# Towards Better Management of Obstructive Sleep Apnoea in Tetraplegia

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# Abstract

Obstructive sleep apnoea (OSA) is a highly prevalent complication of tetraplegia that worsens health and quality of life. There are effective treatments available yet access to OSA diagnosis and treatment is poor. The overall aim of this research was to document, understand and address some of the knowledge gaps and issues preventing the optimal management of OSA for people with tetraplegia.

Four separate but related research projects have been conducted, using a variety of methods. The research questions were chosen because the findings will guide future interventions aiming to improve the clinical management of OSA in tetraplegia, with the ultimate goal of improving quality of life. The aims of the individual projects were:

1. To develop and validate a simple method for detecting OSA in tetraplegia that does not require full in-laboratory sleep study.
2. To describe CPAP use in acute tetraplegia, including adherence rates, factors associated with adherence, and average pressures and mask leak.
3. To estimate CPAP adherence in people with chronic tetraplegia and OSA, and to understand the experience of using CPAP.
4. To describe the variation in OSA management practices in tetraplegia, and to explore factors influencing clinical practice.

In the first study, a highly feasible two-stage model designed to detect moderate to severe OSA was modified and validated for people with tetraplegia. The model, consisting of a four-item questionnaire followed by portable overnight oximetry, provides a translatable alternative to full in-laboratory sleep study for identifying moderate to severe OSA in people with chronic tetraplegia. As such, this screening model has the potential to substantially increase the detection of OSA and improve access to treatment.

The second study involved secondary analysis of CPAP data from a multicentre trial investigating the effect of CPAP on neurocognitive outcomes in people with acute,

traumatic tetraplegia and OSA. This study found that within the trial adherence to CPAP was low, but similar to that observed in other specialized population groups, such as stroke and aged care. The study confirmed findings of previous research that people with tetraplegia require less pressure to treat OSA than people without disability, and those with more severe OSA are more likely to adhere to CPAP.

Both qualitative and quantitative research methodologies were used in the third project to estimate rates of CPAP adherence in people with chronic tetraplegia and to understand the experience of the treatment. The burden of using CPAP was found to be substantial, and the balance between the perceived benefit and perceived burden appeared to strongly influence ongoing use. CPAP adherence patterns took up to six months to establish in people with tetraplegia; substantially longer than reported in people without disability.

Finally, the fourth study used qualitative methods to describe variations in the clinical management of OSA within the spinal unit environment and to identify factors influencing doctors' ability to practice in accordance with evidence-based recommendations. The clinical management of OSA was highly variable. Many spinal physicians were not routinely screening for OSA because they lacked resources and reminder systems. Few spinal units were independently diagnosing and treating non-complicated OSA. Those that were tended to be well resourced, involved the multidisciplinary team, and had "clinical champions" to lead the program.

This thesis has confirmed that people with tetraplegia are under-diagnosed and under-treated for OSA. Several modifiable contributors have been identified, generating opportunities for further research aiming to improve access to OSA screening, diagnosis and treatment. Shifting current practice has the potential to greatly improve the quality of life and participation outcomes of people with OSA and tetraplegia.

# Declaration

This is to certify that:

- This thesis comprises only my original work towards the Doctor of Philosophy, except where indicated in the ‘Preface’.
- Due acknowledgement has been made in the text to all other material used.
- This thesis is fewer than the 100,000 words in length, exclusive of tables, references and appendices.

Signed:

Marnie Graco

# Preface

This thesis investigates a series of research questions concerned with understanding and improving the management of OSA in tetraplegia. No third party editorial assistance was provided in preparation of this thesis. With appropriate guidance from my supervisors, David Berlowitz and Sally Green, Chapters 1 and 6 are entirely my own work. Chapters 2, 3, 4 and 5 are presented as manuscripts, either published, in press, under review or prepared for submission. I performed over 50% of these original studies. A detailed account of the contribution of others to these four chapters is provided below.

**Chapter 2.** This study was conducted in two stages. The development stage involved secondary analysis of data collected for a population survey investigating OSA prevalence.[1, 2] All analyses in the development stage were performed by me. The prospective validation component of the research was conducted at four international study sites. Under the supervision of David Berlowitz and Sally Green, I primarily designed the study. Additional contributors to study design were: Rachel Schembri, Shirin Shafazand, Najib Ayas, Mark Nash, Warren Ruehland, Ching Li Chai-Coetzer, Peter Rochford, Tom Churchward. Statistical consulting was provided by Rachel Sore. Participant recruitment and data collection at the Austin Hospital was conducted by myself, Carmel Nicholls, Sandra Henderson and Sarah Dahlgren-Allen. Participant recruitment and data collection at Stoke-Mandeville Hospital, Aylesbury UK was coordinated and conducted by Sue Cross under the supervision of Chinnaya Thiyagarajan. Participant recruitment and data collection at GF Strong Rehabilitation Centre, Vancouver, Canada was coordinated and conducted by Nurit Fox under the supervision of Viet Vu and Najib Ayas. Data from Miami were originally collected for another trial (clinicaltrials.gov NCT02176928). De-identified data from Miami were prepared and sent electronically by Shirin Shafazand. The Miami sleep studies were converted from Embletta to Compumedics format with assistance from Warren Ruehland. All sleep studies were staged and scored by Natalie Pournaris from Bayside Sleep Analysis, and Rachel Schembri. I oversaw the conduct of the entire study.

Data collection at Stoke-Mandeville Hospital was supported by a Stoke-Mandeville Masson Research Award grant from the Buckinghamshire NHS Trust Charitable Trust Funds, UK. Data collection at the University of Miami was funded by the Department of Defense (Award No W81XWH-13-1-0479). ResMed donated the ApneaLink Plus monitors.

I conducted all data analysis and interpretation and prepared the manuscript. All authors were given the opportunity to edit the manuscript, and all approved the final version. The manuscript was accepted for publication in *Thorax* on 16 April 2018 and first published online on 7 May 2018.

**Chapter 3.** The research in this chapter involved secondary analysis of data collected within the 'Continuous positive airway pressure for Obstructive Sleep Apnoea in Quadriplegia' (COSAQ) trial, a multicentre multinational randomized controlled trial. Lauren Booker performed additional CPAP data entry and cleaning for this study. Graham Hepworth provided statistical advice. I conducted all analysis and interpretation and prepared the manuscript. Rachel Schembri, Jack Ross, Najib Ayas and Peter Cistulli all contributed to the study design and all named authors were provided the opportunity to edit the manuscript. All approved the final version. The "COSAQ investigator group" is included on all publications arising from COSAQ study data. All members of this group approved the manuscript for submission. At the time of thesis submission, this chapter was unpublished material not yet submitted for publication. It had been prepared for a peer-reviewed journal to be submitted when the primary COSAQ trial, in which this study is embedded and which is not a part of this thesis, had been accepted for publication. The COSAQ trial was accepted for publication while this thesis was under examination, and this chapter was submitted to a peer-reviewed journal.

**Chapter 4.** At the time of thesis submission, this original research was in press, having been accepted for publication in *Spinal Cord* on 4 October 2018. I primarily designed the study. Participants were prescribed CPAP by Maree Barnes. CPAP initiation and support was provided by Carmel Nicholls, Sandra Henderson, Julie Tolson and Bronwyn Stevens. Under the supervision of David Berlowitz and Sally Green, I conducted all data analysis and interpretation and prepared the manuscript. All named

authors were provided opportunity to edit the manuscript and all have approved the final version. ResMed donated the AirSense 10 Autoset devices.

**Chapter 5.** This original research was submitted for publication to *BMC Health Services* Research on 8 June 2018 and was under review at the time of thesis submission. All of the work involved in this study, including the design, participant recruitment, data collection, data analysis and manuscript preparation was conducted by me, under the supervision of Sally Green and David Berlowitz.

During the conduct of this PhD I was supported by an Australian Government National Health and Medical Research Council postgraduate scholarship (grant number 1114181) and an Australasian Spinal Cord Injury Network PhD scholarship.

# Acknowledgements

*“I am not the only man to seek his fortune far from home, and certainly I am not the first. Still, there are times I am bewildered by each mile I have travelled, each meal I have eaten, each person I have known, each room in which I have slept. As ordinary as it all appears, there are times when it is beyond my imagination.” ~ Jhumpa Lahiri.*

I am incredibly grateful for the opportunity to complete this thesis. The personal growth I have experienced during this time has been amazing. Over the last three to four years, as a direct result of undertaking this research, my confidence in my ability to become an independent researcher has steadily increased, and I am excited about what lies ahead.

I have two wonderful supervisors, David Berlowitz and Sally Green, to thank for this positive experience. Firstly David, my manager, supervisor, mentor and friend for more than 13 years now. I have learnt so much from you about how to be a researcher. But the most valuable thing you have taught me is the importance of generosity in a leader. Thank you for truly being a huge part of my last decade.

To Sally, I knew I hit the jackpot when you agreed to supervise me! Thank you for being a wonderful role model for women with careers and young children. I am in awe of your clear vision and inclusive approach to research, and am thrilled at the prospect of learning more from you in the coming years.

To both my supervisors, I can only hope that I am able to find the same balance that you have both perfected as leaders – the ability to provide ample trust and freedom, balanced with guidance and support.

To my beautiful family. My budding scientists, Oscar and Harry, whether or not you grow up to be scientists is not important, but I hope you find careers that excite and inspire you. Thank you both for sacrificing time with mummy so that I can complete this big “experiment”. To Steve, they couldn’t have done this if you weren’t so amazing. Thank you for your selflessness and your courage.

To Simon, thank you for your love and patience, and for making me laugh. I feel so lucky to have had you by my side for most of this journey. Thank you especially for the warmth and kindness you offer my children, and for sharing your beautiful “fur child” with us!

Thank you to my mum and dad who have supported everything I do in life and have a special knack for knowing exactly how and when to help. Thank you for valuing and encouraging my education. To my beautiful sister-in-law Jenny, thank you for all that you give. You are the poster girl for strength and resilience.

Thank you to all the wonderful people at IBAS who helped out with this research. Particularly Rachel, who not only rescored a gazillion sleep studies, but also provided an abundance of love and support during the tough times. Also to Nicole, for upping the ante on our marathon study weekends, and only bringing the good wine and chocolate! To all my hilarious, beautiful, and loving friends, thank you for opening my mind to new ideas and for providing the boys and I with our “village”.

Last but by no means least, I want to thank the wonderful people who so generously volunteered their time to participate in this research. More than once I would leave home of an evening to drive an hour or so to a participant’s home to set-up a sleep study, and (shamefully) find myself thinking that I’d prefer to be climbing in to bed. Yet inevitably I would be warmly welcomed into the participant’s home to spend a wonderful hour in their company. It was a privilege to witness how positively every participant with spinal cord injury was living with his or her disability. Without fail, I would drive home feeling truly inspired and grateful for the experience.

# Research outputs

### Publications arising from thesis:

**Graco M**, Schembri R, Cross S, Thiyagarajan C, Shafazand S, Ayas N, Nash MS, Chai-Coetzer CL, Rochford P, Churchward T, Ruehland WR, Green S, Berlowitz DJ. Diagnostic accuracy of a two-stage screening model for obstructive sleep apnea in chronic tetraplegia, Thorax, 2018 (DOI:10.1136/thoraxjnl-2017-211131).

**Graco M**, Green SE, Tolson, J, Stevens B, Barnes M, Rigoni A, Henderson S, Nicholls C, Berlowitz, DJ. Worth the effort? Weighing up the benefit and burden of continuous positive airway pressure therapy for the treatment of obstructive sleep apnoea in chronic tetraplegia. *Spinal Cord (in press; accepted for publication on 4/10/18).*

### Publications during candidature:

Goh MY, Millard MS, Wong EC, Berlowitz DJ, **Graco M**, Schembri RM, Brown DJ, Frauman AG, O'Callaghan CJ. Comparison of diurnal blood pressure and urine production between people with and without chronic spinal cord injury. Spinal cord. 2018 Mar 2:1.

Noonan VK, Chan E, Bassett-Spiers K, Berlowitz DJ, Biering-Sørensen F, Charlifue S, **Graco M**, Hayes KC, Horsewell J, Joshi P, Markelis D. Facilitators and barriers to international collaboration in spinal cord injury: results from a survey of clinicians and researchers. Journal of Neurotrauma. 2017 Jul.

Peters AE, van Silfhout L, **Graco M**, Schembri R, Thijssen D, Berlowitz DJ. Periodic Limb Movements in Tetraplegia. The Journal of Spinal Cord Medicine. 2017 May 3:1-8.

Schembri R, Spong J, **Graco M**, Berlowitz D. Neuropsychological function in patients with acute tetraplegia and sleep disordered breathing. Sleep. 2017 Feb 1;40(2).

Gainche L, Berlowitz DJ, LeGuen M, Ruehland WR, O'Donoghue FJ, Trinder, **Graco M**, Schembri R, Eckert DJ, Rochford PD and Jordan AS. Nasal resistance is elevated in people with tetraplegia and is reduced by topical sympathomimetic administration. Journal of Clinical and Sleep Medicine. 2016 Nov 15;12(11):1487-92.

van Silfhout L, Peters AE, Berlowitz DJ, Schembri R, Thijssen D, **Graco M**. Long-term change in respiratory function following spinal cord injury. Spinal cord. 2016 Jan 12.

van Silfhout L, Peters AE, **Graco M**, Schembri R, Nunn AK, Berlowitz DJ. Validation of the Dutch clinical prediction rule for ambulation outcomes in an inpatient setting following traumatic spinal cord injury. Spinal cord. 2015 Nov 10.

Shields P, Bradley R, **Graco M**, Hutchinson A. Descriptive Evaluation of a Smoking Cessation Support Service for Chronic Disease Clients Within a Hospital Admissions Risk Program. Journal of Smoking Cessation, 2015 June, pp.1-10.

Spong J, **Graco M**, Brown DJ, Schembri R, Berlowitz DJ. Subjective sleep disturbances and quality of life in chronic tetraplegia. Spinal Cord. 2015. Aug;53(8):63

Hutchinson AF, **Graco M**, Rasekaba TM, Parikh S, Berlowitz DJ, Lim WK. Relationship between health-related quality of life, comorbidities and acute health care utilisation, in adults with chronic conditions. Health Qual Life Outcomes. 2015 May 29;13:69.

**Conference workshops during candidature:**

O'Connell C, Sheers N, **Graco M**, Berlowitz DJ, "A is for Airway - the ABCs of Airway Clearance in Spinal Cord Injury." (Workshop) 57th Annual Scientific Meeting of the International Spinal Cord Society, Sydney, September 2018.

**Graco M**. & Berlowitz D., "Towards better management of Obstructive Sleep Apnoea in tetraplegia" (Invited workshop), National Canadian Spinal Cord Injury conference, Niagara Falls November 2017.

**Conference presentations (oral) during candidature:**

**Graco M**, Schembri R, Cross S, Thiyagarajan C, Shafazand S, Ayas N, Nash MS, Chai-Coetzer CL, Rochford P, Churchward T, Ruehland WR, Green S, Berlowitz DJ, "Diagnostic accuracy of a two-stage screening model for obstructive sleep apnoea in chronic tetraplegia", 57th Annual Scientific Meeting of the International Spinal Cord Society, Sydney, September 2018.

**Graco M**, Berlowitz DJ, Green SE, "Understanding the clinical management of obstructive sleep apnoea (OSA) in tetraplegia: a qualitative study using the theoretical domains framework (TDF)", 57th Annual Scientific Meeting of the International Spinal Cord Society, Sydney, September 2018.

**Graco M**, Green S, Berlowitz DJ. Initial validation of a simplified screening model of questionnaire and oximetry for detecting moderate to severe obstructive sleep apnoea in chronic tetraplegia. Australian and New Zealand Spinal Cord Society (ANZSCoS) Annual Scientific Meeting, Perth, November 2015. *Winner of Best Scientific Oral Presentation Award.*

**Graco M**, Nunn A, Booker L, Sinnott R, Stell A, Berlowitz D. SpinalCARE: From inception to implementation. Australian and New Zealand Spinal Cord Society (ANZSCoS) Annual Scientific Meeting, Auckland, November 2014.

**Graco M**, Nunn A, Booker L, Sinnott R, Stell A, Berlowitz D. Embedding the International Spinal Cord Injury (SCI) datasets into usual care. 53rd Annual Scientific Meeting of the International Spinal Cord Society, Maastricht, The Netherlands, September 2014.

**Conference presentations (poster) during candidature:**

**Graco M** Green SE, Tolson, J, Stevens B, Barnes M, Rigoni A, Henderson S, Nicholls C, Berlowitz, DJ. "Burden versus benefit of Continuous Positive Airway Pressure therapy for the treatment of obstructive sleep apnoea in chronic tetraplegia: a mixed methods study." 57th Annual Scientific Meeting of the International Spinal Cord Society, Sydney, September 2018.

**Graco M**, Schembri R, Cross S, Thiyagarajan C, Shafazand S, Ayas N, Nash MS, Chai-Coetzer CL, Rochford P, Churchward T, Ruehland WR, Green S, Berlowitz DJ. "Validation of a two-stage screening model to predict moderate to severe obstructive sleep apnoea in chronic tetraplegia" (poster), National Canadian Spinal Cord Injury conference, Niagara Falls November 2017. *Winner Best Student Poster Presentation Award.*

**Graco M**, Schembri R, Berlowitz DJ. Continuous Positive Airway Pressure (CPAP) adherence rates and influencing factors following acute, traumatic tetraplegia. European Respiratory Society Meeting, London, September 2016.

**Graco M,** Schembri R, Berlowitz DJ. Continuous Positive Airway Pressure (CPAP) adherence rates and influencing factors following acute, traumatic tetraplegia. International Spinal Cord Conference, Vienna, September 2016.

**Graco M**, Green S, Berlowitz DJ. Initial validation of a simplified screening model of questionnaire and oximetry for detecting moderate to severe obstructive sleep apnoea in chronic tetraplegia. Sleep DownUnder 2015. 27th Annual Scientific Meeting of the Australasian Sleep Association, Melbourne, October 2015.

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# Table of acronyms and abbreviations

| | |
|---|---|
| AASM | American Academy of Sleep Medicine |
| APAP | Auto-titrating positive airway pressure |
| AHI | Apnoea Hypopnoea Index |
| AI | Arousal Index |
| AIS | ASIA (American Spinal Injury Association) Impairment Scale |
| ASIA | American Spinal Injury Association |
| AUC | Area Under Curve |
| BMI | Basal Metabolic Rate |
| BNSQ | Basic Nordic Sleep Questionnaire |
| BoT | Burden of Treatment |
| COSAQ | CPAP for OSA in Quadriplegia (trial) |
| CPAP | Continuous Positive Airway Pressure |
| CQ-5 | Congestion Quantifier 5 item questionnaire |
| ECG | Electrocardiograph |
| EEG | Electroencephalogram |
| EMG | Electromyogram |
| EOG | Electrooculogram |
| ESS | Epworth Sleepiness Scale |
| GP | General Practitioner |
| GSES | General Self-Efficacy Scale |
| IQR | Inter-quartile range |
| ISNCSCI | International Standards for Neurological Classification of SCI |
| KSS | Karolinska Sleepiness Scale |
| MID | Minimal Important Difference |
| MS-OSA | Moderate to Severe OSA |
| NAART | North American Adult Reading Test |
| NHMRC | National Health and Medical Research Council |
| NREM | Non Rapid Eye Movement |
| NPV | Negative Predictive Value |
| ODI | Oxygen Desaturation Index |

| | |
|---|---|
| OECD | Organisation for Economic Co-operation and Development |
| OSA | Obstructive Sleep Apnoea |
| PAP | Positive Airway Pressure |
| PPV | Positive Predictive Value |
| PSG | Polysomnography |
| REM | Rapid Eye Movement |
| ROC | Receiver Operating Characteristic |
| SAVE | Sleep Apnea Cardiovascular Endpoints |
| SCI | Spinal Cord Injury |
| SCI-QUERI | Spinal Cord Injury Quality Enhancement Research Initiative |
| SCIRE | Spinal Cord Injury Rehabilitation Evidence |
| SD | Standard Deviation |
| SOSAT | Screening for OSA in Tetraplegia |
| TDF | Theoretical Domains Framework |
| TIA | Transient Ischaemic Attack |

*“Sleep that knits up the ravell'd sleave of care, the death of each day's life, sore labour's bath, balm of hurt minds, great nature's second course, chief nourisher in life's feast.” ~ William Shakespeare, Hamlet.*

# 1 INTRODUCTION, LITERATURE REVIEW AND THESIS AIMS

## 1.1 Overview of Chapter 1

The overall aim of this body of work is to improve the health and quality of life of people with tetraplegia by investigating and translating clinical management options for obstructive sleep apnoea (OSA). This first chapter provides contextual information to position this thesis within the body of existing knowledge and to demonstrate the need for the research.

The research presented in this thesis traverses two areas of clinical medicine (spinal cord injury (SCI) and OSA) and is framed by knowledge translation theory. This introductory chapter provides a brief background on the relevant clinical information about SCI and OSA separately, followed by a more detailed literature review of OSA in people with tetraplegia, including epidemiology, aetiology, morbidity, and diagnosis and treatment options. Later in the chapter, a high level overview of knowledge translation theory and methodology is provided, before a discussion of the current state of knowledge translation research aiming to improve outcomes for people with SCI.

The chapter conclude with the rationale and aims of the four individual research studies presented in subsequent chapters, and positions each study within the context of knowledge translation theory.

## 1.2 Spinal Cord Injury

### 1.2.1 What is Spinal Cord Injury?

SCI occurs when damage to the spinal cord results in a loss of function below the level of the lesion. The spinal cord element of the central nervous system connects the brain to the peripheral nervous system and is contained by the spinal column. The spinal cord extends from the brain down to the L1-2 vertebral level, with the cauda equina continuing to travel caudally and exiting through the sacral levels. The spinal cord has 31 pairs of spinal nerve roots or "neurological levels" (eight cervical (C1-C8), 12 thoracic (T1-T12), five lumbar (L1-L5), five sacral (S1-S5) and one coccygeal, each exiting the spinal column between the vertebrae.[3] Within each nerve root pair, the anterior carries the motor nerves and the posterior carries the sensory nerves.

Damage to the spinal cord can be due to trauma (e.g. car accidents, assault or falls), or non-traumatic causes, usually involving pathology (e.g. tumour, congenital malformations or osteoarthritis). Such damage can be temporary or permanent. Depending on the level and the extent of the damage, the symptoms can involve loss of motor and sensory function to the limbs and trunk and loss of autonomic function. Generally speaking, the higher the level of the injury and the more "complete" the injury, the greater the impairment. Those with injuries at levels C1-T1 are classified as having "tetraplegia" (sometimes called "quadriplegia") because innervation to all four limbs is disrupted, while those with injuries from T2 down are classified as having "paraplegia". People with paraplegia have no impairment of upper limb function from the spinal cord. The population of interest in this thesis is traumatic tetraplegia.

SCI is classified according to the International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI). The ISNCSCI examination involves a thorough motor and sensory assessment to ascertain left and right motor and sensory levels, one overall level, and the American Spinal Injury Association (ASIA) Impairment Scale to indicate injury completeness. Motor level is assessed by testing the strength of key muscles on both sides of the body that correspond to each myotome from C5 to T1, and L2 to S1. The motor level for each side of the body is determined by the most caudal (lowest) myotome with normal muscle strength. Similarly, right and left sensory levels

are obtained by testing areas of the body corresponding to the dermatomes with light touch and pinprick sensations. The sensory levels are determined by the most caudal dermatome with normal sensation. The overall neurological level is the highest of the left and right motor and sensory levels, in other words, the highest level with normal motor and sensory function.[4] See Figure 1.1 for the ISNCSCI exam sheet.

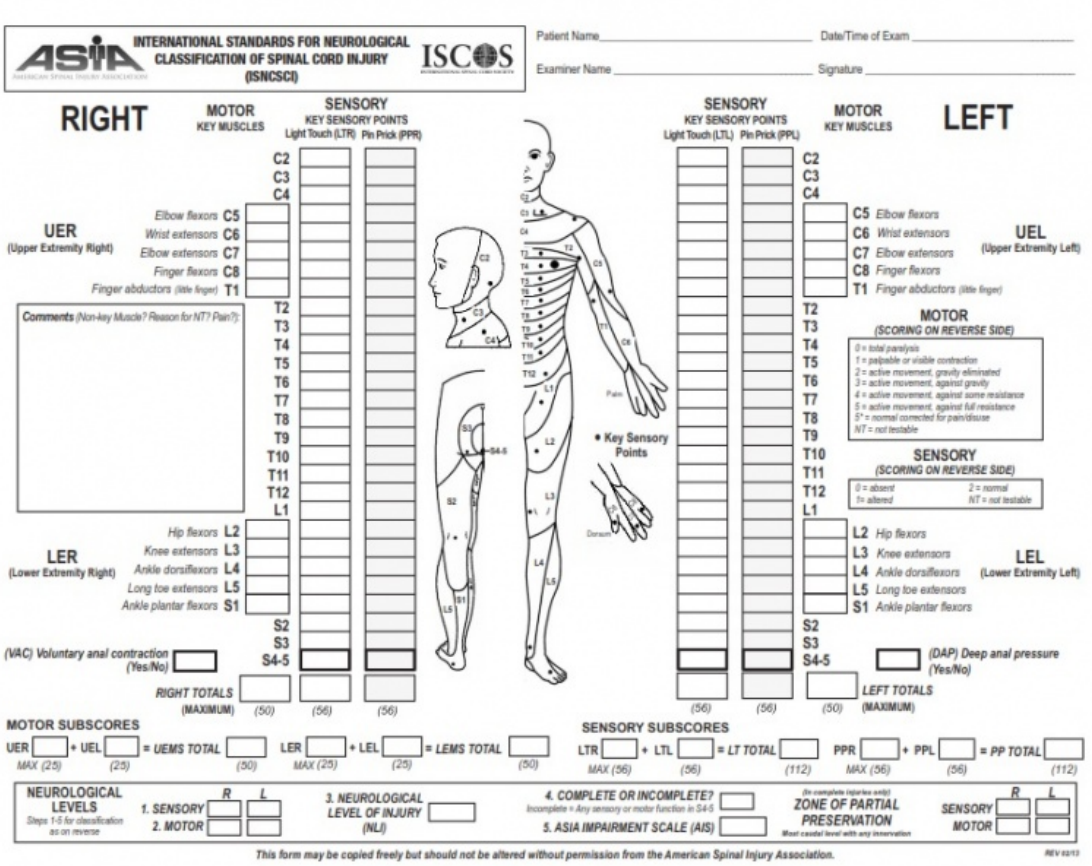


**Figure 1.1 International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI) Examination Sheet**

The ASIA Impairment Scale is used to describe injury completeness and is an important predictor of prognosis and recovery. Classifications range from A to E, with A indicating complete injury, and B, C, D and E indicating varying levels of incomplete injury. The definitions of each can be found in Table 1.1.

**Table 1.1 ASIA Impairment Scale**

| ASIA Impairment Scale classification | Description | Definition |
|---|---|---|
| A | Complete | No sensory or motor function is preserved in the sacral segments S4-S5. |
| B | Sensory incomplete | Sensory but not motor function is preserved below the neurological level and includes the sacral segments S4-S5, AND no motor function is preserved more than three levels below the motor level on either side of the body. |
| C | Motor incomplete | Motor function is preserved below the neurological level, and more than half of key muscle functions below the single neurological level of injury have a muscle grade less than 3 (Grades 0–2). |
| D | Motor incomplete | Motor function is preserved below the neurological level, and at least half (half or more) of key muscle functions below the neurological level of injury have a muscle grade >3. |
| E | Normal | If sensation and motor function as tested with the ISNCSCI are graded as normal in all segments, and the patient had prior deficits, then the ASIA Impairment Scale grade is E. Someone without a SCI does not receive an ASIA Impairment Scale grade. |

Whilst a component of the peripheral nervous system, the autonomic nervous system can be affected by SCI because some sections travel to and from the brainstem via the spinal cord. The autonomic nervous system provides involuntary control of bodily functions, including (but not limited to) blood pressure, heart rate, sexual function, temperature control, bladder and bowel emptying, appetite and sleep. The autonomic nervous system is composed of two components: sympathetic nervous system and parasympathetic nervous system, which differ in both function and structure. The two systems operate as functional opposites enabling the body to maintain equilibrium. Balance is achieved by the autonomic nervous system adjusting the relative inputs from both systems. The sympathetic nervous system prepares the body for stress by expending energy, while the parasympathetic nervous system is responsible for everyday functions and conserving energy. The fibres of the sympathetic nervous system travel from the brainstem with the spinal cord and exit the spinal cord with the thoraco-lumbar nerve roots (T1 to L3). In contrast, the parasympathetic nervous system fibres exit the brainstem via two paths: the cranial nerves, and the sacral nerve roots (S2 and S3). Therefore both components of the autonomic nervous system can be affected with cervical SCI. Following cervical SCI, outflow of the sympathetic nervous system and the sacral component of the parasympathetic nervous system are disrupted, while the cranial nerve components of the parasympathetic nervous system remain intact. Unopposed parasympathetic nervous system activity will upset the body's equilibrium in a number of ways, primarily affecting cardiovascular, urinary, gastrointestinal, sexual and thermoregulatory systems.[5, 6]

While the sympathetic nervous system continues to exit the spinal cord until L3, most fibres involved in cardiovascular and pulmonary function have left the by T6. Thus people with lesions below this level have intact sympathetic and parasympathetic control of the heart and lungs, although other organs (e.g bladder, bowel) can still be affected. Conversely, those with high cervical injury experience the most disruption to autonomic function and usually suffer from abnormal blood pressure control throughout their lives.[6]

### 1.2.2 Secondary complications of SCI

Because the majority of SCI occurs in young people, people typically live with their injury and the associated complications for several decades. Motor, sensory and autonomic compromise are responsible for the many secondary complications of SCI. Common SCI-related complications include pneumonia, pressure ulcers, urinary tract infections, autonomic dysreflexia, pain, and spasticity, among many others.[7] A meta-synthesis of qualitative research investigating quality of life following SCI supports quantitative findings that secondary complications have a significant impact on the lives of people with SCI.[8] In particular, neurogenic pain, spasticity and neurogenic bladder and bowel problems have been strongly associated with worse quality of life. These secondary complications of SCI are reported to have a greater negative effect on quality of life than the SCI impairment itself.[9]

Loss of motor, sensory and autonomic control following SCI also leads to respiratory system compromise, particularly for those with higher and more complete injuries. The ability to breathe deeply and to generate a strong, effective cough is primarily affected by respiratory muscle paralysis. Injuries at C5 or above can affect all respiratory muscles, and are more likely to need ventilatory support. Unopposed parasympathetic nervous system activity further compromises respiratory function by increasing bronchial reactivity. People with cervical SCI are particularly vulnerable to respiratory complications in the first year but continue to be at risk throughout their lives.[6, 10]

Poor sleep is a common secondary complication of SCI. A higher prevalence of sleep disorders has been demonstrated in a number of population surveys of people with SCI. The Stockholm spinal cord study of a near-total regional SCI population found that 35% regularly experience sleep disturbances, and that the odds of having a sleep disturbance were 3.5 times higher in people with SCI than the general population.[11] A Danish postal survey evaluating subjective sleep disturbances in SCI found that individuals with SCI were more likely than the general population to have problems falling asleep, to wake during the night, use sleeping pills, sleep longer at night and during the day, and to snore.[12] Similarly, another large survey in the USA found people with SCI experienced greater levels of sleep disturbance, snoring, respiratory problems, poor or

inadequate sleep and daytime sleepiness than a normative population.[13] Although the causes of poor sleep in people with SCI are not clear, tendency towards obesity, sleeping in supine, nasal congestion, disruption of the melatonin pathway, pain, spasm, and medications are all thought to contribute to the increased prevalence of sleep disorders in this population.[14] Sleep disordered breathing, including OSA, is highly prevalent in SCI, with a demonstrated negative impact on quality of life.[1, 15, 16] The prevalence, potential aetiology and morbidity of OSA in SCI are discussed later in Section 1.6.

The experience of sleep in people with SCI has been investigated using qualitative methods.[17] Poor sleep quality and quantity, including frequent disturbances, and poor sleep patterns were identified as major issues. Three factors contributing to poor sleep were documented in this study: SCI dysfunction and care, such as bladder management, medications, and positioning; the sleep environment, particularly for those in institutions such as hospitals or care homes; and pain and mental health issues. Importantly, participants in this study attributed occupational disengagement, daytime fatigue and impaired cognitive functioning to their poor sleep.[17]

### 1.2.3 Epidemiology of traumatic SCI

The global incidence of traumatic SCI varies significantly by country and is estimated at 13 to 53 new cases per million population per year.[3] The annual incidence of traumatic SCI in Australia is estimated at approximately 12-14 new cases per million population.[18] Whilst the incidence of traumatic SCI is relatively stable in Australia, the prevalence is thought to be increasing, which is likely to reflect both population increases and increasing life-expectancy of people with SCI attributable to improvements in health care.[19] Prevalence data is scarce worldwide, including in Australia. In 1997 it was estimated that there were approximately 10,000 people living with SCI in Australia, or 681 per million of population. Unfortunately there have been no recent estimates of SCI prevalence in Australia, however, statistical modeling has predicted that by 2021, the number of individuals living with SCI in Australia could rise to 12,000.[19]

The National Injury Surveillance Unit at Flinders University in South Australia produces an annual report on incident cases of SCI in Australia using data from the Australian Spinal Cord Injury Register. The most recent report published in 2018 shows that 80% of traumatic SCI injuries are in males, and traumatic SCI is most likely to occur in young adults (aged 15-24) and those between 65 and 74 years old. Almost half of SCI is caused by transport-related accidents, with falls accounting for over a third of injuries. Tetraplegic injuries account for approximately half of incident cases and a third of the tetraplegic injuries are complete (ASIA Impairment Scale A).[18] These Australian data are broadly consistent with international estimates.[3]

Although the incidence is relatively low, the lifetime care costs are enormous and estimated in Australia to be $9.5 million per person with tetraplegia and $5 million per person with paraplegia. The majority of these costs are attributable to long-term care, loss of productivity, aids and modifications, and healthcare.[20]

Fortunately SCI is a rare condition, however for the afflicted individual it has a life-altering impact and can have permanent effects on almost every system of the body. Improvements in the management of SCI in high-income countries have resulted in a steady increase in life expectancy, mostly due to increased survival in the first two years.[21-23] Despite this, people with SCI still die younger than people without SCI, with life expectancy most reduced in those with higher injuries and greater impairment.[24] Mortality in people with SCI in Australia is most commonly from pneumonia and influenza, diseases of the urinary system and suicide.[24]

## 1.3 Sleep Disordered Breathing

Whilst the focus of this thesis is OSA, other forms of sleep-disordered breathing are also commonly reported in people with tetraplegia. As discussed later in this chapter and throughout the thesis, the literature on the prevalence of these different types of respiratory sleep disorders in people with tetraplegia is conflicting and at times contentious. A basic understanding of the different types of respiratory sleep disorders, including mechanisms, measurement and management, is therefore provided below.

### 1.3.1 What is Sleep Disordered Breathing?

Sleep disordered breathing is an umbrella term representing a group of sleep disorders involving the respiratory system. According to the International Classification of Sleep Disorders, sleep disordered breathing consists of three main categories of disorders: OSA, central sleep apnoea disorders, and sleep-related hypoventilation disorders. All of these are known to affect people with SCI. Sleep disordered breathing is characterized by repetitive periods of total cessation in airflow (i.e. apnoeas) or reductions in airflow (i.e., hypopnoeas) that occur during sleep. These events are typically associated with a reduction in oxygen saturation and an arousal from sleep.[25]

The pathophysiological mechanisms underpinning the breathing disruption define the different groups of disorders. OSA is characterised by complete or partial obstruction of the upper airway resulting in complete or reduced airflow. In contrast, central sleep apnoea is primarily a result of reduced respiratory drive mediated by the brain. Whilst the reduction in airflow is essentially the same, it is the absence of respiratory effort at the time of reduced airflow that distinguishes central sleep apnoea from OSA. In reality there is much overlap between the two disorders with few patients experiencing purely “central” or “obstructive” events. Additionally, obstructive and central apnoeas can, and frequently do, overlap within the same event. This is reported as a “mixed” apnoea, when an apnoea begins with loss of central drive to breathe and then continues with increasing effort against an obstructed airway.[25]

The other common group of disorders of breathing and sleep are sleep-related hypoventilation disorders which are characterized by abnormal ventilation and gas exchange during sleep. Ventilation naturally decreases during sleep in response to decreased metabolic activity, however certain pathologies can result in hypoventilation, defined as an excessive reduction in ventilation. These abnormalities result in increased blood carbon dioxide levels (hypercapnia) and associated low blood oxygen concentrations (hypoxemia). Common causes of hypoventilation include obesity, medications and substance use, and neuromuscular diseases (e.g. motor neurone disease and SCI) whereby respiratory muscle weakness impairs gas exchange during sleep.[25]

### 1.3.2 Measurement and diagnosis of sleep disordered breathing

Sleep disordered breathing is usually assessed with a combination of clinical presentation and an objective sleep study. Sleep studies can be divided into four categories, from Level I to Level IV, depending on the number and type of channels. They can be supervised or unattended, and their duration can be full night, split night (diagnostic followed by treatment) or restricted.[26]

The “gold-standard” sleep study is a Level I, overnight, attended polysomnography (PSG). Level I studies involve an overnight stay in a sleep laboratory where the individual is connected to a multichannel device, which takes a comprehensive recording of the biophysiological changes that occur during sleep. It is a highly specialised test, which requires a sleep scientist and sleep physician for analysis and reporting. Level I studies are often accompanied by arterial blood gas analysis and/or transcutaneous monitoring of $CO_2$ pressure for detection of hypoventilation.

The signals required for a Level I PSG include:

- Two electroencephalograms to record brain waves, required for analysis of sleep and its stages.
- Electromyogram to record muscle activity (e.g masseter muscle), required for detection of Rapid Eye Movement (REM) sleep.
- Bilateral electrooculogram to record eye movements in sleep, required for detection of REM sleep.
- Airflow sensor (nasal pressure and oronasal thermistor)
- Respiratory effort sensors. These are bands around the thorax and abdomen to detect movement of the chest wall and abdomen.
- Pulse oximeter, to detect oxygen saturation and pulse.
- Electrocardiograph to detect heart rate and rhythm.
- Body position sensor, which detects whether the patient is lying on their back, front, right or left side.
- Leg movement sensors, usually electromyogram of tibialis anterior to detect periodic leg movements during sleep.
- Snoring sensor, usually by microphone.[25-27]

By contrast, Level II sleep studies are conducted with a portable PSG device and are "unattended" by staff, enabling them to be performed at home rather than in a sleep laboratory. Level II studies can be performed in a number of ways: the patient attends the laboratory to be "set-up" and is sent home to sleep; a technician travels to the patient's house to "set-up" the study and then leaves; or the patient is mailed the kit with instructions to "set-up" at home without technician assistance. Level II studies must still include electroencephalograms, electrooculogram, electromyogram, electrocardiograph, oxygen saturation, airflow and respiratory effort recordings. As a result the same sleep and respiratory indices can be calculated. Evaluation of Level II studies has demonstrated good agreement with Level I studies, and Level II studies have been endorsed by the Australasian Sleep Association as a diagnostic technique for sleep disordered breathing. However due to the practical issues and a higher failure rate, they are not commonly used in clinical practice.[26] However the use of home-based sleep studies is likely to increase in Australia, which has recently authorised billing for Level II studies when an approved questionnaire indicates high probability of moderate to severe OSA.[28]

The data from a Level I or II study are collated and displayed on a computer screen in a "montage". A typical montage showing five minutes of recording is presented in Figure 1.2. These data are "staged and scored", either manually by a sleep scientist or automatically using software, to generate sleep and respiratory indices. The staging process involves categorising sleep in 30 second "epochs" into the following stages: wakefuleness, non-rapid eye movement (NREM) stage 1, NREM stage 2, NREM stage 3, and REM. Following this, the respiratory events are marked, or "scored", according to rules devised by the American Academy of Sleep Medicine (AASM). As previously mentioned, respiratory events can be apnoeas (cessation in breathing for a defined period of time) or hypopnoeas (reduction in breathing). Both apnoeas and hypopnoeas can be classified as obstructive, central or mixed in nature. The scoring rules for respiratory events have undergone several iterations and different sleep laboratories employ different rules. Table 1.2 summarises the AASM respiratory event rules.[27, 29, 30] Following the staging and scoring process, various indices required for the diagnosis of sleep-disordered breathing are calculated.

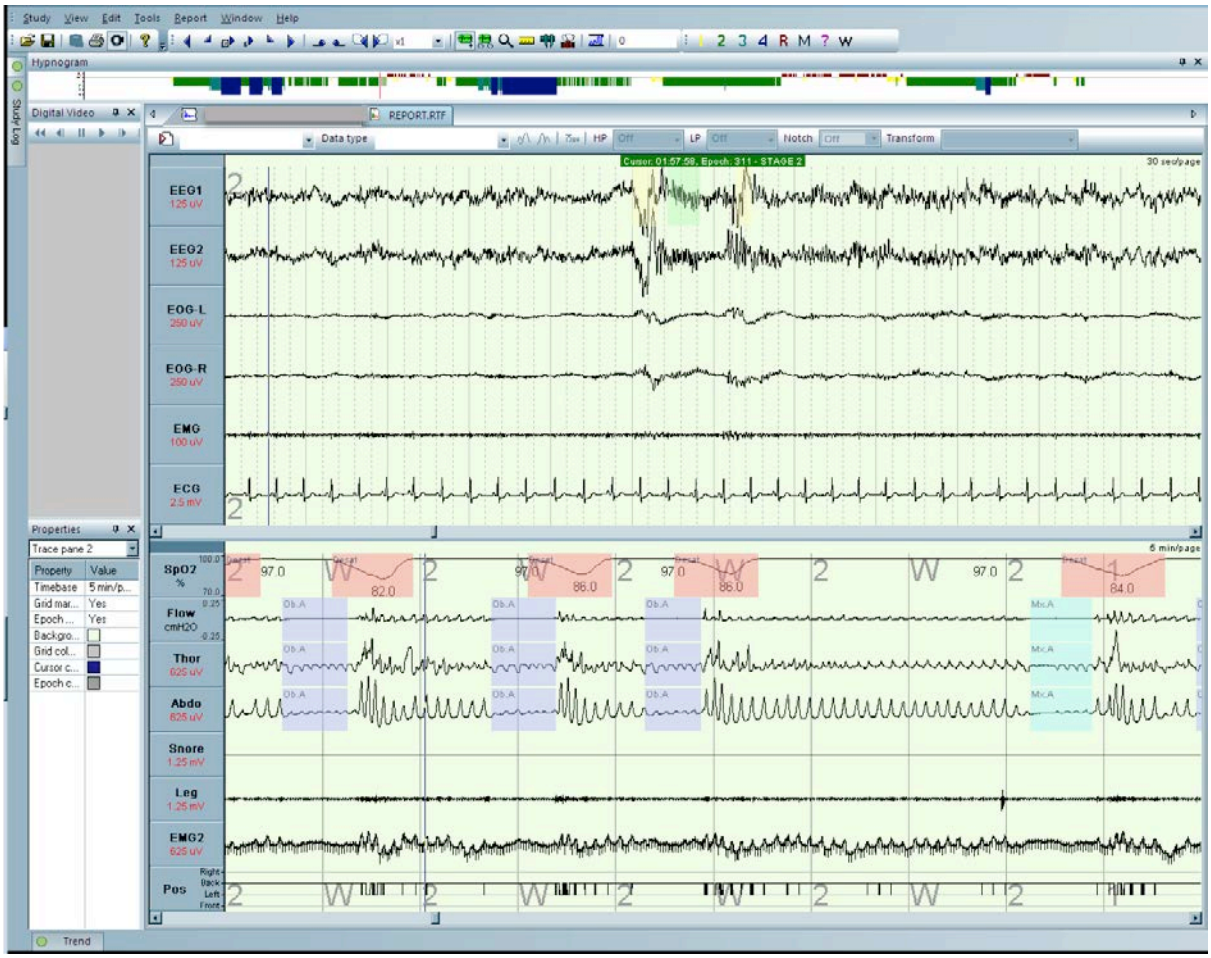


**Figure 1.2 A typical PSG montage, showing 30 seconds of electroencephalogram recording and five minutes of respiratory data recording.**

**Table 1.2 Overview of the American Academy of Sleep Medicine (AASM) respiratory event rule differences**

| | **Chicago** | **AASM 2007** | **AASM 2007** | **AASM 2012** |
|---|---|---|---|---|
| **Hypopnoea** | Clear decrease in breathing of >50%<br><br>OR<br><br>a lesser reduction in breathing associated with a >3% desaturation or arousal | (***alternative* definition**)<br><br>≥50% airflow reduction<br><br>AND<br><br>a ≥3% desaturation or arousal | (recommended definition)<br><br>≥ 30% airflow reduction<br><br>AND<br><br>a >= 4% desaturation | ≥ 30% airflow reduction<br><br>AND<br><br>a ≥3% desaturation or arousal |
| **Obstructive apnoea** | Complete cessation in breathing | ≥90% reduction in airflow, with continued inspiratory effort | ≥90% reduction in airflow, with continued inspiratory effort | ≥90% reduction in airflow, with continued inspiratory effort |
| **Central apnoea** | Absence of breathing and respiratory effort | ≥90% reduction in airflow and inspiratory effort | ≥90% reduction in airflow and inspiratory effort | ≥90% reduction in airflow and inspiratory effort |
| **Mixed apnoea** | Absence of breathing and an initial absence of respiratory effort, followed by gradually increasing effort | ≥90% reduction in airflow and inspiratory effort, with a resumption of inspiratory effort in the second portion of the event | ≥90% reduction in airflow and inspiratory effort, with a resumption of inspiratory effort in the second portion of the event | ≥90% reduction in airflow and inspiratory effort, with a resumption of inspiratory effort in the second portion of the event |
| **RERA (respiratory event related arousal)** | Increased respiratory effort, leading to an arousal from sleep | Increased respiratory effort or flattening of airflow leading to an arousal | | |
| **Event duration** | ≥ 10 seconds | ≥ 10 seconds with the event meeting criteria for at least 90% of the duration | | |

Level III and IV sleep studies record fewer signals and are frequently referred to as “limited channel studies”. The data analysis is commonly automated. These studies typically do not measure electroencephalogram, rendering sleep staging impossible. Level III studies record at least four signals of which three should be oximetry, airflow and respiratory effort. By comparison Level IV studies include only one or two signals; usually oximetry and/or airflow. Oximetry has been suggested as the single most important signal for the diagnosis of sleep disordered breathing and is discussed in more detail in Chapter 2.[26]

## 1.4 Obstructive Sleep Apnoea

Most of our knowledge about OSA comes from research in non-disabled populations. A high-level summary of what is known about OSA from these populations is included here as this information can inform research in other specialised populations, such as SCI. An understanding of the similarities and differences between the epidemiology and aetiology of OSA in non-disabled and tetraplegic populations is necessary for the design and interpretation of the research presented in this thesis.

### 1.4.1 Prevalence, risk factors and symptoms of OSA

OSA is the most prevalent form of sleep-disordered breathing. Population estimates in the non-disabled suggest that the prevalence of OSA is 10-17% in men, 3-9% in women and has substantially increased over the last two decades.[31] A more recent survey of people over the age of 40 has found OSA is prevalent in up to 50% of men and 23% of women in this older age group.[32] A meta-analysis published in 2017 estimated OSA prevalence to range between 9 and 38%, higher in men and increasing with age.[33] The well-established risk factors include obesity, central body fat distribution, large neck circumference, increasing age and craniofacial and upper airway abnormalities. Being male and obese is a major risk factor for OSA. Other suspected risk factors for OSA include genetics, smoking, menopause, alcohol use and nasal congestion.[34, 35] Common symptoms of OSA in adults include snoring, daytime sleepiness, witnessed apnoeas and/or waking up with a choking sensation.[35]

### 1.4.2 Pathophysiology of OSA

Several underlying physiological mechanisms have been suggested to cause OSA. These factors vary substantially among individuals whose disease may predominantly arise from one predisposing factor or a combination. In 2014, Jordan et al[35] summarised several key pathophysiological factors associated with OSA. Upper airway anatomy, causing a reduction in the size of the pharyngeal airway lumen, is one such factor, often caused by increased body fat or craniofacial anatomy. During sleep, upper airway dilator muscle activity naturally reduces, predisposing a narrower airway to collapse. Instability of the respiratory control system during sleep, characterised by large shifts in respiratory output, can also lead to a reduction in upper airway dilator muscle activity, higher airway resistance and consequent upper airway collapse. This is often referred to as “high loop gain”.[35, 36]

Another important variable is waking prematurely to airway narrowing, or having a “low respiratory arousal threshold”. This can upset the stability of the respiratory system by causing disruptions to gas exchange and respiratory drive, leading to further abnormal respiratory events. Low lung volumes may also contribute to OSA. Lower lung volumes are associated with a smaller and more collapsible upper airway and a less stable respiratory control system, all of which are known to contribute to OSA. Finally, dysfunctional upper airway dilator muscles during sleep have also been attributed to OSA pathogenesis. Poor responsiveness of these muscles to airway collapse can be the result of fatigue, neural injury or myopathy.[35, 36]

In reality, a combination of these pathophysiological causes occurs in most individuals with OSA. In 2013 Eckert and colleagues quantified the relative contribution of each of these causes in a large sample of people with OSA, compared to those without OSA. They found that the causes varied significantly among patients, and have proposed three phenotypes for characterising individuals based on the presence or absence of these traits.[36]

1. Patients with a highly collapsible airway and severe OSA, as defined by a high passive critical closing pressure. Approximately 23% of patients belong to this category.

2. Patients with a moderately collapsible upper airway with a range of OSA severities. Approximately 58% of patients belong to this category.
3. Patients with some vulnerability to upper airway collapse and milder OSA, but one or more non-anatomical causes of OSA (e.g poor muscle responsiveness, waking up prematurely and/or having an oversensitive ventilatory control system). Approximately 19% of patients belong to this category.

The authors of this scale reason that understanding the different phenotypic causes of OSA will help direct new treatments. However more research is needed to determine whether these categories are both valid and useful for prescribing targeted therapy.[36]

### 1.4.3 Morbidity of OSA

Economic modelling has estimated that people with untreated OSA have a two-fold increase in healthcare costs compared to controls.[37] Daytime sleepiness is considered a direct consequence of OSA, and is likely to contribute to the higher risk of someone with OSA having a motor vehicle accident.[38] While causality has not been established, OSA is independently associated with disorders of mood and neuropsychological function. A meta-review of several systematic reviews and meta-analyses assessing the effects of OSA on cognition concluded that OSA is associated with deficits in memory, attention, executive function and visuospatial abilities.[39] People with OSA also have a significantly higher risk of depression than those without.[25]

Several studies have established that OSA contributes to hypertension.[34] However the link remains controversial with other research showing that the association is weak when covariates are accounted for.[35] Whilst any causal association is unproven, OSA is commonly pre-morbid with a number of other chronic diseases, including diabetes, stroke, myocardial infarction and congestive heart failure.[35] A meta-analysis investigating the relationship between OSA and cardiovascular disease concluded that the positive relationship exists for moderate to severe OSA but not mild.[40] Whether or not treatment of OSA can alleviate and prevent some of these associated conditions is yet to be fully established.

## 1.5 OSA management in non-disabled

### 1.5.1 Diagnosis of OSA

As discussed in Section 1.3.2 above, Level I PSG is considered the "gold-standard" diagnostic test for OSA. A staged and scored Level I or II PSG will produce a metric known as the Apnoea Hypopnoea Index (AHI). This is the number of apnoeas and hypopnoeas per hour of sleep. Different thresholds for the AHI are used to diagnose OSA and its severity. The AASM has defined mild OSA as an AHI of between 5 and 15, moderate OSA as an AHI of between 15 and 30 and severe OSA as an AHI of greater than 30, but only when respiratory events are scored according to the 1999 AASM "Chicago" rules.[29] Unfortunately these diagnostic thresholds have not been updated to reflect more recent changes in the AASM scoring criteria (Table 1.2). The newer rules alter the AHI substantially and have major implications for the diagnosis of OSA in non-disabled populations[41, 42] and in SCI.[16] This issue is discussed in further detail in Chapter 2.

There have been many attempts at finding alternative methods for detecting and predicting OSA in people without disability. The most commonly used and well known tools include the Berlin questionnaire, STOP questionnaire, STOP-Bang questionnaire, Multivariate Apnea Prediction Index, American Society of Anesthesiologists checklist, Wisconsin questionnaire, and the Sleep Disorders questionnaire.[43, 44] Overnight oximetry (Level IV studies) and partial channel/partial time devices (Level III studies) have also been studied as cheaper and more accessible alternatives to full PSG.

Several systematic reviews and meta-analyses have attempted to compare and rate these alternative screening methods.[43-45] Heterogeneity in study designs has limited the ability of these reviews to compare model performance and to make strong recommendations. In general, questionnaires and clinical prediction models were found to predict severe OSA with a high degree of accuracy but miss a significant proportion of those with mild disease. Clinical prediction models typically include algorithms based on multivariate analysis of risk factors, and usually contain a combination of demographic variables, symptoms and clinical test results such as respiratory, morphometric or cephalometric measures. One review found clinical prediction models

performed better than questionnaires[44], and another concluded that partial channel/partial time studies were the most accurate alternatives to full PSG. [45] The application of some of these alternative methods are discussed later in Section 1.5.3.

### 1.5.2 Treatment for OSA

Applying positive airway pressure (PAP) via a mask to stabilise the upper airway is the primary respiratory treatment for sleep-disordered breathing, including OSA, central sleep apnoea, and sleep-related hypoventilation. Continuous Positive Airway Pressure (CPAP) and bi-level PAP are the most widely known and prescribed forms of PAP.

CPAP remains the first-line treatment for OSA. CPAP maintains a continuous PAP throughout inspiration and expiration with most CPAP devices providing pressure settings between 4 and 20 $cmH_2O$. The goal of CPAP is to splint open the upper airway with pressurised air during sleep to prevent its collapse. Typically patients attend a sleep laboratory for initiation of CPAP. Manual pressure titration is performed overnight to determine the optimal level that abolishes hypopnoeas and apnoeas. Alternatively auto-adjusting CPAP (APAP) devices can be used to determine CPAP requirements. APAP devices detect respiratory events and adjust the pressure automatically to maintain and optimise respiratory flow patterns, whilst still maintaining the same pressure throughout the respiratory cycle.[46] Fixed CPAP prescription can be based on the $90^{th}$ percentile pressures provided from up to one week of APAP.[47]

CPAP has been shown to improve daytime sleepiness, measures of sleep quality, health related quality of life, and mood in people without disability.[48-50] Systematic reviews demonstrate clinically significant improvements in blood pressure, endothelial function and insulin sensitivity from CPAP.[51-53] However until recently no studies had investigated whether treating OSA could prevent major cardiovascular events. The SAVE (Sleep Apnea Cardiovascular Endpoints) study was a large randomised controlled trial of CPAP for people with OSA and cardiovascular disease, which found that treating OSA with CPAP in an at-risk population did not prevent cardiovascular events.[49]

There have been several studies investigating the effect of CPAP on neuropsychological function, with frequently conflicting and inconclusive findings. The conflicting findings may reflect heterogeneity in both the populations studied (i.e. different severities of OSA), and the outcome measures employed. [54] A meta-review of neurocognitive function in OSA concluded that CPAP appears to improve executive function, memory, attention and global cognitive function.[39] Greater improvements in measures of daytime sleepiness, depression, anxiety and quality of life were seen in the group receiving CPAP in the SAVE trial, who also took significantly fewer days off work because of poor health.[49] Improvements in these secondary outcomes suggest that societal participation also improved, although this was not directly measured.

A significant limitation of CPAP effectiveness is poor adherence and acceptance of the therapy. When adherence is defined as greater than four hours per night, rates of 30-60% are reported in the non-disabled with OSA.[55] The CPAP literature is ambiguous on what constitutes “adherence”, at least partly because the amount of CPAP resulting in optimal outcomes has not yet been established. Several studies have observed a dose-response relationship for improvements in sleepiness and cognitive function, suggesting that any CPAP use is better than none. At least four hours seems to be required for normalization of daytime sleepiness, quality of life and neurocognitive function, and average doses of six hours a night and higher are associated with better clinical outcomes.[56-59] Achieving a minimum of four hours per night is considered by experts to be “adherent” to the therapy.[60]

Factors associated with poor CPAP use in the non-disabled include lower OSA severity, less subjective sleepiness, increased nasal resistance, psychological problems, mask discomfort and side-effects, poor self-efficacy with CPAP use, worse coping skills, and lack of spousal support.[57] In reality, optimal adherence is difficult to achieve in the real world. A systematic review of CPAP adherence over a 20 year period, including a total of 66 randomised controlled trials with recorded CPAP usage, reported that non-adherence was 34% overall. Furthermore there was no significant improvement in adherence over the 20 year period.[61] However this study estimated non-adherence by calculating the mean CPAP use across all studies (4.6 hours), subtracting this from “optimum use”, defined by the authors as seven hours, and converting to a percentage.

