Fitness to drive and accident risk assessment in patients with Obstructive Sleep Apnoea Syndrome (OSAS)

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Intellectual Property and Publication Statements

The candidate confirms that the work submitted is his own, except where work which has formed part of jointly authored publications has been included. The contribution of the candidate and the other authors to this work has been explicitly indicated below. The candidate confirms that appropriate credit has been given within the thesis where reference has been made to the work of others

- The design and the driving simulator (MUoLDS) manual were provided by the Institute of Transport Studies, University of Leeds.

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Abstract

Obstructive Sleep Apnoea Syndrome (OSAS) is the most common form of sleep disordered breathing characterised by snoring, apnoeic episodes, sleep fragmentation at night and excessive daytime sleepiness. Some patients with OSAS are at increased risk of being involved in road traffic accidents (RTA). Compared to other individuals, some OSAS patients are at 2-6 times at risk of having a RTA. Clinicians are not only involved in screening, diagnosing, managing patients with OSAS but are often asked to make recommendations about fitness to drive and this is likely to be inconsistent in the absence of objective criteria. Some clinicians advise against driving in high-risk patients and in certain situations inform the licensing authorities. Driving simulators have been used in the research setting to predict fitness to drive in various situations. Many studies have used simple simulators that were unrealistic. The Institute for Transport Studies at the University of Leeds has developed a sophisticated driving simulator (UoLDS). Alongside this, a PC-based simulator (Mini University of Leeds Driving Simulator, MUoLDS) has been developed using the same software. Using continuously measured variables it has been possible to identify, with a high degree of accuracy, a subset of patients with OSAS who fail a simulated driving test. This has the potential to identify at-risk drivers and improve the reliability of a clinician's decision-making. Before the MUoLDS can become useful as a clinical tool there are a number of further questions to be answered and the thesis will address some of these.

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AHI- Apnoea-Hypopnoea Index

ARTP- Association for Respiratory Technology and Physiology

ATS- American Thoracic Society

BRAKE-RT- Brake Reaction Time

BSS- British Sleep Society

BTS- British Thoracic Society

CPAP- Continuous Positive Airway Pressure

CFQ- Cognitive Failure Questionnaire

DASS- Divided Attention Steering Simulator

DSS- Driving Sleepiness Score

DL- Driving Licence

DVLA- Driving Vehicle Licensing Authority

DQ- Driving Questionnaire

EEG- Electroencephalogram

EDS- Excessive Day time Sleepiness

EU- European Union

ERS- European Respiratory Society

ESS- Epworth Sleepiness Score

GMC- General Medical Council

HFS- High Frequency Steering

HGV- Heavy Goods Vehicle
Hw1s- Time Headway in 1 second
ITS- Institute of Transport Studies
MUoLDS- Mini University of Leeds Driving Simulator
MSLT- Multiple Sleep Latency Test
MWT- Maintenance of Wakefulness Test
M1- Motorway one
NICE- National Institute of Clinical Excellence
ODI- Oxygen Desaturation Index
OSA- Obstructive Sleep Apnoea
OSAS- Obstructive Sleep Apnoea Hypopnoea Syndrome
OSLER- Oxford Sleep Latency Test
PSV- Public Service Vehicle
RTA- Road Traffic Accidents
RT- Reaction Times
SDB- Sleep Disordered Breathing
SDLP- Standard Deviation of Lane Position
SF 36- Short Form 36 health survey
SSS- Stanford Sleepiness Score
TTC- minimum time to collision
UoLDS- University of Leeds Driving Simulator

VEER-RT- Veer Reaction Time
WHO- World Health Organisation

Publications

Variability in clinicians' opinions regarding fitness to drive in patients with obstructive sleep apnoea syndrome (OSAS)

Dwarakanath A, Twiddy M, Ghosh D, Jamson SL, Baxter PD, Elliott MW; Thorax. 2015 May; 70(5):495-7. PMID: 25410186

The qualitative analysis was provided by Maureen Twiddy, Leeds Institute of Health Sciences, University of Leeds.

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Sleepiness at the wheel, real and simulated driving in patients with Obstructive Sleep Apnoea Syndrome (OSAS) and controls; what is normal?

Dwarakanath A, Ghosh D, Baxter PD, Jamson SL, Elliott MW

Under review- European Respiratory Journal

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A randomised trial evaluating the issue of repeatability and the effect of incentives on an office based advanced driving simulator (MUoLDS) in patients with Obstructive Sleep Apnoea Syndrome (OSAS)

Dwarakanath A, Ghosh D, Baxter PD, Jamson SL, Elliott MW

Completed- Due for submission

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Use of fatigue related counter measures (Coping Strategies) while driving in patients with Obstructive Sleep Apnoea Syndrome (OSAS) and controls

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Cognitive dysfunction and road traffic incidents (RTA) in Obstructive Sleep Apnoea Syndrome (OSAS) patients and controls

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Completed- Due for submission

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Media releases

Sleep apnoea patients are more likely to report nodding at the wheel and fail driving simulator tests

- European Lung Foundation- 12th February 2013

- The Irishhealth.com- 1st April 2013

- Science Daily -11th April 2013

- The Huffington Post- 14th April 2013

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Driving and Obstructive Sleep Apnoea (OSA) /Obstructive Sleep Apnoea Syndrome (OSAS) - British Thoracic Society Position Statement June 2014.

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- Science Daily- 6th September 2016

- Eurek Alert- 6th September 2016

- Daily Mirror- 6th September 2016

- Yorkshire Evening Post- 6th September 2016

- European Respiratory Society- 7th September 2016

- American Sleep Association- 4th October 2016

Oral Presentations

Comparing coping strategies while driving in patients with Obstructive Sleep Apnoea Syndrome (OSAS) and in controls

A Dwarakanath, D Ghosh, S L Jamson, M W Elliott- Thorax 2012; 67(Suppl 2): A24

Presented at the BTS winter meeting- London

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Establishing a normal range in driving simulator performance using standard deviation of lane position (SDLP) in an advanced PC –based driving simulator (MUoLDS)

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A.Dwarakanath, D.Ghosh, S L Jamson, M W Elliott- European Respiratory Journal Sep 2016, 48 (Suppl 60)

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- **Assessment of cognitive dysfunction using the Cognitive Failures Questionnaire (CFQ) tool in patients with Obstructive Sleep Apnoea Syndrome (OSAS)**

  A Dwarakanath, D Ghosh, S L Jamson, M W Elliott- Thorax 2012; 67(Suppl 2):A182

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- **Residual drowsiness and CPAP compliance in OSAS patients and the DVLA- on behalf of the British Thoracic Society Sleep Apnoea SAG**

  A Dwarakanath, D Ghosh, S L Jamson, P D Baxter, M Twiddy, M W Elliott – Thorax 2013; 68(Suppl 3) A191

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- **Impact of gender on driving performance on an office based advanced driving simulator (MUoLDS)**

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- **Comparing simulator parameters between Obstructive Sleep Apnoea Syndrome (OSAS) patients and controls in an office based advanced driving simulator (MUoLDS)**

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- **Comparing outcomes on an office based advanced driving simulator (MUoLDS) between Obstructive Sleep Apnoea Syndrome (OSAS) patients and controls**

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- **Reported incidence of nodding whilst driving and its impact on simulator outcomes in Obstructive Sleep Apnoea Syndrome (OSAS) patients and controls**

  A Dwarakanath, D Ghosh, S L Jamson, M W Elliott- ERS sleep and breathing conference, Berlin 2013.

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- **Impact of speed and age on an office based advanced driving simulator (MUoLDS) between Obstructive Sleep Apnoea Syndrome (OSAS) patients and controls**

  A Dwarakanath, D Ghosh, S L Jamson, M W Elliott- Eur Respir J 2014; 44: Suppl (58).

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- **Evaluation of cognitive dysfunction using the Cognitive Failures Questionnaire (CFQ), driving incidents and driving simulator (MUoLDS) outcome in Obstructive Sleep Apnoea Syndrome (OSAS) patients and controls**

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  A Baluwala, D Ghosh, A Dwarakanath, M Twiddy, PD Baxter, SL Jamson, MW Elliott- Thorax 2016; 71(Suppl 3) A120.

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Chapter-1

Introduction

Obstructive Sleep Apnoea Syndrome (OSAS) is the most common form of sleep disordered breathing characterised by snoring, apnoeic episodes during sleep and day time excessive sleepiness. It is a prevalent condition affecting up to 20% of the population in first world countries [1] and has a major impact on general health and functional status [2]. It can seriously affect the quality of life of the patient and their immediate family [3]. Previously considered to be a medical curiosity, snoring; more a subject of humour than one of serious investigation, has witnessed a paradigm shift and is being increasingly being recognized as a major health problem. Despite increased awareness, a majority of those affected are still undiagnosed [4]. According to a recent survey, 50-60% of the general public have heard of OSAS [5] and up to 80% of people with OSA have not been diagnosed [6]. The syndrome was first described in the latter half of the 19th century by Sir William Osler where he described obese persons suffering from extreme daytime sleepiness and coined the term "Pickwickian syndrome" inspired after a character in Charles Dickens, The Pickwick Papers [7]. After the introduction of sleep studies, new pathophysiological mechanisms were identified; one of these mechanisms was mechanical obstruction of the upper airways during inspiration and the term "obstructive sleep apnoea syndrome" was introduced [8]. The landmark discovery of Continuous Positive Airway Pressure (CPAP) treatment [9] revolutionised the clinical management of OSAS. Over the last few decades there have been countless studies looking into various aspects of OSAS that has led to better understanding of this chronic condition.

1.1- Definition of OSA and OSAS

OSA is characterized by repetitive episodes of partial or complete upper airway

obstruction occurring during sleep with brief cessation of air flow but continuing thoraco-abdominal movements. A reduction in airflow and peak signal excursion by 30% is termed a "hypopnoea" and complete cessation of airflow for at least 10 seconds despite ongoing inspiratory efforts termed an "apnoea". These episodes lead to inadequate alveolar ventilation, usually result in oxygen desaturation and in prolonged events, a gradual increase in $PaCO_2$. The events are often terminated by arousals which may be described by patients or their partners as gasps, choking episodes or snorting but most go unrecognised. OSAS is defined as the combination symptoms and five or more documented obstructive breathing events per hour [10].

1.2- Pathophysiology of OSA

A vicious cycle of events commences at the onset of sleep (figure-1). Neural activation of the upper airways and pharyngeal muscles is reduced leading to muscular inactivity and atony. Partial or complete obstruction of the airways ensues which leads to hypoxia and/or hypercapnia and this leads to arousal from sleep. This cycle repeats continuously over the course of night leading to fragmented and unrefreshing sleep. OSA presents with a multitude of symptoms including snoring, witnessed apneas, nocturnal sweating, choking episodes, dry mouth, nocturia, excessive sleepiness, tiredness, poor work performance. The presence of day time sleepiness leads to a number of other problems such as driving impairment, accidents at work, cognitive decline, personality changes, mood disturbances, reduced libido secondary to low testosterone levels, martial disharmony and reduced quality of life.

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                          ┌──────────────────┐
                          │   Sleep Onset    │
                          └──────────────────┘
                         ↗                    ↘

        ┌──────────────────┐          ┌──────────────────────┐
        │    Arousal       │          │  Reduced CNS reflex  │
        └──────────────────┘          └──────────────────────┘
              ↑                                  │
              │                                  ↓

   ┌──────────────────────┐    ┌──────────────────────────────────┐
   │  Hypoxia/ Hypercapnia │    │  Loss of muscle tone and activity │
   └──────────────────────┘    └──────────────────────────────────┘
              ↖                          ↘

                     ┌──────────────────┐
                     │   Obstruction    │
                     └──────────────────┘
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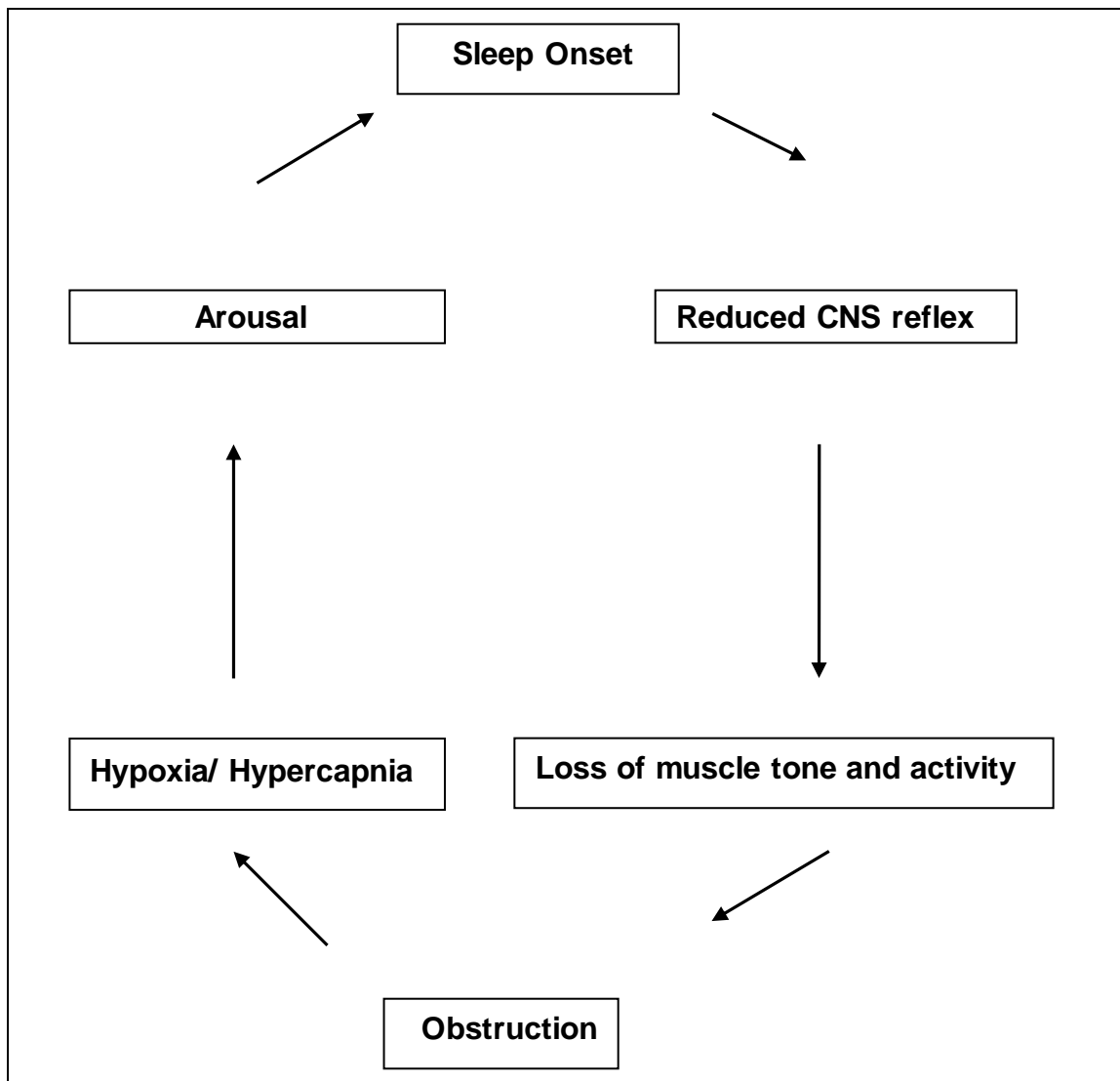
Figure 1-1, adapted from Neil and McEvoy, Medical Journal of Australia 1997 [11] showing the pathophysiology of OSA.

A study evaluating clinical predictors for sleep apnoea showed that snoring (P-0.001, OR= 2.5), excessive day time sleepiness (P- 0.002, OR= 1.7), witnessed apnoeas (P- 0.001, OR= 2.9) and impotence (P- 0.001, OR= 3.5) were the significant factors predicting OSA [12]. OSAS is diagnosed when there are symptoms of excessive daytime sleepiness or cognitive impairment along with an abnormal sleep investigation (overnight oximetry or limited channel sleep study or polysomnography). A number of factors should be taken into consideration such as shift work, sleep insufficiency, psychiatric disorders, metabolic disorders and

nutritional deficiencies, which may be the true cause of the sleepiness rather than objective measures on sleep diagnostics.

1.3- History of Road Safety

The first motor vehicle fatality in the United Kingdom and possibly the world was reported after a 44 year old mother of two, Bridget Driscoll died after being struck by a vehicle. The coroner at the inquest stated "I trust this sort of nonsense will never happen again" [13]. Sadly, the coroner, medical practitioners and general public would be deeply and repeatedly disappointed. It was 1896 and motor vehicles were a curiosity. Drivers did not undergo any form of testing, be it medical fitness, driving ability or otherwise, and there were no licensing regulatory agencies [14]. According to the World Health Organization (WHO), Road traffic accidents (RTA) were one of the top ten causes of death and in 2015 leading to 1.25 million injuries worldwide [15]. In the United Kingdom, a total of 195,723 casualties of road traffic accidents were reported by the public to the police in 2012 [16] and of these 1754 were fatal. For every death on Europe's roads there are an estimated four permanently disabling injuries such as damage to the brain or spinal cord, eight serious injuries and fifty minor injuries [17]. 2011- 2020 was proclaimed by a United Nations General Assembly resolution (64/255) as the "Decade of Action" for road safety with a main goal of reducing the road fatalities at various levels world-wide [18].

The time line in the history of road safety, Highway Code and the various milestones achieved [19] are shown in table 1.1.

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Table 1.1 showing the time line in the history of road safety and Highway Code

Year	Event
1888	First recorded sale of a motor car (petrol driven Benz)
1903	Driver licences were first introduced in Britain by the Motor Car Act, 1903, purely a means of identifying vehicles and their drivers
1930	Regulations introduced covering endorsements and fitness declaration. The Road Traffic Act 1930 introduces licensing system for PSV
1931	The Highway Code was launched and the first edition urged all road users to be careful and considerate towards others, putting safety first
1932	Diagrams of road signs as a warning about the dangers of driving when affected by alcohol or fatigue were seen in the second edition
1933	Stopping distances made their first appearance in the third edition, along with new sections giving hints on driving and cycling
1934	Licenses for lorry drivers were introduced on under the Road Traffic Act
1935	Compulsory driver testing introduced
1937	Speedometers and safety glass in windscreens made compulsory
1950s	The arrival of motorways led to the inclusion of a new section on motorway driving in the fifth edition of the Highway Code, advising drivers to avoid drowsiness by stretching their legs at the parking or service areas
1965	DVLA set up
1973	Centralised computer based licensing system was brought in to cope with the huge increase in demand for both driver and vehicle licences
1990s	Introduction of theory test
2002	Hazard perception element was introduced in the theory test
2011	Highway Code joined social networking websites Twitter and Facebook to share reminders of the road rules
2012	The Official Highway Code app for smart phones was launched
2017	Car driving test included following directions form a sat nav

1.4- The relationship between OSAS and driving

RTA can be caused by human error, environmental issues such as bad weather, poor road maintenance or issues with the vehicle. Up to one fifth (20%) of accidents on the UK motorways and other monotonous types of roads may be caused by driver

fatigue and sleepiness [20]. The morbidity and mortality associated with a sleep related RTA is high due to greater speed on impact and poor reaction to an impending event [20, 21]. RTAs related to sleepiness are common if driving alone or for a long distance without a break, in shift workers and those with untreated sleep disorders [21]. Sleep related RTA can also occur during the time of circadian rhythm change when vigilance is low (afternoon and nights), driving under the influence of alcohol or medications sleep deprivation and in shift workers [22]. Two thirds of drivers who fall asleep at the wheel are car drivers, 85% of the drivers causing sleep related RTA are men, and over one third are under 30 years of age [23]. 300 deaths in UK are caused by drivers falling asleep at the wheel every year [24]. RTA's are extremely expensive to society, with fatal accidents costing over £1 million [25]. Poor sleep hygiene is the commonest cause of excessive daytime sleepiness (EDS) and untreated OSAS is the most common medical condition causing EDS [26]. One of the common causes for sleep related RTA is OSAS. It is well known that some OSA patients are at increased risk of being involved in a RTA and many population and various case control studies have reported this issue previously (Table 1-2). However many studies had relatively unmatched controls and were based on self-reported accidents rather than an objective record from police or licensing authorities. The other limitations in these studies were that there was a lack of robust questionnaire data, issue about recall bias, gender bias, underreporting of RTA's and no data on the severity of sleep disordered breathing.

Table 1-2 showing the risk of RTA in OSA

Author	Type of study	Risk of RTA in OSA
Findley et al (1988) [27]	Case control (n = 29/35)	OR-7.0
Haraldsson et al (1990) [28]	Case control (n = 140/142)	OR-12.0
Young et al (1997) [29]	General population (n = 913)	OR-3.4
George et al (1999) [30]	Case control (n = 460/581)	OR-2.0
Teran Santos et al (1999) [31]	Case control (n = 102/152)	OR-6.3 if AHI > 10/hour
Horstmann et al (2000) [32]	Case control (n = 156/160)	OR-12.0
Mulgrew et al (2008) [33]	Case control (n = 783/783)	Severe OSA- RR 2.0

A recent systemic review and meta-analysis by Garbarino et al [34] has shown that compared to controls, the odds of an accident at work was found to be nearly double in workers with OSA (OR = 2.18; 95% CI = 1.53 to 3.10). A meta-analysis comparing the risks for RTA in all medical conditions reported showed that OSAS has an increased risk between 1.2- and 2-fold with respect to a healthy population. It has the highest increased risk, with a relative risk of 3.71, which is second only to age and sex as a general risk factor for RTA [35]. Sleepiness is the greatest risk factor for RTA [36] and the risk of having a crash with untreated moderate to severe OSAS is superseded only by age and time of the day as risk factors [37]. Studies have shown that patients are reluctant to report accidents and under report symptoms [38, 39]. Data from police, relevant licensing authorities and insurers tend to underestimate the issue as not all incidents are reported, particularly near misses of nodding episodes that have not resulted in an accident.

Driving a vehicle is a skill that requires a combination of multiple factors. It involves complex integrated higher cortical function, alertness, concentration and eye to hand coordination [40]. A lapse in either of these may lead to increased RTA as evidenced by the study by McEvoy et al [41] who reported that driver's using a mobile phone up to 10 minutes prior to a crash have a four fold increase in the likelihood of crashing. Sagaspe et al [42] undertook telephone interviews with French drivers and found that 11.8% had an ESS =/> 11; 28.6% reported sleepiness at the wheel severe enough to require stopping, 46.8% felt sleepy during night-time driving and 39.4% during day time driving, 10% had had a near-miss during the previous year and 6% had had a driving accident. OSA is associated with focal loss of grey matter which may have an impact on an individual's driving abilities [43]. Tippin et al [44] reported that drivers with OSA have reduced visual vigilance for peripheral targets and is postulated that this effect is due to decline in attention and fatigue. However it is not entirely clear what aspects of OSA increase the likelihood for poor driving ability. Potential confounders such as obesity and alcohol that may influence mechanical aspects of driver ability, reduced reaction times and poor evasive action respectively further complicate this. A recent study has shown that the rate of sleepiness and sleep-related accidents among commercial drivers is high [45] and Howard et al [46] showed that 60% of drivers had sleep disordered breathing and 24% were excessively sleepy. Commercial drivers are considered as high risk because they operate larger vehicles, transport hazardous materials, carry multiple passengers, operate for long stretches of time and have an economic incentive to continue driving when non-commercial drivers may choose to stop. Multiple risk factors may synergistically increase the risk of accidents [47].

1.4.1- Position statements about OSAS and driving by various medical societies

In population terms undiagnosed and untreated OSAS, irrespective of the severity is not compatible with safe driving and poses a serious public health concern with respect to road safety. The increased risk of RTA has prompted a specific consideration of OSA in the framework of the legislation for driving licenses. Rules for medical assessment before obtaining a driving licence differ from country to country. Position statements in recent years by various medical bodies [48,49] and licencing authorities [50] have attempted to tackle this issue. The American Thoracic Society (ATS) clinical practise guideline on Sleep Apnoea, sleepiness and driving risk in non-commercial drivers considers patients to be high-risk drivers if there is moderate-to-severe sleepiness plus previous RTA's [49]. Annexe iii of the European Union (EU) directive on driving licences was revised in 2014 on the recommendations from a working group established by the transport and mobility directorate of the European commission in 2012 [51]. The new directive, which is subject to mandatory implementation by all member states from December 2015 states that 'Applicants or drivers in whom a moderate or severe obstructive sleep apnea syndrome is suspected shall be referred to further authorised medical advice before a driving licence is issued or renewed [51]. They may be advised not to drive until confirmation of the diagnosis. Driving licences may be issued to applicants or drivers with moderate or severe OSAS who show adequate control of their condition and compliance with appropriate treatment and improvement of sleepiness, if any, confirmed by authorised medical opinion. Applicants or drivers with moderate or severe obstructive sleep apnea syndrome under treatment shall be subject to a periodic medical review, at intervals not exceeding 3 years for drivers of group 1 (i.e.

non-commercial drivers) and 1 year for drivers of group 2 (i.e. commercial drivers), with a view to establish the level of compliance with the treatment, the need for continuing the treatment and continued good vigilance [51]. The European Respiratory Society has established a task force in the area of driving and OSA to develop guidance and help ensure that any adoption of EU 2014/85/EU is undertaken in a reasoned, sustainable and fair manner in line with each country's legislative procedures and economic resources [52, 53].

1.4.2- OSAS and Driving Vehicle Licensing Authority (DVLA) - The current state of affairs

Currently in the UK, the Driving Vehicle Licensing Authority (DVLA) [50] has specific guidelines that are applicable to all drivers who have OSAS. The current interpretation of the EU directive by the DVLA has caused some consternation among patients, sleep apnoea support groups and the clinicians (personal communications). The DVLA has focussed on both sleepiness sufficient to impair driving along with severity of sleep apnoea based on Apnoea- Hypopnea Index (AHI). Based on the current guidelines the relevant patients by law should inform DVLA and complete the relevant form (SL1 for class one and SLV1 for class two licences) after a diagnosis has been confirmed. Once DVLA is informed, medical enquiries are undertaken to establish whether the driver should retain their licence. Driving will normally be allowed to continue once satisfactory control of the condition is achieved with CPAP, the gold standard in the management of OSAS.

	Group 1 car and motorcycle	Group 2 bus and lorry
Excessive sleepiness due to a medical condition (see relevant chapter) including mild obstructive sleep apnoea syndrome (AHI below 15) or medication.	🔴 Must not drive. Driving may resume only after satisfactory symptom control. If symptom control cannot be achieved in three months the DVLA must be notified.	🔴 Must not drive. Driving may resume only after satisfactory symptom control. If symptom control cannot be achieved in three months the DVLA must be notified.
Excessive sleepiness due to obstructive sleep apnoea syndrome – moderate and severe: ▪ AHI 15 to 29 (moderate) ▪ AHI 30 or more (severe) on the apnoea-hypopnoea index or equivalent sleep study measure.	🔴 Must not drive and must notify the DVLA. Subsequent licensing will require: ▪ control of condition ▪ sleepiness improved ▪ treatment adherence. The DVLA will need medical confirmation of the above, and the driver must confirm review to be undertaken every three years at the minimum.	🔴 Must not drive and must notify the DVLA. Subsequent licensing will require: ▪ control of condition ▪ sleepiness improved ▪ treatment adherence. The DVLA will need medical confirmation of the above, and the driver must confirm review to be undertaken annually at the minimum.
Excessive sleepiness due to suspected obstructive sleep apnoea syndrome.	🔴 Must not drive. Driving may resume only after satisfactory symptom control. If symptom control cannot be achieved in three months the DVLA must be notified. See above when diagnosis is confirmed.	🔴 Must not drive. Driving may resume only after satisfactory symptom control. If symptom control cannot be achieved in three months the DVLA must be notified. See above when diagnosis is confirmed.

Figure 1-2 adapted from DVLA [50] showing the current DVLA guidelines

Randomised controlled trials have shown that CPAP improves subjective and objective sleepiness [54-56]. Adequate control of the underlying symptoms and sleep disordered breathing is essential before driving can be recommended. This should be confirmed by the clinician, as there may be insurance implications in the event of a crash if unfit drivers drive against medical advice. Not reporting to the DVLA about a diagnosis of OSAS could result in a £1,000 fine. 99% of those with OSAS keep their licence [22]. By law, it is the patient's responsibility not to drive if sleepy and the DVLA remains the final arbiter.

1.5- Assessment of fitness to drive in OSAS patients

Driving is an essential part of modern life and most patients with OSAS drive motor vehicles. A survey in 2013 by the British Lung Foundation (BLF) showed that among

a cohort of OSAS patients (n= 2671) attending sleep clinics in the UK, 82% of responders held a current driving licence, 62% drove a motor vehicle and 16% held a professional driving licence or drove for a living [57]. Some clinicians are not only involved in screening and treating OSAS patients but are often asked to make recommendations about fitness to drive which can be challenging with major implications on patients livelihood, in particular professional drivers. There is evidence that the risk of accidents increases with increasing daytime sleepiness [58]. Although there is a trend towards increased likelihood of accidents with more severe sleep disordered breathing there is no sufficient robust data on which to base decisions for an individual [59]. There is a duty of care on clinicians to discourage those patients who are at high risk of causing an accident from driving or even to report them to the licensing authorities. OSAS patients have a moral obligation (a duty which one owes, and which he or she ought to perform, but which he or she is not legally bound to fulfil) to obey the law but due to the fear of losing their driving licence or livelihood may under report sleepiness at the wheel. A meta-analysis showed that making patients take the issue of potential unsafe driving seriously; using threat appeal generates fear and does not translate into positive change resulting in less risky driving behaviour [60]. DVLA remains the final arbiter and has the right to know about one's driving fitness [50]. The advice that a patient will receive about driving will depend upon their doctor's attitude to risk and this is likely to be inconsistent between clinicians in the absence of objective criteria. Clinician's warnings to patients who are potentially unfit to drive may contribute to a decrease in subsequent RTA, but may also exacerbate mood disorders and compromise the doctor-patient relationship [61]. It may also dissuade others from seeking treatment for their own symptoms. General Medical Council (GMC) has published guidance

about breaching patient confidentiality in certain extreme circumstances in the interest of public safety [62]. Currently advice about an individual's fitness to drive is based upon the severity of the sleep disordered breathing, with or without some objective measure of daytime sleepiness and the patient's account of their driving [63, 64]. There are conflicting data about the relationship between perceived sleepiness and the likelihood of being involved in an accident. There is a problem inherent in the ascertainment of risk in an individual patient upon initial presentation.

