting on the computer screen. The second part

of the PRM is followed by the Adjective Checklist, a subjective measure of current emotional state, the Digit Symbol Substitution Task, which assesses response times and error rates on a simple psychomotor task, and the Time Estimation Task, which involves estimating time of presentation of a visual stimulus. Finally, subjects complete a computerised version of the POMS, another survey of emotional state, and the Subjective Effort Questionnaire (SEQ), where subjects rate their own perceived performance on the NAB.

For technical reasons, the NAB is best administered in a fixed fashion from start to finish. The whole automated battery usually takes between 30 to 40 minutes to complete. The NAB was administered in its entirety in this way for each testing session in this study. However, analysis of NAB outcomes was limited to the PVT, DSST, PRM, SSS and POMS tests. This was done in order to focus on the NAB outcomes that were most relevant to the objectives of this project and, hence, to reduce the risk of Type 1 error in the data analysis.

2.2.4.4.1 Psychomotor Vigilance Task

See discussion above

2.2.4.4.2 Digit Symbol Substitution Task

The Digit Symbol Substitution Task (DSST) of the NAB is a computerized test of attention based on the pen and paper version from the standardized Wechsler Adult Intelligence Scale Revised (WAIS-R), of which there is normative data available

(Wechsler 1981a). The original version presented a table of nine line symbols with associated numbers, followed by 175 boxes, each containing a number from one to nine. The subject was instructed to draw the symbol associated with that number into the box. The NAB computerized version has inverted the task by showing all the symbols with associated numbers and then presenting stimulus symbols, one at a time, and asking the subject to type the associated number. As soon as a response is made a new symbol is presented. The same symbol will not be presented twice in succession. An initial practice period of 15 seconds is allowed in every presentation of the DSST, in which no score is kept but feedback is provided to the subject by signaling correct choices with a screen message. After the practice period, scoring of responses begins and no feedback is provided. The test terminates automatically after a total time of 105 seconds (15 seconds practice + 90 seconds test time).

By computerizing the DSST, further information relating to performance and specifically reaction times can be calculated. The outcome measures from each DSST test include the number correct, number wrong, % correct, number of times the 10 second 'wake-up' reminder had to be flashed on the screen, mean response time of all items, and the response rate (number of seconds per item).

2.2.4.4.3 Probed Recall Memory Test

The Probed Recall Memory test (PRM) measures short-term memory. This test is based on a standardised paired word memory test developed by Wechsler which was incorporated into the Wechsler Memory Scale (WMS-R) (Wechsler 1945; Wechsler

1981a). In the original format subjects were presented with 10 word pairs, of which six were 'easy' associations such as "dog – barks", and then four were 'hard' associations such as "onion – floor". The paired words were read to the subjects three times and the subject was given a memory trial after each reading. All the associations in the NAB are 'hard' associations, for example "seed – aeroplane", and there is no memory trial after the initial presentation. The addition of a 10 minute task following the initial presentation of the paired words allows for the measurement of retention.

The words used in this test are randomly selected from a reference list of 450 most commonly used English nouns. Six paired words are initially presented on the screen for 30 seconds from 1 of 24 predetermined patterns. The subject is prompted by the instructions on the screen to memorize the words paired together. Following an intervening task (the PVT), the left-hand word of each word pair previously presented is shown, but in a different order. The subject is instructed to type the missing (right-hand) word for all six pairs, guessing if he/she can't remember. The program allows the subject to enter or edit words in any order at any of the assigned screen locations. The program halts automatically after 150 seconds even if word spaces are blank. The subject is prompted to press the <ESC>ape key if he/she finishes the task before the time limit. This option is not allowed until all the blanks have an entry. The actual working time is logged.

2.2.4.4.4 Stanford Sleepiness Scale

The Stanford Sleepiness Scale (SSS) is a quick and simple test, which measures subjective sleepiness at a particular moment in time. It is one of the most widely used subjective scales in sleep research. The SSS consists of seven statements relating to subjective sleepiness, which range from 1 – “feeling active and vital” to 7 – “almost in reverie; sleep onset soon; lost struggle to remain awake” (Hoddes *et al.* 1972). The SSS was first validated in 1973 with college students in a protocol involving sleep deprivation and performance testing (Hoddes *et al.* 1973). Some researchers have found that the SSS is poorly correlated with objective sleepiness parameters (Carskadon and Dement WC 1985; Dement WC *et al.* 1978). However, this is also true of other subjective scales of sleepiness (Cook *et al.* 1988; Johns 1991). Nonetheless, the SSS is a useful and commonly applied tool that can measure subjective sleepiness at a particular time.

2.2.4.4.5 Profile of Mood States

The Profile of Mood States (POMS) is a validated 65-item mood questionnaire which asks subjects to mark on a five point Likert scale (ranging from 1 “not at all” to 5 “extremely”) how affected they currently feel by certain common feelings (eg, being “worn out”, “unhappy”, “tense”, “friendly”) (Nyenhuis *et al.* 1999). These 65 different feelings cover six main emotional domains - fatigue (f), confusion-bewilderment (cb), tension-anxiety (ta), vigour (v), depression-dejection (dd) and anger-hostility (ah). The POMS has been used in research with cancer patients, head injury patients, epilepsy patients and HIV/AIDS patients (Lezak 1995). Recently, the POMS has been applied to sleep research, where it has been shown to be altered after partial sleep deprivation

(Dinges *et al.* 1997). This is also consistent with a recent meta-analysis which has shown that the effects of sleep deprivation on mood are greater than the effects of sleep deprivation on cognitive or motor performance (Pilcher and Huffcutt 1996).

2.2.4.5 AusEDTM Driving Simulator

A 30 minute run on the AusEdTM driving simulator was performed after each sequence of the NAB. See discussion above.

2.2.4.6 Oxford Sleep Resistance Test (OSLER)

This test was used to provide an objective measure of daytime sleepiness. It was commenced immediately following the completion of the driving simulator testing. Compared to conventional polysomnographic tests of daytime sleepiness (MWT, MSLT), this test offers the advantage of simplicity, low cost, automatic reading, and low requirements for technical personnel. In this test, subjects are asked to press a switch in response to a light emitting diode (LED) regularly illuminated for one second in three. When the subject fails to respond for 21 seconds (i.e. seven illuminations) the test is terminated and sleep is concluded to have occurred. In this way the test is based on a behavioural, rather than a polysomnographic, definition of sleep. This is particularly important, as the polysomnographic definition of sleep is still debated and also open to subjective interpretation.

The OSLER test has been shown to discriminate normal subjects from sleep apnoea subjects (mean sleep latency (min) normal group 39.8, OSA group 10.5) as well as the

traditional MWT (normal group 38.1, OSA group 7.3) (Bennett *et al.* 1997). Sleep latency on the OSLER is also significantly shorter after sleep deprivation, compared with no sleep deprivation, in normal subjects (25 minutes versus 38 minutes) (Priest *et al.* 2001).

When the number of consecutive missed responses during the OSLER test increases from zero to seven, generally the probability that the subject is asleep (defined electrophysiologically) during the intervening period also increases and is equal to or greater than 95% for four or more consecutive missed responses. In addition, the total number of missed responses per OSLER session has been shown to correlate very highly with cumulative microsleep time within an OSLER session ($r = 0.94$, $p < 0.005$), suggesting that the total number of missed stimuli per minute duration of the test could also add valuable information as a quantification of sleep pressure or propensity, perhaps allowing for additional discrimination between subjects (Priest *et al.* 2001).

2.2.4.7 Polysomnography

See discussion above

2.2.4.8 Urine Drug Screen

A urine drug screen was performed on all subjects on both testing weekends. See discussion above.

2.2.5 Statistical Analysis

Determinants of daytime driving performance and cognitive function were evaluated using three-way analysis of variance (ANOVA). There were two within subject variables, sleep condition (baseline, sleep deprivation) and time of day (1900, 0700, 1100, 1500, 1900), and one between subject variable, the presence or absence of mild OSA. During the sleep deprivation condition, an additional night time (0300) time point was analysed. Hence, a separate two-way ANOVA (subject group and time) was conducted to fully evaluate the effect of diurnal variation on driving performance and cognitive function in the sleep deprived state. .

Because of missing data in five subjects for the baseline weekend's final testing battery (1900), ANOVAs were performed with and without data from this final time point included. When the final time point was included, the analysis of daytime outcomes was limited to 24 subjects with complete data sets (primary analysis). When the final time point was excluded, 28 subjects had complete daytime data sets and could be analysed (secondary analysis). One subject failed to complete the baseline weekend's final two testing battery's (1500, 1900), and hence his data was not included in either the primary or secondary analyses for the daytime outcomes.

For the driving performance and cognitive function outcomes, the following potential confounding factors were tested as covariates and retained where they were significant predictors of the outcome variable: age, sleep hours in preceding four nights, average

caffeine or alcohol intake, and caffeine intake on day of admission. Of these, only age and average alcohol intake were significant predictors ($P < 0.05$) in any of the analyses.

The effect of sleep deprivation on polysomnographic measures in subjects with and without OSA was evaluated using two-way analysis of variance (subject group and intervention).

All interactions were tested and, where these were significant ($P < 0.05$), separate models were constructed for each level of the interaction. Pairwise comparisons between levels of each factor were assessed where the factor was found to be significantly associated with the outcome in the ANOVA model. Effects sizes were estimated with 95% confidence intervals. P values < 0.05 were considered statistically significant and are presented in the results.

Differences in preceding sleep hours and questionnaire data were assessed with t tests, and results expressed as mean differences with 95% confidence intervals.

The data analysis described above was undertaken using the SPSS statistical package 10.0.05 (SPSS Inc., Chicago).

2.3 Medico-Legal Case Series

In order to evaluate the effects of OSA on driver fatigue in a broader and more clinically relevant way, a review was conducted of consecutive referrals to the Sleep Disorders Centres at Royal Prince Alfred Hospital (n = 6) and Westmead Hospital (n = 1), Sydney, for medico-legal opinions in fall asleep fatality associated road accidents where the driver who caused the accident survived. Each subject underwent detailed sleep investigations to identify sleep disorders that might have contributed to the fall-asleep road accident. In all cases, the driver had at least one overnight sleep study. In six of the seven cases, an objective test of daytime sleepiness was also performed.

2.3.1 Polysomnography

See discussion above

2.3.2 Objective Tests of Daytime Sleepiness

The extent of daytime sleepiness was objectively measured by one of two different polysomnographic tests.

The Maintenance of Wakefulness Test (MWT) consists of four trials, two hours apart, where the subject is seated in a dark, quiet room, in a comfortable chair, and instructed to stay awake for 40 or 20 minutes at a time, depending on the specific protocol used (Doghranji *et al.* 1997;Mitler *et al.* 1982). While sitting, the subject is monitored polysomnographically for sleep onset. When 20 minute trials are used and sleep onset is defined as the first occurrence of one epoch of any stage of sleep, excessive daytime

sleepiness exists if the mean latency to sleep onset for all trial periods is less than 11 minutes (Doghramji *et al.* 1997).

The Multiple Sleep Latency Test (MSLT) is very similar to the MWT. In this test, the subject is offered four or five opportunities to fall asleep, every two hours, in an environment conducive to sleep (dark, quiet room, comfortable bed) (Association of Sleep Disorders Centers Task Force on Daytime Sleepiness 1986). The average time from lights out to the first epoch of sleep measures the multiple sleep latency (MSL). In the first MSLT studies, Richardson *et al.* investigated 14 control subjects and compared them to 27 narcoleptics (Richardson *et al.* 1978). They reported that an MSL < 5 minutes is indicative of pathological sleepiness, while an MSL > 10 is normal. This test lacks good normative data and these first recommendations remain accepted norms. Scores between these pathological and normal ranges are regarded as a diagnostic gray area (Association of Sleep Disorders Centers Task Force on Daytime Sleepiness 1986; Kreiger J 2000).

An overnight polysomnogram is always performed on the night prior to a MWT or MSLT, so that factors such as the previous night's sleep quality and sleep length, and the presence or absence of sleep disorders can be considered when interpreting the results. In addition, urine samples are collected on the day of MWT or MSLT testing to detect any pharmacological agents that may affect the test results.

Chapter 3: Results: Prevalence of OSA

3.1 Response rates

3.1.1 Drivers surveyed in the field

In total, the questionnaire was administered at 42 sites around NSW. The exact locations, dates of the visits, numbers of drivers surveyed and types of sites visited are set out below in table 1¹. By the end of the recruitment period, 1002 drivers had completed the field survey.

The overall response rate was 83% among the drivers who were at the above locations at the time of the sampling and who had at least 10 minutes available for the questionnaire completion. In other words, 17% of the drivers at the above locations at the time of the sampling and who had at least 10 minutes available for the questionnaire completion refused to participate. Few drivers who presented to the above locations did not have at least 10 minutes available for potential questionnaire completion.

¹ the small discrepancy between the total number of drivers in table 1 and the total number of drivers surveyed arises because the drivers who underwent sleep studies also completed the same survey that was administered in the field and these numbers are not recorded in table 1

Table 1 Site visits for drivers surveyed in the field

<i>DATE</i>	<i>LOCATION</i>	<i>No. SURVEYED</i>	<i>SITE</i>
Jun 1 2000	Wentworthville Leagues Club	206	meeting
Jul 24 2000	Campsons, Minchinbury	6	truck yard
Aug 17 2000	Tolls, Smithfield	17	truck yard
Aug 24 2000	Mobil, Silverwater	15	meeting
Aug 29 2000	First Fleet, Wetherill Park	4	truck yard
Sep 7 2000	Refrigerated Roadways, Ardell Park	11	truck yard
Sep 14 2000	Tolls Coca-Cola, Northmead	30	truck yard
Oct 24 2000	Mains Paper/APM, Chullora	7	truck yard
Oct 26 2000	Refrigerated Roadways, Girraween	8	truck yard
Nov 5 2000	Orange	25	meeting
Nov 8 2000	Blackwoods, Smithfield	14	truck yard
Nov 23 2000	Caltex, Wyong, north bound	37	truck stop
Dec 7 2000	Caltex, Wyong, north bound	35	truck stop
Dec 13 2000	Caltex, Newell Highway, Dubbo	17	truck stop
Jan 22 2001	Mobil, Marrangaroo	6	truck stop
Jan 31 2001	Mobil, Pheasants Nest	5	truck stop
Feb 20 2001	Caltex, Wyong north bound	29	truck stop
Mar 7 2001	BP Marulan, south bound	18	truck stop
Mar 9 2001	BP Marulan, south bound	20	truck stop
Mar 12 2001	BP Potts Hill	13	truck stop
Mar 14 2001	BP Potts Hill	16	truck stop
Mar 15 2001	Toll Ipec Villawood	30	truck stop
Mar 20 2001	Tarcutta café	32	truck stop
Mar 21 2001	Tarcutta café	25	truck stop
Mar 26 2001	Shell, Sutton Forest, south bound	16	truck stop
Apr 2 2001	Caltex, Dubbo	10	truck stop
Apr 3 2001	Ampol, Gilgandra	5	truck stop
Apr 5 2001	Hardware and General, Brookvale	28	truck yard
Apr 10 2001	Shell, Sutton Forest	15	truck stop
Apr 18 2001	Shell, Tomingley	24	truck stop
Apr 19 2001	Shell, Tomingley	24	truck stop
May 14 2001	BP Marulan south bound	17	truck stop
May 16 2001	Caltex Wyong north bound	20	truck stop
May 22 2001	BP Willow Tree	19	truck stop
May 23 2001	BP Willow Tree	15	truck stop
May 31 2001	Shell Sutton Forest	16	truck stop
Jun 6 2001	Shell Wyalong	31	truck stop
Jun 13 2001	Shell Gundagai South	16	truck stop
Jun 14 2001	Shell Gundagai	22	truck stop
Jun 19 2001	BP Potts Hill	18	truck stop
Jun 27 2001	Caltex Coolongolook	5	truck stop
Aug 19 2001	Star Track Express, Minchinbury	47	truck yard

3.1.2 Drivers undergoing sleep studies

Sixty one NSW drivers had sleep laboratory investigations as part of this study.

In total, 149 letters introducing this part of the study were sent to a randomly selected population of NSW transport drivers. Only 106 of these drivers (71%) were subsequently contactable by telephone, either at home or through work, and were current drivers. Sixty one (58%) of these contactable, current drivers agreed to participate in the laboratory investigations. In other words, the response rate for eligible drivers was 58%, which represented 41% of drivers from the overall mail out.

Seven and a half percent of the eligible drivers had already been diagnosed with OSA when the study was discussed with them on the telephone; most were on CPAP treatment for this. Five of these were subsequently enrolled and re-tested. Three drivers with already diagnosed OSA refused involvement in the study.

Forty two percent of eligible drivers refused to participate in the study. Most drivers refused to become involved because they were too busy and couldn't afford the time commitment. Others could never be certain of their roster, so were not willing to commit to a definite date for their sleep study. A small proportion felt that "they had no problem", so could not foresee any need for their involvement, and a smaller proportion were uncomfortable because of the RTA or TWU collaboration. Seventy six percent of these 'non-participants' agreed to provide their age, height and weight, so that these

characteristics could be compared between those who did and did not participate in the laboratory investigations.