In reality, an average of seven hours a night is difficult to achieve. Nonetheless, the finding that CPAP adherence had not improved over 20 years despite significant research investment is an interesting one.

Bi-level PAP can also be used to treat OSA, although it is more commonly used to provide respiratory support to treat hypoventilation disorders. Bi-level PAP provides a higher pressure during inspiration and lower pressure during expiration, which may be more comfortable for the individual.[46] Bi-level PAP is often trialled clinically after the patient has failed to tolerate CPAP, however clinical trials investigating this method have reported mixed results.[62] A Cochrane review found no difference in adherence between bi-level and CPAP devices and recommended further research into whether bi-level PAP is a viable alternative for those who are unable to tolerate CPAP.[63]

Mandibular advancement splints are often prescribed as an alternative to CPAP or as a first-line treatment for mild OSA. These mouth guard-like devices pull the lower jaw forwards to open up the upper airway and generate tension in the soft tissues and muscles of the upper airway, thereby making it less likely to collapse during sleep. Similar improvements to sleepiness, neurocognitive performance and functional outcomes have been observed with a mandibular advancement splint compared to CPAP, although they do not reduce the AHI to the same degree.[25]

While CPAP and mandibular advancement splints are the most common OSA treatments, several alternative treatments are also available. Positional therapy may be effective for patients whose respiratory events are predominantly supine. In these cases devices can be worn at night to prevent the person from sleeping on their back, which can lead to improvements in AHI. Weight loss and bariatric surgery has also been found to alleviate OSA severity in obese patients. Surgery on the upper airway (e.g. tonsillectomy, nasal septoplasty) may be effective for patients whose upper airway anatomy has been assessed as contributing to OSA and is suitable for the procedure.[25]

In 2009 the Adult OSA taskforce of the AASM released clinical guidelines for the overall management of OSA in adults. These recommendations include the routine screening for OSA followed by comprehensive sleep evaluation for those with

suspected OSA. According to these guidelines, those diagnosed with OSA should be actively involved in selecting a treatment regime that may include CPAP, mandibular advancement splint, behavioural treatments, surgery, and/or adjunctive therapies.[64] Similarly, in 2013 the American College of Physicians released clinical practice guidelines for the management of OSA in adults[48] with the following three recommendations:

> **Recommendation 1:** American College of Physicians recommends that all overweight and obese patients diagnosed with OSA should be encouraged to lose weight. *(Grade: strong recommendation; low-quality evidence)*
>
> **Recommendation 2:** American College of Physicians recommends continuous positive airway pressure treatment as initial therapy for patients diagnosed with OSA. *(Grade: strong recommendation; moderate-quality evidence)*
>
> **Recommendation 3:** American College of Physicians recommends mandibular advancement devices as an alternative therapy to continuous positive airway pressure treatment for patients diagnosed with OSA who prefer mandibular advancement devices or for those with adverse effects associated with continuous positive airway pressure treatment. *(Grade: weak recommendation; low-quality evidence)*

### 1.5.3 Alternative OSA management models

In most countries in the Organisation for Economic Cooperation and Development (OECD), the diagnosis of OSA involves referral of patients suspected to have OSA to specialist physicians at sleep centres for diagnostic PSG. While PSG is the gold-standard, definitive test for OSA, it is largely considered to be a cumbersome, labour intensive and expensive procedure.[35, 65] In 2010, the fee for a full PSG in Australia was US$580, costing Medicare Australia over US$48 million in just one year of claims.[66] The requirement for in-laboratory attendance creates a barrier for patients. Furthermore, lack of trained sleep specialists relative to the high prevalence of OSA have led to prolonged waiting times for sleep services.[65] In 2004 the mean wait time from referral to CPAP provision was estimated to be 14 months in the UK, 24 months in Canada and 7-8 months in Australia.[67] Up to 93% of women and 82% of men with moderate to severe OSA have been estimated as undiagnosed.[68] While it is likely that

the delay to sleep services and OSA diagnosis rates have improved since these studies were published, more recent estimates have unfortunately not been produced.

As a result of these issues, several alternative models have been suggested and investigated to hasten diagnosis, improve access to treatment and reduce costs. These include home-based diagnostic models that do not require overnight laboratory testing (i.e. Level II to IV sleep studies). In 2007 a task force of the AASM published clinical guidelines for the use of unattended portable monitors for the diagnosis of OSA.[69] This was the first document supporting the use of portable monitoring for diagnosis of OSA and for prescribing therapy. All reviews published prior to this document dismissed the use of portable monitoring due to insufficient evidence. The 2007 guidelines recommended portable monitoring as an alternative to PSG for patients with high pre-test probability of moderate to severe OSA, and in those without significant comorbid medical conditions. According to these guidelines, the portable monitoring equipment must record airflow, effort and oximetry at a minimum. The paper also recommended portable monitoring is performed under the auspices of an AASM accredited sleep medicine program, conducted by experienced sleep technician, and the data reviewed by a specialist sleep physician.

Alternative treatment initiation practices have also been investigated. Increasingly APAP devices are being used at home (unattended) to determine the ongoing pressure requirements, eliminating the need for in-laboratory titration of CPAP. Recommendations for the use of APAP to treat OSA were also published in 2007 by the AASM.[70] This report included two practice parameters regarding unattended APAP:

- “certain APAP devices may be initiated and used in the self-adjusting mode for unattended treatment of patients with moderate to severe OSA without significant comorbidities (CHF, COPD, central sleep apnoea syndromes, or hypoventilation syndromes).”
- “certain APAP devices may be used in an unattended way to determine a fixed CPAP treatment pressure for patients with moderate to severe OSA without significant comorbidities (congestive cardiac failure, chronic obstructive pulmonary disease, central sleep apnoea syndromes, or hypoventilation syndromes).”

Also in 2007, an international workshop was held in Virginia USA to determine research priorities for incorporating ambulatory models of managing OSA into healthcare systems. Eight recommendations were made, with participants identifying the most important priority as “conducting adequately powered, high quality research studies to generate the evidence needed to incorporate ambulatory management into current practice.”[71]

In 2009 the Adult OSA taskforce of the AASM released updated clinical guidelines for the overall management of OSA in adults.[64] These recommendations include routine screening of symptoms of OSA followed by comprehensive sleep evaluation for those with suspected disease. The recommendations were similar to those published two years earlier.[69] Regarding the use of unattended auto-titrating CPAP for OSA, the 2009 guidelines similarly deferred to previously published practice recommendations.[70]

Since 2007 there have been many clinical research studies comparing portable, ambulatory models of OSA diagnosis and management to the traditional in-laboratory specialist model.[47, 72-78] All studies have concluded that the alternative model was non-inferior to the specialist approach. As yet, there have been no updated AASM practice guidelines since the publications in 2007 and 2009,[64, 69, 70] however in 2013 and 2014 the American College of Physicians produced two clinical guidelines for the diagnosis and management of OSA in adults.[48, 79] These guidelines recommended “portable sleep monitors in patients without serious comorbidities as an alternative to PSG when PSG is not available for diagnostic testing”, and “continuous positive airway pressure treatment as initial therapy for patients diagnosed with OSA.” While the American College of Physicians guidelines acknowledged the evidence that CPAP and APAP are equally efficacious, it did not discuss the use of APAP in an unattended way for determining fixed pressure requirements.

Whether the diagnosis and management of OSA requires oversight from a specialist physician has also been questioned. At least three randomised controlled trials have investigated alternatives to this specialist model in the non-disabled population. Antic et al 2009[80] compared a nurse-led model to standard physician led care. The nurse-led

model included overnight oximetry to detect OSA, and prescription of home APAP. The standard physician led model included in-laboratory diagnostic PSG and a CPAP titration study. This non-inferiority study, with change in subjective sleepiness as the primary outcome, randomised participants within a specialist sleep unit to the nurse-led or physician led models. After three months of CPAP, there were no differences between the groups in sleepiness or CPAP adherence, and the nurse-led model was found to be significantly cheaper.[80]

Another randomized controlled non-inferiority study, led by Chai-Coetzer et al[81] compared an alternative model to standard specialist sleep centre care. In this study the care in the alternative model was provided by a primary care physician and community based nurse. Again, the alternative model employed ambulatory management strategies, while the sleep specialists were instructed to manage OSA as they would normally. Participants were recruited from within the primary care clinic and screened for eligibility with a validated two-stage model of a four item screening questionnaire followed by overnight oximetry.[82] Eligible participants were then randomized to receive either primary care management or specialist sleep centre management. The primary outcome measure was change in subjective daytime sleepiness at six months. At six months, primary care management was found to be non-inferior to specialist management and significantly cheaper.[81]

A similar multicentre non-inferiority randomised controlled trial investigating an alternative model of care was recently conducted in Spain.[83] Participants of this study were also randomised to primary care with portable monitoring, or in-hospital specialised management. Again there was no difference between the groups in the primary outcome (subjective sleepiness) or any secondary outcomes. Again the primary care protocol was substantially cheaper. The populations studied in each of these three randomised controlled trials were non-disabled and without major co-morbidities. Whether non-sleep specialists can safely and effectively manage more complicated population groups has not yet been investigated.

Two review papers have summarised this literature and questioned the traditional model of in-laboratory, specialist management of OSA. The reviews have highlighted the

number of high quality clinical trials that have clearly and consistently demonstrated non-inferiority of alternative ambulatory management strategies.[65, 84] Chai-Coetzer et al [65] cites emerging evidence to support the role of other health-care providers, such as nurses and GPs, in providing an ambulatory management strategy for OSA, and argues that primary care may be the ideal setting for such strategies. Similarly, in 2016 Suarez et al [84] reason that for prevalent diseases with high costs and significant comorbidities, all levels of medical care must be involved, including primary care physicians and nurses. The Suarez et al paper calls for the primary care management of "non-difficult" OSA patients, with specialized sleep centres remaining responsible for "difficult" patients, including those with co-morbidities and poor adherence.

## 1.6 Obstructive Sleep Apnoea in Spinal Cord Injury

### 1.6.1 Epidemiology of OSA in SCI

OSA is likely to be the most common sleep disorder in SCI.[85] Berlowitz et al[86] established that OSA was highly prevalent within weeks of cervical SCI, peaked at 83% at three months and then stabilised at 60-70% after six to 12 months. Similarly, another cohort study in acute SCI (T12 and higher) reported 73% prevalence of OSA at 6-8 weeks post injury, and 75% at six months.[87] Both studies assessed OSA with full PSG.

Population surveys have estimated OSA prevalence in people with chronic SCI to be between 28% and 77%[1, 15, 16, 88-92]. Heterogeneity in study design is primarily responsible for the wide range of prevalence estimates reported in the literature. Testing methods for OSA, scoring methods for respiratory events and definitions of OSA vary enormously between studies. In general, older studies (published >10 years ago) and those not using PSG tended to report lower prevalence of disease. The populations studied also varied significantly. Some studies limited inclusion to those with tetraplegia only, others included thoracic lesions of varying levels, and one included all levels of SCI. [1, 15, 16, 88-92]

OSA surveys published in the last decade suggest that the prevalence of OSA in tetraplegia lies somewhere between 56% and 93%.[1, 15, 16] Leduc et al[15] performed unattended home PSG on 41 adults with cervical injuries, and identified OSA in 56% of participants. In this study OSA was defined as an AHI of greater than five, scored according to the AASM "Chicago" criteria. Similarly Berlowitz et al[1] performed unattended PSG on 78 community dwelling individuals with tetraplegia (T1 level or higher) and reported that that 72% of the sample had OSA, as defined by an AHI > 10 (AASM "Chicago"). When separated into complete and incomplete injuries, OSA prevalence was 91% and 56% respectively. In 2013 Sankari and colleagues[16] performed unattended PSG in 28 people with SCI from level T6 and above. Approximately three quarters (77%) of participants had sleep disordered breathing (AHI>5), when scored using the AASM 2012 criteria. When the sample was divided into cervical and thoracic injuries, the reported prevalence of sleep disordered breathing was 93% and 55% respectively.[16]

Several of the population surveys also investigated associations between patient characteristics and the presence of OSA in SCI. Characteristics significantly associated with OSA have included: higher (cervical) lesions, complete injuries, larger neck circumference, obesity, supine sleeping position, increasing age, increasing time since injury, male gender, cardiac and antispasmodic medications, daytime sleepiness, self-reported snoring and awakenings.[1, 15, 16, 88, 90-93] However the risk factors identified were often conflicting across studies with several found to be significantly associated in one or more studies, and insignificant in others. Differences in study methodologies have hindered pooling of data and meta-analyses of both the prevalence estimates and the risk factors for OSA in SCI.

### 1.6.2 Screening for OSA in SCI

As alternatives to full PSG, few screening tools developed for non-disabled populations have been tested in people with SCI. The Multivariate Apnea Prediction Index [94] was found to have a low sensitivity (16-17% in those with complete and incomplete injuries) and high specificity (100%) for predicting OSA (AHI≥10) in chronic tetraplegia.[1]

Another study found that 47% of those with cervical lesions reported high risk scores on the Berlin questionnaire[95], while 93% had evidence of OSA (AHI≥5).[16]

More recently, Sankari et al [96] investigated whether several self-reported sleep questionnaires could predict OSA in SCI, using threshold scores previously established to predict OSA in non-disabled populations. The questionnaires and the corresponding thresholds investigated were: the Epworth Sleepiness Scale (ESS) (≥10);[97] the Pittsburg Sleep Quality Index(>5);[98] the Berlin Questionnaire (high risk categorisation);[95] and the Fatigue Severity Scale (≥2).[99] Bivariate analyses were undertaken to determine whether these pre-determined thresholds were associated with at least mild OSA (defined as AHI≥5) and at least moderate OSA (AHI≥15) in 28 patients with SCI. The analyses established that none of the questionnaire thresholds were significantly associated with at least mild OSA or at least moderate OSA in SCI.[96] However the thresholds investigated were established for non-disabled populations. Whether alternative thresholds for this population are any better at predicting mild, moderate or severe OSA is yet to be determined.

Another study purported to evaluate whether home based testing could diagnose OSA in people with SCI (T6 lesion or higher). The authors of this study concluded that use of a Level III portable monitoring device and a transcutaneous partial pressure $CO_2$ device can effectively identify sleep-disordered breathing. However, there was no comparator diagnostic technique (i.e. full PSG) to verify the accuracy of the two ambulatory testing methods. Rather, this study demonstrated that home based testing was feasible.[93]

### 1.6.3 Aetiology of OSA in SCI

A seminal study by Berlowitz et al[86] investigated incidence of OSA in acute tetraplegia by following a cohort of people with new tetraplegic injuries for 12 months. PSG was performed within 48 hours of injury, finding none of the 30 participants had evidence of OSA at this time point. Within two weeks 60% of the sample had developed OSA, which peaked at 83% at three months post injury. Only three (10% of the sample) were predicted to have OSA prior to their injury.[86] As a result of this study, OSA is considered a direct consequence of tetraplegia.

Tendency towards obesity, high proportion of males, sleeping in supine, and medication use have all been suggested to contribute to the increased prevalence of sleep disordered breathing in this population.[14] Until recently the phenotypic causes of OSA in people with tetraplegia had not been investigated nor understood. Gainche and colleagues [100, 101] compared the upper airway physiology of people with tetraplegia with non-disabled controls (matched for OSA severity, gender, and age) and found nasal resistance to be up to seven times higher in people with tetraplegia. This discovery may represent a specific phenotype contributing to the high prevalence of disease in this population. Following the administration of a topical sympathomimetic (a nasal decongestant), the high nasal resistance in those with tetraplegia and OSA dropped to the same levels as the non-disabled control group. Sympathetic outflow to the upper airway is disrupted following cervical SCI and the subsequent unopposed parasympathetic activity results in engorgement of the nasal mucosa, raising nasal resistance and providing one possible explanation for the high prevalence of OSA in people with tetraplegia.[102]

Wijesuriya et al[103] also found higher nasal resistance in people with tetraplegia and OSA compared to a control group with OSA. However, despite the higher nasal pressures found using gold-standard laboratory techniques, patients in this study were unable to perceive high nasal resistance, effectively ruling out the potential for clinically useful self-reported measures of nasal congestion.

The study by Gainche et al also discovered that people with SCI and OSA had a slower and smaller cortical reflex response to upper airway occlusion than the non-disabled control group, suggesting that the upper airway dilator muscles may respond too late to prevent upper airway collapse.[100, 101] These findings highlight the need for more research into therapies that lower nasal resistance and improve reflex responsiveness in people with tetraplegia, which may in turn reduce OSA severity.

Other physiological determinants of OSA have also been postulated in SCI. In a review paper, Sankari and colleagues[85] highlight that sleep is a physiological challenge for the respiratory system for healthy individuals, and that unfortunately high SCI causes

many changes that impair the ability of the respiratory system to compensate for these challenges. Problematic changes that occur after high SCI include neuromuscular weakness, reductions in lung volume, disruptions to the autonomic nervous system and abnormal mechanics of the chest wall. More research is required to understand the aetiology of OSA in SCI, which will hopefully lead to more effective therapeutic interventions.

### 1.6.4 Morbidity of OSA in SCI

People living with OSA and tetraplegia have a substantially lower health utility value than their tetraplegic peers without OSA. The difference is almost five times the minimal important difference, which raises the possibility that effectively treating OSA may substantially improve health and quality of life.[1] Although it has not specifically been investigated in SCI, there is no reason to believe that the cardiovascular and metabolic complications associated with OSA in the non-disabled would not be present in SCI.[104] Sankari et al[85] point to a strong relationship between OSA and cardiovascular disease in SCI, citing an audit of 168 veterans with SCI which found one in five had either hypertension or cardiovascular disease.[105] Unfortunately no statistical associations were made between the presence (or severity) of OSA and the presence (or severity) of cardiovascular disease, which has been repeatedly confirmed in the non-disabled.[34, 106] Research investigating the relationships between OSA and morbidity from cardiovascular and metabolic diseases is needed in this population with many additional risk factors for poor cardiovascular health.[105, 107]

OSA is associated with impaired cognition in people with chronic tetraplegia, particularly in the areas of attention, concentration, memory and learning skills.[108] Analysis of neuropsychological function in people with OSA following acute tetraplegia (approximately two to three months after injury) found that more severe OSA was associated with poorer attention, information processing, and immediate recall. However the neuropsychological deficits did not extend to memory, as was previously demonstrated in chronic tetraplegia, suggesting that deficits in memory associated with OSA may take longer to form.[109] Impairment in neuropsychological

function is likely to impact vocational outcomes, particularly for people with tetraplegia, whose physical disabilities usually limit engagement in physical jobs.

### 1.6.5 Treatment for OSA in SCI

There is a general paucity of research investigating OSA treatments in SCI. To date, only one randomised controlled trial has investigated the effect of PAP on the outcomes of people with SCI and OSA. The COSAQ study ('Continuous positive airway pressure (CPAP) for Obstructive Sleep Apnoea in Quadriplegia) was a multicentre randomised controlled trial that examined the effect of CPAP on neuropsychological function, sleepiness, quality of life, anxiety and depression. One hundred and sixty participants with acute, traumatic tetraplegia and OSA were randomly assigned to receive auto-adjusting CPAP for three months or to wait for the treatment. The study found that whilst CPAP significantly improved sleepiness after acute quadriplegia, it did not improve the neurocognitive function beyond that seen with post-injury, spontaneous recovery.[110]

Overall CPAP use in the COSAQ study averaged 2.9 hours (SD=2.3) per night with 21% of those randomised to CPAP classified as fully "adherent", defined as at least four hours of use on 71% (5 of 7) nights over the three-month trial.[110] However in accordance with the protocol, only those who could tolerate at least four hours on one of three nights were randomised. Given those who failed this hurdle requirement were unlikely to be long-term users,[111] CPAP adherence in the acute tetraplegic population is likely to be even lower. This randomised controlled trial was preceded by a smaller feasibility study of treating OSA with CPAP after acute tetraplegia. After three months of CPAP treatment, seven of the 14 participants (50%) were adherent, defined as using the device for more than four hours on at least five nights in the final week.[111]

Whilst there are few studies reporting PAP use in people with chronic SCI, those that exist suggest that CPAP acceptance and use is low, and may be lower in SCI than in non-disabled populations. A handful of highly heterogeneous studies have followed PAP use in people with chronic SCI diagnosed with OSA. [88, 92, 96, 112, 113] Only

one of these studies clearly defined adherence using objectively measured PAP usage data,[112] with others relying on self-report.

Stockhammer et al[92] offered 31 people with tetraplegia treatment with bi-level PAP for OSA. Only 16 accepted the trial and 11 continued with the therapy, representing 36% of the initial cohort. How and when adherence was measured was not reported, though almost certainly through self-report. Burns et al[88] identified eight men with OSA in a prevalence study of 40 individuals with SCI of any level. Of the eight individuals, only two (25%) were able to tolerate CPAP and reported continuing nightly CPAP use approximately one year post CPAP prescription. Sankari et al[96] studied 28 people with SCI (T6 or higher) of whom 22 (79%) had OSA. In this study, those with a positive diagnosis of OSA were encouraged to follow-up with their health care provider for treatment. They were contacted between six and 12 months later, and 50% had discussed their diagnosis with their health care provider. Six people were prescribed PAP therapy, and four reported using it at the time of follow-up.[96] Finally, a postal survey of 72 SCI patients with diagnosed OSA aimed to identify long-term treatment outcomes. Of the 40 respondents, 32 (80%) had tried CPAP and 20 (63%) reported continuing to use it at the time of the survey, for a self-reported average of 7 hours on 6.5 nights per week.[113]

These four studies are likely to be subject to significant response bias in their estimates of PAP acceptance and use. Much larger and more rigorous studies are needed to confirm rates of PAP use in chronic SCI and to understand the different factors contributing to poor adherence. Recently Brown et al[112] used objective data from device downloads to assess PAP use in chronic SCI (T6 lesion or higher). Bi-level PAP was prescribed to 63 people with OSA; after three declined, 60 were initiated with the therapy. Device data were obtained at three, six and 12 months. After three months 17 of the original cohort were classified “good users”, defined as at least 4 hours on 70% of nights. The reported adherence rate was 38% (17/44). However 16 participants withdrew from the study between CPAP initiation and three months. Assuming those who withdrew would not have been adherent at three months, the PAP adherence rate would be 28%. Furthermore, the number of “good users” fell to 11 (18% of the original cohort) at six months, and 10 (17%) at 12 months.[112]

Few alternatives to PAP therapy to treat OSA have been investigated in SCI. An uncontrolled, safety and feasibility trial of using a mandibular advancement splint to treat OSA in eight people with tetraplegia found that the mandibular advancement splint was effective in treating OSA and was well tolerated. However titration of the device, which takes an average of six to 12 weeks in the non-disabled, took up to 12 months in people with tetraplegia. (Unpublished data; personal communication with DJ Berlowitz) As yet there have been no randomised controlled trials investigating mandibular advancement splint to treat OSA in SCI.

Our group has investigated whether topical application of phenylephrine can improve OSA severity in a single night. This within-subjects cross-over randomised trial concluded that phenylephrine was effective in reducing nasal resistance, but this did not translate into a significant reduction in the AHI.[114]The manuscript for this study is currently under review. Whether or not a longer acting agent that is suitable for ongoing use can impact OSA severity is yet to be explored.

### 1.6.6 Clinical Practice Guidelines for the Management of OSA in SCI

Although the evidence supporting treatments for OSA in SCI is limited, current guidelines developed by the Consortium for Spinal Cord Medicine recommend PSG evaluation for all people with SCI with excessive daytime sleepiness or other symptoms for sleep disordered breathing.[115] These guidelines also recommend the prescription of PAP therapy, starting with CPAP, for those with a positive diagnosis of OSA. Similar recommendations have been published by the Spinal Cord Injury Rehabilitation Evidence (SCIRE) project.[116] The SCIRE recommendations include vigilance for suggestive signs and symptoms and further testing with oximetry or PSG when these signs are present. Both guidelines are underpinned by evidence from non-controlled studies, and based on strong clinical opinion.

In reality, little is known about the current management of OSA in people with tetraplegia. An audit of 584 medical records from a Veterans Affairs SCI service revealed only 15% of those with tetraplegia had received a diagnosis of OSA, despite

prevalence estimates of up to 93%. Of those with a diagnosis, only 47% were receiving treatment with CPAP, bi-level PAP or nocturnal oxygen (due to CPAP intolerance). Intolerance or refusal of PAP explained the majority of non-treated cases. Those not using PAP therapy were more likely to have motor-complete lesions at C5 or above.[117] Similarly, a recent audit by Sankari et al[105] revealed that only 37 of 168 (22%) veterans with SCI had been evaluated for OSA, and of the 34 who had a diagnosis of OSA confirmed, only six (18%) were using PAP. This indicates an enormous burden of disease that is both undetected and untreated.

## 1.7 Knowledge Translation

### 1.7.1 Background

Knowledge translation is the process of facilitating the uptake of evidence from research into clinical practice and health related policy. It has been defined as *"the synthesis, exchange and application of knowledge by relevant stakeholders to accelerate the benefits of global and local innovation in strengthening health systems and improving people's health"*.[118] Recognizing its importance, in 2005 the WHO held a meeting to discuss "Knowledge Translation in Global Health". Arising from this meeting was the published statement: *"Bridging the know–do gap is one of the most important challenges for public health in this century. It also poses the greatest opportunity for strengthening health systems and ultimately achieving equity in global health."*[118] Since then there have been a number of global initiatives aiming to bridge the evidence-practice gap in various clinical areas.

An evidence-practice gap exists when there is a lack of concordance between evidence-based recommendations based on research; and healthcare policy, systems and practice. Implementing the findings of research ensures our investment in research is not wasted and patients ultimately benefit. It can take one to two decades for the publication of high quality, synthesized evidence to be taken up into routine clinical care.[119, 120] In a seminal paper highlighting the failure of clinical care to meet recommended standards, McGlynn et al[121] estimated that patients in the USA received 55% of recommended care as measured on 439 indicators of quality. Quality of care varied by medical

condition from 79% with senile cataracts receiving recommended care compared to just 11% with alcohol dependence.[122] Similar findings were reported in a replicate Australian study evaluating compliance with 522 expert consensus indicators for 22 common conditions. Guideline-compliant health care was provided in 57% of the total encounters evaluated, which ranged by condition from 13% for alcohol dependence to 90% for coronary artery disease.[123]

Failure to translate current research evidence into practice and policy results in suboptimal outcomes for patients and enormous economic impacts on the healthcare system. Evidence-practice gaps can occur in the form of underuse of proven therapies and overuse of treatments shown to be ineffective.[124] At a systems level, it has been suggested that evidence practice gaps are caused by four key factors: the growing complexity of medical knowledge and technology; the rise in chronic and comorbid conditions associated with a higher life expectancy; a complicated and poorly organized health-care delivery system; and constraints on exploiting the revolution in information technology.[124] At the clinician level, a systematic review of the barriers to guideline adherence among physicians identified many factors that may be important, including lack of awareness of new research, lack of familiarity and agreement with guidelines, poor self-efficacy, low outcome expectancy, falling back on previous practice and external barriers such as lack of time, environmental factors and staff shortages.[125]

According to Grimshaw et al[126] producing up to date systematic reviews that are accessible to clinicians and policy makers should be the foundation of knowledge translation activities. A high quality evidence-based clinical practice guideline is considered to be the "basic unit of knowledge translation"[126] and tools for assessing the quality of the guidelines have been validated and widely used.[127] Beyond this, there are several methodologies designed to assist clinicians to interpret synthesised evidence and develop and implement interventions to increase the uptake of evidence. While *knowledge translation* is the process of moving evidence into clinical practice and health policy, *implementation science* involves systematically testing interventions that implement the evidence in real-world settings, although both terms are often used inter-changeably.[128] Implementation science has emerged as a field of research

concerned with reducing the lag between the availability of high-quality evidence and its implementation into clinical practice.

### 1.7.2 The Knowledge to Action Cycle

The Knowledge to Action Cycle (Figure 1.3), first published by Graham in 2006, is a useful model for understanding the scope of knowledge translation activities. The cycle divides the process into two categories: the creation and synthesis of new knowledge; and the action cycle, where that knowledge is transferred into clinical practice. Graham et al stress that the processes are often iterative and fluid, and can occur concurrently or sequentially, by the same research groups or in isolation.[129]

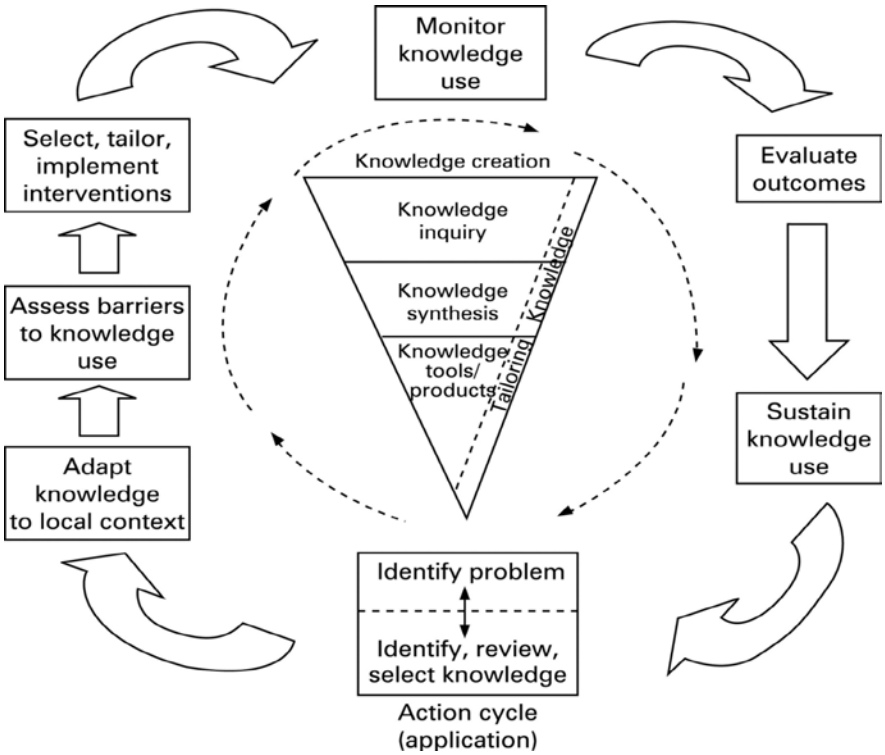


**Figure 1.3 The Knowledge to Action cycle [129]**

In the centre of the model is a pyramid representing the creation of knowledge, which organises knowledge from least to most tailored forms. At the base is “Knowledge inquiry”, which encompasses the many primary studies that investigate a research question, e.g. a randomised controlled trial of the effects of a new treatment. The second tier is “Knowledge synthesis,” e.g. systematic reviews and meta-analyses of like studies representing a body of evidence about a given topic. Finally, “Knowledge

tools/products" (e.g. clinical practice guidelines, patient management pathways) are based on these research syntheses and include context and local application tailored to a given setting. [129]

The action cycle surrounding the knowledge creation triangle represents the activities required to translate and sustain the knowledge into clinical practice. In developing the model, Graham and colleagues identified over 60 theories that have been employed to change clinical practice and the steps common to all are presented in this action cycle.[129]

#### *1.7.2.1 Identify the problem and adapt knowledge to the local context*

In most cases the first step in translating research evidence into practice is identifying and prioritising the problem. This step involves recognizing and where possible, quantifying where there is a gap between evidence and practice in the local setting. For example, a hospital may conduct an audit of their medical records to identify whether clinical practice recommendations for dementia screening are being adhered to.

Once the problem has been identified, the knowledge tools (e.g. clinical practice guidelines) need to be adapted to the local context. For example, in some rural settings it may not be possible to provide access to state-of-the-art equipment within a certain timeframe, requiring the existing clinical practice guidelines to be adapted to meet the abilities of the local facility.[129] Tools and frameworks are available to guide the process of local adaptation of clinical practice guidelines.[130, 131]

#### *1.7.2.2 Assess barriers to knowledge use*

A recent systematic review has concluded that interventions that are tailored to address identified barriers to knowledge use are more likely to improve clinical practice than simple dissemination of guidelines or no intervention.[132] Prior to developing an intervention to improve the uptake of evidence, the barriers that may be impeding practice and the facilitators that are likely to enhance practice should be assessed.

One approach to this assessment is to use the Theoretical Domains Framework (TDF). The TDF was developed by a group of psychologists and researchers to facilitate

research aiming to improve the uptake of evidence into practice.[133] To develop the TDF, Michie and colleagues simplified the plethora of existing psychological theories and constructs into a set of 12 relevant behaviour change domains, thereby providing an accessible framework for other disciplines to explore clinical behaviours.[133]

The 12 domains of TDF are: knowledge; skills; social/professional role and identity; beliefs about capabilities; beliefs about consequences; motivation and goals; memory, attention and decision processes; environmental context and resources; social influences; emotion regulation; behavioural regulation; and nature of the behaviour. The authors reason that the TDF enables a comprehensive, systematic and precise approach to defining the behaviours that need to be changed, thereby identifying opportunities for improved practice.[133] The TDF has subsequently been validated and is commonly used in knowledge translation research. [134-138]

#### *1.7.2.3 Select, tailor and implement intervention*

Using a framework like the TDF to systematically assess and understand barriers to knowledge uptake and enabling factors, facilitates the development of a tailored intervention. French et al [136] have published an operational four step approach to developing "theory-informed" behaviour change interventions for knowledge translation research.[139] The four steps, and the guiding tasks for each step, are set out in Table 1.3.

**Table 1.3 Steps for developing a theory-informed implementation intervention[136]**

| Step | Tasks |
|---|---|
| STEP 1: Who needs to do what, differently? | · Identify the evidence-practice gap<br>· Specify the behaviour change needed to reduce the evidence-practice gap<br>· Specify the health professional group whose behaviour needs to change |
| STEP 2: Using a theoretical framework, which barriers and enablers need to be addressed? | · From the literature, and experience of the development team, select which theory(ies), or theoretical framework(s), are likely to inform the pathways of change<br>· Use the chosen theory(ies), or framework, to identify the pathway(s) of change and the possible barriers and enablers to that pathway<br>· Use qualitative and/or quantitative methods |
| STEP 3: Which intervention components (behaviour change techniques and mode(s) of delivery) could overcome the modifiable barriers and enhance the enablers? | · Use the chosen theory, or framework, to identify potential behaviour change techniques to overcome the barriers and enhance the enablers<br>· Identify evidence to inform the selection of potential behaviour change techniques and modes of delivery<br>· Identify what is likely to be feasible, locally relevant, and acceptable and combine identified components into an acceptable intervention that can be delivered |
| STEP 4: How can behaviour change be measured and understood? | · Identify mediators of change to investigate the proposed pathways of change<br>· Select appropriate outcome measures<br>· Determine feasibility |

#### *1.7.2.4 Monitor intervention and evaluate outcomes*

As with all quality improvement activities, once the intervention has been developed and implemented, it must be monitored (*is the knowledge being applied?)* and evaluated (*what impact has it had on patient/practitioner/system outcomes?*). Knowledge translation interventions can be challenging to evaluate, reflecting the complex nature of their development and implementation.[140] Study designs commonly used to evaluate knowledge translation interventions include randomised designs such as individual

patient and cluster randomised controlled trials, and also non-randomised designs such as interrupted time series or simple before and after studies.[141] Choice of study design should be based on the research question, the local context and the resources available.

#### *1.7.2.5 Sustain knowledge use*

The final stage of the knowledge-to-action cycle is to sustain knowledge use. Graham suggests that the sustainability phase requires ongoing identification of new problems, new barriers, and changes to the local context; thus continuing the cycle.[129]

### 1.7.3 Limitations of knowledge translation research in the field of SCI and OSA

A significant barrier to knowledge translation activities aiming to improve the health of people with SCI and OSA is the lack of robust, synthesised evidence to guide practice, and the corresponding absence of high quality clinical practice guidelines.

A recent systematic review of knowledge translation research in SCI care found that of the 10 studies identified, at least seven did not translate robust evidence from randomised trials, but rather from expert clinical opinion and studies of weaker methodological design.[142] The relatively low incidence and prevalence of SCI and the highly specialised care required poses significant challenges to the conduct of high quality, adequately powered clinical trials. With so many systems of the body affected from SCI, competition for recruitment and limited funding often result in smaller, less robust clinical trials being undertaken.[143] Moreover, large randomised controlled trials are rarely repeated in this population; robust meta-analyses are rarely achieved; and SCI clinical practice guidelines are usually supported by weaker evidence and clinical opinion.[115] As a consequence, knowledge translation research in SCI is still in its infancy.[142]

This population with high disability and disadvantage deserve the best available care. Knowledge translation interventions should therefore focus on translating the best available evidence into practice, despite the limitations. The US Department of Veterans Affairs “SCI Quality Enhancement Research Initiative” (SCI-QUERI) is adopting this approach. SCI-QUERI is committed to promoting the quality of life of US veterans with

SCI by implementing clinical practice guidelines. Some of the projects to date have focussed on improving influenza vaccinations, MRSA infection prevention and pressure ulcer prevention, by implementing guidelines that are based on best available evidence.[144]

Similarly, the Rick Hansen Institute in Canada has developed a model for addressing evidence-practice gaps in SCI research and care. The “Praxis Model” includes three essential components: a coordinated program strategy to foster collaboration between all stakeholders; a method for knowledge translation in the form of an action cycle; and resources and infrastructure to help overcome known obstacles to effective translation.[143] The model is currently being applied to pressure ulcer prevention in SCI with a range of activities completed or underway. One component of this program was the development of clinical practice guidelines and the subsequent development of a “Pressure Ulcer Prevention Initiative”. This project provides another example of knowledge translation of the best available evidence in SCI.[143, 145]

Coordinated knowledge translation activities aiming to improve the care delivered to people with SCI within our region are in the early stages of development. This is enabled by the development of a regional SCI research strategy for Australia and New Zealand which commenced in 2012. This strategy was developed in three stages: a review of the SCI prioritisation literature;[146] a qualitative study involving interviews with key SCI research stakeholders to develop a draft research strategy framework;[147] and a one day structured dialogue with 23 experts to develop clear objectives for further development.[148] The resulting strategy identified a series of key objectives that broadly fit within four main themes: collaboration, coordination, consumer engagement, and resources. The importance of conducting research to improve the quality of life of people living with SCI, by researching issues that are important to them and engaging them in the process, was a recurrent theme in this series of papers. The importance of implementation research was also highlighted, particularly in relation to concerns about the lack of standards of care, and inconsistency in clinical practice.[146-148]

## 1.8 Rationale and aims for this thesis

OSA is a highly prevalent and deleterious secondary complication of tetraplegia that is under-diagnosed and under-treated. The two available clinical practice guidelines on management of OSA in SCI are based on the best available evidence. [115, 116] The practice recommendations within these guidelines have been described earlier in this chapter,(Section 1.6.6) and are similar to the more evidence-based recommendations guiding practice for a non-disabled population.[64] To date, there is no reason to suggest that OSA should be treated vastly differently in SCI than in the non-disabled population. Much can be done to improve the management of OSA in people with tetraplegia, to ultimately improve their quality of life.

This thesis aims to address some of the practical knowledge gaps and issues preventing the optimal management of OSA in the SCI population. As described by Graham et al,[129] the path from evidence to practice is usually a complex, dynamic one where several steps may be occurring simultaneously and iteratively. The ultimate aim for anyone conducting research in the field of OSA in tetraplegia is to improve the quality of life of people living with these two conditions, and the final step to achieving this is to implement evidence-based practice. As the knowledge to action cycle describes, we need to first generate knowledge about how to improve patient management and then apply this knowledge to routine clinical care. However there is much to be done in-between and this thesis addresses several impending and, as yet unanswered, questions necessary for the development of tailored interventions. Four separate but related research projects have been conducted. The objectives and rationale for each are described below.

### 1.8.1 Study 1: Can moderate to severe OSA be identified in chronic tetraplegia without PSG?

#### *1.8.1.1 Aim*

To develop and validate a simple method for detecting OSA in tetraplegia that does not require PSG.

#### *1.8.1.2 Rationale*

OSA is a highly prevalent secondary complication of SCI yet essentially no research has sought to determine how to identify this problem without using PSG; an expensive, onerous and frequently inaccessible test. Improving OSA diagnosis rates has the potential to increase access to treatment and prevent the undesirable quality of life and long-term health consequences for the individuals concerned. This project investigates a pragmatic approach to detecting moderate to severe OSA in traumatic tetraplegia, using a similar methodology to that developed and validated in a non-disabled, primary care population.[82] A tool that accurately detects moderate to severe OSA in people with tetraplegia could provide both a readily accessible and a cost-effective alternative to full PSG for units and countries with poor access to sleep studies. This research is presented in Chapter 2.

### 1.8.2 Study 2: Understanding adherence to CPAP in acute tetraplegia

#### *1.8.2.1 Aim*

To describe CPAP use in acute tetraplegia, including adherence rates, factors associated with adherence, and average pressures and mask leak.

#### *1.8.2.2 Rationale*

Our limited understanding of adherence rates and factors associated with poor CPAP adherence in people with tetraplegia means there is no ability to identify which patients are more likely to be adherent with therapy prior to, or after, CPAP implementation. A better understanding of CPAP adherence rates and the predictors of adherence is required to develop and test screening models and interventions that may improve the management of OSA in this population. This research involves the secondary analysis of data from a large multicentre randomised controlled trial of CPAP for OSA in acute tetraplegia.[110] It is presented in Chapter 3.

### 1.8.3 Study 3: Understanding adherence to CPAP in chronic tetraplegia

#### *1.8.3.1 Aim*

To estimate CPAP adherence in people with chronic tetraplegia and OSA, and to understand the experience of using CPAP.

#### *1.8.3.2 Rationale*

No research has previously sought to understand the experience of using CPAP from the perspective of people with SCI, nor to identify the patient level barriers and enablers to CPAP use. A more in-depth understanding of the unique experiences of CPAP use in this population is required to facilitate the development of targeted interventions to improve adherence. This study utilises a mixed methods design including both quantitative and qualitative methods and is presented in Chapter 4.

### 1.8.4 Study 4: Documenting and understanding clinical practice

#### *1.8.4.1 Aim*

To describe the variation in OSA management practices in tetraplegia, and to explore factors influencing clinical practice.

#### *1.8.4.2 Rationale*

No previous research has aimed to systematically describe the clinical management of OSA in tetraplegia, nor investigate the influences on these clinical practices. Anecdotally, practice is highly varied and is likely to be heavily influenced by access to sleep laboratories and expertise, and physician knowledge and beliefs about OSA. This qualitative research utilises the Theoretical Domains Framework to explore the influences on clinical behaviours, to ultimately facilitate the development of effective interventions to improve the management of OSA in tetraplegia. This research is presented in Chapter 5.

*"Someone is sitting in the shade today because someone planted a tree a long time ago." ~ Warren Buffett*

# 2 DEVELOPMENT AND VALIDATION OF A TWO-STAGE MODEL FOR DETECTING OBSTRUCTIVE SLEEP APNOEA IN CHRONIC TETRAPLEGIA

## 2.1 Overview of Chapter 2

This chapter presents the findings of comprehensive study aiming to validate a simple and accessible method for detecting moderate to severe OSA (MS-OSA) in chronic tetraplegia. This is the first study to investigate the accuracy of an alternative approach to full overnight polysomnography in this population. The Screening for OSA in Tetraplegia (SOSAT) study was conducted between September 2015 and April 2017, submitted for publication to *Thorax* in October 2017 and accepted in April 2018.[149] It was published with an accompanying editorial which is discussed at the end of this chapter (Section 2.7.2).[150] This chapter is presented in five main sections. Section 2.2 provides an overall introduction and rationale for the project. In particular it includes detailed information about the original development and validation of the two-staged screening model for identifying moderate to severe OSA (MS-OSA) in a primary care, non-disabled population.[82] It includes additional information on pulse oximetry as a method of detecting OSA, and further justification for the decision to investigate a screening model aiming to detect *moderate to severe* OSA, rather than *any* OSA. The introduction also includes background information and rationale for a side-study into the relationship between subjectively measured nasal congestion and MS-OSA, which was not presented in the main manuscript.

Section 2.3 is presented as a manuscript published in *Thorax*, and section 2.4 includes the online supplementary file accompanying the manuscript. While the supplementary file has been reformatted for this thesis, the content is unchanged from that published online. Section 2.5 includes methods for the subjective nasal congestion side-study. Section 2.6 contains some additional results from the SOSAT study that were not

presented in the main manuscript and online supplement. It also presents the results of the subjective nasal congestion side-study. Finally Section 2.7 provides a high level overview of this chapter, some limitations of the SOSAT study that were not provided in the manuscript, and a new discussion about the results of the nasal congestion side-study.

## 2.2 Introduction

### 2.2.1 Introduction and rationale for the SOSAT study

#### *2.2.1.1 Screening for OSA*

PSG is considered the "gold-standard" method for diagnosing sleep disordered breathing, including OSA, and is currently recommended by the Consortium for Spinal Cord Medicine for all people with SCI with excessive daytime sleepiness or other symptoms for sleep disordered breathing. [115]

However full PSG typically involves an overnight stay in a sleep laboratory. It uses highly specialised and expensive equipment, and usually requires access to a sleep scientist and sleep physician to analyse and report the data. Anecdotally, very few spinal units have access to PSG. Existing models of referral to a specialist sleep centre for initial consultation, followed by overnight, in-laboratory testing and review, have ensured that diagnoses and subsequent treatments have remained out of reach for the bulk of the SCI community. Even if the disorder is suspected, essentially all sleep laboratories are physically constructed assuming the clientele will be able-bodied, community dwelling people. People with tetraplegia often require overhead lifts, specialty mattresses, frequent overnight turning and wheelchair access, all of which are rarely provided in a sleep laboratory. Thus, the typical sleep laboratory environment is rarely able to effectively manage people with substantial physical disability and attendant care needs.

Available evidence points to massive under-diagnosis of OSA in tetraplegia. Two clinical practice audits, conducted within specialized SCI services, found that only 15-20% of patients had been diagnosed with OSA.[105, 117] This is despite prevalence

estimates of up to 93%.[16] Limited access to in-laboratory testing for people with SCI is a recognized contributor to the under-diagnosis of OSA.[85]

As discussed in Chapter 1, few OSA screening questionnaires have been tested in SCI. Those that have investigated whether threshold scores developed and validated in the non-disabled could predict OSA in high SCI. Sankari et al [16] investigated whether established threshold scores for the Epworth Sleepiness Scale (ESS),[97] the Pittsburg Sleep Quality Index,[98] the Berlin Questionnaire[95] and the Fatigue Severity Scale[99] were associated with at least mild OSA (defined as AHI≥5) and at least moderate OSA (AHI≥15) in 28 patients with SCI. Using this method, none of the questionnaires were significantly associated with mild or moderate OSA, although their abilities to screen out those who do not require further objective testing have not been investigated.

Bauman et al[93] evaluated the use of home based testing with a Level III portable monitor and a transcutaneous $CO_2$ recording device to diagnose sleep disordered breathing in chronic SCI (T6 lesion or higher). While they found similar prevalence estimates of OSA (81%) to studies using PSG, in the absence of a reference standard (PSG), they were unable to report the accuracy of the home testing method. The diagnostic model was found to be feasible, however the diagnostic accuracy remains unknown.[93]

Berlowitz et al[86] established that OSA was highly prevalent within weeks of cervical SCI and is a direct consequence of the injury. Whilst the aetiology of OSA following SCI remains largely unknown, the rapid onset in SCI is markedly different to that observed in people without disability who experience a slow, insidious development of disease over time. Thus it is likely that the risk factors are also different, and questionnaires and screening models developed specifically for people with SCI may perform better than those developed for non-disabled populations. To date, no OSA screening methods have been developed specifically for people with SCI.

#### *2.2.1.2 Chai-Coetzer two-stage screening model*

As discussed in Chapter 1, several systematic reviews and meta-analyses have summarised alternative OSA screening methods for people without disability.[43-45] Since publication of these reviews, a two stage model of screening questionnaire and home monitoring to detect MS- OSA has been developed and validated in a primary care, non-disabled, population. This model consists of a simple four item questionnaire to rule out OSA, followed by overnight pulse oximetry for those with a positive questionnaire result.[82]

The authors of this study defined MS-OSA as an apnoea-hypopnoea index (AHI)≥30, with respiratory events scored with the AASM 1999 "Chicago" criteria. As discussed in Chapter 1, the AASM assigned mild, moderate and severe OSA severities to various ranges of the AHI, when scored using the "Chicago" rules. According to these rules, an AHI of 5 to 15 indicates mild disease, 15 to 30 indicates moderate and over 30 indicates severe disease. However the rules for scoring respiratory events have undergone two further iterations since the 1999 "Chicago" criteria. The 2007 AASM rules result in markedly lower AHI scores, and Ruehland et al showed that an AHI of ≥30 scored according to "Chicago" criteria is equivalent to an AHI of approximately 10.8 when scored according to the 2007 criteria.[42] Using these data, Chai-Coetzer et al justified their decision to define MS-OSA as an AHI of ≥30 using the "Chicago" criteria.[82]

Their two-stage model was developed in a group of 79 people attending one of six primary care clinics. Participants underwent unattended, home-based PSG and oximetry monitoring, and also completed a questionnaire battery including a general health questionnaire, the ESS and the Berlin questionnaire. Following regression analysis, four variables were found to be predictive of MS-OSA. The regression coefficients were subsequently used to develop a questionnaire, called the "OSA50" with a simple scoring algorithm out of 10. (Table 2.1) ROC curve analysis identified the optimal threshold for the screening questionnaire to be ≥5/10, with a sensitivity of 100% and specificity of 29%.

Overnight oximetry in the Chai-Coetzer two-stage model was recorded with a ResMed ApneaLink device and the 3% oxygen desaturation index (ODI) was obtained

automatically using ApneaLink software. Receiver Operating Characteristic (ROC) curve analysis identified a 3%ODI of greater than or equal to 16 as the optimal threshold for diagnosing MS-OSA.[82] When the two-stages were combined in the development group, the overall diagnostic accuracy of the model was 91%.

**Table 2.1 The four-item OSA50 questionnaire**

| | If YES, score: |
|---|---|
| Obesity: Waist circumference (Males>102cm or Females>88cm) | 3 |
| Snoring: Has your snoring ever bothered people? | 3 |
| Apneas: Has anyone noticed that you stop breathing during your sleep? | 2 |
| 50: Are you aged 50 years or over? | 2 |
| Total | 10 |

The model was then prospectively applied to an independent validation group of 78 people, recruited with the same method as the development group. The two-stage model was found to have a sensitivity of 88% and a specificity of 82%, with an overall diagnostic accuracy of 83%. This model has subsequently been used to detect OSA in a clinical trial investigating primary care management of OSA.[81]

*2.2.1.3 Pulse oximetry*

Pulse oximetry is a simple non-invasive method of estimating the percentage of haemoglobin molecules in arterial blood that are bound with oxygen, and is a useful indicator of oxygenation. Pulse oximetry plays a role in detecting OSA, both within a PSG study and increasingly in portable, limited channel devices. OSA is characterized by repetitive episodes of desaturation followed by re-saturation, as a direct result of the airway obstruction that impairs breathing. As in the Chai-Coetzer two-stage model, the oximeter recordings can be used to calculate the Oxygen Desaturation Index (ODI), which is the number of times in one hour that the oxygen saturation dips by a predetermined amount (e.g 3%, 4%).[151]

Oximetry has been described as the “cornerstone” of OSA detection because it is the most accurate, quantifiable, reliable and informative signal. For these reasons it is the most commonly used signal in any limited-channel sleep study. One major advantage of the oximeter is that an automated algorithm can generate an ODI in place of a manual scorer, which can be more expensive and less reliable.[65] According to the Australasian Sleep Association “Guidelines for Sleep Studies in Adults”, oximetry should only be used to diagnose MS-OSA in populations with a high pre-test probability. This is because the ODI performs well at “ruling in” MS-OSA (sensitivity>85%) but less well at “ruling out” the disease (specificity~40-70%).[26, 151] The 3%ODI has been found superior to the 4%ODI in detecting moderate to severe OSA across a range of Body Mass Indices (BMIs).[152]

#### *2.2.1.4 OSA severity*

As discussed in Chapter 1, systematic reviews have concluded that screening models for OSA tend to be good at predicting severe OSA and poor at identifying mild disease. However there are also clinical imperatives for focusing on identifying more severe disease.

In people without disability there is growing evidence to suggest that all-cause mortality, stroke and cardiovascular disease are all strongly associated with OSA severity, with those with moderate to severe disease carrying the highest risk.[153-158] Whilst these serious health outcomes of OSA have not been studied in SCI, there is no reason to believe that they would be substantially different.

There is evidence from literature in non-disabled populations to suggest that severity of OSA and oxygen desaturations are associated with poorer neuropsychological function.[159-161] Large and frequent desaturations, a common feature of more severe OSA, have also been associated with worse neuropsychological function in chronic tetraplegia.[108] A recent study investigating the relationships between OSA and neuropsychological function in acute tetraplegia found that severe OSA (AHI≥30) was associated with worse neuropsychological function in the domains of attention, information processing, immediate recall, executive function and freedom from distractibility.[109]

As previously discussed in Chapter 1, CPAP improves daytime sleepiness and sleep quality, and is the first-line treatment for OSA.[48] However available literature indicates that only 30-60% of people without disability are adherent with the treatment.[55] More severe disease and greater daytime sleepiness have been consistently found to predict CPAP adherence.[48, 57] In fact, a meta-analysis investigating the relationship between OSA severity and CPAP adherence found the AHI to be, on average, six events per hour higher in adherent than in non-adherent groups.[162]

Predictors of CPAP adherence have not yet been investigated in tetraplegia, however chapters 4 and 5 of this thesis present original research investigating adherence rates and predictors in acute and chronic tetraplegia.

### 2.2.2 Subjective nasal congestion and OSA

OSA is a multifactorial and highly heterogeneous disease. As discussed in Chapter 1, the phenotypic causes of OSA in the non-disabled are thought to include upper airway collapsibility, upper airway anatomy, and other pathophysiologic factors such as upper airway muscle responsiveness and respiratory system stability.[35] The phenotypical traits of OSA have not been fully defined in SCI, however recent research by our group indicates that nasal resistance is up to seven times higher in people with tetraplegia and OSA when compared with controls, and may be a specific factor contributing to the high prevalence of disease in this population.[40] Elevated nasal resistance is a known risk factor for OSA in people without disability.[42]

Whether subjectively measured nasal congestion is associated with OSA in people with tetraplegia has never been investigated. We hypothesized that subjectively measured nasal congestion is associated with MS-OSA in chronic tetraplegia. If true, the accuracy of the prediction model could be improved with the addition of a subjective nasal congestion estimate.

### 2.2.1 Study rationale

OSA is a highly prevalent secondary complication of SCI yet essentially no research has sought to determine how to identify this problem without PSG. Untreated OSA is associated with significant neurocognitive deficits and substantially lower quality of life in tetraplegia, which likely reduces independence and limits vocational options.[1, 108] Improving the diagnosis of OSA has the potential to prevent these undesirable consequences for the individuals concerned. This project investigates a pragmatic approach to detecting MS-OSA in chronic, traumatic tetraplegia, using a similar methodology to that developed and validated in a non-disabled, primary care population. If successful, a screening model that accurately detects MS-OSA in people with tetraplegia could provide a readily accessible and a cost-effective alternative to full PSG.

## 2.3 Diagnostic accuracy of a two-stage model for detecting obstructive sleep apnoea in chronic tetraplegia

ORIGINAL ARTICLE

# Diagnostic accuracy of a two-stage model for detecting obstructive sleep apnoea in chronic tetraplegia

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## ABSTRACT

**Background** Obstructive sleep apnoea (OSA) is highly prevalent in people with spinal cord injury (SCI). Polysomnography (PSG) is the gold-standard diagnostic test for OSA, however PSG is expensive and frequently inaccessible, especially in SCI. A two-stage model, incorporating a questionnaire followed by oximetry, has been found to accurately detect moderate to severe OSA (MS-OSA) in a non-disabled primary care population. This study investigated the accuracy of the two-stage model in chronic tetraplegia using both the original model and a modified version for tetraplegia.

**Methods** An existing data set of 78 people with tetraplegia was used to modify the original two-stage model. Multivariable analysis identified significant risk factors for inclusion in a new tetraplegia-specific questionnaire. Receiver operating characteristic (ROC) curve analyses of the questionnaires and oximetry established thresholds for diagnosing MS-OSA. The accuracy of both models in diagnosing MS-OSA was prospectively evaluated in 100 participants with chronic tetraplegia across four international SCI units.

**Results** Injury completeness, sleepiness, self-reported snoring and apnoeas were included in the modified questionnaire, which was highly predictive of MS-OSA (ROC area under the curve 0.87 (95% CI 0.79 to 0.95)). The 3% oxygen desaturation index was also highly predictive (0.93 (0.87–0.98)). The two-stage model with modified questionnaire had a sensitivity and specificity of 83% (66–93) and 88% (75–94) in the development group, and 77% (65–87) and 81% (68–90) in the validation group. Similar results were demonstrated with the original model.