1.5.1- Assessment of sleepiness in OSAS patients

A- Subjective sleepiness

Using validated questionnaire such as the Epworth Sleepiness Score (ESS) and the Stanford Sleepiness Score (SSS), a subjective assessment is carried out. ESS is a well-validated tool to assess subjective sleepiness in OSAS. It is easy to administer and is useful in measuring changes in sleepiness over time. It is intended to measure daytime sleepiness on a probability scale of 0 to 3 in eight different situations during the day [65]. It was introduced in 1991 by Dr. Murray Johns of Epworth Hospital in Melbourne, Australia [65]. It has a total score of 24 and a score of less than 10 is considered as normal. A score of more than 10 is considered as abnormal and warrants further assessment. It is simple and easy to complete. However the disadvantages are that since it is subjective, patients may underplay their responses leading to bias. SSS utilizes a 7-point scale (1- fully alert, 7- struggling to stay awake) and the immediate state of sleepiness is assessed. However there is no relation to the severity of OSAS and is used only in prior to MSLT [2]. Guaita et al [66] recently developed the Barcelona Sleepiness Index which is a brief questionnaire of just two items, which correlates well with objective

sleepiness measures, oxyhemoglobin desaturation and is sensitive to change with therapy. This instrument could be helpful in the evaluation of sleepiness, both during routine clinical interviews as well as a screening method in epidemiological studies. Masa et al [67] suggested that enquiring about sleepiness specifically while driving may better predict accident risk rather than sleepiness in general.

B- Objective tests of sleepiness

Daytime sleepiness is influenced by an individual characteristics, sleep needs, psychologic condition, physical and mental activity. Objective tests for assessment of driving abilities are limited. No test is considered as a gold standard to assess excessive daytime sleepiness, which is considered as the most disabling symptom in OSAS. Multiple Sleep Latency Test (MSLT) [68], Maintenance of Wakefulness Test (MWT) [69] and Oxford sleep resistance (OSLER) test [70] are useful clinical tests for the evaluation of excessive sleepiness but with limitations. The MSLT assesses an individual's ability to fall asleep during the day and is not appropriate to assess a patient's fitness to drive [71]. Young et al [29] found no difference in MSLT test scores between subjects involved in a RTA and those who were not. The MWT is a validated, objective measure of the ability of an individual to stay awake. However its relevance to driving in which an individual has to interact with their environment is questionable. The same is true of the OSLER, a behavioural equivalent of the MWT [70]. Evidence suggests a relationship between driving ability and the MWT in patients with untreated obstructive sleep apnoea [72, 73]. A pathological MWT is associated with simulated driving impairment; sleepy patients had more inappropriate line crossings than control drivers ($p < 0.05$) [72]. In a small study comparing patients with untreated OSAS and controls, Philip et al [73] showed that

the number of inappropriate line crossings correlated with MWT scores (r^2= -0.339; P= < 0.05) but its suitability to evaluate real world performances and/or risks has been questioned [74].

1.6- OSAS and driving simulator performance

Undertaking studies during real time driving is not feasible and is unethical. Evaluating many aspects of safe driving is the key and driving simulators have been used in the research setting to predict fitness to drive in various situations and understand the driving behaviour under safe conditions. This is an alternative approach to identify those patients who are at high risk of having a RTA and there is evidence to show a good correlation between simulator performance and real time driving experience [75]. Various studies have been performed reporting the driving simulator performance in OSAS and controls. Findley et al [76] using a personal computer program simulating a monotonous highway drive showed that OSAS patients when compared to controls perform worse on the driving simulation lasting for 30 minutes. OSAS patients had significantly higher events as compared to controls (44 +/- 52 versus 9 +/- 7, P= < 0.05). George et al [77] developed a laboratory based divided attention driving test and studied the ability to detect impaired performance in sober controls, controls under the influence of alcohol (mean blood alcohol level, 95+/-25 mg/dl) and male OSAS patients. The simulator performance was worse in OSAS patient than controls in all measures, with the largest difference noted in tracking error. Half of the patients were worse than any control subject, with some showing performance worse than control subjects impaired by alcohol. Barbe et al [78] using the Steer-Clear computer program investigated the association between OSAS, RTA and simulator performance. OSAS

patients reported more real life accidents than controls (OR= 2.3; 95% CI: 0.97 to 5.33) and were more likely to have had more than one accident (OR= 5.2; 95% CI: 1.07 to 25.29, P= < 0.05). They had a lower level of vigilance and poorer driving performance (P= < 0.01). However there was no correlation between the degree of daytime sleepiness, the severity of SDB, level of vigilance, simulator performance and the risk of automobile accidents. Risser et al [79] in a case control study using a computer based driving simulator recorded lane position variability, speed variability, steering rate variability, and crash frequency. The frequency and duration of EEG-defined attention lapses were also measured. They showed that OSAS patients as compared to controls demonstrated greater variability in speed, lane position, steering rate and had more crashes. EEG-defined attention lapses of longer duration, which increased with time, were noted in OSAS patients. Measures of lane position variability and crash frequency had a significant positive correlation with attention lapse frequency and duration. The poor performance appeared related to the EEG-defined attention lapses. Lane position variability appeared to be the most sensitive measure for assessing and quantifying impairment. This study showed that poorer driving performance and crashes are not entirely due to excessive sleepiness, but inattention due to sleepiness. Juniper et al [80] developed a steering simulator with a realistic view of the road ahead that allowed separate assessment of the two visual tasks required for steering a car, immediate positioning on road with reference to the road edges, and assessment of the curve of the oncoming road which allows faster driving. This was a case control study and both the groups performed three 30-min drives with the entire oncoming road or only the near part of the road or only the distant part of the road visible. OSAS patients performed significantly worse on the three different drives as measured by steering error (P=

<0.001), time to detect the target number (P = <0.03), and off road events (P = <0.03). Turkington et al [81] have shown that age, female sex and alcohol were the greatest determinants of a task failure on the divided attention steering simulator (DASS). A self-reported near miss was independently associated with a poor performance. The number of off-road events on the simulator was independently associated with a history of previous RTA (OR= 1.004, 95% CI 1.0004 to 1.008, P= <0.03). The ESS was independently associated with episodes of falling asleep at the wheel (OR= 1.21, 95% CI 1.12 to 1.31, P= <0.0001). They concluded that there was an independent relationship between driving ability in OSAS patients and performance on a simple computer based simulator. Pichel et al [82] in a study involving 129 OSAS patients and using both a steer clear simulator and the DASS showed that alcohol and SF-36, a measure of self-reported health status were associated with poor simulator outcome. Philip et al [73] showed that the driving outcome in OSAS patients with a 90-minute real life driving session correlated with MWT and ESS. The AusEd driving simulator has been validated and shown to be sensitive to fatigue in a range of experimental settings [83]. A recent study using the MUoLDS [84] has shown that variables recorded during approximately fifty minutes of simulated motorway driving on the MUoLDS can predict with reasonable accuracy the patients with OSAS who will be involved in a crash in the simulated scenario. Three groups of patients can be identified; those who crash when they really should not, those who do not crash at all and an intermediate group who crash in a situation in which even a reasonably alert driver might crash. In this study 72 patients were included in the exploratory phase of the study and 133 patients in the validation phase. Prediction models could predict "fails" with a sensitivity of 82% and specificity of 96%. The models were subsequently confirmed in the validation phase. These

were based on the SDLP and the reaction time to an event. Fully immersive simulators may be considered as a surrogate for real time driving, but are not cost effective and most importantly not easily available.

1.7- Effect of CPAP treatment on driving simulator performance in OSAS patients

Various studies have shown that CPAP can improve driving simulator performance in OSAS patients. The studies are shown in Table 1-3.

Table 1-3 showing the effect of CPAP treatment on driving simulator performance

Vakulin et al [83]	Driving simulator performance improved after 3 months of CPAP treatment with high adherence in patients with severe OSA but performance remained impaired compared to control subjects
Findley et al [85]	CPAP treatment improved driving simulator performance.
Cassel et al [86]	Accident rate significantly reduced on an 80 minute vigilance test with 12 months CPAP treatment.
Hack et al [87]	Improvement in simulator performance after 1 month of CPAP treatment.
Turkington et al [88]	Improvement in simulator performance after 7 days of CPAP treatment.
Orth et al [89]	Improve simulator performance with reduced accident rates after CPAP treatment.
Mazza et al [90]	CPAP treatment reduced the reaction time on simulator performance

1.8- Effect of CPAP treatment on real life road traffic accidents in OSAS patients

There is also evidence that treatment with CPAP reduces real life RTA. Krieger et al [90] showed reduction in RTA and near miss events after CPAP. Yamamoto et al [92] reported that 33% of OSAS patients had accident/near miss before treatment and no mishaps after CPAP. In a study by George et al [93] comparing motor vehicle crash records between OSAS patients treated with CPAP and controls, increased accident events were noted in untreated OSAS patients prior to CPAP; post CPAP the number of accident events was similar to the control group. Barbe et al [94] showed that after 2 years of CPAP treatment the RR for RTA reduced from 2.57 to 0.41. A meta-analysis that reviewed various observational studies that reported accident risk with OSA before and after treatment with CPAP found a significant reduction in risk following CPAP treatment [95]. Studies discussed so far have consistently shown that OSAS patients perform worse on any driving simulator and studies have also reported improvement in simulator performance and reduction in real time RTA in OSAS patients following CPAP treatment.

1.9- My research

My work focussed on the following aspects:

I. To evaluate the degree of variability in clinician's opinions regarding fitness to drive in patients with OSAS.

This study focused on the current practice of advice given by clinicians regarding fitness to drive in patients with OSAS. This is discussed in Chapter-3.

II. **To establish a normal range based on self- report measures of sleepiness, sleepiness specifically whilst driving, safety-critical driving incidents based on a driving questionnaire, Mini University of Leeds Driving Simulator (MUoLDS) outcome and performance based on continuously measured variables in untreated OSAS patients and controls.**

The aims of this exploratory cohort study were to define a normal range in controls and to compare them with a group of untreated OSAS patients in the following domains:

- Self- reported sleepiness while driving

- Safety – critical driving incidents

- MUoLDS simulator performance

in order to establish objective criteria to help inform the decision making process about an individual's driving risk and investigate the role of an advanced PC based driving simulator as an objective tool for assessment. This is discussed in Chapter-4.

III. **Evaluate the issue of repeatability and the effect of an incentive on performance on the MUoLDS in untreated OSAS patients.**

This was a randomised trial which evaluated as a primary outcome the test-retest reliability (repeatability) and the effect of motivation (incentive effect) on continuously measured driving parameters.

    a. Primary Outcome

        Standard Deviation of Lane Position (SDLP) in epoch 3 and "veer" reaction times (Veer-RT) were the primary outcome variables.

b. Secondary Outcome

"Fail" or "Pass" during the simulated "drive".

This is discussed in Chapter-5.

IV. To explore the use of fatigue related counter measures (coping strategies) as a potential surrogate marker of sleepiness while driving in untreated OSAS patients and controls.

This was an observational study that identified various behaviours adopted by controls and untreated OSAS patients to counter fatigue and sleepiness whilst driving. This study identified surrogate markers of fatigue and sleepiness. This is discussed in Chapter-6.

V. To study cognitive dysfunction using the cognitive failure questionnaire and it's impact on road traffic accidents in untreated OSAS patients and controls.

This study tested the hypothesis that patients with OSAS exhibit worse cognitive dysfunction as compared to OSA patients and controls and higher CFQ score predicts accident risk. This study was divided into exploratory and validation phases. The outcomes were to explore the relationship between CFQ score versus general sleepiness, severity of sleep disordered breathing, accidents and to compare driving incidents between controls and patients. This is discussed in Chapter-7.

Chapter 2

Mini University of Leeds Driving Simulator (MUoLDS)

2.1- University of Leeds Driving Simulator (UoLDS)

The Institute of Transport Studies in the University of Leeds consists of a multidisciplinary research team from engineering, psychology and computing back ground who have a research interest in traffic safety and human factors, road design, driver distraction and driver impairment. The previous UoLDS consisted of a 1991 Rover 216GTi. Through government funding the existing space was refurbished and through competitive tender and negotiated budget of £911,952 the new UoLDS was developed between 2003- 2006. The cost covered motion system, vehicle cab, dome, projection, software and building. The design included real time controls, vehicle dynamics, motion sensors, image generation, eye tracking and in-vehicle touch- screen display.

The UoLDS is a fully dynamic driving simulator located within the Institute for Transport Studies. The full simulator has a Jaguar s-type vehicle located inside a dome which sits on a motion system that can move in 6 degrees of freedom and slide along an x-y table as shown in figure 2-1.

Figure 2-1 showing the University of Leeds Driving Simulator

A driver has a near 360 degree view inside the dome of a road layout and surrounding area. In addition to the visual scene the driver will feel the physical sensation of accelerating, braking and turning the car. Third party applications may be run alongside the simulator to allow for more detailed data collection. Examples include the tracking of head & eye movements and measuring heart beats per minute.

2.2- Mini University of Leeds Driving Simulator (MUoLDS)

In addition to the full simulator above, the same software was installed on a single computer with one monitor. A single computer can easily be deployed in most indoor environments provided there is mains power. This allows for a single experiment to be run from more than one site at different times. However all the simulator tests in this research were conducted in St. James's University Hospital. The software program was installed in two computer desktop (Windows-7) thus allowing multiple participants to run the same experiment at the same time. For the purposes of various studies in patients with OSAS the simulator was used on two computers inside a hospital and was termed as the Mini University of Leeds Driving Simulator (MUoLDS). This is shown in 2-2.

Figure 2-2 showing a photograph of the MUoLDS

2.3- Running the MUoLDS

Before running the simulator a subject number and a run number was created. Each participant had a unique subject number and could do one of two runs:

a. Run 1 involved driving along a motorway for four junctions.

b. Run 2 involved driving along a motorway for seven junctions and encountering drone vehicles.

Provided that the subject and run numbers are valid then the software will start with a similar screen to that shown in figure 2-3.

Figure 2-3 showing the road layout (dash board view)

Figure 2-4 shows a subject seated on the MUoLDS prior to the test.

Figure 2-4 showing a subject on the MUoLDS (subject consent obtained)

Once the simulation test has started then the participant can start the engine. Figure 2-5 shows the steering wheel, gearbox and pedals for the Logitech G27 racing wheel. Although this setup can be used to simulate a manual gearbox the simulator for Sleep Apnoea uses an automatic gearbox. In the middle of the gearbox there are four red buttons. Pressing the red button on the right starts the engine. The rev counter will idle around 500 rpm. To engage the drive gear the red button that is second to the right should be pressed and the car will automatically move unless the brake is applied.

Figure 2-5 showing the logitech G27 racing wheel, gear box and foot pedals

Once the drive gear is engaged there is no need to disengage. Equally there is no facility to turn off the engine. Once the participant has finished their drive, pressing the Esc key on the keyboard ends the simulation.

2.4- Post processing the results

Post processing the results was done in two parts. The first part extracted all the required information from a binary file (as generated by the real-time software) and saves the results to different text files (one file for the subject car information and another file for each of the drone vehicles). The second part extracted relevant information from the text files, using MATLAB or Octave and generated summary results. The script for processing was provided by Michael Daly and Tony Horrobin from the Institute of Transport Studies, University of Leeds. I installed the software for the MUoLDS runs, processing and extracting the results. After the one raw dataset has been processed then there were three choices for processing more data.

a. Process more data as above.

b. Place multiple commands like the one above inside a batch file and process more than one dataset.

c. Move on to processing the text files.

2.5- Processing the text files

After the raw binary files have been processed the resulting text files were generated and placed in a subdirectory called debug. A typical file for the participant vehicle is shown in figure 2-6.

Figure 2-6 showing the text summary file

The debug directory contained one file for the participant vehicle per run and one file per drone vehicle per run. The drone files were used for the analysis of the wobble and hard braking events in run 2. Although files were created for each of the drone vehicles, in practice only the drone vehicles involved with the wobble and hard braking events were needed for analysis. Therefore these files needed to be copied elsewhere and the remainder were deleted.

2.6- Transferring the data files

To transfer the correct drone files, the octave icon was double clicked and the octave program launched. To transfer the relevant files out of debug, the following transfer command was followed:

a. transfer (start subject, stop subject, run number) or:

b. transfer (1,1,2)

In this case only one subject run was done because the first and second numbers were the same. Multiple subjects can be transferred by entering a range of subjects. For example to transfer subjects 1 to 101 for run 2: transfer (1,101,2).

To process the text files the octave icon was double clicked in order to start a second copy of octave. To process data for a single run the command shown was entered. This command processed the data for subject 1 run 2. To process multiple runs, a separate command was entered. This processed subjects 1 to 101 for runs 1 and 2. It takes octave 2-3 hours to process 100 subjects.

2.8- Generate a summary of the results

Many results files were generated after all subject runs have been processed. One last step was to combine all the required results and save them into two summary files (sleep_all.dat and sleep_lanes.dat). This was done for an efficient analysis of the simulator runs. To generate the results a specific command was entered. The resulting files sleep_all.dat and sleep_lanes.dat were tab delimited and were exported to Microsoft excel.

2.9- MUoLDS road layout

In line with the UK highways agency road standards, a three-lane motorway was developed with UK standard lane markings and signage. The road is 90 km long and comprises of 8 junctions, including entry, hard shoulder and exit slip roads, separated by 8 sections of road (each 9km in length). The designed road starts from junction 35 to 42 on M1. It takes approximately 7 minutes to drive one section at 70mph. This will be called as one epoch. The complete scenario comprises eight similar epochs.

2.10- MUoLDS scenario

All OSAS patients and controls had the scenario explained and had a 20 minute practice run before commencing the test proper. All through the test, drone vehicles will drive in and out of the subjects' lane and it is expected that drivers would react to them as they would in real life. In the test proper a "minor" or "veer" event was choreographed within epoch 4. This was a scenario whereby a vehicle swerves briefly into the driver's lane just ahead of them. This requires an avoidance manoeuvre such as braking or swerving (or both), but the vehicle is sufficiently far ahead that it was anticipated that an alert, competent driver should easily be able to avoid a collision. A "major" or "brake" event was inserted into epoch 8 which signalled the end of the run. Here, a vehicle ahead brakes heavily, requiring the driver to be fully attentive and reactive in order to avoid a collision. However, even with full attention some subjects might not be able to avoid a crash. The scenario was coordinated such that all drivers would be at the same time to collision when the car ahead starts to brake; thus all drivers are faced with a comparable task. Previous simulator studies suggest that "minor" events may precede "major" events [88]. All subjects were instructed to drive in the middle lane and were asked not to change lanes to overtake the vehicle in front but to try to keep up with it. This was to generate comparable and consistent data.

2.11- Measures and end points

Task failure was initially defined as unprovoked crash, veer event crash, unable to complete the test or spending more than 5% of the total study time (2 ½ minutes) with two wheels out of the middle lane. Unprovoked task failure and crashes at the minor event should not happen during normal simulated driving and any subject

falling into this category was considered to have "failed" the simulator test. Subjects who completed the test without meeting any of the task failure criteria defined above were deemed to have "passed". The major event was choreographed such that it was harder to avoid a crash and those who only crashed at this event were deemed to be "indeterminate".

Various continuous variable parameters of driving behaviour were recorded at 60 Hz. These included minimum time headway (Hw), percentage time spent with minimum headway of less than 1 second (Hw1s), minimum time to collision (TTC) to the preceding vehicle, high frequency steering (HFS), mean speed and speed variation, standard deviation of lane position (SDLP), lane changes. For the purpose of analysis we used the mean values for each parameter in epochs 3, 5, 6 and 7, which were free of events and just require steady driving at approximately 70 mph. In addition, specific measures at the programmed events were also recorded, including: speed on approach to collision and reaction times (RT).

2.12- Definitions of various driving simulator parameters

2.12.1- Time to Collision (TTC)

This is defined as the instantaneous time it would take to collide into the lead vehicle if vehicle speeds are kept constant. It is measured in seconds. TTC reflects risk margin; the lower the TTC, the less margin for error, the lower the value of TTC minima, higher the risk [96].

2.12.2-Time Headway (Hw)

This defined as the time it would take to collide into the lead vehicle were it to stop dead. Time Headway is a measure of longitudinal risk margin. The closer and faster

a subject travels behind a lead vehicle, the less the chance of managing to avoid a collision if the lead vehicle reduces their speed. For a small headway, the time a subject can be distracted by another task without a highly increased risk of accident, is much less than if the time headway is large. The proportion of the time headway less than one second (Hw1s) has been used as a risk indicator for car following situations. A higher proportion of time spent with headway less than 1 second (Hw1s) is an indicator of worse performance and dangerous driving [97, 98]. Minimum time headway is the minimum value of headway reached in a particular epoch; a lower value indicates poorer driving performance. It is measured in seconds.

2.12.3- Standard Deviation of Lateral Position (SDLP)

Less lateral control may be observed as an increase in SDLP. In several studies, driver sleepiness (drugs, sleep deprivation) has been shown to cause an increase in SDLP; the steering control has become less stable. However, SDLP is influenced by overtaking and voluntary changes in lateral position due to road curvature; effects that may not be related to driving performance. Hence in all the studies subjects were asked to stay in the middle lane all through the runs and we took into account the SDLP only from the straight sections of the road. Higher SDLP relates to worse vehicle control [80, 99]. It is measured in meters.

2.12.4- High frequency steering activity (HFS)

The high frequency component of steering activity is measured as a ratio between steering movements of 3- 6 Hz to all other steering activity. Higher HFS indicates poorer control [100, 101].

2.12.5- Reaction time (RT)

Time between the lead vehicle commencing veering or braking manoeuvre and participant commencing braking. If the patients failed to brake the reaction time was infinity and if they veered out of lane to avoid crash no RT was recorded. It is measured in seconds.

Chapter-3

Variability in clinicians' opinion regarding fitness to drive in patients with OSAS

3.1- Abstract

OSAS is an important risk factor for RTAs. Clinicians have to advise patients about driving but there are no clear standards or guidelines. The current practice of advice given by clinicians regarding fitness to drive in OSAS patients was evaluated. Clinicians were invited to complete a web-based survey, including vignettes of patients with OSAS at diagnosis and following treatment with CPAP. Clinicians were asked to indicate the advice they would give about driving and what they considered to be residual drowsiness and adequate compliance following treatment with CPAP. 467 respondents (58% males) completed the survey. 53% were consultants who saw patients with OSAS. Conflicting advice was given by different clinicians for each vignette at diagnosis. In the least contentious, 94% of clinicians would allow driving; in the most contentious a patient had a 50% chance of being allowed to drive. Following treatment with CPAP clinicians' interpretation of what constituted residual drowsiness was also conflicting. In each vignette the same clinician was more likely to say "yes" to "excessive" than to "irresistible" (71+/12% v/s 42+/-10%, P-0.0045), consistent with a higher standard being applied to vocational drivers, as intended by the DVLA. There was also a lack of consensus regarding "adequate CPAP compliance"; "yes" responses ranged from 13% to 64%. Analysis of responses to an open question revealed that driving and sleep apnoea was a difficult issue for clinicians to manage (qualitative analysis). There is considerable variability in the advice likely to be given by clinicians about driving. It is an area that clinicians found difficult and in which they feel vulnerable. There is a desire for clearer guidance.

3.2- Introduction

OSAS is prevalent in approximately 4% of men and 2% of women, and is characterised by sleep fragmentation and excessive daytime sleepiness [102-105]. Excessive daytime sleepiness decreases reaction times, vigilance and alertness, which affect certain tasks requiring sustained attention, such as driving. Sleepiness at the wheel is estimated to cause about 20% of motorway accidents, which usually occur at high speed without avoidance reactions [20, 30, 32]. OSAS patients are 2 to 6 times more prone to RTAs when compared to other individuals [29, 78] and a meta-analysis has shown that OSAS carries the highest risk for RTAs amongst a variety of medical conditions [31, 35]. However not all OSAS patients are unsafe drivers [106]. Clinicians diagnosing OSAS will need to advise patients about driving. Furthermore they are often asked by the DVLA and employers to make recommendations about a patient's fitness to drive. There is an obligation on clinicians to discourage those patients who are at high risk of causing an accident while driving or to report them to the DVLA. This survey was carried out to gauge the advice patients are likely to be given about driving by clinicians.

3.3- Methods

Clinicians who saw patients with OSAS were invited to participate in a web-based survey, conducted under the auspices of the British Thoracic Society (BTS) in collaboration with the British Sleep Society (BSS) and the Association for Respiratory Technology and Physiology (ARTP, UK). A link to the survey was sent out by email to all members of these societies. Recipients were asked to complete the survey only if they saw patients with OSAS and to forward the link to colleagues who might see patients with OSAS, but who were not members of the above

societies. We conceived and designed the survey and I supervised and analysed the survey results.

3.4- Survey Questionnaire

The survey was divided into two parts. The first was completed by all the respondents and included six vignettes. These presented a variety of patients with OSAS; for each the respondent chose from one of five recommendations regarding the patient's driving ranging from no restriction to advising not to drive at all. The second part was limited to clinicians who completed DVLA medical forms (SL2C and SL2VC). Respondents were presented with further vignettes of patients who had been offered CPAP, focusing on the questions posed by the DVLA. Additional information was requested, including on the use of objective tests for assessing fitness to drive. Three sleep specialists from the BTS Specialist Advisory Group reviewed the vignettes and confirmed that they were reflective of everyday clinical practice. Respondents were reminded twice to answer as if there was a real patient before them and not how they thought they would be expected to respond.

3.5- Clinical Vignettes

Each vignette described an OSAS patient who either had one or more of the following factors; normal or abnormal ESS; sleepiness specific whist driving such as episodes of nodding and/or driving on the rumble strip; moderate or severe sleep disordered breathing and any other significant factor contributing to their underlying clinical condition such as shift working pattern or BMI. Respondents were asked to choose one option from five of the advice they would give in a real time clinical situations for each of the vignettes. Part 2 presented further vignettes from patients

who had been treated with CPAP and focussed on questions asked by the DVLA. All the vignettes are described below.

Part-1 Vignettes (To all the respondents)

1- The patient had a sleep study because of loud snoring. No daytime sleepiness and in particular no problems driving. A sleep study has shown AHI 18 events per hour; the Epworth score is 7. How would you advise the patient about driving?

A- Can drive without restriction, but like anyone else should not drive if feel sleepy

B- Can drive, but should avoid long journeys, motorway driving etc, until satisfactorily treated

C- Should not drive at all, until satisfactorily treated

D- I would not offer the patient any advice about driving

E- Others, please specify

……………………………………………………………………………………..

2- The Patient presented to their GP because of loud snoring and concern about occasional witnessed apnoeas. They deny daytime sleepiness and in particular say no problems driving; even long distances. A sleep study has shown AHI 45 events per hour; Epworth score 3. How would you advise the patient about driving?

A- Can drive without restriction, but like anyone else should not drive if feel sleepy

B- Can drive, but should avoid long journeys, motorway driving etc, until satisfactorily treated

C- Should not drive at all, until satisfactorily treated

D- I would not offer the patient any advice about driving

E- Others, please specify

……………………………………………………………………………………..

3- Patient consulted GP because of tiredness. GP elicited a history of snoring and questioned possibility of obstructive sleep apnoea. Sleep study: AHI 25 events / hour; Epworth score 15. Says no problems at all with sleepiness while driving- recently drove 4 hours on a motorway without a break and with no problems. How would you advise the patient about driving?

A- Can drive without restriction, but like anyone else should not drive if feel sleepy

B- Can drive, but should avoid long journeys, motorway driving etc, until satisfactorily treated

C- Should not drive at all, until satisfactorily treated

D- I would not offer the patient any advice about driving

E- Others, please specify

....

4- Patient referred by ENT to whom had presented with troublesome snoring. This was prompted by the partner; patient denies a problem. Sleep study: AHI 17 events / hour; Epworth 17. Shift worker (alternating 4 days 3 nights with breaks between). Patient only falls asleep if relaxing or bored. Never if occupied. Patient says that this is typical of most of work colleagues. Says that has never had any problems driving; apart from once year ago on a very long drive; 10 hours; returning from holiday; when nodded off very briefly. How would you advise the patient about driving?

A- Can drive without restriction, but like anyone else should not drive if feel sleepy

B- Can drive, but should avoid long journeys, motorway driving etc, until satisfactorily treated

C- Should not drive at all, until satisfactorily treated

D- I would not offer the patient any advice about driving

E- Others, please specify
....

5- A sleep study was performed as part of routine work up of a patient being assessed for bariatric surgery. The patient admits to being "a little sleepy occasionally" but had not thought much of it until now. They would not have bothered to see their GP about it. During motorway driving gets tired after 1 hour. Has nodded on one occasion a couple of years ago - since then says always stops for a rest as soon as starts to feel tired. Sleep study: AHI 30 events per hour; Epworth 18. How would you advise the patient about driving?

A- Can drive without restriction, but like anyone else should not drive if feel sleepy

B- Can drive, but should avoid long journeys, motorway driving etc, until satisfactorily treated

C- Should not drive at all, until satisfactorily treated

D- I would not offer the patient any advice about driving

E- Others, please specify

....

6- AHI 55 events per hour; Epworth score 18. Patient denies any problems driving but then recounts a recent journey on a motorway during which describes nodding at the wheel and hitting the rumble strip on several occasions. Says it was a one off after an early start; a much longer drive than does normally and a particularly hard day's work. Says does not normally drive on motorways; driving usually confined to maximum 20 minutes to and from work; to shops etc. How would you advise the patient about driving?

A- Can drive without restriction, but like anyone else should not drive if feel sleepy

B- Can drive, but should avoid long journeys, motorway driving etc, until satisfactorily treated

C- Should not drive at all, until satisfactorily treated

D- I would not offer the patient any advice about driving

E- Others, please specify

……………………………………………………………………………………………………..

Part-2 Vignettes (Only for clinicians completing DVLA forms)

The DVLA forms sometimes ask about "irresistible" and sometimes about "excessive" drowsiness and about whether the patient is adequately compliant with treatment. We would like you to answer these questions for each of the following patients. PLEASE ANSWER ALL QUESTIONS AS IF THIS WAS A REAL PATIENT - SAY WHAT YOU WOULD DO IN EVERYDAY CLINICAL PRACTICE.

1- Patient with AHI 35/hr Epworth 22. Now established on CPAP. Recent AHI 10/hr on CPAP - machine used 7 hours that night. Epworth 14. Patient says feels much better and that he is no longer having problems driving.   He does still fall asleep watching television in the evening, but not at other times. A download from the machine reveals that he is using it for an average of 3.2 hours per night with a range of 0 to 7 hours. He had stopped driving (his decision) but has now restarted.

A- Is the patient adequately compliant with treatment-?

Yes/ No

B- Does the patient continue to experience irresistible drowsiness-?

Yes/No

C- Does the patient continue to experience excessive drowsiness-?

Yes/No
……………………………………………………………………………………………………..

2- At diagnosis - AHI 28 events per hour, Epworth 15. On CPAP AHI 3, Epworth 5. Average use 6 hours per night. Patient regularly spends weekends in a caravan, a 3 hour drive away. Does not use CPAP in caravan because there is no electricity and admits to sometimes feeling drowsy at the wheel returning home on Sunday night. His partner does not drive.

A- Is the patient adequately compliant with treatment-?

Yes/ No

B- Does the patient continue to experience irresistible drowsiness-?

Yes/No

C- Does the patient continue to experience excessive drowsiness-?

Yes/No

....

3- Diagnostic AHI 45 events / hr, Epworth 14. Now established on CPAP AHI 7 Epworth 9. Average use 4 hours per night, but wide range. Usually does not use at all two nights per week. The days following a night without CPAP admits to falling asleep during breaks at work, but says has no problems driving.