3.2 Demographic and Physical Characteristics

3.2.1 Physical Characteristics

Basic demographic and physical characteristic data are presented below for both the drivers surveyed in the field and those who underwent sleep laboratory studies. Data are compared with those for ‘non-participants’ in the laboratory study.

In the field cohort, all drivers were male, except three (99.7% male). In the laboratory cohort, all drivers were male. The main difference in the demographic data presented between the field cohort and the laboratory cohort is in age. Members of the laboratory cohort of drivers (both participants and non-participants) were older than those surveyed in the field. Body Mass Index (BMI), a measure of obesity, and measured neck circumference, did not differ between the field and the laboratory groups.

Table 2 Age and obesity: comparison between subjects in the field study and laboratory study

	<i>Age (years)*</i>	<i>BMI (kg/m²)</i>	<i>Neck Circumference (cm)</i>	<i>N</i>
Field	41.6 (41.0 to 42.3)	29.8 (29.4 to 30.1)	41.9 (41.7 to 42.1)	925
Laboratory	48.3 (46.1 to 50.6)	30.2 (28.8 to 31.6)	42.2 (41.4 to 43.0)	61
Difference	6.7 (4.2 to 9.2)	0.4 (-1.8 to 1.0)	0.3 (-1.3 to 0.7)	

Table 3 Age & obesity in laboratory study: comparison of participants and non-participants

	<i>Age (years)</i>	<i>BMI (kg/m²)</i>	<i>N</i>
Laboratory	48.3 (46.1 to 50.6)	30.2 (28.8 to 31.6)	61
Non-Participants	45.7 (42.3 to 49.1)	28.8 (27.3 to 30.3)	35
Difference	-2.6 (-6.5 to 1.2)	-1.4 (-3.5 to 0.7)	--

values for tables 2 & 3 are means \pm 95% confidence intervals (CI)

3.2.2 Driving Characteristics 1

Further descriptive data about the transport drivers that were studied is set out below in table 4. In both cohorts, company drivers were more frequently studied than owner drivers. Most drivers undergoing sleep laboratory investigations reported metropolitan driving, while approximately half of the drivers surveyed in the field reported interstate driving. Similarly, a much greater proportion of the drivers surveyed in the field were long distance drivers (defined as driving > 100,000 km/yr at work) – 47% compared to 23% of those who underwent sleep laboratory testing. Approximately one half of the drivers in both cohorts reported night driving shifts and approximately one quarter reported rotating shifts.

Table 4 Driving characteristics of participants in the field study and the laboratory study

	<i>Field Drivers</i>	<i>Laboratory Drivers</i>	<i>Mean Diff (CI)</i>
% Company Drivers	72%	62%	10 (-3 to 23) %
% Owner Drivers	25%	38%	13 (-2 to 27) %
% Metropolitan Driving*	52%	79%	27 (18 to 40) %
% Country Driving	28%	39%	11 (-1 to 25) %
% Interstate Driving*	48%	18%	30 (21 to 42) %
% Long Distance Drivers*	47%	23%	33 (21 to 43) %
% Driving at Night	56%	46%	10 (-3 to 23) %
% Rotating Shifts	25%	30%	5 (-7 to 16) %
% NSW Residence*	70%	100%	30 (18 to 48) %

3.2.3 Driving Characteristics 2

Drivers surveyed in the field drove more kilometres per year, worked and drove more hours per week, and on average reported a greater longest work shift. However, the number of days worked per week was approximately the same between the two cohorts. Both groups reported sleeping only just over 6 hours per day while at work, and both groups compensated for this by attempting to catch up their sleep hours on days off. Intake of caffeine beverages per day was high in both groups, averaging around five per day. Similarly, many drivers admitted to taking tablets to stay awake while driving (see table 6). However, reported alcohol consumption was more modest, averaging approximately one drink per day for both groups.

Table 5 Sleep and other habits of drivers in the field study and laboratory study

	<i>Field Drivers</i>	<i>Laboratory Drivers</i>	<i>Difference</i>
Longest shift worked (hours)*	15.7	13.7	2.0 (0.6 to 3.3)
Number of days worked per wk	5.5	5.4	0.1 (-0.003 to 0.326)
Number of hours worked per wk*	63.6	54.7	9.3 (5.9 to 12.7)
Number of driving hours per wk at work*	52.3	42.2	10.7 (6.8 to 14.6)
Number of km driven per yr for work*	135,265	76,156	61,998 (42,736 to 81,260)
Number of hours of sleep on work days	6.2	6.4	-0.2 (-0.5 to 0.1)
Number of hours of sleep on days off*	8.5	7.6	0.9 (0.6 to 1.3)
Number of glasses of alcohol each day*	0.7	1.2	0.5 (0.01 to .9)
Number of cups of caffeine beverages each day	5.6	4.9	0.7 (-0.3 to 1.7)

Values for table 5 are means \pm 95% CI

3.2.4 Medical Health

Medical health data for the two groups is presented below in table 6. The drivers undergoing sleep laboratory testing reported more medical illnesses in general, including hypertension and ‘sleep apnoea’. The high reported prevalence of illicit drug taking in the groups of drivers has already been commented on above.

Table 6 Medical health of drivers in the field study and laboratory study

	<i>Field Drivers</i>	<i>Laboratory Drivers</i>
% with medical illnesses (other than OSA)	20%	48%
% reporting hypertension	9%	20%
% reporting heart disease	2%	2%
% reporting 'sleep apnoea'	4%	10%
% using 'tablets to stay awake while driving'	24%	11%

3.2.5 Accident rates

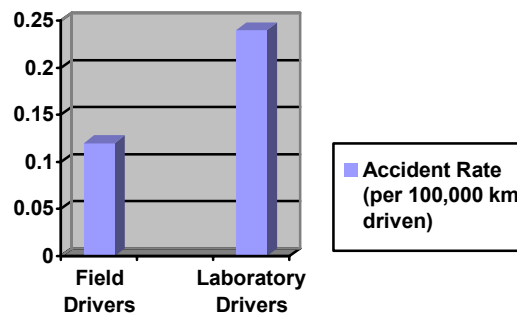
Information regarding self-reported motor vehicle accidents is presented below in table 7. For the 1002 drivers surveyed in the field, 270 (27%) reported at least one motor vehicle accident in the last three years. In comparison, 26 (43%) of the 61 drivers undergoing sleep laboratory investigations reported at least one motor vehicle accident. This is equivalent to 7% and 16% of drivers respectively reporting at least one motor vehicle accident in a year/100,00km driven.

In total 471 and 38 accidents respectively were reported in the two groups over a three year period. This represents an accident rate of 0.12 and 0.24 accidents per year per 100,000 km driven for the two groups respectively (figure 12).

Table 7 Self-reported accidents for field and laboratory drivers

<i>Number of Accidents</i>	<i>Field Drivers Frequency</i>	<i>Percent</i>	<i>Laboratory Drivers Frequency</i>	<i>Percent</i>
0	732	73.1	35	57.4
1	147	14.7	15	24.6
2	79	7.9	10	16.4
3	25	2.5	1	1.6
4	10	1	0	0
5	4	0.4	0	0
6	4	0.4	0	0
7	1	0.1	0	0
	1002	100	61	100

Figure 12 Accident rate of drivers in the 2 study groups



3.3 Prevalence of Daytime Sleepiness

In the group who were surveyed in the field, 258 (26%) of the 996 drivers who completed the Epworth Sleepiness Scale fully, had an Epworth Score of greater than 10, a score which is consistent with pathological daytime sleepiness. Similarly, 20% of the drivers undergoing sleep investigation in the laboratory had pathological daytime sleepiness. There was no statistical difference between the two groups in terms of their Epworth Sleepiness Scores (figures 13 and 14).

Figure 13 Driver sleepiness: drivers surveyed in the field

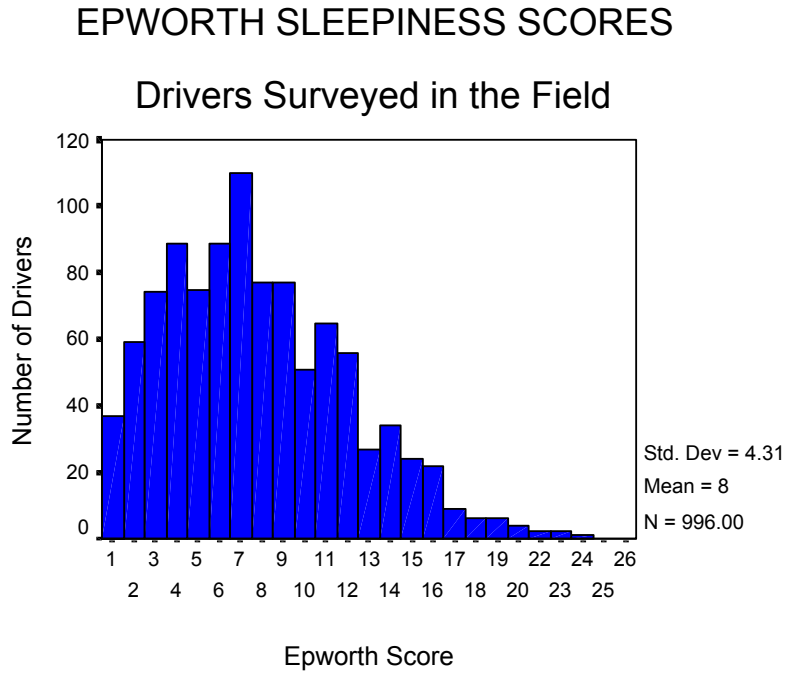
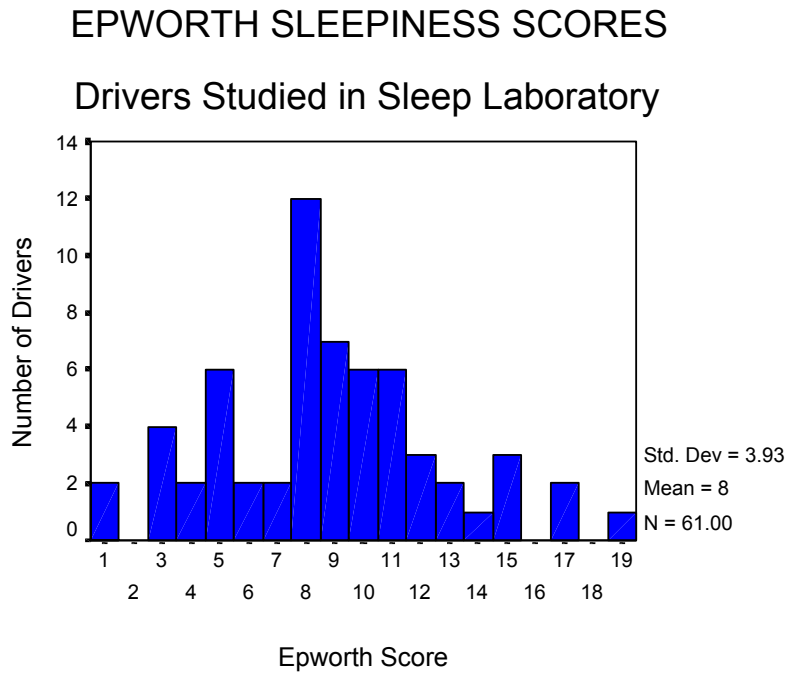


Figure 14 Driver sleepiness: drivers studied in the laboratory



3.4 Prevalence of Obstructive Sleep Apnoea

3.4.1 Prevalence of OSA and Sleep Apnoea Syndrome

In the group of transport drivers surveyed in the field, the prevalence of OSA was estimated using the Maislin questionnaire and equation. From this, the estimated prevalence of OSA for an RDI ≥ 10 was found to be 41%. Furthermore, 14% of the drivers had both an RDI ≥ 10 and an Epworth score > 10 , i.e. met the diagnostic criteria of sleep apnoea syndrome. This is illustrated below in table 8.

Table 8 Relation between OSA and pathological sleepiness in drivers in the field study

	<i>Maislin score < 0.5</i>	<i>Maislin Score ≥ 0.5</i>	<i>TOTAL</i>
ESS ≤ 10	44%	25%	70%
ESS > 10	11%	14%	25%

The drivers who underwent sleep laboratory investigation had their degree of OSA exactly quantified using the gold standard for diagnosis, an overnight sleep study. Table 9 shows the prevalence of OSA in this group of drivers for different diagnostic cut-offs and different degrees of severity.

Table 9 Prevalence of OSA for drivers studied in laboratory

<i>OSA Definition</i>	<i>% Of Laboratory Drivers</i>
RDI \geq 5	71%
RDI \geq 10	51%
Mild OSA (RDI 5 –15)	36%
Moderate OSA (RDI 15 – 30)	20%
Severe OSA (RDI > 30)	15%

The prevalence of sleep apnoea syndrome in this group of drivers is illustrated below in table 10. Importantly, 15% of the drivers studied in the sleep laboratory had both OSA on their overnight sleep study and a history of excessive daytime sleepiness. Only one third of the drivers with sleep apnoea syndrome came from the severe OSA group, indicative of the weak relationship between severity of polysomnographically identified OSA and the presence of excessive daytime sleepiness (this is discussed more fully in the next chapter, section 4.1). The percentages in the first two columns of table 10 represent the minimum true prevalence of sleep apnoea syndrome, assuming all those who did not have sleep investigations (from the original mail out list or telephone contact) did not have sleep apnoea syndrome.

When the group of drivers with sleep apnoea syndrome (RDI \geq 5, Epworth > 10) was directly compared with the group who did not have sleep apnoea syndrome, the mean difference in RDI between the groups was 15/hr (CI: 3 – 26/hr) and in Epworth 8 (CI: 6 – 10).

Table 10 Prevalence of sleep apnoea syndrome for drivers studied in laboratory

	<i>% Of Mail Out Group</i>	<i>% Of Contactable Group</i>	<i>% Of Laboratory Studied Drivers</i>
RDI \geq 5	29%	41%	71%
ESS > 10	8%	11%	20%
“Sleep Apnoea Syndrome” RDI \geq 5 + ESS > 10	6%	9%	15%

Although an overnight sleep study is the most accurate way of diagnosing OSA, drivers who underwent sleep laboratory testing were also asked to complete the Maislin questionnaire and equation, so that their Maislin scores could be compared with the scores of those drivers who were surveyed with the Maislin in the field. Using the Maislin, their estimated prevalence of OSA for an RDI \geq 10 was found to be 60%. This compares to the prevalence figure of 51% that was found for an RDI \geq 10 using the overnight sleep study data (table 9). This suggests that the Maislin tends to overestimate the number of drivers with sleep apnoea.

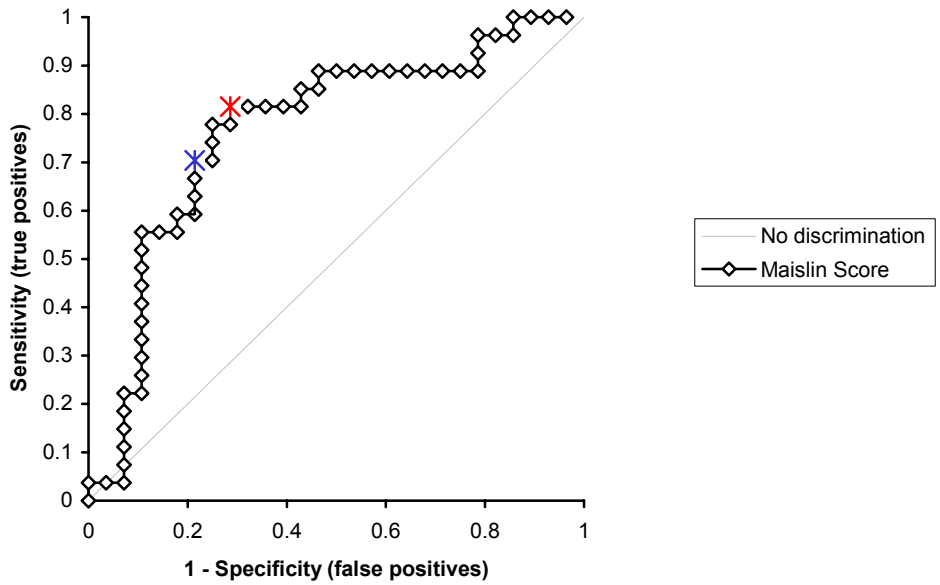
3.4.2 Analysis of Accuracy of Maislin Prediction of OSA

Because of the small difference in the prevalence of OSA in this group when it was estimated using the Maislin (60%), compared to when it was measured using the overnight sleep study data (51%), which is the gold standard of diagnosis, the accuracy of the Maislin as a screening tool for OSA in this group of transport drivers was further evaluated. To do this the drivers Maislin scores were compared with their sleep study results directly.