**Conclusion** Implementation of this simple alternative to full PSG could substantially increase the detection of OSA in patients with tetraplegia and improve access to treatments.

**Trial registration number** Results, ACTRN12615000896572 (The Australian and New Zealand Clinical Trials Registry) and pre-results, NCT02176928 (clinicaltrials.gov).

## Key messages

### What is the key question?

► Can a two-stage model of questionnaire followed by overnight oximetry accurately detect moderate to severe obstructive sleep apnoea in people with chronic tetraplegia?

### What is the bottom line?

► This model could substantially increase the detection of obstructive sleep apnoea in people with tetraplegia and subsequently improve access to treatment.

### Why read on?

► This is the first time a model for detecting obstructive sleep apnoea has been adapted and applied in people with tetraplegia, a population with a high burden of disease but limited access to full diagnostic services.

## INTRODUCTION

People with tetraplegia have a higher prevalence of sleep disorders than the non-disabled population.[1] The most widely studied sleep disorder in tetraplegia is obstructive sleep apnoea (OSA). More recent estimates of OSA prevalence in chronic tetraplegia range from 56% to 77%[2–4] which is higher than in people over the age of 40 without disability (up to 50% in men and 23% in women).[5] OSA is associated with both substantial neurocognitive impairment and reduced quality of life in people with tetraplegia.[2 6 7] People living with OSA and tetraplegia have a substantially lower health utility value than their tetraplegic peers without OSA. This difference is almost five times the minimally important difference and as such effectively treating OSA is likely to translate into an improved quality of life.[2]

Current guidelines recommend polysomnography (PSG) for all people with spinal cord injury (SCI) and excessive daytime sleepiness or other symptoms of sleep disordered breathing.[8] Full PSG is the 'gold-standard' method for diagnosing OSA[9] and involves an overnight sleep laboratory stay and connection to a multichannel polygraph during sleep. Very few spinal units have access to PSG, and specific care needs of people with tetraplegia can prohibit access to full PSG in standard sleep laboratories. Even portable PSG requires expensive equipment and specialised staff to apply, score and

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► http://dx.doi.org/10.1136/thoraxjnl-2018-211954

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report the study. Although there are no published estimates on the proportion of people with SCI and OSA who remain undiagnosed, it is likely to be high. It is well recognised that access to PSG is poor and commonly results in long waiting times for diagnosis and subsequent treatment.[10 11]

The high costs and limited access to PSG have resulted in the development of simpler methods for detecting OSA in people without disability. These simpler methods tend to predict severe OSA with a high degree of accuracy but miss a substantial proportion with milder disease.[12–14] More recently, a two-stage model to detect moderate to severe OSA (MS-OSA) has been developed and validated in a primary care, non-disabled population.[15] The model, with an overall accuracy of 83%, consists of a simple four-item screening questionnaire (the OSA50) to rule out OSA, followed by overnight oximetry for those with a positive questionnaire result.[15]

Two OSA screening questionnaires, the Multivariate Apnea Prediction Index and the Berlin Questionnaire, have been tested in the SCI population and both performed poorly at identifying OSA.[2 16] OSA is highly prevalent within weeks of cervical SCI and is considered a direct consequence of the injury,[17] in contrast to the progressive onset of OSA in people without disability. As such, it is possible that the risk factors also differ, and questionnaires developed specifically for the SCI population may perform better than those developed for the non-disabled population. This project aimed to determine the accuracy of the original two-stage model, developed for the non-disabled population, for diagnosing MS-OSA in people with chronic tetraplegia. Furthermore, the study tested whether inclusion of readily obtainable tetraplegia-specific risk factors would improve model accuracy.

## METHODS

The reference standard for this study, MS-OSA, was defined as an Apnea Hypopnea Index (AHI)≥21, scored with the American Academy of Sleep Medicine (AASM) 2012 criteria. We considered this threshold equivalent to an AHI≥30 scored using AASM 'Chicago' criteria; the reference standard used in the original two-stage model validation in a non-disabled population.[15 18 19] Further details are provided in online supplementary material including eTable2).

### Stage 1: initial validation and modification of the two-stage model with OSA50 questionnaire

An existing data set, including a questionnaire battery and full PSG in a sample of 78 people with chronic tetraplegia, was used to validate and modify the original two-stage model.[2 20] Demographic data coupled with questionnaire responses from the Basic Nordic Sleepiness Questionnaire[21] enabled derivation of the OSA50 scores (online supplementary eFigure 1 and eTable1). The overnight oximetry was simulated by analysing the raw oximetry signal from the PSG independently of all other signals and scored events. The 3% oxygen desaturation index (3%ODI) was generated by Compumedics (Abbotsford, Vic, Australia) ProfusionPSG software (V.3.4). To mirror the conditions of the original study, the 3%ODI was calculated over total (study) recording time.[15] Full PSG data were independently staged and scored as per AASM 2012 criteria to calculate the reference standard AHI.[18] Further details are provided in online supplementary material.

Receiver operating characteristic (ROC) curve analyses of the OSA50 and 3%ODI were performed to assess the accuracy of the two stages separately and to determine optimal thresholds. Following application of the model to the data set, sensitivity and specificity, positive and negative predictive values, positive and negative likelihood ratios and overall test accuracy were calculated for the two-stage model as a whole and the 3%ODI alone. This was performed using the original thresholds (ie, OSA50 ≥5/10 and 3%ODI ≥16/hour) and repeated with the optimised thresholds.

A 95% CI for the 3%ODI threshold was calculated by obtaining 999 bootstrap replicate samples.[22] Resampling separately the 'OSA negative' and 'OSA positive' cases and determining the optimal threshold for each sample provided the 95% CI as the 2.5th and 97.5th percentiles of the 999 thresholds.

### Stage 2: development of the tetraplegia-specific questionnaire (Screening for OSA in Tetraplegia) and two-stage model

Using the same data set (n=78) a modified version of the questionnaire was developed by investigating previously identified, tetraplegia-specific risk factors and their associations with MS-OSA. The risk factors investigated were age, gender, American Spinal Injury Association (ASIA) Impairment Scale (AIS), lesion level, neck and waist circumference, body mass index, time since injury, daytime sleepiness, self-reported snoring and self-reported apnoeas. Non-binary variables were dichotomised to enable simple questionnaire administration. Further details are provided in online supplementary material.

Univariate associations between the binary risk factors and an AHI≥21 were investigated. Variables with a $p<0.1$ on univariate analysis were entered into a backward, stepwise, multivariable logistic regression model. Weightings of the regression coefficients of variables significantly associated with MS-OSA ($p<0.05$) were used to develop a simple scoring algorithm for a new questionnaire, called Screening for OSA in Tetraplegia (SOSAT).[23]

The same diagnostic accuracy statistics used in stage 1 were calculated for the SOSAT questionnaire alone and, after inclusion of the 3%ODI, for the two-stage model as a whole.

### Stage 3: validation of two-stage models

Stage 3 involved validation of the two-stage models (with both OSA50 and SOSAT screening questionnaires) against the reference standard (PSG derived AHI≥21) in a prospective sample. Study design complied with the Standards for Reporting of Diagnostic Accuracy Studies (STARD) statement .[24] The study was prospectively registered in the Australia and New Zealand Clinical Trials Registry (ACTRN12615000896572). The University of Miami provided baseline data from a concurrent randomised controlled trial which was prospectively registered on clinicaltrials.gov (NCT02176928).

#### Sample size

The sample size calculation for the prospective validation was based on the estimated sensitivity, given its relative importance for diagnosis of this disease. Assuming a 50% prevalence of MS-OSA,[2 4] 98 participants were required for a sensitivity of 0.85 (95% CI 0.75 to 0.95). Assuming a home sleep study failure rate of approximately 9%,[15] we aimed to recruit 108 participants.

#### Participant recruitment

Consecutive patients, with chronic (>1 year postinjury), traumatic tetraplegia (level T1 or higher; AIS A, B, C or D), attending the spinal outpatient or inpatient units between September 2015 and April 2017 at Austin Hospital, Stoke-Mandeville Hospital and GF Strong Rehabilitation Centre were invited to participate.

All participants with chronic, traumatic tetraplegia recruited to the University of Miami study between April 2015 and November 2016 were also assessed for inclusion. Participants were excluded if they were: being treated for OSA; an inpatient with a cardiorespiratory complication; medically unstable; or unable to provide informed consent.

### Data collection

Unattended PSGs were conducted in the participants' homes or the spinal inpatient units and set up by two trained staff. PSGs were conducted with a SomtePSG device (Compumedics, Abbottsford, Australia) except in Miami where an Embla Emblettax100 PSG device (Natus Medical, Pleasanton, USA) was used. All studies were sleep staged, and respiratory scored by an independent, experienced sleep scientist in Melbourne using Profusion software (Compumedics).

Oximetry was collected within the PSG devices and the 3%ODI generated as described in stage 1. To determine whether a different oximeter could be confidently used in the model, oximetry was also collected with a ResMed (San Diego, CA, USA) ApneaLinkAir device in a subset of 20 participants, and the 3%ODI was calculated using ApneaLink software (V.10.20). The ApneaLink oximeter was placed on the same finger of the opposite hand to the SomtePSG oximeter. Detailed descriptions of PSG devices and oximeters are provided in online supplementary material.

Demographic data were collected from the medical record. Abdominal girth (at end expiration) and neck circumference were measured immediately prior to the sleep study with the patient in the supine position. If weight and height were not recorded in the medical record, participants provided estimates. The Berlin Questionnaire[25] and Karolinska Sleepiness Scale[26] were collected before the sleep study.

### Data analysis

Baseline characteristics of participants in the development and the validation groups were compared with Student's t-tests (or Wilcoxon signed-rank test if non-normally distributed) and $X^2$ analyses.

The accuracy of both two-stage models and the ODI alone were evaluated with the same diagnostic accuracy statistics described previously. Differences in overall accuracy of the models were evaluated with a McNemar $X^2$ test.

Sensitivity analyses of model accuracy examined the potential effects of study site ($X^2$) and PSG quality. High-quality sleep studies were defined as 3 hours of sleep plus 6 hours of concurrent EEG, oxygen saturation and either nasal flow and/or thoracic/abdominal excursion traces.

Agreement between the 3%ODIs generated by both the ApneaLink and Compumedics devices was compared using a Bland-Altman plot, Pearson's correlation and the proportion changing categories.

## RESULTS

Participants of the development (n=78) and validation (n=100) groups were predominantly male, slightly overweight and less than half had complete injuries (AIS A). Participants of the validation group were on average 6 years older and 6 years longer postinjury than those in the development group. Prevalence of OSA was high in both groups, although significantly higher in the validation group (table 1). See online supplementary material for the characteristics of sleep disordered breathing in both samples.

**Table 1** Characteristics of participants in development and validation groups

| | Development group (n=78) | Validation group (n=100) | P values |
|---|---|---|---|
| Age, years (SD) | 43.9 (12.3) | 49.6 (13.9) | 0.01 |
| Gender male, % (n) | 75.6 (59) | 79.0 (79) | 0.59 |
| Time since injury, median years (IQR)* | 10.0 (11.0) | 12.7 (17.7) | 0.03 |
| AIS A, % (n) | 44.9 (35) | 38.0 (38) | 0.36 |
| AIS B, % (n) | 11.5 (9) | 21.0 (21) | 0.09 |
| AIS C, % (n) | 11.5 (9) | 19.0 (19) | 0.18 |
| AIS D, % (n) | 32.1 (25) | 22.0 (22) | 0.13 |
| C1-C4, % (n) | 30.8 (24) | 20.0 (20) | 0.10 |
| C5-T1, % (n) | 69.2 (54) | 80.0 (80) | 0.13 |
| BMI, kg/m$^2$ (SD) | 25.0 (4.0) | 26.4 (6.1) | 0.07 |
| Waist circumference, cm (SD) | 104.9 (15.9) | 104.0 (16.8) | 0.71 |
| Neck circumference, cm (SD) | 41.3 (5.4) | 42.3 (5.9) | 0.26 |
| KSS, median (IQR)* | 3 (2) | 3 (4) | 0.81 |
| AHI†, median events/hour (IQR)* | 13.3 (28.2) | 22.3 (30.0) | <0.01 |
| AHI≥21, % (n) | 38.5 (30) | 53.0 (53) | 0.05 |
| AHI≥5, % (n) | 73.1 (57) | 97.0 (97) | <0.01 |
| AHI≥15, % (n) | 48.7 (38) | 72.0 (72) | <0.01 |

*Non-normally distributed.
†AASM 2012 scoring criteria.[18]
AASM, American Academy of Sleep Medicine; AHI, Apnea Hypopnea Index; AIS, ASIA Impairment Scale; BMI, body mass index; KSS, Karolinska Sleepiness Scale.

### Stage 1: initial validation and modification of two-stage model with OSA50 questionnaire

In the development data set, the OSA50 questionnaire alone was significantly predictive of MS-OSA with an ROC area under the curve (AUC) of 0.83 (95% CI 0.73 to 0.92, figure 1). When using the original threshold (≥5/10), the sensitivity and specificity of the questionnaire were 86.7% and 52.1%, respectively. A threshold of ≥3/10 with a sensitivity of 100% and a specificity of 29.2% gave the best performance for ruling out OSA.

The ROC AUC for the 3%ODI alone was 0.93 (0.87–0.98, figure 1). When using the original threshold of ≥16, sensitivity and specificity of the ODI were 80.0% and 87.5%. A threshold of ≥13 was deemed the optimal threshold for classifying MS-OSA (86.7% and 83.3%, respectively), and the 95% CI was 9.5 to 22.2.

Sensitivity and specificity of the two-stage model (OSA50 questionnaire and ODI in combination) with original thresholds (OSA50 ≥5/10 and 3%ODI ≥16) were 70.0% and 91.7%. Sensitivity and specificity with optimised thresholds (OSA50 ≥3/10 and 3%ODI ≥13) were 83.3% and 85.4% (table 2 and online supplementary eTable 3A–C).

### Stage 2: development of the tetraplegia-specific questionnaire (SOSAT) and two-stage model

The ROC analyses for non-binary predictor variables, the thresholds selected and the subsequent univariate analyses can be found in online supplementary eTables 4 and 5. Multivariable analysis established that four variables were predictive of MS-OSA (table 3). The multivariable factor weightings were simplified to generate a scoring algorithm out of 10 for the SOSAT questionnaire (figure 2). Two variables were given a

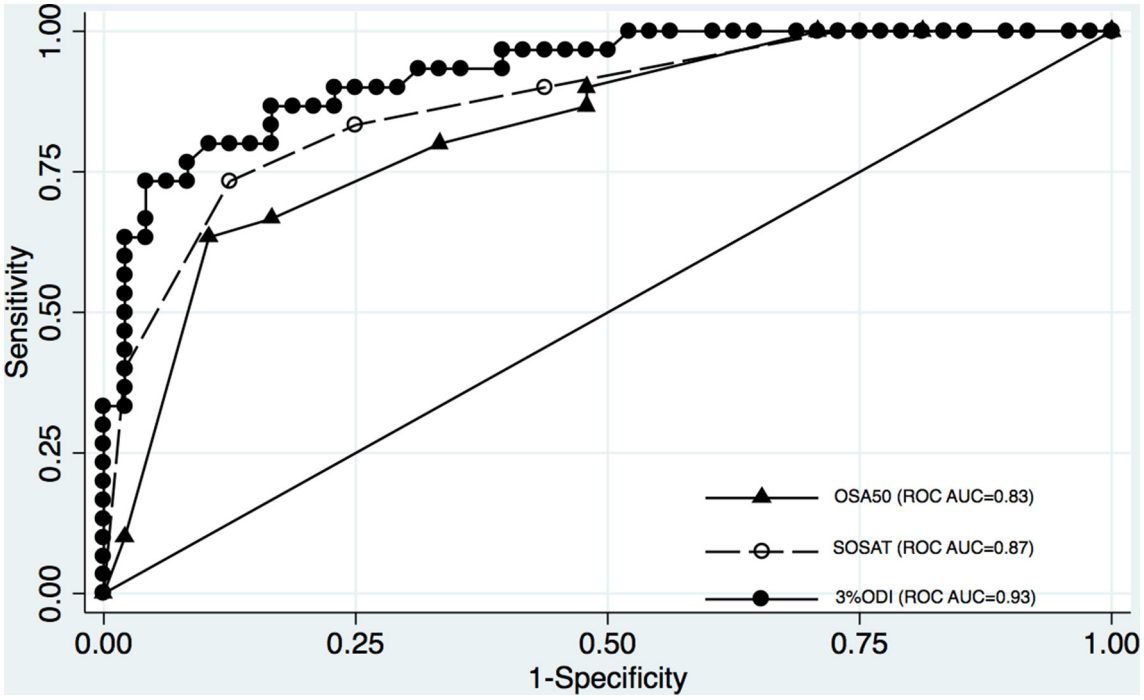


**Figure 1** ROC curve showing performance of two questionnaires (OSA50 and SOSAT) and the 3%ODI in discriminating MS-OSA in people with tetraplegia in development group. AUC, area under the curve; MS-OSA, moderate to severe OSA; ODI, oxygen desaturation index; OSA, obstructive sleep apnoea; ROC, receiver operating characteristic; SOSAT, Screening for OSA in Tetraplegia.

weighting of 3 (AIS A, B or C and self-reported snoring) and two variables a weighting of 2 (self-reported apnoeas and sleepiness).

The ROC AUC for the SOSAT questionnaire was 0.87 (0.79–0.95, figure 1). Sensitivity and specificity at a threshold of ≥5/10 were 100.0% and 27.1%, respectively. When combined with oximetry the sensitivity and specificity of the two-stage model (SOSAT ≥5/10 and 3%ODI ≥13) were 83.3% and 87.5% (table 2 and online supplementary eTable 6).

### Stage 3: validation of two-stage models

Figure 3 shows the participant recruitment pathway for the validation group. Three models were applied to the validation data set for comparison: the two-stage model with OSA50 (with optimised thresholds), the two-stage model with SOSAT and the 3%ODI alone (tables 2 and 4A–C). No differences in the overall accuracy of the three models were observed (p=0.56, 0.48, 0.56 for the three pairwise comparisons). The OSA50 and SOSAT questionnaires excluded 19% and 22%, respectively, from further testing with oximetry.

The SOSAT questionnaire incorrectly excluded three people with MS-OSA and 3%ODI ≥13. In the model using SOSAT, the 3%ODI was responsible for 18 of the 21 incorrectly classified cases. Of these, eight (44%) were within the 95%CI for the 3%ODI (9.5 to 22.2). The AHIs for the 12 incorrectly missed and the nine incorrectly diagnosed ranged from 21.5 to 37.9, and 12.6 to 20.3 respectively (online supplementary eTable 7).

There was no effect of study site (model with SOSAT p=0.40; OSA50 p=0.54), nor PSG quality on overall accuracy (high quality (n=76) vs all (n=100); model with SOSAT=79% vs 79%; with OSA50=82% vs 80%).

#### Oximetry device data comparisons

Oximetry data from simultaneously collected ApneaLink and Compumedics devices revealed four technical failures when using the ApneaLink. Mean 3%ODI scores from the 16 participants with both ApneaLink and Compumedics devices were 20.0 (SD=16.7) and 21.6 (17.2) (p=0.36). Correlation was high (0.92; p<0.01). Two (12.5%) participants whose Compumedics derived 3%ODI was ≥13 were <13 on ApneaLink (online supplementary eFigure2 for Bland-Altman plot).

## DISCUSSION

This study evaluated the accuracy of a two-stage model of a screening questionnaire followed by overnight oximetry as an alternative to PSG for diagnosing MS-OSA in people with chronic tetraplegia. The model was tested using both the OSA50 questionnaire, as originally developed and validated for the non-disabled primary care population[15] and a modified version developed specifically for chronic tetraplegia. To our knowledge, this is the first time an OSA diagnostic model has been adapted and applied in people with tetraplegia, a population with a high burden of disease but limited access to full diagnostic services. Both models performed similarly, correctly classifying 80% (OSA50) and 79% (SOSAT) of participants.

We hypothesised that the model with SOSAT questionnaire would be more accurate than with OSA50 questionnaire. However, two of the four items (self-reported snoring and apnoeas) were identical. Despite the strong association found on univariate analysis, waist circumference (an item of the OSA50) was excluded from the SOSAT questionnaire because it is a highly impractical measurement to obtain in tetraplegia. The absence of waist circumference may partly explain why SOSAT did not outperform the OSA50. Given the performance of SOSAT was comparable to the OSA50 with simpler administration we recommend using SOSAT.

The two-stage model with SOSAT incorrectly diagnosed nine participants with MS-OSA. Their AHIs ranged from 12.6 to 20.3. All had evidence of at least mild OSA and would potentially benefit from therapy. Of greater concern were the 12 participants who were incorrectly 'missed' in the model (AHIs

**Table 2** Diagnostic accuracy statistics for three models in development and validation data sets

| | Sensitivity (%) | Specificity (%) | Correctly classified (%) | Positive predictive value | Negative predictive value | Positive likelihood ratio | Negative likelihood ratio | Requiring oximetry (%) |
|---|---|---|---|---|---|---|---|---|
| Development group (n=78) | | | | | | | | |
| Two-stage model with OSA50 (original thresholds): OSA50 ≥5/10 and 3%ODI ≥16 | 70.0 (52.1–83.3) | 91.7 (80.5–96.7) | 83.3 | 84.0 (66.6–93.3) | 83.0 (73.8–89.5) | 8.4 (3.2–22.1) | 0.33 (0.19–0.57) | 63 |
| Two-stage model with OSA50 (optimised thresholds): OSA50 ≥3/10 and 3%ODI ≥13 | 83.3 (66.4–92.7) | 85.4 (72.8–92.8) | 84.6 | 78.1 (63.9–87.9) | 89.1 (78.5–94.9) | 5.7 (2.8–11.5) | 0.20 (0.09–0.44) | 82 |
| Two-stage model with SOSAT: SOSAT ≥5/10 and 3%ODI ≥13 | 83.3 (66.4–92.7) | 87.5 (75.3–94.1) | 85.9 | 80.7 (66.0–90.0) | 89.4 (78.9–95.0) | 6.7 (3.1–14.3) | 0.19 (0.08–0.43) | 83 |
| 3%ODI ≥13 | 83.3 (66.4–92.6) | 83.3 (70.4–91.3) | 83.3 | 75.7 (61.9–85.7) | 88.9 (78.1–94.7) | 5.0 (2.6–9.6) | 0.20 (0.09–0.45) | 100 |
| Validation group (n=100) | | | | | | | | |
| Two-stage model with OSA50 (optimised thresholds): OSA50 ≥3/10 and 3%ODI ≥13) | 79.3 (66.5–88.0) | 80.9 (67.5–89.6) | 80.0 | 82.4 (71.9–89.5) | 77.6 (66.7–85.6) | 4.1 (2.3–7.6) | 0.26 (0.15–0.44) | 81 |
| Two-stage model with SOSAT: SOSAT ≥5/10 and 3%ODI ≥13 | 77.4 (64.5–86.6) | 80.9 (67.5–89.6) | 79.0 | 82.0 (71.3–89.3) | 76.0 (65.4–84.2) | 4.0 (2.2–7.4) | 0.28 (0.17–0.47) | 78 |
| 3%ODI ≥13 | 83.0 (70.8–90.8) | 70.2 (56.0–81.4) | 77.0 | 75.9 (66.6–83.2) | 78.6 (66.3–87.3) | 2.8 (1.8–4.4) | 0.24 (0.13–0.45) | 100 |

ODI, oxygen desaturation index; OSA, obstructive sleep apnoea; SOSAT, Screening for OSA in Tetraplegia.

**Table 3** Multivariable logistic regression analysis: associations between significant baseline variables and MS-OSA

| Variable | Beta coefficient | OR | P values | 95% CI |
|---|---|---|---|---|
| AIS A, B or C | 2.88 | 17.81 | <0.01 | 1.25 to 4.50 |
| Self-reported snoring | 2.42 | 11.25 | 0.01 | 0.74 to 4.09 |
| Self-reported apnoeas | 1.71 | 5.53 | 0.01 | 0.38 to 3.04 |
| How sleepy did you feel at midday today? (KSS≥3/9) | 1.82 | 6.17 | 0.02 | 0.32 to 3.33 |

AIS, ASIA Impairment Scale; KSS, Karolinska Sleepiness Scale; MS-OSA, moderate to severe OSA.

21.5–37.9). In six of these cases the SOSAT questionnaire failed to identify individuals at risk, and in nine the ODI was too low. In settings where PSG is readily available, clinicians could order full PSG for patients whose unexplained symptoms persist, despite the negative result in this model.

Despite sensitivity and specificity results that were comparable to the original Chai-Coetzer *et al*'s validation study,[15] the negative predictive value (76%) is low in our sample, indicating a 24% chance of a false-negative result. The high prevalence of MS-OSA in this population poses challenges for any diagnostic model to modify post-test probability. The use of CIs partially addresses this issue. A bootstrapping technique determined the optimal threshold for the 3%ODI was ≥13 with a 95% CI of 9.5 to 22.2. Application of the CI could reduce the risk of misclassification. We suggest that clinicians use the 95% CI for the 3%ODI as an 'uncertain' category where, with clinical judgement, they could further investigate OSA and/or proceed to treatment, based on the symptoms and desires of the individual patient. In our study, removing the incorrectly classified participants with 3%ODIs within the CI would have improved the sensitivity and specificity of the two-stage model with SOSAT to 80% and 93%, with an overall accuracy of 86% (n=92).

When OSA is defined as AHI≥5, the prevalence in our validation sample was found to be 97%. This is substantially higher than in the retrospective sample used to develop the model (73%), yet similar to that recently reported in a prevalence study using comparable methods (93%).[4] Unfortunately, methodologies vary substantially among prior prevalence studies and as such, there are no meta-analyses that estimate the population prevalence of OSA in SCI.[1] Undertaking screening tests for a highly prevalent disease could be considered redundant. However, funding for treatment is usually dependent on a clinician's diagnosis of OSA, and few clinicians and patients would prescribe and accept treatment without solid evidence of disease. We have focused on detecting MS-OSA, for which the prevalence was 38% and 53% in our two samples. In people without disability, all-cause mortality, stroke and cardiovascular disease are strongly associated with more severe OSA.[27–30] In people with acute and chronic tetraplegia, more severe OSA has been associated with worse neuropsychological function.[6 7] Further, those with more severe disease and more daytime sleepiness are more likely to adhere to CPAP treatment, the first-line therapy for OSA.[31]

There is currently no agreed threshold for the diagnosis of OSA or its severity[9] and furthermore, the AHI is poorly correlated with symptoms.[32] There are also significant problems with intra-rater and inter-rater reliability of AHI scoring and different laboratories use different scoring rules for hypopnoeas which substantially impact the AHI.[9] Reliability studies have demonstrated high night-to-night variability in the AHI, affecting OSA diagnosis at various thresholds.[33 34] Other

| | If YES, score: |
|---|---|
| Is your spinal cord injury classified as an ASIA impairment scale A, B or C? | 3 |
| Do you snore? | 3 |
| Has anyone noticed that you stop breathing during your sleep? | 2 |
| How sleepy did you feel at midday today? (Karolinska Sleepiness Scale≥3/9) | 2 |
| **Total** | **10** |

**Figure 2** Screening for OSA in Tetraplegia (SOSAT) questionnaire. ASIA, American Spinal Injury Association.

research suggests the ODI has relatively low variability[35] and a comparison of the night-to-night variability of respiratory sleep indices found that the ODI was substantially more reliable than the AHI.[36] Additionally, the ODI, and not the AHI, has been significantly associated with cardiovascular disease in a large non-disabled population with suspected OSA.[37] This evidence suggests that ODI is a more reliable and, potentially, a better marker of cardiovascular risk than the 'gold-standard' AHI. Researchers and clinicians must be mindful of the limitations of the AHI for diagnosing OSA, and the implications for diagnostic accuracy studies investigating alternative models. Evaluating the effectiveness of alternative tests on patient outcomes rather than traditional diagnostic accuracy methods has been suggested to address this issue.[9]

While central sleep apnoea has previously been identified in tetraplegia,[38] our data suggest that it is not the predominant characteristic of sleep disordered breathing, accounting for just 4% of the classified events on average. Only 2% of our combined sample (3/178) had predominant central sleep apnoea. Hypoventilation is a risk in patients with neuromuscular weakness, however its frequency and severity in tetraplegia is yet to be established. Assessment for hypoventilation

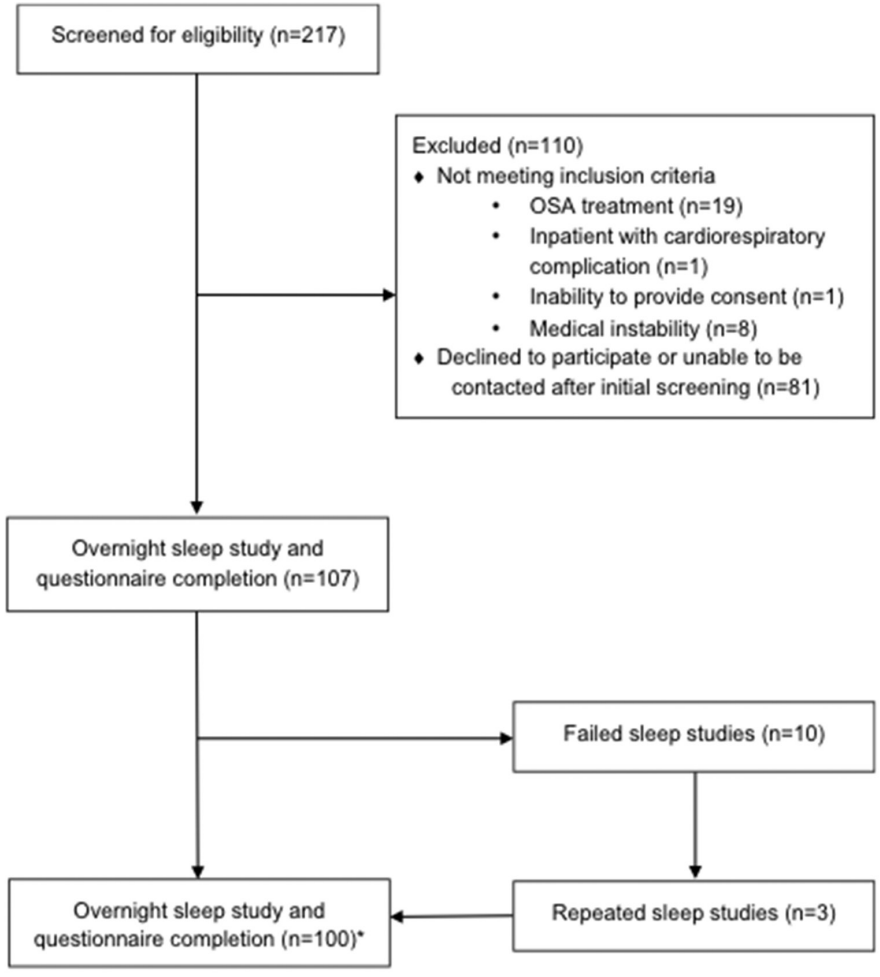


**Figure 3** Participant recruitment pathway (validation group). OSA, obstructive sleep apnoea.

**Table 4A** Contingency table for two-stage model with OSA50 questionnaire (optimised thresholds)

| | | MS-OSA (AHI≥21/hour) | | |
|---|---|---|---|---|
| | | Positive | Negative | |
| OSA50 ≥3/10 and 3%ODI ≥13/hour | Positive | 42 | 9 | 51 (51%) |
| | Negative | 11 | 38 | 49 (51%) |
| | | 53 (53%) | 47 (47%) | 100 (100%) |

AHI, Apnea Hypopnea Index; MS-OSA, moderate to severe OSA; ODI, oxygen desaturation index; OSA, obstructive sleep apnoea.

**Table 4B** Contingency table for two-stage model with SOSAT questionnaire

| | | MS-OSA (AHI≥21/hour) | | |
|---|---|---|---|---|
| | | Positive | Negative | |
| SOSAT ≥5/10 and 3%ODI ≥13/hour | Positive | 41 | 9 | 50 (50%) |
| | Negative | 12 | 38 | 50 (50%) |
| | | 53 (53%) | 47 (47%) | 100 (100%) |

AHI, Apnea Hypopnea Index; MS-OSA, moderate to severe OSA; ODI, oxygen desaturation index; SOSAT, Screening for OSA in Tetraplegia.

**Table 4C** Contingency table for 3%ODI alone

| | | MS-OSA (AHI≥21/hour) | | |
|---|---|---|---|---|
| | | Positive | Negative | |
| 3%ODI ≥13/hour | Positive | 44 | 14 | 58 (58%) |
| | Negative | 9 | 33 | 42 (42%) |
| | | 53 (53%) | 47 (47%) | 100 (100%) |

AHI, Apnea Hypopnea Index; MS-OSA, moderate to severe OSA; ODI, oxygen desaturation index.

would be an important component of any OSA management pathway using our two-stage model. Further research is required to assess the safety and feasibility of using this model in an OSA management pathway. Consideration of symptoms, individual patient comorbidities, assessment for hypoventilation and the availability of full PSG for ambiguous or complicated cases would also be important components of this pathway.

The scope of our study was limited to testing the accuracy of a two-stage model of questionnaire followed by overnight oximetry (a level IV portable device). As yet, the accuracy of level III portable monitors, including airflow, respiratory effort and oximetry recordings, has not been tested in people with tetraplegia, although they have been assessed as feasible in this population.[39] Level III monitors are an accepted alternative for OSA diagnosis in non-disabled populations.[40] Based on research showing similar effectiveness of level III devices to PSG and substantially lower costs, others have suggested that PSG is no longer necessary for most patients with clinical suspicion of OSA.[41] Further research into the accuracy of level III devices and their safety and acceptability in tetraplegia is warranted.

### Limitations

The ODIs were obtained from the PSG oximeter and the Compumedics software. A recent study comparing the ODIs generated by a ResMed system with those from a Compumedics system found the ResMed system generated higher values. The source of the difference was in the data collection processes rather than the algorithms built into the software.[42] This finding has major implications for the use of ODIs to diagnose OSA and may limit translation of models using oximetry into clinical practice. It highlights a sleep industry-wide failure to develop reference criteria for oximeters, analysis software and algorithms. Our addition of the ODI CI to the two-stage model partially addresses this issue. In our substudy there were two participants with conflicting OSA classifications from the ApneaLink and Compumedics systems. In both cases, the wrongly classified ODI was within the CI.

The development and validation samples in this study were recruited with different methods and approximately 10 years apart. The validation group were older, longer postinjury and had more severe OSA, which may reflect a selection bias and have affected the performance of the model.

## CONCLUSION

The two-stage model of SOSAT questionnaire followed by overnight oximetry provides a potential alternative to full PSG for identifying MS-OSA in people with chronic tetraplegia. This model could be considered in settings where PSG is inaccessible or when patients are unable or unwilling to attend an overnight sleep study, in conjunction with comprehensive assessment of symptoms, comorbidities and hypoventilation. Some patients with MS-OSA may be missed; however, the addition of CIs to the 3%ODI may reduce this risk. Despite the limitations, this translatable model has the potential to substantially increase the detection of OSA in people with tetraplegia and subsequently improve access to treatment.

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**Patient consent** Obtained

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## REFERENCES

1 Giannoccaro MP, Moghadam KK, Pizza F, *et al*. Sleep disorders in patients with spinal cord injury. *Sleep Med Rev* 2013;17:399–409.
2 Berlowitz DJ, Spong J, Gordon I, *et al*. Relationships between objective sleep indices and symptoms in a community sample of people with tetraplegia. *Arch Phys Med Rehabil* 2012;93:1246–52.
3 Leduc BE, Dagher JH, Mayer P, *et al*. Estimated prevalence of obstructive sleep apnea-hypopnea syndrome after cervical cord injury. *Arch Phys Med Rehabil* 2007;88:333–7.
4 Sankari A, Bascom A, Oomman S, *et al*. Sleep disordered breathing in chronic spinal cord injury. *JCSM* 2013;10:65–72.
5 Heinzer R, Vat S, Marques-Vidal P, *et al*. Prevalence of sleep-disordered breathing in the general population: the HypnoLaus study. *Lancet Respir Med* 2015;3:310–8.
6 Sajkov D, Marshall R, Walker P, *et al*. Sleep apnoea related hypoxia is associated with cognitive disturbances in patients with tetraplegia. *Spinal Cord* 1998;36:231–9.
7 Schembri R, Spong J, Graco M, *et al*. Neuropsychological function in patients with acute tetraplegia and sleep disordered breathing. *Sleep* 2017;40.
8 Spinal Cord Medicine. *Respiratory management following spinal cord injury: a clinical practice guideline for health-care professionals: consortium for spinal cord medicine*. Washington, DC: Paralyzed Veterans of America, 2005.
9 Chai-Coetzer CL, Antic NA, McEvoy RD. Ambulatory models of care for obstructive sleep apnoea: Diagnosis and management. *Respirology* 2013;18:605–15.
10 Mansfield DR, Antic NA, McEvoy RD. How to assess, diagnose, refer and treat adult obstructive sleep apnoea: a commentary on the choices. *Med J Aust* 2013;199:21–6.
11 Suárez M, Osorio J, Torres M, *et al*. Should the diagnosis and management of OSA move into general practice? *Breathe* 2016;12:243–7.
12 Abrishami A, Khajehdehi A, Chung F. A systematic review of screening questionnaires for obstructive sleep apnea. *Can J Anaesth* 2010;57:423–38.
13 Ramachandran SK, Josephs LA. A meta-analysis of clinical screening tests for obstructive sleep apnea. *Anesthesiology* 2009;110:928–39.
14 Ross SD, Sheinhait IA, Harrison KJ, *et al*. Systematic review and meta-analysis of the literature regarding the diagnosis of sleep apnea. *Sleep* 2000;23:1–14.
15 Chai-Coetzer CL, Antic NA, Rowland LS, *et al*. A simplified model of screening questionnaire and home monitoring for obstructive sleep apnoea in primary care. *Thorax* 2011;66:213–9.
16 Sankari A, Martin JL, Bascom AT, *et al*. Identification and treatment of sleep-disordered breathing in chronic spinal cord injury. *Spinal Cord* 2015;53:145–9.
17 Berlowitz DJ, Brown DJ, Campbell DA, *et al*. A longitudinal evaluation of sleep and breathing in the first year after cervical spinal cord injury. *Arch Phys Med Rehabil* 2005;86:1193–9.
18 Berry RB, Budhiraja R, Gottlieb DJ, *et al*. Rules for scoring respiratory events in sleep: update of the 2007 AASM manual for the scoring of sleep and associated events. Deliberations of the sleep apnea definitions task force of the American Academy of Sleep Medicine. *J Clin Sleep Med* 2012;8:597.
19 Flemons W, Buysse D, Redline S, *et al*. Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research. *Sleep* 1999;22:667–89.
20 Spong J, Graco M, Brown DJ, *et al*. Subjective sleep disturbances and quality of life in chronic tetraplegia. *Spinal Cord* 2015;53:636–40.
21 Partinen M, Gislason T. Basic Nordic Sleep Questionnaire (BNSQ): a quantitated measure of subjective sleep complaints. *J Sleep Res* 1995;4(S1):150–5.
22 Efron B, Tibshirani RJ. *An Introduction to the Bootstrap: Monographs on Statistics and Applied Probability*. 57. New York and London: Chapman and Hall/CRC, 1993.
23 Mehta HB, Mehta V, Girman CJ, *et al*. Regression coefficient-based scoring system should be used to assign weights to the risk index. *J Clin Epidemiol* 2016;79:22–8.
24 Bossuyt PM, Reitsma JB, Bruns DE, *et al*. The STARD statement for reporting studies of diagnostic accuracy: explanation and elaboration. *Ann Intern Med* 2003;138:W1–12.
25 Netzer NC, Stoohs RA, Netzer CM, *et al*. Using the Berlin Questionnaire to identify patients at risk for the sleep apnea syndrome. *Ann Intern Med* 1999;131:485–91.
26 Gillberg M, Kecklund G, Akerstedt T. Relations between performance and subjective ratings of sleepiness during a night awake. *Sleep* 1994;17:236–41.
27 Arzt M, Young T, Finn L, *et al*. Association of sleep-disordered breathing and the occurrence of stroke. *Am J Respir Crit Care Med* 2005;172:1447–51.
28 MARIN J, CARRIZO S, Vicente E, *et al*. Long-term cardiovascular outcomes in men with obstructive sleep apnoea-hypopnoea with or without treatment with continuous positive airway pressure: an observational study. *The Lancet* 2005;365:1046–53.
29 Marshall NS, Wong KK, Liu PY, *et al*. Sleep apnea as an independent risk factor for all-cause mortality: the Busselton Health Study. *Sleep* 2008;31:1079.
30 Punjabi NM, Caffo BS, Goodwin JL, *et al*. Sleep-disordered breathing and mortality: a prospective cohort study. *PLoS Med* 2009;6:e1000132.
31 Qaseem A, Holty JE, Owens DK, *et al*. Management of obstructive sleep apnea in adults: a clinical practice guideline from the American College of Physicians. *Ann Intern Med* 2013;159:471–83.
32 Weaver EM, Kapur V, Yueh B. Polysomnography vs self-reported measures in patients with sleep apnea. *Arch Otolaryngol Head Neck Surg* 2004;130:453–8.
33 Ahmadi N, Shapiro GK, Chung SA, *et al*. Clinical diagnosis of sleep apnea based on single night of polysomnography vs. two nights of polysomnography. *Sleep Breath* 2009;13:221–6.
34 Levendowski DJ, Zack N, Rao S, *et al*. Assessment of the test-retest reliability of laboratory polysomnography. *Sleep Breath* 2009;13:163–7.
35 Fietze I, Dingli K, Diefenbach K, *et al*. Night-to-night variation of the oxygen desaturation index in sleep apnoea syndrome. *Eur Respir J* 2004;24:987–93.
36 Aber WR, Block AJ, Hellard DW, *et al*. Consistency of respiratory measurements from night to night during the sleep of elderly men. *Chest* 1989;96:747–51.
37 Tkacova R, McNicholas WT, Javorsky M, *et al*. Nocturnal intermittent hypoxia predicts prevalent hypertension in the European Sleep Apnoea Database cohort study. *Eur Respir J* 2014;44:931–41.
38 Sankari A, Bascom AT, Chowdhuri S, *et al*. Tetraplegia is a risk factor for central sleep apnea. *J Appl Physiol* 2014;116:345–53.
39 Bauman KA, Kurili A, Schotland HM, *et al*. Simplified approach to diagnosing sleep-disordered breathing and nocturnal hypercapnia in individuals with spinal cord injury. *Arch Phys Med Rehabil* 2016;97.
40 Collop NA, Anderson WM, Boehlecke B, *et al*. Clinical guidelines for the use of unattended portable monitors in the diagnosis of obstructive sleep apnea in adult patients. *J Clin Sleep Med* 2007;3:737–47.
41 Corral J, Sánchez-Quiroga MÁ, Carmona-Bernal C, *et al*. Conventional polysomnography is not necessary for the management of most patients with suspected obstructive sleep apnea. noninferiority, randomized controlled trial. *Am J Respir Crit Care Med* 2017;196:1181–90.
42 Ng Y, Joosten SA, Edwards BA, *et al*. Oxygen desaturation index differs significantly between types of sleep software. *J Clin Sleep Med* 2017;13:599–605.

## 2.4 Online supplement

Section 2.4 was published online with the *Thorax* manuscript. It has been reformatted for this thesis but the wording, tables and figures are unchanged. The table and figure numbering system is also unchanged from the online publication because the original numbers have been cross-referenced in the *Thorax* manuscript.

### 2.4.1 Additional methods

#### *2.4.1.1 Stage One: Initial validation and modification of two stage model with OSA50 questionnaire*

Establishing the definition of moderate to severe OSA with new respiratory scoring rules.

Moderate to severe obstructive sleep apnoea (MS-OSA) was originally defined by Chai-Coetzer et al as an apnoea-hypopnoea index (AHI) ≥30 scored according to the 1999 American Academy of Sleep Medicine (AASM) "Chicago" criteria.[82] When the "Chicago" criteria were formulated, the AASM defined an AHI threshold of ≥30 as "severe OSA", with 5 to 15 indicating mild disease, and 15 to 30 indicating moderate disease.[29] However the rules for scoring of respiratory events have undergone two further iterations since the 1999 "Chicago" criteria.[27, 30] The 2007 AASM rules result in markedly lower AHI scores, and Ruehland et al showed that an AHI of ≥30 scored according to "Chicago" criteria is equivalent to an AHI of approximately 10.8 when scored according to the 2007 criteria.[42] Based on this information, Chai-Coetzer et al chose to define moderate to severe OSA as an AHI of ≥30 using the "Chicago" criteria.[82] We have chosen to replicate this definition in our study but with use of the current 2012 AASM scoring criteria. It was therefore necessary to establish the $AHI_{2012}$ equivalent of an $AHI_{Chicago} \geq 30$.

An existing dataset of 78 sleep studies in people with chronic tetraplegia was used for this purpose. These sleep studies were conducted for a different research project aiming to examine the relationships between demographics, symptoms and objectively measured sleep in people with chronic tetraplegia.[1, 2] Full PSG was performed in the participants' homes with the Compumedics SomtePSG (Version 1) portable devices (Compumedics™, Abbottsford, Australia) collecting EEG, EOG, EMG (mentalis and

diaphragm), electrocardiograph, respiratory motion, nasal pressure, arterial oxygen saturation, snoring and body position. An experienced sleep scientist originally analysed the PSG data using AASM "Chicago" rules.[1]

The AASM 2012 rules are less inclusive of respiratory events, and as such, existing respiratory events were reviewed for compliance with AASM 2012, and removed if they no longer met criteria.[42] The re-scoring enabled Receiver Operating Characteristic (ROC) curves and sensitivity and specificity tables to be calculated in order to estimate an equivalent threshold for MS-OSA as per the original two-stage model validation.[82] The equivalent $AHI_{2012}$ threshold for MS-OSA was subsequently used as the reference standard for Stages One, Two and Three of this study. Results are provided below.

Derivation of the OSA50 questionnaire

The OSA50 questionnaire contains four questions detailed in eFigure 1.[82] Each question was derived from the retrospective dataset of 78 people with chronic tetraplegia (described above) to enable calculation of the questionnaire. Waist circumference and age were available in the retrospective dataset, allowing simple calculation of these scores. However the Berlin questionnaire,[95] which was originally used by Chai-Coetzer to derive the self-reported snoring and apnoea questions, was not available. Similar questions regarding self-reported snoring and apnoeas are contained within the Basic Nordic Sleep Questionnaire (BNSQ, eTable 1).[163] BNSQ Question 16 asks "Do you snore whilst sleeping?", and BNSQ Question 18 asks "Have you had breathing pauses (sleep apnoea) during sleep? Have other people noticed that you have pauses in respiration when you sleep?" Responses for BNSQ questions 16 and 18 are on a 5-item Likert scale (Never or less than once a month; less than once per week; on 1-2 days per week; on 3-5 days per week; daily or almost daily). Both variables were dichotomized as "never or less than once per month" versus all other responses because this was thought to best reflect the "all or nothing" nature of the OSA50 responses. eTable 1 details the OSA50 questions and the corresponding data from the retrospective dataset.

| | If YES, score: |
|---|---|
| Obesity: Waist circumference (Males>102cm or Females>88cm) | 3 |
| Snoring: Has your snoring ever bothered people? | 3 |
| Apnoeas: Has anyone noticed that you stop breathing during your sleep? | 2 |
| 50: Are you aged 50 years or over? | 2 |
| Total | 10 |

**eFigure 1: OSA50 questionnaire**

**eTable 1: Derivation of the OSA50 questionnaire**

| OSA50 questionnaire | Corresponding variable in retrospective dataset |
|---|---|
| Obesity: Waist circumference (Males>102cm or Females>88cm) | Waist circumference (cm; at time of sleep study) |
| Snoring: Has your snoring ever bothered people? (Berlin questionnaire, Question 4) | BNSQ question 16: Do you snore whilst sleeping (ask other people)? |
| Apnoeas: Has anyone noticed that you stop breathing during your sleep? (Berlin questionnaire, Question 5) | BNSQ question 18: Have you had breathing pauses (sleep apnoea) during sleep (have other people noticed that you have pauses in respiration when you sleep? |
| 50: Are you aged 50 years or over? | Age (at time of sleep study) |

*2.4.1.2 Stage Two: Development of the tetraplegia-specific questionnaire.*

Dichotomising non-binary variables

Potential risk factors and their associations with MS-OSA were investigated for inclusion in the new questionnaire. The following risk factors were available for investigation in the retrospective dataset of 78 people with chronic tetraplegia: age, gender, American Spinal Injury Association Impairment Scale (AIS), lesion level, neck circumference, waist circumference, Body Mass Index (BMI), time since injury, daytime sleepiness, self-reported snoring, and self-reported apnoeas. Daytime sleepiness was assessed with the Karolinska Sleepiness Scale (KSS), an assessment of state sleepiness. The KSS asks participants to rate their level sleepiness at midday of the day the questionnaire is completed on a scale from 1 (very alert) to 9 (extremely sleepy; fighting sleep).[164] Self-reported snoring and self-reported apnoeas were assessed with questions 16 and 18 of the BNSQ, as described previously.

The tetraplegia specific questionnaire was developed for use in busy outpatient and primary care locations. As such it was important to dichotomize the non-binary outcomes to facilitate simple scale development. To determine the optimal point for dichotomising variables, ROC curves were calculated for all continuous variables and categorical variables with more than two categories. Only variables where the 95%CI for ROC area under curve (AUC) did not cross 0.5 were dichotomised and progressed to univariate analysis. The ROC curves for these variables were examined and dichotomised at the point that maximized sensitivity and specificity. Univariate and multivariable regressions of the binary risk factors were then performed as outlined in the methods of the main paper.

*2.4.1.3 Stage Three: Validation of two-stage models*

Home sleep studies

Full PSG was conducted on all participants, using Type II ambulatory devices. Sleep studies from all sites except the University of Miami were conducted with SomtePSG (Compumedics™, Abbottsford, Australia) units, measuring EEG, EOG, EMG (mentalis and diaphragm), ECG, respiratory motion, nasal flow estimated from nasal pressure cannula, oronasal thermistor, arterial oxygen saturation, snoring and body position. Sleep studies from the University of Miami were conducted with Embla®

Embletta®x100 (Natus Medical Inc.®, Pleasanton, USA) portable units. These units recorded EEG, EOG, EMG, nasal flow, respiratory motion and arterial oxygen saturation. Oronasal thermistor and ECG were not recorded in the 10 studies from the University of Miami.

Attended, in-laboratory PSG is considered to be the "gold standard" test for the diagnosis of OSA. However the unattended, portable SomtePSG unit has been validated against the "gold-standard" with the manually scored AHIs from the two systems showing good agreement.[165] Similarly, the Emblettax100 unit has been validated against a standard in laboratory attended PSG with good performance characteristics and accuracy in detecting OSA.[166]

The raw PSG data from the University of Miami were de-identified and electronically sent to the Austin Health site for central independent analysis. These studies were exported to European Data Format and imported into Profusion software (Compumedics™) for manual scoring by the same experienced sleep scientist. The sleep scientist was blinded to the questionnaire data and the automatically generated 3%ODI data. Sleep, arousals and respiratory events were scored according to the most recent AASM standard criteria. Apnoeas were defined as ≥90% reduction in airflow. Hypopnoeas were defined as a ≥30% reduction in airflow with a ≥3% desaturation or arousal.[27]

Oximeters

The Resmed ApnoeaLink oximetry system uses a Nonin pulse oximetry sensor (Nonin Medical, Minnesota, USA), and the Compumedics SomtePSG (Version 1) uses a Compumedics oximeter. The Compumedics oximeter samples oxygen saturation ($SpO_2$) every heartbeat and uses the seven most recent measures to calculate $SpO_2$. The largest and smallest values are removed from the analysis, and the remaining five are averaged to give the $SpO_2$ result. The ApnoeaLink oximeter samples data at 1Hz and averages the signal every three seconds to generate the $SpO_2$ value.[167] How each system automatically calculates the ODI from the $SpO_2$ data is unknown and at the discretion of the companies who do not publish their algorithms. The researcher performing the 3%ODI analysis was blinded to the full PSG data, including the AHI.

### 2.4.2 Additional results

#### *2.4.2.1 Stage One: Initial validation and modification of two stage model with OSA50 questionnaire*

Establishing the definition of MS-OSA with new respiratory scoring rules.

The AHIs scored using the AASM 2012 criteria ($AHI_{2012}$) were significantly lower than those scored with AASM "Chicago" ($AHI_{Chicago}$) rules. Mean (median) AHIs were 22.4 (13.3) and 26.9 (18.9), respectively. The equivalent threshold for $AHI \geq 30_{Chicago}$ was $AHI \geq 21_{2012}$, which had sensitivity and specificity of 100%. eTable 2 shows the sensitivity and specificity of the various thresholds.

**eTable 2. Sensitivity and specificity of $AHI_{2012}$ in classifying MS-OSA ($AHI \geq 30_{Chicago}$)**

| Cutpoint | Sensitivity | Specificity | Correctly Classified |
|---|---|---|---|
| ( >= .9 ) | 100.00% | 0.00% | 38.46% |
| ( >= 1 ) | 100.00% | 0.00% | 38.46% |
| ( >= 1.1 ) | 100.00% | 4.17% | 41.03% |
| ( >= 1.5 ) | 100.00% | 6.25% | 42.31% |
| ( >= 2 ) | 100.00% | 8.33% | 43.59% |
| ( >= 2.4 ) | 100.00% | 10.42% | 44.87% |
| ( >= 2.5 ) | 100.00% | 16.67% | 48.72% |
| ( >= 2.7 ) | 100.00% | 18.75% | 50.00% |
| ( >= 3 ) | 100.00% | 20.83% | 51.28% |
| ( >= 3.1 ) | 100.00% | 22.92% | 52.56% |
| ( >= 3.2 ) | 100.00% | 25.00% | 53.85% |
| ( >= 3.6 ) | 100.00% | 29.17% | 56.41% |
| ( >= 3.7 ) | 100.00% | 31.25% | 57.69% |
| ( >= 3.8 ) | 100.00% | 33.33% | 58.97% |
| ( >= 4.1 ) | 100.00% | 35.42% | 60.26% |
| ( >= 4.9 ) | 100.00% | 39.58% | 62.82% |
| ( >= 5.3 ) | 100.00% | 41.67% | 64.10% |
| ( >= 6.1 ) | 100.00% | 43.75% | 65.38% |
| ( >= 6.7 ) | 100.00% | 45.83% | 66.67% |
| ( >= 7 ) | 100.00% | 47.92% | 67.95% |
| ( >= 7.1 ) | 100.00% | 50.00% | 69.23% |
| ( >= 7.8 ) | 100.00% | 52.08% | 70.51% |
| ( >= 8.2 ) | 100.00% | 54.17% | 71.79% |
| ( >= 9 ) | 100.00% | 58.33% | 74.36% |
| ( >= 9.1 ) | 100.00% | 60.42% | 75.64% |
| ( >= 9.9 ) | 100.00% | 62.50% | 76.92% |
| ( >= 10 ) | 100.00% | 64.58% | 78.21% |
| ( >= 10.2 ) | 100.00% | 66.67% | 79.49% |
| ( >= 10.4 ) | 100.00% | 68.75% | 80.77% |

| | | | |
|---|---|---|---|
| ( >= 12 ) | 100.00% | 77.08% | 85.90% |
| ( >= 12.1 ) | 100.00% | 79.17% | 87.18% |
| ( >= 14.4 ) | 100.00% | 81.25% | 88.46% |
| ( >= 15.2 ) | 100.00% | 83.33% | 89.74% |
| ( >= 15.3 ) | 100.00% | 85.42% | 91.03% |
| ( >= 15.5 ) | 100.00% | 87.50% | 92.31% |
| ( >= 16.7 ) | 100.00% | 89.58% | 93.59% |
| ( >= 19 ) | 100.00% | 91.67% | 94.87% |
| ( >= 19.2 ) | 100.00% | 93.75% | 96.15% |
| ( >= 19.7 ) | 100.00% | 97.92% | 98.72% |
| **( >= 21.2 )** | **100.00%** | **100.00%** | **100.00%** |
| ( >= 21.7 ) | 96.67% | 100.00% | 98.72% |
| ( >= 24.4 ) | 90.00% | 100.00% | 96.15% |
| ( >= 27.9 ) | 86.67% | 100.00% | 94.87% |
| ( >= 28.1 ) | 83.33% | 100.00% | 93.59% |
| ( >= 29.1 ) | 80.00% | 100.00% | 92.31% |
| ( >= 30.1 ) | 76.67% | 100.00% | 91.03% |
| ( >= 30.2 ) | 66.67% | 100.00% | 87.18% |
| ( >= 31.2 ) | 63.33% | 100.00% | 85.90% |
| ( >= 32.3 ) | 60.00% | 100.00% | 84.62% |
| ( >= 34.3 ) | 56.67% | 100.00% | 83.33% |
| ( >= 35.8 ) | 53.33% | 100.00% | 82.05% |
| ( >= 36.6 ) | 46.67% | 100.00% | 79.49% |
| ( >= 41 ) | 43.33% | 100.00% | 78.21% |
| ( >= 41.4 ) | 40.00% | 100.00% | 76.92% |
| ( >= 44.8 ) | 36.67% | 100.00% | 75.64% |
| ( >= 46.9 ) | 33.33% | 100.00% | 74.36% |
| ( >= 48.4 ) | 23.33% | 100.00% | 70.51% |
| ( >= 51.5 ) | 20.00% | 100.00% | 69.23% |
| ( >= 53 ) | 16.67% | 100.00% | 67.95% |
| ( >= 57.5 ) | 13.33% | 100.00% | 66.67% |
| ( >= 59.3 ) | 10.00% | 100.00% | 65.38% |
| ( >= 62.1 ) | 6.67% | 100.00% | 64.10% |
| ( >= 63.3 ) | 0.00% | 100.00% | 61.54% |

Contingency tables for two-stage models in development group

Contingency tables showing accuracy of the two-stage model with OSA50 questionnaire (using original and optimized thresholds) and the 3%ODI alone in the development group can be found in Tables 3A-C.