A- Is the patient adequately compliant with treatment-?

Yes/ No

B- Does the patient continue to experience irresistible drowsiness-?

Yes/No

C- Does the patient continue to experience excessive drowsiness-?

Yes/No

....

4- Diagnostic AHI 80 events per hour, Epworth 22, patient admitted falling asleep regularly while driving. On CPAP AHI 10 events per hour Epworth 12. Says feels

44

much better and no longer having any problems driving but continues to fall asleep watching television, while reading and if a passenger in a car.

A- Is the patient adequately compliant with treatment-?

Yes/ No

B- Does the patient continue to experience irresistible drowsiness-?

Yes/No

C- Does the patient continue to experience excessive drowsiness-?

Yes/No

…………………………………………………………………………………………..

5- Patient with AHI 35 events/hour, Epworth score 13. Prior to diagnosis the patient admits that continued to drive despite regularly nodding at the wheel, because "had to". On a couple of occasions had found himself driving over the rumble strip onto the hard shoulder. Tried CPAP but could not tolerate it at all. Has decided to lose weight and has lost 3 kg so far over two months. Says feels better. Epworth score is 12. There is a moderate chance of dozing or falling asleep watching TV, reading, sitting quietly after lunch, lying down for a rest in the afternoon and as a passenger in a car for an hour without a break. Says that has now realised the importance of not driving when tired and whenever starts to feel tired always stops for a rest and a cup of coffee. Says that since tried CPAP has never nodded while driving nor driven over the rumble strip.

A- Is the patient adequately compliant with treatment-?

Yes/ No

B- Does the patient continue to experience irresistible drowsiness-?

Yes/No

C- Does the patient continue to experience excessive drowsiness-?

Yes/No

....

3.6- Objectives

3.6.1- Primary Objective

To assess the degree of variation in advice a patient with OSAS might receive in everyday clinical practice at diagnosis and after starting CPAP.

3.6.2- Secondary Objectives

To establish which factors, if any, influenced the advice given, to evaluate the use of objective tests in assessing fitness to drive and whether clinicians report patients to the DVLA.

3.7- Statistical analysis

The statistical analysis was carried out using Graph Pad Prism 6 software, San Diego California USA and SPSS version 20. Statistical significance was set at $p < 0.05$. Chi-square tests were used to evaluate which factors influenced the advice given. As the respondents were matched pairs of subjects, McNemar's test was used to establish the significant difference in the residual drowsiness. Binary logistic regression analysis was performed to evaluate the significant variables. Data that were not normally distributed are presented as median and Inter quartile range. Qualitative analysis was done using thematic analysis [107].

3.8- Results

Approximately 3150 members of the BTS, BSS and ARTP were invited to complete the survey. 467 (15%) respondents completed the first stage of the survey, 210 said they completed forms for the DVLA and of these 178 completed the second stage.

Although the response rate of 15% appears low it should be stressed that those who received the e-mail were told they should only complete the survey if they saw patients with OSAS and advised them about driving; for reference 538 BTS members indicate that sleep medicine is one of their 3 specialty interests. In the ERS there are 461 members affiliated to Group 04.02 (Sleep and Control of Breathing) as main group, among which 27 are from UK. I believe therefore that the survey results reflect the views of clinicians working in this field.

3.8.1- Demographics (Table 3-1)

Table 3-1 showing the demographical details of the respondents

Professional background	
Sleep Consultant	109 (23%)
Non Sleep Consultant	138 (30%)
Specialist Trainee	103 (22%)
General Practitioner	3 (1%)
Nurse	44 (9%)
Physiologist	48 (10%)
Others	22 (5%)
Gender	
Males	272 (58%)
Females	195 (42%)
OSAS patients seen per month	
None	21 (4%)
1-5/month	167 (36%)
6-20/month	119 (26%)
> 20/month	160 (34%)
Age of the respondents	
Less than 35 Years	115 (24%)
36-50 Years	251 (54%)
More than 50 Years	101 (22%)
Region of Work	
Northern Ireland	6 (2%)
Wales	17 (3%)
East Of England	23 (5%)
South East Coast	23 (5%)
South Central	25(5%)
North East	34 (7%)
East Midlands	32 (7%)
Scotland	31 (7%)
West Midlands	36 (8%)
South West	46 (10%)
North West	50 (11%)
London	63 (13%)
Yorkshire and Humber	81 (17%)

3.8.2- Advice given at diagnosis of OSAS

There was wide variability in the advice given in all the six vignettes (Figure 3-1). To a patient what matter is whether driving is permitted or not. For this reason, and for subsequent ease of presentation and analysis, responses "would not give advice" or "other" are omitted and data presented in table 3-2 as "yes" would allow driving [no restriction (option 1) and would allow driving but should avoid long journeys and motorways (option 2)] versus "no" should not drive at all (option 3). Respondents who chose "would not give advice" and "other" were specialist nurses and non-medically qualified professionals including sleep physiologists. Conflicting advice was given by different clinicians for each vignette. In the least contentious (vignette-1) 94% of clinicians would allow driving. In the most contentious (vignette-3) a patient had a 50% chance of being allowed to drive.
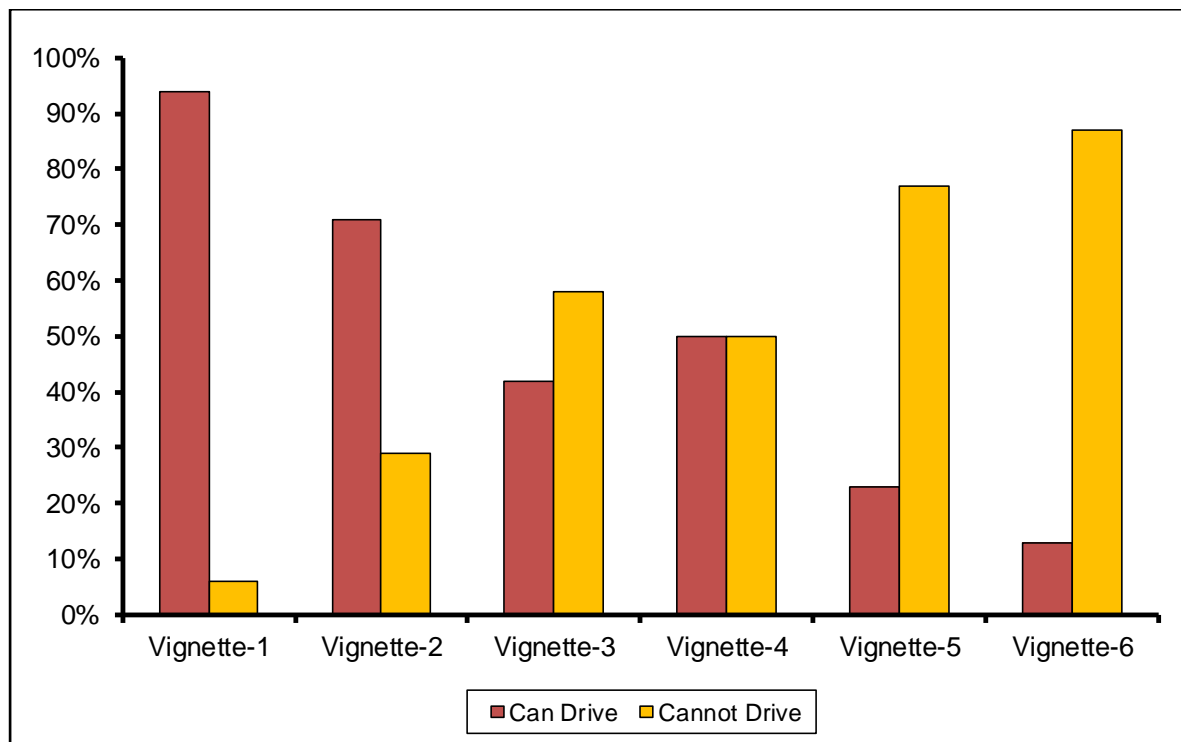
Figure 3-1 showing the likelihood of conflicting advice given by the clinicians at diagnosis of OSAS.

Table 3-2 showing the percentage of patients who would be advised they could and could not drive. Key information from each vignette is also presented.

Vignette	ESS	Any sleepiness while driving	AHI	Other Factors	"Yes" (%)	"No" (%)	"Yes" (%) 95% CI	"No" (%) 95% CI
1	7	Nil	18/hr	Nil	94%	6%	92%-96%	4%-8%
2	3	Nil	45/hr	Nil	71%	29%	61%-81%	19%-39%
3	15	Nil	25/hr	Nil	42%	58%	32%-52%	48%-68%
4	17	Nodded briefly	17/hr	Shift worker	50%	50%	40%-60%	40%-60%
5	18	Nodded Once	30/hr	Bariatric surgery assessment	23%	77%	15%-31%	69%-85%
6	18	Nodded, hit rumble strip	55/hr	Nil	13%	87%	9%-17%	83%-91%

3.8.3- Reasons for variability in the advice given

3.8.3.1- Gender

There was a statistically significant difference in the driving advice given in vignettes 2 to 5 respectively depending on the gender of the respondent (Table 3-3). Female clinicians are more likely than male clinicians to advise patients to continue driving.

Table 3-3 showing the gender variation in various clinical vignettes

Vignette	Females "Can Drive"	Females "Cannot Drive"	Males "Can Drive"	Males "Cannot Drive"	P- Value	OR (95% CI)
1	161 (95%)	9 (5%)	233 (94%)	16 (6%)	0.63	1.22 (0.5-2.8)
2	105 (66%)	55 (33%)	185 (75%)	62 (25%)	0.04	0.63 (0.4-0.9)
3	84 (49%)	89 (51%)	89 (36%)	155 (64%)	0.01	1.64 (1.1-2.4)
4	101 (59%)	73 (41%)	114 (45%)	139 (55%)	0.008	1.68 (1.1-2.4)
5	50 (27%)	132 (73%)	50 (19%)	209 (81%)	0.04	1.58 (1.0-2.4)
6	29 (16%)	155 (84%)	31 12%)	234 (88%)	0.21	1.41 (0.8-2.4)

3.8.3.2- Professional background

Consultants with a special interest in sleep medicine are more likely to advise patients to continue driving in vignettes 2, 5 and 6 respectively when compared to those without a special interest in sleep medicine (Table 3-4). However there was no difference in the advice given when the consultant grade was compared to non consultant grade (trainees, general practitioner and allied health care professionals) (Table 3-5).

Table 3-4 showing the difference in advice given in various clinical vignettes between sleep and non-sleep consultants

Vignette	Sleep Consultant "Can Drive"	Sleep Consultant "Cannot Drive"	Non Sleep Consultant "Can Drive"	Non Sleep Consultant "Cannot Drive"	P- Value	OR (95% CI)
1	94 (94%)	7 (6%)	116 (94%)	7 (6%)	0.70	0.81 (0.2-2.3)
2	75 (83%)	15 (17%)	81 (64%)	45 (36%)	0.002	2.7 (1.4-5.3)
3	39 (41%)	56 (59%)	43 (35%)	80 (65%)	0.35	1.2 (0.74-2.2)
4	47 (48%)	50 (52%)	58 (47%)	65 (53%)	0.84	1.0 (0.61-1.7)
5	29 (29%)	71 (71%)	21 (13%)	107 (87%)	0.02	2.08 (1.1-3.9)
6	18 (19%)	85 (81%)	10 (8%)	121 (92%)	0.02	2.5 (1.1-5.8)

Table 3-5 showing the difference in advice given between consultants and other health care professionals in various clinical vignettes

Vignette	Consultant "Can Drive"	Consultant "Cannot Drive"	Non Consultant "Can Drive"	Non Consultant "Cannot Drive"	P- Value	OR (95%CI)
1	210 (94%)	14 (6%)	156 (95%)	9 (5%)	0.74	0.86 (0.36-2.0)
2	156 (72%)	60 (28%)	116 (71%)	47 (29%)	0.82	1.05 (0.67-1.6)
3	82 (38%)	136 (62%)	61 (41%)	87 (59%)	0.48	0.85 (0.56-1.3)
4	105 (48%)	115 (52%)	94 (55%)	77 (45%)	0.15	0.74 (0.5-1.1)
5	50 (22%)	178 (78%)	42 (24%)	131 (76%)	0.57	0.87 (0.54-1.3)
6	28 (12%)	206 (88%)	25 (14%)	150 (86%)	0.48	0.81 (0.45-1.4)

3.8.3.3- Number of patients seen

The advice given to OSAS patients was dependent on the number of patients seen per month by the clinician. Respondents who saw more than 5 patients per month were more likely to advise patients to continue driving compared to those who saw less than 5 patients per month. This was statistically significant in vignette 2 and 6 respectively (Table 3-6).

Table 3-6 showing the differing advice given in various clinical vignettes depending on the number of patients seen per month by the health care professionals

Vignette	> 5/month "Can Drive"	> 5/month "Cannot Drive"	< 5/month "Can Drive"	<5/month "Cannot Drive"	P- Value	OR (95% CI)
1	238 (95%)	13 (5%)	154 (92%)	12 (8%)	0.38	1.4 (0.6-3.2)
2	183 (87%)	57 (13%)	108 (64%)	59 (36%)	0.01	1.7 (1.1-2.7)
3	110 (45%)	136 (55%)	63 (37%)	108 (63%)	0.10	1.3 (0.9-2.0)
4	121 (49%)	128 (51%)	94 (53%)	84 (47%)	0.39	0.8 (0.5-1.2)
5	64 (25%)	193 (75%)	36 (20%)	148(80%)	0.18	1.3 (0.8-2.1)
6	41 (15%)	225 (85%)	16 (8%)	168 (92%)	0.03	1.9 (1.0-3.5)

3.8.3.4- Age

The advice given to the patients was not dependent on the age of the clinicians. This was not significant in all the vignettes (Table 3-7).

Table 3-7 showing no difference among the age group of the clinicians and the advice given

Vignette-1	Less than 35 Years	36-50 Years	More than 50 Years	P- Value
Can Drive	95 (98%)	94 (92%)	91 (93%)	0.16
Cannot Drive	2 (2%)	8 (8%)	7 (7%)	
Vignette-2				
Can Drive	69 (76%)	69 (69%)	70 (73%)	0.56
Cannot Drive	22 (24%)	31 (31%)	26 (27%)	
Vignette-3				
Can Drive	41 (44%)	42 (42%)	35 (36%)	0.51
Cannot Drive	52 (56%)	59 (59%)	62 (64%)	
Vignette-4				
Can Drive	52 (54%)	53 (51%)	56 (56%)	0.81
Cannot Drive	45 (46%)	50 (49%)	44 (44%)	
Vignette-5				
Can Drive	23 (23%)	23 (22%)	25 (25%)	0.88
Cannot Drive	76 (76%)	82 (78%)	76 (75%)	
Vignette-6				
Can Drive	15 (16%)	14 (13%)	10 (10%)	0.42
Cannot Drive	85 (85%)	93 (87%)	93 (90%)	

3.8.4- Advice given following treatment with CPAP

210 (45%) of clinicians completed forms for the DVLA. 32 responses were excluded as the questions were unanswered or were incomplete leaving 178 responses for analysis.

3.8.4.1- Residual Drowsiness

The DVLA forms enquire whether the patient still suffers from "irresistible" (SL2C) or "excessive" (SL2VC) drowsiness. There was inconsistency in the assessment of residual drowsiness when completing the form. The advice depended on the choice of words "irresistible" and "excessive" on the DVLA form. In each vignette the same clinician was more likely to say "yes" to "excessive" than to "irresistible" (71+/12% v/s 42+/-10%, P-0.0045) (Table 3-8).

3.8.4.2-CPAP Compliance

Across the vignettes there was a disagreement between clinicians regarding what constituted adequate compliance with CPAP (Figure 3-2); "yes" responses ranged from 13% to 64%.

Table 3-8 showing the key factors in the vignettes of patients after CPAP treatment and the McNemar's test showing significant variability in what a patient will be told by the same clinician depending on whether the DVLA form asks about "irresistible" or "excessive" drowsiness

Vignette	Pre CPAP AHI	Pre CPAP ESS	Post CPAP AHI	Post CPAP ESS	CPAP use	Other factors	"Excessive" "Yes"	"Irresistible" "Yes"	McNemar's Test	
									P-value	OR (95% CI)
7	35/hr	22	10	14	3.2 hr	Had stopped driving (his decision) but has now restarted	116(65%)	46(26%)	<0.0001	6.8(3.7-13.7)
8	28/hr	15	3	5	6 hr	Does not use CPAP during weekend	94 (53%)	69(39%)	0.0009	2.3 (1.4-4.1)
9	45/hr	14	7	9	4 hr	Does not use CPAP for 2 days in a week	128(72%)	92(52%)	<0.0001	2.7 (1.6-4.7)
10	80/hr	22	10	12	N/A	No longer having any problems driving but continues to fall asleep watching television, while reading and if a passenger in a car.	140(79%)	77(43%)	<0.0001	6.7(3.5-14)
11	35/hr	13	Nil	12	N/A	Intolerant to CPAP, lifestyle modifications, weight loss 4 kilograms	151(85%)	87(49%)	<0.0001	13.8 (5-43)
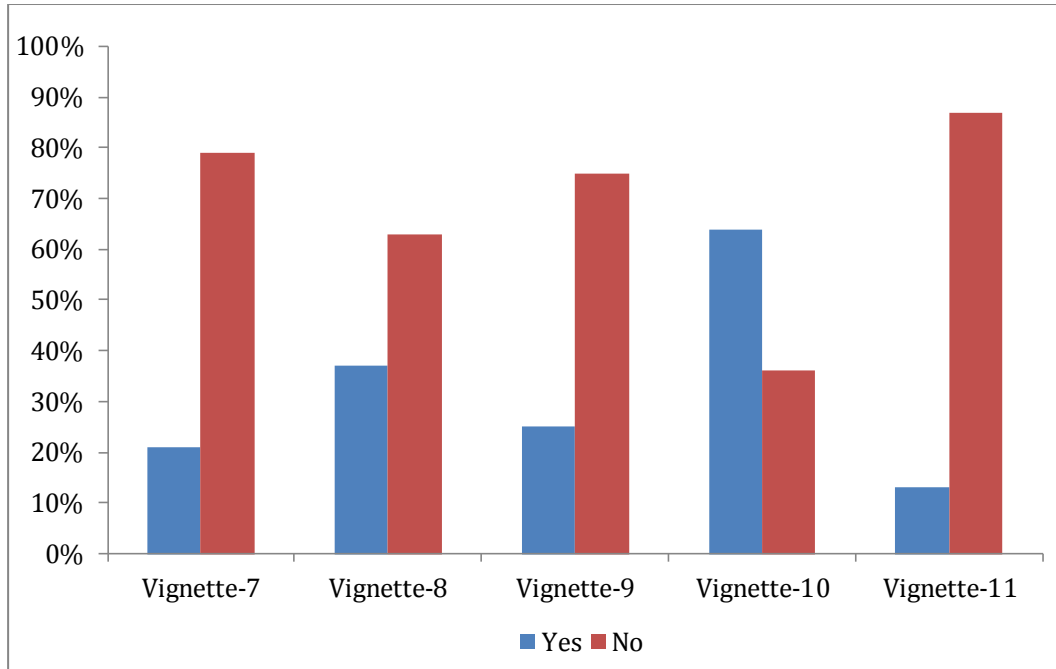
Figure 3-2 showing the disagreement between clinicians regarding adequate CPAP compliance

3.8.5- Drivers reported to the DVLA

131 (74%) of the clinicians who completed the DVLA form had never reported patients to the DVLA, 42 (23%) had reported 1-4 times and 5 (3%) had reported more than 5 times.

3.8.6- Influence of sleepiness in different situations

Respondents were asked to weigh the value given to ESS, description of general sleepiness and sleepiness specifically whilst driving when assessing a patient's fitness for driving. On average clinicians gave equal importance to all three but with a wide range (Table 3-9)

Table 3-9 showing the influence of sleepiness contributing to the clinicians' assessment of driving fitness in OSAS patients

	Median	Inter Quartile Range	Range
ESS	3	2-4	0-10
General Sleepiness	3	2-4	0-7
Sleepiness whilst Driving	3	2-4	0-7

3.8.7- Use of Objective Tests

1% of clinicians always and 4% frequently use objective tests to help in their assessment. Professional drivers are more likely to undergo objective tests than non professional drivers (52% v/s 38%, P-0.0002, OR-1.75) (Table 3-10).

Table 3-10 showing the current practice of using objective tests by the clinicians' prior giving advice to patients regarding driving

	MSLT	MWT	OSLER	DADS
Never	123 (69%)	133 (75%)	131 (74%)	165 (93%)
Occasionally	52 (29%)	39 (22%)	39 (21%)	11 (6%)
Frequently	3 (2%)	4 (2%)	7 (4%)	2 (1%)
Always	0 (0%)	2 (1%)	1 (1%)	0 (0%)
	HGV	Taxi	High mileage	Others
Never	79 (44%)	92 (52%)	107 (60%)	113 (63%)
Occasionally	62 (35%)	53 (30%)	52 (29%)	49 (27%)
Frequently	17 (10%)	16 (9%)	8 (4%)	8 (5%)
Always	20 (11%)	17 (9%)	11 (7%)	8(5%)

MSLT- Multiple Sleep Latency Test, MWT- Maintenance of Wakefulness Test, OSLER- Oxford Sleep Resistance, DADS- Divided Attention Driving Simulator

3.8.8- Qualitative analysis

Seventy nine (38%) of respondents provided additional information. Forty (50%) were sleep consultants, representing the most experienced clinicians. Most responses related to the complexity of the issue of driving and OSAS and where the responsibility lies in negotiating this challenge, with the role of DVLA, clinician and patient all discussed.

3.8.8.1- Understanding current DVLA guidance

Twenty six respondents commented on the complexity of advising OSAS patients about driving. Responses were about the guidance provided by the DVLA and views about its usefulness were divided, even amongst experienced sleep specialists. A few sleep consultants felt the guidance was adequate, but most viewed it as open to interpretation. Others felt it placed too much responsibility on health professionals, a view echoed by non-specialist consultants and trainees who a found advising patient not to drive was stressful as they felt guidance was not clear.

Terms such as *'pragmatic'*, *'common sense'* and *'proportionate'* were used by experienced sleep consultants to describe their approach, which considered the patient's lifestyle, vocation and symptoms. Some sleep consultants expressed the view that less experienced physicians were more likely to be *'harsher'* than more experienced colleagues. In contrast, some non sleep specialists felt that some sleep consultants do not take the problem seriously enough; a view echoed by a small number of sleep consultants who expressed the opinion that much stricter, standardised, guidance is needed.

"The medico-legal frame is currently flimsy and inadequate to the point neither patients, community nor sleep specialists are properly informed and duly protected" (Sleep Consultant).

"The DVLA guidelines are rather open to interpretation. Devolving the responsibility to the clinician caring for the patient to give his/her interpretation of the DLVA's advice is not good enough" (Trainee).

3.8.8.2- Responsibility

The issue of responsibility appeared repeatedly; 55 respondents mentioned it and 21 provided a clear statement of their views. It was broadly agreed that it is the doctor's responsibility to advise the patient of the DVLA rules about driving and OSAS. However, most felt non-compliance was high and views about how to manage this and whose responsibility it is to manage this varied. Although few had reported patients to the DVLA, others had used this as a threat if the patient did not stop driving.

"DVLA tell us they want everyone to notify them of a new diagnosis and that it's up to them to say if they can drive or not – not us!" (Sleep Consultant)
"*The medical professional is not facing up to our responsibility to protect the public from drivers who are not fit to drive. "* (Sleep Consultant).

Persuading patients to report their diagnosis to DVLA was challenging; some tried to couch their advice in terms of doing what is morally right, others appealed to the patient's sense of responsibility.

"I take the view that this is an issue of individual responsibility and stress this to patients, explaining the serious consequences to them and others if they get it wrong" (Sleep Consultant).

Although the responsibility not to drive was seen to rest with the patient, respondents were concerned if patients had an accident whilst driving Clinicians reiterated the importance of ensuring patients are aware of their responsibility; and used letters and leaflets to back up their advice. However,

many said that documenting advice in this way was a way of defending themselves from criticism.

"[I]*insist on the patient reporting to the DVLA, even though I know they often don't, makes me feel like I have covered my tail"* (Sleep Consultant).

Whilst respondents agreed they would advise professional HGV/PSV drivers not to drive until they received treatment and were stable, there was less consistency when it came to people who rely on their cars for other reasons.

*"[I have]… mentioned to HGV drivers and a train driver that I would consider reporting them" (*Sleep Consultant)*.*

"can be damaging to stop driving in someone whose livelihood may depend on it (salesman or driving to work). Obviously need stricter controls for vocational drivers" (Non-Sleep Consultant).

3.8.8.3- Dealing with patients sensitively

The need to deal with patients sensitively and not penalise them for seeking help was viewed as vital. There was a tension between a physician's responsibility to advise patients not to drive, and keeping them in treatment. Many felt that being too prescriptive would be counter-productive and discourage some patients from seeking treatment. A few were of the opinion that they would be prepared to advise patients not to drive until treated if they could start treatment immediately.

"It is frustrating that patients who have had this for months (or more likely years) are penalised and a more supportive approach is often helpful in practice. However, that leaves the patient in the position of driving illegally" (Consultant)

3.8.8.4- Assessment and Treatment

Ten respondents specifically discussed concerns about a lack of reliable, objective measures of sleepiness and many mentioned this in passing. The ESS was viewed as too easy for patients to manipulate and many of the objective tests, whilst viewed as more reliable are often only available at specialist or tertiary centres requiring referral, and potential delay.

"I do think it would be useful if the DVLA had a robust, objective scheme for assessing vigilance […] it is very hard to deprive someone of their livelihood without something objective" (Sleep Specialist).

3.9- Discussion

This survey has shown that there is considerable variability in clinician's opinions regarding whether a patient with OSAS should drive or not. The vignettes were deliberately chosen to be contentious; less variability may have been seen if less contentious vignettes had been presented. However all were within the range of what is seen regularly in sleep clinics. There can be a wide range of opinion, even about issues that may not appear contentious. This is also true in the healthcare arena [108] where attempts have been made to reduce variability by the development of guidelines, care pathways and protocols and these have been shown to improve outcomes [109]. When possible they are based on evidence but in the absence of evidence; expert consensus. The results of this survey, particularly the qualitative analysis of free text, suggest that consensus may be difficult to achieve. Clinicians do not appear to differentiate between sleepiness generally and specifically while driving. Despite the fact that ESS correlates poorly with road accidents and performance on driving simulators, it is still considered in the decision-making

process.

Objective tests are seldom used and while it could be argued that this is because of lack of access there is little evidence that these tests are useful in determining whether a patient is safe to drive or not. When they were used, the most common was the MSLT, which although an objective tests of sleepiness has little relationship to driving. The MWT or the behavioural alternative the OSLER test is more logical ; a pathological MWT is associated with simulated driving impairment- very sleepy and sleepy patients had more inappropriate line crossings than control drivers (P= < 0.05) [73]. In a small study comparing patients with untreated OSAS and controls, the number of inappropriate line crossings correlated with MWT scores (r^2= -0.339; P= < 0.05) [72]; however this is not sufficiently discriminating for everyday practice. The lack of reliable objective tests means that the clinician is dependent on the account given by the patient; fear of losing their licence may lead them to underplay symptoms. The DVLA is the ultimate arbiter of whether an individual can hold a licence or not. What constitutes adequate compliance with CPAP and residual drowsiness are both contentious, however there is some evidence to suggest adequate compliance if the mean CPAP usage is more than 4 hours per night for more than 70% of nights [110]. Clinicians are more likely to consider drowsiness "excessive" (vocational form) than "irresistible"(standard form) consistent with a higher standard being applied to vocational drivers, as intended by the DVLA. However the DVLA is also concerned specifically with sleepiness while driving (personal communication); a number of vignettes (7, 9, 10 and 11) were of patients with general sleepiness, but who denied problems while driving. Many clinicians

appear either to be answering the question about residual drowsiness literally or do not believe the patient; these questions could be improved by including the words "while driving".

3.10- Conclusion

The current DVLA and EU statements are discussed in Chapter-1. Clinicians want better guidance from the DVLA. This must include clear definitions of residual sleepiness, that the key issue is of whether persists during driving, and what is meant by adequate compliance. Research needs to be directed towards a better understanding of what factors in OSAS impair driving performance, how these can be assessed and the development and use of objective tests which can inform decision-making and lead to greater consistency in the decisions reached. If not patients will lose confidence in a process that is inconsistent and therefore unfair.

Chapter-4

Sleepiness at the wheel, real and simulated driving in untreated male Obstructive Sleep Apnoea Syndrome (OSAS) patients and controls; what is normal?

4.1- Abstract

Advising patients with OSAS about driving is challenging. By integrating self-reported measures of sleepiness, safety-critical driving incidents and performance on a driving simulator task in male controls and untreated male OSAS patients we have established what constitutes "normal". 129 untreated OSAS patients (Age= 53 $\pm$ 12 years, ESS= 14 $\pm$ 5, ODI= 41 $\pm$ 26 dips/hour, BMI= 36 $\pm$ 8 kg/m2, driving license years= 31 $\pm$ 12) and 79 controls (Age= 56 $\pm$ 15 years, ESS= 4 $\pm$ 3, BMI= 28 $\pm$ 8 kg/m2, driving license years= 34 $\pm$ 17) completed a driving questionnaire prior to a simulator session. Questionnaire responses, simulator outcome and various continuously measured variables were compared between the two groups. OSAS patients, but no control reported episodes of nodding (> 2 times), admitted to high chance of sleepiness while driving and a DSS of more than 7. All controls completed the simulator test and none had an unprovoked crash whereas 11% of OSAS patients had an unprovoked crash and 9% were unable to complete the test. SDLP, a marker of poor driving performance was significantly worse in the OSAS group as compared to controls (P= 0.03, 95% CI= 0.0043 to 0.0095) and this predicts MUoLDS failure. The group at risk can be identified by key questions about sleepiness during driving, real driving incidents, driving sleepiness score, simulator outcome and outputs from an advanced PC based simulator. Defining what constitutes "normal" and risk stratification based on various parameters holds promise and may aid the clinician in better decision making.

4.2- Introduction

Patients with OSAS are at increased risk of being involved in a RTA because of increased sleepiness and poor concentration. However RTAs are not the sole preserve of patients with OSAS and not all patients are unsafe drivers. Clinicians are often asked to make recommendations about fitness to drive and many find this challenging [111]. There is considerable variation in the advice that a patient is likely to receive [112]. Guidelines [48, 49] are largely based on expert opinion and there is a need for more evidenced based recommendations. Although there is a trend towards increased likelihood of accidents with more severe sleep-disordered breathing (SDB), the relationship is not sufficiently robust on which to base decisions about driving for an individual [59]. Furthermore there are conflicting data about the relationship between perceived sleepiness and the likelihood of being involved in an RTA [31,113]; Sleepiness specifically while driving rather than in general, is a better predictor of which OSAS patients are at increased risk of RTAs [67]. There are also conflicting data about the relationship between objective tests for increased daytime sleepiness and driving [70,114,115].