This analysis found that for the Maislin cut-off (0.5) that was used, the sensitivity for diagnosing OSA (RDI > 10) is 82% and the specificity is 66% (for definitions, see attachment 3). The sensitivity and specificity of the Maislin for diagnosing OSA can be further discussed in the context of its receiver operator characteristic (ROC) curves (figure 15). This illustrates some additional points about the Maislin as a screening tool for OSA in this population:

- As the sensitivity of the Maislin rises above 70% (marked with blue asterisk “*”), the specificity of the test drops rapidly. In other words, the number of false positive test results dramatically increases.
- The optimal Maislin cut-off (marked with red asterisk “**”) that combines both good levels of sensitivity and specificity appears to be around 0.51, where sensitivity is 82% and specificity is approximately 70%. A cut-off of 0.5 was used for the analysis above.

Figure 15 ROC curve: Maislin prediction of OSA



Using the Maislin and sleep study data, likelihood ratios (see Attachment 3) for predicting OSA for four different ranges of Maislin scores were calculated (table 11). This data illustrates that in a population of transport drivers, a Maislin score above 0.55 increases the odds for having OSA almost three fold.

Table 11 Likelihood ratios for predicting OSA for Maislin score quartiles

<i>Maislin Quartile</i>	<i>Likelihood Ratio</i>
< 0.4	0.45
0.4 to 0.55	0.36
0.55 to 0.75	2.9
> 0.75	2.9

Chapter 4: Results: Correlates of OSA

4.1 Relationship of Obstructive Sleep Apnoea to Driver Sleepiness

As discussed in the introduction, not all patients with OSA report excessive daytime sleepiness. There are potentially many reasons for this, including a lack of awareness or under-reporting of daytime sleepiness in patients suffering from OSA prior to treatment (Engleman H *et al.* 1997a). In Chapter 3, the percentage of drivers with both OSA and excessive daytime sleepiness (i.e., those drivers with ‘sleep apnoea syndrome’) was given for both of the groups of drivers tested. These results are again summarised below in Table 12.

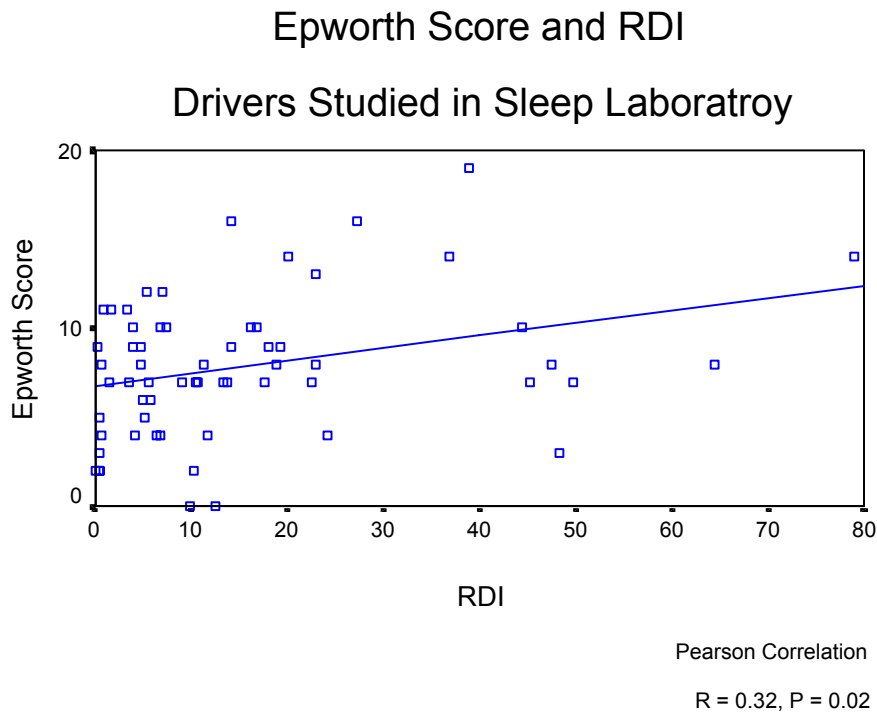
Table 12 Prevalence of sleep apnoea syndrome for drivers in the field and laboratory

	<i>Field Drivers (RDI \geq 10 (Maislin), Epworth > 10)</i>	<i>Laboratory Drivers (RDI \geq 5, Epworth > 10)</i>	<i>Laboratory Drivers (RDI \geq 10, Epworth > 10)</i>
Sleep Apnoea Syndrome (OSA, Epworth > 10)	14%	15%	12%

In this section the relationship between having OSA and reporting excessive daytime sleepiness has been examined further in the study populations. In the group of drivers surveyed in the field, those with suspected OSA reported higher Epworth scores (mean difference in Epworth =1.79; CI: 1.23 to 2.35) and were 2.1 times more likely to have an Epworth score > 10 (CI: 1.5 to 2.8). Further, a 0.1 unit increase in their Maislin scores led

to a 1.2 fold increase in the odds of being pathologically sleepy (i.e. Epworth > 10) (OR = 1.2 (1.1 to 1.3)). In the drivers who underwent sleep laboratory investigation, there was a significant, but weak, correlation between actual RDIs and Epworth scores (Pearson Correlation R=0.32, P=0.02, N=61). This is illustrated in figure 16.

Figure 16 Correlation between driver sleepiness and OSA



4.2 Relationship of OSA to Self-Reported Accident Rates

4.2.1 Drivers Surveyed in the Field

For the drivers surveyed in the field, there was a very weak but significant relationship between reporting motor vehicle accidents in the last three years and the drivers Epworth scores ($R^2 = 0.005$; $P = 0.04$). Further, a one unit increase in the drivers Epworth scores

was associated with a four percent increase in the odds of reporting one accident or more (OR = 1.04; CI: 1.001 to 1.072). However, there was no relationship between reporting a motor vehicle accident and having OSA ($R^2=0.0002$; $P=0.6$). Similarly, no relationship was found between reporting multiple accidents (i.e. more than one in a three year period) and Epworth or Maislin scores.

Because of the lack of association between OSA and self-reported accidents, the subgroup of drivers who had sleep apnoea syndrome were analysed separately to see if this group was associated with increased self-reported motor vehicle accidents. This analysis was performed for three levels of reported accidents – total reported accidents, at least one reported accident, and multiple accidents. Table 13 illustrates that there was no significant difference in any of the self-reported accident outcomes between drivers with and without sleep apnoea syndrome.

Table 13 Comparison of accident rates between drivers with and without sleep apnoea syndrome

	<i>Mean Difference</i>	<i>Lower 95% CI</i>	<i>Upper 95% CI</i>
Total Reported Accidents	-0.15	-0.37	0.07
At Least 1 Accident	-0.04	-0.12	0.04
Multiple Accidents	-0.01	-0.07	0.04

4.2.2 Drivers Studied in the Sleep Laboratory

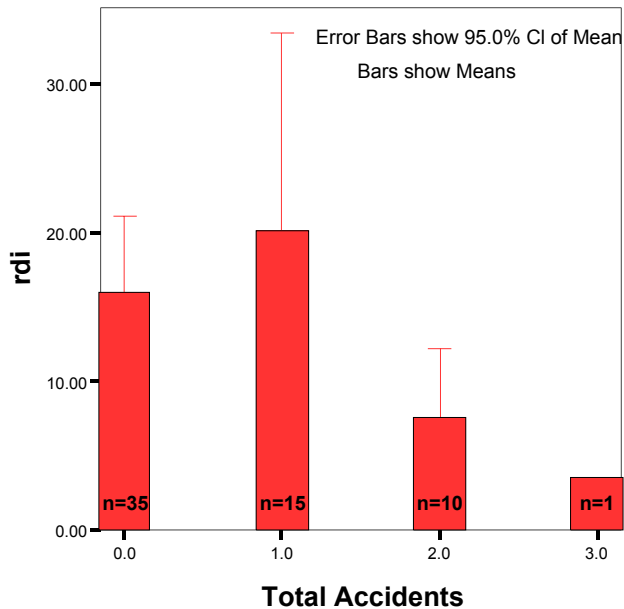
For the group of drivers studied in the sleep laboratory, RDI was not significantly correlated with the total number of accidents (P=0.2, R= -0.130, N=57). Similarly, there was no statistically significant difference in the RDIs of those drivers with one or more accidents compared to those drivers with no accidents (Table 14, Figure 17).

Table 14 OSA (RDI) in drivers with and without a history of accidents

<i>Mean RDI of drivers with no accidents (n=35)</i>	<i>Mean RDI of drivers with at least 1 accident (n=26)</i>	<i>Difference*</i>
15.9	14.6	1.3 (-10.2 to 7.5)

* mean difference \pm 95% confidence interval

Figure 17 Accidents compared to RDI for drivers studied in the laboratory



Other analyses to assess for a relationship between self-reported accidents and RDI in this small cohort of drivers did not show any significant associations. Similarly, those drivers with sleep apnoea syndrome did not show increased accidents. However, statistical significance was not expected given the very small numbers in these later analyses.

4.3 Relationship of OSA to Driving Impairment (Driving Simulator)

The drivers studied in the sleep laboratory had their driving performance objectively measured using a driving simulator. Each driver performed a 30 minute driving simulator task at 8 pm on the day of admission, then again at 7 am and approximately 10 am the next day after their sleep study. Repeated measures analysis of variance was used to

assess differences in driving simulator performance between drivers with and without various risk factors.

4.3.1 Obstructive Sleep Apnoea

The effects of OSA (classified as no OSA (RDI <5), mild OSA (RDI 5-15), moderate OSA (RDI 15-30), severe OSA (RDI >30)), pathological sleepiness (ESS > 10) and time of day (8pm, 7am, 10am) on driving simulator performance were assessed by repeated measures analysis of variance.

This analysis demonstrated that neither the presence nor level of OSA, the time of day, nor the interaction between these, had any significant effect on the driving simulator outcomes. Similarly drivers with pathological sleepiness (Epworth > 10) were not significantly different to other drivers in driving simulator performance.

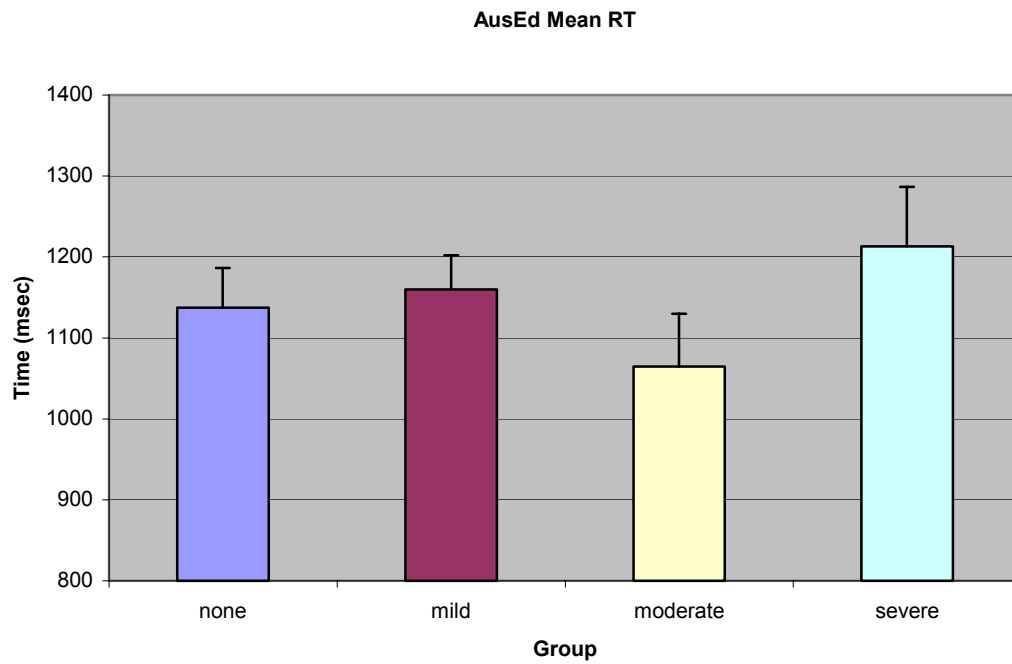
Table 15 below shows the AusEdTM mean reaction time (RT), averaged for the three time periods, by OSA status. Figure 18 illustrates the same information graphically. This was one of approximately 15 driving simulator outcome variables that were compared between the groups

Table 15 AusEd mean reaction time by OSA status

	<i>Mean RT</i>	<i>95% upper CI</i>	<i>95% lower CI</i>
No OSA	1137.5	1039.6	1235.4
Mild OSA	1159.7	1074.2	1245.1
Moderate OSA	1064.7	934.2	1195.2
Severe OSA	1213.0	1065.0	1361.0

P = 0.5

Figure 18 AusEd mean reaction time by OSA status



4.3.2 Sleep Apnoea Syndrome

The effect of sleep apnoea syndrome on some aspects of driving simulator performance differed according to the time of day at which the test was done. However, other driving simulator performance measures were worse at all times of day for the sleep apnoea syndrome group (table 16). After adjustments were made for age, and this analysis was repeated, there was little change in the results.

Table 16 Effect of sleep apnoea syndrome on driving simulator performance

(adjusted for diurnal variation)

<i>Dependent Variable</i>	<i>Time of day</i>	<i>Effect of Sleep Apnoea Syndrome</i>	<i>P</i>	<i>Interaction¹</i>
Median Lane Position	All	None	0.1	0.6
Sd lane position median	8pm	Worse performance	0.04	0.02
Sd lane position median	10am	Worse performance	0.02	0.02
Sd lane position median	7am	None	0.2	0.02
Area dev steering centre	All	None	0.3	0.1
Av dev steering centre	All	None	0.97	0.3
Area steer dev median	All	None	0.09	0.3
Av steer dev median	All	Worse performance	0.02	0.3
RT Mean	10am	Worse performance	0.00	< 0.001
RT Mean	8pm	None	0.2	<0.001
RT Mean	7am	None	0.07	<0.001
RT sd mean	10am	Worse performance	0.00	< 0.001
RT sd mean	8pm	None	0.3	<0.001
RT sd mean	7am	None	0.9	<0.001
RT median	All	Worse performance	0.01	0.2
RT sd median	10am	Worse performance	0.00	0.001
RT sd median	8pm	None	0.8	0.001
RT sd median	7am	None	0.2	0.001
RT 95% percentile	10am	Worse performance	0.00	< 0.001
RT 95% percentile	8pm	None	0.9	<0.001
RT 95% percentile	7am	None	0.4	<0.001
Area speed dev zone	All	None	0.9	0.5
Av speed dev zone	All	None	0.3	0.4
Crashes	8pm	Worse performance	0.02	0.02
Crashes	7am	None	0.2	0.02
Crashes	10am	None	0.1	0.02

1. Significant test for diurnal variation in the effect of SAS on driving performance.

In summary, the drivers with sleep apnoea syndrome performed worse than drivers without sleep apnoea syndrome in three key driving simulator performance outcome measures:

1) Tracking (steering) – drivers with sleep apnoea syndrome showed greater variability in the lane positions they adopted on the road, i.e., more erratic driving. This is demonstrated by a difference between the groups in the variable “Av steer dev median” (average steering deviation outside the median lane position adopted for the 30 minute drive – see figure 20) and “sd lane position median” (standard deviation of the lane position from the median lane position for the 30 minute drive).

2) Reaction time – drivers with sleep apnoea syndrome showed longer reaction times, as measured by both the mean and median reaction times, together with greater variability in reaction times (standard deviation and 95% percentile of reaction times were greater in the sleep apnoea syndrome group). Many of these changes were seen at the 10 am time point. See figure 19.

3) Number of crashes – drivers with sleep apnoea syndrome crashed more than those drivers without sleep apnoea syndrome (at 8 pm).

Figure 19 is a plot of the AusEd™ mean reaction times for drivers with sleep apnoea syndrome and without sleep apnoea syndrome across the three time periods tested. The graph shows that the effect of sleep apnoea syndrome on this driving performance measure varied with time; an important difference was apparent only at the 10 am test.