**eTable 3A: Contingency table for two-stage model with OSA50 (using original thresholds).**

| | | Moderate to severe OSA (AHI≥21/hour) +ve | -ve | |
|---|---|---|---|---|
| OSA50≥5/10& 3%ODI≥16/hour | +ve | 21 | 4 | 25 (32%) |
| | -ve | 9 | 44 | 53 (68%) |
| | | 30 (38%) | 48 (62%) | 78 (100%) |

**eTable 3B: Contingency table for two-stage model with OSA50 (using optimised thresholds) in development dataset**

| | | Moderate to severe OSA (AHI≥21/hour) +ve | -ve | |
|---|---|---|---|---|
| OSA50≥3/10& 3%ODI≥13/hour | +ve | 25 | 7 | 32 (41%) |
| | -ve | 5 | 41 | 46 (59%) |
| | | 30 (38%) | 48 (62%) | 78 (100%) |

**eTable 3C: Contingency table for validation of 3% ODI alone in development dataset**

| | | Moderate to severe OSA (AHI≥21/hour) +ve | -ve | |
|---|---|---|---|---|
| 3%ODI≥13/hour | +ve | 25 | 8 | 33 (42%) |
| | -ve | 5 | 40 | 45 (58%) |
| | | 30 (38%) | 48 (62%) | 78 (100%) |

*2.4.2.2 Stage Two: Development of the tetraplegia-specific questionnaire.*

SOSAT questionnaire development

ROC curve analyses were performed for 10 non-binary potential risk factors against AHI≥21 (eTable4). The ROC AUC with confidence intervals for each variable can be found in eTable4. Reasoning that anthropometry measures differed substantially

between men and woman, neck and waist circumference were split in to male and female subgroups. Seven of the potential risk factors were significantly predictive of MS-OSA. The thresholds that optimized sensitivity and specificity, the corresponding sensitivity and specificity, and the percentage of participants who were excluded at this threshold are detailed for each variable in eTable 4.

**eTable4: ROC-AUC for "non-binary" variables, threshold selected, and sensitivity, specificity and % excluded for given threshold.**

| Variable | ROC AUC | Optimal threshold | Sensitivity | Specificity | % excluded |
|---|---|---|---|---|---|
| AIS | 0.70 (0.59-0.81) | ABC vs DE | 90.0% | 45.8% | 32% |
| Lesion level | 0.49 (0.36-0.62) | NA | NA | NA | NA |
| Neck circumference ALL | 0.71(0.59-0.83) | ≥41cm | 80.0 | 47.9 | 37% |
| Neck circumference MALES | 0.71(0.57-0.83) | ≥42cm | 80.0 | 50.0 | 28% (37% males) |
| Neck circumference FEMALES | 0.80 (0.59-1.0) | ≥35cm | 100.0 | 50.0 | 9% (35% females) |
| BMI | 0.61(0.49-0.78) | NA | NA | NA | NA |
| Waist circumference ALL | 0.75 (0.63-0.86) | ≥103 | 80.0 | 66.7 | 49% |
| Waist circumference MALES | 0.74 (0.61-0.87) | ≥103 | 84.0 | 64.7 | 33% (43% males) |
| Waist circumference FEMALES | 0.70 (0.35-1.0) | ≥99 | 80.0 | 64.3 | 13%(50% females) |
| Age | 0.65 (0.53-0.77) | ≥40 | 73.3 | 56.3 | 45% |
| Time since injury | 0.52(0.38-0.66) | NA | NA | NA | NA |
| KSS | 0.63 (0.50-0.75) | ≥3 | 86.9 | 31.3 | 24% |
| Snoring BNSQ16 | 0.70 (0.58-0.82) | Not never (>1) | 90.0 | 36.4 | 26% |
| Apnoeas BNSQ18 | 0.68 (0.57-0.79) | Not never (>1) | 56.7 | 78.3 | 65% |

The seven significant ($p<0.05$) variables on ROC AUC analysis were then dichotomized at the selected thresholds and, along with gender, underwent univariate logistic regression analysis to determine association with MS-OSA (AHI≥21). The regression co-efficients and p-values for these variables can be found in eTable5. All except gender were significantly associated with MS-OSA ($p<0.1$) and were therefore candidates for multivariable regression. However given that waist and neck circumference are both measures of adiposity and likely to be collinear, only neck circumference was selected for multivariable analysis. Waist circumference was not chosen because of the difficulty in obtaining this measurement in people with tetraplegia in the outpatient setting. Six variables were therefore entered into the multivariable model and the results are detailed in the main paper.

**eTable5: Univariate logistic regression analysis: associations between binary variables and MS-OSA**

| Variable | Co-efficient | P value |
|---|---|---|
| AIS (ABC)** | 2.03 | <0.01* |
| Neck circumference (Males≥42cm, Females≥35cm)** | 1.61 | 0.01* |
| Waist circumference (Males≥103cm, Females≥99cm) | 2.21 | <0.01* |
| Age (≥40)** | 1.26 | 0.01* |
| Daytime sleepiness (≥3KSS)** | 1.08 | 0.08* |
| Snoring (BNSQ16>1; not never)** | 1.86 | 0.01* |
| Apnoeas (BNSQ18>1; not never)** | 1.60 | <0.01* |
| Gender (male) | 1.08 | 0.22* |

*p<0.1; **entered into multivariable model

Contingency table for two-stage model in development group

The contingency table showing accuracy of the two-stage model with SOSAT questionnaire in the development group can be found in eTable6.

**eTable6: Contingency table for two-stage model with SOSAT in development dataset**

| | | Moderate to severe OSA (AHI≥21/hour) +ve | -ve | |
|---|---|---|---|---|
| SOSAT ≥5/10 & 3%ODI≥13/hour | +ve | 25 | 6 | 31 (40%) |
| | -ve | 5 | 42 | 47 (60%) |
| | | 30 (38%) | 48 (62%) | 78 (100%) |

*2.4.2.3 Stage Three: Validation of two-stage models*

The characteristics of the 21 incorrectly classified participants in the two-stage model with SOSAT questionnaire in the validation group are shown in eTable7.

**eTable7: Characteristics of incorrectly classified participants**

| Gender | Age | AIS | Level | KSS | Snore | Apnoea | Waist | SOSAT | OSA50 | ODI | AHI |
|---|---|---|---|---|---|---|---|---|---|---|---|
| *Incorrectly classified as having moderate to severe OSA* | | | | | | | | | | | |
| M | 44 | C | C4 | 1 | Yes | No | 112 | 6 | 6 | 20.1 | 12.6 |
| F | 62 | C | C7 | 1 | Yes | No | 131 | 6 | 8 | 16.7 | 13.7 |
| M | 64 | B | C6 | 3 | Yes | No | 113 | 8 | 8 | 16.1 | 14.3 |
| M | 72 | D | C6 | 3 | Yes | No | 95 | 5 | 5 | 14.8 | 14.5 |
| M | 25 | A | C8 | 3 | Yes | Yes | 105 | 10 | 8 | 21.8 | 14.9 |
| M | 44 | A | C5 | 7 | Yes | No | 103 | 8 | 6 | 22.4 | 15.0 |
| F | 32 | A | C3 | 9 | Yes | Yes | 98 | 10 | 8 | 23.7 | 16.0 |
| M | 62 | A | C6 | 5 | Yes | No | 115 | 8 | 8 | 19.9 | 20.2 |
| M | 37 | A | C5 | 7 | Yes | Yes | 91 | 10 | 5 | 25 | 20.3 |
| *Incorrectly classified as not having moderate to severe OSA* | | | | | | | | | | | |
| F | 61 | D | C4 | 7 | No | No | 107 | 2 | 5 | 5.0 | 21.5 |
| F | 39 | B | C7 | 3 | No | No | 90 | 5 | 3 | 3.1 | 22.6 |
| M | 43 | D | C5 | 4 | Yes | No | 82 | 5 | 3 | 3.7 | 22.9 |
| M | 54 | D | C3 | 1 | No | No | 102 | 0 | 2 | 25.2 | 23.2 |
| M | 67 | A | C6 | 5 | Yes | No | 83 | 8 | 5 | 6.7 | 26.2 |
| M | 56 | D | C5 | 2 | Yes | Yes | 98 | 5 | 7 | 10.6 | 29.9 |
| M | 61 | D | C8 | 3 | No | No | 98 | 2 | 2 | 9.0 | 31.3 |
| M | 36 | A | C5 | 3 | Yes | No | 91 | 8 | 3 | 2.8 | 31.5 |
| M | 49 | D | C4 | 1 | Yes | No | 93 | 3 | 3 | 33.7 | 34.8 |
| F | 24 | A | C6 | 1 | No | No | 138 | 3 | 3 | 16.5 | 35.4 |
| M | 63 | D | C3 | 6 | Yes | No | 123 | 5 | 8 | 12.3 | 37.6 |
| M | 62 | B | C4 | 2 | No | No | 105 | 3 | 5 | 6.5 | 37.9 |

**eTable8a: Classification of event types in development group (n=78)**

| | N | Hypopnoea Index | Obstructive Apnoea Index | Central Apnoea Index | Mixed Apnoea Index | AHI |
|---|---|---|---|---|---|---|
| All, mean(SD) | 78 | 17.4(14.5) | 7.9(15.6) | 1.4(6.0) | 0.2(0.7) | 27.0(23.4) |
| All (%) | 78 | 80% | 16% | 4% | <1% | 100% |
| AHI<10 (%) | 22 | 95% | <1% | 5% | <1% | 100% |
| 10≤AHI<30 (%) | 26 | 87% | 11% | 2% | <1% | 100% |
| AHI≥30 (%) | 30 | 62% | 32% | 6% | <1% | 100% |

*AASM 1999 Chicago criteria

**eTable8b: Classification of event types in validation group (n=100)**

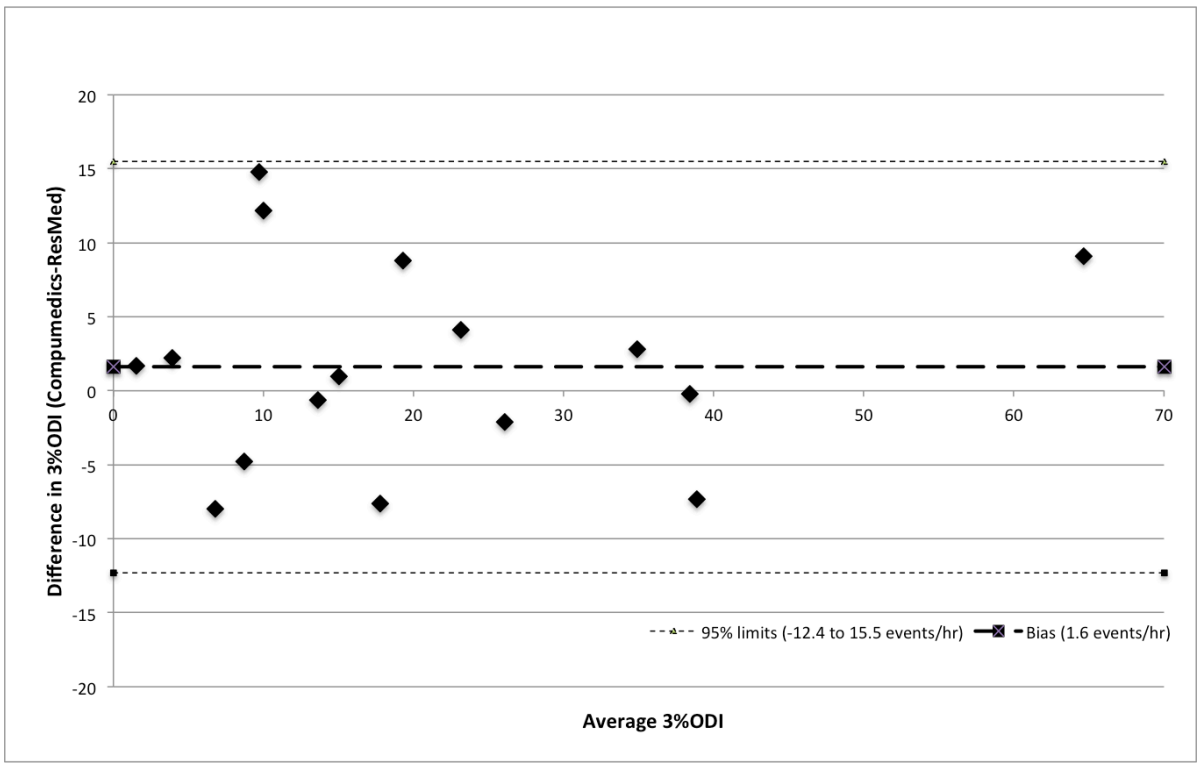
| | N | Hypopnoea Index | Obstructive Apnoea Index | Central Apnoea Index | Mixed Apnoea Index | AHI |
|---|---|---|---|---|---|---|
| All, mean(SD) | 100 | 19.9(14.4) | 11.6(21.2) | 1.4(5.3) | 1.0(3.6) | 33.7(26.9) |
| All (%) | 100 | 74% | 20% | 4% | 2% | 100% |
| AHI<10 (%) | 13 | 91% | 4% | 4% | 1% | 100% |
| 10≤AHI<30 (%) | 47 | 88% | 8% | 3% | 1% | 100% |
| AHI≥30 (%) | 40 | 54% | 39% | 4% | 3% | 100% |

*AASM 2012 criteria

The proportions of central and mixed apnoeas are low and relatively stable as OSA severity increases in both datasets. Only three participants in the combined samples of 178 (2%) had predominant central sleep apnoea, with 56%, 62% and 67% of events classified as central apnoea. Central sleep apnoea is observable in this population; but is not the predominant characteristic of sleep disordered breathing in people with tetraplegia.

Oximetry device data comparisons

The Bland-Altman plot of differences in the 3%ODIs measured simultaneously by the Compumedics and ApnoeaLink oximeters (eFigure2) shows the overall bias is low at 1.6 events/hour and, whilst the 95% limits of agreement are wide (-12.4 to 15.5), all differences are within two standard deviations of the mean. However there appears to be larger differences in 3%ODIs at the lower range of the measure, which could result in disagreement when various OSA diagnostic thresholds for the 3%ODI are applied. Ng et al found the ApnoeaLink oximeter generated higher 3%ODI values than the Compumedics oximeter by an average of 7.1 events/hour (95% limits of agreement -6.4 to 20.6).[167] This was not replicated in our small sample of 16 participants, however the width of the 95% limits was comparable, suggesting a similar clinical impact on diagnostic thresholds for OSA.




**eFigure2: Bland-Altman plot of mean difference in 3%ODIs from Compumedics and Resmed oximeters**

## 2.5 Additional methods

The following sections (2.5, 2.6 and 2.7) contain new material associated with the SOSAT study that was not published in the main manuscript (Section 2.3) or online supplement (Section 2.4).

### 2.5.1 Subjective nasal congestion and MS-OSA

To test whether subjectively measured nasal congestion is associated with MS-OSA in chronic tetraplegia, two self-reported nasal congestion questionnaires were included in the questionnaire battery during the SOSAT validation phase.

At the time of study development, our group had obtained funding for a National Health and Medical Research Centre (NHMRC) trial of treating nasal resistance in people with tetraplegia and OSA and this trial was underway at our centre. The aim of the study was to determine whether topical application of phenylephrine prior to sleep onset could reduce the AHI.[114] In addition to objective measures of nasal resistance, two questionnaires assessing subjective nasal congestion were also being collected in this trial: the Congestion Quantifier five-item (CQ-5) questionnaire[168] and a Borg scale of nasal obstruction. The CQ-5 asks five questions about symptoms and impact of nasal congestion over the past week, and is scored on a likert scale from “none of the time” to “all of the time”. The range of possible scores is 5-25. (See Appendix 8.1) This questionnaire was previously found to be a reliable, valid and responsive measure for evaluating the severity of nasal congestion in non-disabled populations.[168] The Borg scale of nasal obstruction asks participants to rate how blocked their nose is “right now” on a scale of 0-10, with verbal descriptors placed at different numbers to guide participants (e.g 1=slight blockage; 9= very, very severe (almost maximal) blockage). This scale was adapted from the Modified Borg Dyspnoea Scale[169], a valid measure of breathlessness during exercise, specifically for this trial.[103] (See Appendix 8.2)

These two questionnaires were included in the protocol for the prospective validation component of the SOSAT study, and administered immediately prior to the sleep study along with the other self-report measures. Descriptive analysis of the questionnaire scores included measures of central tendency and spread. The relationships between the

overall scores for both questionnaires and the AHI were investigated with correlation statistics and univariate linear regression analysis. Whether these questionnaire scores could predict the presence or absence of MS-OSA was investigated with univariate logistic regression analysis.

## 2.6 Additional results

### 2.6.1 Development of the SOSAT questionnaire

As detailed in Section 2.4 (Online supplement) non-binary potential risk factors for MS-OSA were dichotomized prior to univariate and multivariate analyses to determine associations with MS-OSA. Additional results showing the ability these non-binary variables to discriminate MS-OSA and the process of selecting the thresholds are presented here.

ROC curves were established for each of the following continuous variables and categorical variables with more than one category: AIS, injury severity,[170] injury level, neck circumference, BMI, waist circumference, age, years since injury, daytime sleepiness (as measured by the Karolinska Sleepiness Scale[171] (KSS)), self-reported snoring (as measured by Basic Nordic Sleep Questionnaire (BNSQ) question 16), and self-reported apnoeas (as measured by BNSQ question 18).[163] Results are summarized below. The ROC curves and sensitivity and specificity tables for each variable can be found in Appendix 8.3. From these tables the thresholds deemed to optimize sensitivity and specificity were selected for each variable.

#### *2.6.1.1 ASIA Impairment Scale (AIS)*

Possible responses for this ordinal variable were A, B, C, D and E. Table 2.2 shows the frequency of responses.

**Table 2.2 Frequency of AIS categories**

| AIS category | Frequency | Percentage |
|---|---|---|
| AIS A | 35 | 44.9 |
| AIS B | 9 | 11.5 |
| AIS C | 9 | 11.5 |
| AIS D | 22 | 28.2 |
| AIS E | 3 | 3.9 |
| Total | 78 | 100 |

ROC AUC for AIS was 0.70 (95% CI 0.59-0.81). (Figure 8.1) The AIS threshold selected for univariate analysis was ABC vs DE, which had a sensitivity of 90.0% and a specificity of 45.8%. At this threshold 32% of the sample were excluded. (Table 8.1 )

*2.6.1.2 Injury severity*

Possible responses for injury severity included: C1-C4, AIS A, B or C; C5-C8, AIS A, B or C; T1-S5 AIS A, B or C; AIS D; Ventilator Dependent at any level. Table 2.3 shows the frequency of responses.

**Table 2.3 Frequency of injury severity categories**

| | Frequency | Percentage |
|---|---|---|
| C1-C4, AIS A, B or C | 13 | 16.7 |
| C5-C8, AIS A, B or C | 37 | 47.4 |
| T1-S5 AIS A, B or C | 3 | 3.9 |
| AIS D or E | 25 | 32.0 |
| Ventilator dependent | 0 | 0 |
| Total | 78 | 100 |

ROC AUC for injury severity was 0.74 (0.64-0.84). (Figure 8.2) The threshold selected for further analysis was between *C5-C8, AIS A, B or C* and *T1-S5, AIS A, B or C,* which had a sensitivity of 90.0% and a specificity of 52.1%. This threshold excluded 32% of the sample. (Table 8.2)

There were only three participants with T1 lesions in this dataset and consequently the optimal threshold for this variable divided the sample in almost the same manner as the

optimal threshold for the AIS. Only the AIS was selected to progress to univariate and multivariate analysis.

#### *2.6.1.3 Injury level*

Possible responses for injury level included: C1, C2, C3, C4, C5, C6, C7, C8 and T1. Table 2.4 shows the frequency of responses.

**Table 2.4 Frequency of injury level categories**

| | Frequency | Percentage |
|---|---|---|
| C1 | 1 | 1.3 |
| C2 | 0 | 0 |
| C3 | 3 | 3.9 |
| C4 | 20 | 25.6 |
| C5 | 25 | 32.1 |
| C6 | 18 | 23.1 |
| C7 | 7 | 9.0 |
| C8 | 1 | 1.3 |
| T1 | 3 | 3.9 |
| Total | 78 | 100 |

ROC AUC was 0.51 (0.38-0.64), indicating that this variable was no better than chance at predicting OSA. (Figure 8.3) This variable did not progress to univariate and multivariate analysis. ((Table 8.3)

#### *2.6.1.4 Neck circumference*

Neck circumference was measured in centimeters as a continuous variable. ROC AUC for neck circumference was 0.71 (0.59-0.83). (Figure 8.4) When all subjects were included in the analysis a threshold of ≥41cm, with a sensitivity of 80.0% and a specificity of 47.9%, was selected. (Table 8.4) This excluded 37% of the sample. ROC AUC for males and females separately were 0.71 (0.57-0.84) and 0.80 (0.59-1.0). (Figure 8.5; Table 8.5) A threshold score of ≥42cm, with a sensitivity and specificity of 80.0% and 50.0%), was deemed to be optimal for males, excluding 37% of the male sample (28% of the total sample). The optimal threshold for women in this sample was

≥35cm, with a sensitivity and specificity of 100.0% and 50.0%, excluding 35% of the female sample (9% of the total sample). (Figure 8.6; Table 8.6)

#### *2.6.1.5 BMI*

BMI was measured as a continuous variable in kilograms per metre squared. With an AUC of 0.62 (0.49-0.75), BMI was a poor discriminator of MS-OSA. (Figure 8.7; Table 8.7). This variable did not progress to univariate and multivariate analysis.

#### *2.6.1.6 Waist circumference*

Waist circumference was measured in centimetres as a continuous variable. The ROC for waist circumference was 0.75 (0.63-0.86). (Figure 8.8). A threshold of ≥103cm in the total sample was deemed to optimize sensitivity and specificity (80.0% and 66.7% respectively) and eliminated approximately 50% from further testing. (Table 8.8)

When males and females were separated, thresholds of ≥103cm for males (sensitivity=84.0 and specificity=64.7), and ≥99cm in females (sensitivity=88.0% and specificity=64.3%) were selected as optimal. (Figure 8.9; Figure 8.10; Table 8.9; Table 8.10)

#### *2.6.1.7 Age*

Age was measured in years as a continuous variable. ROC AUC for age was 0.65 (0.53-0.77). (Figure 8.11) The optimal threshold was deemed to be ≥40 years with a sensitivity of 73.3% and a specificity of 56.3%, which excluded 45% of the sample. (Table 8.11)

#### *2.6.1.8 Years since injury*

ROC AUC for years since injury was 0.52 (0.38-0.67). (Figure 8.12; Table 8.12) This was no better than chance at discriminating moderate to severe OSA. This variable did not progress to univariate analysis.

#### *2.6.1.9 Karolinska Sleepiness Scale (KSS)*

The KSS is scored on a nine point scale (from 1-9). ROC AUC for the KSS was 0.63 (0.50-0.75), and the optimal threshold was deemed to be ≥3 with a sensitivity of 86.7% and a specificity of 31.3%.(Figure 8.13, Table 8.13) This score eliminated 24% of the sample from further testing.

*2.6.1.10 Self-reported snoring (BNSQ16)*

Possible responses for this question of the BNSQ ("Do you snore whilst sleeping (ask other people)?") included: never or less than once a week; less than once per week; on 1-2 days per week; on 3-5 days per week; daily or almost daily. Table 2.5 shows the frequency of responses.

**Table 2.5 Frequency of BNSQ Question 16 responses**

| | Frequency | Percentage |
|---|---|---|
| Never or less than once a week | 19 | 25.7 |
| Less than once per week | 13 | 17.6 |
| On 1-2 days per week | 11 | 14.9 |
| On 3-5 days per week | 7 | 9.5 |
| Daily or almost daily | 24 | 32.4 |
| Total | 74 | 100 |

ROC AUC was 0.70 (0.58-0.82). (Figure 8.14) A threshold of ≥2 (never or less than once a month vs everything else) demonstrated a sensitivity of 90.0% and a specificity of 36.4%, and eliminated 26% of the sample from further testing. This dichotomization is closest to that in the OSA50 questionnaire, which asks, "Has your snoring ever bothered people?" In both cases the questions are asking for "never" vs "not never" responses. (Table 8.14)

*2.6.1.11 Self-reported apnoeas (BNSQ18)*

The responses for this question of the BNSQ ("Have you had breathing pauses (sleep apnoea) during sleep (have other people noticed that you have pauses in respiration when you sleep?)" included: never or less than once a week; less than once per week; on 1-2 days per week; on 3-5 days per week; daily or almost daily. Table 2.6 shows frequency of responses.

**Table 2.6 Frequency of BNSQ Question 18 responses**

| | Frequency | Percentage |
|---|---|---|
| Never or less than once a month | 49 | 64.5 |
| Less than once per week | 6 | 7.9 |
| On 1-2 days per week | 7 | 9.2 |
| On 3-5 days per week | 4 | 5.3 |
| Daily or almost daily | 10 | 13.2 |
| Total | 76 | 100 |

ROC AUC was 0.68 (0.57-0.79). (Figure 8.15) A threshold of ≥2 (never or less than once a month vs everything else) had a sensitivity of 56.7% and a specificity of 78.3%, and ruled out 65% of the sample. Whilst this sensitivity is low, it is the highest of all possible thresholds. As with the previous question about self-reported snoring, this dichotomization is closest to that in the OSA50 questionnaire, which asks, “Has anyone noticed that you stop breathing in your sleep?” (Table 8.15)

The thresholds that optimized sensitivity and specificity for each of these variables, the corresponding sensitivity and specificity values, and the percentage of participants who were excluded at the selected threshold are summarized in eTable 4 of Section 2.4 (Online supplement).

### 2.6.2 Thresholds for questionnaires and ODI for identifying MS-OSA

The ROC curves (including AUC) demonstrating the ability of the two questionnaires (OSA50 and SOSAT) and the 3%ODI to discriminate MS-OSA are presented in the main manuscript (Section 2.3). The sensitivity and specificity tables, used to select the thresholds for examination in validation group are provided in Appendix 8.4 (Table 8.16; Table 8.17; Table 8.18). As detailed in the manuscript, the thresholds selected for prospective validation were: OSA50 questionnaire ≥3/10 (sensitivity=100%, specificity=29%); SOSAT questionnaire ≥5/10 (sensitivity=100%, specificity=27%); 3%ODI≥13/hr (sensitivity=87%, specificity=83%).

### 2.6.3 Subjective nasal congestion and MS-OSA

Summary statistics for both measures of subjective nasal congestion are summarized in Table 2.7. Both questionnaires were significantly skewed towards the lower end of the scale ($p<0.01$), with the Borg scale in particular demonstrating a substantial “floor

effect" in this sample. Almost 40% of the sample recorded the lowest possible score in the scale, and over 80% scored in the bottom 10% of available scores. The mean and median scores for the Borg scale of nasal obstruction were 1.0 (SD=1.4) and 0.5 (IQR=0-1), respectively. Of the 85 responders, five scored higher than two (out of a possible 10), and were considered outliers. (Figure 2.1)

The CQ-5 questionnaire was less skewed than the Borg with a mean of 8.7 (SD=4.1) and a median of 7 (IQR=5-11) (Table 2.7 and Figure 2.2). However 37% of the sample still recorded the lowest possible score for this questionnaire. (Table 2.8)

**Table 2.7 Summary statistics for subjective nasal congestion questionnaires**

| | N | Mean (SD) | Median | Range |
|---|---|---|---|---|
| Borg scale of nasal obstruction | 85 | 1.0 (1.4) | 0.5 | 0-7 |
| CQ-5 | 90 | 8.7 (4.1) | 7 | 5-20 |

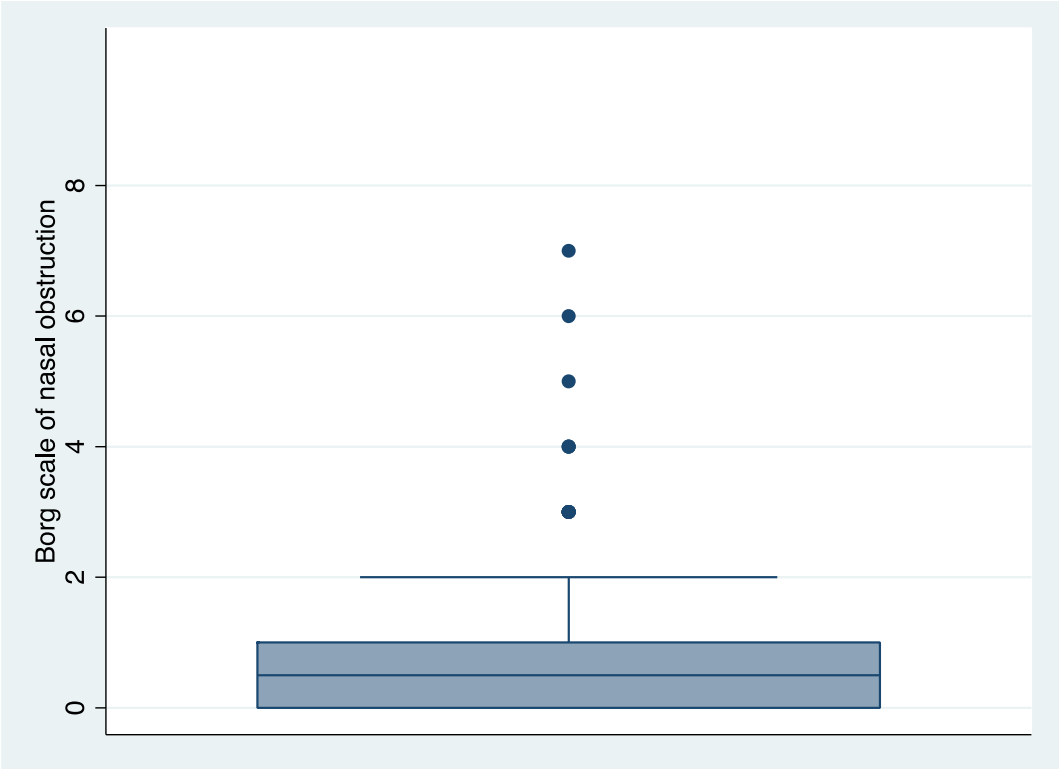



**Figure 2.1 Boxplot of Borg scale of nasal obstruction**

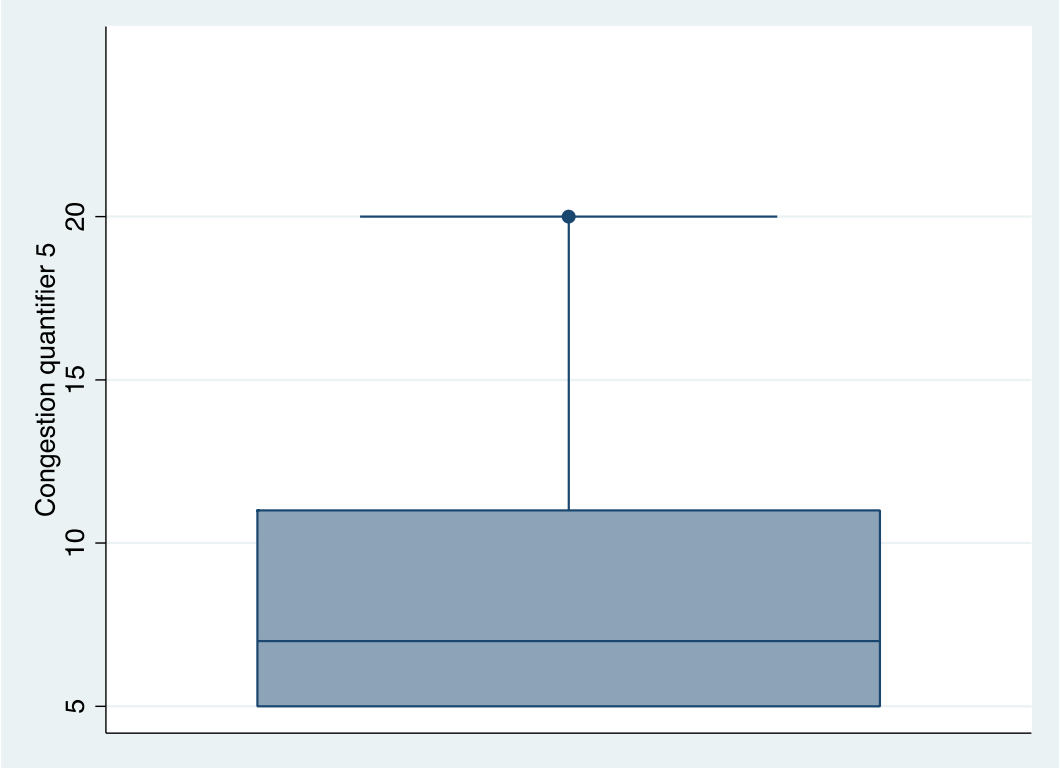



**Figure 2.2 Boxplot of congestion quantifier 5 item questionnaire**

**Table 2.8 Distribution of scores of Borg scale of nasal obstruction**

| Borg scores | Frequency | Percent | Cumulative percent |
|---|---|---|---|
| 0 | 34 | 37.78 | 37.78 |
| 0.5 | 25 | 27.78 | 65.56 |
| 1 | 15 | 16.67 | 82.22 |
| 2 | 1 | 1.11 | 83.33 |
| 3 | 9 | 10 | 93.33 |
| 4 | 3 | 3.33 | 96.67 |
| 5 | 1 | 1.11 | 97.78 |
| 6 | 1 | 1.11 | 98.89 |
| 7 | 1 | 1.11 | 100 |
| **Total** | **90** | **100** | |

The two questionnaires were significantly correlated (Pearson's R=0.64, p<0.01). However there was no evidence of correlation between the Borg scale of nasal congestion and the AHI (Pearson's R=0.11, p=0.30), nor the CQ-5 questionnaire and the AHI (Pearson's R=0.06, p=0.62).

Similarly, linear regression analysis found there were no associations between either questionnaire and the AHI (p>0.05). Nor was either questionnaire associated with having MS-OSA (AHI≥21; p<0.05) with logistic regression analysis.(Table 2.9)

**Table 2.9 Associations between subjectively measured nasal obstruction and OSA severity**

| | Linear association with AHI | | Logistic association with MS-OSA | |
|---|---|---|---|---|
| | Co-efficient | p-value | Co-efficient | p-value |
| Borg scale of nasal obstruction | 2.11 | 0.30 | 0.09 | 0.56 |
| CQ-5 | 0.37 | 0.61 | 0.01 | 0.92 |

## 2.7 Discussion

### 2.7.1 Limitations

The dataset used for this retrospective analysis was initially collected for a population study that examined the relationships between quality of life, sleep symptoms, and objectively measured sleep, and sleep disorders in chronic tetraplegia.[1] The initial survey battery response rate was 38%, which may have introduced a non-responder bias. However, only small and clinically insignificant differences in basic demographic information were found between responders and non-responders, indicating that the data obtained were likely to be representative of the population. It is possible that those with sleep problems preferentially completed the questionnaires. If so, this may have introduced a selection bias to the study and inflated the estimated prevalence of OSA. We believe this is unlikely because the OSA prevalence in this sample was similar to comparable studies and lower than that found in the validation group.[15, 16]

The self-reported snoring and apnoea questions in the OSA50 questionnaire were obtained from the Berlin questionnaire.[82] Our retrospective dataset did not include this questionnaire, and as such, these responses were derived from similarly worded questions in the BNSQ. It is possible that the derived responses may have differed from those otherwise collected from the Berlin questionnaire and affected the results. However both apnoea and snoring questions were significantly associated with MS-OSA in the development dataset and therefore included in the SOSAT questionnaire for prospective validation.

The KSS[171] was used in this study to measure daytime sleepiness. The KSS is a measure of “state” not “trait” sleepiness. State sleepiness is a short-term measure and therefore susceptible to random variation in sleep.[172] Sleepiness from OSA is more likely to become trait sleepiness because dysfunction occurs over a longer period of time. The ESS is the most common measure of trait sleepiness in people with OSA[97] however in 2002 it was reported to be difficult to administer in people with SCI because of the questions about driving and outdoor activities, which are less likely to be undertaken in this population.[92] The ESS is made up of eight questions, which asks

people to rate how likely they are to fall asleep during common situations, and is scored out of 24. Scores of ≥10 are generally considered to be abnormal. In 2015, Sankari and colleagues reported the ESS was significantly associated with OSA in people with SCI.[96] Over 60% of the SCI sample in this study scored 10 or higher on the ESS, although central tendency and spread of the questionnaire data were not reported.[96] More information about the performance of the ESS and other measures of trait sleepiness in SCI is required to understand whether trait sleepiness can be accurately and reliably measured in people with SCI. Anecdotally, people with tetraplegia are increasingly living more active lives, and the reasons this questionnaire was avoided previously may no longer be valid.

### 2.7.2 Thorax editorial

The publication in *Thorax* attracted an accompanying editorial by Alder and Janssens.[150] The editorial discusses the need for assessment of hypoventilation and raises concerns about the potential of undiagnosed central respiratory events, and the inability of the SOSAT model to detect these. Research examining the extent of central sleep apnoea in tetraplegia is conflicting. Our group has previously reported low prevalence of central events.[149] In the SOSAT study, the central apnoea index was low at 1.4/hour, with central events accounting for an average of 4% of the total events. Only 2% of the combined sample (3/178) had predominant central sleep apnoea. By contrast Sankari et al[16, 173] have reported central sleep apnoea to be the predominant pattern of sleep disordered breathing in tetraplegia. In neither the SOSAT nor the Sankari et al[16, 173] studies were hypopnoeas classified as central, obstructive or mixed according to recommended criteria published in the 2012 AASM guidelines.[27] Given the high proportion of hypopnoeas found in our study, Adler and Janssens[150] highlight the possibility that some of these hypopnoeas may be central in nature, and that our assessment of central events may be an underestimate. This is a possibility and a study proposed in Chapter 6 will test this hypothesis.

Clinically, concerns about hypoventilation and predominant central sleep apnoea are related to treatment prescription. In some cases, central sleep apnoea is associated with nocturnal hypoventilation, causing $CO_2$ retention, which may worsen with CPAP. Usually bi-level PAP is prescribed in these circumstances. Adler and Janssens[150]

have recommended using manually scored Level III portable devices alongside transcutaneous $CO_2$ monitoring as an alternative to full PSG in this population, but provide no evidence of increased diagnostic sensitivity or specificity with such an approach. As discussed in the main manuscript (Section 2.3), our group agrees that the SOSAT model should be accompanied by transcutaneous $CO_2$ monitoring to assess nocturnal hypoventilation.[149] We also acknowledge that further research is required to determine how the SOSAT model could be incorporated into a comprehensive OSA management pathway. Our concern about manually scored Level III studies is that they limit the diagnosis of OSA to those with specialist respiratory or sleep qualifications. While this home-based approach will overcome the access barriers to overnight sleep testing in a laboratory, it will not address the barriers to specialist sleep service access. As discussed in the main manuscript (Section 2.3), our group agrees that further research comparing different models of OSA diagnosis in tetraplegia is warranted. However we hypothesise that, compared to manual scoring, automatic scoring of Level III and IV devices with assessment for hypoventilation will not alter treatment outcomes. Furthermore, automatically scored devices will improve access to diagnostic investigation and are therefore likely to lead to improved OSA diagnosis rates and patient outcomes.

Stroke survivors have similarly high prevalence of OSA to people with tetraplegia, and a similarly low prevalence of predominant central sleep apnoea.[174, 175] There are several papers demonstrating the feasibility of early screening for OSA with Level III portable devices following stroke and transient ischaemic attack (TIA). The authors of these studies have similarly argued that this method facilitates rapid diagnosis and improved access to treatment.[176, 177]

### 2.7.3 Subjective nasal congestion and MS-OSA

The side study investigating the relationship between subjectively measured nasal congestion and OSA severity demonstrated that subjectively measured nasal congestion was not associated with OSA severity in tetraplegia. Furthermore, perceived nasal congestion was low.

Since completion of this project, Wijesuriya et al [103] published the results of a study investigating the relationships between three measures of nasal congestion in a group

with tetraplegia and OSA (n=8) and a non-disabled control group (n=6). Nasal congestion was measured with the Borg scale of nasal obstruction, and posterior and anterior rhinometry. They found that subjectively measured nasal congestion was significantly lower in the control group than the tetraplegic group, but that perceived nasal obstruction was essentially the same. They concluded that people with tetraplegia have poor perception of elevated nasal resistance, and furthermore, that subjective measures should not be used to identify people with high nasal resistance.

The mean (SD) Borg score in the tetraplegic group was 0.5 (1.8); similar to that reported in our study. The authors did not consider whether this finding could have been the result of a "floor effect" in the questionnaire responses. As previously discussed, this scale was adapted from the Modified Borg Dyspnoea Scale [169] which is a valid measure of breathlessness during exercise. This is the first time it has been used in tetraplegia to assess nasal congestion, and as such, its validity, reliability and responsiveness have never been assessed. That it may not be a valid or sensitive measure of subjective nasal obstruction in this population was also not discussed by Wijesuriya et al.[103]

Wijesuriya et al [103] also reported that subjectively measured nasal congestion is not correlated with objectively measured nasal resistance in people with tetraplegia. Correlations were completed between the Borg scale and both objective measures of nasal congestion. Nasal congestion measures obtained from the Borg scale and anterior rhinometry were correlated in the tetraplegic group (Pearson's R=0.19, p=0.02) and the control group (R=0.3, p=0.01). Both were measured at four time points for each participant, creating a sample size of 32 in the tetraplegic group and 24 in the control group. The authors report that there was no correlation between the Borg scale and the "gold-standard" posterior rhinometry measurement, however the correlation statistics are not provided in the paper. Posterior rhinometry was measured twice, thereby halving the sample size of this correlation analysis and reducing its power. Without the correlation statistics it is impossible to estimate whether this non-finding may have been the result an under-powered analysis. In my opinion, the scatterplots provided in the paper do suggest that a weak relationship existed.[103]

Data presented in this chapter and in the paper by Wijesuriya et al [103] indicate that the Borg scale of nasal obstruction suffers from a significant floor effect, and is not a valid and sensitive measure of subjective nasal obstruction in people with tetraplegia. The double blinded cross-over randomised controlled trial of topical phenylephrine to reduce OSA severity in people with tetraplegia, conducted by our group at the same time as the SOSAT study, concluded that whilst nasal resistance improved with topical phenylephrine, the AHI was not significantly lowered.[114]Nasal resistance is a known risk factor for OSA in the non-disabled[178] and is higher in people with tetraplegia and OSA than in non-disabled controls with OSA.[100] Further research into whether longer acting drugs, suitable for long-term use, can reduce OSA severity or improve adherence to CPAP is warranted. If nasal resistance is found to be an effective therapeutic target for OSA in people with tetraplegia, more research into whether a more sensitive measure of subjective nasal resistance can estimate total nasal resistance may also be warranted.

### 2.7.4 Overall summary and conclusion

Within this chapter, the comprehensive rationale, methods and results of the SOSAT study have been presented. In conclusion, this model provides an alternative to full PSG for identifying MS-OSA in people with tetraplegia. It should be combined with a thorough clinical assessment of symptoms, comorbidities and hypoventilation. Further research is required to assess the safety and feasibility of using this model in a comprehensive OSA management pathway. These ideas are discussed in further detail in Chapter 6.

*"He who has a why to live can bear almost any how."~ Friedrich Nietzsche*

# 3 CONTINUOUS POSITIVE AIRWAY PRESSURE USE FOR OBSTRUCTIVE SLEEP APNOEA IN ACUTE, TRAUMATIC TETRAPLEGIA

## 3.1 Overview of Chapter 3

While the research presented in Chapter 2 investigated a potential solution to a known barrier to OSA detection in tetraplegia, the focus of Chapter 3 is on understanding the barriers to treatment. CPAP is the first-line treatment for OSA in tetraplegia, yet little is known about its uptake in acute tetraplegia, nor the factors associated with adherence. For the person with a new spinal cord injury, the first 12 months is usually a time of enormous change and significant challenges. A better understanding of CPAP use in this period is essential for the development future of interventions that may improve the management of OSA in this population. Improving OSA treatment adherence in the acute period is likely to enhance rehabilitation outcomes.

This research involved the secondary analysis of data from a large multicentre randomised controlled trial of CPAP for OSA in acute tetraplegia (the COSAQ study). It is the largest study to evaluate CPAP use in acute tetraplegia.

At the time of thesis submission, the manuscript for the COSAQ study was under review and the published abstract was referenced throughout the chapter. The manuscript has since been accepted for publication, and the referencing has been updated accordingly. This chapter is presented as a manuscript. Since the publication of the COSAQ trial, this chapter has been submitted to a peer-reviewed journal and at the time of thesis confirmation (March 2019), it was under review.

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## 3.3 Abstract


### 3.3.1 Study objectives

Up to 80% of people with acute tetraplegia have obstructive sleep apnoea (OSA). Continuous positive airway pressure (CPAP) is the recommended treatment for OSA but its use is poorly understood in tetraplegia. The aim of this study was to describe CPAP use in acute tetraplegia, including adherence rates and associated factors.

### 3.3.2 Methods

CPAP data from a multinational randomized controlled trial of auto-titrating CPAP for OSA for three months after acute, traumatic quadriplegia (the COSAQ study) were analysed. Adherence was measured as mean daily hours of use. Adherent (yes/no) was defined as an average of at least four hours a night throughout the study. Regression analyses determined associations between baseline factors and adherence. CPAP device pressure and leak data were analysed descriptively.

### 3.3.3 Results

79 participants from 10 spinal units (91% male, mean age 46 (SD=16), 78 (SD=64) days post-injury) completed the study in the treatment arm and 33% were adherent. Mean daily CPAP use was 2.9 hours (SD=2.3). Better adherence was associated with more severe OSA ($p=0.04$), and greater CPAP use in the first week ($p<0.01$). Average $95^{th}$ percentile pressure was low (9.3cmH2O; SD=1.7) and $95^{th}$ percentile leak was high (27.1L/min; SD=13.4). Overall CPAP adherence in acute, traumatic tetraplegia was estimated at 21%.

### 3.3.4 Conclusion

Adherence to CPAP following acute, traumatic tetraplegia is low. Early acceptance of therapy and more severe OSA predict CPAP use over three months. People with acute tetraplegia require less pressure to treat their OSA than the non-disabled; however, air leak is high. These findings highlight the need for further investigation of OSA treatment in acute tetraplegia.

## 3.4 Background

Obstructive sleep apnoea (OSA) is thought to be a direct result of traumatic tetraplegia. A seminal paper examining the sleep and breathing of people with tetraplegia in the first year post injury found that OSA was not apparent until two weeks post injury, and peaked at 83% after 3 months, before dropping to 62% at 12 months.[86] Another study of OSA prevalence in acute spinal cord injury (SCI) found similarly high prevalence (75%) at six months post-injury. These prevalence estimates are significantly higher than those in people without disability; estimated at 10-17% in men and 3-9% in women.[31]

Analysis of neuropsychological function in people with OSA following acute tetraplegia (approximately two to three months after injury) found that more severe OSA was associated with poorer attention, information processing, and immediate recall.[109] Acute impairment in neuropsychological function is likely to impact on rehabilitation outcomes in this population.

Continuous positive airway pressure (CPAP) therapy is the first-line treatment for OSA, and has been shown to improve daytime sleepiness, and some measures of sleep quality, health related quality of life and mood in people without disability.[48, 49, 54] Efficacy of CPAP therapy for people with acute tetraplegia has recently been investigated with a multicenter randomized controlled trial design.[110] While this trial reported no effect of CPAP on neurocognitive function, the CPAP group experienced greater improvements in subjective daytime sleepiness, and furthermore, weekly changes in subjective sleepiness were sensitive to CPAP use that week.

A significant limitation to CPAP effectiveness is poor adherence and acceptance of the therapy. CPAP adherence in non-disabled populations is reported to range between 30 and 60%.[55] Factors associated with better CPAP use in people without disability have included more severe OSA, subjective sleepiness, decreased nasal resistance, better self-efficacy with CPAP use, and social and spousal support.[57] Early acceptance of therapy is a strong predictor of long-term use.[179-183] This information has enabled

the development of intensive interventions aiming to improve the uptake of CPAP in people without disability. [57]

To our knowledge, only one study has previously investigated CPAP adherence in the acute inpatient SCI setting. Of the 14 participants, seven (50%) were adherent with the therapy in the final week of the three month trial.[111] Risk factors for non-adherence have not yet been thoroughly investigated in SCI but are likely to be different to people without disability because of the additional physical and psychosocial issues they face.[184] People with tetraplegia require significantly less CPAP to treat their OSA (for any severity) than those without disability and OSA, however the mechanisms leading to this difference remain unknown.[185]

A better understanding of CPAP use in acute tetraplegia will assist clinicians and researchers to develop new strategies for maximising CPAP uptake in this population. The aim of this study was to describe autoset CPAP use in people with acute, traumatic tetraplegia, including adherence rates, average pressures and leak, night-to-night variability in pressure requirements, and to determine the predictors of adherence.

## 3.5 Methods

### 3.5.1 The COSAQ study

This study involved secondary data analysis of CPAP use in a multinational randomized controlled trial of auto-titrating CPAP treatment for OSA for three months after acute, traumatic tetraplegia (the COSAQ study). The methods for the COSAQ trial have been detailed previously.[186] Briefly, consenting participants who met the inclusion and exclusion criteria were screened for OSA with overnight polysomnography, and those with an Apnoea Hypopnoea Index (AHI) greater than or equal to 10 were provided a trial of auto-titrating CPAP (S8 and S9; Resmed Autoset, San Diego USA). Participants were only randomised to three months of CPAP or usual care if they could first tolerate CPAP for greater than four hours on one of three consecutive nights. Training in CPAP set-up, mask selection and troubleshooting was provided to each site by the central study team. ResMed nasal pillows, face and oro-nasal masks were available and the mask selection was individualised for each participant to maximise fit and comfort and

to minimise leak.[110, 186] Following randomization, weekly CPAP usage data were recorded for each participant.

### 3.5.2 CPAP adherence in the three month study

Adherence within the 13-week study was measured as mean nightly hours of use. Adherent (yes/no) was defined as recorded device use of at least four hours average per night throughout the study.

### 3.5.3 Predictors of CPAP adherence in the three month study

Univariate linear analyses were undertaken to determine associations between baseline factors and adherence. Baseline factors collected within the COSAQ study and included in the analysis were: age, gender, injury severity,[170] time since injury, OSA severity (AHI, 4% oxygen desaturation index (ODI), arousal index (AI) and number of awakenings), quality of life,[187] premorbid intelligence,[188],anxiety and depression,[189] mood,[190] daytime sleepiness,[171] anthropometry (waist circumference, neck circumference and BMI) and early CPAP use (hours on night one, and average hours in week one). Variables were assumed to be collinear if the bivariate correlation co-efficient was greater than 0.3. Non-collinear variables associated with CPAP adherence on univariate analysis ($p<0.1$) were entered into a multivariate linear regression model.

### 3.5.4 Overall estimate of adherence in acute, traumatic tetraplegia

An overall estimate of CPAP adherence in the acute, traumatic tetraplegic population was made with the assumption that those who initially failed the three night trial of CPAP, and thus were excluded from the study, would not have been adherent during the subsequent 13 week study. These participants were pooled with the sample of non-adherent participants in the three-month trial. Differences in various demographic and sleep variables between those who failed the initial three-night trial and those who failed to adhere during the three-month study were first assessed to ensure the two groups were demographically similar.

### 3.5.5 Average daily pressures and leak and their associations with CPAP use

In addition to weekly summary data, daily CPAP data were collected in a convenience sample of 47 of the 79 participants. The COSAQ study protocol did not require these data to be collected; nonetheless the data were available for many of the sites. The daily data included average pressure ($cmH_2O$), average leak (L/min) and use (hours), were collected for 47 of the 79 participants administered CPAP in the three-month study. Median, maximum and 95th percentile pressure and leak data were analysed with descriptive statistics.

Night to night variability in average 95th percentile pressure per patient was estimated by calculating the average co-efficient of variation (SD/mean) for each patient, and reporting the mean, median and range for the co-efficient of variation of the sample. Whether $95^{th}$ percentile leak and pressure were associated with hours of use were analysed with a generalized linear regression model in this sub-set of participants, using daily hours of use as the dependent variable, 95th percentile pressure and $95^{th}$ percentile leak as covariates and participant as the random effect.