The Institute for Transport Studies at the University of Leeds, UK has developed a sophisticated fully immersive driving simulator (UoLDS). Alongside this full-scale simulator, a PC-based mini simulator has been developed using the same software (MUoLDS). In a previous study over 50% of patients with significant OSAS, sufficient to warrant a trial of CPAP completed approximately one hour of "motorway driving" without incident [83] suggesting that it is a more credible reflection of driving and by using standard

deviation of lane position (SDLP) a subset of patients with OSAS who failed a simulated driving test could be identified. A normal range for sleepiness while driving and driving simulator performance particularly based on SDLP and other continuously measured variables have not been described. Furthermore the criteria used to indicate "fail" in the previous study [84], while intuitively reasonable, need to be validated against a control group.

4.3- Aims

The aims of this exploratory cohort study were to define a normal range in controls and to compare them with a group of untreated OSAS patients against this in the following domains:

- Self-reported sleepiness while driving

- Safety – critical driving incidents

- MUoLDS performance

4.4- Methods

Patients attending the sleep clinic at St. James's University Hospital with a confirmed diagnosis of OSAS [Apnoea Hypopnea Index (AHI) of > 10 hour and/or Oxygen Desaturation Index (ODI) of 4% dips in saturation >10/hour] on respiratory variable overnight sleep study (Embletta, Resmed; Abingdon, Oxford) or overnight oximetry and who drove regularly with a full valid UK driving licence were approached. Majority (n=110, 85%) of OSAS patients had a sleep study and the rest (n=19, 15%) had an oximetry. All OSAS patients who had an oximetry had moderate to severe sleep disordered breathing. The study was exclusively focused on males because in a previous

study significant difference in MUoLDS performance was found between the genders [31]. Subjects with no symptoms of OSAS and with an ESS of < 10 were recruited as controls. Participants who were taking sedating medications were excluded. Participants in both groups were provided with an information leaflet and written consent was obtained. The MUoLDS runs were done during the day between 0900-1700 hours. Both the practice and the test runs were done in a single sitting. The MUoLDS has been validated by a study done by Ghosh et al [84]. Ethics approval for this study was obtained from the NHS Research Ethics Committee (09/H1311/58).

4.4.1- Inclusion and exclusion criteria for the study

The inclusion and exclusion criteria for this study are listed below.

<u>Inclusion Criteria</u>

- Age more than 18 years

- Males

- Should possess a full valid UK driving licence

- Previous experience of driving on a UK motor way

- Able to drive on an automatic mode for more than an hour on the MUoLDS

- Able to consent

- Documented evidence of OSA either on an overnight oximetry and or a home variable sleep study

- ESS of more than 10

- No previous CPAP treatment

- No regular use of sedatives or stimulants

Exclusion Criteria

- Females

- Unable to consent

- Non OSA sleep disordered breathing

- Previous diagnosis of OSA and or previous use of CPAP

- ESS of less than 10

- No previous experience of UK motor way driving

- Having a provisional driving licence

- Use of sedation or stimulants

- Unable to drive for more than an hour on the MUoLDS

4.4.2- Scoring of Sleep Disordered Breathing

The overnight oximetry and the home variable sleep study were scored as per the American Association of Sleep Medicine scoring Manual [10]. The definitions for scoring are as follows

- **Apnoea** – 10 seconds or more duration of 90% or more flow reduction

- **Obstructive apnoea** – 10 seconds or more duration of 90% or more reduction in flow with effort being made to breathe

- **Hypopnoea-** 10 seconds or more of a 30% reduction in flow and effort with a 3% or more dip in desaturation

- **Oxygen desaturation Index-** 4% dip rate with severity classifications similar to Apnoea/Obstructive hypopnoea. The classification is shown in 4.4.2.1 sub section.

4.4.2.1- Severity classifications

- 0-5 events/hour - Normal

- 6-15 events/hour - Mild

- 16-30 events/hour - Moderate

- More than 30 events/hour - Severe

4.5- Questionnaire

All completed a questionnaire about sleepiness while driving and whether they had an accident, near miss or nodded off at the wheel in the previous year. This was developed with the input of patients and healthcare professionals and has not been validated. The same questionnaire was used in a previous study [84]. All were informed that responses were anonymised and would not be used to make fitness-to-drive decisions. Using a four-point scale, based on that used for ESS, participants were asked to rate their chance of feeling sleepy whilst driving at different times of the day (early morning, mid-morning, noon, mid-afternoon, evening and late at night) and durations of journey (less than 30 minutes, 30 minutes-1hour, 1-2 hours and more than 2 hours). The maximum score was 30 and was termed their "Driving Sleepiness Score" (DSS). The fatigue and driving questionnaire is listed in appendix III.

4.6- Statistical analysis

Statistical analysis was carried out using Graph Pad Prism 6 software (San Diego, California, USA) and SPSS statistics (Version 24; IBM, New York, USA). The level of significance was set at $P = <0.05$. Unpaired t test was used to evaluate for baseline demographics and MUoLDS specific measures

between the two groups. To exclude ambiguity, SDLP-3 of more than one or infinity were scored as one. Chi-square test was used to evaluate the safety-critical driving incidents and MUoLDS performance. Binary regression analysis was used for univariate and multivariate analysis to predict MUoLDS outcome. Receiver operating characteristic (ROC) curve analysis to calculate the discriminative power, positive predictive value (PPV) and negative predictive value (NPV) were performed to predict "failure" on MUoLDS. For the post hoc analysis, one- way ANOVA with Bonferroni's multiple comparison test (corrected) was used for univariate analysis to evaluate the different variables between the high risk, intermediate risk and low risk groups.

4.7- Results

4.7.1- Demographics (Table 4-1)

Table 4-1 Demographics: controls and OSAS patients

Mean +/- SD	Controls (n=79)	Patients (n=129)	P- Value	CI of difference
Age (Years)	56 ± 14	54 ± 11	0.16	-0.97 to 5.8
ESS	4 ± 2	13 ± 5	< 0.0001	7.7 to 10.1
BMI (Kg/m2)	28 ± 5	36 ± 8	< 0.0001	5.9 to 6.8
Licence (years)	34 ± 17	31 ± 12	0.25	-6.0 to 1.8
ODI		41 ± 26		

ESS: Epworth Sleepiness Score, BMI: Body Mass Index (kg/m2), ODI: Oxygen Desaturation Index, CI: Confidence interval

Controls and OSAS patients were well matched for age and driving experience, but OSAS patients had a significantly higher BMI and were more sleepy as evidenced by the higher ESS.

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4.7.2- Driving Questionnaire (Table 4-2 and 4-3)

OSAS patients compared to controls admitted to significantly more nodding episodes whilst driving, had significantly more near misses, a worse accident history and also admitted to more sleepiness while driving. This is shown in detail in table 4-3. No control admitted to nodding more than 2 times, high chance of sleepiness whilst driving or had a total DSS of more than 7 compared to 28% of OSAS patients (Table 4-2). A univariate analysis was performed between the two groups (Table 4-3). There was a statistically significant difference between the percentage of OSAS patients admitting to nodding 1 to 2 times, having a near miss or an accident in the last year or to a moderate chance of sleepiness while driving than controls.

Table 4-2 showing the DSS between controls and OSAS patients

DSS	Controls (n=79)	OSAS patients (n=129)
Score 0	46% (36)	33% (43)
Score 1-7	54% (43)	39% (50)
Score more than 7	0% (0)	28% (36)

Table 4-3 showing the real time driving events between controls and OSAS patients

Events (In the last one year)	Controls (n=79)	Patients (n=129)	P- Value	OR (95% CI)
Nodding (Never)	94% (74)	74% (95)	0.0003	5.2 (1.97 - 14.2)
Nodding (1-2 times)	6% (5)	17% (22)	0.02	3.0 (1.1 - 8.4)
Nodding (more than 2 times)	0% (0)	9% (12)	0.003	18.0 (1.0 – 317)
Near miss	19%(15)	32% (41)	0.04	1.98 (1.0 - 3.8)
Accident history*	4% (3)	13% (17)	0.02	3.8 (1.0 - 13.5)
Sleepiness while driving (Never)	49% (39)	34% (44)	0.02	1.8 (1.0 - 3.3)
Sleepiness while driving (Slight chance)	47% (37)	31% (40)	0.02	1.96 (1.0 - 3.5)
Sleepiness while driving (Moderate chance)	4% (3)	15% (19)	0.01	4.3 (1.2 - 15.3)
Sleepiness while driving (High chance)	0% (0)	20% (26)	<0.0001	36 (2.4 – 678)
Driving Sleepiness Score (DSS) < 7	100% (79)	75% (97)	<0.0001	53 (3.1- 878)
Driving Sleepiness Score (DSS) >7	0% (0)	25% (32)		

* Minor damage, Major damage, Garage work, Insurance claims in the last one year

4.7.3- MUoLDS outcome (Table 4-4)

No controls had an unprovoked crash and none were unable to complete the simulator run but more crashed at the brake event. In contrast 11% of OSAS patients had an unprovoked crash but completed the test; 9% were unable to complete the test. No control had an unprovoked crash or was unable to complete the test these were considered a "fail" in OSAS patients on the MUoLDS. The MUoLDS outcome is shown in table 4.4.

Table 4-4 showing the MUoLDS outcome in controls and OSAS patients

Criteria	Controls (n=79)	OSAS patients (n = 129)	P- Value	OR (95% CI)
Unprovoked crash	0% (0)	11% (14)	0.002	20 (0.002 - 0.85)
Unable to complete	0% (0)	9% (12)	0.005	17 (0.003 - 1.01)
< 95% in lane-2	3 % (2)	4% (5)	0.6	1.5 (0.12 - 3.4)
Veer- event crash	5% (4)	10% (13)	0.2	2.1 (0.66 - 6.6)
Brake event crash	49% (39)	35% (45)	0.03	1.8 (1.0 - 3.2)
No events	43% (34)	31% (40)	0.07	1.6 (0.94 - 3.2)

Discriminatory factors between the pass and fail group were evaluated. On univariate analysis, ESS, BMI and ODI were significant (Table 4-5).

Table 4-5 showing the univariate variables between the two groups

Variables (mean +/-SD)	"Pass Group" (n=103)	" Fail Group" (n=26)	P- Value
Age (Years)	53 $\pm$ 11	50 $\pm$ 13	0.18
ESS	13 $\pm$ 5	15 $\pm$ 5	0.04
BMI (Kg/m2)	35 $\pm$ 7	42 $\pm$ 8	< 0.0001
ODI	39 $\pm$ 24	53 $\pm$ 31	0.01
Licence (Years)	34 $\pm$ 17	32 $\pm$ 12	0.28

BMI-Body mass index, ESS- Epworth Sleepiness Score, ODI-Oxygen desaturation index, DL- Driving licence in years

4.7.4- MUoLDS performance based on measured variables (Table 4-6)

There was a significant difference in SDLP-3 between controls [mean $\pm$ SD (0.39 $\pm$ 0.10), 95% CI (0.37- 0.42)] and OSAS patients [mean $\pm$ SD (0.44 $\pm$ 0.18), 95% CI (0.41- 0.48)], P= 0.04. 15% of OSAS patients had SDLP-3 more than the 95th centile for controls and 9% had SDLP-3 greater than the worst control (figure 4-1).

Table 4-6 shows the measured variables between controls and OSAS patients

Parameters (mean +/- SD)	Controls (n=79)	OSAS patients (n= 129)	P= Value
Veer-RT	1.5 $\pm$ 0.45	1.5 $\pm$ 0.57	0.77
TTC 3	13 $\pm$ 21	9 $\pm$ 12	0.12
Min Hw 3	0.61 $\pm$ 0.26	0.58 $\pm$ 0.36	0.47
HFS 3	0.58 $\pm$ 0.07	0.57 $\pm$ 0.07	0.32
SDLP 3	0.39 $\pm$ 0.12	0.44 $\pm$ 0.18	0.04
Brake-RT	2.9 $\pm$ 1.4	2.9 $\pm$ 1.4	0.65
Speed (miles)	64 $\pm$ 5	62 $\pm$ 8	0.07

Veer RT- veer reaction time, TTC 3- time to collision in epoch 3, Min Hw- minimum headway, SDLP 3- standard deviation of lane position in epoch 3, Brake RT- brake reaction time
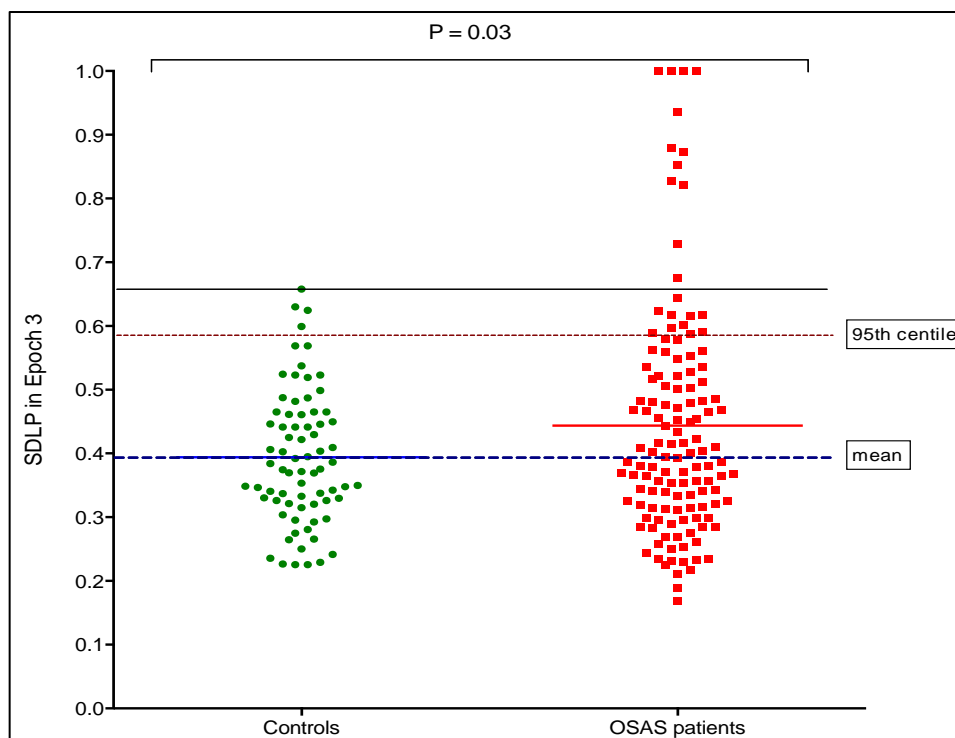
Figure 4-1 showing the SDLP-3 between controls and OSAS patients

4.7.5- Predictors of MUoLDS failure (Table 4-7)

Binary logistic regression analysis was performed to predict "failure" on MUoLDS.

BMI, ESS, ODI and SDLP-3 were significant factors on univariate analysis.

Table 4-7 showing the predictors of "failure" on MUoLDS

Parameters (Unpaired- t test)	Fail (n=26) (20%)	Pass (n=103) (80%)	P= Value	Mean difference
Age	50+/-13	53+/-11	0.18	3.4 +/- 2.6
BMI	42+/-8	35+/-7	<0.0001	- 6.7 +/- 1.5
ESS	15+/-5	13+/-5	0.04	-2 +/- 1
ODI	53+/-31	39+/-24	0.01	-14.4 +/- 5.6
DL (years)	32+/-12	34+/-17	0.28	2.2 +/-1.8
DSS (Total)	6+/-7	5+/-5	0.41	-1 +/- 1.3
SDLP-3	0.64 +/-0.21	0.40 +/-0.14	< 0.0001	-0.24 +/- 0.03
Parameters (Chi-square test)				**OR (95% CI)**
DSS < 7	69% (18)	77% (79)	0.43	0.68 (0.26 to 1.8)
DSS > 7	31% (8)	23% (24)		
No Nodding	77% (20)	73% (75)	0.67	1.2 (0.45 to 3.4)
Nodding (1-2 times)	15% (4)	17% (18)	0.8	0.85 (0.26 to 2.8)
Nodding (> 2 times)	8% (2)	10% (10)	0.75	0.77 (0.16 to 3.8)
Near Miss	42% (11)	29% (30)	0.19	1.8 (0.73 to 4.3)
Accidents	12% (3)	14% (14)	0.78	0.82 (0.22 to 3.1)
BMI- Body mass index, ESS- Epworth sleepiness score, ODI- Oxygen desaturation index, DL- Driving licence, DSS- Driving sleepiness score, SDLP- Standard Deviation of Lane Position(in epoch 3) Difference in mean is shown with unpaired t tests and OR (95% CI) is shown with chi-square tests				

However on multivariate analysis, only BMI (P = 0.008) and SDLP-3 (P = < 0.0001) predicted "failure" on MUoLDS. The area under the curve (AUC) was 0.87. This is shown in figure 4-2. The positive predictive value (PPV) was 96.30% (95% CI, 91.24% to 98.48%) and negative predictive value (NPV) was 60.47% (95% CI, 49.06% to 70.84%).
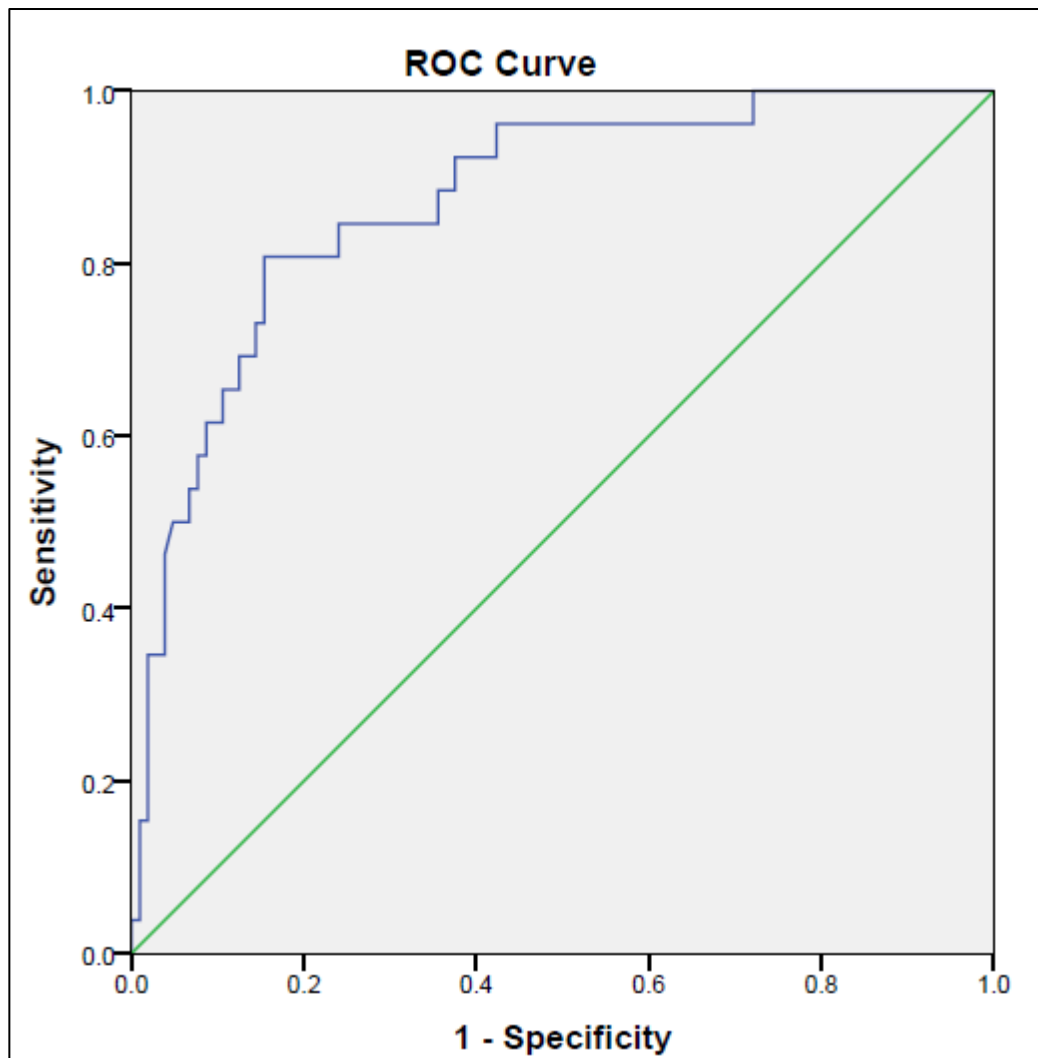
Figure 4-2, showing the Area under Curve (AUC) in predicting MUoLDS failure

4.7.6- Defining criteria to identify the "at risk driver" (Risk stratification)

I defined "flags", based upon comparisons with controls, to stratify patients driving risk (Tables 4-8 and 4-9). Red flags were factors that were not seen at all in controls,

amber flags were seen in some controls but patients were statistically significantly worse.

4.7.6.1- Red flags / High risk group (Table 4-8)

Table 4-8 Red flag criteria

1	Admitting to nodding at the wheel 2 or more times in the last year
2	Admitting to high chance of sleepiness while driving
3	Driving Sleepiness Score of more than 7
4	Failure to complete the MUoLDS test run
5	Unprovoked crash on the MUoLDS
6	SDLP-3 greater than 0.66

4.7.6.2- Amber flags / Intermediate risk group (Table 4-9)

Table 4-9 Amber flag criteria

1	Admitting to nodding at the wheel 1-2 times in the last year
2	Accident history or a near miss in the last year
3	Moderate chance of sleepiness while driving
4	SDLP-3 more than 0.59 (95th percentile) and below 0.66

On multiple comparison testing (Bonferroni's) there was a significant difference between the high risk and the other two groups but not between the group with intermediate risk and the group with the same risk as the control population. BMI and ESS were significantly worse in the high risk group as compared to the other groups (Table 4-10).

Table 4-10 showing the various variables between the three groups

Univariate Analysis (mean +/-SD)	High risk (n=55) (43%)	Intermediate risk (n=54) (42%)	Low risk (n=20) (15%)	P- Value (One-way ANOVA)
Age	51+11	53+12	56+11	0.26
BMI (Kg/m2)	39+8	34+6	34+8	0.001
ESS	16+-5	12+5	12+4	<0.0001
ODI	46+-28	37+25	38+20	0.16

BMI-Body mass index, ESS- Epworth Sleepiness Score, ODI-Oxygen desaturation index

4.8- Discussion

Ideally accident risk should be predicted using an objective test; the limitations of self-reporting, particularly when the licence may be at risk, are well recognized [37]. However this is always likely to be difficult in a condition which is variable; even patients who fall asleep during real driving and have an accident will have been driving, often for prolonged periods, on many other days, without incident. It is therefore not surprising that I was not able to demonstrate a relationship between failure on the simulator and real life events. However I was able to demonstrate, in a test which is a more credible test of the ability to maintain alertness while driving than for instance the MWT [73] that a subset of patients with OSAS performed differently to control subjects. This study confirms the findings of a previous study [84] that over 50% of patients were able to drive for approximately one hour without incident. Furthermore I have shown that there was a difference in SDLP in epoch 3 between patients and controls and there were a significant number of patients with values much worse than controls. SDLP has the advantage that it is measured continuously, has been shown to predict task failure accurately on the MUoLDS [84] and it, or a similar measure, has been shown to indicate the at risk driver in other

studies [75,116]. The brake event at the end of the drive was designed such that even controls would find it difficult to avoid a crash and indicated the end of the test. That more controls than patients failed the brake event is surprising, but patients who had had an unprovoked crash, failed to complete the test or the veer event did not reach the brake event. It is possible that had they got to the end of the test most of these would also have failed the brake event. If available sophisticated PC based simulators with realistic graphics may be of some help in indicating which patients are not safe to drive, but further work needs to be done before these can be considered robust enough for routine clinical use. My data suggest that patients with severe OSA, very high BMI and a high ESS (Table 4-10) who deny problems driving, or those, in whom there is concern, should be tested on such a simulator. Failure to complete, an unprovoked crash or high SDLP should be taken as evidence to support recommending that driving cease. Accepting the limitations of self-reporting it will always be important even if a robust objective test becomes available; however many patients are honest and if they admit to high risk driving behaviour they should cease driving regardless of the results of any other tests. Any driver may experience sleepiness while driving and it is important to understand what is "normal". I have suggested factors that indicate that an individual differs markedly from controls indicating potentially unsafe driving. Red flags were those factors which were not seen at all in controls and amber those where there was a statistically significant difference between patients and controls. These were defined post hoc. As with the use of symptoms to indicate the likelihood of cancer these should not be used in an all or nothing way. The circumstances surrounding an event are important; for instance the significance of haemoptysis in a non-smoking young individual, with frequent nosebleeds, is very different to that when it is seen in a middle aged

smoker, occurring persistently over time. In the same way an episode of nodding at the wheel after a very long journey has a different significance to nodding repeatedly during short journeys. Similarly accidents, and near misses, may not be the fault of the individual, nor attributable to sleepiness. However the attribution of "fault" is not straight forward either. While there are clearly some situations in which the driver cannot be blamed, for instance an individual parked by the roadside and hit by another car, there are many when both drivers feel that the accident was not their fault. The same is true with regard to what constitutes a "near miss". The questionnaire did not allow participants to provide any further information; I did not want events to be dismissed that they considered, erroneously, to not be their fault. I suggest that the "flags" that my study has identified are important questions to ask; positive answers to any raise concerns about that individual's continued driving, but do not of themselves suggest that driving must cease. Negative responses however should not be taken to indicate that the patient does not have a problem. This is a situation common to many other aspects of medicine.

The "likelihood" of sleepiness is subjective; one person's "high" is another's "moderate" chance. However nodding at the wheel is an all or nothing phenomenon; an individual either has or has not nodded at the wheel Nodding at the wheel indicates that the driver has fallen asleep, albeit transiently; a few seconds longer and an accident is likely. It also shows that the individual has made an error of judgement by continuing to drive despite increasing sleepiness; accidents due to driver sleepiness are always preceded by a period of time when the individual is fighting sleep [117]. However patients involved in an accident, when it is likely that it is due to them falling asleep at the wheel may deny this either because they do not

recall doing so or because they understand the implications of admitting such [118]. The same may be true with regard to admitting to nodding at the wheel; however a positive response to this question, particularly more than twice in the last year, indicates a high risk driver. The questionnaire relies upon an individual telling the truth and patients may underestimate or deny problems. Patients are more likely to answer an anonymous questionnaire truthfully and the data presented here are more likely to represent the true situation, but the possibility that individuals were not truthful, or underestimated their symptoms, cannot be discounted. My data shows that as compared to controls, untreated male OSAS patients report frequent nodding more than 2 times in the last year (OR= 18), near miss (OR=2), history of accidents (OR=3.8) and admit to high chance of sleepiness (OR= 36). This is consistent with other case control and population based studies (Table 1-1, Chapter-1). When discussing driving restriction patients sometimes state "everyone struggles to stay awake driving occasionally" or similar and challenge the advice. Any sleepiness at the wheel is potentially dangerous and is unacceptable; these data justify restricting driving in certain OSAS patients by showing them that their sleepiness is not "normal". My data also indicate which patients, who deny problems driving, should be tested upon an advanced PC-based driving simulator and criteria on which they should then be advised not to drive.

4.9- Study limitations

This study focused only on males. A previous study has shown that MUoLDS performance and task failure is gender dependent [119]. It is likely that the questionnaire responses are still valid in females, but this will need to be confirmed in future studies. I only studied patients with OSAS of sufficient severity to warrant a

trial of CPAP; this is the group in which a risk assessment needs to be made about an individual's continued driving. It would not be appropriate to say that someone did not have OSAS of sufficient severity to warrant treatment but severe enough that a patient should not drive. Annex III of the European Union (EU) Directive on Driving Licences, states that patients with OSAS, needing treatment in the opinion of a physician and not receiving it, should not receive an unconditional licence [51]. However this study needs to be extended to patients with milder OSAS, as they may still be at increased risk of an accident. I did not perform sleep studies in controls. However the questionnaire included questions about symptoms of snoring or OSA and controls were only included if they had a low probability for OSAS. I think it is very unlikely that I included any controls with significant OSAS and the results of the driving simulation and the questionnaire would support this. I only used data from the third epoch as a previous study showed that on average this is representative of the whole study. However it is possible, on an individual basis that more detailed analysis including other epochs may pick up other at risk drivers. The driver seat used was not a standard driving seat and thus some patients may have found it cumbersome whilst driving (personal feedback) and thus may have had issues with accelerator and brake pedals. This may have impacted upon the reaction times and outcome. Finally seeking information from licensing authorities or police has limitations also as not all accidents, and certainly not near misses or episodes of nodding at the wheel, are reported.

4.10- Conclusion

In common with many other situations in medicine a decision about whether an individual should cease driving is complex and cannot be based on simple yes or no

criteria. I suggest several factors, each of which needs to be weighed for significance. Licensing authorities remain the final arbiter of who should cease driving but they should be guided by clinicians. Individuals should be advised of their personal responsibility; they may be safe to drive most of the time, but not after a poor night's sleep. No one should drive if they cannot guarantee to maintain full concentration and vigilance. Advanced PC based driving simulators have a role in identifying the at risk driver, but further research is required.

Chapter-5

A randomised trial evaluating the issue of repeatability and the effect of incentives on an office based advanced driving simulator (MUoLDS) in OSAS patients

5.1- Abstract

On average, patients with OSAS are at higher risk of being involved in road traffic accidents. No objective tests have been shown to predict reliably whether an individual is safe to drive or not and there is significant variation in the advice given by the clinicians. Using continuously measured variables in an advanced PC-based driving simulator the at risk patients can be identified with a high degree of accuracy. Individuals may "raise their game" if they know that their licence is at stake. 150 untreated OSAS patients (males-131) were randomised to either test repeatability (n=50) or the effect of an incentive (n=100). All performed a simulator run, after initial acclimatisation. For the repeatability test, patients performed the simulator run on two separate occasions; they were not informed about how well they had performed during the test. To test the effect of an incentive patients again performed the simulator run on two separate occasions but just prior to the second run they were told they would be given a prize if they could improve their performance by 10%. SDLP in epoch 3 and "veer" reaction time (Veer-RT) were the co-primary outcome variables. Classification of patients based on pre-set criteria into "fail" and "pass" were the secondary outcome variables.137 patients (repeatability -48, incentive -89) completed the trial. The median duration between the two simulator runs was 13 days (range, 5-55). There was no difference in the SDLP in epoch 3 (P = 0.54, Δ change = -0.01) and Veer-RT (P = 0.37, Δ change = 0.13) in the repeatability arm. There was no effect of an incentive on SDLP in epoch 3 (P= 0.39) and Veer-RT (P= 0.15). 67% of OSAS patients passed the MUoLDS on both the occasions, 12% failed on both the MUoLDS run. However 21% of OSAS patients either passed on run one and failed on run two or the vice versa. Continuously measured variables (SDLP and Veer-RT) on the MUoLDS are consistent. There is no effect of a simple incentive;

hence no effect on motivation. Although a majority of OSAS patients did not change the MUoLDS outcome, one in five patients changed categories from either a pass to fail or vice versa.