Figure 19 AusEd mean reaction times for drivers with and without sleep apnoea syndrome

(illustrated across the three time periods)

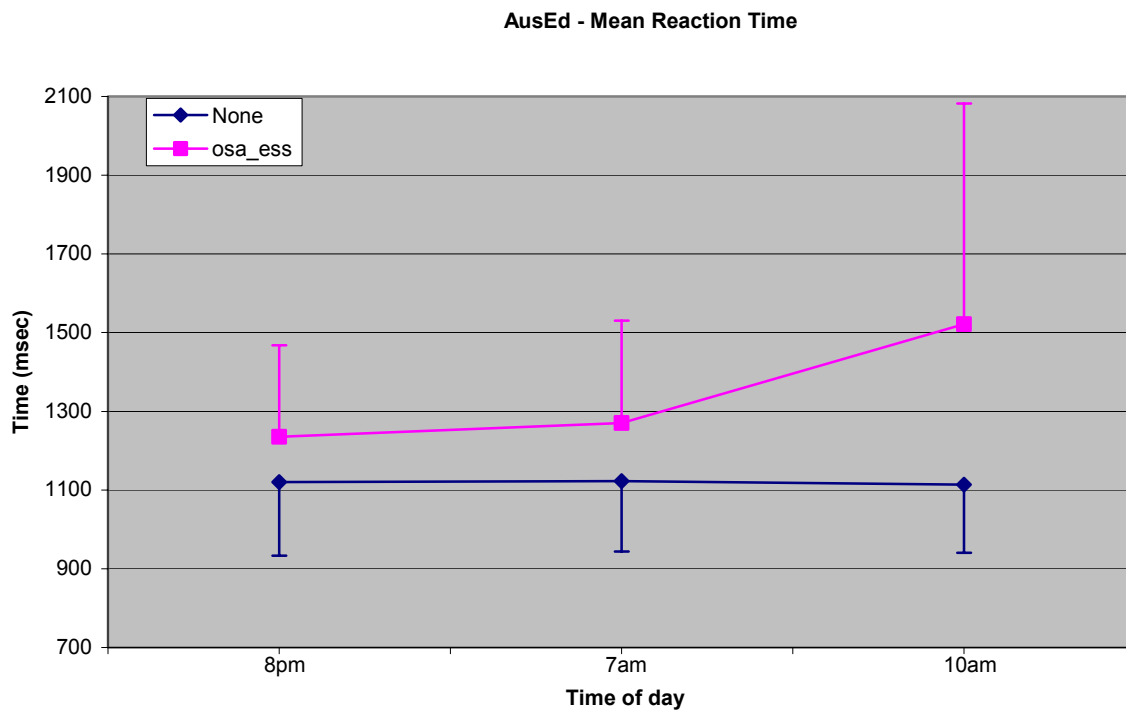
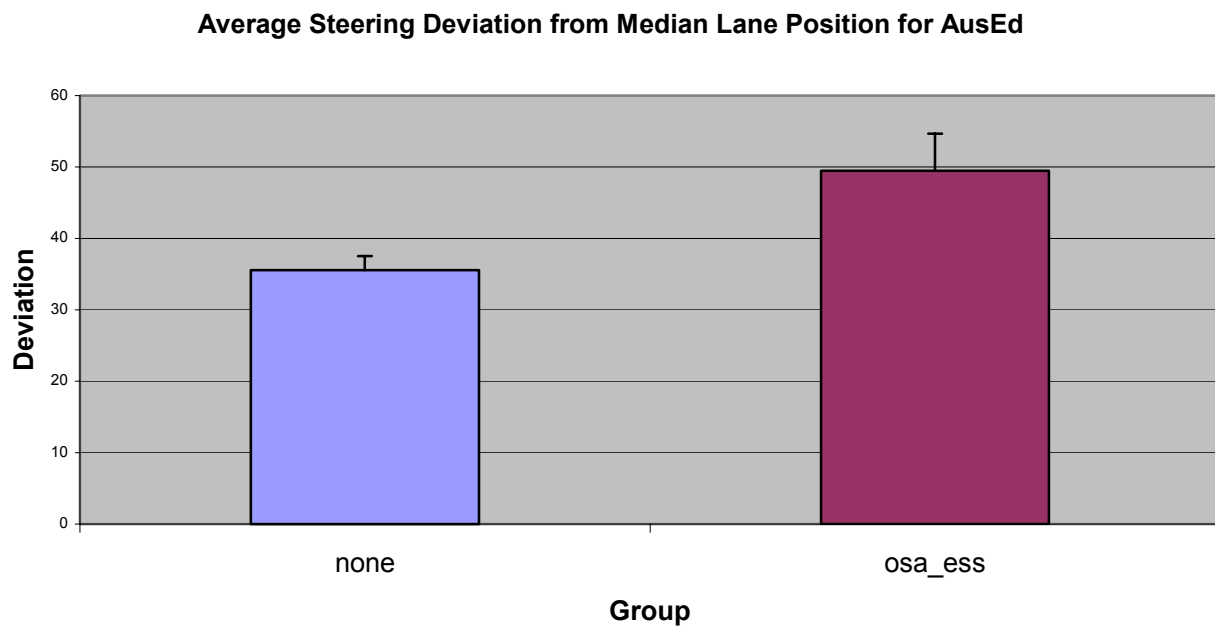


Figure 20 shows that average steering deviation from the median lane position, a measure of tracking, was worse overall in the drivers with sleep apnoea syndrome.

Figure 20 Tracking ability in drivers with and without sleep apnoea syndrome



These analyses were repeated using a broader definition of sleep apnoea syndrome (RDI ≥ 5 , ESS > 10 . See table 12). The findings were broadly consistent with those described above: drivers with sleep apnoea syndrome performed worse than drivers without sleep apnoea syndrome on several reaction time variables and crashes.

4.4 Regression Models

4.4.1 Factors Predicting Driver Sleepiness

The effect of various lifestyle, work and medical factors (Table 17) on the risk of reporting excessive daytime sleepiness (Epworth Sleepiness Scale > 10) was assessed using logistic regression modeling with stepwise selection.

Table 17 Predictor variables for driver sleepiness

<i>Variable</i>	<i>Type of Variable</i>
Maislin Score \geq 0.5*	Medical
Body Mass Index	Medical
Age	Medical
> 2 hours sleep difference between work and off-work days*	Lifestyle
At least 3 caffeine drinks per day*	Lifestyle
Less than 6 hours sleep per work night*	Lifestyle
At least 6 day working week*	Work
At least 10 hours driven per day*	Work
Greater than 50 hours worked per week*	Work
At least 14 hours longest work shift*	Work
Rotating shifts*	Work
Night shifts*	Work
Interstate driving*	Work
Metropolitan driving*	Work
Country driving*	Work
Long distance driving*	Work

* = dichotomised variable

Of the 16 medical, lifestyle and work factors that were tested, only three were found to be statistically significant predictors of excessive driver sleepiness: Maislin score ≥ 0.5 , > 2 hours sleep difference between work and off-work days, and at least a six day working week. Table 18 presents the odds ratios and 95% confidence intervals for these independent, significant predictors of sleepiness. It illustrates that individuals with OSA (Maislin ≥ 0.5) are 2.9 times more likely to be pathologically sleepy (Epworth > 10) compared to individuals without OSA, when corrected for the effects of factors reflecting lifestyle and work habits.

Importantly, Maislin ≥ 0.5 (i.e., having OSA) was the most important factor predicting driver sleepiness in this population. It was more important than many of the traditionally recognized fatigue promoting factors, such as night driving, chronic sleep deprivation (represented by the variable “less than 6 hours sleep per work night”), driving many hours per day (represented as “at least 10 hours driven per day” and “at least 14 hours longest work shift”), and long distance driving, all of which failed to be statistically significant predictors of driver sleepiness in this group.

Table 18 Predictors of excessive driver sleepiness

<i>Variable</i>	<i>OR</i>	<i>95% CI</i>
Maislin score > 0.5	2.9	1.9 - 4.6
> 2 hours sleep difference between work and off-work days	1.6	1.1 – 2.4
At least 6 day working week	1.5	1.01 - 2123

4.4.2 Factors Predicting Reported Accidents

A multiple logistic regression analysis was performed to look for factors predicting self-reported accidents for the drivers surveyed in the field. All the work, lifestyle and medical factors used in the last analysis (table 17) were tested, together with driver sleepiness (dichotomised at Epworth > 10). Metropolitan drivers (OR 1.9, 95% CI 1.2 – 3.2) and those reporting a longest work shift duration of at least 14 hours (OR 1.46, 95% CI 1.01 – 2.08) had significantly increased odds for reporting at least one accident. None of the other variables significantly predicted self-reported accidents.

When the outcome of multiple self-reported accidents (i.e. more than one) was assessed using a similar multiple logistic regression analysis, metropolitan drivers were 2.7 times more likely to report multiple accidents compared to non-metropolitan drivers (OR 2.7, 95% CI 1.3 – 5.7), and country drivers showed a significantly lower odds for reporting multiple accidents than non-country drivers (OR 0.54, 95% CI 0.29 – 0.99). No other variables were significant.

To assess whether driving simulator performance could predict self-reported accidents in the drivers who underwent sleep laboratory testing, several multiple logistic regression analyses were performed for the outcome variables of reporting at least one accident and reporting multiple accidents. Several driving simulator variables representing reaction time, steering, and speed were entered as independent predictors. None of these variables at any of the 3 times (8 pm, 7 am, 10 am) or averaged across all three times were statistically significant predictors of self-reported accidents.

4.4.3 Factors Predicting Driving Impairment (Driving Simulator)

The effect of age, RDI and pathological sleepiness (Epworth > 10), and time of testing, was tested for each of the driving simulator performance measures by linear regression modeling. Age explained up to 15% of the variance in 13 of the tracking and reaction time measures in these models. In total 48 performance measures were modeled. Sleepiness was not a statistically significant independent predictor of driving simulator performance and RDI partially explained two tracking measures (Table 19).

Table 19 Driving simulator variables partially explained by RDI

<i>Driving Variable - outcome measure</i>	<i>Explained variance of RDI (P value, adjusted for age and ESS)</i>
Area of steering deviation from median	7% (P = 0.047)
Average of steering deviation from median	7% (P = 0.047)

In separate models, the effect of sleep apnoea syndrome (RDI \geq 10, Epworth > 10) was tested, with adjustment for the effects of age. Similar to the results in section 4.3.2 above, sleep apnoea syndrome was a significant independent predictor of tracking, reaction time and crash outcomes on the driving simulator, explaining up to 26% of the variance in some of these outcomes. This was apparent at all three testing sessions. See table 20.

Table 20 Driving simulator variables explained by sleep apnoea syndrome

<i>Driving Variable - outcome measure</i>	<i>% of variance explained by SAS (P value, corrected for Age)</i>
Standard deviation of lane position from median, 10 am	11% (P = 0.02)
Area steering deviation of lane position from median, 10 am	11% (P = 0.02)
Average steering deviation of lane position from median, 10 am	11% (P = 0.02)
Mean reaction time, 10 am	24% (P = 0.00)
Standard deviation of mean reaction time, 10 am	24% (P = 0.00)
Median reaction time, 10 am	16% (P = 0.00)
95'th percentile of median reaction time, 10 am	26% (P = 0.00)
Mean reaction time, 7 am	7% (P = 0.045)
Median reaction time, 7 am	9% (P = 0.02)
Median reaction time, 8 pm	9% (P = 0.02)
Number of crashes, 8 pm	9% (P = 0.02)

4.4.4 Factors Predicting Obstructive Sleep Apnoea

The value of simple medical evaluation in screening for the presence of OSA was assessed by logistic regression analysis. For the drivers studied in the sleep laboratory, reporting the combination of snorting or gasping (one or more nights per week), loud snoring (one or more nights per week), and breathing pauses (once or more nights per week) increased the odds for having an RDI ≥ 10 by 3.4 times (OR = 3.4, 95% CI 1.2 – 10.2).

Neck circumference was a significant independent predictor of an RDI ≥ 10 in this population (OR= 1.7, corrected for age and BMI, CI 1.2 – 2.6), but BMI and age were not. See table 21.

Table 21 Predictor variables of OSA

<i>Predictor of OSA</i>	<i>OR</i>	<i>CI</i>
Neck Circumference	1.74	1.17 – 2.59
Body Mass Index	.87	0.70 – 1.07
Age	1.07	0.99 – 1.15

Similarly, neck circumference was correlated with RDI (R=0.389; P=0.002), but BMI was not (R=0.228; P=0.08).

4.5 Effect of OSA/Sleepiness on Vigilance (Psychomotor Vigilance Task)

The effect of RDI, pathological daytime sleepiness (Epworth > 10) and age on PVT outcomes was assessed by multiple linear regression.

After accounting for the effects of age and OSA (measured as RDI), the presence of pathological sleepiness was significantly related to PVT lapses (i.e. poor reaction time performance) at 10 am (R = 0.30, P = 0.03). Age also had an independent effect on several PVT outcome measures, but RDI did not predict PVT performance.

In a separate model, sleep apnoea syndrome (corrected for age) was a significant independent predictor of 3 PVT outcomes at 10 am (PVT median, $R^2 = 13\%$ $P = 0.008$; PVT lapses, $R^2 = 18\%$ $P = 0.001$; PVT 1/reaction time slowest 10%, $R^2 = 12\%$ $P = 0.01$)

After adjusting for age, the effect of sleep apnoea syndrome ($RDI \geq 10$, Epworth > 10) on PVT performance at various times of the day was assessed by analysis of variance. Where the interaction between sleep apnoea syndrome and time of testing was significant, the significant effects of sleep apnoea syndrome have been analysed and presented at the time points at which they occurred (table 22). When the interaction was not significant, any significant group effects have been presented. Table 22 shows that drivers with sleep apnoea syndrome had poorer PVT reaction time performance than those drivers without sleep apnoea syndrome, mainly at 10 am. After adjusting for age, differences in PVT reaction time between groups of drivers were not seen when drivers with OSA ($RDI > 10$) were compared with drivers without OSA. However, drivers with pathological sleepiness (Epworth > 10) had significantly more lapses at 10am ($P=0.03$) than drivers without pathological sleepiness.

Table 22 Effect of sleep apnoea syndrome on PVT performance, adjusted for diurnal variation

<i>Dependent Variable</i>	<i>Interaction</i>	<i>Interpretation</i>
PVT Median	.02	Drivers with SAS had slower median reaction times at 10 am (49ms, 95% CI 14-83, p=0.01)
Lapses	.001	Drivers with SAS had more lapses at 10 am (3, 95% CI 1-5, p=0.00)
Fast 10%	.90	
1/RT Slow 10%	.08	Drivers with SAS showed poorer performance, averaged across all 3 times (Effect of group -0.4, P=0.03)
Errors	.93	

4.6 Effect of OSA/Sleepiness on neuropsychological measures

After controlling for IQ, there was no significant relationship between RDI and any of the normed neuropsychological test results. However, those drivers with sleep apnoea syndrome ($RDI \geq 10$, Epworth > 10) had a significantly lower Trails B Z score (a test of psychomotor speed) than those drivers without sleep apnoea syndrome ($P=0.049$). In other words, drivers with sleep apnoea syndrome performed poorer on a motor and visual search task.

4.7 Summary of Results for Chapters 3 and 4

4.7.1 Response Rates

- For the transport drivers surveyed in the field, 42 randomly selected NSW truck yards or truck stops were visited over an approximate 15 month period. The overall response rate for the 1002 questionnaires completed by the drivers at these sites was 83%.
- Sixty one randomly selected transport drivers were studied in the sleep laboratory over a 20 month period. The response rate for the eligible drivers in this cohort was 58%.

4.7.2 Demographic and Physical Characteristics

- The drivers surveyed in the field had an average age of 42 years, an average Body Mass Index of 30 kg/m², and an average neck circumference of 42 cm.
- The drivers who underwent sleep laboratory investigations were older (average age of 48 years), but otherwise their body mass index and neck circumference did not differ from the other cohort.
- In both cohorts, company drivers were more frequently studied than owner drivers
- Drivers surveyed in the field performed more interstate and long distance driving than the drivers studied in the sleep laboratory, who reported more metropolitan driving.
- Drivers surveyed in the field drove more kilometres per year, worked and drove more hours per week, and on average reported a greater longest work shift.

- Both cohorts slept on average just over six hours per day while at work, and reported high caffeine and illicit drug use.
- The drivers undergoing sleep laboratory testing reported more medical illnesses in general, including hypertension and ‘sleep apnoea’.
- Seven percent of the drivers surveyed in the field and sixteen percent of the drivers who were studied in the sleep laboratory reported at least one motor vehicle accident in a year/100,00km driven

4.7.3 Prevalence of Daytime Sleepiness

- In the group who were surveyed in the field, 26% reported pathological daytime sleepiness. For the other cohort of drivers, this was reported in 20%.

4.7.4 Prevalence of Obstructive Sleep Apnoea

- For the drivers surveyed in the field, the prevalence of OSA was estimated at 41%. Furthermore, 14% of the drivers had both OSA and excessive daytime sleepiness, i.e., sleep apnoea syndrome.
- The drivers studied in the sleep laboratory showed a prevalence of OSA of 51% (RDI \geq 10). Fifteen percent of the drivers had severe OSA. The prevalence of sleep apnoea syndrome in this cohort was 12% (RDI \geq 10, Epworth > 10).
- When the Maislin Questionnaire was ‘re-validated’ within the laboratory cohort, the Maislin threshold score of 0.5 that was used showed a sensitivity of 82% and a specificity of 66% for diagnosing OSA (RDI > 10). This threshold score

compared very favourably to the optimal threshold suggested by the Maislin's ROC curve.