## 3.6 Results

Eleven spinal cord injury centres participated in the study and 332 patients consented and underwent overnight PSG. 78% of participants with an Apnoea Hypopnoea Index (AHI) greater than or equal to 10 passed the initial three night CPAP trial (165/213). Forty-eight could not tolerate CPAP and were excluded from the COSAQ study. 160 participants were randomized, 80 of whom were in the CPAP arm. 149 participants (134 men, mean age 47) completed the study.[110]

Allowing for withdrawals and cross-over from one group to another, 79 participants from 10 of the 11 sites (91% male, mean age 46 (SD=16), 78 (SD=64) days post-injury, and mean baseline AHI of 49 (SD=28)) completed the study in the treatment arm. (See Figure 3.1)

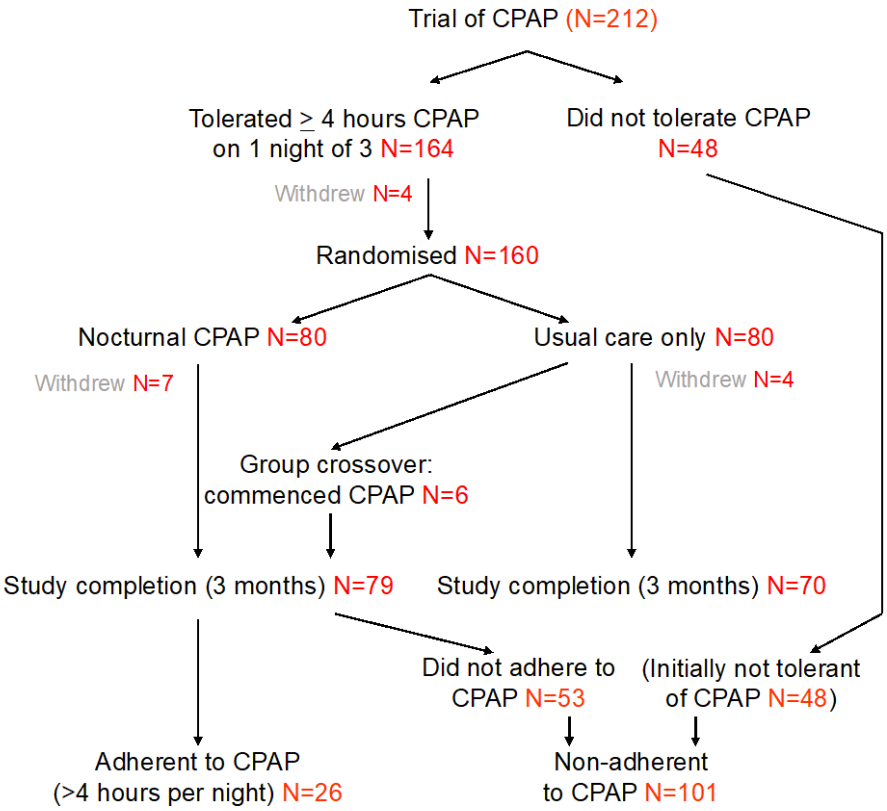


**Figure 3.1 Participant CPAP flowchart**

### 3.6.1 CPAP adherence in the three month study

The mean daily CPAP use was 2.9 hours (SD=2.3). Median CPAP use was 2.5 hours. Of the 79 participants receiving CPAP, 33% (N=26) were adherent over the three month study with average daily use of greater than four hours. Forty-three percent (N=34) used CPAP for less than 2 hours per night, and 24% (N=19) used CPAP for between two and four hours per night on average. (Figure 3.2)

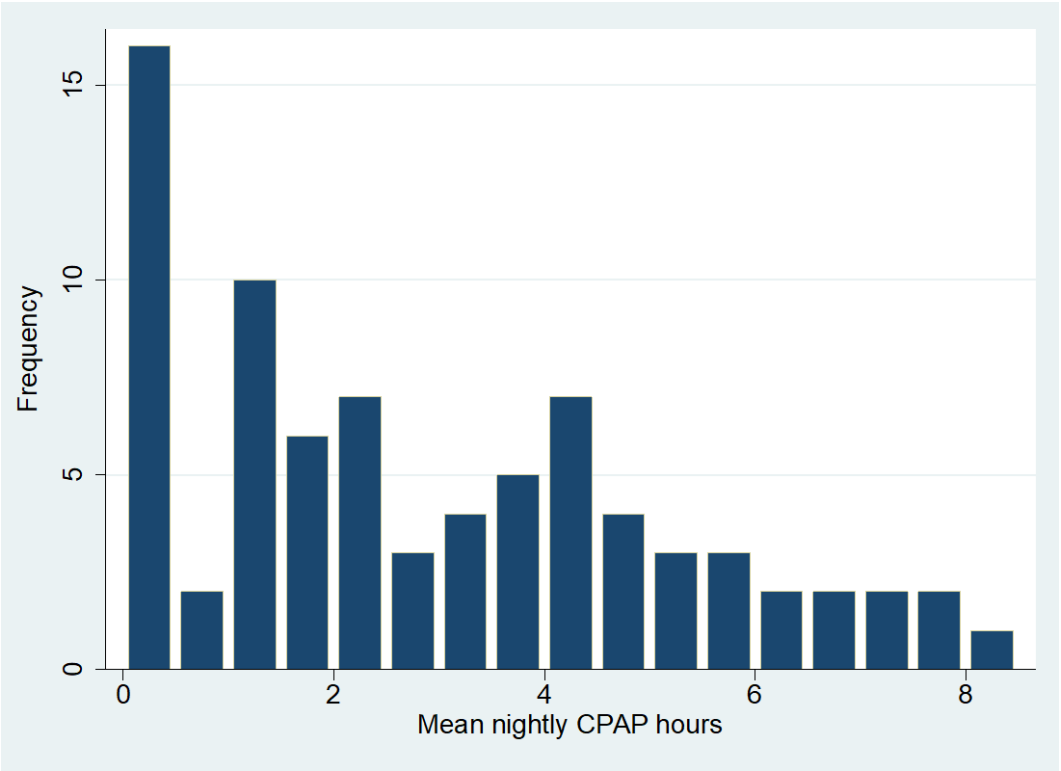


**Figure 3.2 Histogram of average daily use for CPAP administered patients.**

Ten of the 11 sites administered CPAP to one or more participants, with the number of participants per site ranging from 1 to 19. Average CPAP use by site ranged from 0.6 hours to 6.3 hours per night, however whether study site was statistically associated with adherence was unable to be determined due to the low numbers of participants from some sites. (Figure 3.3)

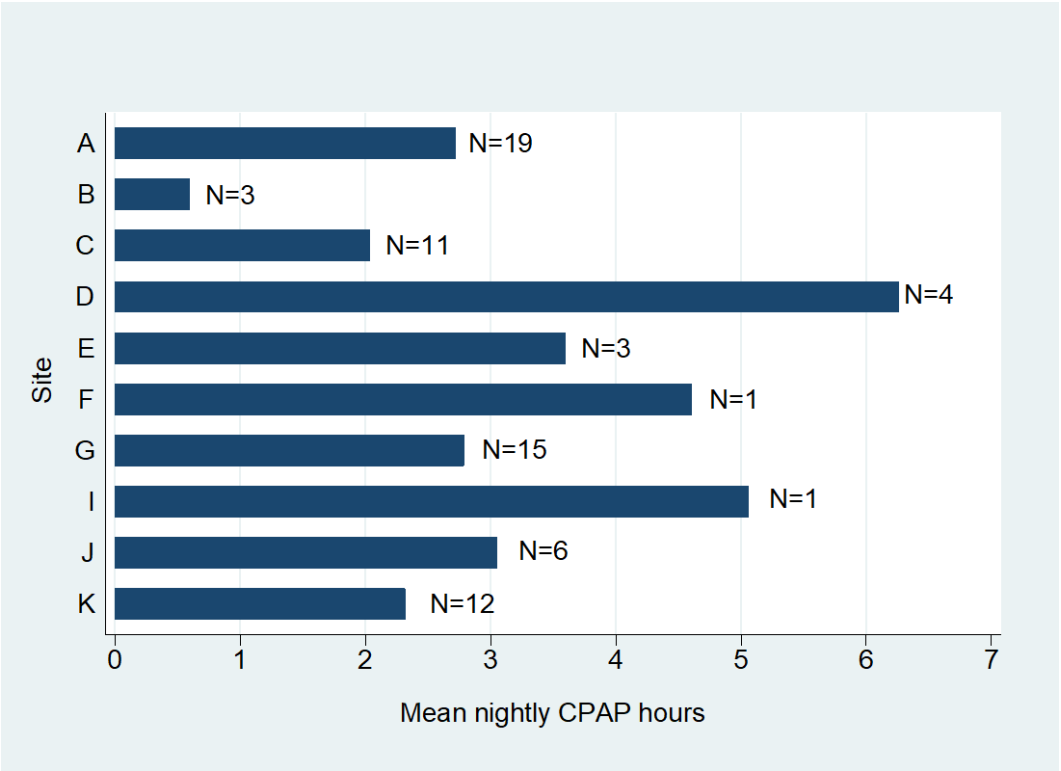


**Figure 3.3 CPAP use by site in the 13 week study (n=79)**

### 3.6.2 Predictors of CPAP adherence in the three month study

Univariate linear regression analysis found that greater CPAP use over the 13 week trial was associated ($p<0.1$; Table 1) with CPAP use in the first week, higher premorbid intelligence as estimated by the North American Adult Reading Test (NAART), higher abdominal girth, increasing age and more severe OSA, as measured by Apnoea Hypopnoea Index (AHI), Arousal Index (AI), awakenings and 4% oxygen desaturation index (4% ODI). (Table 3.1)

**Table 3.1 Univariate associations between average daily CPAP use and baseline predictor variables.**

| Variable | Coefficient (95% CI) | p- value |
|---|---|---|
| Gender (male) | -1.07(-2.83-0.70) | 0.23 |
| Age (years) | 0.03(-0.00-0.06) | 0.06 |
| ASIA impairment scale (A-D) | 0.18(-0.28-0.65) | 0.44 |
| Injury level (C2-T1) | 0.07(-0.34-0.48) | 0.73 |
| Time since injury (years) | 0.00(-0.01-0.01) | 0.60 |
| Baseline AHI | 0.03(0.02-0.05) | <0.01* |
| AHI>30 | 1.70 (0.68-2.71) | <0.01* |
| Baseline AI | 0.03(0.01-0.05) | 0.02* |
| Baseline awakenings | 0.02(0.01-0.03) | 0.01* |
| Baseline 4% ODI | 0.03(0.01-0.05) | <0.01* |
| Baseline KSS | 0.18(-0.04-0.40) | 0.11 |
| Baseline NAART | 0.04(0.00-0.08) | 0.049* |
| Baseline AQoL | -1.73(-5.43-1.97) | 0.35 |
| Baseline HADS anxiety | -0.05(-0.18-0.08) | 0.47 |
| Baseline HADS depression | 0.00(-0.13-0.13) | 0.97 |
| POMS total mood disturbance | -0.00(-0.02-0.02) | 0.99 |
| Abdominal girth (cm) | 0.03(-0.00-0.06) | 0.08 |
| Neck Circ. (cm) | 0.07(-0.05-0.20) | 0.25 |
| BMI ($kg/m^2$) | 0.02(-0.04-0.07) | 0.59 |
| CPAP use week 1 (hours) | 0.46(0.30-0.62) | <0.01* |
| KSS change in week 1 | -0.12(-0.32-0.09) | 0.26 |

**<0.05. KSS=Karolinska Sleepiness Scale; NAART=North American Adult Reading Test; AQoL=Assessment of quality of life questionnaire; HADS=Hospital Anxiety and Depression Scale; POMS=Profile of Mood States.*

Variables associated with CPAP use ($p<0.1$) were considered for the multivariate model. Arousals, awakenings and oxygen desaturation all contribute to the AHI, and were therefore not included. Evidence of collinearity was found between AHI and abdominal girth (Pearson's $R=0.44$, $p<0.01$) and AHI and age (Pearson's $R=0.43$, $p<0.01$). Therefore variables selected for multivariate analysis included baseline AHI, average hours of CPAP use in week one, and NAART. Higher baseline AHI and higher

CPAP use in week one remained significantly associated with more CPAP use in the three month study. (Table 3.2) The adjusted R-squared for this model was 41%.

**Table 3.2 Multivariate linear regression analysis: associations between significant baseline variables and average nightly CPAP use (hours)**

| Variable | Beta co-efficient | P value | 95% CI |
|---|---|---|---|
| Average CPAP use in week 1 (hours) | 0.43 | <0.01 | 0.28-0.58 |
| Baseline AHI (OSA severity) | 0.02 | 0.04 | 0.00-0.03 |
| Baseline NAART (pre-morbid intelligence) | 0.03 | 0.06 | -0.001-0.06 |

### 3.6.3 Overall estimate of CPAP adherence in acute, traumatic tetraplegia

Assuming those who did not pass the initial three night trial (n=48) would not have achieved long-term adherence, the overall estimate of CPAP adherence in the acute, traumatic tetraplegic population was 21% (26/127).

There was no difference in age, injury severity classification,[170] time since injury, baseline AHI, NAART or abdominal girth ($p<0.05$) between participants who initially failed the three-night trial (N=48) and those who failed to adhere (>4 hours on average per night) in the study period (N=53). However the proportion of women who failed the three night trial (14/48 =29%) was three times higher than the proportion of women who failed to adhere in the 13 week study (5/53= 9%; $p=0.01$).

### 3.6.4 Average daily pressures and leak

Daily CPAP data, including pressure, leak and hours used were available for 47 of the 79 participants. Three were excluded from analysis because the CPAP device was used for three nights or less, and for short periods only (<2 hours). On average each participant had 49 daily recordings, providing a total of 2160 observations. There was no difference in gender, age, injury severity, NAART, time since injury, abdominal girth or baseline AHI ($p<0.05$) between those with daily CPAP (n=44) data and those without (n=35).

Mean 95th percentile pressure was 9.3 $cmH_2O$ (SD=1.7), and mean $95^{th}$ percentile leak was 27.1 L/min (SD=13.3). (Table 3.3) Excessive leak (>24 L/min) was present in 46% of patient*nights (2160 observations). Over half of participants (53%, n=44) experienced mean $95^{th}$ percentile leak of >24L/minute. Whilst statistically significant ($p<0.05$), the absolute difference in $95^{th}$ percentile pressure between observations (n=2160) with excessive leak and those without was small (mean = 9.6 (SD=2.4) versus 9.3 (2.6) $cmH_2O$). There was no difference in mean $95^{th}$ percentile pressure between individuals (n=44) with mean $95^{th}$ percentile leak above and below 24L/min (9.2(SD=1.6) vs 9.5 (1.8) $cmH_2O$, p=0.50). There was no relationship between baseline AHI and mean $95^{th}$ percentile pressure (Pearson's R= 0.12, p=0.43).

**Table 3.3 Mean nightly CPAP pressures and leak per patient (N=44).**

| | **Mean** | **SD** | **Median** |
|---|---|---|---|
| Median pressure ($cmH_2O$) | 7.36 | 1.73 | 7.30 |
| $95^{th}$ percentile pressure ($cmH_2O$) | 9.28 | 1.65 | 9.56 |
| Maximum pressure ($cmH_2O$) | 9.94 | 1.83 | 9.98 |
| Median Leak (L/min) | 10.20 | 9.34 | 7.18 |
| $95^{th}$ percentile leak (L/min) | 27.10 | 13.39 | 25.14 |
| Maximum leak (L/min) | 51.64 | 23.34 | 45.13 |

### 3.6.5 Night to night variability in 95% pressure

The mean co-efficient of variation of $95^{th}$ percentile pressure in 44 people with an average of 49 recordings (SD/mean) was 0.21 (SD= 0.15, range 0.05-0.93), indicating low variability. In this sample there were three outliers, whose average co-efficient of variation was greater than 0.4. (Figure 3.4)

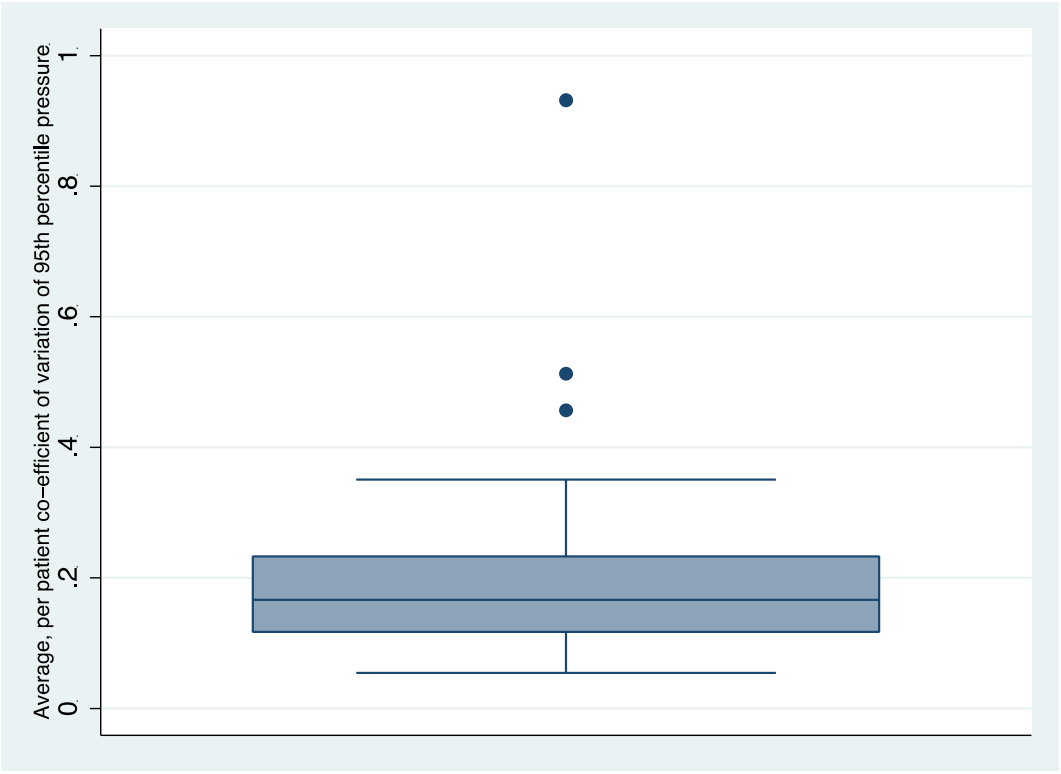


**Figure 3.4 Boxplot of average, per patient co-efficient of variation of 95th percentile pressure.**

### 3.6.6 Effect of pressure and leak on average daily hours of CPAP use

Covariates included in the generalized linear model were 95th percentile pressure and leak. Baseline AHI was also included given the association found in the larger sample (N=79). Collinearity was not present between any covariates (Pearson's R correlation co-efficient<0.1). After accounting for individual variation in the generalized linear model, only 95th percentile pressure ($cmH_2O$) was significantly associated with daily hours of use (co-efficient=0.20; 95%CI=0.16-0.25; p<0.001). Baseline AHI (co-efficient=0.01; p=0.08) and 95th percentile leak (co-efficient=-0.001; p=0.68) were not associated with daily hours of use in this model.

## 3.7 Discussion

This study has established that CPAP adherence in people with acute, traumatic tetraplegia is low, even within the setting of inpatient spinal units participating in a clinical trial. Within the 13 week trial, participants averaged 2.9 hours of CPAP per night, and the proportion of those using CPAP for greater than four hours per night was

33%. Better adherence over the three month period was observed in those with more severe OSA and greater early CPAP use.

Similar CPAP adherence rates have been observed in other disabled and special needs populations. A randomized controlled trial of treating OSA with CPAP in an aged care population found adherence (>4 hours per night) within the trial was 35% and median CPAP use was approximately one and a half hours per night.[191] Estimates of CPAP adherence for OSA after stroke vary considerably from 1.4 hours per night [192] to 4.1 hours per night.[193] Differences in methodology have undoubtedly contributed to the wide variation.

Unfortunately the CPAP literature is ambiguous on what constitutes “adherent”. CPAP adherence is inconsistently defined at least partly because the amount of CPAP required for optimal outcomes has not yet been established. Several studies in people without disability have observed a dose-response relationship for improvements in sleepiness and cognitive function, suggesting that any CPAP use is better than none. At least 4 hours seems to be required for normalization of daytime sleepiness, quality of life and neurocognitive function, and average doses of six hours and higher per night are associated with better clinical outcomes.[55-59] Based on these findings, experts have recently recommended that greater than four hours per night be used to define “adherent”,[60] which is the definition used in this paper. This target is challenging for people with acute tetraplegia who are subject to much nighttime disruption associated with acute illnesses, skin and bladder care. Reduced upper limb function makes adjusting the mask difficult and they are also dealing with the psychological and social impacts of their new injury.

Moreover, these recommendations are based on data from non-disabled populations. The amount of CPAP required to improve outcomes in populations with special needs, like tetraplegia, remains unknown. For people without disability, research has aimed to identify individuals at risk and their modifiable risk factors, with the intention of developing targeted interventions to improve adherence. There is some evidence to suggest that, in the non-disabled populations, intensive intervention can improve CPAP

adherence rates. Integrative interventions employing psychological therapies, support and education appear to be the most effective.[55]

Our limited understanding of the factors associated with poor CPAP adherence in people with tetraplegia means we cannot confidently predict which of these patients are more likely to be adherent with therapy prior to, or after, CPAP implementation. None of the prediction tools tested in the non-disabled following CPAP initiation have ever been examined in people with SCI. Furthermore, there have been no intervention studies aiming to increase adherence in this population. There remains a scarcity of research in this area. Qualitative research could provide detailed information from participants to help explain why this therapy is so readily accepted by some and poorly tolerated by others.

Secondary analysis of CPAP data from a large multicentre trial of CPAP to reduce cardiovascular events in non-disabled people with OSA found adherence to be 39% at 12 months, with average daily use of 3.3 hours.[180] Multivariate analysis of baseline variables identified that early use and early side effects (both measured at one month) were significantly associated with adherence. While side effects were not measured in our study, early CPAP use (measured at one week) was a significant predictor. Early acceptance of therapy has consistently been found to predict longer term CPAP use in the non-disabled.[181]

Increasing OSA severity has also been identified as a predictor of CPAP adherence in the non-disabled [57, 162] and was significantly associated with adherence in this study also. Our group previously conducted a study of the feasibility and effectiveness of early CPAP treatment for OSA; the results of which informed the COSAQ trial.[111] Adherent patients were found to be older, heavier, sleepier and with more severe OSA at baseline than those who did not tolerate CPAP. Early use was also found to be a strong predictor of adherence at three months. The 50% adherence rate was acknowledged to be the best possible in routine clinical care and was attributed to the significant amount of support provided by highly skilled staff. Time spent with CPAP

implementation and staff experience was not measured in this study, but it may have influenced adherence rates.

Air leak was high in this study with over 50% of participants averaging 95$^{th}$ percentile leak over the accepted range of 24L/min. CPAP leak has received very little attention in the SCI literature but it may be a bigger problem for people with tetraplegia who, with impaired upper limb function, may have difficulty performing simple mask adjustments. Higher levels of air leak have been associated with poor adherence in a non-disabled population, although high air leak did not influence CPAP use in this study.[194]

The average per-patient coefficient of variation in 95$^{th}$ percentile pressure was 0.2. Statistically this indicates low variability, however we were unable to locate any literature that quantitatively reports night-to-night variability in pressure for comparison to our sample, and are therefore unable to offer a clinical interpretation of this value. Several studies have calculated within night variability in pressure using a variability index,[195, 196] however we could not perform this analysis because our data provided daily summaries only. High variability in pressure could support a case for autoset over fixed pressure CPAP in this population, as was prescribed in the COSAQ trial.

LeGuen et al[185] compared CPAP requirements of people without disability and people with tetraplegia and found mean required pressure was approximately 50% less in tetraplegia. The mean 95$^{th}$ percentile pressure reported in our study (9.3cm$H_2O$) is similar to that reported by Le Gruen et al (9.0cm$H_2O$),[185] supporting their conclusion that people with tetraplegia require less CPAP to treat OSA. They postulate that people with tetraplegia may have a more distensible and/or a less collapsible upper airway. There may also be other unknown factors influencing the pressure requirements in tetraplegia.

Our generalized linear model found that higher 95$^{th}$ percentile pressure was associated with greater daily CPAP use in the participants with daily CPAP data (n=44, 2160 observations). OSA severity is a known predictor of CPAP adherence [162] and higher pressures are correlated with increasing OSA severity[185, 197] in the non-disabled

literature. In contrast, in both our data and the report by Le Guen,[185] more severe OSA was not associated with higher pressures in tetraplegia. As such, when both variables are included in the generalized linear model, baseline AHI was not associated with daily CPAP hours, while 95$^{th}$ percentile pressure remained highly significant.

A recent study by Brown et al,[112] found that severity of sleep disordered breathing did not predict bi-level positive airway pressure (PAP) adherence in a linear regression model, but higher PAP significantly predicted adherence. Unfortunately, the paper does not contain the absolute levels of PAP applied and as such it is difficult to establish whether the AHI and pressure relationship held in their data. Nonetheless, we confirmed the findings of Brown et al that higher pressures were associated with better usage despite controlling for OSA severity. This was a surprising finding, with the authors highlighting the common belief among clinicians that higher pressures would have a negative impact on adherence. More research is required to unpack the relationships between CPAP use, pressure and OSA severity.

### 3.7.1 Limitations

An overall estimate of CPAP adherence in acute tetraplegia was made by assuming that those who failed the initial three night trial, and therefore not randomized, would not have met the criteria for adherence in the 13 week study. Some may have become adherent, and as such our estimate of overall adherence is conservative. The only statistical difference we identified between the two non-adherent groups was that those who failed the three night trial were three times more likely to be women. Daily CPAP data were only available for 47 of the 79 participants. This is a possible source of bias, however there were no differences in baseline demographics between those with and without these data. This study did not record type of mask selected, therapist experience or time spent troubleshooting CPAP issues, all of which may have influenced adherence.

## 3.8 Conclusion

When defined as an average of at least of four hours use per night, adherence to CPAP following acute, traumatic tetraplegia is low. CPAP is particularly challenging for people with acute tetraplegia who are dealing with their new injury and its devastating

effects on the body. More information about the minimum dose required for improvements in daytime function for people with tetraplegia is warranted. People with acute tetraplegia require less pressure to treat their OSA than the non-disabled, however air leak is high. This study has found that those with more severe OSA and/or higher pressures are more likely to adhere CPAP, and early acceptance of therapy is a strong predictor of longer-term use. A better understanding of the relationships between CPAP use, pressure requirements and OSA severity could lead to interventions aiming to improve CPAP adherence in people with acute, traumatic tetraplegia. Additionally, our study supports the need for research to assess the role of non-CPAP treatment alternatives in these patients.

*“I have never been disabled in my dreams.” ~ Christopher Reeve*

# 4 WORTH THE EFFORT? WEIGHING UP THE BENEFIT AND BURDEN OF CONTINUOUS POSITIVE AIRWAY PRESSURE THERAPY FOR THE TREATMENT OF OBSTRUCTIVE SLEEP APNOEA IN CHRONIC TETRAPLEGIA.

## 4.1 Overview of Chapter 4

The previous chapter sought to understand CPAP use in people with acute tetraplegia, using data from a large clinical trial. It demonstrated that CPAP adherence is low in this setting. Chapter 4 focuses on CPAP use in those who have been living with their injury for greater than 12 months. Using a mixed methods design, it aims to understand the experience of using CPAP from the perspective of people with SCI. This study is the first to use qualitative methods to capture this perspective from people with the lived experience. It is also the first study to objectively measure CPAP use over a 12 month period in tetraplegia, thereby providing an estimate of long-term adherence.

This chapter is presented in two parts: as a journal article that was accepted for publication in *Spinal Cord* on 4 October 2018; and the online supplementary material. The accepted version of the manuscript and online supplement are provided, with minor formatting changes only.

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## 4.3 Abstract


### 4.3.1 Study design

Mixed methods: cohort /qualitative study.

### 4.3.2 Objectives:

Continuous Positive Airway Pressure (CPAP) therapy is the recommended treatment for obstructive sleep apnoea (OSA). The aim of this study was to estimate CPAP adherence in people with tetraplegia and OSA, and to explore the barriers and facilitators to CPAP use.

### 4.3.3 Setting:

Hospital outpatient department in Melbourne, Australia

### 4.3.4 Methods:

People with chronic tetraplegia and OSA were commenced with auto-titrating CPAP and supported for one month. Semi-structured interviews were conducted with participants at one month and analysed thematically. CPAP usage was measured at one, six and 12 months, with “adherent” defined as achieving more than four hours average per night.

### 4.3.5 Results:

Sixteen participants completed the study (80% male; mean age 56(SD=15)). Mean nightly CPAP use at one month was 3.1 hours (SD=2.53; 38% adherent), and at 6 months and 12 months were 2.6 hours (SD=2.8; 25% adherent) and 2.1 hours (SD=3.2; 25% adherent). The perceived benefit/ burden balance strongly influenced ongoing use. Burden attributed to CPAP use was common, and included mask discomfort, and physical and emotional problems. Adherent participants were motivated by the immediate daytime benefits to mood, alertness and sleepiness. There was a tendency to not recognise symptoms of OSA until after they were treated.

### 4.3.6 **Conclusion:**

CPAP use is challenging for people with tetraplegia, who experience substantial burden from using the device. When tolerated, the proximate benefits are substantial. People with tetraplegia need more intensive support for longer to help them overcome the burdens of CPAP and benefit from the treatment.

## 4.4 Introduction

People with spinal cord injury (SCI) experience worse sleep than people without disability, as a consequence of a range of sleep disorders.[14] The most common sleep disorder in tetraplegia is obstructive sleep apnoea (OSA), with prevalence estimates from 56 to 97%.[1, 15, 16, 149] For the individual, OSA has been associated with worse quality of life and substantial neurocognitive deficits in people with tetraplegia.[1, 108, 109] Common symptoms of OSA in tetraplegia include snoring, daytime sleepiness and witnessed apnoeas.[149] It is thought that neuromuscular weakness, reduced lung volumes, disruptions to the autonomic nervous system, obesity, medications and supine sleeping position all contribute to higher OSA prevalence in tetraplegia.[85]

Clinical practice guidelines for non-disabled populations and those with SCI recommend Continuous Positive Airway Pressure (CPAP) therapy for OSA.[48, 115] CPAP has been shown to effectively prevent the repetitive closure of the airway that occurs with OSA, and improve daytime sleepiness, quality of life and blood pressure in the non-disabled.[48, 49, 54] CPAP has also been found to improve daytime sleepiness in specialised populations such as stroke survivors and the elderly.[191, 198]

Despite its benefits, CPAP effectiveness is limited by poor adherence to, and acceptance of, the therapy. Adherence to CPAP in the non-disabled is reported to range between 30 and 60%.[55] Two small studies have followed CPAP uptake in people with chronic SCI and OSA, reporting adherence rates to be 25% (2/8) and 67% (4/6).[88, 96] However in both studies adherence was determined through self-report, which has been found an unreliable method.[55]

CPAP acceptance and adherence is a complex phenomenon that is not adequately explained through the quantitative analysis of risk factors. Several studies have attempted to understand the factors associated with CPAP adherence in the non-disabled using qualitative methodology.[199-203] Family and spousal support, beliefs about OSA, self-efficacy, and perceived barriers and facilitators to treatment are among the factors found to be influential. [202, 203]

Factors associated with CPAP adherence in chronic tetraplegia have not been thoroughly investigated but are likely to be different to those of people without disability because of additional physical and psychosocial issues; including poor upper limb function, increased tactile sensitivity to the face, increased nasal congestion, reduced likelihood of bed partner, competing medical issues, socio-demographic differences, and additional causes of poor sleep such as pain and spasms.[184] To our knowledge, there have been no qualitative studies investigating the unique influences on CPAP use in people with SCI, although the experience of sleep *per se* has been investigated using secondary analysis of qualitative data collected for a larger ethnographic study. This study identified poor sleep quality and quantity among participants, including frequent disturbances, and poor sleep patterns. Importantly, participants attributed their poor sleep to occupational disengagement, daytime fatigue and impaired cognitive functioning.[17]

Given the high prevalence and impact of OSA in tetraplegia, a more in-depth understanding of the unique experiences of CPAP use in this population is required to develop targeted interventions that improve adherence. The aims of the study were: 1. To estimate adherence to CPAP in people with tetraplegia and explore associations between baseline factors and adherence. 2. To understand the individual experiences of using CPAP; including barriers and enablers to CPAP use.

## 4.5 Methods

### 4.5.1 Design

Mixed methods study, including an observational study and qualitative semi-structured interviews, with a cohort of people with tetraplegia and OSA commencing CPAP therapy. Refer to online supplement (Section 4.9.1) for additional methods.

### 4.5.2 Setting

Hospital outpatient department in Melbourne, Australia.

### 4.5.3 Participants and data collection

Consecutive patietns with chronic (>1year post-injury), traumatic tetraplegia (level T1 or higher; American Spinal Injuries Association (ASIA) Impairment Scale (AIS) A, B, C or D) attending spinal outpatient departments were recruited for a larger multicentre study (Screening for OSA in Tetraplegia; SOSAT).[149] SOSAT data utilised for this study included: demographic information, Karolinska Sleepiness Scale (KSS),[204] Borg scale of nasal obstruction,[103] Congestion quantifier 5-item questionnaire,[168] General self-efficacy scale (GSES)[205] and sleep study data. (Online supplement Section 4.9.1). The sleep studies undertaken for the SOSAT study were unattended and performed in the participants' homes.

Upon receiving their sleep study results, all SOSAT participants recruited from the spinal outpatient clinic at the Austin Hospital in Melbourne, Australia were offered an outpatient appointment with a sleep physician. To access this service a referral from their treating doctor was required. Participants prescribed CPAP for OSA at this appointment were offered daytime auto-titrating CPAP implementation with an experienced sleep scientist at the CPAP clinic of the Austin Hospital, Melbourne. The autotitrating CPAP devices (AirSense 10 Autoset, ResMed, San Diego USA) wirelessly delivered real-time usage data to the treating clinical team. The sleep scientist contacted participants by telephone after three days, and at least weekly thereafter for four weeks. Additional support was available during the one-month period if required.

The sleep physician reviewed participants after four weeks. Immediately following this appointment, participants completed an in-depth semi-structured interview, the KSS, and a 7-item CPAP adverse events questionnaire.[180] The interview consisted of open-ended questions focusing on the experience of using CPAP, including barriers and enablers to CPAP use. CPAP usage data were obtained from the CPAP devices at one, six and 12 months. Interviews were conducted by an experienced interviewer with a clinical background in physiotherapy (MG).

### 4.5.4 Data analysis

Quantitative data, including CPAP usage, pressure and leak, patient reported questionnaires and demographic information, were analysed and reported descriptively.

CPAP usage data (mean hours per night) were reported over three time periods: Date of CPAP initiation to one month; one to six months; and six to 12 months. CPAP "adherent" was defined as achieving more than four hours average per night over the entire period.[60] Potential associations between baseline factors and mean nightly CPAP usage were explored with univariate linear regression analyses.

Interviews were audiotaped, anonymised and transcribed. Qualitative data were analysed using a general thematic approach.[206] Comparisons between "adherent" and "non-adherent" participants were made to identify patterns in the data and develop interpretations. Refer to Table 4.3 (Online supplement; Section 4.9.1.3) for for coding framework.

The study was approved by the Austin Health research ethics committee; AU/1/5FB02015. All applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during the course of this research.

## 4.6 Results

Of 44 eligible participants, 21 were referred to the sleep physician, 17 were prescribed CPAP, and 16 completed the study. (Figure 4.1) Participants were predominantly male (81%), mean age 56 years (SD=16) and mean body mass index (BMI) 27 (SD=6). On average they were two decades post injury, and had severe OSA. (Table 4.1) Refer to Online supplement (Section 4.9.2) for additional results.

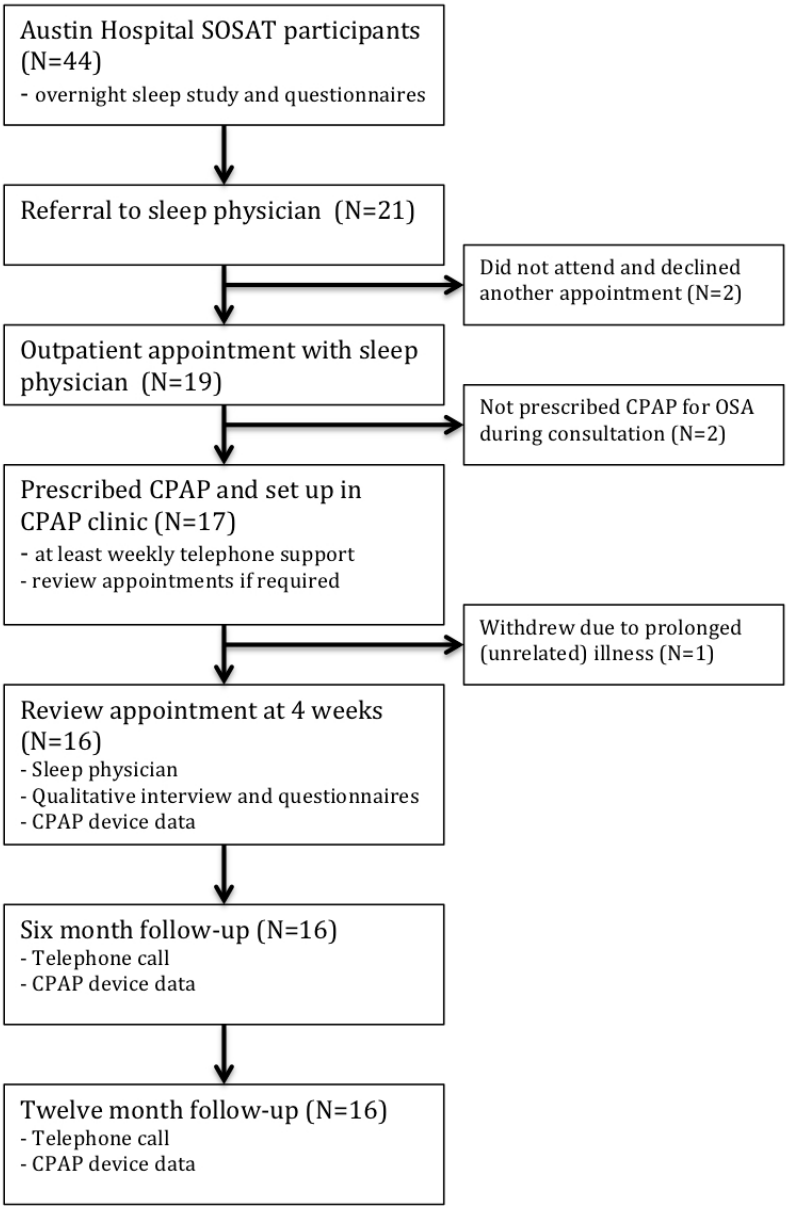


**Figure 4.1 Recruitment flowchart**

**Table 4.1 Demographic characteristics and other baseline data**

| | **N=16** |
|---|---|
| Age, years | 56.3 (15.5) |
| Gender male, %(n) | 81.3 (13) |
| Time since injury, years | 21.0 (14.9) |
| C1-C4, ASIA Impairment Scale (AIS) A,B,C, %(n) | 6 (1) |
| C5-C8, AIS A,B,C, %(n) | 81 (13) |
| T1-S3, AIS A,B,C, %(n) | 0 (0) |
| AIS D, at any level, %(n) | 13 (2) |
| C1-C4, %(n) | 6 (1) |
| C5-T1, %(n) | 94 (15) |
| AIS A, % (n) | 25 (4) |
| Body Mass Index (BMI), $kg/m^2$ | 27.2 (5.7) |
| Waist circumference, cm | 109.9 (19.4) |
| Apnoea Hyponoea Index (AHI), events/hour | 49.5 (30.0) |
| 3% Oxygen Desaturation Index (ODI), events/hour | 36.9 (27.0) |
| Borg scale of nasal obstruction, score/10 | 1.0 (1.4) |
| Congestion quantifier 5-item questionnaire, score range 0-20 | 3.8 (4.0) |
| General self-efficacy scale (GSES), score range 10-40 | 33.6 (4.3) |
| Karolinska Sleepiness Scale (KSS), score range 0-9: baseline | 4.3(2.1) |
| Karolinska Sleepiness Scale (KSS), score range 0-9: one month review | 2.9 (2.1) |
| Number of CPAP adverse events: one month review | 3.4 (1.8) |

**DeVivo et al classification of SCI severity [170]* *Values are mean (SD) unless otherwise indicated*

On average, the CPAP implementation appointment took 1.7 hours (SD=0.4). Participants were telephoned an average of six times between CPAP implementation and the review appointment. Seven participants required additional appointments with the sleep scientist, including nine additional face-to-face appointments and three home visits. The average time the sleep scientist spent with each participant in the first month was 3.1 hours (SD=1.5), including implementation, telephone calls and review appointments. On average, participants tried three different models of CPAP mask. Most settled with nasal pillows (n=10); while others opted for nasal masks (n=3), and full face masks (n=3); nine used a chinstrap.

At one month, mean nightly CPAP use was 3.1 hours, with 38% achieving at least four hours per night. Mean nightly use dropped to 2.6 hours at six months and 2.1 hours at 12 months, with one quarter of the sample achieving at least four hours per night in these time periods. (Table 4.2) Individual participant CPAP usage data are displayed in Figure 4.2 and Table 4.5 (Online supplement, Section 4.9.2), showing six participants swapping their "adherent status" between months one and six (two became adherent and four became non-adherent). No participant changed adherent status after six months. By 12 months CPAP usage was distinctly bimodal and stable, with either high usage (>6 hours per night) or low usage (<3 hours per night). Average 95$^{th}$ percentile pressure ranged from 10 to 13 cm$H_2O$ during the three time periods, while average 95$^{th}$ percentile leak ranged from 21 to 26 litres/minute. (Table 4.2)

**Table 4.2 CPAP data (usage, 95$^{th}$ percentile pressure and 95$^{th}$ percentile leak)**

| | 0 to 1 month (N=16) | 1 to 6 months (N=16) | 6-12 months (N=16) |
|---|---|---|---|
| Mean nightly use, hours | 3.1 (2.5) | 2.6 (2.8) | 2.1 (3.2) |
| Proportion with > 4 hours use per night, % (n) | 37.5 (6) | 25 (4) | 25 (4) |
| Mean nightly 95$^{th}$ percentile pressure, cm$H_2O$ | 13.1 (3.2) [a] | 12.2 (2.1) [a] | 10.0 (4.6) [b] |
| Mean nightly 95$^{th}$ percentile leak, L/min | 25.7 (19.6) | 20.8 (10.0) [c] | 22.8 (13.6) [d] |

*Values are mean (SD) unless otherwise indicated* *[a] N=13, [b] N=8, [c] N=14, [d] N=9*

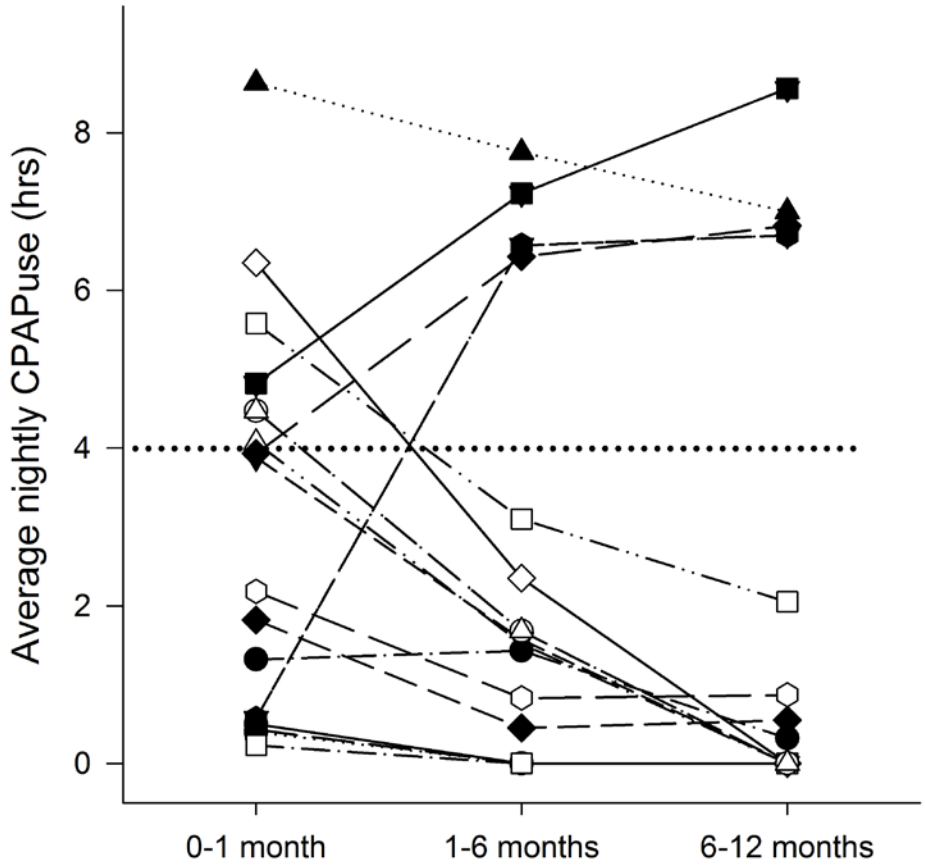


**Figure 4.2 Individual average nightly CPAP usage, measured at one, six and 12 months.**

CPAP use (average nightly hours) at six and 12 months were strongly associated with more hours spent with the sleep scientist in the first month and greater years since injury ($p<0.05$; Table 4.4, Online supplement, Section 4.9.2). Improvements in subjective daytime sleepiness in the first month appeared weakly associated with greater CPAP use at six ($p=0.06$) and 12 months ($p=0.05$; Table 4.4) No associations between any other baseline variables with CPAP use were identified.

## 4.7 Qualitative interview results

### 4.7.1 The burden of CPAP versus the benefit: "the love-hate relationship"

*(72 year old male, C6 AIS-D)*

Most people in this study described the active, conscious decisions they made about whether the benefits of CPAP outweighed the burdens and hence whether to continue use. All participants experienced burdens and adverse events from using CPAP, and the

trade-off between the perceived burden and the perceived benefit appeared to impact adherence to the therapy. For some, the perceived benefits and burdens were negligible, requiring the participant to decide whether the treatment was worthwhile. These participants spoke of their plans to discontinue CPAP for a specified period of time to better understand the benefits and to enable an informed decision of whether to continue. None of the participants in this group were CPAP users at six or 12 months.

> *I think the only way to prove it to myself is if I go off the machine for two weeks and then go back on and just see the difference. And that will probably convince me one way or the other. (79 year old female, C5 AIS-C)*

For others, both the immediate daytime benefits and the burdens were substantial. Three participants belonging to this group actively engaged with health professionals to troubleshoot issues and were able to overcome the burdens to become CPAP users. For those with high burden and little benefit, or low burden and substantial benefit, the decision of whether to continue with CPAP was easier, and their user status tended to be determined earlier. Unfortunately some participants did not experience any benefits from CPAP because they were unable to overcome the substantial burdens encountered from the beginning.

> *I've never been able to fall asleep with it. I want to, but at the same time, am I fooling myself? (49 year old male, C5 AIS-C)*

The majority of participants were motivated by the immediate daytime benefits of having better sleep. Most were not concerned by the long-term health consequences of untreated OSA.

> *For me [the main reason I am using CPAP is], so I'll have better days, physically and mentally. (65 year old female, C6 AIS-C)*

> *I know how the professionals would put it, and that's sleep apnoea can cause strokes or heart attack or whatever. I've never been one to worry about anything*

*like that, and I'm probably still not. If I didn't use it, it wouldn't overly concern me in that respect. (72 year old male, C6 AIS-D)*

This concept of burden versus benefit of CPAP is represented in Figure 4.3, which describes four groups defined according to their perceived benefit and burden. Participants were retrospectively categorised to the most appropriate group (A-D) based on their interview data, and average nightly CPAP use over the three time periods were calculated for each group (Table 4.6, Online supplement, Section 4.9.2). This pilot exercise demonstrated that those whose perceived benefit from CPAP was high (B&D) had substantially higher CPAP use than those reporting low benefit (A&C). Perceived burden impacted CPAP use to a lesser degree than perceived benefit.

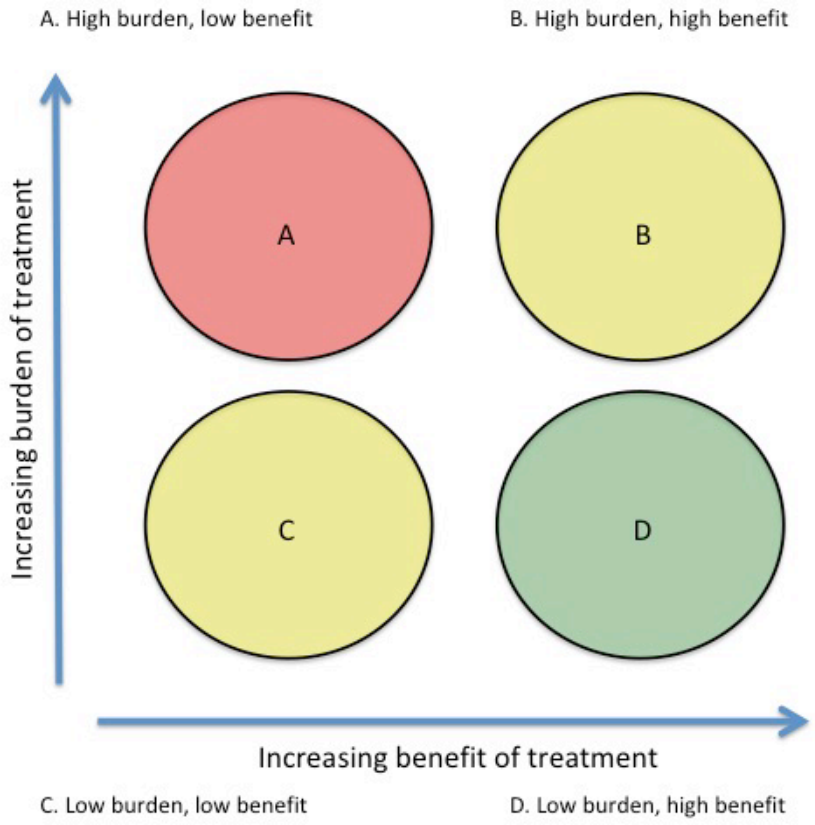


**Figure 4.3 CPAP burden versus benefit matrix**

The specific burdens and benefits are described in detail in the online supplement. Briefly, common burdens included issues with mask discomfort and fit, causing air leak,

skin irritation and breakdown, and dry eyes and mouth. Considerable trial and error was required to overcome these issues. Participants also described psychosocial and emotional problems, including guilt about additional partner burden, claustrophobia, frustration and fear. Some participants had difficulty sleeping with the device. These problems were exacerbated by their physical disability, particularly limited upper limb function, and the already substantial workload associated with managing their SCI and the associated complications. At the six and 12 month review phone calls, several participants reported discontinuing CPAP when unwell in order to simplify their healthcare routines.

Benefits included improvements to sleep quality and sleep hygiene. Less daytime napping, reduced snoring, waking up refreshed, and fewer leg spasms at night were commonly reported. Other reported benefits included improvements in mood, energy levels, productivity, alertness and concentration.

Additional barriers and enablers to CPAP use, such as partner/family support and health professional support are also discussed in detail in the online supplement (Section 4.9.3). Briefly, partner/family support appeared moderately important for some, but merely having this support did not ensure CPAP adherence. Overall, participants of this study were highly satisfied with the assistance they received from the health professionals involved in CPAP implementation.

### 4.7.2 Barriers to OSA diagnosis

While not an *a priori* focus of the interviews, two themes emerged relating to OSA diagnosis barriers.

#### *4.7.2.1 Poor recognition of OSA symptoms prior to diagnosis and treatment*

Several participants were surprised by the improvements they experienced from CPAP. Many felt they had incorrectly attributed daytime sleepiness to aging with a SCI, and did not realise the extent of their symptoms of OSA until after they had been treated. For these reasons many had not reported any symptoms of OSA to a health professional, and were initially surprised by their OSA.

*No, I didn't realise, I just took it for granted that this is what happens as you get old with quadriplegia. I thought, 'well, just suck it up'. But now I realise what I've been missing out on. (71 year old male, C6 AIS-A)*

*Personally, I was not aware of any problem whatsoever. I thought 'I'm not concentrating enough, I'm getting old, I haven't got enough to do.' That has turned around now, so it is obvious. It's made me aware of what the situation was. (72 year old male, C6 AIS-D)*

#### *4.7.2.2 Overnight in-laboratory sleep studies are prohibitive to diagnosis*

Most participants felt that having an overnight sleep study in a hospital or sleep laboratory would have been too difficult, and had it not been for the SOSAT study offering the test in their home, they would never have been diagnosed and subsequently treated for OSA. Their concerns centred on the potential disruption to their daily routines, and the inability of sleep laboratories to cater for the needs of people with disability.

*A couple of years ago the Austin contacted me and wanted me to come in to do it [overnight sleep study], but three kids, work, my wife's work; it was just too hard. I look back and now think I should have done it years ago. (43 year old male, C6 AIS-B)*

*And being in a wheelchair, the thought of having to travel somewhere to go and do a sleep study and stay overnight, it's not very appealing. But obviously since you came out to the house it meant that I didn't have to leave home so it made it a lot easier. (49 year old male, C5 AIS-B)*

## 4.8 Discussion

CPAP adherence was low in this sample of people with chronic tetraplegia and OSA. Half of the participants were regularly using CPAP at one month, however this had reduced to a quarter by six months. Between one and six months, six (38%) participants changed their "adherence status", from above to below four hours per night or vice

versa. Adherence status was then stable for all participants in the following six months. This suggests that CPAP patterns, which are established within a week in the non-disabled with OSA,[182] can take up to six months in people with tetraplegia.

In this small study, we found that greater CPAP use at six months was strongly associated with more time spent with the sleep scientist in the first month. We speculate that participants who were more engaged were more likely to overcome the initial problems and continue with the treatment. Our qualitative data suggest it was the perceived benefit that drove the participants to seek solutions. These solutions required more time from the sleep scientist, but it was the perceived benefit, not simply "more therapy" that drove the improvements.

The perceived burdens relative to the perceived benefits of CPAP were identified as a major theme in this study. This same 'trade-off' has also been described in non-disabled populations.[203] However for people with tetraplegia, this decision is also made in the context of living with SCI. Most people with tetraplegia experience multiple secondary complications, with bladder and bowel dysfunction, spasms, pain, and pressure injuries being the most common.[207-209] The decision about whether CPAP is worthwhile was strongly influenced by the overall, ongoing burden of managing these SCI complications. Unfortunately the complexity of living with SCI often tipped the balance in the direction of discontinuing the therapy.

The concept of burden of treatment (BoT) has grown in the literature in the last decade in response to the rising prevalence of multi-morbidity. A recent meta-analysis of qualitative studies investigating BoT in people with chronic diseases found that the magnitude of the burden is related to the workload required, the individual's capacity, and the environmental context. Patients often prioritise treatments to reduce the workload, and try to integrate the treatments into their daily lives.[210] Data from our study are concordant with these findings. At the six and 12 month reviews, our participants commonly reported discontinuing CPAP during times of illness. This phenomenon has been reported previously. In another study investigating OSA treatment adherence in people with SCI, participants reported only tolerating bi-level

positive airway pressure when their health was stable, and frequently suspended treatment during periods of illness.[112]

Patient reported measures of BoT have been developed for people with multi-morbidity.[211, 212] Rosbach et al[210] reason that the weight of BoT should be assessed in those with multi-morbidity, and health care providers should aim to reduce treatment burden where possible. Given the nature of SCI, BoT should arguably be considered in this population when prescribing new and challenging treatment regimes, such as CPAP.

The simple matrix assessing perceived burden and benefit from CPAP in the first few weeks of treatment (Figure 3) could potentially be applied to predict long-term CPAP adherence. Further research could establish the clinical utility of this model to categorise patients into the four types of early CPAP users, in order to guide interventions to improve adherence. For example, those in the high burden, high benefit group (Group B) might be offered intensive support including home visits and/or additional appointments with health professionals to help them to overcome their substantial burdens. Given our finding that CPAP use takes longer to establish in this population, this support should be offered for a longer period of time. Potential strategies for those with low burden and low benefit (Group C) might include more education about the longer-term consequences of OSA and benefits of CPAP treatment. Those with high burden and low benefit (Group A) could be offered alternative treatments for OSA; and finally, those with high benefit and low burden (Group D) could be reviewed periodically to monitor adherence and encourage continuation of the therapy during or after illness.

With the exception of reduced leg spasm, the daytime benefits described by participants of this study, such as improved sleep quality, reduced daytime sleepiness, and improvements in mood and cognition, were all common to other population groups.[213] In contrast, many of the burdens were either unique to people with SCI or augmented by their disability. Guilt about the additional burden using CPAP placed on partners was a major concern for many participants in this study. Conversely, qualitative research in adults without disability has identified that guilt about the impact on partners by *not* using the therapy is a motivator for use.[112] Fear of problems,

particularly recurrent skin break down, was another significant barrier for participants in this study, potentially exacerbated from previous experiences of pressure injuries. Frustration was usually described in relation to the participant's inability to independently adjust the mask, and we hypothesise that claustrophobia is also magnified in this population because of reduced independence and hypersensitivity to the face. These additional and amplified burdens are likely to contribute to lower CPAP adherence in this population.

That participants in this study were not motivated by the long-term consequences of untreated OSA may reflect health information fatigue from managing multiple co-morbidities. In contrast, several qualitative studies in non-disabled populations have reported that fear of long-term consequences of OSA is an important motivator to CPAP use.[201, 202, 214]

Given the unique and complex burdens and motivations for CPAP use in tetraplegia, we speculate that non-complicated OSA may be better managed within a specialist spinal unit. Specialised spinal units are generally responsible for the overall management of the person's SCI and associated complications, coordinating care with other specialists as required. Diagnosis and treatment of non-complicated OSA is managed independently of respiratory/sleep specialists in several spinal units around the world, although this is not the usual model. We hypothesise that patient outcomes and satisfaction would improve with either enhanced disability training for respiratory/sleep units, or enhanced OSA management training for spinal units. Either way, research into alternative models of OSA care for people with tetraplegia is needed.

Despite the low adherence to CPAP and the high treatment burden reported by many participants in this study, the daytime benefits for those adherent to the therapy appeared to be substantial. One quarter of our sample was adherent at six and 12 months, with average nightly use of approximately seven hours among these four individuals. Given the positive effect CPAP had on our adherent participants, our data would suggest that it remains a worthwhile therapy in this population with such high prevalence of OSA. Ultimately, a better therapy will replace CPAP as the first line treatment for OSA, but until then, research investigating interventions to reduce burden and improve adherence is warranted.[115]

While not a focus of the study, barriers to OSA detection emerged as a major issue. Participants reported their reluctance to attend an overnight sleep study in a sleep laboratory, citing the potential disruption to healthcare routines and the inability of non-spinal health services to meet the needs of people with tetraplegia. Available data suggest that OSA is largely under-diagnosed and under-treated in SCI.[105] Our qualitative data also suggest that many patients are not being screened, diagnosed and treated for OSA, despite the high prevalence. A simplified ambulatory model for diagnosing moderate to severe OSA in tetraplegia has recently been published, offering an alternative to overnight sleep laboratory testing.[93, 149] By overcoming this major barrier to OSA diagnosis, ambulatory diagnostic models have the potential to substantially increase diagnosis rates in this population.

### 4.8.1 Limitations

This was a small study of 16 people living with chronic tetraplegia. As such the quantitative analysis should be considered as exploratory and hypothesis generating. Only five of the 16 interviews were double-coded by two researchers (MG and AR), however the coding framework was revised after the first five interviews and guided the analysis of the remaining 11. Our sample of convenience did not allow for sampling until saturation of themes; nonetheless saturation was achieved with no new themes emerging for at least the last five interviews.