5.2- Introduction

Driving a vehicle is a skill that involves complex integrated higher cortical function, alertness, concentration and eye to hand coordination [40]. The risk assessment of any OSAS patient should include a combination of subjective and objective assessment that leads to greater consistency in the decisions reached. An objective test should evaluate many aspects of safe driving and thus should aid in the decision-making. If the MUoLDS is to be useful in the clinical setting it is important that the test should be consistent. A major concern about the use of any test, the result of which will be dependent upon the motivation of the subject, is that the individual may be able to "raise their game" if their driving licence is at stake. I hypothesised that the variables (SDLP in epoch 3 and Veer-RT) recorded on the MUoLDS could be repeated on different runs and patients cannot improve the simulator performance despite an incentive offer. I have therefore evaluated these factors further by conducting a randomised trial.

5.3- Methods

This was a single centre randomised trial conducted at St James's University Hospital, Leeds, UK. Ethical approval was obtained from the local NHS Research Ethics Committee (12/YH/0168). Untreated patients with a confirmed diagnosis of OSAS [apnoea hypopnoea index (AHI) and/or oxygen desaturation index (ODI- 4% dips in saturation of more than 10/hour) on respiratory variable overnight sleep study

(Embletta; ResMed, Abingdon, UK) or overnight oximetry who possessed a full UK valid driving licence (Group 1 or Group 2) and who drove on the motorways were approached. Patients with nocturnal symptoms and excessive day time sleepiness and an ESS of more than 10 were classified as OSAS patients. All patients were told not to drink any caffeinated drinks within two hours of the start of the study and all completed a driving questionnaire. The MUoLDS practice and test run were done in a single sitting between 0900 and 1700 hours on two separate days.

5.4- Study design and randomisation

The randomisation was done using a computer-generated random number sequence for both the arms. The process was supervised by an independent clinical trials co-ordinator who was not associated with the study. I was completely blinded to the randomisation process. Patients (n=150) were randomised into two arms, repeatability (n=50) or effect of incentive (n=100) respectively. The sample size was based on Martin Bland's work [120]. To assess the repeatability issue patients performed the simulator run on two separate occasions. To assess the effect of a simple incentive patients performed the simulator run on two separate occasions but just prior to the second run were offered a prize (a gift voucher of £25) if they could improve their performance by 10% (in SDLP during Epoch 3). All simulator runs were undertaken prior to starting CPAP treatment. The trial protocol is listed in appendix IV.

5.4.1- Inclusion and exclusion criteria for the study

The inclusion and exclusion criteria for this study are listed below.

Inclusion Criteria

- Age more than 18 years

- Should possess a full valid UK driving licence

- Previous experience of driving on a UK motor way

- Able to drive on an automatic mode for more than an hour on the MUoLDS

- Able to consent

- Documented evidence of OSA either on an overnight oximetry and or a home variable sleep study

- ESS of more than 10

- No previous CPAP treatment

- No regular use of sedatives or stimulants

Exclusion Criteria

- Unable to consent

- Non OSA sleep disordered breathing

- Previous diagnosis of OSA and or previous use of CPAP

- ESS of less than 10

- No previous experience of UK motor way driving

- Having a provisional driving licence

- Use of sedation or stimulants

- Unable to drive for more than an hour on the MUoLDS

5.5- Simulator road layout and scenario

This is described in detail in Chapter 2.

5.6- Measures and end points

Task failure was defined as unprovoked crash or unable to complete the test. Unprovoked task failure and failure to complete the test should not happen during normal simulated driving and any subject falling into this category was considered to have "failed" the simulator test. Subjects who completed the test or had either a veer event crash or brake event crash or spending less than 5% of the study time (2½) minutes were deemed to have "passed". Continuous variable parameters of driving behaviour were recorded at 60 Hz and these included SDLP and Veer-RT. Definitions of various driving simulator parameters are described in Chapter 2.

5.6.1- Primary Outcome

SDLP in epoch 3 and "veer" reaction time (Veer-RT) were the primary outcome variables.

5.6.2- Secondary Outcome

Classification of patients into "Fail" and "pass" were the secondary outcome variables.

5.7- Statistical analysis

The statistical analysis was carried out using Graph Pad Prism 6 software, San Diego California USA and SPSS version 20. Statistical significance was set at $P= < 0.05$. Data are presented as mean +/- SD. Both in the repeatability and incentive arm, SDLP in epoch 3 and Veer-RT in run 1 were compared with run 2 in using

paired t tests (2-tailed). The difference in SDLP in epoch 3 and Veer-RT in run two were compared between groups A and B, using unpaired t tests (2-tailed) to evaluate the effect of incentives. Chi-square contingency test was used to evaluate the MUoLDS outcome between run-1 and 2 respectively. Unpaired t tests (2- tailed) and Chi-square contingency test were used for post hoc analysis.

5.8- Results

150 patients were randomised to assessment of repeatability arm (n=50) or the effect of an incentive (n=100). 137 patients completed the trial (figure 5-1). The baseline demographics of the patients are shown in Table 5-1. The median duration between the two runs on the MUoLDS was 13 days (range, 5-55).

Table 5-1: Demographics of OSAS patients in the two arms

	Repeatability Arm (n= 48)	Incentive Arm (n= 89)	P- Value
Age (Years)	55 +/- 12	52 +/- 10	0.11
Males (%)	88% (n= 42)	85% (n= 76)	
Females (%)	12% (n=6)	15% (n=13)	
BMI (mean +/-SD) (kg/m2)	36 +/- 7	37 +/- 8	0.5
ESS (mean+/-SD)	15 +/- 3	16 +/-3	0.16
ODI (mean +/-SD)	40 +/- 29	38 +/- 23	0.7
DL (mean +/- SD) (Years)	30 +/- 2	29 +/- 4	0.3

BMI, body mass index; ESS, Epworth Sleepiness Score; ODI, oxygen desaturation index, DL; Driving Licence
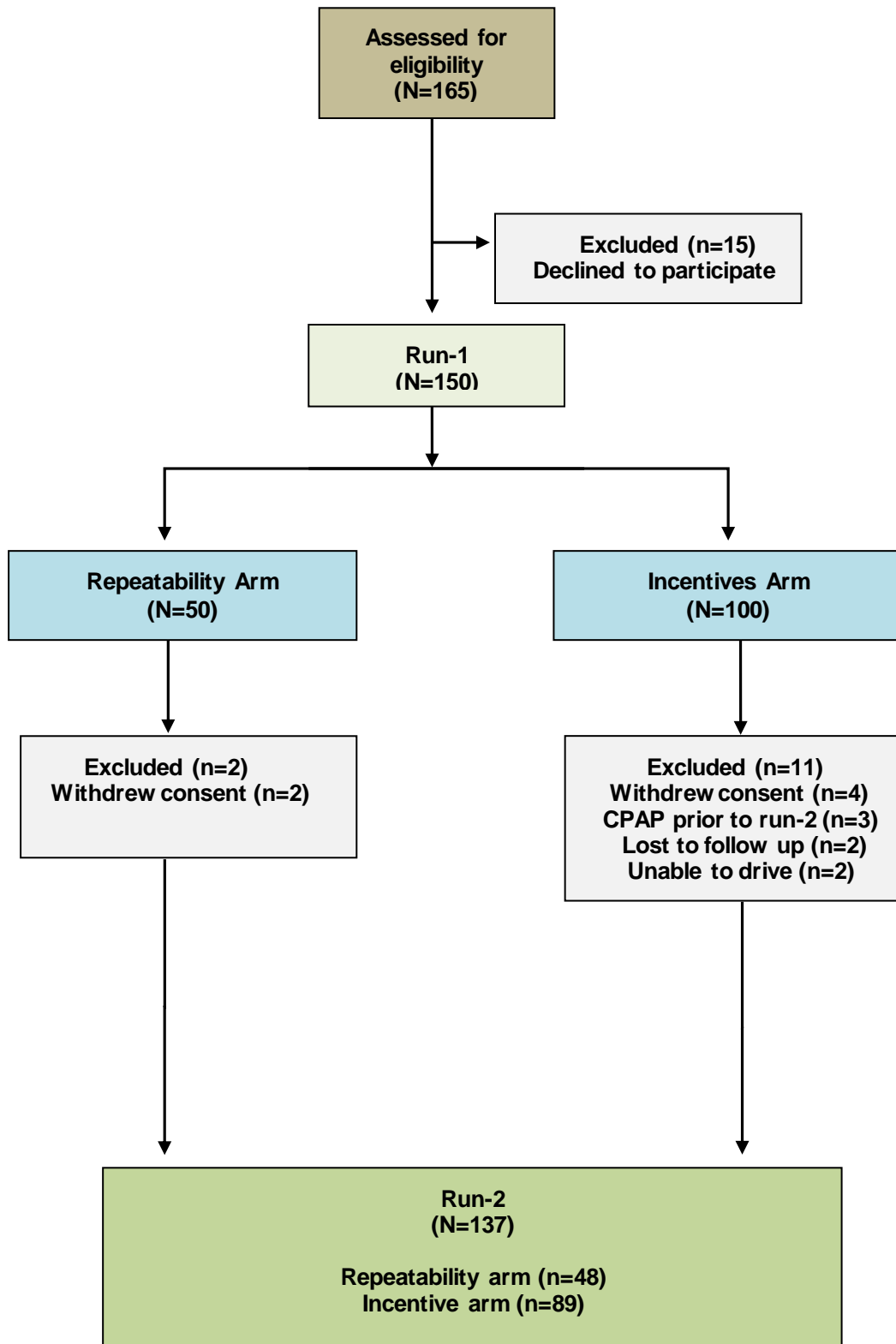
Figure 5-1, CONSORT flow diagram of the trial randomisation

5.8.1- Primary Outcome

5.8.1.1- Effect of repeatability

There was no statistically significant difference in the SDLP in epoch 3 and Veer- RT during MUoLDS run one and two respectively. The continuously measured variables were consistent and thus were repeatable (Table 5-2; figure 5-2 and 5-3).

Table 5-2, showing the SDLP-3 and Veer-RT in run one and two (effect of repeatability)

Variable	MUoLDS- Run 1	MUoLDS- Run 2	Δ change	P- Value
SDLP-3 (mean +/- SD)	0.45 +/- 0.16	0.44 +/- 0.16	-0.01	0.54
Veer-RT(mean +/- SD)	1.58 +/- 0.51	1.72 +/- 0.30	0.13	0.37

SDLP-3, standard deviation of lane position in epoch-3, Veer-RT, veer reaction time.
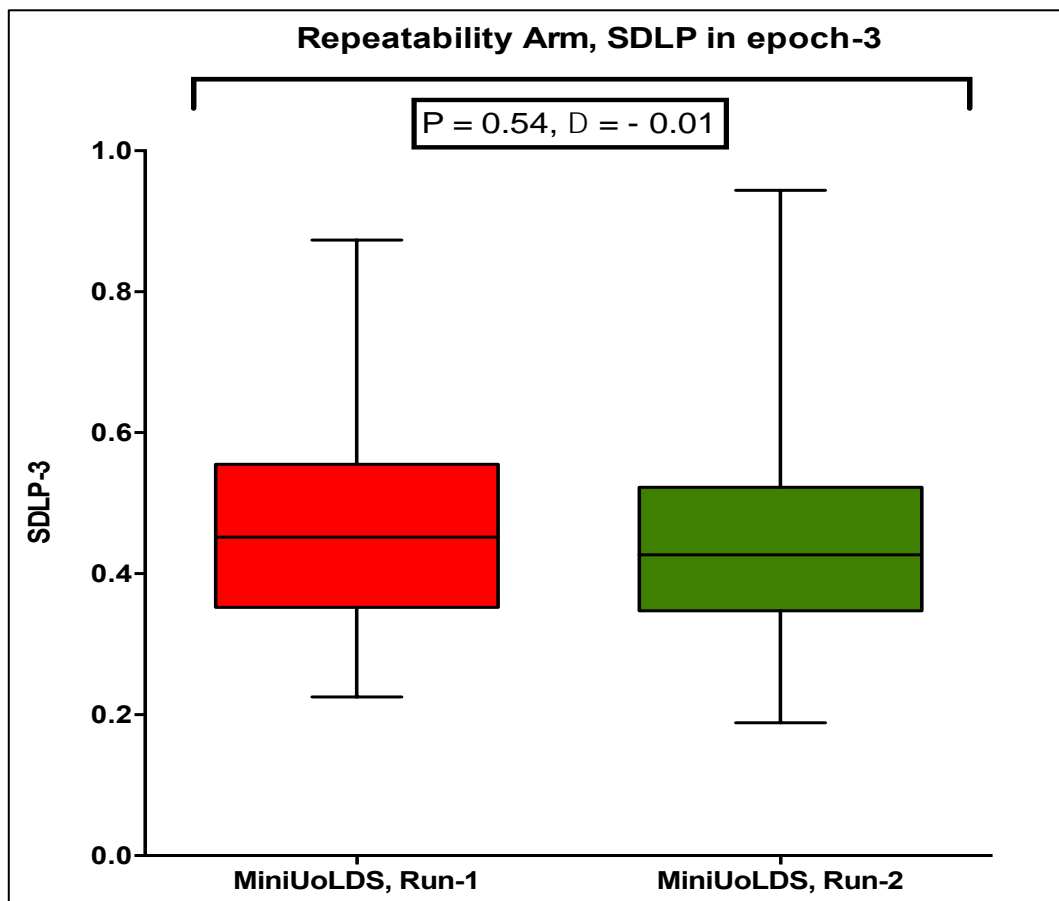
Figure 5-2 showing the repeatability of SDLP-3 between the two MUoLDS runs
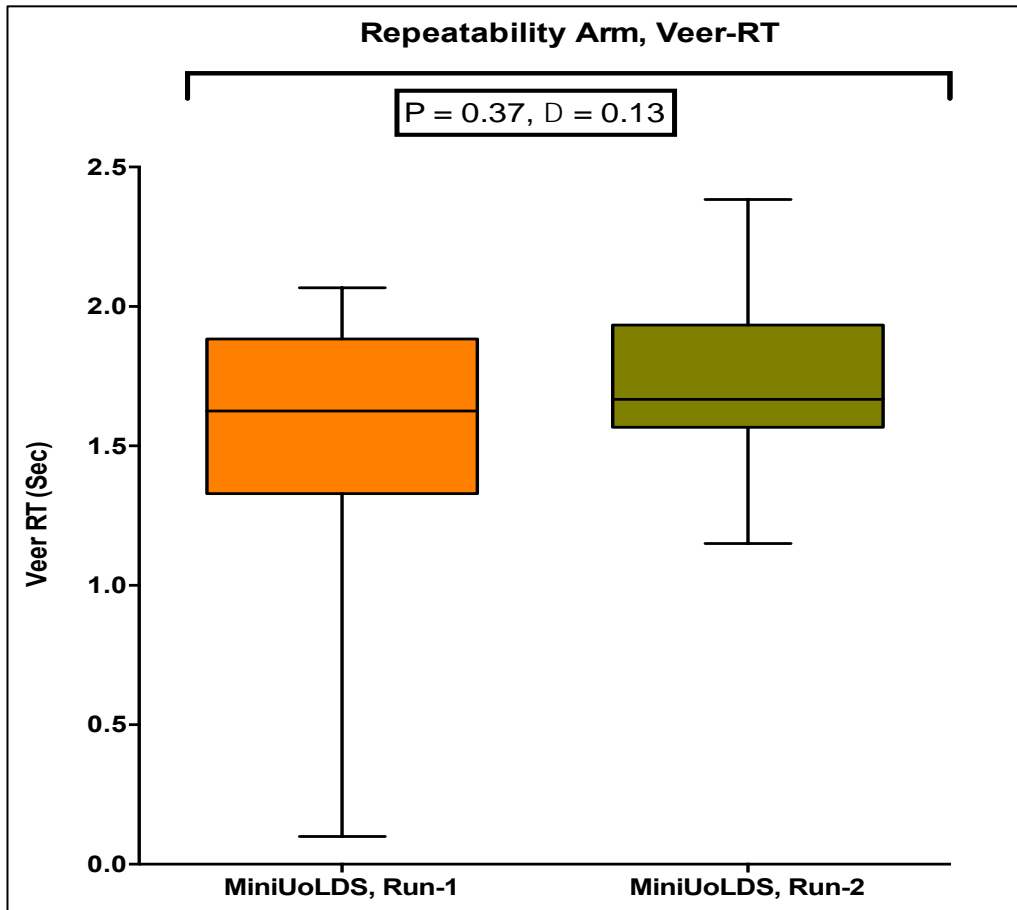
Figure 5-3 showing the repeatability of Veer-RT between the two MUoLDS runs

5.8.1.2- Effect of incentives

The difference in the SDLP-3 and Veer-RT between run-1 and 2 in both the repeatability and the incentive arms were compared using unpaired-t tests and there was no significant difference observed and hence there was no effect of a simple incentive (Table 5-3 & figure 5-4 and 5-5).

Table 5-3, showing the Δ change in SDLP-3 and Veer-RT between run one and run two (effect of incentive)

Arm	Repeatability	Incentive	P- Value
Δ SDLP 3 (mean +/- SD)	-0.01 +/- 0.11	0.01 +/- 0.16	0.39
Δ Veer RT (mean +/- SD)	0.13 +/- 0.53	-0.12 +/- 0.57	0.15
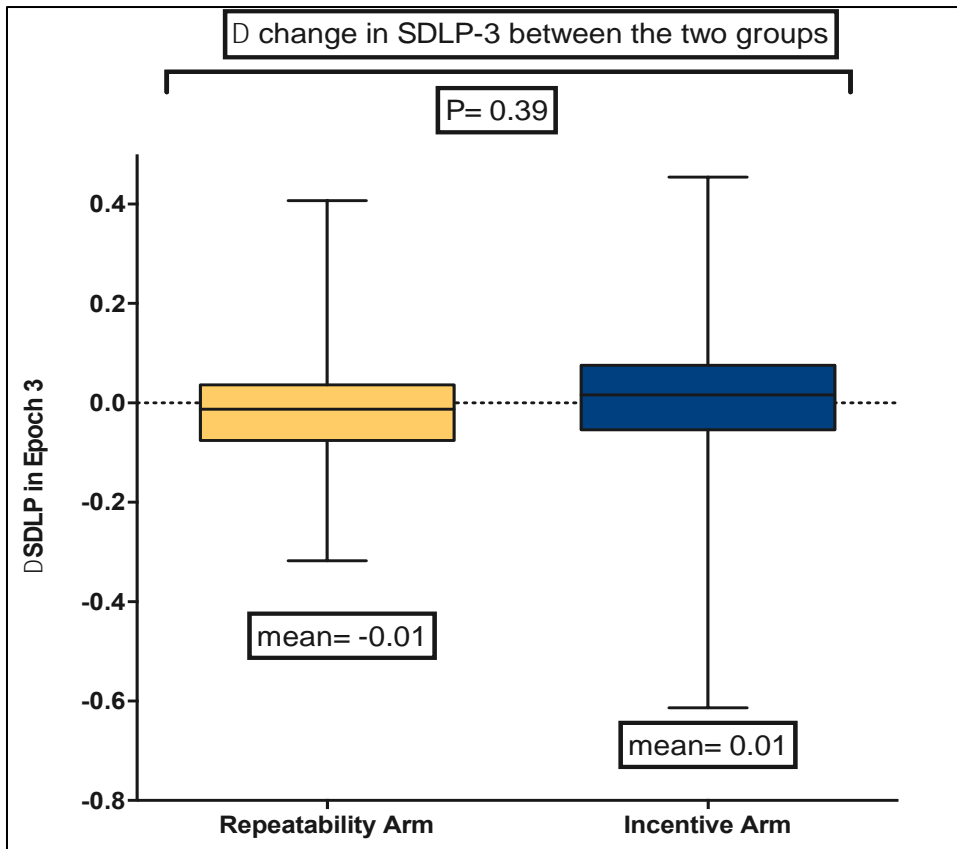
Figure 5-4 showing the Δ change in SDLP-3 between the two groups
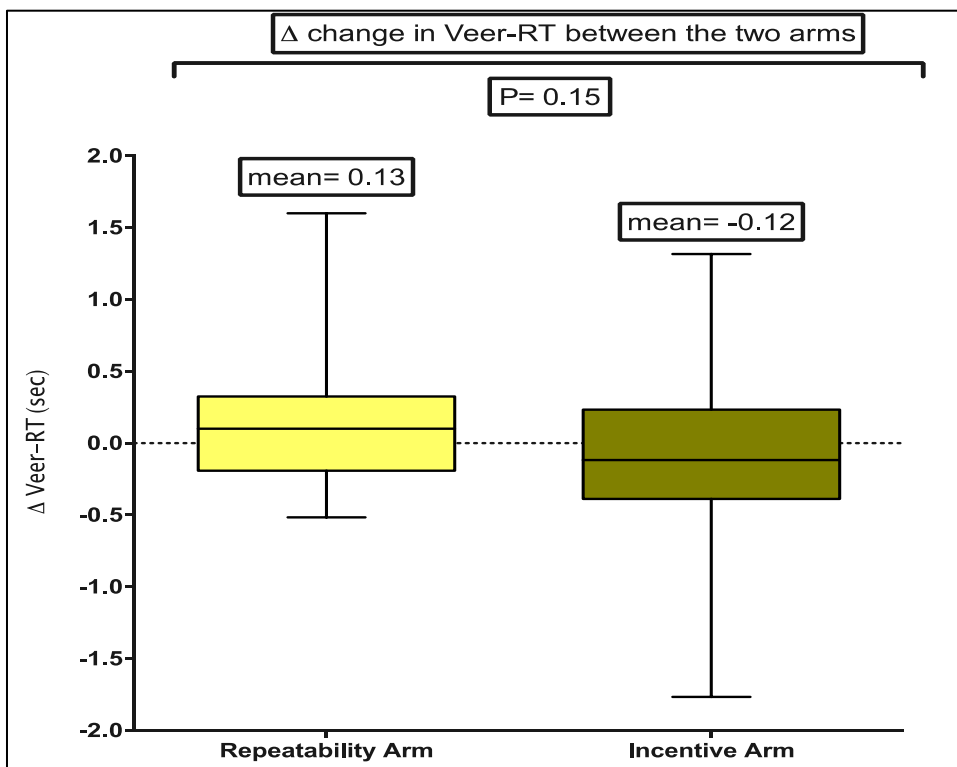
Figure 5-5 showing the Δ change in Veer-RT between the two groups

5.8.2- Secondary outcome

There was no statistically significant difference in the MUoLDS outcome between run-1 and run-2 respectively (P- value= 0.29, OR= 1.37). This is shown in table 5-4.

Table 5-4 showing the secondary outcome

Overall	Run-1	Run-2	P- Value	Odds Ratio
Fail	18% (n=24)	23% (n= 31)	0.29	1.37
Pass	82% (n=113)	77% (n=106)		

Most patients (79%) did not change category between the two MUoLDS outcome but a significant proportion (21%) either failed on run-1 and passed run-2 or vice versa. This is shown in table 5-5.

Table 5-5 showing the MUoLDS outcome between run1 and 2

MUoLDS Outcome (Run-1 and Run-2)	
Pass/ Pass	67% (92)
Fail/ Fail	12% (16)
Others (Fail/ Pass or Pass/ Fail)	21% (29)

5.8.2.1- Subgroup analysis (Repeatability and Incentive arm)

There was no difference in the secondary outcome in either the repeatability or the incentive arm. This is shown in table 5-6 and 5-7 respectively.

Table 5-6 showing the sub group analysis of the secondary outcome between the two arms

Outcome	Repeatability arm (n=48)		P- Value	Odds Ratio
	MUoLDS Run-1	MUoLDS Run-2		
Fail	25% (n=12)	29% (n=14)	0.64	1.2
Pass	75% (n=36)	71% (n=34)		
	Incentive Arm (n=89)			
	MUoLDS Run-1	MUoLDS Run-2		
Fail	13% (n=12)	19% (n=17)	0.31	1.5
Pass	87% (n=77)	81% (n=72)		

Table 5-7 showing the MUoLDS outcome between the two arms in run1 and 2

Outcome	Repeatability Arm	Incentive Arm	P- Value	OR
Pass/ Pass	63% (n= 30)	74% (n= 66)	0.15	1.7
Fail/ Fail	17% (n= 8)	7% (n= 6)	0.06	2.7
Others (Fail/ Pass or Pass/ Fail)	20% (n= 10)	21% (n= 17)	0.98	1.0

5.8.3- Post hoc analysis

Although there was no significant difference in the secondary outcome, 1 in 5 OSAS patients either pass on run one and fail on run two or vice versa irrespective of the randomised arms. Gender has shown to be a factor responsible for simulator performance [119] and therefore to evaluate this further I performed a post hoc analysis in males and females OSAS patients separately. The results are shown in table5-8. There was no statistically significant difference in the baseline demographics and in the MUoLDS outcome between males and females. However males were more likely to change the outcome (22% versus 10.5%) but this was not statistically significant.

Table 5-8 showing the post hoc analysis between males and females

	Males	Females		
Total	86% (n= 118)	14% (n= 19)		
Repeatability Arm	36% (n= 42)	32% (n= 6)		
Incentive Arm	64% (n= 76)	68% (n= 13)		
Parameters (Unpaired- t test)			**P- Value**	**Mean difference**
Age (mean+/- SD)	54 +/- 12	50 +/- 9	0.18	3.6+/- 2.8
BMI (mean+/-SD)	36 +/- 8	38 +/- 8	0.23	2.1 +/- 1.2
ESS (mean +/-SD)	13 +/- 5	15 +/- 3	0.11	2 +/- 1
ODI (mean +/-SD)	40 +/- 25	34 +/- 25	0.31	-14 +/- 5.6
DL (Mean +/SD) (Years)	30 +/- 2	29 +/- 4	0.3	1.1 +/- 1.2
Parameters (Chi-square test)				**Odds ratio**
Pass/Pass	66% (n= 78)	79% (n= 15)	0.26	0.52
Fail/ Fail	12% (n= 14)	10.5% (n= 2)	0.86	1.1
Others (Pass/ Fail or Fail/Pass)	22% (n= 26)	10.5% (n= 2)	0.24	2.4

BMI, body mass index (kg/m2); ESS, Epworth Sleepiness Score; ODI, oxygen desaturation index, DL; Driving Licence

5.8.3.1- Comparing old and new criteria for MUoLDS failure

In Chapter-4, I have shown that a SDLP-3 of more than 0.66 to be a high risk group. However this is applicable only to males as there is no data available regarding the normal range in MUoLDS performance in females. Thus I compared the MUoLDS outcome based on two criteria's.

    I.   Criteria A- unprovoked crash, unable to complete.

    II.   Criteria B- unprovoked crash, unable to complete, SDLP-3 of > 0.66.

There was no significant difference in the MUoLDS outcome and this is shown in figure 5-6.
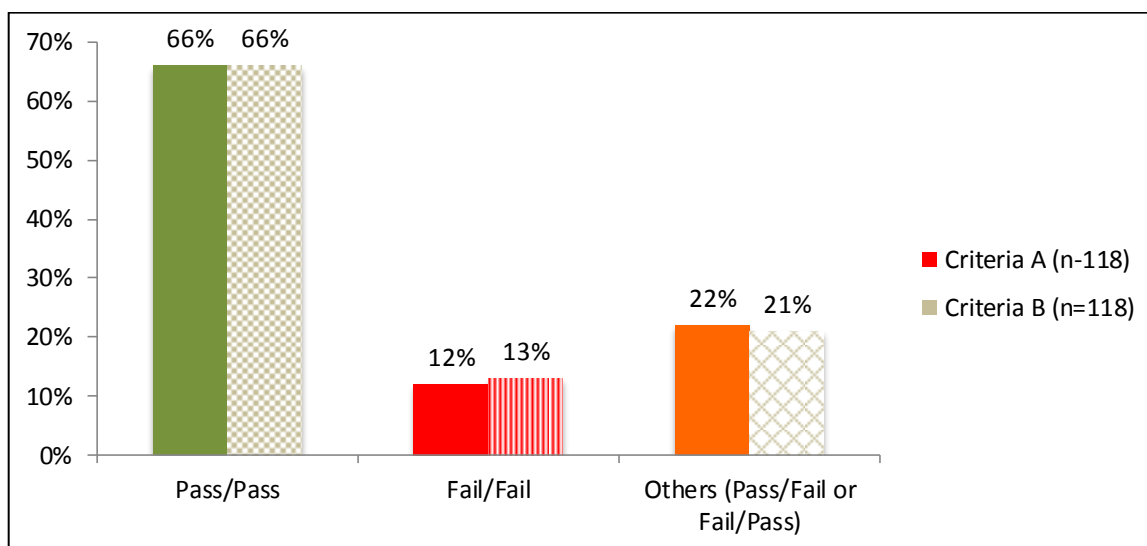
Figure 5-6 showing the MUoLDS outcome based on two different criteria

5.8.3.2- Comparing SDLP-3 with MUoLDS outcome on both run-1 and run-2

In the previous Chapter, I have shown that SDLP-3 is a predictor of MUoLDS outcome and hence I compared this with MUoLDS outcome on run-1 and run-2 respectively. There was no statistically significant difference between the three groups. This is illustrated in figures 5-7, 5-8 and 5-9 respectively. The red dotted line represents mean SDLP-3 and the green dotted line represents 95th centile in male controls.