4.7.5 Relationship of Obstructive Sleep apnoea to Driver Sleepiness

- Obstructive sleep apnoea was related to driver sleepiness. In the group of drivers surveyed in the field, those with OSA reported higher Epworth scores and were 2.1 times more likely to report pathological daytime sleepiness. In the drivers who underwent sleep laboratory investigation, there was a statistically significant correlation between actual RDIs and Epworth scores (Pearson Correlation $R=0.32$).

4.7.6 Relationship of Obstructive Sleep Apnoea to Self-Reported Accident Rates

- For the drivers surveyed in the field, there was a very weak but significant relationship between reporting motor vehicle accidents in the last three years and the driver's Epworth scores.
- However, there was no relationship between reporting a motor vehicle accident and having OSA or sleep apnoea syndrome in either of the study groups

4.7.7 Relationship of Obstructive Sleep Apnoea to Driving Impairment (Driving Simulator)

- Drivers with sleep apnoea syndrome performed worse than drivers without sleep apnoea syndrome in three key driving simulator performance outcomes – steering,

reaction time and number of crashes. Driving simulator differences between the groups were not apparent for RDI alone or pathological sleepiness alone.

4.7.8 Predictors of pathological sleepiness, accident risk, poor performance on the driving simulator and OSA

- $\text{Maislin} \geq 0.5$ (i.e., having OSA) was the most important factor predicting pathological sleepiness in the drivers surveyed in the field. It was more important than many of the traditionally recognized fatigue promoting factors, such as night driving, chronic sleep deprivation, driving for many hours per day, and long distance driving, all of which failed to be statistically significant predictors of driver sleepiness in this group.
- Metropolitan driving and having a longest work shift duration of at least 14 hours were the only significant predictors for reporting at least one accident. Metropolitan drivers were also 2.7 times more likely to report multiple accidents compared to non-metropolitan drivers, while country drivers showed a significantly lower odds for reporting multiple accidents than non-country drivers. Driving simulator performance did not predict self-reported accident rates.
- Sleep apnoea syndrome was a significant independent predictor of tracking, reaction time and crash outcomes on the driving simulator (when adjusted for the effects of age).
- Simple medical questioning about sleep apnoea symptoms and neck circumference measurements were the most significant clinical predictors for the presence of OSA

4.7.9 Effect of OSA/Sleepiness on Vigilance (Psychomotor Vigilance Task)

- Sleep apnoea syndrome was a significant independent predictor of several PVT reaction time outcomes (when adjusted for the effects of age). RDI alone did not predict PVT outcomes, while pathological sleepiness alone predicted one PVT outcome.
- After adjusting for age, drivers with sleep apnoea syndrome showed poorer performance on PVT reaction time tests compared to drivers without sleep apnoea syndrome. These differences in PVT reaction time between groups of drivers were not seen for OSA alone ($RDI \geq 10$). However, drivers with pathological sleepiness (Epworth > 10) showed significant differences on one PVT outcome.

4.7.10 Effect of OSA/Sleepiness on Neuropsychological Measures

- After controlling for IQ, drivers with sleep apnoea syndrome performed worse on a test of psychomotor speed than those drivers without sleep apnoea syndrome. However, there was no significant relationship between RDI alone and any of the normed neuropsychological test results.

Chapter 5: Results: Interactive Effects of Mild OSA

5.1 Demographic and Physical Measures

Subjects with OSA did not differ in age from control subjects, but they were more obese, as indicated by a higher body mass index and larger neck circumference. See table below.

Table 23 Demographic & physical measures: comparison between OSA & control groups

	<i>Mean Age (years)</i>	<i>Mean BMI (kg/m²)</i>	<i>Mean Neck Circumference (cm)</i>	<i>N</i>
Controls	38	25.5	38.9	16
OSA	45	30.3	41.4	13
Difference*	7 (-18 to 4)	4.7 (1.1 to 8.3)	2.5 (0.4 to 4.5)	

*values are mean differences \pm 95% confidence intervals (CI)

5.2 Lifestyle Details

Subjects with OSA tended to report less sleep on work days and have less actual recorded sleep in the four nights preceding their laboratory admissions, compared to subjects without OSA (although these differences were not statistically significant). Both subject groups reported consuming several caffeine drinks per day, but there was no significant difference in amount consumed between the two groups. See table below.

Table 24 Lifestyle details: comparison between OSA and control groups

	<i>Controls</i>	<i>OSA</i>	<i>Difference*</i>
Av. reported sleep work days (hours)	7.0		1.2 (-0.01 to 2.4)
Av. reported sleep days off (hours)	8.2	8.0	0.2 (-1.0 to 1.4)
Av recorded sleep preceding 4 nights (average sleep hours/night)	7.1	6.6	0.5 (-0.3 to 1.2)
Av. caffeine intake (drinks/day)	2.9	4.3	1.4 (-0.8 to 3.6)
Av. ETOH work days (drinks/day)	0.3	1.0	0.6 (-0.5 to 1.8)
Av. ETOH days off (drinks/day)	1.1	2.8	1.7 (-0.1 to 3.5)
N	16	13	

*Values are mean differences \pm 95% Confidence Intervals (CI)

There was no difference in caffeine intake on the day of admission or in average sleep hours during the preceding four nights in the subjects prior to the two testing weekends. Thus, neither of these factors could be expected to explain differences in performance outcomes between the two testing weekends. See table below.

Table 25 Caffeine intake and sleep hours immediately prior to testing weekends

	<i>Baseline Weekend</i>	<i>Sleep Deprivation Weekend</i>	<i>Difference*</i>
Caffeine intake on day of admission (drinks/day)	1.72	1.67	0.05 (-0.55 to 0.66)
Sleep preceding 4 nights (average sleep hours/night)	6.7	6.9	0.3 (-.006 to 0.6)
N	29	29	

*values are mean differences \pm 95% confidence intervals (CI)

5.3 Driver Details

Neither of the subject groups showed pathological daytime sleepiness, as measured by the Epworth Sleepiness Scale. There was no difference in Epworth scores or self-reported motor vehicle accident rates between the two groups. See table below.

Table 26: Driver details: comparison between OSA and control groups

	<i>Epworth Sleepiness Score</i>	<i>Reported Motor Vehicle Accidents (number in 3 years)</i>	<i>N</i>
Controls	7	0.6	16
OSA	9	0.3	13
Difference*	2 (-6 to 2)	0.3 (-0.5 to 1.1)	

*values are mean differences \pm 95% confidence intervals (CI)

5.4 Baseline Polysomnography

Table 27 confirms that the OSA status was different between the two groups. Subjects with OSA had a mean total RDI of 12, compared to a mean total RDI of 2 in the control group. Similarly, there was a significant difference between the groups in NREM RDI, arousal index and minimum oxygen saturation. Based on these polysomnographic results, OSA subjects had mild disease, whereas controls had no OSA.

Table 27 Baseline polysomnography: comparison between controls and OSA subjects

	<i>Controls</i>	<i>OSA</i>
Total RDI (events/hr)	1.9 (-0.7 to 4.4)	12.1 (9.2 to 15.0)
NREM RDI (events/hr)	0.7 (-2.5 to 3.8)	10.1 (6.6 to 13.5)
REM RDI (events/hr)	7.9 (1.4 to 14.5)	19.9 (12.7 to 27.1)
Arousal Index (arousals/hr)	9.3 (6.2 to 12.4)	17.2 (13.8 to 20.7)
Minimum O₂ saturation (%)	92 (90.8 to 93.2)	89.2 (87.7 to 90.7)

* values are mean +/- 95% confidence intervals

5.5 Daytime Driving Performance and Cognitive Function Outcomes

The effects of mild OSA, sleep deprivation and time of day on daytime driving performance and cognitive function were assessed by analysis of variance. No subjects had any crashes in any of the driving simulator testing sessions, so this AusEdTM outcome could not be analysed.

5.5.1 Effect of Time of Day and Sleep Deprivation

There was an effect of sleep deprivation and diurnal variation, or an interaction between these, for many of the daytime driving performance and cognitive function outcomes. Sleep deprivation consistently resulted in poorer driving and cognitive performance for many of the outcome measures. Time of day influenced performance, and the worst daytime performance was most often seen at 1500. These data are presented in tables 28 and 29 below. Data from subjects with mild OSA and subjects without OSA have been grouped together in these tables because the effect of sleep deprivation, time of day and

the interaction between them did not differ between OSA patients or controls for any of these outcomes. However, this was not the case for the Stanford Sleepiness Score and the PVT reaction time mean fastest 10% outcome. Both of these are discussed separately below.

5.5.1.1 Effect of Sleep Deprivation

Table 28 shows that the effect of sleep deprivation on most of the daytime driving performance and cognitive function outcomes differed according to the time of day at which the test was done. Impairments due to sleep deprivation were seen for tests of driving ability (AusEdTM reaction time, steering and speed outcomes), vigilance (PVT lapses), sleepiness (OSLER sleep latency), and mood (POMS fatigue and vigour subscores). However, there was no effect of sleep deprivation on the DSST, a test of attention, or the PRM test, a test of memory.

Table 28 Effect of sleep deprivation on outcomes (adjusted for diurnal variation)

Table 28 legend:

1. Interaction between time of day and sleep deprivation ('Intervention'). A significant result for this interaction indicates that there was significant diurnal variation in the effect of sleep deprivation on the outcome.
2. Results of secondary analysis presented
3. Age significant covariate
4. "All": 1900, 0700, 1100, 1500, 1900

<i>Dependent Variable</i>	<i>Time of day</i>	<i>Effect of Sleep Deprivation</i>	<i>Effect Size (95% CI)</i>
OSLER sleep latency (Interaction ¹ , p=0.00)	7 am	shorter sleep latency	851 (466 to 1236) secs, p=0.00
	11 am	shorter sleep latency	551 (181 to 921) secs, p=0.01
	3 pm	shorter sleep latency	566 (233 to 899) secs, p=0.00
	7 pm	none	359 (-12 to 731) secs, p=0.06
AusEd mean reaction time (RT) ^{2,3} (Interaction ¹ , p=0.03)	7 am	longer RT	127 (21 to 232) ms, p=0.02
	11 am	longer RT	127 (0.5 to 254) ms, p=0.05
	3 pm	longer RT	125 (26 to 224) ms, p=0.02
Aus Ed standard deviation mean RT ² (Interaction ¹ , p=0.12)	All ⁴	greater variability RT	97 (36 to 157) ms, p=0.00
AusEd average Steering Deviation from median position (Interaction ¹ , p=0.43)	All ⁴	none	7.6 (-3.1 to 18.3) cm, p=0.16
AusEd standard deviation of lane position (Interaction ¹ , p=0.00)	7 am	greater variability position	24 (13 to 35) cm, p=0.00
	11am	greater variability position	20 (10 to 29) cm, p=0.00
	3 pm	greater variability position	23 (9 to 37) cm, p=0.00
	7 pm	greater variability position	18 (6 to 29) cm, p=0.00
AusEd average speed deviation ² (Interaction ¹ , p=0.02)	7 am	greater variability speed	1.7 (0.1 to 3.3) km/h, p=0.03
	11 am	none	1.5 (-0.2 to 3.2) km/h, p=0.08
	3 pm	greater variability speed	2.3 (0.2 to 4.4) km/h, p=0.03
PVT transformed lapses (Interaction ¹ , p=0.01)	7 am	more lapses	1.8 (0.5 to 3.0) lapses, p=0.01
	11 am	more lapses	1.8 (0.8 to 2.9) lapses, p=0.00
	3 pm	more lapses	2.2 (0.9 to 3.5) lapses, p=0.00
	7 pm	more lapses	1.6 (0.6 to 2.7) lapses, p=0.00
POMS fatigue sub-score (Interaction ¹ , p=0.00)	7 am	greater reported fatigue	8.6 (5.8 to 11.3), p=0.00
	11 am	greater reported fatigue	9.3 (6.1 to 12.6), p=0.00
	3 pm	greater reported fatigue	9.3 (6.5 to 12.0), p=0.00
	7 pm	greater reported fatigue	8.5 (5.9 to 11.1), p=0.00
POMS vigour sub-score (Interaction ¹ , p=0.00)	7 pm	lesser reported vigour	7.6 (4.3 to 10.9), p=0.00
	11 am	lesser reported vigour	6.8 (4.3 to 9.3), p=0.00
	3 pm	lesser reported vigour	6.3 (3.8 to 8.8), p=0.00
	7 pm	lesser reported vigour	4.5 (2.2 to 6.8), p=0.00
PRM number correct (Interaction ¹ , p=0.55)	All ⁴	none	0.2 (-0.1 to 0.6), p=0.22
DSST % correct (Interaction ¹ , p=0.42)	All ⁴	none	0.1 (-0.5 to 0.8) %, p=0.67
DSST mean RT ³ (Interaction ¹ , p=0.27)	All ⁴	none	0.01 (-0.002 to 0.18) sec, p=0.11
DSST response rate ³ (Interaction ¹ , p=0.30)	All ⁴	none	0.01 (-0.002 to 0.19) sec/item, p=0.10

5.5.1.2 Effect of Time of Day

Table 29 shows that the daytime diurnal effect on most of the driving performance and cognitive function outcomes differed according to whether the subject was sleep deprived or not ('Intervention'). When daytime driving and cognitive performance was compared to the pre-intervention time point, i.e. first 1900 evening testing session prior to either a normal nights sleep or sleep deprivation, the worst performance was most often seen at 1500, the expected time of the circadian nadir in performance and alertness. This physiological circadian effect was seen for AusEdTM reaction time and PVT outcomes. However, subjective mood outcomes (POMS fatigue and vigour sub-scores) and sleepiness measures (OSLER sleep latency) showed an earlier maximal impairment (0700, 1100). There was no effect of time of day on the DSST, PRM test, or AusEdTM average speed deviation.

Table 29 Effect of time of day on outcomes (adjusted for intervention)

Table 29 legend

1. Differences are relative to pre-intervention time point, i.e. first 1900 evening testing session prior to either a normal nights sleep or sleep deprivation
2. Interaction between time of day and sleep deprivation ('Intervention')
3. Results of secondary analysis presented
4. Age significant covariate
5. Whether a significant effect was present for time of day at that level of intervention; '*' with no overall significant effect of time of day, the significance of the maximal differences presented in the last column is questionable

<i>Dependent Variable</i>	<i>Intervention</i>	<i>Effect of Time of Day</i> ⁵	<i>Maximal mean difference from 1900¹ (95% CI)</i>
OSLER sleep latency	Baseline	none	1900: 117 (-85 to 320) secs, p=0.24
(Interaction ² , p=0.00)	Sleep deprived	sleep onset quickest 0700	0700: 934 (534 to 1335) secs, p=0.00
AusEd average reaction time (RT) ^{3,4}	Baseline	RT longest 1500	1500: 90 (36 to 143) ms, p=0.00
(Interaction ² , p=0.03)	Sleep deprived	RT longest 1500	1500: 218 (115 to 321) ms, p=0.00
AusEd standard deviation of average RT ³	Both	variability greatest 1500	1500: 106 (42 to 169) ms, p=0.00
(Interaction ² , p=0.12)			
AusEd average steering deviation from median position (Interaction ² , p=0.43)	Both	none	0700: 21 (-0.7 to 42.3) cm, p=0.06
AusEd standard deviation of lane position	Baseline	none	1900: 5.3 (-6.0 to 16.7) cm, p=0.34
(Interaction ² , p=0.00)	Sleep Deprived	variability greatest 0700	0700: 29 (18 to 39) cm, p=0.00
AusEd average speed deviation ³	Baseline	none	1500: 0.2 (-0.6 to 0.9) km/h, p=0.69
(Interaction ² , p=0.02)	Sleep Deprived	none *	1500: 2.4 (0.1 to 4.8) km/h, p=0.04
PVT transformed lapses	Baseline	none	0700: 0.5 (-0.3 to 1.3) lapses, p=0.23
(Interaction ² , p=0.01)	Sleep Deprived	lapses greatest 1500	1500: 2.7 (1.5 to 3.9) lapses, p=0.00
POMS fatigue sub-score	Baseline	none	0700: 1.2 (-1.5 to 3.9), p=0.36
(Interaction ² , p=0.00)	Sleep Deprived	fatigue greatest 1100	1100: 8.7 (6.0 to 11.4), p=0.00
POMS vigour sub-score	Baseline	none	1900: 2.5 (-0.2 to 5.1), p=0.06
(Interaction ² , p=0.00)	Sleep Deprived	vigour least 0700	0700: 8.9 (6.2 to 11.5), p=0.00
PRM number correct (Interaction ² , p=0.55)	Both	none	0700: 0.5 (-0.2 to 1.1), p=0.18
DSST % correct (Interaction ² , p=0.42)	Both	none	1500: 0.6 (-0.3 to 1.5) %, p=0.21
DSST mean RT ⁴ (Interaction ² , p=0.27)	Both	none	0700: 0.01 (-0.002 to 0.16) sec, p=0.86
DSST response rate ⁴ (Interaction ² , p=0.30)	Both	none *	0700: 0.01 (-0.0005 to -0.17) sec/item, p=0.04 s

5.5.2 Effect of Obstructive Sleep Apnoea Status

Consistent with the effect of sleep deprivation on objective sleepiness (OSLER sleep latency) shown in table 28, sleep deprivation was also associated with increased subjective sleepiness (Stanford Sleepiness Score), compared with the non-sleep deprived state, in subjects with mild OSA (difference 1.3, 0.8 to 1.7, $p=0.00$) and subjects without OSA (difference 1.9, 1.5 to 2.3), $p=0.00$). However, the extent of increased subjective sleepiness due to sleep deprivation was less in those subjects with OSA than in those without OSA ($p=0.03$). This difference was not due to differences in initial sleepiness between the OSA and control groups (pairwise comparison of initial difference, $p=0.77$). This interaction suggests that the OSA subjects were less aware of their impairment due to sleep deprivation. The effect of sleep deprivation on all other daytime outcomes, except one described below, did not differ between subjects with OSA and controls. Similarly, there was no difference in the effect of daytime diurnal variation between subjects with mild OSA and subjects without OSA. Further, subjects with mild OSA did not show different driving performance and cognitive function compared with subjects without OSA.