### 4.8.2 Conclusion

Adherence to CPAP is low among people with tetraplegia and OSA. However the benefits described in this study by the quarter that used it well were substantial. People with tetraplegia experience high burden from CPAP, exacerbated by their disability. More intensive support, for a longer period of time is recommended to help them to overcome these burdens and to allow them to be established on treatment. Individuals' adherence patterns were set by six months and remained relatively unchanged out to 12 months.

## 4.9 Online supplement

### 4.9.1 Additional Methods

#### *4.9.1.1 Participants*

Consecutive patients, with chronic (>1 year post injury), traumatic tetraplegia (level T1 or higher; ASIA Impairment Scale A, B, C or D), attending the spinal outpatient or inpatient units between September 2015 and April 2017 at three spinal units were invited to participate to the Screening for OSA in Tetraplegia (SOSAT) study.[149] Only participants from the Austin Hospital, Melbourne Australia site were also invited to participate in this sub-study (N=44). All participants provided informed consent in accordance with the ethics approval from The Austin Hospital Ethics Committee.

#### *4.9.1.2 Data collection*

As part of the SOSAT study, unattended polysomnography was conducted in the participants' homes. Sleep studies were sleep staged and respiratory scored by an experienced sleep scientist. Demographic data were collected from the medical record and abdominal circumference was measured in supine on the night of the sleep study. The following questionnaires were also obtained on the night of the sleep study and reported in this study: Karolinsksa Sleepiness Scale (KSS),[204] Borg scale of nasal obstruction,[103] Congestion quantifier 5-item questionnaire,[168] General self-efficacy scale (GSES).[205]

Immediately prior to the interview, participants repeated the KSS; and on conclusion of the interview, the 7-item CPAP adverse events questionnaire.[180] Following the one month review, participants were offered ongoing clinical support through the CPAP clinic at the Austin Hospital.

#### *4.9.1.3 Qualitative data analysis*

The researcher conducting the interviews (MG) had experience with qualitative research methods and the clinical area.[149, 215] The first two interviews were open-coded by two researchers together (MG and AR) to identify recurrent themes and develop the initial coding framework for analysis of subsequent interviews. The researchers viewed

the data through a "theoretical" lens, specifically the barriers and enablers to CPAP use, and as such the coding framework reflected this.[206] Despite this general approach, themes in addition to barriers and enablers of CPAP use were inductively identified in the data and also included in the analysis. The same two researchers then independently coded the next three interviews and met to discuss and resolve any differences, and update the coding framework. MG coded the remaining interviews and further refinement to the coding framework was discussed with AR. See Table 4.3 for the coding framework.

**Table 4.3 Qualitative coding framework**

<table>
<tr><td colspan="2">1. Burdens VS Benefit = overall trade-off between burden of the CPAP machine and the daytime benefits.</td></tr>
<tr><td>Common burdens:<br>Mask issues<br>• Mask discomfort/ fit/air leak<br>• Skin irritation/breakdown/dry eyes and mouth/ blood nose<br>• Trial and error required<br>Psychosocial/emotional<br>• Concerns about attractiveness<br>• Guilt about partner burden<br>• Claustrophobia<br>• Frustration<br>• Fear of problems<br>Difficulty sleeping</td><td>Common benefits:<br>Sleep quality/sleep hygiene<br>• Easier to get to sleep<br>• Waking up brighter/ready to get up in the morning<br>• Less snoring<br>• Less napping<br>• Less spasm<br>Less daytime sleepiness<br>Psychosocial benefits<br>• Improved mood<br>• Partner sleeping better<br>• More energy / productivity<br>• Increased social activity<br>Cognitive benefits<br>• Increased alertness<br>• Improved concentration</td></tr>
<tr><td colspan="2">Other barriers and enablers (influencing factors)<br>• Cost of device and masks etc<br>• Partner/family support<br>• Health professional support</td></tr>
</table>

| |
|---|
| ○ Understanding of the limitations association with SCI that may impact CPAP usage (i.e. mask adjustment)<br>○ Face-to-face monitoring of CPAP usage<br>• Self-efficacy<br>• SCI related physical limitations (Difficulty adjusting mask because of SCI related physical limitations, especially upper limb)<br>• Complicated health and social circumstances associated with SCI |
| **2. Motivations**<br>• Motivated by immediate daytime benefits rather than long-term health consequences (e.g stroke, CVD) |
| **3. Barriers to OSA diagnosis in SCI**<br>• Poor recognition of OSA symptoms prior to diagnosis and treatment<br>• Overnight stay in sleep lab prohibitive to diagnosis |
| **4. Equipment modifications for people with SCI**<br>• Remote on-off switch would be very helpful |

### 4.9.2 Additional results

Thirteen participants lived with family (10 with their partner). Three lived alone. Six of the participants were in regular employment, and six drove a car.

**Table 4.4 Univariate linear regression: associations between baseline variables and hours of CPAP use at three timepoints.**

| | 0-1 month | | 1-6 months | | 6-12 months | |
|---|---|---|---|---|---|---|
| Variable | Co-efficient | P value | Co-efficient | P value | Co-efficient | P value |
| Age, years | 0.01 | 0.90 | 0.04 | 0.40 | 0.04 | 0.50 |
| Gender, male | 1.60 | 0.34 | 2.04 | 0.27 | 1.81 | 0.39 |
| AIS A | -1.12 | 0.46 | -0.19 | 0.91 | -0.51 | 0.79 |
| BMI, kg/m2 | 0.01 | 0.95 | 0.08 | 0.57 | 0.10 | 0.50 |
| Waist circumference, cm | 0.001 | 0.98 | 0.06 | 0.10 | 0.08 | 0.08 |
| AHI, events/hour | -0.01 | 0.83 | 0.01 | 0.76 | 0.01 | 0.71 |
| 3% ODI, events/hour | -0.004 | 0.87 | 0.02 | 0.59 | 0.02 | 0.49 |
| Borg scale of nasal obstruction | -0.70 | 0.15 | 0.39 | 0.47 | 0.62 | 0.31 |
| Congestion quantifier 5-item | -0.31 | 0.06 | 0.07 | 0.71 | 0.02 | 0.93 |
| General self-efficacy scale | -0.09 | 0.58 | 0.12 | 0.49 | 0.21 | 0.29 |
| Change (improvement) in KSS | 0.06 | 0.75 | 0.38 | 0.06 | 0.45 | 0.045* |
| Time with clinician scientist, hours | 0.70 | 0.11 | 1.26 | <0.01* | 1.22 | 0.02* |
| Time since injury, years | 0.07 | 0.10 | 0.12 | 0.01* | 0.12 | 0.02* |

*p<0.05

Appointments with the sleep physician were conducted between May 2016 and July 2017. The average time from date of referral to appointment was 55 days (range 15-105). Fourteen participants were initiated with CPAP immediately following the appointment with the sleep physician; the remaining two were initiated within two weeks.

**Table 4.5 Individual patient data: CPAP usage, adverse events, subjective sleepiness, and time with clinician scientist for CPAP initiation and troubleshooting.**

| ID | CPAP hr/n 0-1mth | CPAP hr/n 1-6mth | CPAP hr/n 1-6mth | KSS B/L | KSS F/U 1mth | Hours with SS | No. hospital appts. | No. home visits | AE Dry mouth | AE Nasal | AE Eye | AE Claustr ophobia | AE Facial /skin | AE Mask fit | AE Noise | Total No. AE |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 2.18 | 0.83 | 0.87 | 3 | 7 | 2.25 | 0 | 0 | Y | N | N | N | N | N | N | 1 |
| 2 | 1.32 | 1.43 | 0.32 | 5 | 2 | 3 | 0 | 0 | N | Y | N | Y | N | Y | Y | 4 |
| 3 | 1.82 | 0.45 | 0.55 | 1 | 3 | 2.5 | 0 | 0 | Y | Y | Y | Y | N | Y | Y | 6 |
| 4 | 0.57 | 6.57 | 6.7 | 5 | 2 | 5.5 | 1 | 1 | Y | Y | N | Y | N | Y | Y | 5 |
| 5 | 0.43 | 0 | 0 | 3 | 7 | 3 | 0 | 1 | Y | Y | N | Y | Y | Y | N | 5 |
| 6 | 4.82 | 7.23 | 8.56 | 6 | 1 | 2.25 | 0 | 0 | N | N | N | N | N | N | N | 0 |
| 7 | 3.93 | 6.43 | 6.82 | 9 | 1 | 4 | 2 | 0 | Y | Y | N | Y | N | Y | N | 4 |
| 8 | 4.47 | 1.68 | 0 | 2 | 3 | 3 | 0 | 0 | Y | Y | N | N | Y | Y | Y | 5 |
| 9 | 6.35 | 2.35 | 0 | 3 | 3 | 3 | 0 | 0 | Y | N | Y | N | N | Y | N | 3 |
| 10 | 8.63 | 7.75 | 7 | 3 | 1 | 7.5 | 4 | 0 | Y | Y | Y | N | Y | Y | Y | 6 |
| 11 | 3.88 | 1.57 | 0 | 3 | 2 | 3 | 1 | 0 | Y | Y | N | N | Y | N | N | 3 |
| 12 | 0.5 | 0 | 0 | 7 | 1 | 1.75 | 1 | 0 | Y | N | N | N | N | N | Y | 2 |
| 13 | 0.23 | 0 | 0 | 6 | 1 | 2 | 0 | 0 | N | N | N | N | Y | Y | N | 2 |
| 14 | 4.07 | 1.52 | 0 | 6 | 5 | 2.9 | 0 | 1 | Y | Y | N | N | Y | Y | N | 4 |
| 15 | 0.4 | 0 | 0 | 3 | 6 | 2.25 | 0 | 0 | N | Y | N | N | Y | Y | N | 3 |
| 16 | 5.58 | 3.1 | 2.05 | 3 | 2 | 1.5 | 0 | 0 | Y | N | N | N | Y | N | N | 2 |

*Variable names: Participant ID; Average CPAP hours per night 0-1 month; Average CPAP hours per night 1-6 months; Average CPAP hours per night 6-12 months; Baseline Karolinska Sleepiness Scale; Follow-up Karolinska Sleepiness Scale at 1 month; Number of additional face to face hospital appointments; Number of home visits; 7 item adverse event questionnaire: Dry mouth; 7 item adverse event questionnaire: Nasal symptoms; 7 item adverse event questionnaire: Eye problems; 7 item adverse event questionnaire: Claustrophobia; 7 item adverse event questionnaire: Facial soreness or skin irritation from the mask; 7 item adverse event questionnaire: Mask fit; 7 item adverse event questionnaire: Noise problems; Total number of adverse events reported on 7 item adverse event questionnaire.*

**Table 4.6 Mean nightly hours at months one, six and 12 for participants categorised into groups defined by the CPAP burden versus benefit matrix.**

| | Mean nightly CPAP use (SD): 0-1 month | Mean nightly CPAP use (SD): 1-6 months | Mean nightly CPAP use (SD): 6-12 months |
|---|---|---|---|
| Group A (N=6) | 1.6 (1.9) | 0.5 (0.8) | 0.0 (0.0) |
| Group B (N=4) | 4.3 (3.8) | 4.3 (3.4) | 3.6 (3.8) |
| Group C (N=3) | 2.7 (1.6) | 1.3 (0.4) | 0.4 (0.4) |
| Group D (N=3) | 4.8 (0.8) | 5.6 (2.2) | 5.8 (3.4) |

### 4.9.3 Qualitative interviews: Additional results

#### *4.9.3.1 Common benefits: "you end up getting a better sleep" (64 year old male, C6 AIS-B)*

Many participants described with enthusiasm the improved quality of their sleep and improved sleep patterns. Most commonly, they reported waking up feeling refreshed and ready to start the day.

> *On days where I do use CPAP and I sleep fine with it, I feel like I can just fly out of bed. (23 year old male, C7 AIS-A)*

Many reported snoring less, with obvious benefits to partners and family members. Deeper, longer sleep, ease of getting to sleep and less daytime napping were commonly cited changes to sleep hygiene and quality. Several participants noticed that with CPAP they were waking less from leg spasms during the night.

> *Going back to before [using CPAP], the sleep was spread over the 24 hours. It's getting more compacted now. (75 year old male, C6 AIS-B)*

> *With the CPAP I'm finding that I'm more alert and I don't need a nap. I can stay awake in the afternoon. (65 year old female, C6 AIS-C)*

*But with the sleep machine I am able to sleep throughout the night without the spasm or without being woken up by the spasm. (43 year old male, C6 AIS-A)*

These improvements in sleep quality resulted in functional, psychosocial and cognitive benefits for many participants. Several participants reported feeling more alert, having more energy and more ability to concentrate during the day. Functional gains included increased productivity at work, increased social activity and driving more.

*I feel so refreshed. I've got more energy, more get up and go. Not that physically I can do a great deal, but there are a lot of things that I didn't accomplish during the day that I'm doing now. (71 year old male, C6 AIS-A)*

*I'm definitely thinking clearer. (72 year old male, C6 AIS-D)*

Improvements in mood were also cited by many, who had either noticed this themselves, or were told by family and friends. In particular, they described feeling less irritable, and having more tolerance with others.

*Even the carers have said that my moods are better. (64 year old male, C6 AIS-B)*

*My family notice that I'm not as short and as sharp. (75 year old male, C6 AIS-B)*

### 4.9.4 Common burdens: "where do I start?"

Most of the burdens from CPAP were associated with wearing a mask. Issues with mask fit and discomfort were common and often led to physical problems such as skin breakdown, a sore, bleeding nose, and dry eyes and mouth.

*My eyes are very sore of a morning, and my mouth gets very dry. (65 year old female, C6 AIS-C)*

*I finished up with pressure marks on the inside of my septum and then I think I had a scab under my nose, which has gone now. (71 year old male, C6 AIS-A)*

Air leak was a problem for many, who also described feeling intense frustration from not being able to adjust the mask when this occurred.

*And because of every slight movement you make during your sleep also moves the nasal mask, and so that caused a lot of leakage and also discomfort. (43 year old male, C6 AIS-A)*

*And leaking air and blowing air in my eyes during the night, it's really frustrating. (23 year old male, C7 AIS-A)*

"Trial and error" and perseverance was a common theme in the qualitative data. Participants reported making adjustments to pressure, ramp time, humidity and temperature, and trying different masks and attachments, such as a chin strap, in order to overcome some of the problems.

*I reckon it takes you easy six weeks to three months. I'm only just there now. (79 year old female, C5 AIS-C)*

*I think for most people it would be trial and error because you're not going to all of a sudden put something over your mouth and it's going to be perfect. I don't think that's going to happen. (65 year old female, C6 AIS-C)*

Some were not prepared to persevere because they were fearful that the problems they had experienced, such as skin breakdown, would occur again.

*I wasn't game to try it again because I don't want to get blisters again. (65 year old male, C4 AIS-C)*

Unfortunately many reported psychosocial burdens from the CPAP. Feelings of guilt associated with increased partner and carer burden were common. They spoke of the

amount of assistance already required from their carers, and the inclusion of CPAP at night was seen to be unfairly adding to the workload.

> *It makes me feel like I'm a nuisance. Waking up my husband once a night is fine, but four to five times, I think that's a bit unfair. It's a big ask. (65 year old female, C6 AIS-C)*

Others resented having another health problem to manage and another piece of equipment to service and clean. Many described having complicated night-time routines for other SCI related care, such as spasm and pain management, skin care and bladder complications. Some participants felt that CPAP was adding further burden to an already difficult schedule.

> *I guess it's just another thing you have to do. Just another thing that you need to worry about, to annoy you. (43 year old male, C6 AIS-A)*

For these reasons, participants reported discontinuing CPAP when they became unwell with regular illnesses such as colds, or with SCI related complications. At the six and 12 month review phone calls, many participants reported stopping CPAP because of an unrelated health issue, as a way of simplifying their routines. In some cases, they did not recommence CPAP after recovering from their illness.

Feelings of frustration and claustrophobia were usually associated with impaired physical function from the SCI, particularly upper limb function. Participants described a sense of loss of control and fear from not being able to adjust or remove the mask, or turn off the machine if required.

> *I also found that lying down flat, and I couldn't move, that anything could have happened to me. I had no control over it, and being claustrophobic, that made it worse as well. (65 year old female, C6 AIS-C)*

Related to this were suggestions to modify the CPAP device to make it easier for people with SCI to use it independently. Modifications to the "on-off" switch, so they could turn it off in the night rather than waking their carer to do so, was proposed by several

participants. Others had ideas for different designs to the strapping mechanism holding the mask to the face.

> *What I thought with the machine is it could have some sort of control where you can turn it on and off from in the bed, because there'd be a lot of people who'd want to turn it off and they can't. (65 year old female, C6 AIS-C)*

Concerns over the appearance of the mask were apparent for some. This was either related to seeming unwell and disabled, or feeling unattractive.

> *When I have it on and I'm in bed, I feel like a Martian, I feel very unattractive and very ugly. (65 year old female, C6 AIS-C)*

#### *4.9.4.1 Partner and family support*

Partners and family were supportive and encouraging for some, and not for others. Whilst CPAP adherent participants tended to have supportive partners, families and carers, merely having this support did not ensure CPAP use.

> *Oh, she's quite happy [with CPAP], because any diagnosis that I get she always sees the darkest side of it, and thinks, you could have a stroke, or you could have a heart attack, where I'm totally the opposite. (72 year old male, C6 AIS-D)*

> *But her words are "you should be using it, that's what it's there for". I'll get around to it one day, I suppose. (65 year old male, C4 AIS-C)*

Four participants reported their partners and families were not supportive of their CPAP use, mostly because it negatively impacted their own sleep, and this appeared to strongly influence the participant's decision to discontinue the therapy.

> *I want to [use CPAP] but I'm not going to do it if I'm going to disturb her or interrupt her. (49 year old male, C5 AIS-C)*

#### *4.9.4.2 Health professional support*

Overwhelmingly, participants were satisfied with the support they received from the health professionals involved in their CPAP prescription, implementation and troubleshooting. In particular, participants appreciated the weekly phone calls, and the ability to speak with a health professional whenever they needed to troubleshoot issues.

> *I know I could have called whenever I needed to, and [health professional name] rang me a few times and said "I noticed this or that" or "Are you right?", so that was helpful. (56 year old male, C5 AIS-B)*

> *They were great because [health professional name] rang me a few times just to check up. She was able to turn the pressure down from her end. And then I was able to use it so that was great. (44 year old woman, C6 AIS-C)*

One participant felt that the health professionals who treated him lacked understanding of the health issues and physical limitations associated with having a SCI, in particular the difficulties he experience donning and doffing and adjusting the mask with limited upper limb function.

> *The people here bent over backwards to help but didn't appreciate the problem of quadriplegia and our inability to handle things. I think they have to look more at people's ability to do stuff without the use of fingers. (71 year old male, C6 AIS-A)*

While most participants were happy with the ambulatory model of care, which minimised the need to travel for appointments, two participants suggested that more face-to-face monitoring of CPAP might have hastened the process of overcoming problems.

> *It wouldn't hurt for either the patient to come in and spend an hour in the hospital with it on and let the people at the sleep clinic actually see the problems first hand. (71 year old male, C6 AIS-A)*

*If it wasn't for me working it'd be easier to go in for appointments and get it sorted. I would have liked to go in and stay a night, so I can talk to them during the night about it. (23 year old male, C7 AIS-A)*

*"The truth is rarely pure and never simple." ~ Oscar Wilde*

# 5 UNDERSTANDING THE CLINICAL MANAGEMENT OF OBSTRUCTIVE SLEEP APNOEA IN TETRAPLEGIA: A QUALITATIVE STUDY USING THE THEORETICAL DOMAINS FRAMEWORK.

## 5.1 Overview of Chapter 5

The research presented in the previous two chapters has described CPAP use and identified many patient-level barriers and enablers to optimal OSA management. Chapter 5 presents original research to systematically describe the clinical management of OSA in tetraplegia, and investigate the influences on these clinical practices. The participants of this research were the doctors responsible for the overall rehabilitation and management of people SCI, within a specialist spinal rehabilitation unit. This qualitative research utilised the Theoretical Domains Framework to explore the influences on clinical behaviours.

This chapter is presented as a journal article that was submitted for publication in a peer-reviewed journal in May 2018. The online supplementary file that accompanies this manuscript contains only the interview guide. This is located in Appendix 8.5. The submitted version of the manuscript and online supplement are provided, with minor changes to the formatting. An addendum to the manuscript is provided at the end of the chapter (Section 5.7.3). The addendum provides additional discussion of material that had not been published at the time of manuscript submission.

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## 5.3 Abstract


### 5.3.1 Background

Clinical practice guidelines recommend further testing for people with tetraplegia and signs and symptoms of obstructive sleep apnoea (OSA), followed by treatment with positive airway pressure therapy. Little is known about how clinicians manage OSA in tetraplegia. The theoretical domains framework (TDF) is commonly used to identify determinants of clinical behaviours. This study aimed to describe OSA management practices in tetraplegia, and to explore factors influencing clinical practice.

### 5.3.2 Methods

Semi-structured interviews were conducted with 20 specialist doctors managing people with tetraplegia from spinal units in Europe, UK, Canada, USA, Australia and New Zealand. Interviews were audiotaped for verbatim transcription. OSA management was divided into screening, diagnosis and treatment components for inpatient and outpatient services, allowing common practices to be categorised. Data were thematically coded to the 12 constructs of the TDF. Common beliefs were identified and comparisons were made between participants reporting different practices.

### 5.3.3 Results

Routine screening for OSA signs and symptoms was reported by 10 (50%) doctors in inpatient settings and eight (40%) in outpatient clinics. Doctors commonly referred to sleep specialists for OSA diagnosis (9/20 in inpatients; 16/20 in outpatients), and treatment (12/20; 17/20). Three doctors reported their three spinal units were managing non-complicated OSA internally, without referral to sleep specialists. Ten belief statements representing six domains of the TDF were generated about screening. Lack of time and support staff (*Environmental context and resources)* and no prompts to screen for OSA *(Memory, attention and decision processes)* were commonly identified barriers to routine screening. Ten belief statements representing six TDF domains were generated for diagnosis and treatment behaviours. Common barriers to independent management practices were lack of skills *(Skills)*, low confidence (*Beliefs about*

*capabilities)*, and the belief that OSA management was outside their scope of practice *(Social/Professional role and identity)*. The three units independently managing OSA were well resourced with multidisciplinary involvement *(Environmental context and resources)*, had 'clinical champions' to lead the program *(Social influences)*.

### 5.3.4 **Conclusion**

Clinical management of OSA in tetraplegia is highly varied. Several influences on OSA management within spinal units have been identified, facilitating the development of future interventions aiming to improve clinical practice.

## 5.4 Introduction

People with tetraplegia experience a range of complications from their injury, affecting almost every system of their body. Obstructive sleep apnoea (OSA) is one such complication, with prevalence estimates of up to 83% in the acute phase, and up to 97% in the community dwelling chronic population.[86, 216] The quality of life of people with tetraplegia and OSA is up to five times the minimally important clinical difference worse than their peers without OSA.[1] OSA has been associated with daytime sleepiness, poor memory, attention and information processing in both the acute and chronic populations, and is therefore likely to impact on rehabilitation and vocational outcomes.[108, 109] Improving the management of OSA has the potential to prevent these undesirable consequences of spinal cord injury (SCI).

Guidelines developed by the Consortium of Spinal Cord Medicine recommend diagnostic testing with polysomnography for all people with SCI with excessive daytime sleepiness or other symptoms of sleep disordered breathing.[115] These guidelines also recommend the prescription of positive airway pressure (PAP) therapy for those with a positive diagnosis of OSA. Similar recommendations have been published by the Spinal Cord Injury Rehabilitation Evidence (SCIRE) project, a Canadian research collaboration that produces evidence-based practice recommendations for health professionals working in SCI rehabilitation.[116] The SCIRE recommendations include vigilance for suggestive signs and symptoms and further testing with oximetry or polysomnography when these signs are present. Management adherent to these recommendations therefore requires routine screening for the signs and symptoms of OSA, and subsequent investigation.

Both guidelines are not explicit in fully detailing the recommended clinical practices, potentially hampering efforts by clinicians aiming to practice according to evidence-based guidelines.[217] In particular, screening practices are recommended with little indication of how, when or where screening for signs and symptoms of OSA should be undertaken. Diagnosis of OSA is recommended with polysomnography in one guideline, and polysomnography or oximetry in the other, with no indication of who would perform these tests and what the clinical criteria for diagnosis should be.

Furthermore, only one guideline recommends a specific type of treatment; initially with continuous positive airway pressure (CPAP), and with bi-level PAP as a second option for those unable to tolerate CPAP.

The lack of actionable recommendations in the OSA in SCI guidelines reflects a lack of robust clinical evidence. While the guidelines are based on evidence from non-randomised studies and the expert panel consensus was reported to be strong, there is little randomised trial evidence in this setting. SCI is a relatively small and specialised clinical area, and as such, there are significant challenges for the conduct of clinical trials.[218] Thus, few guidelines in SCI are based on strong evidence. A review of knowledge translation research in SCI revealed almost all interventions were based on the findings of individual studies and expert opinion, with only one citing evidence from a randomised control trial.[142] Given the high prevalence and significant morbidity of OSA in tetraplegia, practice concordant with the best available evidence in the form of the current guidelines is important, and will contribute to reducing variation in practice and improving the clinical management of OSA.

Very little is known about the current management of OSA in chronic tetraplegia. An older study investigating OSA treatment in people with chronic SCI found that in a service providing care to approximately 600 veterans with chronic SCI, approximately 15% of people with tetraplegia had received a diagnoses of OSA.[117] Given the high prevalence estimates in this population, this is likely to reflect low screening and subsequent testing for OSA. More current research is required to determine the extent of OSA under-diagnosis in the present clinical environment.

To our knowledge, there have been no studies that systematically describe the current management of OSA in SCI, nor what influences the clinical behaviours of health professionals involved in the care of people with SCI and OSA. Anecdotally, practice is highly varied. A systematic review of barriers to physician adherence to clinical practice guidelines generally (not specifically in SCI) identified many factors that may influence practice, including lack of awareness, familiarity and dis/agreement with the guidelines, poor physician self-efficacy, low outcome expectancy, inertia of previous practice and external barriers such as lack of time, environmental factors and staff shortages.[125] Understanding the prevailing and contextual influences on clinical practice is essential

for the development of any intervention aiming to improve the management of OSA in people with tetraplegia.

The Theoretical Domains Framework (TDF) is a validated and commonly used set of 12 behavioural domains for use when exploring factors that influence clinical behaviours.[133] The 12 domains of the TDF include: knowledge; skills; social/professional role and identity; beliefs about capabilities; beliefs about consequences; motivation and goals; nature of the behaviour; memory, attention and decision processes; environmental context and resources; social influences; emotion; and behavioural regulation. The TDF enables a comprehensive, theory-based approach to recognising the behaviours that need to be changed, thereby identifying opportunities for improved practice.

The aims of this study are: 1. To describe the OSA screening, diagnosis and treatment practices of specialist doctors managing the rehabilitation of people with tetraplegia. 2. To explore factors that influence the management of OSA in tetraplegia, informed by the Theoretical Domains Framework.

## 5.5 Method

In-depth semi-structured interviews were conducted with specialist doctors managing the rehabilitation of people with tetraplegia in the inpatient and outpatient settings of spinal rehabilitation services, between August 2016 and March 2018. Names and contact details of doctors were obtained from websites of hospitals with a specialised SCI Unit. Additionally, a snowball sampling technique, where existing participants recommended future participants from among their professional networks, was utilized. In recognition that practice may vary in different regions because of cultural and healthcare model influences, a purposeful sample was drawn to include a range of regions in the Organisation for Economic Co-operation and Development (OECD; e.g. Australia/New Zealand, North America, Europe, UK). Low and middle-income countries were not included because the availability of resources and infrastructure required to undertake OSA management, and hence culture and subsequent practice, were likely to be very different. Potential participants were approached by telephone or email and invited to participate in the study. All participants provided written, informed

consent prior to the interview. Ethical approval for the study was obtained from the University of Melbourne (School of Health Sciences Human Ethics Advisory Group; Ethics ID 1545475).

Interviews were conducted face to face or via online video technology (e.g. Skype) or telephone at a time suitable to the participants. The researcher conducting the interviews (MG) had experience with qualitative research methods and the clinical area. An interview schedule, based on the TDF, was used to prompt the discussion and guide the analysis (see Appendix 8.4). The interview questions focused on describing current practices in the identification and management of OSA, and exploring the domains of the TDF to understand factors that influence practices.

All interviews were audio recorded for verbatim transcription. Transcripts were de-identified and imported into NVivo qualitative data analysis software (QSR International Pty Ltd. Version 12, 2018) to aid data management and analysis. The OSA management pathway was divided into screening, diagnosis and treatment components for inpatient and outpatient services, creating six categories. Self-reported practice was initially content analysed into these six categories. Data from the first five interviews were then independently analysed by two researchers (MG and DJB) to identify common clinical practices within each of the categories. For example, for inpatient diagnosis, clinical practice was found to fall within three main clinical practices. They were: conducted by spinal unit (with three sub-clinical practices), referral to sleep specialist and not undertaken. After the first five interviews, the two researchers discussed and resolved any differences in their identified clinical practices. Some changes to wording were required to ensure consistency and clarity. The clinical practices are presented in Figure 5.1.

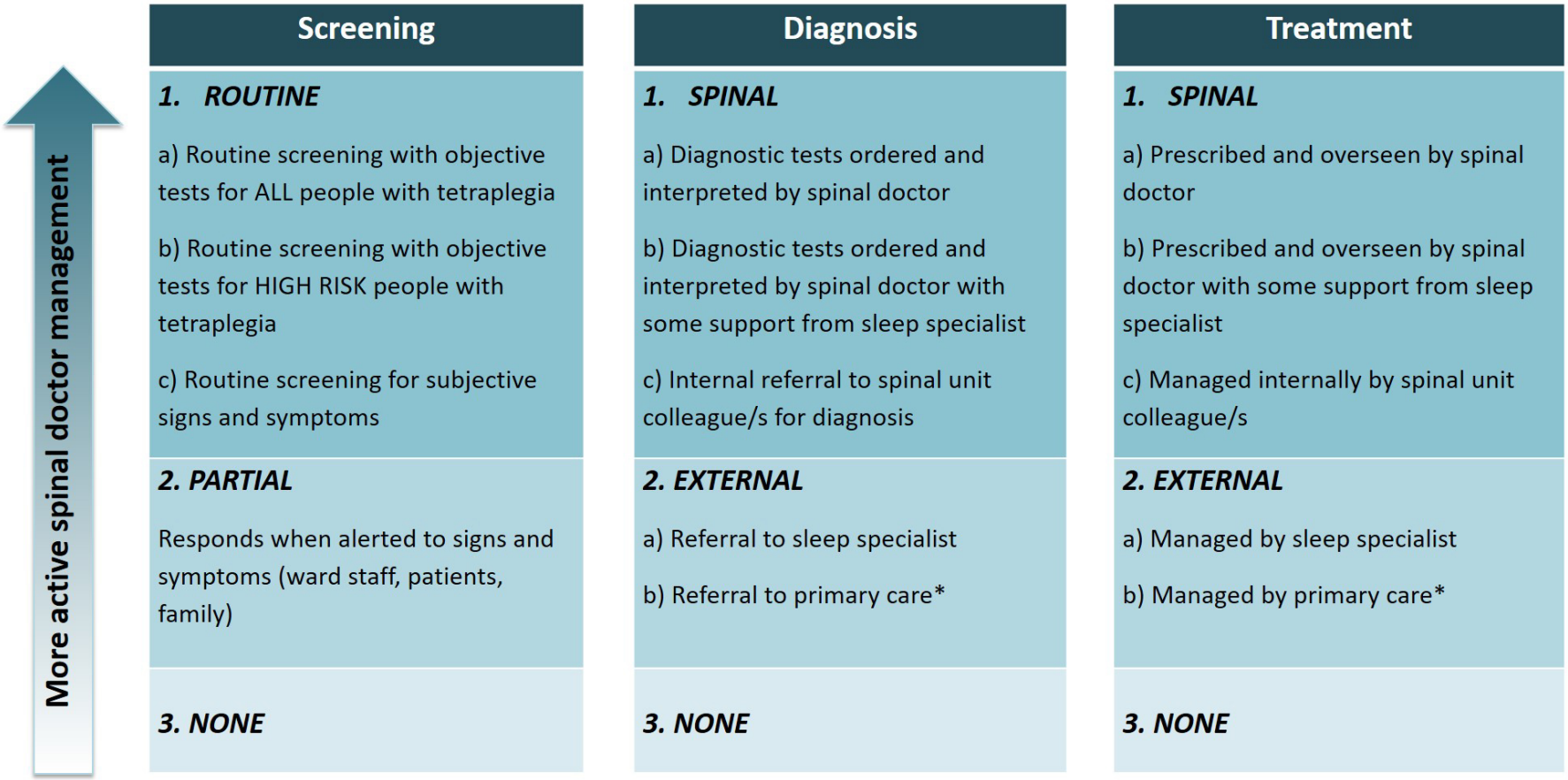


**Figure 5.1 Predominant clinical practices**

This matrix formed the coding structure for the remaining interviews, and as such, six clinical practice categories were assigned for each participant. When clinicians reported more than one clinical practice (e.g. referring to sleep specialist and general practitioner in outpatients), the predominant practice was selected.

Data were next thematically coded according to the 12 constructs of the TDF to assess influences on clinical practice and develop theoretical explanations about the influences on practice. The first five interviews were analysed independently by two researchers (MG and DJB). MG and DJB met after coding two interviews, and again after five, to discuss and resolve any differences and to revise the coding guideline. The remaining interviews were analysed by MG, who discussed any instances of ambiguity with DJB.

Following coding to the TDF domains, common "belief statements" were generated. A belief statement has been defined as a collection of responses with a similar core belief about the barrier or enabler to the behaviour under investigation.[219] Comparisons in belief statements were made between participants with different clinical practices. For example, the influences identified for those routinely screening all their patients with tetraplegia were compared to those who were not. Similarly, the influences of those who were diagnosing and/or prescribing treatment for OSA themselves were compared to those who were referring to sleep specialists for OSA diagnosis and treatment.

After the first five interviews were analysed, sampling continued until saturation of themes was achieved. Saturation was defined as when five consecutive interviews had been analysed with no new belief statements emerging [220].

## 5.6 Results

Interviews were conducted with 20 doctors, from 19 spinal units, from Australia and New Zealand (6), North America (6), mainland Europe (4), and UK/Ireland (4). Five were conducted face-to-face, 10 with online video technology, and five over telephone. Nine of the doctors were women. Interviews ranged in length from 22 to 66 (average 41) minutes. Specialist sleep laboratories were on site for six doctors, available in nearby affiliated hospitals for seven, and not available for another seven.

### 5.6.1 **Predominant clinical practices**

Of the five interviews double-coded, there were three differences in categorization of clinical practices (6 practice types, 5 interviews = 30 cells), which were resolved on discussion. Table 5.1 summarises the self-reported clinical practices of the 20 doctors.

**Table 5.1 Results of categorisation into common clinical practices**

| | **Inpatient N (%)** | **Outpatient N (%)** |
|---|---|---|
| **SCREENING** | | |
| **1. Routine** | **10 (50%)** | **8 (40%)** |
| a Routine screening with objective tests for all people with tetraplegia | 8 (40%) | 0 (0%) |
| b Routine screening with objective tests for high risk people with tetraplegia | 2 (10%) | 0 (0%) |
| c Routine screening for subjective signs and symptoms | 0 (0%) | 8 (40%) |
| **2. Partial** Responds when alerted to signs and symptoms | **10 (50%)** | **12 (60%)** |
| **3. None** | **0 (0%)** | **0 (0%)** |
| **DIAGNOSIS** | | |
| **1. Spinal** | **10 (50%)** | **4 (20%)** |
| a Diagnostic tests ordered and interpreted by spinal doctor | 5 (25%) | 3 (15%) |
| b Diagnostic tests ordered and interpreted by spinal doctor with some support from sleep specialist | 2 (10%) | 0 (0%) |
| c Internal referral to spinal unit colleague/s for diagnosis | 3 (15%) | 1 (5%) |
| **2. External** | **9 (45%)** | **16 (80%)** |
| a Referral to sleep specialist | 9 (45%) | 13 (65%) |
| b Referral to primary care | | 3(15%) |
| **3. None** | **1 (5%)** | **0 (0%)** |
| **TREATMENT** | | |
| **1. Spinal** | **8 (40%)** | **3 (15%)** |
| a Prescribed and overseen by spinal doctor | 4 (20%) | 3 (15%) |
| b Prescribed and overseen by spinal doctor with some support from sleep specialist | 1 (5%) | 0 (0%) |
| c Managed internally by spinal unit colleague/s | 3 (15%) | 0 (0%) |
| **2. External** | **11 (55%)** | **17 (85%)** |
| a Managed by sleep specialist | 11 (55%) | 16 (80%) |
| b Managed by primary care | | 1 (5%) |
| **3. None** | **1 (5%)** | **0 (0%)** |

In the inpatient unit, 10 (50%) of physicians reported routine screening for OSA, with eight of these screening all patients with tetraplegia using objective tests (e.g. overnight oximetry). Ten (50%) reported diagnosing OSA within the spinal unit. Three of these

referred internally to their colleague(s) for diagnosis, and two were provided with some assistance from a sleep physician. Of the spinal units diagnosing OSA, most used polygraphy (8/10) with two relying solely on overnight oximetry. Eight (40%) reported the prescription of treatment for OSA occurred within their spinal unit, with four prescribing treatment independently of any sleep specialist. Of these, seven offered CPAP as first-line treatment, and one predominantly prescribed bi-level PAP.

In the outpatient environment, eight (40%) reported routine screening for OSA in all patients with tetraplegia, with questions about signs and symptoms. The remaining 12 (60%) did not consider screening for OSA unless alerted to signs and symptoms from patients and/or their carers. These doctors also estimated that less than 10% of their patients were identified at risk for OSA, requiring further investigations. Three (15%) reported responsibility for diagnosing OSA in their outpatients with tetraplegia, and one referred internally to a spinal unit colleague. Of those diagnosing OSA, two used polygraphy and one predominantly used overnight oximetry. Doctors diagnosing OSA also reported managing the treatment and follow-up. The remaining 16 (80%) referred to a sleep specialist or the primary care physician for OSA diagnosis and ongoing management.

In summary, three doctors (15%) reported that their spinal unit was predominantly diagnosing and treating non-complicated OSA in their inpatients and outpatients with tetraplegia. Eleven (55%) were predominantly referring all inpatients and outpatients with signs and symptoms of OSA to sleep specialists or GPs for diagnosis and management. The remaining six (30%) were practicing a “hybrid management model”; that is, predominantly diagnosing and treating OSA in their inpatient units, and referring to external specialists in their outpatient clinics.

### 5.6.2 Factors influencing practice

For the qualitative analysis of factors influencing practice, OSA management practices were divided into *screening practices* and *diagnosis and treatment practices.* Diagnosis and treatment practices were not analysed separately as they were considerably related to one another. For example if a doctor referred for diagnosis of OSA, the referral also covered treatment. Similarly if a doctor diagnosed OSA, s/he tended to also prescribe

the treatment. If the influences on clinical practice were specific to the inpatient or outpatient settings, these were clearly reflected in the belief statements.

#### *5.6.2.1 Factors influencing screening practices*

Key themes regarding screening behaviours represented six domains of the TDF: Knowledge, Social/Professional role and identity, Beliefs about capabilities, Beliefs about consequences, Memory, attention and decision processes, and Environmental context and resources. Within these domains, 10 belief statements were generated, of which three were separated into opposite beliefs. Table 5.2 summarises the belief statements, corresponding TDF domains and representative quotes.

**Table 5.2 Summary of relevant TDF domains, belief statements and representative quotes about screening for OSA in tetraplegia**

| Domain | Belief statements | Representative quotes | Frequency of belief out of 20 |
|---|---|---|---|
| Knowledge | I don't know of any clinical practice guidelines recommending management of OSA in tetraplegia. | "No I don't know or aware of any existing clinical guidelines."<br><br>Regarding clinical practice guidelines: "I assume they [clinical practice guidelines] exist. But I wouldn't go hunting for them because I don't disagree with the concept that they should be screened." | 10 |
| | I know that the prevalence of OSA is very high in tetraplegia and that OSA causes negative outcomes. | "So the paper that I usually refer to…where they followed acute spinal cord injuries, so it was within the first year, and they test for sleep apnoea and it was up to like 80%. And then most other papers say, you know, up to 60% of spinal cord injury will have sleep apnoea."<br><br>"Yes. I'm aware it is high. It is definitely high in the first 2-3 months, but I can see a lot of the studies from one year post injury, that's quite variable, it's varies from 40-70%." | 14 |
| Social/Professional Role and Identity | As the doctor managing the patients' rehabilitation and spinal cord injury needs, screening for OSA is my clinical responsibility. | "I think it should be the physician's role. I think that's the most appropriate person because if the symptoms come back positive, it does have to be a medical referral onto the respiratory clinic."<br><br>"I think it is our responsibility as their spinal cord injury doctor to understand sleep apnoea and understand respiratory; it falls under the umbrella of respiratory management, right. Especially somebody with a cervical injury, like you have to know what MIPS and MEPS are, vital capacities are, what their PFTs are. And sleep apnoea is just another component of that." | 17 |

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| Beliefs about Capabilities | I am confident/not confident that I am identifying OSA in most of my patients. | "I think we get everything, we get all patients we need, well we catch all the patients who are in need of ventilation, yes."<br><br>"I'd say I'm pretty confident, yeah I don't miss it in many patients."<br><br>"I wouldn't be very confident [to identify OSA symptoms]. The symptoms, there are so many other contributors to the symptoms that are described, I wouldn't be very confident."<br><br>"In the acute phase, I think I'm probably missing a good proportion. Just ballparking, maybe 30%, 30 to 40%, I might be missing. In the community phase, of those that I follow regularly, probably missing less, but I'm sure I'm still missing some. Maybe 10%, 10–20%." | 8<br><br>8 |
| Beliefs about Consequences | Routine screening may identify non-symptomatic OSA that does not need to be treated. | "Okay, but even if you screen symptoms, and they have some symptoms, people can be affected by their symptoms in a different way. Did he have a problem? If he didn't have a problem, why suddenly I found a problem with him and I start him to sleep with a machine on. The problem is blanket screening and blanket investigation we'll end up having more people on a treatment that otherwise may not need to be. That is my worry."<br><br>"From my point of view, in the clinic, I'd probably be most interested in following up patients who had symptoms that were relevant to them. I guess a disincentive for me is to be actively pursuing investigation results of patients who don't seem to have symptoms of that. Because what's the point? I mean, like, with any test or referral, there's a saying in medicine, don't do it if it's not going to change the treatment. Yeah, well it would be a waste of resources, but also it's inconvenient for the | 3 |

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| | | patient." | |
| | Routine screening helps prevent patients who are poor at recognizing their symptoms from being missed. | "Yeah because patients do not complain about that, that you have to measure it before you know that they have it, so sometimes they have the complaints of tiredness and that kind of stuff and then you have a trigger but if they don't have that complaint then the screening might disappear." | 3 |
| | I am/I am not sure that the benefits of routine screening would outweigh the costs. | "No question about it, yes. Because most patients, when they're eventually getting ventilation during the night, they feel a lot better and they can have more… what do you call it, they can do much better during the day, so I think most patients will benefit from it (screening)."<br><br>"Have to do it. Yeah, of course. The only long run if you ignore something which is there and you don't treat it, you don't manage it, of course at the end of the day that will cost you even more. And also you have to respect the patient's wellbeing and their needs."<br><br>"I wouldn't be convinced. I'm not convinced of that at the moment, no. Should I just screen them all? I don't know if that would be cost-effective, I don't think so."<br><br>"I think it's probably only worthwhile when the patient initiates the concern about fatigue and sleepiness because, otherwise, my experience is that if they're really not troubled by symptoms in the day, they do not tolerate CPAP." | 13<br><br>5 |
| Memory, Attention and Decision Processes | A checklist/form is helpful/would be helpful to prompt me to screen for OSA in the inpatient unit | "With our clinics we do have a template, we always get prompted to ask these questions about sleep, excessive snoring, does your partner notice you are not breathing for a while, and then we check the risk factors. So as long as the template is there we usually – I usually, you get prompted to ask it and I would." | 14 |

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| | and outpatient clinic. | "Inpatients definitely, so we have some standing orders ... And on there it was just immediate, everyone gets overnight oximetry and pulmonary function tests, and then in outpatient I do have like a template I use when I see patients, so there's a respiratory heading which usually prompts me to ask about that."<br><br>"And I often think, "Oh, gosh, I should remember to ask the patients about their breathing but I never seem to. So, I think that if there was a box, like, are you having sleep-disordered breathing symptoms, I mean, most doctors have an idea what those symptoms are, you could just quickly ask the patient four or five questions."<br><br>"I think it will be nice if we can come up with a routine screen that we will screen everybody on admission, like an admission ASIA, something like that, we could do an admission and a discharge. If it's a very short questionnaire that we can do. I think it would be worthwhile." | |
| Environmental Context and Resources | I don't have enough time in outpatients to screen for OSA symptoms. | "I think it's, for us like, probably the time that I am allotted with patients, so there's a lot of things to cover.<br><br>"In our current setup we don't have time. We still allocate an hour for the patient, there are so many things to discuss, especially if they come once a year. And we don't have any allied health clinic." | 6 |
| | Patients often have more important medical issues to discuss in their outpatient appointment than OSA. | "So they're having a very hard time with bladder, with bowel, with pain, spasticity, and then unfortunately the respiratory system does fall on the wayside a little bit. And if you – if they are really worried about their bladder, and you finish talking about their bladder, and they're thinking about their bladder, and start talking about sleep apnoea, they tend not to take it – it's hard to then take on so much information." | 6 |

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| | | “Usually I’ll have the patient kind of lead the discussion as to what their most important thing they want to talk about that day is and I’ll kind of ask them prompting questions just to see a more general review of systems, but in that appointment, like, yeah I think that might be why things are getting missed because they may just want to talk about pain that day or they may just want to talk about their bladder or their pressure ulcer; we don’t get around to discussing sleep apnoea as well as we should.” | |

Most doctors were not aware of any clinical practice guidelines about OSA management in tetraplegia, although they did know of research establishing high prevalence of OSA in tetraplegia (*Knowledge*). There was a strong belief that, as the person responsible for the holistic management of the person with SCI, screening for OSA was their responsibility *(Social/professional role and identity).* However many reported a lack of confidence in their ability to identify OSA in their patients. For some this was because they lacked confidence in identifying risk factors and symptoms, and for others, it was reflective of their incomplete screening practices *(Beliefs about capabilities).*

Some doctors were fundamentally opposed to routine screening for a condition that the patient may not recognise as a problem. In contrast, others felt that routine screening was important because patients often have difficulty recognizing their symptoms of OSA. Most thought that the benefits of routine screening would outweigh the costs. However some doctors were not convinced of the need for routine screening for OSA, which appeared to reflect a lack of confidence in the outcomes of the treatment. *(Beliefs about consequences).*

Those who reported routine screening practices for OSA tended to use reminders. These were usually a checklist or form in the outpatient clinic, standard orders for testing (e.g overnight oximetry) in the inpatient unit, or an agreed protocol for OSA screening within the spinal unit. Those who were not routinely screening for OSA, but believed that screening was their responsibility, commonly reported forgetting to screen in a busy clinical environment. When asked what they would change in their practice to improve the management of OSA, the most common response was the introduction of some sort of physical reminder, such as a form or checklist, to screen for likelihood of OSA (*Memory, attention and decision processes*).

Related to this was lack of time and resources, particularly in the outpatient environment, which was commonly cited as a barrier to screening. Nursing and allied health support were not available for most doctors in the outpatient clinic. Doctors spoke passionately about the patients' competing medical problems, and the lack of available time to discuss all of their medical issues. Screening for signs and symptoms

of a condition that the patient was not complaining about was not a priority when the patient had more significant medical problems such as bladder or bowel issues, pressure sores or pain. Most surveillance clinics for chronic spinal cord injury offered annual appointments. For one doctor, patients were reviewed twice yearly, enabling one of these visits to be dedicated to proactive screening for conditions such as OSA, while the other was focused on managing existing health problems (*Environmental context and resources*).

#### *5.6.2.2 Factors influencing diagnosis and treatment practices*

Key themes regarding diagnosis and treatment behaviours emerged as representing six domains of the TDF: Skills, Social/Professional role and identity, Beliefs about capabilities, Beliefs about consequences, Environmental context and resources, and Social influences. Within these domains, 10 belief statements were generated, of which three could be divided into conflicting beliefs (Table 5.3).

**Table 5.3 Summary of relevant TDF domains, belief statements and representative quotes about diagnosing and treating OSA in tetraplegia**

| Domain | Belief statement | Representative quotes | Frequency of belief out of 20 |
|---|---|---|---|
| Skills | I don't have the necessary skills to interpret diagnostic tests and prescribe treatments for OSA. | "I don't order oximetry or spirometry or something myself because I'm not sure how to interpret it."<br><br>"Lack of confidence and lack of training. Especially about the machines and about what pressures, and so on, to start with. I know that we would titrate it depending on the oximetry or the sleep study, but I would not know exactly how to start." | 11 |
| Social/Professional Role and Identity | The diagnosis and treatment of OSA is outside my scope of practice. It should be managed by a sleep/respiratory specialist. | "If I was looking up the literature that wouldn't be something I'd look up because it would never be appropriate for me to be the one prescribing the treatment for sleep-disordered breathing."<br><br>"I don't have the appropriate speciality qualification to interpret the results and prescribe the treatment. So, it would be sort of a, I'm trying to think of the word, it would be breaching my scope of practice. It would be implying to the patient that I know what I'm talking about when I don't."<br><br>"The way our system works is once I get pulmonologists involved it's sort of like their thing."<br><br>"I don't consider myself a sleep specialist so if they've got symptoms that are consistent with that and there's concerns on the oxygen saturation, that's when I take them to the respirologist to see." | 6 |

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| Beliefs about Capabilities | I am not confident to diagnose and treat OSA without sleep/respiratory specialist involvement. | "But I think I like having the respirologist there to discuss sort of a game plan of what pressures to start them at, even though it's auto CPAP or, you know."<br><br>[Regarding diagnosing OSA] "I've not been trained in it. You know, I can read a graph but just because I can read labels I am not confidently able to say, "Yes, you have sleep apnoea.""<br><br>"Personally, I don't feel confident in prescribing." | 12 |
| Beliefs about Consequences | CPAP is beneficial to my patients with tetraplegia and OSA. | "So once patients are diagnosed and treated successfully, the change in terms of cognitive improvement, we have patients who would sleep through their therapy sessions, their family meetings, because they were so tired. We have patients who are on numerous sleep inducers just to get them to sleep. So once we see that patients can come off of these medications, they're fully participating and learning about their spinal cord injury, that's huge, right, because that will decrease the length of stay in rehab, and all of the other complications associated with them."<br><br>"And then I'd say the more impressive thing that has happened, not uncommonly in patients who use it on our unit, is all of a sudden they do way better in tolerating therapies the next day, even day-to-day, like, "We're going to try this tonight," and the next day the therapists are like, "What did you do differently with Mr Smith? He's like a different guy today." It's like, "Well, I think he has sleep apnoea and used CPAP last night. I guess his sleep apnoea was really affecting him." And we have lots of the patients like that, I would say." | 9 |
| | Adherence to CPAP is poor/good in our unit. | "Of the patients who can't take the mask off themselves, I'd say 80% of them don't tolerate it. It's bad but what are you going to do. I totally understand." | 7 |

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| | | "I think the biggest challenge for us right now is to get people to adhere to the CPAP machine."<br><br>"But patients just find it [CPAP] really difficult to tolerate, so most patients go untreated."<br><br>"No I would say normally we have a high compliance in tetraplegics… I would say 80% is compliant. We have of course some person who are not compliant and we check their compliance with the usual things." | 4 |
| Environmental Context and Resources | We have poor/good access to overnight sleep studies and sleep specialists. | "It's hard to get an in-patient sleep study now…But, yeah, that's been a bit of an inhibitory factor, you know, to ask about patients early on and then say, "Well, you can have a sleep study in 14 months when you're out of hospital."""<br><br>"It's a logistical problem if they need a lot of care or ceiling lifts or anything like that, or an attendant. Because you know what sleep labs look like. They're not designed for people in wheelchairs."<br><br>"Having a sleep study is very difficult, for our inpatients, because [nearby acute hospital] has a sleep service but that is not manned, there is no nursing support."<br><br>"In a few weeks patients can go there and get the measurements, yep. And when we do it in our ward then it's also very quickly, so the waiting list is no problem, no." | 6<br><br>4 |
| | I can't diagnose OSA and/or prescribe treatment because the patient's CPAP machine | "But most commercial payers in [XX country] require that a polysomnography is done, documented before they'll pay for it. So we're kind of hamstrung a little bit in that way." | 7 |

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| | won't be funded. | "I prescribe it, they won't get funded. So there is a minority who can get funding or self-fund, but you still need to involve a respiratory professional in the set-up and reading and the compliance. | |
| | Our spinal unit has trained nurses and allied health to help manage OSA / We would need trained nurses and allied health to help manage OSA. | "Yeah we've got nurses involved in this part of our clinic. The nurses would go to the patients with our CPAPs and then advise them around the mask they would use and instruct them and all that."<br><br>"So, we use a couple of our physios that kind of are the respiratory leads but, actually, any of our physios have the competence to set up BiPAP, CPAP, etcetera."<br><br>"We also need the nurses of course, they have to be knowledgeable about this, we have to train the team, the doctors, everybody else, so maybe in the future we will, yes."<br><br>"I need to have other special respiratory nurse who needs to train and they need to educate." | 9<br><br>4 |
| | I practice in the same way as my colleagues from the same spinal unit. | "We do the same thing. Whoever it is, they'll be doing the same thing in our unit."<br><br>"I think we have a clear policy of all the screening and referring and intervention for sleep apnoea is probably standard practice." | 16 |
| Social influences | Our OSA management program is the result of a "clinical champion" | "It started with my colleague…maybe even 10 years ago or a bit longer he saw [another hospital's] sleep laboratory and you know the screening on sleep apnoea they do in their spinal cord centre … my colleague got inspired and started to set up a similar department here which existed of nurses and himself and later I would take part in that as well and over the years kind of grew in our expertise I guess." | 6 |

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| | | Participant: “You sort of need a champion.” Interviewer: “Right, so you’ve basically, you’re the one who set up this program for your unit?” Participant: “Yep, pretty much, yeah, yeah.”<br><br>“My colleague and I started 20 years ago and realised that our tetraplegic patients were falling asleep during therapies... And then, and then we started assessing our patients, realised this is a problem. And then since this experience done 20 years ago now and then it became the standard. It was just translation from research to daily routine and now it’s well implemented.” | |

Those who were not diagnosing OSA or prescribing treatment did not believe they had the necessary skills or training to both interpret the diagnostic tests, and to prescribe and initiate treatment. They frequently pointed to the nature of SCI medicine, which requires management of multiple systems of the body and demands specialized skills in bladder, bowel, blood pressure, pain, spasticity, respiratory management and more, stating that they could not be "jack of all trades" (*Skills*). Related to the lack of skills in OSA diagnosis and treatment was the lack of confidence in their abilities to manage OSA. Several doctors reported diagnosing respiratory insufficiency and prescribing bi-level PAP treatment in the inpatient units without a respiratory physician, but they were not confident in diagnosing OSA or prescribing PAP for OSA (*Beliefs about capabilities).*

The ability to diagnose and treat some respiratory disorders with bi-level PAP but not treat OSA with CPAP appeared to reflect historical management pathways and beliefs about professional responsibilities. A subset of those who reported referring to sleep specialists for diagnosis and treatment of OSA felt very strongly that OSA should only be managed by a sleep specialist; that it was outside of their scope of practice and that it would be irresponsible to take on management of OSA *(Social/Professional role and identity).* For some this was also related to strict regulations from compensatory funding bodies. Seven of the doctors interviewed reported that funding bodies would only accept applications for PAP funding if the patient had been diagnosed with a full overnight polysomnography, and/or the diagnosis had been made by a sleep specialist. These regulations varied between and within countries (*Environmental context and resources*).

There were conflicting views about the benefit of PAP therapy. Those who were independently managing all aspects of non-complicated OSA were very positive about the benefits of PAP in terms of individual patient outcomes and overall adherence in their units. However many were disappointed in the treatment, reporting poor tolerance in the majority of their patients, which was frequently cited as a disincentive to screen for OSA (*Beliefs about consequences*).

Another commonly cited barrier was poor access to specialist sleep services. Several doctors described long waiting lists for overnight sleep studies and specialist

consultations. For others the poor access was related to the inability of the sleep services to cater for the needs of people with disability. For example, the lack of nursing support provided by the sleep service and the lack of specialized equipment. However, some doctors were satisfied with their local specialist sleep services, describing good relationships and relatively short waiting times for appointments, and consequently reported no need to change their current practice of referring patients with suspected OSA (*Environmental context and resources*).