I also explored any differences in ESS, BMI, ODI between the MUoLDS outcomes. OSAS patients with worse severe SDB, higher BMI and worse sleepiness were more likely to either fail on both the runs or fail in run-1 and pass in run-2 and vice versa. This is shown in table- 5-9.
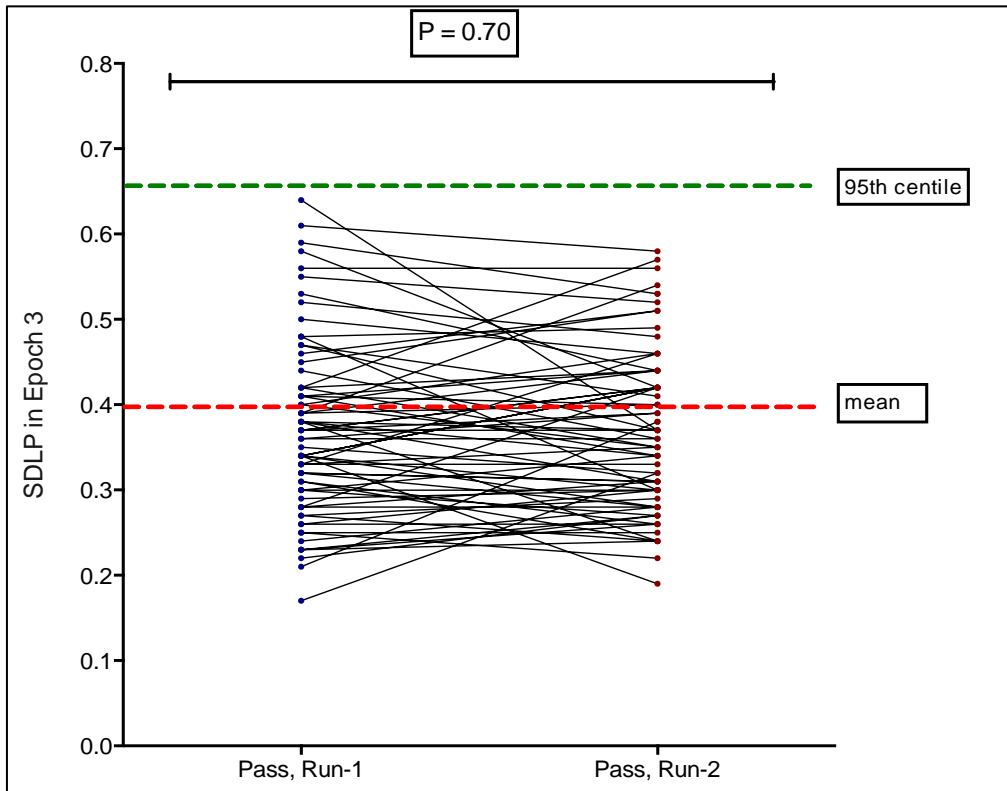
Figure 5-7 showing the SDLP-3 in the pass/pass group
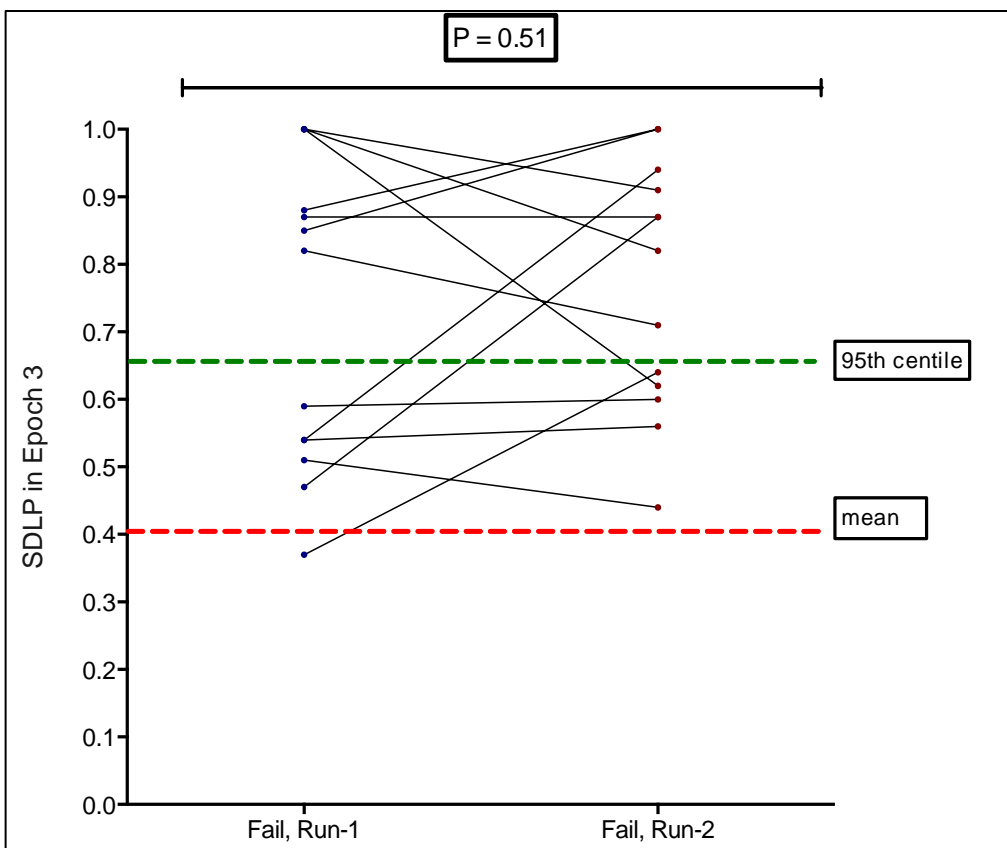
Figure 5-8 showing the SDLP-3 in the fail/fail group
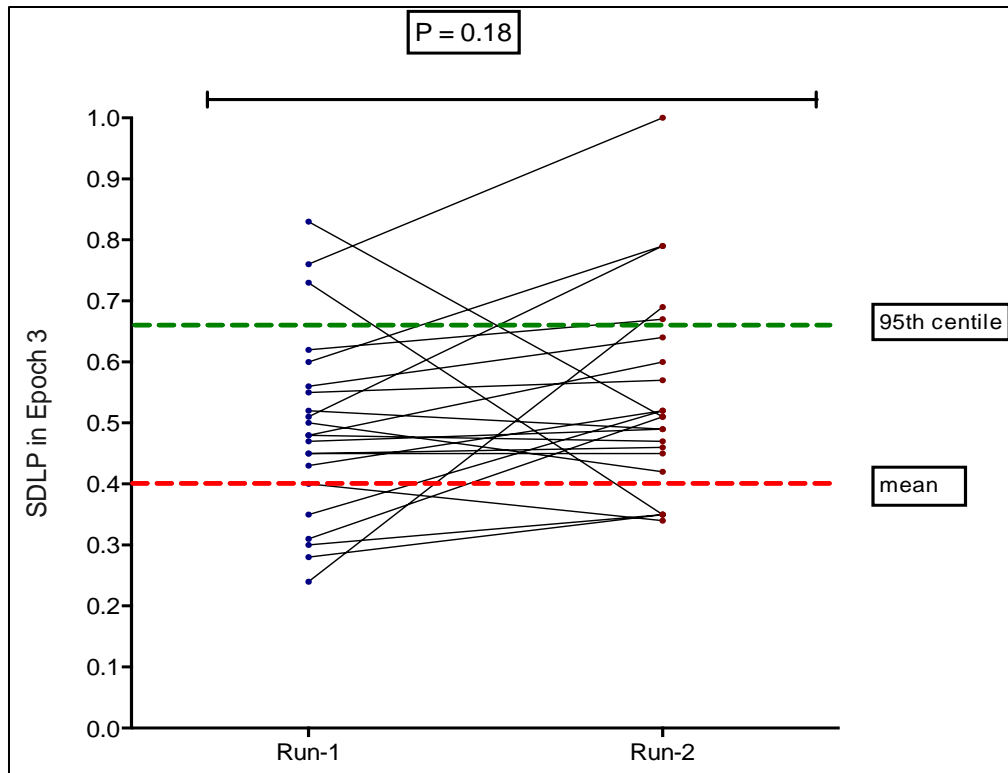
Figure 5-9 showing the SDLP-3 in the pass/fail or fail/pass group

Table 5-9 showing the baseline differences between the two groups

Parameter	Fail/ Fail (n=14) Fail/Pass (n=13) Pass/Fail (n=13)	Pass/Pass (n= 78)	P-Value
Age (mean/SD)	54 (11)	54 (13)	0.72
BMI (mean/SD)	39 (9)	34 (6)	0.003
ESS (mean/SD)	19 (15)	13 (5)	0.007
ODI (mean/SD)	48 (27)	36 (23)	0.01
Time between run-1 & 2 (median/IQR)	15 days (7-25)	13 days (7-23)	0.32

5.9- Discussion

Driving is an essential part of modern life and depriving an individual of their licence has major potential implications for them and society. Assessing and advising whether a patient with OSAS should stop driving is one of the key components in management and therefore it is vital to identify accurately the OSAS patient who is at risk. To do so any results from a potential objective test should be consistent and hence reproducible. It is also true that the general hypothesis regarding the effects of monetary incentives on effort and performance is that incentives lead to greater effort than would have been the case in their absence. Incentives can serve several functions such as initiating action, changing goals and ensuring commitment (121-123). The main objectives in this randomised trial were to evaluate the test-retest reliability in continuously measured variables and to gauge the effect of a financial incentive on driving performance on the MUoLDS.

The main outcomes of this randomised trial were the consistency in the measurement of continuous variables (SDLP-3 and Veer-RT) on successive runs with no effect of motivation factor; hence OSAS patients being assessed could not significantly improve the results despite raising the game and the outcome on MUoLDS. OSAS patients in both the randomisation arms were matched for age, BMI, ESS, severity of OSAS and driving experience. The trial focussed on recruiting symptomatic OSAS patients who were more likely at risk of having problems during driving. It could be argued that some OSAS patients did raise their game and thus did not fail on the second run but there was no improvement in SDLP-3 or the veer-RT. This may imply that the continuously measured variable which both the clinician and the OSAS patient are oblivious to may be a better marker of risk assessment as

compared to the MUoLDS outcome. SDLP3 has the advantage that it is measured continuously, has been shown to predict task failure accurately on the MUoLDS [28] and it, or a similar measure, has been shown to indicate the at risk driver in other studies [22,27]. Ideally an objective test should be used and tests such as the divided attention driving simulator while intuitively reasonable surrogates for real driving lack credibility.

However a fifth of OSAS patients change category in terms of the outcome of the simulator run. The same is also true for SDLP3; on average it did not change but patients did move above or below the thresholds we have identified, indicating increased risk, between the two studies. One possible explanation could be that this is just day to day variability in performance on a simulator. However this is also true of real world driving - the individual who has an accident one day will almost certainly have driven before without having had an accident and will drive afterwards without having an accident. The performance on the simulator therefore reflects the real world. However individuals who have had an accident are more likely to have another accident and the patient who fails on the simulator is therefore at increased risk as no controls did this. However a pass does not necessarily mean that the accident risk is not increased.

OSAS patients who failed the MUoLDS on either of the runs were more sleepy, had a higher BMI and had worse SDB as compared to those who passed the MUoLDS and this was statistically significant. This suggests that patients with high BMI or high ESS or the most severe SDB who pass the test should be considered for retesting, perhaps with some sort of distraction task or a drive of longer duration. There is no

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data available in controls about the issue of repeatability and the effect of incentive and further studies are needed to explore this finding.

5.10- Trial limitations

Apart from the study limitations described in Chapter-4, the specific limitations in this trial were that there was no standard time period between the first and second run and majority of the patients did their second run on the day of their CPAP trial appointment. I did not do a detailed analysis of all the epochs for any change in SDLP. Unlike the patients studied in Chapter-4 this study included females and a post –hoc analysis showed that males were more likely to change the outcome from either a pass to fail or vice versa on successive runs but this was not statistically significant.

5.11- Conclusion

Although the continuously measured variable is repeatable and there is no effect of a simple incentive, the hard outcome on MUoLDS based on pre-set criteria is not repeatable and a fifth of patients change categories. On an individual basis the SDLP3 also changes between runs. Male OSAS patient with higher BMI, worse ESS and worse severe SDB may need to repeat the MUoLDS if the clinician's suspicion is high.

Chapter-6

Use of fatigue related counter measures (Coping Strategies) while driving in male OSAS patients and controls

6.1- Abstract

Sleepiness while driving is potentially fatal and it is recommended that a driver who starts to feel tired should stop and have a rest, but some may use various counter measures to try to stay alert. Using a questionnaire that assessed various potential fatigue related counter measures (coping strategies), I explored whether there was any difference in those used in the last year between OSAS patients and controls. I also compared use with sleepiness generally (ESS), specifically while driving (DSS), accident history and the outcome on the MUoLDS. 98 untreated male OSAS patients [ESS= 14 +/- 9, BMI = 36 +/- 8, ODI = 41 +/- 25] and 53 male controls [ESS = 4 +/- 3, BMI= 28 +/- 5] matched for age and driving experience were recruited. All completed a questionnaire, relating to their experience over the last one year, which included ESS, DSS, ten questions about various strategies they adopt in order to stay awake and their accident history. All performed a 90km motorway driving simulation. Male OSAS patients as compared to male controls frequently use coping strategies (46% versus 17%, P= 0.0004, OR= 4.1), were more sleepy generally (ESS 17 +/- 3 versus 12 +/- 5, P= < 0.0001) and were more likely to have clinically significant sleepiness while driving (DSS 11 +/- 7 versus 4 +/- 5, P= < 0.0001). 10% of patients who had a DSS of less than 7 used 3 or more coping strategies "frequently". History of accidents was significantly higher in patients who used 3 or more coping strategies "frequently" (78% versus 45%, P= 0.005, OR= 4.3). OSAS patients report "frequent" use of coping strategies and some admit to sleepiness both generally and specifically while driving. These counter measures may be surrogate markers of fatigue and sleepiness. Asking about such strategies in clinical practice may aid the clinician in identifying the at risk patients.

6.2- Introduction

Driving is a complex task that involves many aspects such as perception, response time, physical ability and is an essential part of an individual's life. Studies have shown that driving either on a motorway or on an urban road can be fatiguing even for an alert driver [117, 124-125]. Driver stress and fatigue may impair performance; compromise safety [126] and drivers may adapt various counter measures to tackle this issue. A survey among commercial drivers unveiled a series of specific responses related to a feeling of excessive sleepiness at the wheel that were not usually considered in the medical context. These attitudes served as "alerting signals" that the sleepiness level was too high, and that the driver should take a break in order to avoid a possible RTA [127]. I hypothesised that asking about the use of coping strategies might be another way to identify the OSAS patient at risk of RTA. Furthermore while patients might be reluctant to admit to problems driving, because of fear that they might be prevented from driving, they might be more willing to admit to using coping strategies. This might therefore be a less threatening way of identifying the individual who is at increased risk of an accident due to fatigue. It is also possible that such strategies might be effective in preventing accidents.

The aims of this study were to identify strategies to counter feelings of fatigue employed by OSAS patients and controls and compare the use of these with accident history, sleepiness in general and specifically while driving and performance on an advanced office based driving simulator.

6.3- Methods

The methodology including the inclusion/exclusion criteria and the scoring for sleep disordered breathing has been discussed in Chapter-2. Females were included in this study as the main hypothesis was to evaluate the use of fatigue related counter measures rather than the MUoLDS outcome or performance. Ethical approval for the study was obtained by the NHS Research Ethics Committee - 09/H1311/58.

6.4- Questionnaire

All subjects completed a questionnaire about driving and the use of coping strategies (listed in appendix III and V). This was developed with the input of patients and healthcare professionals. This questionnaire has not been validated. The questionnaire included demographic details, ESS; ten questions about various counter measures (coping strategies) patients might adapt in order to stay awake. Admitting to one or more coping strategies "frequently" was compared between OSAS patients and controls. Accident history included nodding events, near miss, minor damage and major damage or insurance claims. Questions about sleepiness while driving were posed, and following the format of ESS, OSAS patients and controls were asked to rate on a scale ranging from "Never" to "High" their chance of dozing or falling asleep while driving at different times of the day and on journeys of different durations. The maximum score was 30 and gave a Driver Sleepiness Score (DSS). This has been discussed in Chapter-4.

6.5- Driving Simulator (MUoLDS)

All performed a 90km motorway driving simulation after 20 min acclimatisation. The simulator outcome was based on preset criteria. The simulator road layout and scenario are described in Chapter-2.

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6.6- Statistical analysis

The statistical analysis was carried out using Graph Pad Prism 6 software (San Diego, California, USA). The level of significance was set at P= <0.05. Normally distributed data are presented as mean/standard deviation. Median/Interquartile range was used for data that are not normally distributed. Unpaired t-test was used to evaluate for subject demographics and for univariate analysis. Chi-square tests were used to evaluate the difference in the use of coping strategies between controls and OSAS patients and accident history. Spearman correlation was performed to evaluate the relationship between ESS, DSS and "frequently" used coping strategies as the data was not normally distrributed. One- way Anova and Bonferroni's multiple comparison tests were used to compare the use of coping strategies and the MUoLDS outcome and SDLP-3 between the three groups.

6.7- Results

98 untreated male OSAS patients and 53 male controls were included in the study. The baseline demographics are shown in table 6-1.

Table 6-1 showing the baseline demographics in OSAS patients and controls

Parameters(mean +/- SD)	Controls (n=53)	Patients (n=98)	P- Value
Age	56 +/- 11	53 +/- 9	0.08
ESS	4 +/- 3	14 +/- 9	<0.0001
BMI (Kg/m2)	28 +/- 5	36 +/- 8	<0.0001
Licence (Years)	34 +/- 13	32 +/- 9	0.21
ODI		41 +/- 25	

ESS- Epworth Sleepiness Scale, BMI- Body mass index, ODI- Oxygen desaturation index.

6.7.1- "Frequently" used coping strategies

OSAS patients were more likely to use at least one coping strategies "frequently" as compared to controls and this was statistically significant (46% versus 17%, P value= 0.0004, OR= 4.1). No control used more than three different strategies as compared to 23% of OSAS patients who used more than three such strategies while driving. This is shown in figure 6-1.
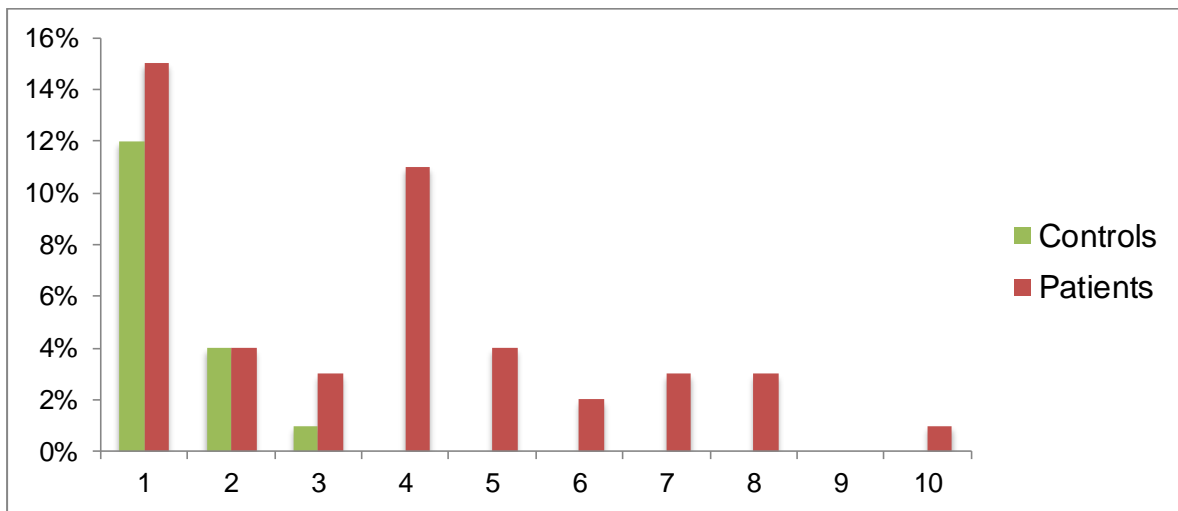
Figure 6-1- showing the number of "frequently" used coping strategies between controls and OSAS patients

6.7.2- Types of "frequently" used coping strategies

The various types of "frequently" used coping strategies by OSAS patients and controls are shown in table 6-2. All were statistically significant except stopping for a nap.

Table 6-2 showing the types of "frequently" used coping strategies between controls and OSAS patients

	Controls (n=53)	Patients (n=98)	P= Value	Odds ratio (OR)
Stopped for a nap	2% (n=1)	9% (n=9)	0.10	5.2
Stopped for a walk/ exercise	0% (n=0)	12% (n=12)	0.007	6.8
Opened the window	13% (n=7)	33% (n=32)	0.01	3.1
Turned up the radio/ stereo	2% (n=1)	21% (n=21)	0.001	14.8
Stopped to drink tea/coffee	6% (n=3)	22% (n=22)	0.01	4.8
Stopped at service area to wash face in cold water	0% (n=0)	12% (n=12)	0.008	15.4
Sing/talk to yourself	0% (n=0)	13% (n=13)	0.004	16.8
Chew gum/eat something	0% (n=0)	14% (n=14)	0.005	18.3
Fidget/ exercise	0% (n=0)	11% (n=11)	0.01	6.6
Changed seat position	2% (n=1)	13% (n=13)	0.03	7.9

A univariate analysis was performed to identify any variables which could predict the group of subjects using more than three coping strategies. This is shown in table 6-3.

Table 6.3 showing the univariate analysis between the two groups

Parameters (mean +/- SD)	Coping Strategies		P- value
	< 3	< or = 3	
Age (years)	53 +/- 6	53 +/- 9	0.91
BMI(kg/m2)	35 +/- 6	36+/- 9	0.86
ESS	17+/- 3	12+/- 5	< 0.0001
ODI	38 +/- 24	41+/- 25	0.53
Licence(years)	33+/- 8	31+/- 10	0.62
DSS	11+/-7	4 +/- 5	< 0.0001

BMI- Body mass index, ESS- Epworth Sleepiness Scale, ODI- Oxygen desaturation index, DSS- Driving Sleepiness Score

6.7.3- Correlation between "frequently" used coping strategies, DSS and ESS

There was a correlation between "frequently" used coping strategies, ESS and DSS. Admitting to general sleepiness, ESS (r=0.37, P= 0.01) (figure 6-2) and sleepiness specifically while driving, DSS (r=0.42, P=0.004) (figure 6-3) were significant in OSAS patients who admit to using more than three coping strategies on a "frequent" basis.
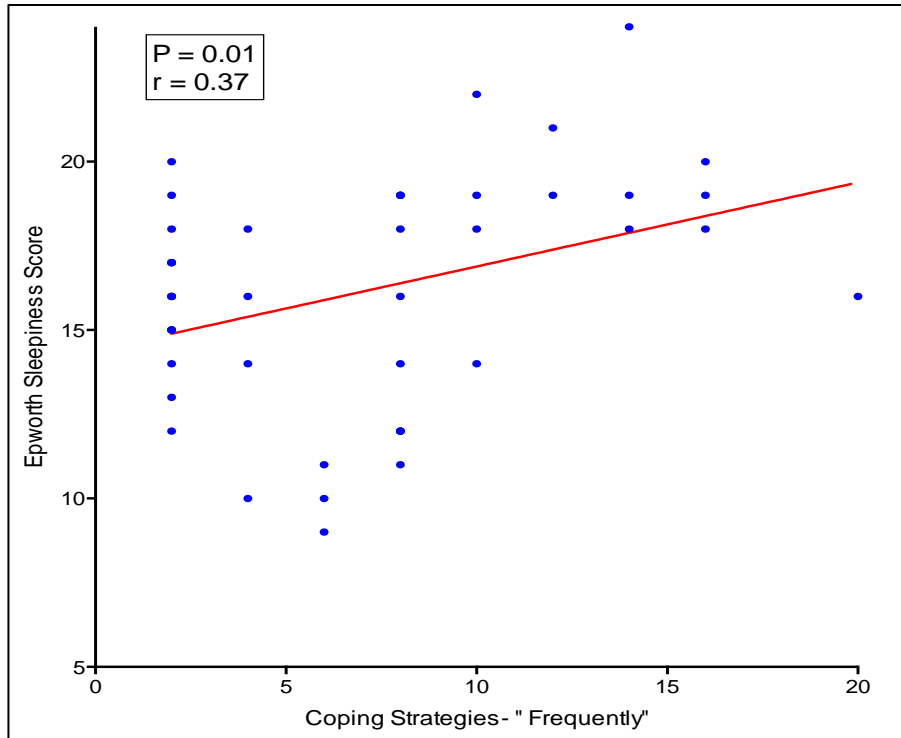
Figure 6-2 showing the spearman's correlation between ESS and coping strategies used "frequently"
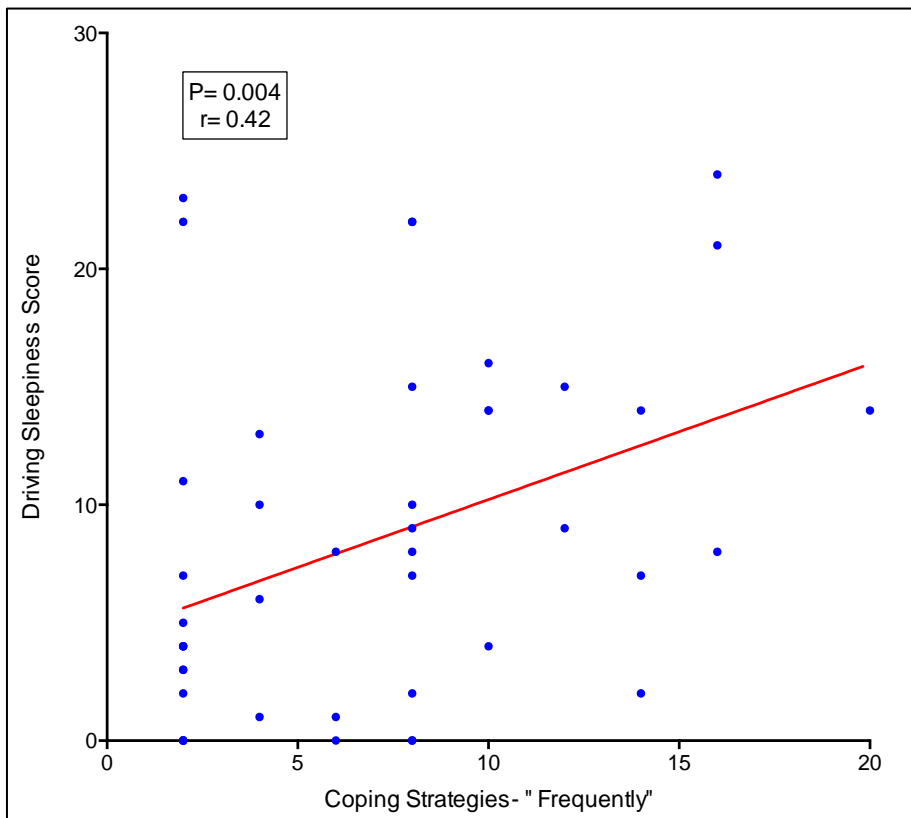
Figure 6-3 showing the spearman's correlation between DSS and coping strategies used "frequently"

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6.7.4- Relationship between Driving Sleepiness Score and Coping Strategies "frequently"

OSAS patients who employed more than three coping strategies on a "frequent" basis were more likely to have had a DSS of more than 7 and this was statistically significant (P= < 0.0001, OR= 12). 10% of patients who had a DSS of less than 7 used any coping strategy "frequently". A proportion of patients (17%) had a DSS of more than 7 and admitted to "frequent" use of more than three coping strategies, some had a DSS of more than 7 only with no "frequent" coping strategies (10%) and some neither to both (63%). This is shown in table 6-4.

Table 6-4 showing the relationship between frequently used coping strategies and DSS

Coping Strategies	DSS > 7	DSS < = 7	P= Value	OR (95% CI)
> 3 frequently	17% (17)	10% (9)	< 0.0001	12 (4.1- 33)
</= 3 frequently	10% (10)	63% (62)		

6.7.5- Relationship between Accident history and Coping Strategies "frequently"

There was a significant difference in accidents (near misses, minor damage, major damage including garage work or insurance claims) or episodes of nodding at the wheel in the last year between OSAS patients who used > 3 coping strategies "frequently" as compared to OSAS patients who used < 3 coping strategies on a "frequent" basis. This is shown in table 6-5.

Table 6-5 showing the relationship between accident history and coping strategies

Accidents, Near miss or Nodding in the last one year			P= Value	Odds Ratio
Coping Strategies	Yes	No		
> 3 " frequently"	18 (78%)	5 (22%)		
</ = 3 " frequently"	34 (45%)	41 (55%)	0.005	4.3

6.7.6- Relationship between MUoLDS outcome, performance based on SDLP-3 on and Coping Strategies "frequently"

No controls and 20% (n= 20) of OSAS patients failed the MUoLDS irrespective of the use of any coping strategy "frequently" (P=value 0.69, OR=1.24). There was no difference in MUoLDS performance based on SDLP-3 between controls and OSAS patients who used more than 3 coping strategies or less than three coping strategies (P= 0.06). There was a hierarchical pattern in the SDLP-3 between controls, OSAS patients who used less than three coping strategies "frequently" and those patients who used more than three coping strategies frequently (mean +/- SD (95% CI); 0.41 +/- 0.12 (0.38-0.44); 0.46 +/- 0.20 (0.41-0.50); 0.50 +/- 0.29 (0.40-0.59) respectively. There was no difference between the three groups when corrected for multiple comparisons. This is shown in figure 6-4.
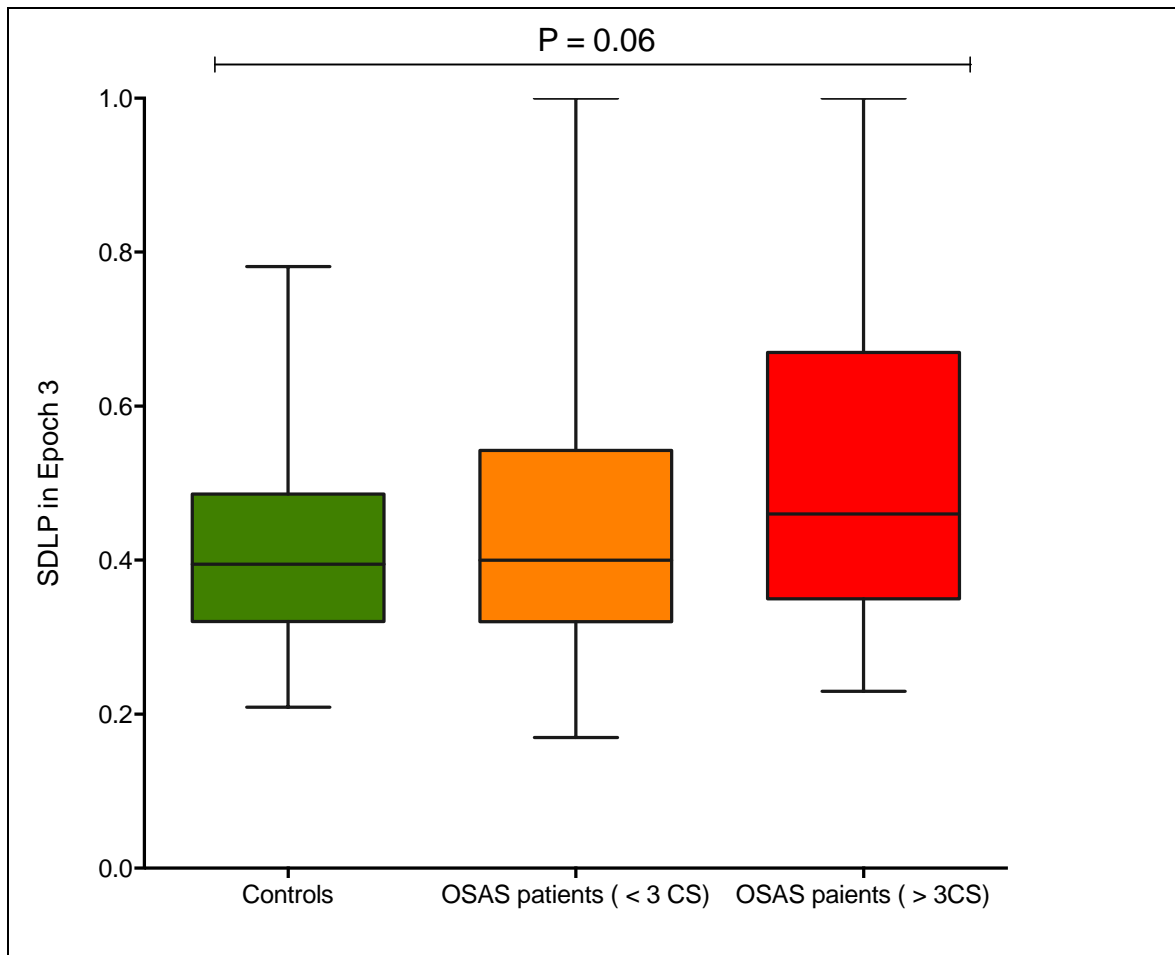
Figure 6-4 showing the relationship between coping strategies and SDLP in epoch -3

6.8- Discussion

The principal outcome from this observational study was that behaviours adopted by untreated OSAS patients may be a useful additional way of identifying an individual who is potentially at risk of an accident, because of sleepiness while driving. I found feeling sleepy generally (ESS) or specifically while driving (DSS) correlate strongly with the adoption of various strategies to counter sleepiness. This confirms the hypothesis that using coping strategies may be a surrogate marker for sleepiness and might be a way of identifying patients who had a problem but did not admit to it directly. Of note 10% of patients admitted to the use of at least one coping strategy

"frequently" but did not admit to significant sleepiness while driving (DSS</=7). I also found that OSAS patients using more than three strategies "frequently" are more likely to admit to a near miss or an accident in the previous year.