5.5.3 Impact of Sleep Deprivation on Diurnal Variation Differed with OSA Status

For one outcome measure, PVT reaction time, mean fastest 10%, there was a significant three-way interaction. In other words, the effect of sleep deprivation on diurnal variation in reaction time differed between OSA subjects and controls ($P = 0.02$). Separate analyses for both subject groups (mild OSA subjects and those without OSA) showed that after sleep deprivation subjects with mild OSA had significantly poorer performance

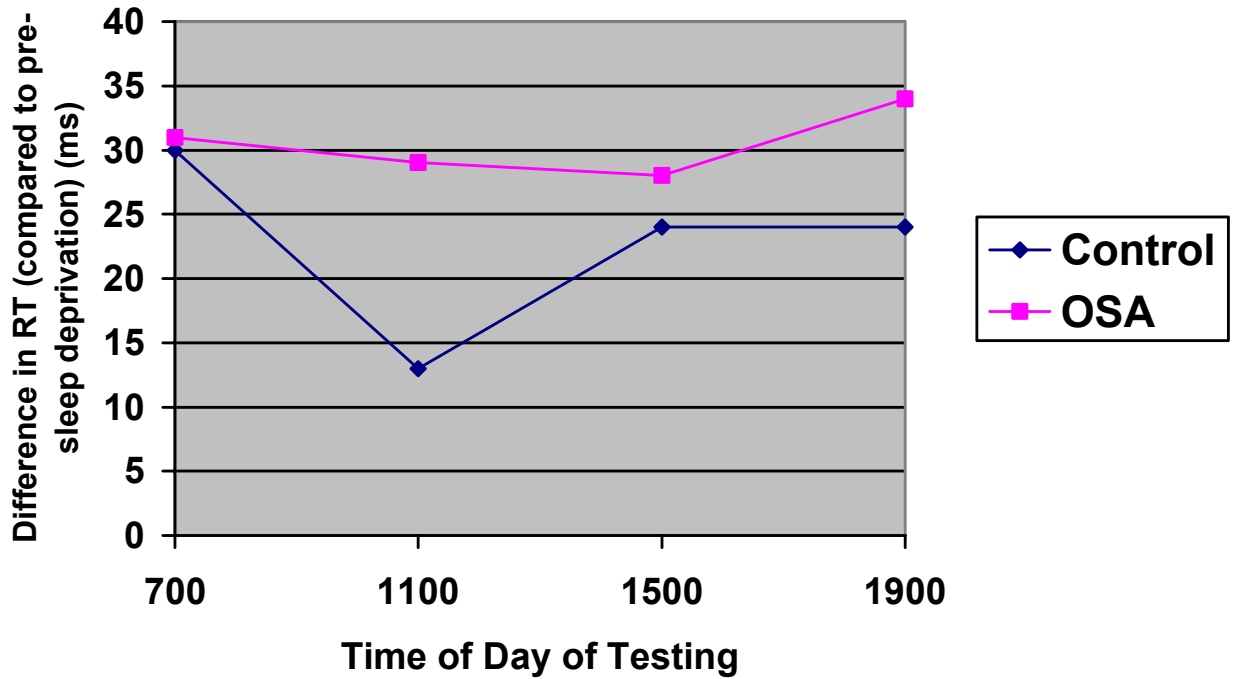
throughout the day and were worst at the end of the day (1900), whereas control subjects showed worst performance at 0700 with a transient relative improvement mid-morning (1100). See table and figure below.

Table 30 Impact of sleep deprivation on diurnal variation differed with OSA status

<i>Group</i>	<i>Intervention</i>	<i>Mean RT Difference from 1900¹</i>	<i>LCI</i>	<i>UCI</i>
Controls²	Sleep Deprived	0700: 30 ms	19	41
		1100: 13 ms	-1	27
		1500: 24 ms	6	41
		1900: 24 ms	6	41
OSA³	Sleep Deprived	0700: 31 ms	16	47
		1100: 29 ms	11	48
		1500:28 ms	5	50
		1900:34 ms	21	47

1. Differences are relative to pre-intervention time point, i.e. first 1900 evening testing session prior to sleep deprivation
2. Intervention by time interaction, $p = 0.01$
3. Intervention by time interaction, $p = 0.00$

Figure 21 Impact of sleep deprivation on diurnal variation differed with OSA status



5.6 Night Time Driving Performance and Cognitive Function Outcomes

5.6.1 Effect of Time of Day

For the analyses that included the night period after sleep deprivation, a time of day effect was again evident, with the worst performance most often seen at 1500. Maximal performance impairment was not seen at 0300 for any of the statistically significant outcomes (Table 31).

Table 31 includes effect estimates of time of day on all the outcomes. The mean difference in the outcome variable due to diurnal variation is presented in units of that variable with 95% confidence intervals. The difference presented is the maximal diurnal difference relative to the pre-intervention 1900 testing session. These effect estimates are

similar to the sleep deprived effect estimates in table 28. Minor differences arise due to a more complete data set for these later analyses (see Statistical Analysis section).

Table 31 legend

1. Age significant covariate
2. Interaction between time of day and OSA status ('Group')
3. Differences are relative to pre sleep deprivation time point, i.e. first 1900 evening testing session of the SD weekend
4. Average alcohol intake significant covariate
5. Whether a significant effect was present for time of day at that level of group; '*' with no overall significant effect of time of day, the significance of the maximal differences presented in the last column is questionable

Table 31 Effect of time of day on outcomes in the sleep deprived state (adjusted for OSA status)

<i>Dependent Variable</i>	<i>Group</i>	<i>Effect of Time of Day⁵</i>	<i>Maximal mean difference from 1900³ (95% CI)</i>
OSLER sleep latency Interaction ² , p=0.74	Both	sleep onset quickest 0700	0700: 966 (605 to 1327) secs, p=0.00
AusEd av RT ¹ Interaction ² , p=0.39	Both	none *	1500: 225 (125 to 326) ms, p=0.00
Aus Ed sd Av RT ¹ Interaction ² , p=0.30	Both	none *	1500: 188 (60 to 317) ms, p=0.01
AusED av Steer Dev from median position Interaction ² , p=0.54	Both	variability greatest 1500	1500: 21.0 (12.6 to 29.4) cm, p=0.00
AusEd sd Lane Position Interaction ² , p=0.66	Both	variability greatest 1500	1500: 29.2 (16.9 to 41.6) cm, p=0.00
AusEd av Speed Deviation Interaction ² , p=0.80	Both	none *	1500: 2.4 (0.2 to 4.7) km/h, p=0.04
SSS Interaction ² , p=0.98	Both	sleepiness greatest 1100	1100: 2.8 (2.3 to 3.2), p=0.00
PVT transformed lapses Interaction ² , p=0.50	Both	lapses greatest 1500	1500: 2.4 (1.4 to 3.5) lapses, p=0.00
PVT mean fast 10% Interaction ² , p=0.31	Both	reaction time slowest 0700	0700: 27.9 (20.3 to 35.4) ms, p=0.00
POMS Fatigue Interaction ² , p=0.92	Both	fatigue greatest 1900	1900: 8.6 (6.3 to 10.9), p=0.00
POMS Vigour ⁴ Interaction ² , p=0.50	Both	vigour least 0700	0700: 8.5 (6.3 to 10.7), p=0.00
PRM correct Interaction ² , p=0.57	Both	none *	1900: 0.8 (0.03 to 1.5), p=0.04
DSST % correct Interaction ² , p=0.50	Both	correct least 1500	1500: 1.1 (-0.01 to 2.2), p=0.06
DSST mean RT Interaction ² , p=0.62	Both	none *	1100: 0.1 (0.003 to 0.2) sec, p=0.01
DSST response rate Interaction ² , p=0.54	Both	none *	1100: 0.1 (0.003 to 0.2) sec/item, p=0.01

5.6.2 Effect of OSA Status

There was no difference in the effect of diurnal variation between subjects with mild OSA and subjects without OSA after sleep deprivation. Similarly, subjects with mild OSA did not show different driving performance and cognitive function compared with subjects without OSA after sleep deprivation.

5.7 Effect of Sleep Deprivation on Polysomnographic Measures on OSA

After sleep deprivation, subjects slept longer, had greater sleep efficiency and increased amounts of REM sleep (REM rebound). However, RDI, arousal index and the length of the longest apnoea were not different. The effect of sleep deprivation on minimum oxygen saturation differed according to OSA status. Subjects with OSA showed an even lower minimum oxygen saturation after sleep deprivation, whereas control subjects did not. See table below.

Table 32 Effect of sleep deprivation on PSG measures (adjusted for group)

<i>Variable</i>	<i>Group</i>	<i>Effect of Sleep Deprivation: mean difference (95% CI)</i>	<i>P</i>	<i>Interaction¹</i>
Total Sleep Time	both	longer sleep time: 53 min (15 to 91)	0.01	0.91
REM Sleep Time	both	longer REM sleep: 17 min (4 to 30)	0.01	0.40
Sleep Efficiency	both	greater sleep efficiency: 9% (6 to 13)	0.00	0.41
Total RDI	both	none: 1.0 (-1.9 to 3.8)	0.50	0.77
REM RDI	both	none: 1.2 (-3.7 to 6.0)	0.62	0.69
NREM RDI	both	none: 1.4 (-1.5 to 4.2)	0.33	0.58
Arousal Index	both	none: 2.2 (-0.8 to 5.3)	0.14	0.78
Longest Apnoea	both	none: 0.0 (-7.4 to 7.4)	1.0	0.87
Minimum O₂ Saturation	controls	none: 0.1 (-1.3 to 1.6)	0.85	0.03
	OSA	lower saturation: 2.5% (0.70 to 4.3)	0.01	

1. Interaction between sleep deprivation and OSA status ('Group')

Chapter 6: Results: Case Series

6.1 Cases

These cases represent consecutive referrals to the Sleep Disorders Centres at Royal Prince Alfred Hospital (n = 6) and Westmead Hospital (n=1), Sydney, for medico-legal opinions in fall asleep road accidents where the driver who caused the accident survived. Drivers were aged between 30 and 60 years at the time of their accidents. Five of the cases involved commercial drivers and two involved non-commercial drivers. For each case, police investigations did not identify the weather, road environment, or vehicle mechanics as significant contributors to the accidents. The contribution of alcohol was ruled out by breath or blood tests. Each subject underwent detailed sleep investigations to identify sleep disorders that might have contributed to the fall-asleep road accident. In all cases, the driver had at least one overnight sleep study. In six of the seven cases, an objective measurement of daytime sleepiness was also performed. See table 33 below.

Case A: under-treated OSA and undiagnosed Periodic Limb Movement Disorder

In this first case, A's truck ran into the back of a stationary car, killing that vehicle's driver, and injuring two others. A reported drifting off to sleep at the time of the accident. Several years before this accident, A was diagnosed with severe OSA and commenced on continuous positive airway pressure (CPAP), but was not regularly followed up. A's subjective compliance with CPAP was good, but despite this, A remained sleepy, to the extent that, A's spouse would frequently share any long distance driving. Following A's fall asleep accident, A had further sleep studies which showed under-treated OSA

(residual respiratory events on CPAP), and in addition, a new sleep disorder (Periodic Limb Movement Disorder), which was also fragmenting A's sleep. A MWT verified that A had residual severe daytime sleepiness. A's legal case was not billed (i.e. was not prosecuted) and A remained licensed to drive.

Case B: undiagnosed mild OSA and upper airway resistance syndrome

Case B was involved in a fatal road accident where B's car veered to the other side of the road, colliding with an oncoming vehicle, killing that vehicle's driver and seriously injuring the passenger. B has no recollection of the period immediately preceding the accident and there was no evidence of any aversive action taken. B reported 8 hours sleep the night prior to the accident, and 5 ½ hours sleep 2 nights prior. Clinical evaluation after the accident noted that B infrequently snored, was sleepy during the day, and was obese. B's diagnostic sleep study showed an AI of 40 per hour. The arousals were partly due to OSA events (AHI 10 per hour), but mostly due to other more subtle obstructive events that did not reach the full scoring criteria for OSA (upper airway resistance syndrome) (Guilleminault C. *et al.* 2001). An MSLT confirmed pathological daytime sleepiness. B's legal case was not billed and B remained licensed to drive.

Case C: "sleep attack" in a private driver

In case C, C's vehicle veered across the road into the path of an oncoming vehicle, killing multiple occupants in that vehicle. C reported to have fallen asleep suddenly at the time of the accident. C also reported being "slightly sleep deprived" in the preceding week, but did not recall being drowsy prior to the accident occurring. C's history did not suggest an

untreated sleep disorder or a problem with chronic excessive daytime sleepiness (EDS). After the accident, two overnight sleep studies and an objective test of daytime sleepiness have failed to show any abnormalities. In the absence of any other medical explanation, legal counsel argued that cumulative sleep debt from inadequate sleep hours over the preceding week could have caused C's "sleep attack". C was acquitted by a judge and contested his license suspension by the Roads and Traffic Authority.

Case D: undiagnosed OSA in a truck driver

Case D was involved in an accident where D's truck collided with, and over-rode a car, which was stopped in a line of traffic, killing two people and damaging five cars. There was no evidence of braking prior to the accident. Two witnesses at the time noted D to be leaning and apparently looking to the left at the time of the accident. Medical assessment after the accident revealed a long history of snoring, witnessed nocturnal apnoeas, and an easy ability to doze when inactive. In addition, D recalls sleeping six hours the night prior to the accident. Subsequent sleep studies have shown D to have untreated severe OSA with an RDI of 30 per hour. Daytime sleepiness was also objectively confirmed with a MWT. D was subsequently found guilty of culpable driving and was sentenced to a prison term. D still remained licensed to drive immediately after the accident.

Case E: undiagnosed idiopathic hypersomnolence in a truck driver

Case E caused a five vehicle, one fatality accident by failing to stop on approaching a line of traffic in a road work zone. E's accident occurred in the evening towards the end of a 16 hour working day. Just prior to E's accident, E had rested and had dinner at home. On

subsequent medical questioning, E reported being excessively sleepy since childhood, more so than peers. E even felt that the inability to stay awake during class had impaired education. When E later took up work as a truck driver, E noted that, compared to other truck drivers, E needed to pull over to the side of the road more than average to nap. On one occasion, E had even fallen asleep driving, but fortunately no accident had ensued. E's overnight sleep study did not show a sleep disorder, but a MWT confirmed an inability to stay awake. E's objectively confirmed long standing EDS, together with negative polysomnography, suggests a diagnosis of idiopathic hypersomnolence. After the accident, E pleaded guilty to culpable driving. E still remained licensed to drive immediately after the accident.

Case F: undiagnosed OSA in a truck driver

F's semi-trailer collided into the back of a stationary car, which was stopped at traffic lights, killing two people. F has no recollection of the period prior to this accident. F gave a long history of sleep talking and occasional sleep walking. However, in the two years immediately before this accident, F's spouse had also become aware of worsened snoring and apnoeas during F's sleep. During this time, F described a problem with EDS, including a habit of frequently taking pseudoephedrine while driving. An overnight polysomnogram was performed on F after the accident. This showed moderate OSA with an AHI of 23 per hour. F's daytime sleepiness was also objectively confirmed. F's urine was found to be positive for amphetamines on testing at the time of the accident. F pleaded guilty to the culpable driving offence and was jailed. F remained licensed to drive immediately after the accident.

Case G: untreated OSA in a truck driver

In this last case, G's truck veered into the side lane on a major freeway after G fell asleep, killing a cyclist. G's accident occurred in the morning, after G had driven interstate overnight. Importantly, G had been diagnosed with OSA several months prior to this accident and had ignored medical advice to undergo further management. During G's initial medical assessment prior to the accident, G described a history of almost dozing off while driving on a few occasions, in addition to other symptoms of OSA. G's subsequent diagnostic sleep study showed moderate OSA with an AHI of 17 per hour. G failed to return for a follow up appointment to discuss these results, even when reminded to do so by letter. G then went on to have the fall-asleep road accident several months later. Recently, a judge has jailed G for 3 years and withdrawn G's driving license for 5 years.