The availability (and lack) of allied health professionals and nurses with OSA management skills was both an enabler and a barrier to diagnosing and treating OSA within the spinal unit. The doctors who were performing any aspect of diagnosis or treatment in the inpatient or outpatient units reported their reliance on ancillary staff for support. The types of staff involved varied from unit to unit, but were usually nurses, physiotherapists or respiratory therapists. These staff tended to be involved in the application of diagnostic equipment (eg overnight oximetry or polygraphy), and/or treatment initiation and maintenance. Whilst doctors usually made the diagnosis and prescribed treatment, they mostly relied on the allied staff to perform the operational tasks. Conversely doctors not diagnosing or treating OSA tended to report the lack of available ancillary staff to support OSA management as a significant barrier to the practice (*Environmental context and resources*).

Almost every doctor interviewed reported similar OSA practices to his/her colleagues from the same spinal unit, pointing to culture and the local environment as highly significant (*Environmental context and resources*). The three doctors (and units) who were independently managing all aspects of non-complicated OSA spoke extensively of a highly influential "clinical champion" who introduced and led the OSA management program in their unit (*Social influences*).

Most doctors who were referring to specialists for OSA management thought that the diagnosis and treatment of non-complicated OSA could potentially be performed within their unit, provided there was additional training for staff *(Knowledge and skills)*, more resources for equipment and staff and changes to the funding rules for PAP devices (*Environmental context and resources*).

## 5.7 Discussion

This is the first time the breadth of OSA management practices within a spinal unit has been investigated and documented, and the first time a behavioural model, such as the TDF, has been applied to this area of clinical medicine to explore the influences on clinical practice. We found that 40 to 50% of spinal doctors in our sample were undertaking routine screening for signs and symptoms of OSA in their patients with tetraplegia. The remainder reported being alerted to signs and symptoms from the patient, family or ward staff before any investigation for OSA. This reactive practice may have contributed to an under-diagnosis of OSA in this population. Most doctors in this study felt that routine screening for OSA was their responsibility and was a beneficial practice to either continue or initiate. A comparison of the influences on screening practices between those routinely screening and those who were not, found that time available in outpatients, resources for allied health and nursing support, and reminders to prompt screening were likely to be important.

Providing reminders is a common intervention to prompt clinicians to perform tasks such as screening for a condition or ordering an investigation. A 2012 overview of 35 systematic reviews of reminder interventions aiming to change clinical behaviours found that reminders can lead to modest improvements in clinical practice, and concluded they are an effective intervention across a range of healthcare settings.[221] If reminders for OSA screening were to be implemented in a spinal unit, consideration of the local context to determine the most suitable type of reminder would be important. Further research is needed to explore the feasibility and effectiveness of reminders as an intervention to improve rates of screening for OSA in spinal cord injury settings.

The types of screening varied significantly in the inpatient and outpatient environments, with objective tests (e.g. overnight oximetry) predominant in the inpatient unit, and questions about symptoms (e.g. daytime sleepiness, snoring) prevailing in the outpatient clinics. Two OSA screening questionnaires developed for the non-disabled sleep clinic population have been tested in the SCI and both performed poorly in identifying OSA, however their ability to identify individuals at high risk of OSA, who require objective testing has not been evaluated.[1, 96] Recently a two-stage model for identifying moderate to severe OSA in people with chronic tetraplegia has been validated and

published.[216] In this model a screening questionnaire identifies patients who require further testing with overnight oximetry. This simple four-item questionnaire (SOSAT) could be applied in the outpatient setting of a spinal unit to identify high-risk individuals for further investigation.

Within our sample, three doctors reported that their spinal unit (15%) was predominantly managing all aspects of non-complicated OSA. Eleven (55%) described referring all patients with suspected OSA to sleep specialists for ongoing management, and six (30%) were performing some components of the diagnosis and/or treatment prescription, usually in the inpatient setting. Those referring to sleep specialists for OSA management tended to lack confidence and skills in interpreting diagnostic tests and prescribing treatments, and felt that OSA management was outside the scope of their specialty and should be managed by a sleep specialist. Seven (35% of the total sample) were also impeded by restrictive regulations from compensatory bodies that limit the diagnosis of OSA to sleep specialists. Spinal units independently managing non-complicated OSA in their patients were well resourced for staff and training, were not impeded by regulations from compensatory funding bodies, and described “clinical champions” who initiated and led the OSA program within their spinal unit. Most of the doctors who were not diagnosing and treating OSA thought that their unit could do so with additional training, equipment, and greater involvement of allied health professionals and/or nurses.

That almost half of the spinal doctors interviewed in this study were undertaking at least some diagnosis and/or treatment of non-complicated OSA suggests that it is entirely possible for spinal doctors to perform these tasks. The perception that OSA is outside of the scope of practice of a spinal doctor may be more likely to reflect local cultural influences, lack of training and resource constraints. The results of this study suggest that with adequate training and resources, spinal units that currently refer to sleep specialists for OSA management may be able to perform these practices within the unit. This is consistent with a non-randomised study in stroke survivors (reported to have a similarly high OSA prevalence to that observed in tetraplegia [175]) which demonstrated that it is feasible and safe to diagnose and treat OSA within a stroke rehabilitation environment.[222]

Poor access and high costs of in-laboratory specialist sleep services to diagnose and initiate treatment for OSA have been identified as a problem in the non-disabled population.[65, 67] In response, alternative ambulatory techniques, including automated, home-based diagnosis and treatment initiation, have been compared to specialist sleep laboratory management, with all studies demonstrating non-inferiority of the alternative model.[65, 84] There have now been three non-inferiority randomised controlled trials investigating whether non-sleep specialist health professionals can effectively treat OSA in people without disability using these ambulatory techniques. Two investigated OSA management delivered in primary care settings by general practitioners and practice nurses,[81, 83] with the other investigating OSA management provided by nurses in specialist sleep centres.[80] In each of the studies the alternative models were compared to the traditional sleep specialist model, and all concluded that the care provided by non-sleep specialist professionals was not inferior to that provided by the sleep specialists. As yet, there has been no research investigating alternatives to the specialist sleep model for people with tetraplegia.

Ideally, a randomised controlled trial comparing the spinal unit management of non-complicated OSA to specialist sleep laboratory management could determine whether spinal unit management is at least not inferior to the traditional model. The alternative OSA management model could be based on one, or a combination of the three, spinal units found to be independently managing OSA in this study. There are important safety and feasibility considerations, such as the identification and treatment of hypoventilation, to resolve prior to any such clinical trial. However evaluation of safety procedures at the spinal units identified in this study, and consultation with sleep specialists, should enable resolution of these concerns. In addition, our findings suggest that staff training, multi-disciplinary involvement, and resources for equipment are important components of the model.

### 5.7.1 Limitations

Only five of the 20 interviews were independently double-coded in this study by two researchers (MG and DJB). However the coding framework was revised after the first five interviews and guided the analysis of the remaining 15, and any instances of ambiguity were discussed between the two researchers.

It is possible that the snowballing recruitment method resulted in the recruitment of participants with similar practices and beliefs, and thus saturation of themes could have occurred prematurely. However, participants were only asked to recommend doctors from different spinal units, and our purposive sampling method also involved recruiting participants from a range of countries in the OECD. The results demonstrate a wide variation in practice and beliefs. Self-reported clinical practice is also likely to be influenced by these sampling techniques and the small sample size. Whilst we are confident that our matrix of clinical practices describes the range of OSA practices in the OECD, we do not suggest that the proportions of doctors allocated to the different clinical practices in this study can be generalised to all spinal doctors in the OECD.

Interviewing clinicians about their perceived influences on their clinical practice does not necessarily reveal the actual influences on their practices.[223] Triangulation is a commonly used technique in qualitative research, involving the use of multiple data sources to facilitate deeper understanding. Ideally the findings of this study should be compared and complimented with a quantitative clinical practice audit and, given the multi-disciplinary nature of OSA management, more qualitative research involving spinal unit nurses, allied health clinicians and people with tetraplegia.

### 5.7.2 Conclusion

People with tetraplegia experience high disability and disadvantage. In this context, while we recognise that knowledge translation interventions should be primarily focused on clinical areas with robust evidence-based recommendations for clinical practice, we are advocating for the translation of best available evidence into practice. We assert that routine screening for a highly prevalent condition, for which there is a relatively cheap, simple and non-invasive treatment available, is both practical and worthwhile. Given the lack of specific, actionable practice recommendations in the existing guidelines, and the wide variation in OSA management practices described in this study, more research into the feasibility and outcomes of spinal unit management of non-complicated OSA is warranted. Interventions that target the factors identified in this study are likely to improve the management of OSA, which may ultimately improve the quality of life of people living with tetraplegia.

### 5.7.3 **Addendum**

Adler and Janssens[150] recommended that only symptomatic patients with tetraplegia who are likely to accept treatment should be screened for OSA, echoing the beliefs of several of the doctors interviewed in this study. The problem with this approach is that many patients are not aware of their symptoms of OSA until after they have been treated. This was an important finding from the qualitative research presented in Chapter 4, and contrasts starkly with the opinions of some health professionals about the value of screening patients who do not present with symptoms. In this population with profound disability and multiple comorbidities, disentangling fatigue from sleepiness and other symptoms of mental health problems like depression is challenging.[224] By only investigating OSA in those with “symptoms”, it is likely that many patients who would have benefitted from OSA treatment will be missed. Ideally all people with tetraplegia should be screened for OSA.

*“There are known knowns; there are things we know we know. We also know there are known unknowns; that is to say we know there are some things we do not know. But there are also unknown unknowns – the ones we don't know we don't know. And if one looks throughout the history of our country and other free countries, it is the latter category that tend to be the difficult ones.” ~ Donald Rumsfeld*

# 6 SUMMARY, FURTHER RESEARCH AND CONCLUSIONS

## 6.1 Overview of Chapter 6

OSA is highly prevalent in tetraplegia and is associated with poor health-related quality of life.[1] In an ideal healthcare system, all people with tetraplegia would be screened for OSA and offered further investigation and treatment where required. In reality, few people with tetraplegia are screened, and most with the disorder remain undiagnosed and untreated. Given the high prevalence and poor health outcomes associated with OSA in tetraplegia, these known access issues have resulted in the provision of inequitable healthcare, and they must be addressed.

The aim of this research was to document, understand and begin to address the issues that have resulted in under-diagnosis of OSA and poor access to OSA treatment for people with tetraplegia. This information is essential for effective planning of future interventions to improve the clinical management of OSA in tetraplegia. This final chapter recaps the main findings of this thesis, summarises what is known about OSA management practices in tetraplegia, and identifies relevant knowledge gaps. Two areas of future research are proposed, that together aim to advance the care of people with tetraplegia and OSA.

## 6.2 Summary of research findings

### 6.2.1 OSA detection in tetraplegia

Clinical practice guidelines recommend polysomnography for people with SCI and signs and symptoms of OSA.[115] However access to polysomnography is limited,

particularly for people with SCI, whose physical disability can prohibit access to standard sleep laboratories. Whilst the true proportion of people with tetraplegia and undiagnosed OSA is unknown, available data suggest that it is high. Two separate audit studies of spinal units have estimated that only 15-20% of patients are diagnosed with OSA.[105, 117] Given OSA prevalence estimates of 56-97% in people with tetraplegia,[15, 149] this represents an enormous burden of disease that is effectively being ignored. If these data are accurate, the proportion of those with undetected OSA is likely to lie between 45 to 82%. A more precise estimate, derived from systematic review and synthesis of available studies, of the prevalence and proportion of people with tetraplegia who have undiagnosed OSA would help to more accurately assess this burden.

Chapter 2 addresses the problem of poor access to diagnostic investigations by refining and validating a simple two-stage model designed to detect MS-OSA in people with tetraplegia. This is the first time an alternative to full PSG has been thoroughly investigated in this population and demonstrates that full PSG is not necessarily required for accurate detection of MS-OSA in people with chronic tetraplegia. The four-item questionnaire followed by portable overnight oximetry therefore has the potential to substantially increase the detection of OSA and improve access to treatment, particularly in settings where access to services is poor. [149]

### 6.2.2 CPAP use for OSA in tetraplegia

The first-line treatment for OSA is CPAP, which has been found to improve daytime sleepiness in acute tetraplegia.[225] Chapter 3 reports secondary analysis of CPAP data from a multicentre randomised controlled trial investigating the effect of CPAP on neurocognitive outcomes among people with acute, traumatic tetraplegia and OSA.[226] The aims of this secondary analysis were to estimate CPAP adherence, to determine baseline predictors of adherence, and to describe average pressure requirements and unintentional mask leak. This is the largest study to estimate CPAP adherence in acute tetraplegia using objective data from the devices. The novel findings from this study included:

- Adherence to CPAP is low in acute tetraplegia, estimated at 21% of the total population.

- Within trial CPAP adherence was low at 33%, but similar to that reported in other trials in aged care and stroke populations.
- Following acute tetraplegia, those with more severe OSA were more likely to adhere to CPAP.
- People with tetraplegia require less CPAP to treat OSA at any severity than those without disability, however mask leak is high.
- There is a complex relationship between OSA severity, CPAP pressure requirements and CPAP adherence, which is likely to reflect underlying differences in pathophysiology in this population.

Using both qualitative and quantitative research methodologies, Chapter 4 reports estimated rates of adherence to CPAP in people with chronic tetraplegia, and patient level barriers and facilitators to the acceptance of CPAP. The novel findings from this study included:

- The burdens of using CPAP are substantial and unique to this population.
- The balance of perceived burdens relative to the perceived benefits of CPAP appears to influence ongoing use.
- CPAP adherence patterns may take up to six month to establish in people with tetraplegia.
- OSA is often being managed alongside many other secondary complications of SCI, and CPAP contributes to overall burden of treatment.
- There is poor recognition of OSA symptoms among people with tetraplegia.
- Estimated at 25%, CPAP adherence is low in chronic tetraplegia and likely worse than in people without disability.
- For people with tetraplegia, the requirement to stay overnight in a sleep laboratory for OSA testing is a major barrier to diagnosis.

This study is the first to investigate the experience of using CPAP in people with tetraplegia and OSA. It is also the first study to objectively quantify 12 month CPAP adherence in a cohort with chronic tetraplegia. The findings of this study point to new interventions which might improve adherence, such as providing more intensive support over a longer period to overcome the burdens of CPAP. It also highlights the need for more research into alternative treatments.

### 6.2.3 Understanding current clinical practice

Chapter 5 reports the variations in current management of OSA in tetraplegia and identified clinician and health system level factors influencing this management. The overall aim of this study was to document and understand the problems of under-diagnosis of OSA and poor access to treatment. The novel findings from this research included:

- The clinical management of OSA in tetraplegia is highly varied.
- Many spinal physicians/spinal units do not routinely screen for OSA because they lack resources, especially ancillary staff support, and reminder systems.
- Some spinal units independently diagnose and treat non-complicated OSA.
- Most spinal physicians refer to specialist sleep/respiratory services for OSA management because they believe they lack the resources, knowledge and skills to fully diagnose and treat OSA.

That OSA management practices were highly varied enabled comparison of the influences on clinical practice. Perhaps the most significant discovery was that it is feasible for spinal units to screen all patients with tetraplegia for OSA, and manage all aspects of non-complicated OSA. The logical enquiry arising from this finding is a comparison of patient outcomes between those managed by a spinal unit and those managed by specialist sleep services. Opportunities for further research aiming to improve access to OSA treatment are discussed in detail below.

## 6.3 Further research

As a result of this research, we now have a much deeper understanding of the OSA related issues faced by people with tetraplegia and their clinicians. These discoveries will inform a future research agenda to improve clinical practice and quality of life for people with tetraplegia. This thesis has primarily focused on understanding the problem, while the research proposals presented below, informed by this new knowledge, aim to find solutions.

Figure 6.1 provides a summary of what we know and don't know about how to improve access to OSA management in tetraplegia. The figure is divided into four quadrants: the

known problems (barriers and enablers to OSA management) and the unknown problems; the known solutions (interventions that improve access) and the “unknown” solutions (interventions that may improve access). This provides a framework to guide future research in this area.

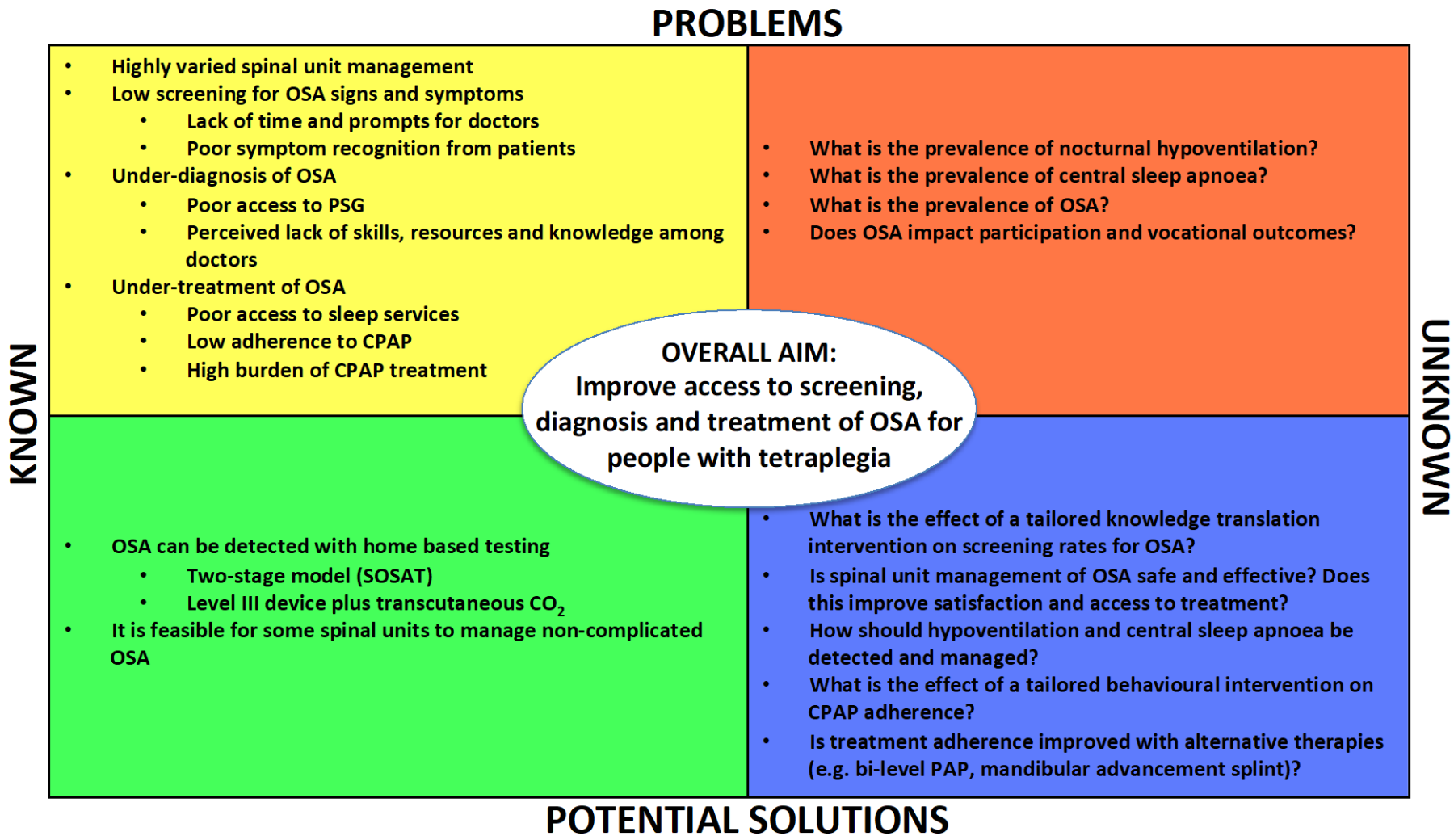


Figure 6.1 The “known” and “unknown” problems and solutions to improved access to OSA services in tetraplegia.

Detailed below is a proposal for two areas of research that aim to improve OSA management in tetraplegia, specifically by improving access to screening, diagnosis and treatment. Broadly, the two research areas are:

1. The design, implementation and evaluation of a knowledge translation intervention to increase screening for symptoms of OSA within the spinal unit environment.
2. Investigation of alternatives to the usual sleep/respiratory specialist model of OSA diagnosis and treatment.

Findings from this thesis suggest that spinal units are not routinely screening for OSA, and furthermore, that with appropriate resources and training the spinal rehabilitation team could take primary responsibility for managing OSA without the need for external referral. I hypothesise that these two shifts in clinical practice could substantially improve OSA diagnosis and access to treatment. A brief summary of these two projects, including the rationale, aims and proposed methods, are presented in the subsequent section.

This is by no means a comprehensive list of research projects that can and should be completed to advance knowledge in this area of medicine. In particular, other research is required to identify alternative treatments for OSA for people with tetraplegia, given the unique causes of OSA and the significant burdens associated with CPAP treatment. Further research into the use of mandibular advancement splits, considered to improve compliance with treatment in non-disabled populations with OSA,[227] warrants further investigation. Similarly, investigation of alternative agents to reduce nasal congestion may lead to new adjuncts to current therapies.[114]

### 6.3.1 Designing and testing a knowledge translation intervention to increase screening for OSA in tetraplegia

#### *6.3.1.1 Background and rationale:*

Clinical practice guidelines recommend screening patients with tetraplegia for signs and symptoms of OSA.[115] As discussed in Chapter 5, these guidelines are not explicit in

their recommended screening practices. More detail about who should be screened and how would enhance knowledge translation activities.

Qualitative research presented in Chapter 5 indicates that approximately half of spinal units are not routinely screening for OSA, despite most spinal doctors believing it is their role and being willing to increase OSA screening in their practice. There is an expressed enthusiasm from several spinal units to collaborate on further research to improve OSA screening. Using the Theoretical Domains Framework[133] to identify the influences on screening practices, this research identified that lack of time, knowledge and the absence of systems to trigger memory were largely responsible for the low screening behaviours.

The Knowledge to Action Cycle[129] (Figure 1.3) describes the steps necessary for effective application of knowledge into practice. The research presented in this thesis has described the barriers to routine screening for OSA. The next stage in the cycle is to use this information to "select, tailor and implement interventions", and to monitor and evaluate the outcomes.

#### *6.3.1.2 Aims:*

To design, implement and evaluate a tailored intervention aiming to increase screening for symptoms of OSA in the outpatient clinics of three spinal units.

#### *6.3.1.3 Proposed method:*

The multifaceted intervention will address knowledge, memory prompts, systems and resources. The setting will likely involve the spinal outpatient departments of several spinal units. Depending on the setting and available resources, effectiveness of the intervention could be evaluated using an interrupted time series design or a step-wedge trial. Medical record audit of monthly screening rates for OSA is the likely primary outcome measure. Secondary outcome measures could include referral rates to specialist sleep physicians and rates of OSA diagnostic testing.

### 6.3.2 Investigating alternative models of OSA management

#### *6.3.2.1 Background and rationale:*

Interventions to improve the diagnosis and treatment of OSA require a different approach to those aiming to improve screening. More knowledge about the most effective way to diagnose and treat OSA in SCI must be generated before implementation research can be undertaken, because the current standard of evidence is relatively weak. Several novel findings from this research have led me to question whether OSA may be better managed by specialised spinal units rather than specialist sleep/respiratory units.

Firstly, the current predominant model of referring to sleep specialists is clearly failing to provide adequate, accessible healthcare. People with tetraplegia are reluctant to attend overnight testing for OSA in a sleep laboratory, and furthermore, spinal doctors report poor access to these tests. People with tetraplegia and OSA describe unique burdens and motivations for CPAP use. Their experience of OSA diagnosis and treatment with CPAP is influenced substantially by their personal experience of living with their disability and its associated secondary complications. Given the unique and complex burdens and motivations for CPAP use in tetraplegia, I have hypothesised in Chapters 4 and 5 that spinal unit management of OSA may be preferable to specialist sleep management. The multi-disciplinary team within a spinal unit is generally responsible for the overall management of the person's SCI and associated complications. They are trained to provide "holistic" care to those with SCI, and therefore are likely to have a deeper understanding of the physical limitations and the medical and psychosocial issues experienced by people with tetraplegia than health professionals outside this specialty.

As discussed in Chapter 5, almost half of the spinal doctors interviewed were undertaking some diagnosis and/or treatment of non-complicated OSA, indicating that it is feasible for spinal doctors to perform and/or oversee these tasks. Three spinal units were independently managing all non-complicated OSA. To enable independent management of OSA, members of the multidisciplinary team would need to adopt new roles, requiring additional training and resources.

Poor access and high costs of in-laboratory specialist sleep services are also a problem for people without disability.[65, 67] In response, alternative ambulatory techniques to diagnose OSA and initiate treatment (under the auspices of sleep specialists) have been rigorously investigated, with all studies demonstrating non-inferiority of the alternative model.[65, 84] As discussed in Chapters 1 and 5, there have now been three non-inferiority randomised controlled trials investigating whether general practitioners (GPs) and nurses can effectively treat OSA in people without disability using ambulatory techniques. In each of the studies the alternative models were compared to the traditional sleep specialist model, and all concluded that the care provided by non-sleep specialist professionals was not inferior to that provided by the sleep specialists.[80, 81, 83]

Stroke survivors have a similarly high OSA prevalence (approximately 62-72%) to that observed in tetraplegia,[174, 175] and research has found that it is feasible and safe to diagnose and treat OSA within a stroke rehabilitation environment.[222] To date, there has been no similar research investigating alternative OSA models of care in tetraplegia.

#### *6.3.2.2 Hypothesis:*

The clinical outcomes of people with tetraplegia and OSA managed by a spinal unit will not be inferior to the outcomes of those managed by a specialist sleep centre.

#### *6.3.2.3 Proposed method:*

This hypothesis could be evaluated with a step-wedge trial design, a multicentre individual participant or cluster randomised controlled trial. In all designs people with tetraplegia would receive either spinal unit management of OSA or specialised sleep centre management. Evaluation of the primary outcome would be based on non-inferiority of the sleep specialist model. The primary outcome is likely to be change in subjective daytime sleepiness on a validated measure. Secondary outcomes could include quality of life, treatment adherence, waiting times to services, patient satisfaction, and adverse events.

I have presented this research idea at the National Canadian SCI Conference in Niagara Falls in 2017, and to Austin Health (Melbourne) Department of Respiratory and Sleep

Medicine in 2017. In both forums the support for the overall concept was positive. Both audiences agreed that before such a trial could commence, several unanswered, critical questions must be addressed. The concerns raised in these two forums related to the assessment and management of hypoventilation, staff training requirements, and appropriate selection of the primary outcome measure. Briefly outlined below are an additional five research questions and proposed methods that aim to address these issues, and inform and strengthen the design of a potential multi-centre trial comparing these two models of care.

### 6.3.3 How do spinal units routinely and independently manage OSA?

#### *6.3.3.1 Background and rationale:*

Qualitative research presented in Chapter 5 identified three spinal units routinely screening, diagnosing and treating uncomplicated OSA in their patients with tetraplegia, without consultation from specialist sleep services. All three spinal unit heads have committed to collaborate on further research to determine the components, feasibility and implementation factors associated with these models of care, and to provide at least two years of data for review. This information will inform the design of the spinal unit care model to be tested.

#### *6.3.3.2 Aim:*

To document and evaluate OSA management models of care in three spinal units.

#### *6.3.3.3 Proposed methods:*

Screening, diagnosis, safety and treatment processes will be thoroughly documented for each unit, ascertained from unit records and from interviews with unit staff. Process outcomes will be assessed (for example: proportion of people with tetraplegia screened; proportion diagnosed with OSA; proportion commenced on therapy; types of therapy prescribed; models for assessment and management of hypoventilation; proportion screened for hypercapnia, proportion with hypercapnia). Prevalence of OSA, determinants and rates of CPAP adherence and cost per patient will be estimated.

### 6.3.4 **Measuring daytime sleepiness in people with tetraplegia.**

#### *6.3.4.1 Background and rationale:*

Change in the patient-reported outcome of subjective sleepiness is the likely primary outcome of the proposed non-inferiority randomised controlled trial. For people with tetraplegia, the Minimal Important Difference (MID) has not been established for the Karolinska Sleepiness Scale (KSS)[204] or the Epworth Sleepiness Scale (ESS),[97] the two most commonly used measures of sleepiness in this population. Understanding how much change on these scales is clinically important is a critical trial element.

As discussed in Chapter 2, the KSS is commonly used to measure daytime sleepiness, especially "state" sleepiness, in OSA and SCI research.[149, 226] However the MID has never been established for the KSS in any population.

The ESS, a measure of trait sleepiness, is the most widely used measure of subjective sleepiness in sleep research.[97] However, as discussed in Chapter 2, its validity in SCI has been questioned because of questions about activities that are less frequently undertaken in this population, such as driving.[92] In my opinion, these dated assumptions should be challenged with future research investigating this common measure of trait sleepiness in tetraplegia.

Until recently, there was no formal estimate of the MID for the ESS. The three published non-inferiority randomised controlled trials discussed in Section 6.3.2.1 all used the ESS as their primary outcome measure.[80, 81, 83] They estimated the MID of the primary outcome to be -2, using a simple, universal method of halving the known standard deviation.[228] Since then, two studies have formally estimated the MID of the ESS using both distribution and anchor based methods. Both provided similar or identical MID estimates to that used previously.[229, 230] However the MID has never been estimated in people with tetraplegia whose disability and associated fatigue may cause them respond differently to questions about sleepiness.

Establishing the responsiveness and the MID of these two sleepiness questionnaires in a population of people with tetraplegia is essential for evaluative research investigating treatments for sleep disorders in tetraplegia. The performance of the two measures will

inform selection of the primary outcome measure, and the MID will enable calculation of the sample size in our planned study.

#### *6.3.4.2 Aim:*

To establish the responsiveness and MID for the KSS and ESS in people with tetraplegia.

#### *6.3.4.3 Proposed methods:*

Prospective cohort study in several spinal units with active OSA management programs. Approximately 100 patients with tetraplegia, assessed for OSA and prescribed treatment, will complete the KSS and ESS pre and post treatment initiation. Distribution and anchor-based methods will be used to determine the MID of both questionnaires.[231]

### 6.3.5 Safety and feasibility of spinal unit management of OSA

#### *6.3.5.1 Background and rationale:*

This study will test whether the model developed following the research proposed above in studies 6.3.3 and 6.3.4 is acceptable (to staff and patients), practical and safe to implement in a spinal unit that currently refers patients to specialist sleep services for OSA management.

#### *6.3.5.2 Aim:*

To determine the safety and feasibility of providing routine OSA screening, diagnosis and treatment to people with chronic tetraplegia in a spinal outpatient clinic setting.

#### *6.3.5.3 Proposed methods:*

A multidisciplinary team from within a spinal unit will be identified, roles delineated and a specialist OSA education package provided. Patients will be screened for OSA and managed by the spinal rehabilitation team according to the protocol developed. Measures of subjective daytime sleepiness and quality of life will be collected from participants, along with patient satisfaction, waiting times and CPAP usage data. Feedback on the model will be sought from staff. Potential adverse effects will be documented to assess safety.

### 6.3.6 **Prevalence of OSA in tetraplegia: a systematic review and meta-analysis.**

#### *6.3.6.1 Background and rationale:*

A precise measure of OSA prevalence in tetraplegia is critical for service and research planning, however reported prevalence estimates range from 15% to 97%.[14, 149, 232] Heterogeneity in study design is primarily responsible for this wide range.[14, 232] Testing methods for OSA, scoring methods for respiratory events, definitions of OSA, and the populations studied have varied enormously between studies. These differences have previously hindered synthesis of data and meta-analyses, however four studies published in the last ~10 years have employed similar rigorous methodologies,[1, 15, 16, 149] and suggest that the prevalence lies between 56 and 97%. Two meta-analyses of OSA prevalence in people with stroke and transient ischaemic attack have previously estimated the prevalence of OSA (defined as AHI≥5) to be 70% and 72%.[174, 175] Meta-analysis of OSA prevalence data in general, non-disabled populations has recently estimated the overall population prevalence to be between 9% and 38%, higher in men and increasing with age.[33] To date, there are no pooled prevalence estimates of OSA in SCI.

#### *6.3.6.2 Aims:*

To determine the prevalence of OSA in people with tetraplegia by conducting a systematic review and meta-analysis of OSA prevalence studies.

#### *6.3.6.3 Proposed methods:*

A systematic review and meta-analysis comprising: systematic searching of Medline, EMBASE and CINAHL databases employing SCI and OSA specific search terms; review of retrieved references against predetermined criteria to exclude ineligible studies; assessment of risk of bias of included studies; data extraction and analysis. Briefly, studies will be considered eligible if they objectively measured OSA in people with SCI using Level I or Level II studies, and reported prevalence with AHI.

### 6.3.7 Understanding the extent of hypoventilation and central sleep apnoea in tetraplegia

#### *6.3.7.1 Background and rationale:*

As previously discussed in Sections 1.6 and 2.7, the nature of respiratory events in tetraplegia remains controversial in the literature, with some research indicating predominance of central sleep apnoea [16, 173] and other studies finding OSA more prevalent.[93, 149, 212] To our knowledge, no research in SCI has investigated whether hypopnoeas are predominantly central or obstructive in nature, though this has been recommended.[85, 150] Very little is known about the prevalence of nocturnal hypercapnia, an indicator of hypoventilation, in people with SCI. Understanding the extent of central sleep apnoea and hypoventilation is essential for planning diagnosis and treatment pathways within the non-inferiority randomised controlled trial.

#### *6.3.7.2 Aims:*

To estimate the prevalence of hypercapnia, central and obstructive sleep apnoea in people with tetraplegia.

#### *6.3.7.3 Proposed methods:*

This study will involve a retrospective audit of data from three research studies led by the Institute for Breathing and Sleep,[1, 149, 226] and clinical data from the Austin Health Respiratory Medicine database. Clinical data extracted will include PSG and $CO_2$ studies in people with tetraplegia over the last 20 years. Descriptive analysis of the prevalence of hypercapnia and various respiratory event types will be undertaken, using previously staged and scored studies. In a sub-set of subjects, hypopnoeas will be classified as obstructive or central according to AASM 2012 guidelines.[27]

## 6.4 Conclusions

In chronic diseases such as stroke, cardiovascular disease, heart failure and diabetes, it is widely accepted that a pathway that incorporates the screening, diagnosis and management of sleep disordered breathing is essential for health and wellbeing.[233] However, for the majority of people with tetraplegia this is not yet available.

All people deserve timely access to evidence-based health care and living with a physical disability should not hinder this. Evidence suggests that OSA contributes to markedly reduced quality of life in tetraplegia, likely mediated through its negative effects on mood, cognition and participation. People living with tetraplegia and their clinicians are appropriately focused on their physical disability and pressing medical problems, however OSA goes mostly undetected.

This thesis has demonstrated that people with tetraplegia are not receiving quality management of OSA. They are under-diagnosed and subsequently under-treated for this highly prevalent secondary complication. Within this thesis several modifiable contributors to sub-optimal clinical management of OSA in tetraplegia have been identified, and two new areas of research have been recommended. The proposed research targets these barriers and enablers to optimal management using knowledge translation and health services research methodologies. By raising awareness of OSA and removing the barriers to investigation and management, it is likely that this silent disease will be better managed. Further knowledge translation research is likely to improve clinical care for people with tetraplegia and OSA, and thus has the potential to greatly impact their quality of life and participation outcomes.

# 7 REFERENCES


1. Berlowitz DJ, Spong J, Gordon I, Howard ME, Brown DJ: Relationships between objective sleep indices and symptoms in a community sample of people with tetraplegia. *Arch Phys Med Rehabil* 2012, 93(7):1246-1252.
2. Spong J, Graco M, Brown DJ, Schembri R, Berlowitz DJ: Subjective sleep disturbances and quality of life in chronic tetraplegia. *Spinal Cord* 2015.
3. WHO: International perspectives on spinal cord injury. In. Edited by Bickenbach J. Malta; 2013.
4. Harvey LPD: Management of spinal cord injuries : a guide for physiotherapists. Edinburgh ;: Butterworth-Heinemann; 2008.
5. Zejdlik CP: Management of spinal cord injury, 2nd ed. edn. Boston :: Jones and Bartlett Publishers; 1992.
6. Krassioukov A: Autonomic function following cervical spinal cord injury. *Respir Physiol Neurobiol* 2009, 169(2):157-164.
7. Haisma JA, Van Der Woude LH, Stam HJ, Bergen MP, Sluis TA, Post MW, Bussmann JB: Complications following spinal cord injury: occurrence and risk factors in a longitudinal study during and after inpatient rehabilitation. *J Rehabil Med* 2007, 39(5):393-398.
8. Hammell KW: Quality of life after spinal cord injury: a meta-synthesis of qualitative findings. *Spinal Cord* 2007, 45(2):124.
9. Westgren N, Levi R: Quality of life and traumatic spinal cord injury. *Arch Phys Med Rehabil* 1998, 79(11):1433-1439.
10. Berlowitz DJ, Wadsworth B, Ross J: Respiratory problems and management in people with spinal cord injury. *Breathe* 2016, 12(4):328-340.
11. Levi R, Hultling C, Nash MS, Seiger A: The Stockholm spinal cord injury study: 1. Medical problems in a regional SCI population. *Paraplegia* 1995, 33(6):308-315.
12. Biering-Sorensen F, Biering-Sorensen M: Sleep disturbances in the spinal cord injured: an epidemiological questionnaire investigation, including a normal population. *Spinal Cord* 2001, 39(10):505-513.
13. Jensen MP, Hirsh AT, Molton IR, Bamer AM: Sleep Problems in Individuals With Spinal Cord Injury: Frequency and Age Effects. *Rehabil Psychol* 2009, 54(3):323-331.
14. Giannoccaro MP, Moghadam KK, Pizza F, Boriani S, Maraldi NM, Avoni P, Morreale A, Liguori R, Plazzi G: Sleep disorders in patients with spinal cord injury. *Sleep Med Rev* 2013, 17(6):399-409.
15. Leduc BE, Dagher JH, Mayer P, Bellemare F, Lepage Y: Estimated prevalence of obstructive sleep apnea–hypopnea syndrome after cervical cord injury. *Arch Phys Med Rehabil* 2007, 88(3):333-337.
16. Sankari A, Bascom A, Oomman S, Badr M: Sleep disordered breathing in chronic spinal cord injury. *Journal of clinical sleep medicine: JCSM: official publication of the American Academy of Sleep Medicine* 2013, 10(1):65-72.

17. Fogelberg DJ, Leland, Blanchard NEJ, Rich TJ, Clark FA: Qualitative Experience of Sleep in Individuals With Spinal Cord Injury. *OTJR: occupation, participation and health* 2017, 37 (2):89-97.
18. AIHW, Tovell A, Harrison J: Spinal cord injury, Australia: summary 2008–09 to 2012–13. In: *Injury research and statistics series no 100 Cat no INJCAT 176.* Canberra: AIHW; 2018.
19. O'Connor P: Prevalence of spinal cord injury in Australia. *Spinal Cord* 2005, 43(1):42-46.
20. Access Economics PL: The economic cost of spinal cord injury and traumatic brain injury in Australia. In. Melbourne; 2009.
21. DeVivo M: Sir Ludwig Guttmann Lecture: Trends in spinal cord injury rehabilitation outcomes from model systems in the United States: 1973–2006. *Spinal Cord* 2007, 45(11):713-721.
22. Saunders LL, Selassie AW, Hill EG, Nicholas JS, Varma AK, Lackland DT, Patel SJ: Traumatic spinal cord injury mortality, 1981-1998. *Journal of Trauma-Injury, Infection, and Critical Care* 2009, 66(1):184-190.
23. Strauss DJ, DeVivo MJ, Paculdo DR, Shavelle RM: Trends in life expectancy after spinal cord injury. *Arch Phys Med Rehabil* 2006, 87(8):1079-1085.
24. Middleton J, Dayton A, Walsh J, Rutkowski S, Leong G, Duong S: Life expectancy after spinal cord injury: a 50-year study. *Spinal Cord* 2012, 50(11):803-811.
25. Kryger MH, Roth T, Dement WC: Principles and practice of sleep medicine. In., Sixth edition. edn. Philadelphia, PA :: Elsevier; 2017.
26. Chai-Coetzer C, Douglas J, McEvoy D: Guidelines for sleep studies in adults. Prepared for the Australasian Sleep Association. 2014. In.
27. Berry RB, Budhiraja R, Gottlieb DJ, Gozal D, Iber C, Kapur VK, Marcus CL, Mehra R, Parthasarathy S, Quan SF: Rules for scoring respiratory events in sleep: update of the 2007 AASM manual for the scoring of sleep and associated events: deliberations of the sleep apnea definitions task force of the American Academy of Sleep Medicine. *Journal of clinical sleep medicine: JCSM: official publication of the American Academy of Sleep Medicine* 2012, 8(5):597.
28. Australasian Sleep Association - MBS changes [https://www.sleep.org.au/professional-resources/mbs-changes-2]
29. Flemons W, Buysse D, Redline S, Oack A, Strohl K, Wheatley J, Young T, Douglas N, Levy P, McNicolas W: Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research. *Sleep* 1999, 22(5):667-689.
30. Iber C, Ancoli-Israel S, Chesson A, Quan S: The AASM Manual for the Scoring of Sleep and Associated Events: Rules, Terminology and Technical Specification, (2007). *Westchester American Academy of Sleep Medicine*:17-19.
31. Peppard PE, Young T, Barnet JH, Palta M, Hagen EW, Hla KM: Increased prevalence of sleep-disordered breathing in adults. *Am J Epidemiol* 2013, 177(9):1006-1014.
32. Heinzer R, Vat S, Marques-Vidal P, Marti-Soler H, Andries D, Tobback N, Mooser V, Preisig M, Malhotra A, Waeber G: Prevalence of sleep-disordered breathing in the general population: the HypnoLaus study. *The Lancet Respiratory Medicine* 2015, 3(4):310-318.

33. Senaratna CV, Perret JL, Lodge CJ, Lowe AJ, Campbell BE, Matheson MC, Hamilton GS, Dharmage SC: Prevalence of obstructive sleep apnea in the general population: a systematic review. *Sleep Med Rev* 2017, 34:70-81.
34. Young T, Skatrud J, Peppard PE: Risk factors for obstructive sleep apnea in adults. *JAMA* 2004, 291(16):2013-2016.
35. Jordan AS, McSharry DG, Malhotra A: Adult obstructive sleep apnoea. *The Lancet* 2014, 383(9918):736-747.
36. Eckert DJ, White DP, Jordan AS, Malhotra A, Wellman A: Defining phenotypic causes of obstructive sleep apnea. Identification of novel therapeutic targets. *Am J Respir Crit Care Med* 2013, 188(8):996-1004.
37. Tarasiuk A, Reuveni H: The economic impact of obstructive sleep apnea. *Curr Opin Pulm Med* 2013, 19(6):639-644.
38. Tregear S, Reston J, Schoelles K, Phillips B: Obstructive sleep apnea and risk of motor vehicle crash: systematic review and meta-analysis. *J Clin Sleep Med* 2009, 5(06):573-581.
39. Bucks RS, Olaithe M, Eastwood P: Neurocognitive function in obstructive sleep apnoea: A meta‐review. *Respirology* 2013, 18(1):61-70.
40. Wang X, Ouyang Y, Wang Z, Zhao G, Liu L, Bi Y: Obstructive sleep apnea and risk of cardiovascular disease and all-cause mortality: a meta-analysis of prospective cohort studies. *Int J Cardiol* 2013, 169(3):207-214.
41. Duce B, Milosavljevic J, Hukins C: The 2012 AASM Respiratory Event Criteria Increase the Incidence of Hypopneas in an Adult Sleep Center Population. *Journal of clinical sleep medicine: JCSM: official publication of the American Academy of Sleep Medicine* 2014, 11(12):1425-1431.
42. Ruehland WR, Rochford PD, O'Donoghue FJ, Pierce RJ, Singh P, Thornton AT: The new AASM criteria for scoring hypopneas: impact on the apnea hypopnea index. *Sleep* 2009, 32(2):150.
43. Abrishami A, Khajehdehi A, Chung F: A systematic review of screening questionnaires for obstructive sleep apnea. *Canadian Journal of Anesthesia/Journal canadien d'anesthésie* 2010, 57(5):423-438.
44. Ramachandran SK, Josephs LA: A meta-analysis of clinical screening tests for obstructive sleep apnea. *Anesthesiology* 2009, 110(4):928-939.
45. Ross SD, Sheinhait I, Harrison KJ, Kvasz M, Connelly JE, Shea SA, Allen IE: Systematic review and meta-analysis of the literature regarding the diagnosis of sleep apnea. *Sleep* 2000, 23(4):519-532.
46. Johnson KG, Johnson DC: Treatment of sleep-disordered breathing with positive airway pressure devices: technology update. *Medical Devices (Auckland, NZ)* 2015, 8:425.
47. Rosen CL, Auckley D, Benca R, Foldvary-Schaefer N, Iber C, Kapur V, Rueschman M, Zee P, Redline S: A multisite randomized trial of portable sleep studies and positive airway pressure autotitration versus laboratory-based polysomnography for the diagnosis and treatment of obstructive sleep apnea: the HomePAP study. *Sleep* 2012, 35(6):757-767.
48. Qaseem A, Holty J-EC, Owens DK, Dallas P, Starkey M, Shekelle P: Management of obstructive sleep apnea in adults: a clinical practice guideline from the American College of Physicians. *Ann Intern Med* 2013, 159(7):471-483.

49. McEvoy RD, Antic NA, Heeley E, Luo Y, Ou Q, Zhang X, Mediano O, Chen R, Drager LF, Liu Z: CPAP for prevention of cardiovascular events in obstructive sleep apnea. *N Engl J Med* 2016, 375(10):919-931.
50. Giles TL, Lasserson TJ, Smith B, White J, Wright JJ, Cates CJ: Continuous positive airways pressure for obstructive sleep apnoea in adults. *Cochrane Database of Systematic Reviews* 2006(1).
51. Iftikhar IH, Valentine CW, Bittencourt LR, Cohen DL, Fedson AC, Gíslason T, Penzel T, Phillips CL, Yu-sheng L, Pack AI: Effects of continuous positive airway pressure on blood pressure in patients with resistant hypertension and obstructive sleep apnea: a meta-analysis. *J Hypertens* 2014, 32(12):2341.
52. Montesi SB, Edwards BA, Malhotra A, Bakker JP: The effect of continuous positive airway pressure treatment on blood pressure: a systematic review and meta-analysis of randomized controlled trials. *Journal of clinical sleep medicine: JCSM: official publication of the American Academy of Sleep Medicine* 2012, 8(5):587.
53. Schwarz EI, Puhan MA, Schlatzer C, Stradling JR, Kohler M: Effect of CPAP therapy on endothelial function in obstructive sleep apnoea: A systematic review and meta‐analysis. *Respirology* 2015, 20(6):889-895.
54. Gay P, Weaver T, Loube D, Iber C: Evaluation of positive airway pressure treatment for sleep related breathing disorders in adults. *SLEEP-NEW YORK THEN WESTCHESTER-* 2006, 29(3):381.
55. Weaver TE, Sawyer AM: Adherence to continuous positive airway pressure treatment for obstructive sleep apnea: implications for future interventions. *The Indian journal of medical research* 2010, 131:245.
56. Antic NA, Catcheside P, Buchan C, Hensley M, Naughton MT, Rowland S, Williamson B, Windler S, McEvoy RD: The effect of CPAP in normalizing daytime sleepiness, quality of life, and neurocognitive function in patients with moderate to severe OSA. *Sleep* 2011, 34(1):111-119.
57. Sawyer AM, Gooneratne NS, Marcus CL, Ofer D, Richards KC, Weaver TE: A systematic review of CPAP adherence across age groups: clinical and empiric insights for developing CPAP adherence interventions. *Sleep Med Rev* 2011, 15(6):343-356.
58. Weaver TE, Maislin G, Dinges DF, Bloxham T, George CF, Greenberg H, Kader G, Mahowald M, Younger J, Pack AI: Relationship between hours of CPAP use and achieving normal levels of sleepiness and daily functioning. *Sleep* 2007, 30(6):711.
59. Zimmerman ME, Arnedt JT, Stanchina M, Millman RP, Aloia MS: Normalization of memory performance and positive airway pressure adherence in memory-impaired patients with obstructive sleep apnea. *Chest Journal* 2006, 130(6):1772-1778.
60. Adherence with continuous positive airway pressure (CPAP) [https://www.uptodate.com/contents/adherence-with-continuous-positive-airway-pressure-cpap ]
61. Rotenberg BW, Murariu D, Pang KP: Trends in CPAP adherence over twenty years of data collection: a flattened curve. *Journal of Otolaryngology-Head & Neck Surgery* 2016, 45(1):43.
62. Antonescu-Turcu A, Parthasarathy S: CPAP and bi-level PAP therapy: new and established roles. *Respir Care* 2010, 55(9):1216-1229.

63. Smith I, Lasserson TJ, Haniffa M: Interventions to improve use of continuous positive airway pressure for obstructive sleep apnoea. *Cochrane Database of Systematic Reviews* 2004(4).
64. Epstein LJ, Kristo D, Strollo Jr PJ, Friedman N, Malhotra A, Patil SP, Ramar K, Rogers R, Schwab RJ, Weaver EM: Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. *J Clin Sleep Med* 2009, 5(3):263-276.
65. Chai‐Coetzer CL, Antic NA, McEvoy RD: Ambulatory models of care for obstructive sleep apnoea: Diagnosis and management. *Respirology* 2013, 18(4):605-615.
66. Economics DA: Re-awakening Australia: The economic cost of sleep disorders in Australia, 2010. *Sleep Health Foundation* 2011.
67. Flemons WW, Douglas NJ, Kuna ST, Rodenstein DO, Wheatley J: Access to diagnosis and treatment of patients with suspected sleep apnea. *Am J Respir Crit Care Med* 2004, 169(6):668-672.
68. Young T, Evans L, Finn L, Palta M: Estimation of the clinically diagnosed proportion of sleep apnea syndrome in middle-aged men and women. *Sleep* 1997, 20(9):705-706.
69. Collop NA, Anderson WM, Boehlecke B, Claman D, Goldberg R, Gottlieb DJ, Hudgel D, Sateia M, Schwab R: Clinical guidelines for the use of unattended portable monitors in the diagnosis of obstructive sleep apnea in adult patients. *J Clin Sleep Med* 2007, 3(7):737-747.
70. Morgenthaler TI, Aurora RN, Brown T, Zak R, Alessi C, Boehlecke B, Chesson A, Friedman L, Kapur V, Maganti R: Practice parameters for the use of autotitrating continuous positive airway pressure devices for titrating pressures and treating adult patients with obstructive sleep apnea syndrome: an update for 2007 An American Academy of Sleep Medicine report. *SLEEP-NEW YORK THEN WESTCHESTER*- 2008, 31(1):141.
71. Kuna ST, Badr MS, Kimoff RJ, Kushida C, Lee-Chiong T, Levy P, McNicholas WT, Strollo Jr PJ: An official ATS/AASM/ACCP/ERS workshop report: research priorities in ambulatory management of adults with obstructive sleep apnea. *Proc Am Thorac Soc* 2011, 8(1):1-16.
72. Mulgrew AT, Fox N, Ayas NT, Ryan CF: Diagnosis and initial management of obstructive sleep apnea without polysomnography: a randomized validation study. *Ann Intern Med* 2007, 146(3):157-166.
73. Masa JF, Duran-Cantolla J, Capote F, Cabello M, Abad J, Garcia-Rio F, Ferrer A, Fortuna AM, Gonzalez-Mangado N, de la Peña M: Efficacy of home single-channel nasal pressure for recommending continuous positive airway pressure treatment in sleep apnea. *Sleep* 2015, 38(1):13.
74. Sánchez-de-la-Torre M, Nadal N, Cortijo A, Masa J, Duran-Cantolla J, Valls J, Serra S, Sánchez-de-la-Torre A, Gracia M, Ferrer F: Role of primary care in the follow-up of patients with obstructive sleep apnoea undergoing CPAP treatment: a randomised controlled trial. *Thorax* 2015, 70(4):346-352.
75. Kuna ST, Gurubhagavatula I, Maislin G, Hin S, Hartwig KC, McCloskey S, Hachadoorian R, Hurley S, Gupta R, Staley B: Noninferiority of functional outcome in ambulatory management of obstructive sleep apnea. *Am J Respir Crit Care Med* 2011, 183(9):1238-1244.

76. Berry RB, Hill G, Thompson L, McLaurin V: Portable monitoring and autotitration versus polysomnography for the diagnosis and treatment of sleep apnea. *Sleep* 2008, 31(10):1423-1431.
77. Andreu AL, Chiner E, Sancho-Chust JN, Pastor E, Llombart M, Gomez-Merino E, Senent C, Barbé F: Effect of an ambulatory diagnostic and treatment programme in patients with sleep apnoea. *Eur Respir J* 2012, 39(2):305-312.
78. Corral J, Sánchez-Quiroga M-Á, Carmona-Bernal C, Sánchez-Armengol Á, de la Torre AS, Durán-Cantolla J, Egea CJ, Salord N, Monasterio C, Terán J: Conventional Polysomnography Is Not Necessary for the Management of Most Patients with Suspected Obstructive Sleep Apnea. Noninferiority, Randomized Controlled Trial. *Am J Respir Crit Care Med* 2017, 196(9):1181-1190.
79. Qaseem A, Dallas P, Owens DK, Starkey M, Holty J-EC, Shekelle P: Diagnosis of obstructive sleep apnea in adults: a clinical practice guideline from the American College of Physicians. *Ann Intern Med* 2014, 161(3):210-220.
80. Antic NA, Buchan C, Esterman A, Hensley M, Naughton MT, Rowland S, Williamson B, Windler S, Eckermann S, McEvoy RD: A randomized controlled trial of nurse-led care for symptomatic moderate–severe obstructive sleep apnea. *Am J Respir Crit Care Med* 2009, 179(6):501-508.
81. Chai-Coetzer CL, Antic NA, Rowland LS, Reed RL, Esterman A, Catcheside PG, Eckermann S, Vowles N, Williams H, Dunn S: Primary care vs specialist sleep center management of obstructive sleep apnea and daytime sleepiness and quality of life: a randomized trial. *JAMA* 2013, 309(10):997-1004.
82. Chai-Coetzer CL, Antic NA, Rowland LS, Catcheside PG, Esterman A, Reed RL, Williams H, Dunn S, McEvoy RD: A simplified model of screening questionnaire and home monitoring for obstructive sleep apnoea in primary care. *Thorax* 2011, 66(3):213-219.
83. Sánchez-Quiroga MÁ, Corral J, Gómez-de-Terreros FJ, Carmona-Bernal C, Asensio-Cruz MI, Cabello M, Martínez-Martínez MÁ, Egea CJ, Ordax E, Barbe F: Primary Care Physicians Can Comprehensively Manage Sleep Apnea Patients: A Non-inferiority Randomized Controlled Trial. *Am J Respir Crit Care Med* 2018(ja).
84. Suárez M, Osorio J, Torres M, Montserrat JM: Should the diagnosis and management of OSA move into general practice? *Breathe* 2016, 12(3):243-247.
85. Sankari A, Martin JL, Badr MS: Sleep-Disordered Breathing and Spinal Cord Injury: Challenges and Opportunities. *Current sleep medicine reports* 2017, 3(4):272-278.
86. Berlowitz DJ, Brown DJ, Campbell DA, Pierce RJ: A longitudinal evaluation of sleep and breathing in the first year after cervical spinal cord injury. *Arch Phys Med Rehabil* 2005, 86(6):1193-1199.
87. Tran K, Hukins C, Geraghty T, Eckert B, Fraser L: Sleep‐disordered breathing in spinal cord‐injured patients: A short‐term longitudinal study. *Respirology* 2010, 15(2):272-276.