Coping is a complex multidimensional process determined by environmental conditions, cognitive abilities, and personality dispositions [128]. A study comparing the driving habits of professional and non-professional drivers has shown that stopping for a short nap is effective in counteracting fatigue and benefits performance [129]. There is some limited data to suggest that stopping for a walk/exercise or stopping for a drink or particularly "washing the face" can have a positive effect, albeit for a short period in the general population [130-132]. It could be argued that measures which involve taking a break from driving are a legitimate and "appropriate" response to fatigue. However measures adopted while the patient continues to drive indicate that the individual is "fighting" sleepiness and might therefore be considered to be "inappropriate". A post hoc analysis of our data comparing accident history and episodes of nodding in patients using coping strategies "appropriately" or "inappropriately" showed no difference, but the study may not have had sufficient numbers of subjects to address this issue definitively. My data suggests that strategies employed to counter fatigue are not effective but rather a marker of a patient who is driving with less reserves of alertness. Whether coping strategies are used "appropriately" or "inappropriately", if it is "frequently", it indicates that drivers are driving with increased sleepiness likely to impair safe driving. I suggest that the use of more than three coping

strategies "frequently" should be considered as a "red flag" with regard to future driving, but that any use of such strategies should raise concerns.

6.9- Study Limitations

Apart from the limitations described in Chapter-4 this study relied on patients' reports of their driving. While it is possible that females use fatigue related counter measures in the same way as males this needs to be evaluated in future studies. I did not enquire when patients used the counter measures; for example stopping for a nap after 30 minutes is likely to be more significant than doing so after several hours. I do not know whether different counter measures were tried in the same journey. If yes it is further evidence that there is a problem; one does not seem to work so the individual tries something else. These are factors that the clinician will have to weigh in their assessment.

6.10- Conclusion

Patients with OSAS of sufficient severity to warrant a trial of CPAP use various coping strategies to deal with sleepiness while driving. Use of more than three such measures "frequently" is associated with an increased risk of accidents and near misses and may be a complementary, and less threatening way to ask about sleepiness likely to impair safe driving. No control admitted to the use of more than three different coping strategies "frequently" and given the relationship with accidents and near misses, I suggest that this should be a "red flag" with regard to continued driving. Any

use of coping strategies should be a factor that is taken into account in assessing whether a patient has sleepiness likely to impair safe driving.

Chapter-7

Cognitive dysfunction and road traffic incidents

in OSAS patients and controls

7.1- Abstract

There has been a growing interest in the evaluation of cognitive deterioration and a wide range of cognitive deficits: general intellectual functioning, attention, memory, executive & motor functioning has been identified in patients with OSAS. Cognitive Failures Questionnaire (CFQ) is an assessment tool that is a measure of self-reported cognitive deficits in the completion of simple everyday tasks that a person should normally be capable of completing without error. I hypothesised those patients with OSAS exhibit worse cognitive dysfunction as compared to OSA patients and controls and higher CFQ score predicts accident risk. All completed a questionnaire that included CFQ, previous driving incidents in the last 1-year, ESS and DSS. They were asked how often they make various common mistakes on a 5-point Likert scale, from 0 (never) to 4 (very often). CFQ was scored by adding up the rating for 25 questions, the highest possible total being 100, with a higher score indicating a higher incidence of cognitive failures. Prediction model using binary regression analysis identified accidents and or near miss and this was validated in a different cohort. 105 controls and 150 patients were included in the exploratory; 68 controls and 198 patients in the validation. Untreated OSAS patients had a statistically significant higher CFQ score as compared to OSA patients and controls. The score remained statistically significant when different components of the CFQ were evaluated. Untreated OSAS patients with higher CFQ score reported increased driving incidents in the last one-year. The model was subsequently validated using ROC analysis. Sleepiness rather than severity of sleep disordered breathing predicts cognitive failure. Higher CFQ score is associated with accident risk.

The CFQ is easy to complete, may identify a different aspect of accident risk and therefore be useful in assessing fitness to drive in OSAS patients.

7.2- Introduction

OSAS is a common disorder with far reaching health implications. Deterioration in some cognitive domains is considered part of the aging process [133] but untreated OSAS results in cognitive dysfunction [134]. There is no consensus regarding the mechanisms by which OSAS affect cognition but it is thought to be multifactorial. Studies have shown deficits in various domains such as executive functions [135], memory [136], alertness [137] and attention [138]. Cognitive deficits in OSAS patients are qualitatively similar to those of elderly individuals, especially in tasks sensitive to frontal lobe dysfunction [139]. Cognitive dysfunction was independently related to both OSA severity and increasing age, but the coexistence of both factors did not result in increased cognitive deficit [140-141]. Impairment in attention plays a pivotal role in all aspects of cognitive deficits and thereby contributes to the poor performance of OSAS patients when compared to that of healthy individuals [138,142]. Brain activation is increased in OSA patients with preserved cognitive function as compared with the activation that occurs in healthy controls performing the same task. The association between preserved cognitive function, and greater activation in OSA patients suggests that increased cerebral recruitment is required to maintain cognitive performance [143]. The hippocampus is a region known to be closely associated with the neural processing of memory [144] and the morphology is altered in patients with OSAS [145-146].

Driving a vehicle is a skill that involves complex integrated higher cortical function, alertness, concentration and hand-to-eye coordination. While errors of judgement cognitive failures occur frequently and many do not produce any serious consequences, some will results in accidents. Evidence suggests that there is a link between cognitive failures and road traffic accidents (RTA), distractibility, poor selective attention and mental error [147-149]. Annex III of the European Union (EU) Directive on Driving Licences was revised in 2014 on the recommendations from a working group established by the Transport and Mobility Directorate of the European Commission in 2012 [51]. The UK Driver and Vehicle Licensing Agency (DVLA) changed their advice regarding who should not drive and who needs to notify them [50]. More over the current guidance [50] enquires about assessment of poor concentration especially in the absence of sleepiness.

The EU Directive states that OSAS patients needing treatment, in the opinion of a physician and not receiving it should not receive an unconditional licence. A driver with moderate or severe OSAS may be permitted to drive based on demonstration of compliance with treatment. Patients with mild OSAS (AHI < 15 events / hour) can drive if they do not have invalidating excessive sleepiness (ESS < 15), deny accidents, are not taking more than two drugs for hypertension, and have a BMI < 35 kg/m2. The UK DVLA regulations are also different for patients with mild compared to moderate and severe OSAS. Patients with mild OSAS and excessive sleepiness must not drive but do not need to inform the DVLA. Patients with moderate or severe sleep apnoea with

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excessive sleepiness must not drive and must notify the DVLA; subsequent licensing will require control of the condition, an improvement in sleepiness and treatment adherence. The cardinal symptom of OSAS is excessive sleepiness and can have an adverse effect on driving [67]. If the patient is not sleepy and has moderate or severe OSAS they must not drive but do not need the DVLA. Driving may resume once associated symptoms, such as poor concentration, have been brought under control. These standards are higher for bus and lorry drivers.

In this study I have evaluated whether the severity of SDB and / or poor decision making function impacts upon the likelihood of RTA.

7.3- Study Outcomes

7.3.3- Primary outcome

To explore the relationship between CFQ score versus general sleepiness, severity of sleep disordered breathing and predicting accidents.

7.3.4- Secondary outcome

Comparing driving incidents between severity of SDB, general sleepiness and specifically whilst driving.

7.4- Methods

This is described in Chapter-4. Females were included in this study due to absence of MUoLDS test. Patients with SDB and an ESS of less than 10, irrespective of other symptoms were classified as OSA and patients with SDB and an ESS of more than 10 were classified as OSAS. Subjects with no symptoms of SDB and with an ESS of < 10 were recruited as controls.

Participants in both the groups were provided with a patient information leaflet and written consent was obtained. Ethics approval for this study was obtained from the NHS Research Ethics Committee (09/H1311/58).

7.5- Questionnaire

7.5.1- Driving Questionnaire (DQ)

This is described in Chapter-4.

7.5.2- Cognitive Failures Questionnaire (CFQ)

To assess decision making function I used the CFQ [150]. This is a cognitive assessment tool which measures self-reported deficits in the completion of simple everyday tasks that a person should normally be capable of completing without error. It includes failures in attention, memory, perception and motor functions [24]. Allahyari et al [151] reported that CFQ could be used to identify drivers susceptible to driving errors. Patients and controls completed the CFQ, which enquired how often they make various common errors on a 5-point Likert scale, from 0 (never), 1 (very rarely), 2 (occasionally), 3 (quite often) and 4 (very often). CFQ was scored by adding up the ratings for twenty-five questions, the highest possible total being one hundred, with a higher score indicating a higher incidence of cognitive failures. Allahyari et al [151] refined this further by performing a principal component analysis with varimax rotation to determine the factor structure of each domain; this gave five domains ("motor function", "memory", "lack of concentration", "social interaction" and "names"). The DQ and the CFQ are described in detail in appendix (III and VI) respectively.

7.6- Study design and statistical analysis

The study was divided into exploratory and validation phase. Statistical analysis was carried out using Graph Pad Prism 6 software (San Diego, California, USA) and SPSS statistics (Version 24; IBM, New York, USA). The level of significance was set at $P= <0.05$. In the exploratory phase we explored the total CFQ score and the five domains between controls, OSA, OSAS patients and controls. One way ANOVA and multiple comparison test (Bonferroni's) was used to evaluate for demographic differences, differences in the total and the five domains of the CFQ between controls, OSA and OSAS patients. Spearman's correlation was used to evaluate the relationship between ESS, DSS and ODI. Binary logistic regression analysis was used to test the hypothesis that an "accident" could be predicted from the either the total CFQ score or from any or all of the domains and thereby explore the possibility of developing a predictive model. Receiver operating characteristic (ROC) curve analysis was performed to calculate the discriminative power of the models and identify optimal cut-offs for probability score. The sensitivity, specificity and predictive powers of the models were calculated using the cut-off values. The curve generated for each model was compared using the two proportion Z-tests in SPSS.

7.7- Results

7.7.1- Baseline demographics

The baseline characteristics in both the exploratory and the validation cohort are shown in table 7-1.

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173 controls and 348 untreated OSAS patients were recruited to the study. In both the cohorts controls and patients were matched for age and driving experience. Patients as compared to controls had a worse ESS, BMI and this was statistically significant.

Table 7-1 Demographics in exploratory and validation cohort: controls and OSAS patients

Controls				
Variables	Exploratory study (n=105)	Validation study (n=68)	P- Value	CI of difference
Age (Years)	55 ± 14	56 ± 14	0.68	-3.5 to 5.4
ESS	4 ± 3	3 ± 2	0.12	-1.4 to 0.17
BMI (kg/m2)	28 ± 6	28 ± 4	0.37	-2.3 to 0.88
DL (years)	32 ± 16	34 ± 15	0.56	-3.4 to 6.3
OSAS patients				
Variables	Exploratory study (n=150)	Validation study (n=198)	P- Value	CI of difference
Age (Years)	53 ± 12	53 ± 11	0.45	-1.4 to 3.2
ESS	14 ± 5	13 ± 6	0.09	-2.2 to 0.03
BMI (kg/m2)	36 ± 8	35 ± 7	0.12	-2.7 to 0.31
DL (Years)	31 ± 12	32 ± 11	0.87	-2.2 to 2.6
ODI	40 ± 26	34 ± 24	0.02	-11.30 to -0.73

Data is presented as mean +/- SD, ESS: Epworth Sleepiness Score, BMI: Body Mass Index (kg/m2), DL: Driving Licence (years), ODI: Oxygen Desaturation Index, CI: Confidence interval

7.7.2- Primary Outcome

7.7.2.1- Exploratory study

A- CFQ score between controls, OSA (ESS </=10) and OSAS (ESS > 10) patients

There was a significant difference in the total CFQ score and in all the five

domains between controls, OSA and OSAS patients. On multiple comparison tests, there was no difference between controls and OSA patients but a significant difference between controls v/s OSAS patients and OSA v/s OSAS patients respectively as shown in table 7-2.

B- CFQ score and severity of SDB

Except for "names", there was a statistically significant difference between the total CFQ score, "memory", "lack of concentration"; "motor function" and "social interaction" between controls and patients with mild, moderate and severe sleep disordered breathing. However on multiple comparison testing (Bonferroni's) there was no significant difference between the severities except between mild versus severe OSA. This was due to a smaller number of patients in the mild OSA subgroup and the mild OSA group being more sleepy compared to severe OSAS [ESS (mean/SD), 16 +/- 3 versus 13 +/- 5, P = 0.01, 95% CI= -4.7 to -0.58]. This is shown in table 7-3.

C- Correlation of total CFQ score with ESS, DSS, ODI and age

There was a good correlation between total CFQ score and ESS (r^2 = 0.45, P = < 0.0001) and DSS (r^2 = 0.39, P = < 0.0001) but a weak correlation with ODI (r^2 = - 0.18, P = 0.02) and age (r^2 = - 0.21, P = 0.007).

Table 7-2, exploratory study; CFQ score between controls, OSA (ESS </=10) and OSAS (ESS>10) patients

Parameter Mean (SD)	Controls (n = 105)	OSA (n = 38)	OSAS (n =112)	One-way ANOVA P-Value	Bonferroni's multiple testing correction: is p<0.05?		
					Control v/s OSA	Control v/s OSAS	OSA v/s OSAS
Total CFQ score	28 (11)	26 (15)	40 (20)	< 0.0001	No	Yes	Yes
Memory	8 (4)	8 (5)	13 (6)	< 0.0001	No	Yes	Yes
Lack of concentration	7 (4)	7 (5)	11 (6)	< 0.0001	No	Yes	Yes
Motor function	4 (2)	4 (3)	7 (4)	< 0.0001	No	Yes	Yes
Social interaction	5 (2)	5 (3)	7 (4)	< 0.0001	No	Yes	Yes
Names	3 (2)	2 (2)	3 (2)	0.02	No	No	Yes

Table7-3, exploratory study; comparison of CFQ score between controls and OSA patients, grouped by severity of SDB

Parameter - Mean (SD)	Controls (n = 105)	Mild (n = 26)	Moderate (n = 40)	Severe (n= 84)	One-way ANOVA (P-Value)
Total CFQ score	28 (14)	45 (24)	40 (18)	32 (19)	< 0.0001
Memory	8 (4)	14 (7)	13 (6)	10 (6)	< 0.0001
Lack of concentration	7 (4)	12 (7)	10 (5)	9 (6)	< 0.0001
Motor function	4 (2)	8 (5)	7 (3)	5 (4)	< 0.0001
Social interaction	5 (2)	8 (4)	7 (4)	6 (3)	0.0001
Names	3 (1)	3 (2)	3 (2)	3 (2)	0.15

Bonferroni's multiple testing correction: is p<0.05?						
Parameter Mean (SD)	Control v/s Mild	Control v/s Moderate	Controls v/s Severe	Mild v/s Moderate	Mild v/s Severe	Moderate v/s Severe
Total CFQ score	Yes	Yes	No	No	Yes	No
Memory	Yes	Yes	No	No	Yes	No
Lack of concentration	Yes	Yes	No	No	Yes	No
Motor function	Yes	Yes	No	No	Yes	Yes
Social interaction	Yes	No	No	No	Yes	No
Names	No	No	No	No	No	No

D- Regression analysis and ROC curve

Binary regression analysis (step wise forward conditional) was done to develop a predictive model for accidents based on CFQ and derived from the individual domain scores. "Memory" (P= 0.01), "lack of concentration" (P= .001), "motor" (< 0.0001), "social interaction" (P= 0.05) and "names" (P= 0.02) were significant but the domain of "motor function" had the highest predictive power [PPV= 56.76%, 95% CI = 42.78% to 69.74% and NPV= 64.60%, 95% CI= 59.76% to 69.16%]. The area under the curve (AUC) was 0.67 (95% CI, 0.58 to 0.74). The ROC curve is shown in figure 7-1.
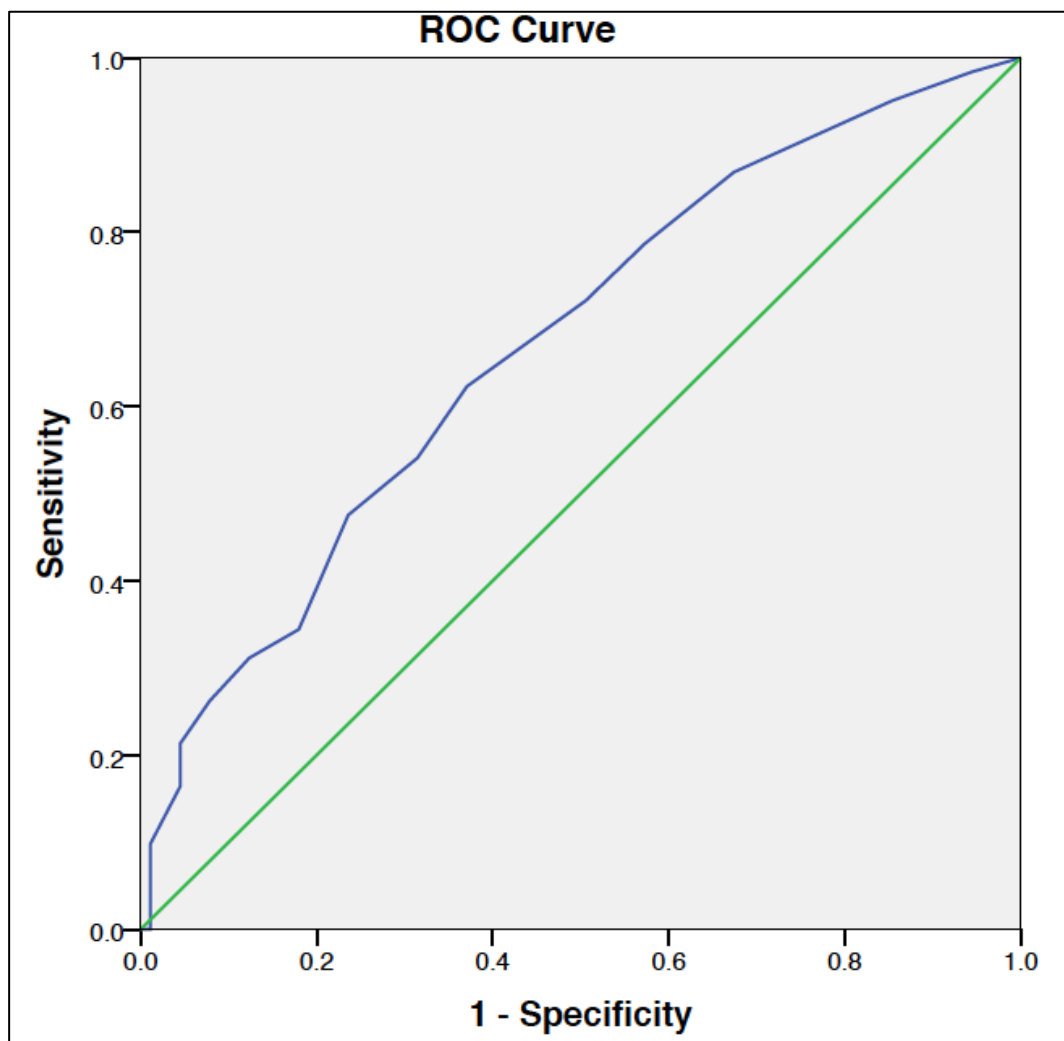
Figure 7-1 showing the ROC in the predictive model

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7.2.2.2- Validation study

The results in the total CFQ score and all the five domains were similar to the exploratory study. There was a good correlation with total CFQ score v/s ESS (r^2 = 0.40, P = < 0.0001) and DSS (r^2 = 0.41, P = < 0.0001) but a weak correlation with age (r^2 = - 0.23, P = 0.0008) and no correlation with ODI (r^2 = -0.06, P = 0.39) respectively. 6 patients had missing data for accident history. The total CFQ including all the domain scores was significantly higher in patients who reported either an accident and/or near miss in the last year. I could apply the exploratory model in 192 patients in the validation cohort. AUC was 0.65, similar to the exploratory model (AUC= 0.67), P= 0.74. The results are shown in Tables 7-4 and 7-5 respectively.

Table 7-4, validation study; CFQ score between controls, OSA and OSAS patients

Parameter Mean (SD)	Controls (n = 68)	OSA (n = 68)	OSAS (n =130)	One-way ANOVA P-Value	Bonferroni's multiple testing correction: is $p<0.05$?		
					Control v/s OSA	Control v/s OSAS	OSA v/s OSAS
Total CFQ score	28 (14)	28 (17)	43 (18)	< 0.0001	No	Yes	Yes
Memory	9 (5)	9 (5)	13 (6)	< 0.0001	No	Yes	Yes
Lack of concentration	7 (4)	8 (5)	12 (5)	< 0.0001	No	Yes	Yes
Motor function	5 (3)	4 (3)	7 (4)	< 0.0001	No	Yes	Yes
Social interaction	5 (3)	5 (3)	8 (3)	< 0.0001	No	Yes	Yes
Names	2 (1)	3 (2)	4 (2)	<0.0001	No	No	Yes

Table 7-5, validation study; CFQ score between controls and OSA severity

Parameter - Mean (SD)	Controls (n = 68)	Mild (n =44)	Moderate (n =67)	Severe (n= 87)	One-way ANOVA (P-Value)
Total CFQ score	28 (14)	41 (20)	37 (20)	37 (18)	0.0005
Memory	9 (5)	12 (7)	11 (6)	11 (5)	0.003
Lack of concentration	7 (4)	12 (5)	10 (6)	10 (6)	0.0001
Motor function	5 (3)	6 (5)	6 (4)	6 (4)	0.13
Social interaction	5 (3)	7 (4)	7 (4)	7 (4)	0.008
Names	2 (1)	4 (2)	4 (2)	4 (2)	< 0.0001

Bonferroni's multiple testing correction: is p<0.05?					
Parameter- Mean (SD)	Control v/s Mild	Control v/s Moderate	Controls v/s Severe	Mild v/s Moderate	Mild v/s Severe	Moderate v/s Severe
Total CFQ score	Yes	Yes	Yes	No	No	No
Memory	Yes	No	Yes	No	No	No
Lack of concentration	Yes	Yes	Yes	No	No	No
Motor function	No	No	No	No	No	No
Social interaction	Yes	Yes	Yes	No	No	No
Names	Yes	Yes	Yes	No	No	No

7.7.3- Secondary outcome

7.7.3.1- Comparing driving incidents between severity of SDB, general sleepiness and specifically whilst driving

As compared to controls, patients were more likely to report either a near miss (25% v/s 7%, P= < 0.0001, OR= 3.9), accidents (8% v/s 2%, P= 0.01, OR= 3.5). This is similar to other studies that are listed in table1-2, Chapter-1. The incidence of driving incidents was significantly higher in patients who reported either a higher degree of sleepiness in general (ESS) or specifically whilst driving (DSS). There was no difference in the severity of sleep disorder breathing as shown in table 7-6.

Table 7-6, showing the driving incidents between severity of SDB, general sleepiness and specifically whilst driving

Parameters	Accidents and or near miss		P- value	OR	95% CI
	Yes	No			
Mild SDB (n=33)	36% (12)	64% (21)	0.81	1.09	0.51- 2.3
Moderate/ Severe SDB (n =315)	34% (108)	66% (207)			
ESS < / = 10 (n =105)	24% (25)	76% (80)	0.005	2	1.2-3.4
ESS > 10 (n = 243)	39% (95)	61% (148)			
DSS </ = 7 (n = 228)	29% (67)	91% (161)	0.009	1.83	1.1-2.9
DSS > 7 (n = 120)	43% (52)	57% (68)			

7.7.3.2- Driving incidents versus CFQ score

The total CFQ including all the domain score was significantly higher in patients who reported either an accident history and/or near miss as shown in table 7-7.

Table 7-7, showing the CFQ v/s accident history and or near miss

Parameter- Mean (SD)	Accidents and or near miss		P= Value
	Yes (n=61) (41%)	No (n=89) (59%)	
Total CFQ score	43 (21)	35 (18)	0.001
Memory	13 (7)	10 (6)	0.01
Lack of concentration	12 (6)	8 (5)	0.0005
Motor function	7 (4)	5 (4)	0.0002
Social interaction	7 (4)	6 (3)	0.004
Names	3 (2)	2 (2)	0.01

7.8- Discussion

In this observational study I have shown that untreated OSAS patients, but not patients with OSA, are more likely to have had a near miss or an RTA in the last one year compared to controls. A higher CFQ score is associated with either a near miss and or an accident in the last one year; the domain of "motor function" being the strongest predictor. In both the exploratory and the validation cohorts I have shown that rather than the severity of sleep disordered breathing it is sleepiness that increases both cognitive dysfunction and accident risk. The presence of sleepiness (ESS > 10) predicts higher CFQ score and there was no difference either in the total CFQ score or any of the subscale scores between patients who were not sleepy (ESS </=10) and controls. Furthermore there was a good correlation with ESS, DSS and a weak correlation with severity of sleep disordered breathing.

Both the DVLA interpretation and the EU directive put emphasis on the severity of SDB based on AHI, in determining how patients with OSA/OSAS should be advised about driving. 34% of our patients, with sleep disordered

breathing and symptoms of sufficient severity to warrant a trial of CPAP reported an accident or near miss in the last year compared to 14% of controls. Data presented here suggest that the severity of the sleep disorder breathing, by itself, is not relevant as there was no difference in the percentage reporting accidents and / or near misses in those with mild compared to those with moderate or severe SDB. Sleepiness, both in general (ESS) and specifically while driving (DSS) appears to be more relevant but even so 24% of patients with an ESS of less than 10 and 29% with a DSS less than 7 reported an accident or near miss in the last year. These figures could be considered to be unacceptably high, being approximately twice the rate seen in controls, raising the question of whether driving should be advised against in any patient with OSAS of sufficient severity to warrant a trial of CPAP. This would be in keeping with the EU Directive regarding the importance of treatment deemed necessary by a physician. It does however have the danger of driving the problem underground, with patients not seeking medical advice or not trying CPAP for fear that they might lose their licence.

The DVLA guidance suggests that in the absence of significant sleepiness other factors, only concentration is specifically mentioned, should be taken into account when advising patients about driving. My data suggest that cognitive function and sleepiness are closely linked and that in the absence of sleepiness patients are unlikely to have significant problems with cognitive function. A number of studies have shown structural brain damage in patients with OSAS [145-146] but it appears that most of the cognitive dysfunction is due to sleepiness and therefore reversible with treatment. This requires

further research. One of the strengths of this study was that the questionnaires were anonymised, making it more likely that patients would tell the truth. The rate of accidents and near misses in our study was similar to other that reported in other studies (table 1-2, Chapter 1). However the previous studies did not take near misses into account. While intuitively reasonable that sleepiness likely to be likely to impair safe driving is more important than sleepiness in general this is not supported by my data. The accident / near miss rate in patients with an ESS greater than 10 was very similar to that in patients with driver sleepiness score greater than 7.

The fact that the cognitive failures questionnaire was predictive of accidents and also correlated with sleepiness suggests that it could be used as an alternative, or complementary, approach in assessing the at risk driver. Patients may realise that admitting to sleepiness, particularly while driving, increases the risk that they will be advised to surrender their licence whereas the cognitive failures questionnaire effectively provides similar information but in a less obvious, and therefore less threatening, manner. However the cognitive failures questionnaire still relies on patient self-report. Objective tests of sleepiness as predictors of driving risk are disappointing and the use of objective tests of cognitive function might be more effective and are worthy of further investigation.

7.9- Study limitations

This study only recruited patients with OSAS of sufficient severity to warrant a trial of CPAP; this is the group in which a risk assessment needs to be made

about an individual's continued driving. It would not be appropriate to say that someone did not have OSAS of sufficient severity to warrant treatment but severe enough that a patient should not drive. The results are consistent with the EU Directive recommendation that a clinician determining that treatment with CPAP necessary is a key factor in determining whether an individual is at increased risk of an accident. However this study needs to be extended to patients with milder OSAS, as they may still be at increased risk of an accident. Controls did not undergo any objective screening. However the questionnaire included questions about symptoms of snoring or OSA and controls were only included if they had a low probability for OSAS. I think it is very unlikely that we included any controls with significant OSAS and the results of the driving simulation and the questionnaire would support this. I used a questionnaire to assess cognitive function and this is subject to the same limitations as a questionnaire about driving behaviours. However it has the advantage that it can be performed easily in patients attending a sleep clinic as it does not involve the same level of supervision as for an objective test. In practical terms a complementary approach could be considered. If a patient admits to cognitive failures there is no need to follow this up with more time consuming objective testing which can be reserved for those who deny problems but in whom there is a high degree of concern. This approach requires further evaluation and in particular the identification of the most appropriate tests of cognitive function relevant to driving accident risk.

7.10- Conclusions

This study suggests that the severity of SDB is not relevant to driving accident risk and that the arbitrary classification of severity should be removed from guidance about driving in patients with OSAS. Sleepiness and cognitive failures appear to be a much better predictor of accident risk. However I found that even patients with a normal ESS or no significant sleepiness during driving, compared to controls, still reported an excessive number of driving events. My study was in patients for whom a trial of CPAP had been recommended by a clinician. However while there is unlikely to be significant disagreement between clinicians as to the appropriateness of CPAP in patients with severe symptomatic OSAS it is likely that different clinicians will draw the line at a different point in those with mild symptoms. Driving is such an important part of most patients everyday life that once it is decided that CPAP is appropriate treatment should be implemented with the minimum of delay. Further studies are needed to establish accident risk in patients with OSAS but not of sufficient severity to warrant treatment.