Table 33 Case details of fall asleep road fatalities

1. Arousal Index (AI): normal range, 0-10/hour
2. Respiratory Disturbance Index (RDI), Apnoea-Hypopnoea Index (AHI): normal range, 0-5/hour
3. Periodic Limb Movement Index (PLMI): normal range, 0-5/hour
4. Maintenance of Wakefulness Test (MWT), 20 minute protocol, sleep onset as the first occurrence of one epoch of any stage of sleep: normal range, 11-20 min
5. Multiple Sleep Latency Test (MSLT): normal range, 10-20 min
6. Maintenance of Wakefulness Test (MWT), 40 minute protocol, sleep onset defined as three consecutive epochs of stage 1 sleep or any single epoch of another sleep stage: normal range, 19-40 minutes.

<i>Case (Diagnosis)</i>	<i>Driver Type</i>	<i>Overnight Sleep Study</i>	<i>MSLT or MWT</i>	<i>Accident Outcome</i>	<i>Legal Outcome</i>	<i>Remained Licensed?</i>
case A (OSA & PLMD)	truck	CPAP review AI ¹ 30 (RDI ² 10; PLMI ³ 20)	MWT ⁴ SL 4.75 min	2 vehicle 1 fatality 2 others injured	no billed	yes
case B (OSA & UARS)	private	diagnostic AI ¹ 41 (AHI ² 10)	MSLT ⁵ SL 9.4 min	2 vehicle 1 fatality 2 others injured	no billed	yes
case C (sleep deprivation)	private	diagnostic RDI ² 2.4, RDI ² 1	MWT ⁶ SL 40 min	4 vehicle 5 fatalities several others injured	acquitted by judge	yes. Later withdrawn by RTA and then contested in court
case D (OSA)	truck	diagnostic RDI ² 30	MWT ⁶ SL 11 min	6 vehicle 2 fatalities 12 others injured	found guilty; jailed	yes
case E (idiopathic hypersomnolence)	truck	diagnostic RDI ² 0.4	MWT ⁴ : SL 8 min	5 vehicle 1 fatality 2 others injured	pleaded guilty	yes
case F (OSA)	truck	diagnostic AHI ² 23	MSLT ⁵ SL 5.5 min	3 vehicle 2 fatalities	pleaded guilty; jailed	yes
case G (OSA)	truck	diagnostic AHI ² 17	not performed	2 vehicles, 1 fatality	found guilty; jailed	Yes. Later withdrawn by Judge

Chapter 7: Discussion

7.1 Commercial Drivers Study

This study was designed to gather in a systematic and scientific way important information about obstructive sleep apnoea in commercial drivers. The impetus for the research was the escalating medical evidence published in the mid to late 1990's, which showed the important role of obstructive sleep apnoea in driver fatigue and road accidents in private drivers, and the hypothesis that commercial drivers would be equally, if not more severely, affected by this medical illness and its road safety consequences. Primarily, the study was designed to determine the prevalence of obstructive sleep apnoea and excessive daytime sleepiness in commercial drivers, and to identify the relationship between OSA and driving. The study involved recruiting two groups of commercial drivers, with the drivers studied in the sleep laboratory undergoing much more detailed testing, including a full overnight sleep study and driving simulator testing.

The response rate for the drivers surveyed in the field was excellent (83%), suggesting that this data was quite representative of the transport drivers in the truck yards and truck stops. However, as only transport drivers who had at least 10 minutes available (time taken to complete the questionnaire) were asked if they would like to participate, this high response rate needs to be interpreted with a little caution. The response rate for the drivers who underwent sleep investigations was lower (58%), but given the much more intensive protocol involved, this was expected. In fact, most of the drivers who declined involvement in this part of the study did so because of the time commitment involved.

Non-participants did not differ from the participants in age or body mass index (table 3), both of which have been shown to be important predictors of OSA (Bearpark *et al.* 1995). The two cohorts of drivers consisted essentially of men, who were middle-aged and overweight (table 2). As discussed in the background section, all three of these characteristics are frequently seen in association with OSA, heralding the high OSA prevalence figures that were subsequently found in both cohorts.

The two groups of drivers did differ in some respects, despite an attempt to obtain a random sample of drivers for both groups. The drivers studied in the sleep laboratory were older, and reported more medical illnesses. This most likely represents a selection bias, with drivers that are older and medically unwell being more likely to volunteer themselves for detailed sleep investigations because of existing concern about their health. The drivers studied in the sleep laboratory also reported more metropolitan driving, while those surveyed in the field performed more interstate and long distance driving. This difference in the groups probably represents two biases. Firstly, since the sleep laboratory investigations were performed in Sydney, those drivers driving and living locally (metropolitan drivers) were more likely to find this part of the study convenient and accessible and hence volunteer to be studied. Secondly, because many drivers from the field study were surveyed at truck stops, which tend to be located on major freeways, this form of recruitment would be expected to pick up more interstate and long distance drivers. This difference in the groups is also reflected in the data showing that the drivers surveyed in the field drove more kilometres per year, worked and drove more hours per week, and on average reported a greater longest work shift.

Of note is the observation that the drivers from both cohorts slept on average just over six hours per day while at work. This suggests that those drivers without OSA are experiencing inadequate sleep on a chronic basis and that those drivers with OSA are being further compromised by sleep deprivation on top of their already broken sleep from OSA. Both groups reported high levels of caffeine use and illicit drug use while driving. This is of concern, because these countermeasures may have limited value and may be ineffective if both sleep loss and sleep apnoea are present. Further, treating daytime sleepiness in transport drivers with alerting agents is inappropriate, as this strategy fails to deal with the underlying causes of their sleepiness, such as sleep deprivation and obstructive sleep apnoea.

The drivers in this study reported an accident rate of 0.12 (field drivers) and 0.24 (laboratory drivers) accidents per year per 100,000 km driven. Maycock and co-workers have reported on accident rates in transport drivers in the UK (Maycock 1997). Their data was collected in a similar way, as it was based on a driver's self-report of motor vehicle accidents in the preceding three year period. All of these drivers had been sampled at motorway service stations (n = 996). Using this similar methodology, they found an accident rate of 0.09 accidents per year (mean annual mileage was 69,700). Stoohs et al used both self reported and company recorded data from the prior five years to measure accident rates in US transport drivers passing through the main hub of a long-haul trucking company (Stoohs *et al.* 1994a). Their results suggest an accident rate of 0.13 per year per 100,000 km driven. The accident rate reported in this study for the group of drivers surveyed in the field (0.12) appears in line with the above estimates from the UK

and USA. However, there are several reasons why this accident data needs to be interpreted with caution. Firstly, these accidents were self-reported and hence subject to recall bias. Secondly, there is likely to be some stigma associated with the self-reporting of motor vehicle accidents for transport drivers and this may have contributed to them being under-reported in this study. Finally, one study has also shown that drivers with OSA under-report accidents or driving impairment prior to CPAP treatment (Engleman H *et al.* 1997a). In this study, 25% of initial deniers retrospectively admitted compromised driving ability after they had been treated with CPAP. This potential measurement error in the estimation of accident rates, affects not only the overall estimate of accident rates, but also the validity of the identification of predictors of accidents.

A major finding of this study is a high prevalence of OSA in NSW transport drivers. This has been shown on the basis of a questionnaire diagnosis in a very large sample of randomly surveyed transport drivers, and also by objective testing, in a smaller subset of randomly selected drivers, who have had full overnight sleep studies in a sleep laboratory, the gold standard for diagnosis of OSA.

The prevalence of OSA in the field was found to be 41%. This was estimated using the Maislin equation, a validated screening tool (Maislin *et al.* 1995), which can be used to predict the likelihood of having OSA, based on the subjects reported symptoms of OSA, their sex, age and body mass index. The Maislin score predicts the likelihood of having OSA at a severity level of at least 10 apnoeas/hour ($RDI \geq 10/hr$). The Maislin was also 're-validated' in this population of transport drivers and the threshold score that was used

in the analyses compared very favorably to the optimal threshold suggested by the Maislin's ROC curve.

For the group of drivers studied in the sleep laboratory, the prevalence of OSA ($RDI \geq 10/hr$) using the sleep study data was 51%, whereas the prevalence using the Maislin was 60%. Both estimates for OSA prevalence are very high, but from an accuracy point of view, it is reassuring that, despite the different measurement techniques (including inherent differences in respiratory scoring definitions for hypopnoeas and apnoeas), the difference in OSA prevalence between the two measurement methods was relatively small. However, there was a more obvious difference in the prevalence of OSA between the two different cohorts of drivers studied, with the drivers studied in the sleep laboratory showing a generally higher prevalence than those surveyed in the field. This most likely represents a selection bias in the drivers studied in the sleep laboratory. Drivers who were concerned about sleep apnoea symptoms, such as snoring or poor sleep, were perhaps more likely to volunteer themselves for the intensive laboratory protocol in the hope of obtaining a diagnosis for their symptoms or perhaps medical advice on further management. Regardless of which prevalence figure is examined, these values are considerably higher than the general population prevalence of OSA for middle-aged men (10% to 15% for $RDI \geq 10/hr$). Prevalence values of 40% to 50% for transport drivers are in line with the prevalence figures previously reported by Stoohs et al (Stoohs *et al.* 1995b) for professional truck drivers in the USA (46% for a similar RDI level) and Hui et al (Hui *et al.* 2002) for commercial bus drivers in Hong Kong (41% had an RDI of at least 10/hr). However, all these values are well above the commercial driver

prevalence figures recently reported in abstract form by Pack et al (Pack *et al.* 2000a) and Diaz et al (Diaz *et al.* 2001). This study differs from those by Stoohs et al and Hui et al in that full overnight sleep studies were used together with a very large questionnaire sample to define OSA prevalence, and from the study by Pack et al because of a much higher response rate and a larger sample of long distance drivers. Further, drivers in this study were randomly selected, an important methodological advantage compared to several of the earlier studies. Clearly this study adds critical and accurate information about the prevalence of OSA in transport drivers to the current literature.

Approximately a quarter of both driver groups reported excessive daytime sleepiness. Previously, the conventional view has been that long work hours and time of day of driving are the dominant causes of fatigue and sleepiness in commercial drivers (Arnold *et al.* 1997;Neville 2000;Williamson *et al.* 1992). However, in the present study, a diagnosis of OSA was the most important factor predicting pathological daytime sleepiness (odds ratio 2.9, $p < 0.05$): OSA (measured by the Maislin questionnaire) was more important than 15 other work-related, lifestyle and medical factors that could be expected to promote, or be associated with, daytime sleepiness.

A few studies have previously found that OSA may be a determinant of driver sleepiness in commercial drivers. In one study, which examined factors associated with falling asleep at the wheel in a sample of 600 truck drivers, symptoms of a sleep disorder (higher body weight, snoring, breathing stopping during sleep, and self-reported poor sleep at home) were one of six variables found to be significant predictors of a driver ever having

fallen asleep at the wheel (odds ratio 1.39, $p < 0.01$) (McCartt *et al.* 2000). Other predictors included more arduous work schedules (odds ratio 1.80, $p < 0.01$), shorter, poorer sleep on the road (odds ratio 1.43, $p < 0.01$), and greater tendency to night time drowsy driving (odds ratio 1.44, $p < 0.01$). In another study, work related factors, such as shift length and shift type, individual factors, such as driver age and experience, and symptoms of sleep apnoea syndrome (snoring, respiratory disturbances, Epworth score) all significantly predicted self-reported difficulties in staying alert while driving, dozing off at the wheel and near misses in commercial drivers (Hakkanen and Summala 2000). However, in this study, each of these three factors predicted only a minority of the driver sleepiness-related problems (in all cases, $R^2 < 10\%$). Finally, in a study of 1000 UK heavy goods vehicle drivers, drivers who reported snoring every night, or who were obese, or who had a large collar size, also suffered from higher levels of daytime sleepiness (Epworth score) (Maycock 1997).

Many of the other fatigue promoting factors (such as sleep deprivation and night driving in transport drivers) that were examined in this study as predictors of excessive driver sleepiness alongside OSA, are known to be associated with increased motor vehicle accident rates. There is no clear reason why OSA in transport drivers should prove to have less impact on accident rates than these other comparable fatigue promoting factors. However, there is very little published literature (section 1.2.3.5) that examines this specific issue. One study, often quoted, reported that accident rates (self reported and company recorded) in community sampled truck drivers with OSA were double of those who did not have OSA (Stoohs *et al.* 1994a). However, this difference was not

statistically significant. The data from this study has not shown an increased motor vehicle accident rate in transport drivers with OSA or sleep apnoea syndrome. This is perhaps not unexpected as the accident data may be potentially flawed for the reasons discussed above.

Nonetheless, this study has shown that those drivers with sleep apnoea syndrome (both OSA and pathological daytime sleepiness) do have an increased driving accident risk, using driving simulator and PVT performance as proxy measures for accident risk. This group of drivers showed poorer reaction time performance, poorer steering performance and an increased number of crashes on a driving simulator task, and poorer reaction time performance on a vigilance task (PVT). Importantly, these abnormalities were generally not present when drivers with OSA alone or sleepiness alone were assessed. This finding that a specific sub-group of transport drivers with OSA do have an increased driving accident risk, using these proxy measures and in particular a PC based driving simulator task, is novel and represents an important discovery in driver fatigue research. Specifically, it suggests which commercial drivers with OSA are at most driving accident risk. Twelve to fourteen percent of drivers had sleep apnoea syndrome in this study. Resources should now be focused on identifying through screening this particular high risk group of NSW drivers, treating their sleep apnoea and hence potentially reducing road accident risk. Apart from the road safety reasons, there are also of course other major medical health and quality of life benefits to be gained from treating these patients. Only one other study, reported in abstract form, has examined predictors of impaired driving ability (PVT, driving simulator) in transport drivers with OSA. This has found

that an increasing RDI was associated with greater impairment on these performance tests (Dinges *et al.* 1998).

This study failed to show a statistically increased motor accident risk for the whole group of drivers with OSA. This however, as discussed in the background section, has been shown for private drivers in many studies. This study was limited in this respect by self-reporting of motor vehicle accidents and by proxy measures of accident risk in a sample of only 60. A more robust study, incorporating objective accident records (e.g., from government, company or insurance databases) in a larger sample of transport drivers, would be important to extend this current research. Other ways of extending this research to more accurately define accident rates due to OSA in this population could be to prospectively follow a cohort of drivers, measuring OSA and actual accidents, or alternatively, to launch a pilot screening and treatment program for OSA to see whether accidents and performance can be improved.

7.2 Mild Obstructive Sleep Apnoea Study

This study primarily sought to examine the added effect of other fatigue promoting factors (sleep deprivation and time of day) on driving performance and cognitive function in mild OSA patients. The results for the most part suggest that this group of drivers with mild OSA were not different to the control group in their response to sleep deprivation or time of day influences. Consistent with previous literature, there were clear effects of sleep deprivation and time of day in all subjects. However, the subjects with mild OSA were less aware of their impairment due to sleep deprivation and in one reaction time task showed greater impairment than controls at certain times of the day after sleep deprivation. These latter results, together with the limitations of this study that are discussed below, suggest that more research is needed in this area before firm conclusions can be made.

The group of subjects with OSA was clearly different in their OSA status from the control group. Table 27 shows that the baseline polysomnography categorised the OSA subjects to be in the mild range of OSA severity, and the controls to have lesser sleep disordered breathing. Consistent with the difference in OSA status between the groups are the results of table 23, which show the OSA subjects to have the expected demographic and physical characteristics associated with this disease; the OSA group tended to be older (though this difference was not statistically significant), and had an increased BMI and neck circumference, compared with the controls. However, table 26 shows that neither group reported excessive daytime sleepiness, as measured by the Epworth Sleepiness Scale. Hence the study subjects with OSA are more representative of

those patients with obstructive sleep apnoea alone (snoring, nocturnal apnoeas, obstructive respiratory events on polysomnography), rather than those with “sleep apnoea syndrome” (clinical combination of OSA *and* excessive daytime sleepiness; see section 1.2.3.1). The implications that this may have had for the study outcomes are discussed in more detail later.

An attempt was made in this study to control for factors outside the study that might affect performance on the testing weekends. All subjects completed a sleep diary and wore actigraphs for four nights prior to their hospital presentations, so that sleep hours or sleep deprivation in the days prior to testing could be controlled for. Table 25 shows that there was no statistical difference in the amount of sleep the subjects had prior to their two testing weekends. Hence, differences in performance between the two testing weekends would not be expected to be explained by differences in sleep debt from the days immediately prior to the subjects’ laboratory admissions. Similarly, caffeine intake on the day of laboratory admission was not different between the two testing weekends. These two variables, together with age, average caffeine intake, and average alcohol intake were also tested as covariates in the analyses and retained where they were significant predictors of the outcome variable.

Table 24 shows the actual recorded sleep that the subjects obtained prior to the two testing weekends. There was no statistically significant difference between the two study groups. Hence, differences in prior sleep debt would not be expected to explain any differences between the two groups during the testing weekends. However, it can be seen

that both groups of subjects obtained less than the ideal average amount of sleep (approximately eight hours per night), consistent with the notion that many individuals in society are chronically and partially sleep deprived (see section 1.2.1.3).

This study found that sleep deprivation resulted in poorer driving and cognitive performance for most of the outcome measures. There was some variation in the effects of sleep deprivation according to the time of day, with the most consistent effect being at three pm, coinciding with the expected circadian drop in performance. Impairments due to sleep deprivation were seen for tests of driving ability (AusEd™ reaction time, steering and speed outcomes), vigilance (PVT lapses), sleepiness (both subjective and objective), and mood (POMS fatigue and vigour sub-scores). However, there was no effect of sleep deprivation on the DSST, a test of attention, or the PRM test, a test of memory.

This study found that time of day influenced performance. For some outcomes, this diurnal effect differed according to whether the subject was sleep deprived or not. However, for other outcomes it was evident with or without sleep deprivation. The worst daytime performance was most often seen at three pm, which is consistent with known circadian effects on performance. However, there was no maximal circadian effect at three am for any of the variables in this study, perhaps due to the fact that subjects had been less sleep deprived at this time point compared with three pm, where the maximal effect was most often seen.

This study found that OSA status influenced the outcome of two variables (Stanford Sleepiness Score and PVT reaction time, mean fastest 10%). Although there is a risk of Type 1 error in the interpretation of these significant results, an attempt was made to minimise this by limiting the analysis of all the outcome variables to only those that were considered most relevant to the study objectives. For the Stanford Sleepiness Score, a measure of subjective sleepiness, the extent of increased subjective sleepiness due to sleep deprivation was less in those subjects with OSA than in those without OSA ($p=0.03$). Given the consistent effect of sleep deprivation on most of the objective outcome measures, where there was no difference between the two groups, this apparently paradoxical result is very important. This is because it suggests that the OSA subjects were less aware of their impairment due to sleep deprivation. This is particularly important if individuals are relying on their degree of subjective sleepiness to make decisions about stopping driving when fatigued. For the outcome measure, PVT reaction time mean fastest 10%, there was a significant three-way interaction. In other words, the effect of sleep deprivation on diurnal variation in reaction time differed between OSA subjects and controls ($P = 0.02$). Further analyses showed that subjects with mild OSA had poorer performance throughout the day, whereas control subjects showed a transient relative improvement mid-morning. This suggests that OSA subjects when sleep deprived may be less affected by circadian improvements in performance for some tasks, compared to controls. Although this study did not show any other differences or interactions for daytime or night time performance outcomes between the OSA and control groups, the effect of OSA status on the above two outcomes within the study limitations that are discussed below, suggests that more work is still needed in this area

before definite conclusions can be made. Such work should also focus on the additive or interactive effects of chronic partial sleep deprivation, as opposed to acute total sleep deprivation, on performance in OSA subjects.

A separate aim of this study was to determine the effect of sleep deprivation on polysomnographic measures of OSA (see table 32). Sleep deprivation was found to significantly increase total sleep time, sleep efficiency and REM sleep time. Because the order of the testing weekends was balanced, with approximately half of the subjects of each group (mild OSA and controls) tested under baseline conditions as their first weekend of testing, and approximately half of the subjects tested under sleep deprivation conditions as their first weekend of testing, these differences in polysomnographic outcomes due to sleep deprivation could not be due to 'first night effects' (subjects sleeping worse on their first weekend of testing because of unfamiliarity). Subjects did not show a different RDI, arousal index or length of the longest apnoea after sleep deprivation. However, subjects with OSA showed an even lower minimum oxygen saturation after sleep deprivation. A reduction in minimum oxygen saturation in OSA patients after sleep deprivation has been noted previously, but others have also found significant worsening of additional OSA parameters after sleep deprivation (e.g., RDI, see section 1.3.2). Given the relatively mild disease of the OSA patients and the small numbers in this study, it is possible that night to night variability in polysomnography blunted some of the potential differences due to sleep deprivation.

This study found that OSA status influenced the outcome of only two variables. One reason why there was little difference between the subjects with mild OSA and the control subjects in driving performance and cognitive function may be lack of sleepiness in the mild OSA group. With minimal daytime symptoms, this group of mild OSA subjects may behave differently to other mild OSA subjects that do report daytime sleepiness (i.e. those with sleep apnoea syndrome); it is possible that daytime sleepiness needs to be present for there also to be impaired cognitive or driving performance in mild OSA subjects. However, as discussed in section 1.2.3.10 above, no studies have yet been able to clearly demonstrate that daytime sleepiness predicts accident risk or driving impairment in subjects with OSA. Further research is urgently needed into predictors of accident risk or driving impairment in OSA drivers, particularly for the mild OSA group. Similar research to this, but studying drivers with mild OSA who have significant daytime sleepiness would be part of such a research agenda.

Another selection bias, which may also partially explain why the mild OSA group was not different in most outcomes compared with the control group, may have occurred because of the way in which the control group was recruited. Part of the control group was recruited from patients presenting to sleep clinics for assessment or from patients who had had negative laboratory sleep studies. All these patients therefore had initially presented with a sleep disturbance to a physician, and were therefore unlikely to be totally disease free with respect to sleep abnormalities. Even the presence of simple snoring or a minimal amount of OSA in the control group, may have blunted the differences that this study might be expected to show between the OSA and “control”

groups. In fact a careful inspection of the baseline polysomnography for the control group (table 27) shows that, although their total RDI was < 5 , their mean REM RDI was 7.9, with a 95% confidence interval of 1.4 to 14.5. The significance of mild REM OSA on its own is uncertain, but it is possible that this has biased the control population against finding a difference between the two study groups. A more ideal control group for this study would consist of subjects with absolutely no sleep disordered breathing (no snoring, total RDI < 5 , REM RDI < 5 , NREM RDI < 5 , oxygen saturation $> 95\%$, arousal index < 10). Such a cohort however would be very hard to find without screening many individuals, as few would qualify, and would also probably include mainly young males, who may not have appropriate driving experience for this kind of research. In addition, because of night-to-night variability in polysomnography results, each potential subject identified in this way would need at least two overnight sleep studies to ensure that they were truly free of sleep disordered breathing.

7.3 Medico-Legal Case Series

This case series describes seven recent medico-legal cases associated with road fatalities on NSW roads since 1995. In each case, the driver who caused the accident suffered from an unrecognised or under-treated sleep disorder. The nature of many of the accidents suggests inattention, with the vehicles crashing into the back of other stationary cars or veering to the other side of the road, while showing little or no preventative action (e.g., braking). The inattention of each of the drivers could have other causes besides the driver having fallen asleep. Neurological clinical assessment and/or further neurological tests did not suggest neurological causes for any of the accidents. When taken together with the results of the driver's clinical history and sleep investigations, each episode of inattention was probably a consequence of sleep or sleepiness. Although untreated sleep disorders could explain these possible episodes of sleep, inappropriate work and sleep schedules may also have compounded driver sleepiness in some of the cases, especially those involving commercial drivers.

The outcomes in these cases were variable in that some of the drivers have been acquitted and other drivers have been jailed. Almost all the drivers remain licensed, even when they successfully used the defence that their accident was caused by a sudden unexpected period of sleep. The cases highlight important medico-legal aspects of driver fatigue, in particular, some of the apparent inconsistencies and difficulties in this area.

It is important to first note the variability in the legal outcomes of some of the cases, despite comparable circumstances. For instance, Case A had a known diagnosis of OSA,

continued to drive while sleepy, and was not billed, whereas Case G also had a known diagnosis of OSA, continued to drive while sleepy, but was jailed. As a second example, the legal outcome of Case B contrasts with that of Case D. Case B had undiagnosed OSA, and a history of excessive daytime sleepiness, yet was not billed, whereas Case D also suffered from undiagnosed OSA but denied an awareness of excessive daytime sleepiness. D in turn was found guilty and jailed. One of the potential reasons for these apparent judicial inconsistencies could relate to current medical difficulties in apportioning blame to OSA in fall asleep road accidents. While drivers with OSA *as a group* show increased sleepiness and driving accident risk, some *individuals* with OSA may in fact be safe drivers (George CF *et al.* 1996). However, there are currently no definite clinical markers or laboratory tests that can identify those drivers with OSA that have the most or least accident risk (see section 1.2.3.10). Another reason for the apparent judicial inconsistencies, may relate to an individual's awareness of their medical illness. It has been held that a person is not liable if they are not aware of their illness (Britts 1998), that is, if their incapacity comes upon them unexpectedly. Many individuals with OSA, including some of the cases presented, are unaware of their diagnosis. However, while an individual with a sleep disorder may not be aware of their specific diagnosis, they may be very aware of their symptom of excessive daytime sleepiness. The majority of the people involved in these cases had prior knowledge of their excessive sleepiness.

The legal proceedings for Cases A, B, and C all took into consideration the *Jiminez* defence, the basis of which is the issue of lack of foreseeability (Commonwealth Law

Reports 1992). In these cases, the claim was that they had no warning that they were going to fall asleep. As discussed in section 1.2.3.8.1, the argument that sleep can occur without warning is very controversial. The Canadian and English courts maintain that, regardless of the circumstances, the ordinary person who allows themselves to fall asleep at the wheel is liable for their actions. These judgements are predicated on the “prior fault” principle (McCutcheon JP 1997) that there was a period of time prior to being asleep, of voluntary conduct when a person chose to take the risk of continuing to drive. This is consistent with medical evidence which suggests that *healthy* people do not fall asleep without significant symptoms of sleepiness for some period of time (Atzram *et al.* 2001;Lisper HO *et al.* 1986;Reyner and Horne 1998). Similar evidence looking at an individual’s perception of sleepiness prior to sleep onset is now needed for other groups, especially for those with OSA.

The fact that individuals have been allowed to continue driving until after their trials seems illogical and dangerous. Whether or not an individual can later escape liability on the basis of a *Jiminez* defence does not remove the implication that they may be unsafe in medical terms to drive (immediately following the accident). Further, if they do later successfully use the Jiminez defence, should they ever be allowed to drive again? The NSW RTA has recently tried to address this apparent licensing inconsistency. An amendment to the NSW Road Transport (Driving Licensing) Regulation 1999 (1999), enacted in 2001, has effectively removed some of the legal constraints on license suspension which had previously handicapped the NSW RTA in managing fall asleep MVA’s. The new regulation gives the RTA explicit power to suspend a license

immediately where the driver has fallen asleep or has lost consciousness and caused death or injury. This can occur regardless of whether the person has been prosecuted for an offence. The courts will only allow an appeal if the person can demonstrate that the individual is medically fit to have their license renewed.

Health practitioners have a duty of care to their patients to provide treatment at the prevailing, acceptable standard. The Australasian Sleep Association guidelines (Australian Sleep Association 2002) recommend that health professionals should refer patients with suspected sleep apnoea to a sleep specialist for assessment and further investigation. These guidelines go on to advise periodic review of drivers with OSA to ensure that adequate treatment is maintained. However, the extent to which a practitioner needs to ensure follow up, and how much responsibility for this the patient must also bear is unclear. In this case series, Case A who was a truck driver, was not followed up by the practitioner to ensure that they no longer posed a significant risk to the public. However, at the same time, A did not follow up the fact that there was persisting sleepiness despite CPAP. In contrast to Case A, the practitioner tried to encourage Case G to have treatment for OSA, but G did not attend follow up appointments and continued to drive.

Legislators, medical and road safety specialists must recognise the change in knowledge in this area and help to clarify the important medico-legal issues. In particular, the Jiminez defence, which is at odds with legal opinion in other countries and current medical evidence, should be challenged. At the same time, more research is needed to further delineate the relationship between the symptoms of sleepiness and falling asleep

(especially for certain at risk groups, such as drivers with OSA), and in trying to identify driver characteristics or tools which predict which drivers with OSA are at most risk of road accidents. Regulation of early assessment and treatment and automatic suspension of licenses until drivers are medically fit to drive are important steps forward in ensuring the safety of individuals and the rest of the community.

7.4 Final Summary and Implications

This body of work has investigated the area of obstructive sleep apnoea and driver fatigue in several ways. The Commercial Drivers Study is a large epidemiological study, which has clearly shown a high prevalence of OSA in commercial drivers, a strong association between OSA and driver sleepiness, and an increased driving accident risk in those commercial drivers with both OSA and daytime sleepiness (sleep apnoea syndrome). The Mild Obstructive Sleep Apnoea Study went on further to explore the interaction between mild OSA, the commonest form of OSA, and other driver fatigue risk factors (sleep deprivation and time of day). This study for the most part suggested that drivers with mild OSA were not different to the control group in their response to sleep deprivation or time of day influences. However, the subjects with mild OSA did show important differences to the control group in two outcome measures, suggesting that the additive effects of OSA and other fatigue risk factors need to be further investigated with more research. This would be particularly important for the commercial driver population, who are often exposed to many fatigue promoting factors, apart from OSA. The case series has demonstrated the day to day potential for devastating road accidents due, at least in part, to un-recognised or untreated sleep disorders. In addition, some of the current medico-legal controversies and difficulties in this area have been discussed.

Two findings from this body of work deserve special emphasis. Firstly, the finding that OSA was the most important predictor of excessive daytime sleepiness in commercial drivers. OSA was shown to be a more important contributor to pathological driver sleepiness than many other commonly recognised causes, such as work hours, sleep hours

and time of day influences. This is important as current fatigue guidelines for transport drivers, including the latest Commonwealth parliamentary report into fatigue in transport drivers (Neville 2000) emphasise work hours and time of day influences, but do not address the issue of OSA as a cause of driver fatigue in any significant way.

Another important finding of this work is the identification of a subgroup of commercial drivers who have increased driving accident risk (those with sleep apnoea syndrome). It seems that those commercial drivers who report daytime sleepiness in association with polysomnographically identified OSA, may be the most vulnerable to driver fatigue effects. As a treatable condition, there is now a compelling argument for screening all commercial drivers for the presence of sleep apnoea syndrome in order to potentially reduce road accident risk through treatment. At the same time, attention should continue to be directed towards reducing other important fatigue promoting factors, such as sleep deprivation.

Finally, future research should examine the relationship between objective accident rates and OSA/sleep apnoea syndrome in commercial drivers, the interaction between mild sleep apnoea syndrome and other fatigue risk factors, and driver perception of sleepiness prior to sleep onset in drivers with sleep disorders.

Chapter 8: Publications

8.1 Papers

1. A. Desai, E. Ellis, J. Wheatley, R. Grunstein. Fatal Distraction. A Case Series of Fatal Fall-Asleep Road Accidents and their Medico-Legal Outcomes, *submitted Medical Journal of Australia*, 30.8.2002

8.2 Abstracts

1. A. Desai, G. Marks, J. Williamson, B. Harris, D. Joffe, R. Grunstein. Driving Impairment In NSW Transport Drivers With Sleep Apnoea Syndrome. Abstract at Annual Scientific Meeting Australasian Sleep Association, Hobart, 10-13/10/2002
2. M. Howard, A. Desai, C. Worsnop, D. Campbell, P. Swann, D. Joffe, R. Grunstein, R. Pierce. Sleep Apnoea Prevalence and Crash Risk in Australian Commercial Vehicle Drivers. Abstract at Annual Scientific Meeting Australasian Sleep Association, Hobart, 10-13/10/2002
3. A. Desai, D. Joffe, R. Grunstein. NSW Transport Drivers have a high prevalence of obstructive sleep apnea. *AJRCCM* 4/2002, 165, 8, A513
4. A. Desai, J. Wheatley, R. Grunstein. Fatal Distraction. A case series of fatal fall-asleep road accidents and their medico-legal outcomes. Does the law need changing? *AJRCCM* 4/2002, 165, 8, A513
5. A. Desai, E. Ellis, J. Wheatley, R. Grunstein. Fatal Distraction. A case series of fatal fall-asleep road accidents and their medico-legal outcomes. Does the law need

changing? Abstract at Annual Scientific Meeting Australasian Sleep Association, Glenelg, 12-14/10/2001.

6. A. Desai, B. Wilsmore , D. Joffe, R. Grunstein. NSW Transport Drivers have a high prevalence of obstructive sleep apnea. Abstract at Annual Scientific Meeting Australasian Sleep Association, Glenelg, 12-14/10/2001.
7. A. Desai, D. Joffe, R. Grunstein. NSW Transport Drivers have a high prevalence of obstructive sleep apnea. *Respirology*, 2001; 6 (suppl.) A56
8. A. Desai, J. Newcombe, D. Bartlett, D. Joffe, R. Grunstein. Sleep Apnea and Driving in NSW Transport Drivers – Abstract at 2000 Road Safety Research, Policing and Education Conference, Brisbane. 26-28/11/2000. Web reference: http://www.transport.qld.gov.au/qt/driver.nsf/index/conference_fatigue

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Attachments