Chapter- 8

Conclusions and future work

Concluding statement

OSAS is an escalating problem with little sign of abating for health care services and clinicians. Many patients with OSAS drive a vehicle both for pleasure and as part of their employment. A key component in the management of OSAS involves appropriate risk assessment about driving in order to prevent RTA that carries a significant socioeconomic burden to society. Current guidelines endorsed by various medical societies and from licencing authorities have led to some consternation among patients, sleep apnoea support groups and clinicians. The research work presented in this thesis has provided significant insights into the fitness to drive and accident risk assessment in OSAS patients.

The BTS driving survey highlighted the variability in the advice given and the discordant views about residual drowsiness and adequate CPAP compliance. Following this study BTS issued a position statement regarding driving and OSAS. However a repeat survey in 2015, using exactly the same vignettes [152] disappointingly suggested that the statement had had little impact. The change in emphasis from excessively sleepy to sleepiness likely to impair safe driving was felt to be helpful by a small majority. There is a clear need for tools which are felt to be robust by clinicians and patients to aid the decision making about fitness to drive.

Neither accidents nor sleepiness while driving are unique to patients with OSAS and deciding which patients should not drive, and then justifying the decision to them, is difficult. Clinicians are dependent upon what patients say and it is considered likely by most clinicians that some patients may underestimate symptoms or not be truthful when answering questions about driving if they think that their licence might be at

risk. When discussing sleepiness at the wheel patients sometimes state "everyone struggles sometimes" or something similar. Previous attempts at devising an objective test lacked credibility as a legitimate test of driving ability. I have therefore attempted to establish what constitutes "normal" sleepiness while driving in controls and contrasted this with patients with significant OSAS. I have described one of the few studies which provides objective criteria to help inform the decision making process and as far as am aware the only one which establishes what is "normal" sleepiness at the wheel (that does not mean that any sleepiness at the wheel is acceptable but does provide a robust justification for restricting driving in certain patients with OSAS). If patients answer questions about driving truthfully clinicians have a justification for their decision to restrict driving, which is based upon evidence. I have also suggested which patients, who deny problems driving, should be tested upon an advanced PC based driving simulator and criteria, and justification, for which should then be advised not to drive. By integrating self- report measures of sleepiness, safety-critical driving incidents and performance based on a driving simulator task, a number of red and amber flags are suggested to indicate that an individual is potentially at higher risk of having an accident due to sleepiness at the wheel and a clinician can have confidence that their decision that the patient be advised not to drive is reasonable and can be justified.

Advanced PC based driving simulators have a role in identifying the at risk driver, and a proportion of OSAS patients who fail the MUoLDS can be reliably identified based on by SDLP. The randomised trial has shown that this continuously measured variable is repeatable with no effect of a simple incentive. However a proportion of patients had a change in MUoLDS outcome. Patients with high BMI or high ESS or

the worse severe SDB who pass the test should be considered for retesting, perhaps with some sort of distraction task or a drive of longer duration.

OSAS patients report frequent use of certain measures or coping strategies to combat fatigue and some admit to sleepiness both generally and specifically while driving. These counter measures may be surrogate markers of fatigue and sleepiness. Asking about such strategies in clinical practice may aid the clinician in identifying the at risk patients.

Sleepiness rather than severity of sleep disordered breathing predicts cognitive failure. Higher CFQ score is associated with accident risk. The CFQ holds promise, is easy to complete, may identify a different aspect of accident risk and therefore be useful in assessing fitness to drive in OSAS patients. Safe driving is not only related to driving without errors, but intentional violations and risky behaviours are also important components [153]. Unsafe behaviours originate from failures of information processing and action execution and also from deliberate deviations from rules and procedures. Therefore a model of cognitive failures causing unsafe behaviour should also be considered [154]. Objective tests of sleepiness as predictors of driving risk are disappointing and the use of objective tests of cognitive function might be more effective and are worthy of further investigation.

Further research

The simulator run on MUoLDS was on in automatic mode with basic driving controls. It lacked certain advanced features such as a comfortable car seat, motion sensors, vehicle gear changes, the ability to measure pupillary changes to choreographed events on the simulator and video recording of both controls and OSAS patients. As a first step a second generation MUoLDS is needed.

I. Further studies are required to validate the driving questionnaire, DSS and the normal range.

II. The normal range described was exclusively in males with significant OSAS and further studies in a wider OSA population and in females are needed.

III. The performance on the MUoLDS was based on SDLP at epoch 3. Further in depth analysis of each epoch should be undertaken for a better understanding of performance on the simulator both in controls and in a wider OSA population.

IV. There is a need for a trial to test the issue of repeatability and the effect of incentives in controls.

V. Coping strategies need to be evaluated in females along with validating these strategies.

VI. A future model to predict accident risk by combing DSS, safety- critical driving incidents, coping strategies, CFQ score, MUoLDS outcome and performance holds promise.

VII. Finally, further simulator studies are needed exploring non-motorway scenarios.

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Appendix

I- PARTICIPANT INFORMATION LEAFLET

Title of the Study

A- Driving simulator performance in obstructive sleep apnoea

Establishing a normal range and determining factors which influence simulator performance & optimal length of study

Introduction

You are being invited to take part in a research study. Before you decide, it is important that you understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Please ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part or talk about it with family or friends before making your decision. Any information you give during this study will not become part of your medical records or be made available to the clinicians involved in your care and will not be used to make any decisions about your ability to drive .

What is the purpose of the study?

Many people suffer from a condition known as obstructive sleep apnoea (OSA). During sleep the muscles of the upper airway relax causing a degree of narrowing. This may lead to partial obstruction which causes vibration and the noise of snoring. If more severe narrowing occurs the airway may be completely obstructed. If this occurs the individual makes increasing efforts to breathe, but these are ineffective because the airway is simply sucked more tightly shut. (It is analogous to trying to suck through a

straw that has lost its rigidity.) After several efforts there is an arousal and the tone is immediately restored to the upper airway. A large breath, and usually snore, ensues and the individual immediately returns to sleep. These arousals may last no more than a few seconds and the individual concerned is usually completely unaware that they are occurring. Occasionally they may awake with a sensation of suffocation or choking. If these episodes occur regularly sleep is disturbed and in particular the individual is prevented from entering the deeper stages of restorative sleep and suffers from sleep fragmentation. As a consequence affected individuals are always tired and tend to fall asleep during the day. This may affect their ability to drive safely.

In the research setting driving simulators (simulated driving using a computer) have been used to investigate some aspects of driving performance but it is not known whether these simulators are helpful in identifying those individuals who may have a problem maintaining concentration and vigilance while driving and those who have no such problems.   We are conducting this research to address this issue.

Why have I been chosen?

We wish to study patients with sleep apnoea & compare them with people who do not have sleep apnoea. You have been chosen because you fall into one of these categories.

Do I have to take part?

Participation is entirely voluntary. If you decide to take part, you will be given this information sheet to keep and asked to sign a consent form. If you decide to take part you are still free to withdraw at anytime and without giving a reason.

If you choose not to join this study or subsequently decide you no longer wish to take part , the hospital care you may receive in the future will not be affected.

What will happen if I decide to take part?

If you agree to take part in this research study, you first will be asked to sign the consent form attached at the back of this information leaflet.

You need to be with us for about 2 hours. You will be asked to complete a questionnaire about your driving habits and various other questions about your health and everyday life.. You will then be asked to "drive" on a computer based driving simulator. The computer will have a large screen, steering wheel, foot pedals, a gear shift and realistic graphics. You will need to react to images on the computer screen just as if you were driving normally. . After a practice run of approximately 20 minutes you will be asked to perform the test, which involves "driving" on a motorway for approximately 50 minutes. You will be asked not to drink any caffeinated drinks (tea, coffee, hot chocolate, etc.) for at least 2 hours before the tests and until the test is completed. The session will be organized on a mutually convenient day.

What are the possible disadvantages and risks of taking part?

There are no risks involved.

What are the possible benefits of taking part?

Your participation in the study is unlikely to be of direct benefit to you. It is possible that performance on the simulator may give you some insights into your own driving performance. It should be stressed that the results from this study will not be used in

any way to advise you on whether you are safe to drive or not and the information derived from the study will not become part of your medical records or be made available to the clinicians responsible for your care.

What if something goes wrong?

If you are harmed by taking part in this research project, which is most unlikely, there are no special compensation arrangements. If you are harmed due to someone's negligence, then you may have grounds for legal action. Regardless of this if you would like to complain about any aspect of the way you have been approached or treated during the course of this study the normal National Health Service compliant mechanism is available to you.

Will my taking part be kept confidential?

All information collected about you during the course of the research will be kept confidential. Identifiers such as your name or address will not be used in any publications or reports. All electronic data will be password protected and stored in a secure location. Each patient will be given a unique identity number from which all their results will be associated. Neither the researchers, nor the doctors involved in your care, will be able to identify an individual from these results.

What will happen to the results of the research study ?

After the completion of our study, which we expect to last about 2 years we wish to publish them in an international medical journal & also would like to present them in conferences. Your identity will not be divulged in any report/publication unless you

have consented to release such information. If you would like to know about the outcomes of the research we would be happy to give it you. For that you need to contact us in the number given below.

Further information

This study is being conducted by Dr. Mark Elliott & his team at Leeds Teaching Hospitals NHS Trust.

If you have any questions or require further information regarding the research, please contact:

<div align="center">

Dr. Mark Elliott

Consultant Chest Physician

St James's University Hospital

Leeds, LS9 7TF

Email: mark.elliott@leedsth.nhs.uk

Tel. 0113 2065683

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<u>**Title of the study**</u>

B- Repeatability and effect of incentives on an office based advanced driving simulator to assess driving performance in Obstructive Sleep Apnoea Syndrome (OSAS)

Introduction

You are being invited to take part in a research study. Before you decide, it is important that you understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Please ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part or talk about it with family or friends before making your decision. Any information you give during this study will not be part of your notes and will not be used to inform your ability to drive in anyway.

What is the purpose of the study?

Many people suffer from a condition known as obstructive sleep apnoea (OSA). During sleep the muscles of the upper airway relax causing a degree of narrowing. This may lead to partial obstruction, which causes vibration and the noise of snoring. If more severe narrowing occurs the airway may be completely obstructed. If this occurs the individual makes increasing efforts to breathe, but these are ineffective because the airway is simply sucked more tightly shut. (It is analogous to trying to suck through a straw that has lost its rigidity.) After several efforts there is an arousal and the tone is immediately restored to the upper airway. A large breath, and usually snore, ensues and the individual immediately returns to sleep. These arousals may last no more than

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a few seconds and the individual concerned is usually completely unaware that they are occurring. Occasionally they may awake with a sensation of suffocation or choking. If these episodes occur regularly sleep is disturbed and in particular the individual is prevented from entering the deeper stages of restorative sleep and suffers from sleep fragmentation. As a consequence affected individuals are always tired and tend to fall asleep during the day. This may affect their ability to drive safely. Continuous Positive Pressure Ventilation or CPAP is the commonest treatment option for this condition.

We are conducting this research in order to develop a test by which we can study driving behaviour in patients with sleep apnoea. In order to do that, we are trying to establish some of the qualities that should be the part of any reliable test.

One of the most important issues to address is whether driving performance can be repeatable and the effect of the incentives on an office based advanced driving simulator. This study will try to address this issue.

Why have I been chosen?

We wish to study patients with sleep apnoea who drive. You have been chosen because you fall into this category.

 Do I have to take part?

Participation is entirely voluntary. If you decide to take part, you will be given this information sheet to keep and asked to sign a consent form. If you decide to take part you are still free to withdraw at anytime and without giving a reason.

If you choose not to join this study or subsequently decide you no longer wish to take part, the hospital care you may receive in the future will not be affected.

What will happen if I decide to take part?

If you agree to take part in this research study, you first will be asked to sign the consent form attached at the back of this patient information form.

You need to be with us for about 2 hours. You will be asked to complete a questionnaire about your driving habits and your sleepiness. You will then undergo driving simulator tests. This will involve "driving" a computer based driving simulator. The computer will have a large screen, steering wheel, foot pedals, a gearshift and realistic graphics. You will need to react to images on the computer screen such as cars in front braking, overtaking, etc. After about 20 minutes of practice session you will be asked to perform the test, which involves "driving" on a motorway for approximately 50 minutes. You will be asked not to drink any caffeinated drinks (tea, coffee, hot chocolate, etc.) for at least 2 hours before the tests and until the test is completed. There will be two such sessions on 2 different days.

What are the possible disadvantages and risks of taking part?

There are no risks as such. Approximately 2% of people develop feelings of sickness with simulated driving. This is usually only mild, but if it occurs the test will be stopped.

What are the possible benefits of taking part?

Your participation in the study is unlikely to be of direct benefit to you. It is possible that performance on the simulator may give you some insights into your own driving

performance. It should be stressed that the results from this study will not be used in any way to advise you on whether you are safe to drive or not.

WARNING This test has not been sufficiently well validated for the results from it to be used, at this stage, to make decisions about whether an individual is safe to drive or not. A good result on this test does not mean that you are safe to drive. Neither does poor performance on the driving simulator mean that you are not safe to drive. Decisions about whether you are safe to drive or not should still be made by you and your doctor (your doctor will not be informed about the results of this test).

What if something goes wrong?

If taking part in this research project harms you there are no special compensation arrangements. If you are harmed due to someone's negligence, then you may have grounds for legal action. Regardless of this if you would like to complain about any aspect of the way you have been approached or treated during the course of this study the normal National Health Service complaint mechanism is available to you.

Will my taking part be kept confidential?

All information collected about you during the course of the research will be kept confidential. Identifiers such as your name or address will not be used in any publications or reports. All electronic data will be password protected and stored in a secure location. Each patient will be given a unique identity number from which all his or her results will be associated. Neither the researchers, nor the doctors involved will be able to identify a patient from their results. Therefore we will not be able to

advise you on how well you have done. This is to protect those patients who may be reluctant to participate for fear they will be told they cannot drive afterwards.

What will happen to the results of the research study?

After the completion of our study, which we expect to last about 12 months we wish to publish them in an international medical journal & also would like to present them in conferences. Your identity will not be divulged in any report/publication unless you have consented to release such information. If you would like to know about the outcomes of the research we would be happy to give it you. For that you need to contact us in the number given below.

Further information

This study is being conducted by Dr.Mark Elliott & his team at Leeds Teaching Hospitals NHS Trust.

If you have any questions or require further information regarding the research, please contact:

<div align="center">

Dr.Mark Elliott
Consultant Chest Physician
St James's University Hospital
Leeds, LS9 7TF
Email: mark.elliott@leedsth.nhs.uk
Tel. 0113 2065683

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II-   <u>**CONSENT FORM**</u>

Patient Label

Patient Identification Number for this trial:

<u>Title of the Study</u>

A- Driving simulator performance in obstructive sleep apnoea: Study A: Establishing a normal range

Name of Researcher: **Dr.M.W.Elliott**

Please initial box

1. I confirm that I have read and understand the information sheet dated 08/02/09

   (version 1.0) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.

2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.

3. I understand that relevant sections of any of my medical notes and data collected during the study, may be looked at by responsible individuals from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records. I also understand that after completion of the research the

   anonymized data might be published in an international journal.

4. I agree to take part in the above study.

_____   _____   _____
Name of Patient   Date   Signature

_____   _____   _____
Name of Person taking consent   Date   Signature
(if different from researcher)

_____   _____   _____
Researcher   Date   Signature

When completed, 1 for patient; 1 for research file; 1 (original) to be kept in medical notes

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Patient Label:

Patient Identification Number for this trial:

Title of the Study

B- Repeatability and effect of incentives on an office based advanced driving simulator to assess driving performance in Obstructive Sleep Apnoea Syndrome (OSAS)

Name of Researcher: **Dr.M.W.Elliott**

Please initial box

1. I confirm that I have read and understand the information sheet dated 23.05.2012

   (Version 2) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.

2. I understand that my participation is voluntary and that I am free to withdraw at any time,

   without giving any reason, without my medical care or legal rights being affected.

3. I understand that relevant sections of any of my medical notes and data collected
   during the study, may be looked at by responsible individuals from the NHS Trust,
   where it is relevant to my taking part in this research.

4. I give permission for these individuals to have access to my records and also
   understand that after completion of the research the anonymized data
   might be published in an international journal.

5. I have read and understood the warning that how I perform on the simulator should
   not be used as evidence of whether I am safe to drive or not.

6. I agree to take part in the above study.

_____   _____   _____
Name of Patient   Date   Signature

_____   _____   _____
Name of Person taking consent   Date   Signature
(if different from researcher)

_____   _____   _____
Researcher   Date   Signature

When completed, 1 for patient; 1 for research file; 1 (original) to be kept in medical not

III-   Fatigue and Driving Questionnaire

This questionnaire will help us to understand your driving habits, whether you are sleepy during the day and if so its effect on your everyday life. **Your answers are confidential and will not be entered into your medical records & will not be used to judge your ability to drive in any way**. Therefore please answer as **honestly and accurately** as possible. Please circle the most appropriate answer. Some questions may require more than one answer.

Section A

1.Do you snore?

        Never

        Occasionally

        Frequently

        Every night

2. Has anyone ever commented that you stop breathing when you are asleep?

        Never

        Occasionally

        Frequently

        Every night

3. Do you fall asleep during the day ?

        Never

        Only if I want to (eg choosing to take a nap)

        Only if bored or relaxing

        Sometimes even if occupied

        Often

Section B

How likely are you to doze off or fall asleep in the following situations, in contrast to feeling just tired ? This refers to your usual way of life in recent times. Even if you have not done some of these things recently try to work out how they would have affected you. Use the following scale to choose the most appropriate number for each question.

0 = would never doze

1 = slight chance of dozing

2 = moderate chance of dozing

3 = high chance of dozing

Situation	Chance of dozing
Sitting & reading	_____
Watching TV	_____
Sitting, inactive in a public place (eg. Theatre or a meeting)	_____
As a passenger in a car for an hour without a break	_____
Lying down for a rest in the afternoon when circumstances permit	_____
Sitting & talking to someone	_____
Sitting quietly after lunch without alcohol	_____
In a car, while stopped for a few minutes in the traffic	_____

Section C

1. How long have you had your driving licence? …….. yrs

2. Does your job involve night shifts?

      Yes   No

If yes please give brief details of shift pattern

3. Are you a HGV/PSV driver?

  Yes   No

4. How many miles would you normally drive in a year?

More than 50,000 miles

20,000 – 50,000 miles

15,000 - 20,000 miles

10,000 -15,000 miles

5,000 -10,000 miles

Less than 5,000 miles

5. Which best describes your pattern of driving ? (*Tick the most appropriate answers)*

    a) Only local journeys of less than 1 hour, never on motorways

    b) Mainly local journeys of less than one hour, occasional (less than once per month) longer journeys, never on motorways

    c) Mainly local journeys of less than one hour, occasional (less than once per month) longer journeys including motorway driving

    d) At least once per month drive for more than one hour, including motorway driving

    e) Regular journeys of at least one hour on all types of road

6. If you were to make a long journey for how long would you generally drive before stopping for a break?

More than 4 hours

3 - 4 hours

2 - 3hours

1- 2hours

Less than 1 hour

Never make long journeys

7. How likely are you to doze off or feel sleepy while driving at each of the following times of day (if you do not drive at these times please try to imagine how you would feel then) ? *(Circle the most appropriate answers)*

Early morning:

Would never doze off / slight chance / moderate chance/ high chance/ don't know

Mid-morning:

Would never doze off / slight chance / moderate chance/ high chance/ don't know

Noon time:

Would never doze off / slight chance / moderate chance/ high chance/ don't know

Mid-afternoon:

Would never doze off / slight chance / moderate chance/ high chance/ don't know

Evening:

Would never doze off / slight chance / moderate chance/ high chance/don't know

Late at night:

Would never doze off / slight chance / moderate chance/ high chance/don't know

8. **How likely are you to doze off or feel sleepy while driving the following types of journey?** (Circle *the most appropriate answers*)

Journeys less than 30 minutes

Would never doze off / slight chance / moderate chance/ high chance/don't know

Journeys 30 minutes to one hour

Would never doze off / slight chance / moderate chance/ high chance/don't know

Journeys one to two hours

Would never doze off / slight chance / moderate chance/ high chance/don't know

Journeys more than two hours

Would never doze off / slight chance / moderate chance/ high chance/don't know

Motorways

Would never doze off / slight chance / moderate chance/ high chance/don't know

Urban roads

Would never doze off / slight chance / moderate chance/ high chance/don't know

Country roads

Would never doze off / slight chance / moderate chance/ high chance/don't know

9.Have you ever nodded off whilst driving? *(Circle the most appropriate answers)*

During last 1 year : Yes > 5 times   Yes 3-4 times   Yes 1-2 times

   Never

During last 3 years : Yes > 5 times   Yes 3-4 times   Yes 1-2 times

   Never

11.Have you ever driven over the rumble strip on the motorway?

(C)ircle the most appropriate answers)

During last 1 year :   Yes > 5 times

Yes 3-4 times

Yes 1-2 times

Never

Don't drive on motorways

During last 3 years :   Yes > 5 times

Yes 3-4 times

Yes 1-2 times

Never

Don't drive on motorways

12. While you were driving, regardless of blame

	1 year?	3 years?
how many near misses have you had in the last		
how many accidents causing only minor damage have you had in the last		
how many accidents causing some damage requiring repair have you had in the last		
how many accidents involving major garage work or write off have you had in the last		

13. Regardless of blame have you reported any accidents to your insurer in the last

1 year? No / Yes (if yes number)……..

3 years? No / Yes (if yes number)……..

14. How much alcohol do you drink in a week?

I don't drink alcohol

Less than 7 units

7-14 units

14-21 units

More than 21 units

(1 Unit = equals half a pint of beer, a small glass of wine or a pub measure of spirits)

Section : D

1. How long since you last had a caffeinated drink (tea, coffee, etc)? ……..hours

2. What time did you go to sleep last night? …………..

3. What time this morning did you get up? ……………

4. How was the quality of sleep last night?

Good   Average   poor

5. How would you rate your quality of sleep last night compared to your normal?

Better   Same   Worse

6. **How alert do you feel now?**

Degree of Sleepiness	Scale Rating
Feeling active, vital, alert, or wide awake	1
Functioning at high levels, but not at peak; able to concentrate	2
Awake, but relaxed; responsive but not fully alert	3
Somewhat foggy, let down	4
Foggy; losing interest in remaining awake; slowed down	5
Sleepy, woozy, fighting sleep; prefer to lie down	6
No longer fighting sleep, sleep onset soon; having dream-like thoughts	7
Asleep	X

IV- Protocol for the issue of repeatability and the effect of incentives on an office based advanced driving simulator (MUoLDS) in OSAS patients

Research Study Protocol

Repeatability and effect of incentives on an office based advanced driving simulator to assess driving performance in Obstructive Sleep Apnoea Syndrome (OSAS)

Department of Respiratory Medicine

St. James University Hospital

Beckett Street, Leeds, LS97TF,

West Yorkshire, United Kingdom

GENERAL INFORMATION

PROJECT TITLE

Repeatability and effect of incentives on an office based advanced driving simulator to assess driving performance in Obstructive Sleep Apnoea Syndrome (OSAS).

PROJECT SUMMARY

Patients with obstructive sleep apnoea syndrome (OSAS) are at increased risk of being involved in a road traffic accident (RTA), but not all patients with OSAS are unsafe drivers. The advice that a patient will receive about driving will depend upon their doctor's attitude to risk and this is likely to be inconsistent between clinicians in the absence of objective criteria. Currently advice about an individual's fitness to drive is based upon the severity of the sleep disordered breathing, with or without some objective measure of daytime sleepiness and their account of their driving. Although there is a trend towards increased likelihood of accidents with more severe sleep disordered breathing there is no sufficient robust data on which to base decisions for an individual. There are conflicting data about the relationship between perceived sleepiness (ESS) and the likelihood of being involved in an accident. Driving requires alertness and also complex integrated higher cortical function; there is evidence that patients with OSA may have cerebellar and other neurological damage, which may impact on driving. Driving may therefore be impaired for reasons other than those just related to maintenance of alertness.

A study done at the St.James University Hospital in collaboration with the Institute of Transport Studies, University of Leeds has shown that variables recorded during approximately fifty minutes of simulated motorway driving on the MiniSim can predict

with reasonable accuracy the patients with OSAS who will be involved in a crash in the simulated scenario. Three groups of patients can be identified; those who crash when they really shouldn't, those who do not crash at all and an intermediate group who crash in a situation in which even a reasonably alert driver might crash. In our study, in which we deliberately tried to recruit patients most at risk of having problems while driving, many completed a 50 minute run on a realistic motorway without crashing, going off-road or veering out of lane. (Paper under review). The criteria that we used for "fail" are realistic and understandable to patients. This is very important if the test is to have credibility; an individual who fails on the simulator because they go off road multiple times might argue, quite reasonably, that this is not what happens when they drive a real car and therefore that the simulation is not valid. This is important if this test is going to be credible to patients and licensing authorities alike. While it might be reasonable to include an event such as our final "brake" event, as failure to avoid this is realistic evidence of sub optimal performance, at least during simulated driving, it has the disadvantage that it may limit the usefulness of the test for repeated use. A patient who is expecting something to happen may perform differently the second time. Furthermore they may drive poorly at other times during the tests but, by chance, perform adequately at the event. Variables that are recorded continuously throughout the test, and of which the patient is unaware, are preferable, for monitoring performance.

In common with previous studies we found that poor lane control (SDLP) was related to a crash even when the lane control information was obtained from an epoch where no crash should have occurred (epochs 3, 5, 6 and 7). We confirm that it is a marker for poor driving performance and is a strong predictor of a crash in simulated

situations. Predictive power was increased by the inclusion of reaction time. Again previous studies have shown that untreated OSAS sufferers have worse reaction times than controls and patients with OSAS after CPAP therapy. Our study shows that there are differences even amongst the OSAS sufferers and this impact upon the likelihood of a crash; the reaction time at the veer event was different between all three groups. This is likely to be an underestimate as we had to exclude some patients from the analysis; some subjects (n=5) did not brake at all at the veer event and avoided a crash by veering out of lane, a legitimate manoeuvre, and others (n=4) did not brake at all and crashed. Although this assessment requires an "event" the one programmed is a subtle extension of routine driving behavior and hence it is unlikely to be memorable. The fact that these abnormalities are detected early in the run means that it may be possible to use a shorter test, important in the clinical setting.

If the MUoLDS is to be useful in the clinical setting it is important that the test should be repeatable; in other words it should give the same result when performed on different occasions. We have already established that there is no significant learning effect between the acclimatisation and definitive runs. A major concern about the use of any test, the result of which will be dependent upon the motivation of the subject, is that the individual may be able to "raise their game" if their driving licence is at stake. We now wish to investigate these issues further.

AIM

To study the repeatability and effect of incentives on an office based advanced driving simulator to assess driving performance in Obstructive Sleep Apnoea Syndrome (OSAS).

METHODS

Patients attending the Sleep Clinic at St James's University Hospital will be asked to participate in the study. All subjects will be asked to perform a simulator run, after an initial acclimatisation, on two separate occasions. Subjects will be randomly allocated to one of two groups. Group A will be asked to perform a similar to run on two separate occasions. Group B will be asked to do the same thing but just prior to the final run will be told that if they can improve their performance by 10% they will be given a £20 gift voucher from the Trust fund. Subjects will not be told how this will be measured but it will be based upon the change in SDLP in epoch 3.

ANALYSIS OF RESULTS

- SDLP in epoch 3 and "veer" reaction time will be the co-primary outcome variables.

- Classification of patients into "pass", "fail" and "indeterminate" will be secondary outcome variables.

- Repeatability - SDLP in epoch 3 and veer reaction time in run 1 will be compared with run 2 in groups A using paired T tests, with the level of significance set at $p < 0.05$

- Effect of incentives - the difference in SDLP and veer reaction time in run two will be compared between groups A and B, using unpaired T tests, with the level of significance set at $p < 0.05$

SAMPLE SIZE

There are standard recommendations for sample size for looking at reproducibility and agreement taken from Martin Bland's work. We will recruit 50 subjects for the repeatability and 100 for the effect of incentive components of the study.

DISSEMINATION OF RESULTS AND PUBLICATION POLICY

The initial results will be presented as abstracts in various national and international meetings and conferences with a view to publish it as a paper in a peer reviewed journal.

DURATION OF THE PROJECT

Recruitment is expected to take 12 months.

ETHICS

Approved by Leeds Ethical Committee

INFORMED CONSENT

All participants will sign a consent form. One copy form will be filed in the case notes, one given to the patient and one retained by the researcher.

V- Coping Strategies Questionnaire

1- Have you ever done any of the following in the last 1 year in order to stay awake whilst driving?

(tick as appropriate)

	Never	Occasionally	Frequently
Stopped for a nap			
Stopped for a walk/exercise			
Opened the window			
Turned up the radio/stereo			
Stopped to drink tea/coffee			
Stopped at service area to wash face in cold water			
Sing / talk to yourself			
Chew gum/ eat something			
Fidget / exercise			
Smoke			
Changed seat position			

VI- Cognitive Failure Questionnaire

The following questions are about minor mistakes which everyone makes from time to time, but some of which happen more often than others. We want to know how often these things have happened to your in the past 6 months. Please circle the appropriate number.

		Very often	Quite often	Occasionally	Very rarely	Never
1.	Do you read something and find you haven't been thinking about it and must read it again?	4	3	2	1	0
2.	Do you find you forget why you went from one part of the house to the other?	4	3	2	1	0
3.	Do you fail to notice signposts on the road?	4	3	2	1	0
4.	Do you find you confuse right and left when giving directions?	4	3	2	1	0
5.	Do you bump into people?	4	3	2	1	0
6.	Do you find you forget whether you've turned off a light or a fire or locked the door?	4	3	2	1	0
	7.					
8.	Do you say something and realize afterwards that it might be taken as insulting?	4	3	2	1	0
9.	Do you fail to hear people speaking to you when you are doing something else?	4	3	2	1	0
10.	Do you lose your temper and regret it?	4	3	2	1	0
11.	Do you leave important letters unanswered for days?	4	3	2	1	0
12.	Do you find you forget which way to turn on a road you know well but rarely use?	4	3	2	1	0
13.	Do you fail to see what you want in a supermarket (although it's there)?	4	3	2	1	0

14.	Do you find yourself suddenly wondering whether you've used a word correctly?	4	3	2	1	0
15.	Do you have trouble making up your mind?	4	3	2	1	0
16.	Do you find you forget appointments?	4	3	2	1	0
17.	Do you forget where you put something like a newspaper or a book?	4	3	2	1	0
18.	Do you find you accidentally throw away the thing you want and keep what you meant to throw away – as in the example of throwing away the matchbox and putting the used match in your pocket?	4	3	2	1	0
19.	Do you daydream when you ought to be listening to something?	4	3	2	1	0
20.	Do you find you forget people's names?	4	3	2	1	0
21.	Do you start doing one thing at home and get distracted into doing something else (unintentionally)?	4	3	2	1	0
22.	Do you find you can't quite remember something although it's "on the tip of your tongue"?	4	3	2	1	0
23.	Do you find you forget what you came to the shops to buy?	4	3	2	1	0
24.	Do you drop things?	4	3	2	1	0
25.	Do you find you can't think of anything to say?	4	3	2	1	0