88. Burns SP, Little JW, Hussey JD, Lyman P, Lakshminarayanan S: Sleep apnea syndrome in chronic spinal cord injury: associated factors and treatment. *Arch Phys Med Rehabil* 2000, 81(10):1334-1339.
89. Klefbeck B, Sternhag M, Weinberg J, Levi R, Hultling C, Borg J: Obstructive sleep apneas in relation to severity of cervical spinal cord injury. *Spinal Cord* 1998, 36(9).
90. McEvoy R, Mykytyn I, Sajkov D, Flavell H, Marshall R, Antic R, Thornton A: Sleep apnoea in patients with quadriplegia. *Thorax* 1995, 50(6):613-619.
91. Short D, Stradling J, Williams S: Prevalence of sleep apnoea in patients over 40 years of age with spinal cord lesions. *J Neurol Neurosurg Psychiatry* 1992, 55(11):1032-1036.
92. Stockhammer E, Tobon A, Michel F, Eser P, Scheuler W, Bauer W, Baumberger M, Müller W, Kakebeeke T, Knecht H: Characteristics of sleep apnea syndrome in tetraplegic patients. *Spinal Cord* 2002, 40(6):286.
93. Bauman KA, Kurili A, Schotland HM, Rodriguez GM, Chiodo AE, Sitrin RG: Simplified Approach to Diagnosing Sleep-Disordered Breathing and Nocturnal Hypercapnia in Individuals With Spinal Cord Injury. *Archives of physical medicine and rehabilitation* 2015.
94. Maislin GP, A I. Kribbs, N B. Smith, P L. Schwartz, A R. Kline, L R. Schwab, R J. Dinges, D F.: A survey screen for prediction of apnea. *Sleep* 1995, 18(3):158-166.
95. Netzer NC, Stoohs RA, Netzer CM, Clark K, Strohl KP: Using the Berlin Questionnaire to identify patients at risk for the sleep apnea syndrome. *Ann Intern Med* 1999, 131(7):485-491.
96. Sankari A, Martin J, Bascom A, Mitchell M, Badr M: Identification and treatment of sleep-disordered breathing in chronic spinal cord injury. *Spinal Cord* 2015, 53(2):145-149.
97. Johns MW: A new method for measuring daytime sleepiness: the Epworth sleepiness scale. *Sleep* 1991, 14(6):540-545.
98. Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ: The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry Res* 1989, 28(2):193-213.
99. Krupp LB, LaRocca NG, Muir-Nash J, Steinberg AD: The fatigue severity scale: application to patients with multiple sclerosis and systemic lupus erythematosus. *Arch Neurol* 1989, 46(10):1121-1123.
100. Gainche L, Berlowitz DJ, LeGuen M, Ruehland WR, O'Donoghue FJ, Trinder J, Graco M, Schembri R, Eckert DJ, Rochford PD: Nasal resistance is elevated in people with tetraplegia and is reduced by topical sympathomimetic administration. *Journal of clinical sleep medicine: JCSM: official publication of the American Academy of Sleep Medicine* 2016, 12(11):1487.
101. Gainche L, LeGuen M, Trinder JA, Rochford PD, O'Donoghue FJ, Berlowitz DJ, Jordan AS: Pathogenesis of obstructive sleep apnoea in quadriplegia. In: *52nd Annual Meeting of International Spinal Cord Society: October 2013 2013; Istanbul, Turkey*; 2013.
102. Mansel JK, Norman J: Respiratory complications and management of spinal cord injuries. *CHEST Journal* 1990, 97(6):1446-1452.
103. Wijesuriya NS, Lewis C, Butler JE, Lee BB, Jordan AS, Berlowitz DJ, Eckert DJ: High nasal resistance is stable over time but poorly perceived in people

with tetraplegia and obstructive sleep apnoea. *Respir Physiol Neurobiol* 2017, 235:27-33.
104. Al Lawati NM, Patel SR, Ayas NT: Epidemiology, risk factors, and consequences of obstructive sleep apnea and short sleep duration. *Prog Cardiovasc Dis* 2009, 51(4):285-293.
105. Sankari A, Martin J, Badr M: A retrospective review of sleep-disordered breathing, hypertenstion and cardiovascular diseases in spinal cord injury patients. *Spinal Cord* 2015, 53(6):496.
106. McEvoy RD, Anderson CS, Antic NA, Chen B, He Q, Heeley E, Huang S, Huang Y, Wang J, Zhong N: The sleep apnea cardiovascular endpoints (SAVE) trial: Rationale and start-up phase. *J Thorac Dis* 2011, 2(3):138-143.
107. Goh MY, Millard MS, Wong EC, Berlowitz DJ, Graco M, Schembri RM, Brown DJ, Frauman AG, O'Callaghan CJ: Comparison of diurnal blood pressure and urine production between people with and without chronic spinal cord injury. *Spinal Cord* 2018:1.
108. Sajkov D, Marshall R, Walker P, Mykytyn I, McEvoy RD, Wale J, Flavell H, Thornton AT, Antic R: Sleep apnoea related hypoxia is associated with cognitive disturbances in patients with tetraplegia. *Spinal Cord* 1998, 36(4):231-239.
109. Schembri R, Spong J, Graco M, Berlowitz D, team Cs: Neuropsychological function in patients with acute tetraplegia and sleep disordered breathing. *Sleep* 2016.
110. Berlowitz DJ, Schembri R, Graco M, Ross JM, Ayas N, Gordon I, Lee B, Graham A, Cross SV, McClelland M *et al*: Positive airway pressure for sleep-disordered breathing in acute quadriplegia: a randomised controlled trial. *Thorax* 2018:thoraxjnl-2018-212319.
111. Berlowitz D, Spong J, Pierce R, Ross J, Barnes M, Brown D: The feasibility of using auto-titrating continuous positive airway pressure to treat obstructive sleep apnoea after acute tetraplegia. *Spinal Cord* 2009, 47(12):868-873.
112. Brown JP, Bauman KA, Kurili A, Rodriguez GM, Chiodo AE, Sitrin RG, Schotland HM: Positive airway pressure therapy for sleep-disordered breathing confers short-term benefits to patients with spinal cord injury despite widely ranging patterns of use. *Spinal Cord* 2018, 56:777-789.
113. Burns SP, Rad MY, Bryant S, Kapur V: Long-term treatment of sleep apnea in persons with spinal cord injury. *Am J Phys Med Rehabil* 2005, 84(8):620-626.
114. Wijesuriya NS, Eckert DJ, Jordan AS, Schembri R, Lewis C, Meaklim H, Booker L, Brown D, Graco M, Berlowitz DJ: A randomised controlled trial of nasal decongestant to treat obstructive sleep apnoea in people with cervical spinal cord injury. *Spinal Cord* 2019:1.
115. Respiratory Management Following Spinal Cord Injury: A Clinical Practice Guideline for Health-Care Professionals. In.: Consortium for Spinal Cord Medicine; Paralyzed Veterans of America; 2005.
116. Sheel AW RW, Townson AF, Ayas N Respiratory Management Following Spinal Cord Injury. , 5 edn. Vancouver; 2014.
117. Burns S, Kapur V, Yin K, Buhrer R: Factors associated with sleep apnea in men with spinal cord injury: a population-based case-control study. *Spinal Cord* 2001, 39(1):15-22.

118. WHO: Bridging the “Know–Do” Gap. Meeting on Knowledge Translation in Global Health. In. Geneva, Switzerland :: World Health Organization; 2006.
119. Sussman S, Valente TW, Rohrbach LA, Skara S, Ann Pentz M: Translation in the health professions: converting science into action. *Eval Health Prof* 2006, 29(1):7-32.
120. Morris ZS, Wooding S, Grant J: The answer is 17 years, what is the question: understanding time lags in translational research. *J R Soc Med* 2011, 104(12):510-520.
121. McGlynn EA, Asch SM, Adams J, Keesey J, Hicks J, DeCristofaro A, Kerr EA: The quality of health care delivered to adults in the United States. *N Engl J Med* 2003, 348(26):2635-2645.
122. Grol R: Successes and failures in the implementation of evidence-based guidelines for clinical practice. *Med Care* 2001, 39(8):II-46-II-54.
123. Runciman WB, Hunt TD, Hannaford NA, Hibbert PD, Westbrook JI, Coiera EW, Day RO, Hindmarsh DM, McGlynn EA, Braithwaite J: CareTrack: assessing the appropriateness of health care delivery in Australia. *Med J Aust* 2012, 197(2):100.
124. Medicine Io: Crossing the Quality Chasm: A New Health System for the 21st Century. Washington, DC: The National Academies Press; 2001.
125. Cabana MD, Rand CS, Powe NR, Wu AW, Wilson MH, Abboud P-AC, Rubin HR: Why don't physicians follow clinical practice guidelines?: A framework for improvement. *JAMA* 1999, 282(15):1458-1465.
126. Grimshaw JM, Eccles MP, Lavis JN, Hill SJ, Squires JE: Knowledge translation of research findings. *Implementation science* 2012, 7(1):50.
127. Terrace L: Development and validation of an international appraisal instrument for assessing the quality of clinical practice guidelines: the AGREE project. *Qual Saf Health Care* 2003, 12:18-23.
128. Khalil H: Knowledge translation and implementation science: what is the difference? In.: LWW; 2016.
129. Graham ID, Logan J, Harrison MB, Straus SE, Tetroe J, Caswell W, Robinson N: Lost in knowledge translation: time for a map? *J Contin Educ Health Prof* 2006, 26(1):13-24.
130. Graham ID, Harrison MB: Evaluation and adaptation of clinical practice guidelines. *Evid Based Nurs* 2005, 8(3):68-72.
131. Harrison MB, Légaré F, Graham ID, Fervers B: Adapting clinical practice guidelines to local context and assessing barriers to their use. *Can Med Assoc J* 2010, 182(2):E78-E84.
132. Baker R, Camosso‐Stefinovic J, Gillies C, Shaw EJ, Cheater F, Flottorp S, Robertson N, Wensing M, Fiander M, Eccles MP: Tailored interventions to address determinants of practice. *Cochrane Database of Systematic Reviews* 2015(4).
133. Michie S, Johnston M, Abraham C, Lawton R, Parker D, Walker A: Making psychological theory useful for implementing evidence based practice: a consensus approach. *Quality and safety in health care* 2005, 14(1):26-33.
134. Bussieres AE, Patey AM, Francis J, Sales AE, Grimshaw JM: Identifying factors likely to influence compliance with diagnostic imaging guideline recommendations for spine disorders among chiropractors in North America: a focus group study using the Theoretical Domains Framework. *Implement Sci* 2012, 7:82.

135. Cane J, O'Connor D, Michie S: Validation of the theoretical domains framework for use in behaviour change and implementation research. *Implement Sci* 2012, 7(1):37.
136. French SD, Green SE, O'Connor DA, McKenzie JE, Francis JJ, Michie S, Buchbinder R, Schattner P, Spike N, Grimshaw JM: Developing theory-informed behaviour change interventions to implement evidence into practice: a systematic approach using the Theoretical Domains Framework. *Implementation Science* 2012, 7(1):38.
137. Murphy K, O'Connor D, Browning CJ, French SD, Michie S, Francis JJ, Russell GM, Workman B, Flicker L, Eccles MP: Understanding diagnosis and management of dementia and guideline implementation in general practice: a qualitative study using the theoretical domains framework. *Implement Sci* 2014, 9(1):31-?
138. Tavender EJ, Bosch M, Gruen RL, Green SE, Knott J, Francis JJ, Michie S, O'Connor DA: Understanding practice: the factors that influence management of mild traumatic brain injury in the emergency department-a qualitative study using the Theoretical Domains Framework. *Implement Sci* 2014, 9(8).
139. McKenzie JE, French SD, O'Connor DA, Grimshaw JM, Mortimer D, Michie S, Francis J, Spike N, Schattner P, Kent PM: IMPLEmenting a clinical practice guideline for acute low back pain evidence-based manageMENT in general practice (IMPLEMENT): cluster randomised controlled trial study protocol. *Implementation Science* 2008, 3(1):11.
140. Curran JA, Grimshaw JM, Hayden JA, Campbell B: Knowledge translation research: the science of moving research into policy and practice. *J Contin Educ Health Prof* 2011, 31(3):174-180.
141. Eccles M, Grimshaw J, Campbell M, Ramsay C: Research designs for studies evaluating the effectiveness of change and improvement strategies. *BMJ Quality & Safety* 2003, 12(1):47-52.
142. Noonan V, Wolfe D, Thorogood N, Park S, Hsieh J, Eng J: Knowledge translation and implementation in spinal cord injury: a systematic review. *Spinal Cord* 2014, 52(8):578-587.
143. Barrable B, Thorogood N, Noonan V, Tomkinson J, Joshi P, Stephenson K, Barclay J, Burns KK: Model for bridging the translational "valleys of death" in spinal cord injury research. *Journal of Healthcare Leadership* 2014, 6:15-27.
144. McQueen L, Mittman BS, Demakis JG: Overview of the veterans health administration (VHA) quality enhancement research initiative (QUERI). *J Am Med Inform Assoc* 2004, 11(5):339-343.
145. PE H, KE C, CPG P: Canadian Best Practice Guidelines for the Prevention and Management of Pressure Ulcers in People with Spinal Cord Injury. A resource handbook for Clinicians. . 2013.
146. Bragge P, Piccenna L, Middleton J, Williams S, Creasey G, Dunlop S, Brown D, Gruen R: Developing a spinal cord injury research strategy using a structured process of evidence review and stakeholder dialogue. Part I: rapid review of SCI prioritisation literature. *Spinal Cord* 2015, 53(10):714.
147. Bragge P, Piccenna L, Middleton J, Williams S, Creasey G, Dunlop S, Brown D, Gruen R: Developing a spinal cord injury research strategy using a

structured process of evidence review and stakeholder dialogue. Part II: Background to a research strategy. *Spinal Cord* 2015, 53(10):721.
148. Middleton JW, Piccenna L, Gruen RL, Williams S, Creasey G, Dunlop S, Brown D, Batchelor PE, Berlowitz DJ, Coates S: Developing a spinal cord injury research strategy using a structured process of evidence review and stakeholder dialogue. Part III: outcomes. *Spinal Cord* 2015, 53(10):729.
149. Graco M, Schembri R, Cross S, Thiyagarajan C, Shafazand S, Ayas NT, Nash MS, Vu VH, Ruehland WR, Chai-Coetzer CL: Diagnostic accuracy of a two-stage model for detecting obstructive sleep apnoea in chronic tetraplegia. *Thorax* 2018:thoraxjnl-2017-211131.
150. Adler D, Janssens J-P: Estimating the probability of OSA in the spinal cord injury population: specific tools are still needed. In.: BMJ Publishing Group Ltd; 2018.
151. Pretto JJ, Roebuck T, Beckert L, Hamilton G: Clinical use of pulse oximetry: official guidelines from the Thoracic Society of Australia and New Zealand. *Respirology* 2014, 19(1):38-46.
152. Ling IT, James AL, Hillman DR: Interrelationships between body mass, oxygen desaturation, and apnea-hypopnea indices in a sleep clinic population. *Sleep* 2012, 35(1):89-96.
153. Arzt M, Young T, Finn L, Skatrud JB, Bradley TD: Association of sleep-disordered breathing and the occurrence of stroke. *Am J Respir Crit Care Med* 2005, 172(11):1447-1451.
154. Marin JM, Carrizo SJ, Vicente E, Agusti AG: Long-term cardiovascular outcomes in men with obstructive sleep apnoea-hypopnoea with or without treatment with continuous positive airway pressure: an observational study. *The Lancet* 2005, 365(9464):1046-1053.
155. Marshall NS, Wong KK, Liu PY, Cullen SR, Knuiman MW, Grunstein RR: Sleep apnea as an independent risk factor for all-cause mortality: the Busselton Health Study. *Sleep* 2008, 31(8):1079.
156. Punjabi NM, Caffo BS, Goodwin JL, Gottlieb DJ, Newman AB, O'Connor GT, Rapoport DM, Redline S, Resnick HE, Robbins JA: Sleep-disordered breathing and mortality: a prospective cohort study. *PLoS Med* 2009, 6(8):e1000132.
157. Redline S, Yenokyan G, Gottlieb DJ, Shahar E, O'Connor GT, Resnick HE, Diener-West M, Sanders MH, Wolf PA, Geraghty EM: Obstructive sleep apnea–hypopnea and incident stroke: the sleep heart health study. *Am J Respir Crit Care Med* 2010, 182(2):269-277.
158. Shahar E, Whitney CW, REdline S, Lee ET, Newman AB, Javier Nieto F, O'Connor GT, Boland LL, Schwartz JE, Samet JM: Sleep-disordered breathing and cardiovascular disease: cross-sectional results of the Sleep Heart Health Study. *Am J Respir Crit Care Med* 2001, 163(1):19-25.
159. Adams N, Strauss M, Schluchter M, Redline S: Relation of measures of sleep-disordered breathing to neuropsychological functioning. *Am J Respir Crit Care Med* 2001, 163(7):1626-1631.
160. Aloia MS, Arnedt J, Davis JD, Riggs RL, Byrd D: Neuropsychological sequelae of obstructive sleep apnea-hypopnea syndrome: a critical review. *J Int Neuropsychol Soc* 2004, 10(05):772-785.

161. Naëgelé B, Thouvard V, Pépin J-L, Lévy P, Bonnet C, Perret JE, Pellat J, Feuerstein C: Deficits of cognitive executive functions in patients with sleep apnea syndrome. *Sleep: Journal of Sleep Research & Sleep Medicine* 1995.
162. Madbouly EM, Nadeem R, Nida M, Molnar J, Aggarwal S, Loomba R: The Role of Severity of Obstructive Sleep Apnea Measured by Apnea–Hypopnea Index in Predicting Compliance With Pressure Therapy, a Meta-analysis. *Am J Ther* 2014, 21(4):260-264.
163. Partinen M, Gislason T: Basic Nordic Sleep Questionnaire (BNSQ): a quantitated measure of subjective sleep complaints. *J Sleep Res* 1995, 4(s1):150-155.
164. Gillberg M, Kecklund G, Åkerstedt T: Relations between performance and subjective ratings of sleepiness during a night awake. *Sleep* 1994, 17(3):236-241.
165. Cunnington D, Garg H, Teichtahl H: Accuracy of an ambulatory device for the diagnosis of sleep disordered breathing. *The Indian Journal of Sleep Medicine* 2009, 4(4):143-148.
166. Chung F, Liao P, Sun Y, Amirshahi B, Fazel H, Shapiro CM, Elsaid H: Perioperative practical experiences in using a level 2 portable polysomnography. *Sleep and Breathing* 2011, 15(3):367-375.
167. Ng Y, Joosten S, Edwards B, Turton A, Romios H, Samarasinghe T, Landry S, Mansfield D, Hamilton G: Oxygen Desaturation Index Differs Significantly Between Types of Sleep Software. *Journal of clinical sleep medicine: JCSM: official publication of the American Academy of Sleep Medicine* 2017, 13(4):599.
168. Stull DE, Meltzer EO, Krouse JH, Roberts L, Kim S, Frank L, Naclerio R, Lund V, Long A: The congestion quantifier five-item test for nasal congestion: refinement of the congestion quantifier seven-item test. *American journal of rhinology & allergy* 2010, 24(1):34-38.
169. Wilson RC, Jones P: A comparison of the visual analogue scale and modified Borg scale for the measurement of dyspnoea during exercise. *Clin Sci* 1989, 76(3):277-282.
170. DeVivo M, Biering-Sørensen F, New P, Chen Y: Standardization of data analysis and reporting of results from the International Spinal Cord Injury Core Data Set. *Spinal Cord* 2010, 49(5):596-599.
171. Åkerstedt T, Gillberg M: Subjective and objective sleepiness in the active individual. *Int J Neurosci* 1990, 52(1-2):29-37.
172. Brown JG, Wieroney M, Blair L, Zhu S, Warren J, Scharf SM, Hinds PS: Measuring subjective sleepiness at work in hospital nurses: validation of a modified delivery format of the Karolinska Sleepiness Scale. *Sleep and Breathing* 2014, 18(4):731-739.
173. Sankari A, Bascom AT, Chowdhuri S, Badr MS: Tetraplegia is a risk factor for central sleep apnea. *J Appl Physiol* 2013, 116(3):345-353.
174. Dong R, Dong Z, Liu H, Shi F, Du J: Prevalence, Risk Factors, Outcomes, and Treatment of Obstructive Sleep Apnea in Patients with Cerebrovascular Disease: A Systematic Review. *J Stroke Cerebrovasc Dis* 2018, 27(6):1471-1480.
175. Johnson KG, Johnson DC: Frequency of sleep apnea in stroke and TIA patients: a meta-analysis. *Journal of clinical sleep medicine: JCSM: official publication of the American Academy of Sleep Medicine* 2010, 6(2):131.

176. Boulos MI, Elias S, Wan A, Im J, Frankul F, Atalla M, Black SE, Basile VS, Sundaram A, Hopyan JJ: Unattended hospital and home sleep apnea testing following cerebrovascular events. *J Stroke Cerebrovasc Dis* 2017, 26(1):143-149.
177. Kepplinger J, Barlinn K, Albright KC, Schrempf W, Boehme AK, Pallesen L-P, Schwanebeck U, Graehlert X, Storch A, Reichmann H: Early sleep apnea screening on a stroke unit is feasible in patients with acute cerebral ischemia. *J Neurol* 2013, 260(5):1343-1350.
178. Lofaso F, Coste A, Zerah‐Lancner F, Delclaux C, Goldenberg F, Harf A: Nasal obstruction as a risk factor for sleep apnoea syndrome. *Eur Respir J* 2000, 16(4):639-643.
179. Budhiraja R, Parthasarathy S, Drake CL, Roth T, Sharief I, Budhiraja P, Saunders V, Hudgel DW: Early CPAP use identifies subsequent adherence to CPAP therapy. *SLEEP-NEW YORK THEN WESTCHESTER-* 2007, 30(3):320.
180. Chai-Coetzer CL, Luo Y-M, Antic NA, Zhang X-L, Chen B-Y, He Q-Y, Heeley E, Huang S-G, Anderson C, Zhong N-S: Predictors of long-term adherence to continuous positive airway pressure therapy in patients with obstructive sleep apnea and cardiovascular disease in the SAVE study. *Sleep* 2013, 36(12):1929.
181. Weaver TE, Grunstein RR: Adherence to continuous positive airway pressure therapy: the challenge to effective treatment. *Proc Am Thorac Soc* 2008, 5(2):173-178.
182. Weaver TE, Kribbs NB, Pack AI, Kline LR, Chugh TK, Maislin G, Smith PL, Schwartz AR, Schubert NM, Gillen KA *et al*: 'Night—To-Night Variability in CPAP Use Over the First Three Months of Treatment. *Sleep* 1997, 20(4):278-283.
183. Aloia MS, Arnedt JT, Stanchina M, Millman RP: How early in treatment is PAP adherence established? Revisiting night-to-night variability. *Behav Sleep Med* 2007, 5(3):229-240.
184. Berlowitz DJ: Neurotrauma and sleep. *Sleep Med Rev* 2013, 17(6):391-393.
185. Le Guen M, Cistulli P, Berlowitz DJ: Continuous positive airway pressure requirements in patients with tetraplegia and obstructive sleep apnoea. *Spinal Cord* 2012, 50(11):832-835.
186. Berlowitz DJ, Ayas N, Barnes M, Brown DJ, Cistulli PA, Geraghty T, Graham A, Lee BB, Morris M, Fergal O: Auto-titrating continuous positive airway pressure treatment for obstructive sleep apnoea after acute quadriplegia (COSAQ): study protocol for a randomized controlled trial. *Trials* 2013, 14(1):181.
187. Hawthorne G, Richardson J, Osborne R: The Assessment of Quality of Life (AQoL) instrument: a psychometric measure of health-related quality of life. *Qual Life Res* 1999, 8(3):209-224.
188. Blair JR, Spreen O: Predicting premorbid IQ: a revision of the National Adult Reading Test. *The Clinical Neuropsychologist* 1989, 3(2):129-136.
189. Zigmond AS, Snaith RP: The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983, 67(6):361-370.
190. McNair DM, Lorr M, Droppleman LF: Profile of mood states: Educational and Industrial Testing Service San Diego, CA; 1981.
191. McMillan A, Bratton DJ, Faria R, Laskawiec-Szkonter M, Griffin S, Davies RJ, Nunn AJ, Stradling JR, Riha RL, Morrell MJ: Continuous positive airway

pressure in older people with obstructive sleep apnoea syndrome (PREDICT): a 12-month, multicentre, randomised trial. *The Lancet Respiratory Medicine* 2014, 2(10):804-812.
192. Hsu C-Y, Vennelle M, Li H-Y, Engleman HM, Dennis MS, Douglas NJ: Sleep-disordered breathing after stroke: a randomised controlled trial of continuous positive airway pressure. *J Neurol Neurosurg Psychiatry* 2006, 77(10):1143-1149.
193. Sandberg O, Franklin K, Bucht G, Eriksson S, Gustafson Y: Nasal continuous positive airway pressure in stroke patients with sleep apnoea: a randomized treatment study. *Eur Respir J* 2001, 18(4):630-634.
194. Valentin A, Subramanian S, Quan SF, Berry RB, Parthasarathy S: Air leak is associated with poor adherence to autoPAP therapy. *Sleep* 2011, 34(6):801-806.
195. Bachour A, Virkkala JT, Maasilta PK: AutoCPAP initiation at home: optimal trial duration and cost-effectiveness. *Sleep Med* 2007, 8(7):704-710.
196. Noseda A, Kempenaers C, Kerkhofs M, Braun S, Linkowski P, Jann E: Constant vs auto-continuous positive airway pressure in patients with sleep apnea hypopnea syndrome and a high variability in pressure requirement. *Chest* 2004, 126(1):31-37.
197. Camacho M, Riaz M, Tahoori A, Certal V, Kushida CA: Mathematical equations to predict positive airway pressures for obstructive sleep apnea: a systematic review. *Sleep disorders* 2015, 2015.
198. Ryan CM, Bayley M, Green R, Murray BJ, Bradley TD: Influence of continuous positive airway pressure on outcomes of rehabilitation in stroke patients with obstructive sleep apnea. *Stroke* 2011:STROKEAHA. 110.597468.
199. Almeida FR, Henrich N, Marra C, Lynd LD, Lowe AA, Tsuda H, Fleetham JA, Pliska B, Ayas N: Patient preferences and experiences of CPAP and oral appliances for the treatment of obstructive sleep apnea: a qualitative analysis. *Sleep and Breathing* 2013, 17(2):659-666.
200. Broström A, Fridlund B, Ulander M, Sunnergren O, Svanborg E, Nilsen P: A mixed method evaluation of a group‐based educational programme for CPAP use in patients with obstructive sleep apnea. *J Eval Clin Pract* 2013, 19(1):173-184.
201. Prashad PS, Marcus CL, Maggs J, Stettler N, Cornaglia MA, Costa P, Puzino K, Xanthopoulos M, Bradford R, Barg FK: Investigating reasons for CPAP adherence in adolescents: a qualitative approach. *Journal of clinical sleep medicine: JCSM: official publication of the American Academy of Sleep Medicine* 2013, 9(12):1303.
202. Sawyer AM, Deatrick JA, Kuna ST, Weaver TE: Differences in perceptions of the diagnosis and treatment of obstructive sleep apnea and continuous positive airway pressure therapy among adherers and nonadherers. *Qualitative health research* 2010.
203. Ward K, Hoare KJ, Gott M: What is known about the experiences of using CPAP for OSA from the users' perspective? A systematic integrative literature review. *Sleep Med Rev* 2014, 18(4):357-366.
204. Åkerstedt T, Anund A, Axelsson J, Kecklund G: Subjective sleepiness is a sensitive indicator of insufficient sleep and impaired waking function. *J Sleep Res* 2014, 23(3):240-252.

205. Schwarzer R, Jerusalem M: Generalized Self-Efficacy scale. In: *Measures in health psychology: A user's portfolio Causal and control beliefs.* edn. Edited by Weinman J, Wright S, Johnston M. Windsor, England: NFER-NELSON; 1995: 35-37.
206. Braun V, Clarke V, Terry G: Thematic analysis. *APA handbook of research methods in psychology* 2012, 2:57-71.
207. Adriaansen JJ, Post MW, de Groot S, van Asbeck FW, Stolwijk-Swüste JM, Tepper M, Lindeman E: Secondary health conditions in persons with spinal cord injury: a longitudinal study from one to five years post-discharge. *J Rehabil Med* 2013, 45(10):1016-1022.
208. Anson C, Shepherd C: Incidence of secondary complications in spinal cord injury. *International journal of rehabilitation research Internationale Zeitschrift fur Rehabilitationsforschung Revue internationale de recherches de readaptation* 1996, 19(1):55-66.
209. Bloemen-Vrencken JH, Post MW, Hendriks JM, De Reus EC, De Witte LP: Health problems of persons with spinal cord injury living in the Netherlands. *Disabil Rehabil* 2005, 27(22):1381-1389.
210. Rosbach M, Andersen JS: Patient-experienced burden of treatment in patients with multimorbidity–A systematic review of qualitative data. *PLoS One* 2017, 12(6):e0179916.
211. Eton DT, Yost KJ, Lai J-s, Ridgeway JL, Egginton JS, Rosedahl JK, Linzer M, Boehm DH, Thakur A, Poplau S: Development and validation of the Patient Experience with Treatment and Self-management (PETS): a patient-reported measure of treatment burden. *Qual Life Res* 2017, 26(2):489-503.
212. Tran V-T, Harrington M, Montori VM, Barnes C, Wicks P, Ravaud P: Adaptation and validation of the Treatment Burden Questionnaire (TBQ) in English using an internet platform. *BMC Med* 2014, 12(1):109.
213. Luyster FS, Dunbar-Jacob J, Aloia MS, Martire LM, Buysse DJ, Strollo PJ: Patient and partner experiences with obstructive sleep apnea and CPAP treatment: a qualitative analysis. *Behav Sleep Med* 2016, 14(1):67-84.
214. Broström A, Nilsen P, Johansson P, Ulander M, Strömberg A, Svanborg E, Fridlund B: Putative facilitators and barriers for adherence to CPAP treatment in patients with obstructive sleep apnea syndrome: a qualitative content analysis. *Sleep Med* 2010, 11(2):126-130.
215. Graco M, Garrard J, Jasper AE: Participation in physical activity: perceptions of women with a previous history of gestational diabetes mellitus. *Health Promot J Austr* 2009, 20(1):20-25.
216. Graco M, Schembri R, Cross S, Thiyagarjan C, Shafazand S, Ayas N, Nash M, Vu V, Ruehland W, Chai-Coetzer C *et al*: Diagnostic accuracy of a two-stage model for detecting obstructive sleep apnea in chronic tetraplegia. *Thorax* 2018.
217. Hoffmann TC, Glasziou PP, Boutron I, Milne R, Perera R, Moher D, Altman DG, Barbour V, Macdonald H, Johnston M: Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. *BMJ* 2014, 348:g1687.
218. Noonan VK, Chan E, Bassett-Spiers K, Berlowitz DJ, Biering-Sørensen F, Charlifue S, Graco M, Hayes KC, Horsewell J, Joshi P: Facilitators and barriers to international collaboration in spinal cord injury: results from a survey of clinicians and researchers. *J Neurotrauma* 2018, 35(3):478-485.

219. Francis JJ, Stockton C, Eccles MP, Johnston M, Cuthbertson BH, Grimshaw JM, Hyde C, Tinmouth A, Stanworth SJ: Evidence‐based selection of theories for designing behaviour change interventions: Using methods based on theoretical construct domains to understand clinicians' blood transfusion behaviour. *Br J Health Psychol* 2009, 14(4):625-646.
220. Francis JJ, Johnston M, Robertson C, Glidewell L, Entwistle V, Eccles MP, Grimshaw JM: What is an adequate sample size? Operationalising data saturation for theory-based interview studies. *Psychology and Health* 2010, 25(10):1229-1245.
221. Cheung A, Weir M, Mayhew A, Kozloff N, Brown K, Grimshaw J: Overview of systematic reviews of the effectiveness of reminders in improving healthcare professional behavior. *Systematic reviews* 2012, 1(1):36.
222. Disler P, Hansford A, Skelton J, Wright P, Kerr J, O'reilly J, Hepworth J, Middleton S, Sullivan C: Diagnosis and treatment of obstructive sleep apnea in a stroke rehabilitation unit: a feasibility study. *Am J Phys Med Rehabil* 2002, 81(8):622-625.
223. Patey AM, Islam R, Francis JJ, Bryson GL, Grimshaw JM: Anesthesiologists' and surgeons' perceptions about routine pre-operative testing in low-risk patients: application of the Theoretical Domains Framework (TDF) to identify factors that influence physicians' decisions to order pre-operative tests. *Implementation Science* 2012, 7(1):52.
224. Craig A, Rodrigues D, Tran Y, Guest R, Middleton J: Daytime sleepiness and its relationships to fatigue and autonomic dysfunction in adults with spinal cord injury. *J Psychosom Res* 2018, 112:90-98.
225. Berlowitz D, Schembri R, Graco M: The effect of treating obstructive sleep apnoea after acute quadriplegia with auto-titrating positive airway pressure on neurocognitive performance and sleepiness (COSAQ); a randomised controlled trial. . *Thorax (under review)* 2018.
226. Berlowitz D: A randomized controlled trial of auto-titrating continuous positive airway pressure treatment for obstructive sleep apnoea after acute quadriplegia (COSAQ). In.: Eur Respiratory Soc; 2016.
227. Sutherland K, Cistulli P: Mandibular advancement splints for the treatment of sleep apnea syndrome. *Swiss Med Wkly* 2011, 141(3940).
228. Norman GR, Sloan JA, Wyrwich KW: Interpretation of changes in health-related quality of life: the remarkable universality of half a standard deviation. *Med Care* 2003:582-592.
229. Crook S, Sievi NA, Bloch KE, Stradling JR, Frei A, Puhan MA, Kohler M: Minimum important difference of the Epworth Sleepiness Scale in obstructive sleep apnoea: estimation from three randomised controlled trials. *Thorax* 2018:thoraxjnl-2018-211959.
230. Patel S, Kon SS, Nolan CM, Barker RE, Simonds AK, Morrell MJ, Man WD-C: The Epworth Sleepiness Scale: minimum clinically important difference in obstructive sleep apnea. *Am J Respir Crit Care Med* 2018, 197(7):961-963.
231. Beaton DE, Boers M, Wells GA: Many faces of the minimal clinically important difference (MCID): a literature review and directions for future research. *Curr Opin Rheumatol* 2002, 14(2):109-114.
232. Chiodo AE, Sitrin RG, Bauman KA: Sleep disordered breathing in spinal cord injury: A systematic review. *The journal of spinal cord medicine* 2016:1-9.

233. Farrell PC, Richards G: Recognition and treatment of sleep-disordered breathing: an important component of chronic disease management. *J Transl Med* 2017, 15(1):114.
234. Cane J, O'Connor D, Michie S: Validation of the theoretical domains framework for use in behaviour change and implementation research. *Implement Sci* 2012, 7(1):37.

# 8 APPENDICES

## 8.1 Congestion Quantifier Five-Item Questionnaire

The following questions ask about the past week. For each question please select one response by checking the appropriate box.

During the past week:

1. How often did you have nasal stuffiness, blockage, or congestion?
    (a) None of the time
    (b) A little of the time
    (c) Some of the time
    (d) Most of the time
    (e) All of the time
2. How often did you have to breathe through your mouth because you could not breathe through your nose?
    (a) None of the time
    (b) A little of the time
    (c) Some of the time
    (d) Most of the time
    (e) All of the time
3. How often did you have difficulty completely clearing your nose even after repeated blowing?
    (a) None of the time
    (b) A little of the time
    (c) Some of the time
    (d) Most of the time
    (e) All of the time
4. How often did any of these symptoms affect your ability to work, learn in school, or do the things you need to do? [SEP]
    (a) None of the time
    (b) A little of the time

(c) Some of the time

(d) Most of the time

(e) All of the time

5. How often was your sleep affected by your nasal stuffiness, blockage, or congestion?

(a) None of the time

(b) A little of the time

(c) Some of the time

(d) Most of the time

(e) All of the time

## 8.2 Borg Scale of Nasal Obstruction

This scale is designed to help us understand how easy or hard you feel it is for you to breathe through your nose right now.

A score of ‘0’ means you feel no blockage in your nasal passage and ‘10’ means your nasal passage is completely blocked.

Please select from the scale below the score that best describes how blocked you feel your nose is right now.

| | |
|---|---|
| 0 | Completely unblocked |
| 0.5 | Very, very slight (just noticeable) blockage |
| 1 | Slight blockage |
| 2 | |
| 3 | Moderate blockage |
| 4 | Somewhat Severe blockage |
| 5 | Severe blockage |
| 6 | |
| 7 | Very Severe blockage |
| 8 | |
| 9 | Very, very Severe (almost maximum) blockage |
| 10 | Maximum (Completely blocked) |

## 8.3 ROC curves and sensitivity and specificity tables of non-binary variables for potential inclusion in SOSAT questionnaire.

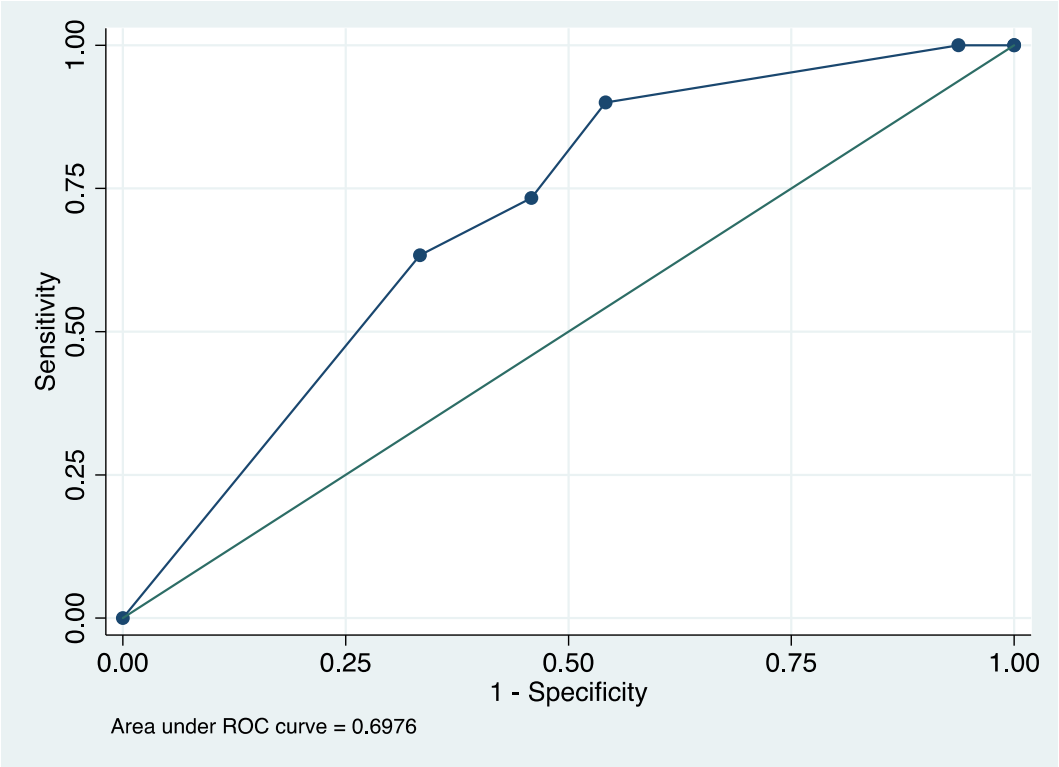


**Figure 8.1** **ROC curve showing performance of AIS in discriminating moderate to severe OSA in people with tetraplegia.**

**Table 8.1** **Sensitivity and specificity at various AIS thresholds for identifying moderate to severe OSA in people with tetraplegia**

| Cutpoint | Sensitivity | Specificity | Correctly Classified | LR+ | LR− |
|---|---|---|---|---|---|
| ( >= 1 ) | 100.00% | 0.00% | 38.46% | 1.0000 | |
| ( >= 2 ) | 100.00% | 6.25% | 42.31% | 1.0667 | 0.0000 |
| ( >= 3 ) | 90.00% | 45.83% | 62.82% | 1.6615 | 0.2182 |
| ( >= 4 ) | 73.33% | 54.17% | 61.54% | 1.6000 | 0.4923 |
| ( >= 5 ) | 63.33% | 66.67% | 65.38% | 1.9000 | 0.5500 |
| ( > 5 ) | 0.00% | 100.00% | 61.54% | | 1.0000 |

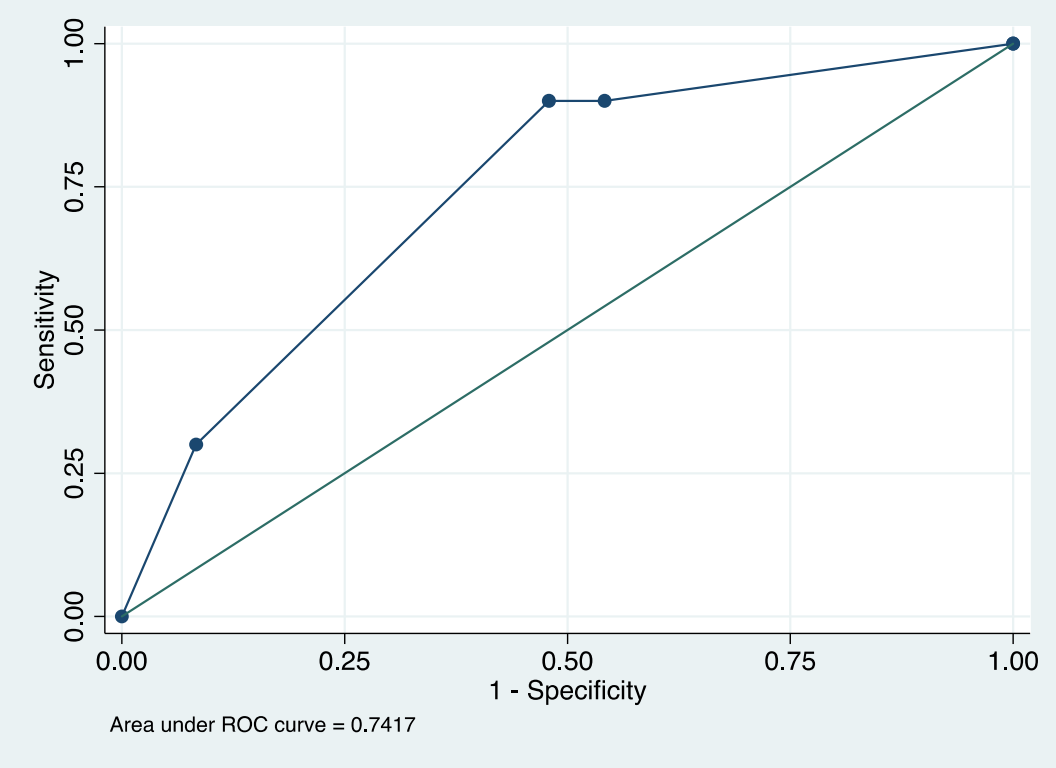


**Figure 8.2** **ROC curve showing performance of injury severity in discriminating moderate to severe OSA in people with tetraplegia.**

**Table 8.2** **Sensitivity and specificity at various injury severity thresholds for identifying moderate to severe OSA in people with tetraplegia**

| Cutpoint | Sensitivity | Specificity | Correctly Classified | LR+ | LR− |
|---|---|---|---|---|---|
| ( >= 3 ) | 100.00% | 0.00% | 38.46% | 1.0000 | |
| ( >= 4 ) | 90.00% | 45.83% | 62.82% | 1.6615 | 0.2182 |
| ( >= 5 ) | 90.00% | 52.08% | 66.67% | 1.8783 | 0.1920 |
| ( >= 6 ) | 30.00% | 91.67% | 67.95% | 3.6000 | 0.7636 |
| ( > 6 ) | 0.00% | 100.00% | 61.54% | | 1.0000 |

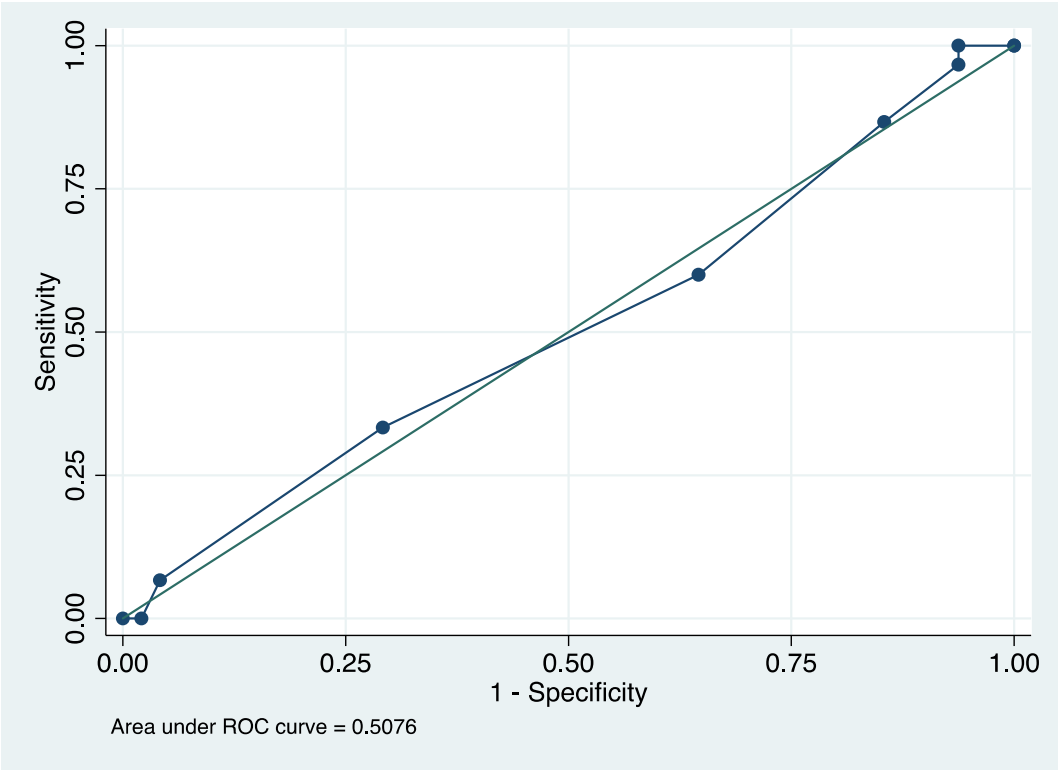


**Figure 8.3** **ROC curve showing performance of injury level in discriminating moderate to severe OSA in people with tetraplegia.**

**Table 8.3** **Sensitivity and specificity at various injury level thresholds for identifying moderate to severe OSA in people with tetraplegia**

| Cutpoint | Sensitivity | Specificity | Correctly Classified | LR+ | LR− |
|---|---|---|---|---|---|
| ( >= 1 ) | 100.00% | 0.00% | 38.46% | 1.0000 | |
| ( >= 3 ) | 100.00% | 2.08% | 39.74% | 1.0213 | 0.0000 |
| ( >= 4 ) | 93.33% | 4.17% | 38.46% | 0.9739 | 1.6000 |
| ( >= 5 ) | 66.67% | 29.17% | 43.59% | 0.9412 | 1.1429 |
| ( >= 6 ) | 40.00% | 64.58% | 55.13% | 1.1294 | 0.9290 |
| ( >= 7 ) | 13.33% | 85.42% | 57.69% | 0.9143 | 1.0146 |
| ( >= 8 ) | 3.33% | 93.75% | 58.97% | 0.5333 | 1.0311 |
| ( >= 9 ) | 0.00% | 93.75% | 57.69% | 0.0000 | 1.0667 |
| ( > 9 ) | 0.00% | 100.00% | 61.54% | | 1.0000 |

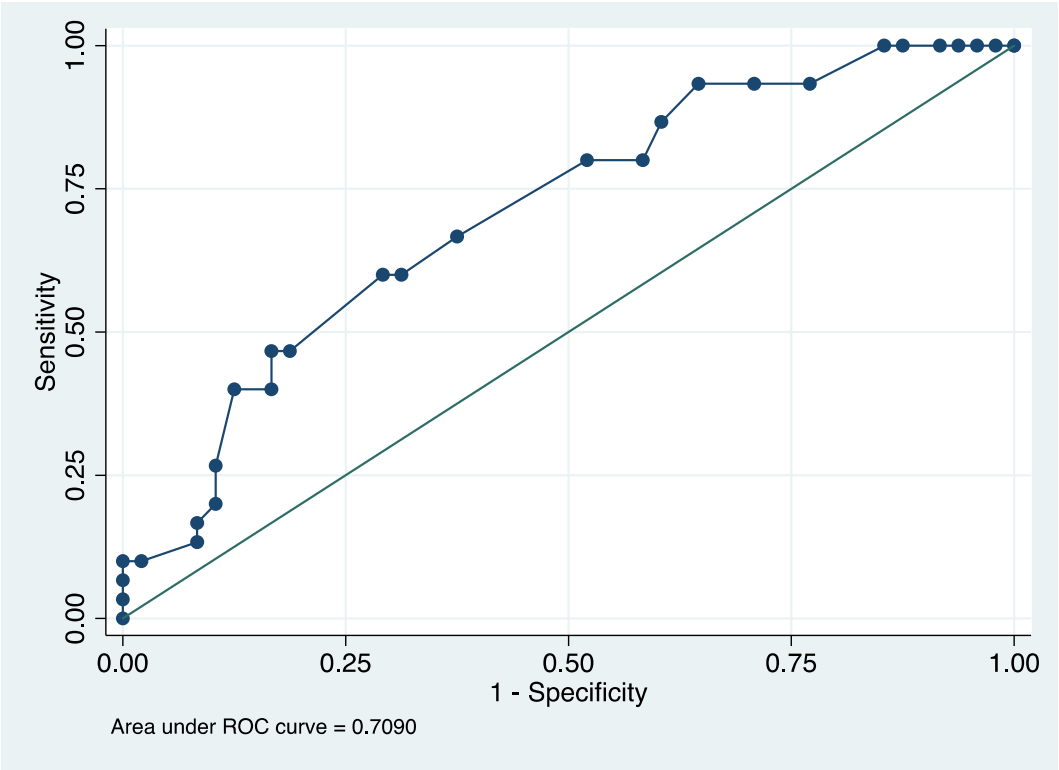


**Figure 8.4** **ROC curve showing performance of neck circumference in discriminating moderate to severe OSA in people with tetraplegia.**

**Table 8.4 Sensitivity and specificity at various neck circumference thresholds for identifying moderate to severe OSA in people with tetraplegia**

| Cutpoint | Sensitivity | Specificity | Correctly Classified | LR+ | LR− |
|---|---|---|---|---|---|
| ( >= 30 ) | 100.00% | 0.00% | 38.46% | 1.0000 | |
| ( >= 31 ) | 100.00% | 2.08% | 39.74% | 1.0213 | 0.0000 |
| ( >= 32 ) | 100.00% | 4.17% | 41.03% | 1.0435 | 0.0000 |
| ( >= 32.5 ) | 100.00% | 6.25% | 42.31% | 1.0667 | 0.0000 |
| ( >= 33 ) | 100.00% | 8.33% | 43.59% | 1.0909 | 0.0000 |
| ( >= 34 ) | 100.00% | 12.50% | 46.15% | 1.1429 | 0.0000 |
| ( >= 35 ) | 100.00% | 14.58% | 47.44% | 1.1707 | 0.0000 |
| ( >= 36 ) | 93.33% | 22.92% | 50.00% | 1.2108 | 0.2909 |
| ( >= 37 ) | 93.33% | 29.17% | 53.85% | 1.3176 | 0.2286 |
| ( >= 38 ) | 93.33% | 35.42% | 57.69% | 1.4452 | 0.1882 |
| ( >= 39 ) | 86.67% | 39.58% | 57.69% | 1.4345 | 0.3368 |
| ( >= 40 ) | 80.00% | 41.67% | 56.41% | 1.3714 | 0.4800 |
| ( >= 41 ) | 80.00% | 47.92% | 60.26% | 1.5360 | 0.4174 |
| ( >= 42 ) | 66.67% | 62.50% | 64.10% | 1.7778 | 0.5333 |
| ( >= 42.5 ) | 60.00% | 68.75% | 65.38% | 1.9200 | 0.5818 |
| ( >= 43 ) | 60.00% | 70.83% | 66.67% | 2.0571 | 0.5647 |
| ( >= 43.5 ) | 46.67% | 81.25% | 67.95% | 2.4889 | 0.6564 |
| ( >= 44 ) | 46.67% | 83.33% | 69.23% | 2.8000 | 0.6400 |
| ( >= 44.5 ) | 40.00% | 83.33% | 66.67% | 2.4000 | 0.7200 |
| ( >= 45 ) | 40.00% | 87.50% | 69.23% | 3.2000 | 0.6857 |
| ( >= 46 ) | 26.67% | 89.58% | 65.38% | 2.5600 | 0.8186 |
| ( >= 47 ) | 20.00% | 89.58% | 62.82% | 1.9200 | 0.8930 |
| ( >= 47.5 ) | 16.67% | 91.67% | 62.82% | 2.0000 | 0.9091 |
| ( >= 48 ) | 13.33% | 91.67% | 61.54% | 1.6000 | 0.9455 |
| ( >= 49 ) | 10.00% | 97.92% | 64.10% | 4.8000 | 0.9191 |
| ( >= 49.5 ) | 10.00% | 100.00% | 65.38% | | 0.9000 |
| ( >= 53 ) | 6.67% | 100.00% | 64.10% | | 0.9333 |
| ( >= 64 ) | 3.33% | 100.00% | 62.82% | | 0.9667 |
| ( > 64 ) | 0.00% | 100.00% | 61.54% | | 1.0000 |

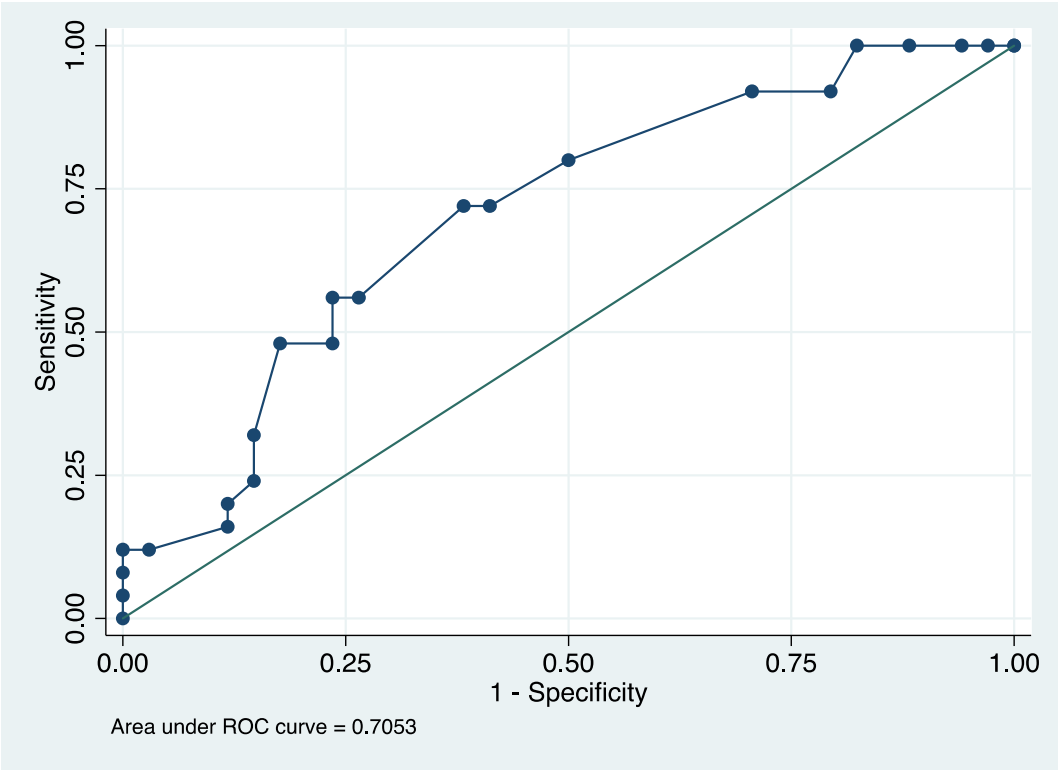


**Figure 8.5** **ROC curve showing performance of neck circumference (males) in discriminating moderate to severe OSA in people with tetraplegia.**

**Table 8.5** **Sensitivity and specificity at various neck circumference thresholds (males) for identifying moderate to severe OSA in people with tetraplegia**

| Cutpoint | Sensitivity | Specificity | Correctly Classified | LR+ | LR− |
|---|---|---|---|---|---|
| ( >= 35 ) | 100.00% | 0.00% | 42.37% | 1.0000 | |
| ( >= 36 ) | 100.00% | 2.94% | 44.07% | 1.0303 | 0.0000 |
| ( >= 37 ) | 100.00% | 5.88% | 45.76% | 1.0625 | 0.0000 |
| ( >= 38 ) | 100.00% | 11.76% | 49.15% | 1.1333 | 0.0000 |
| ( >= 39 ) | 100.00% | 17.65% | 52.54% | 1.2143 | 0.0000 |
| ( >= 40 ) | 92.00% | 20.59% | 50.85% | 1.1585 | 0.3886 |
| ( >= 41 ) | 92.00% | 29.41% | 55.93% | 1.3033 | 0.2720 |
| ( >= 42 ) | 80.00% | 50.00% | 62.71% | 1.6000 | 0.4000 |
| ( >= 42.5 ) | 72.00% | 58.82% | 64.41% | 1.7486 | 0.4760 |
| ( >= 43 ) | 72.00% | 61.76% | 66.10% | 1.8831 | 0.4533 |
| ( >= 43.5 ) | 56.00% | 73.53% | 66.10% | 2.1156 | 0.5984 |
| ( >= 44 ) | 56.00% | 76.47% | 67.80% | 2.3800 | 0.5754 |
| ( >= 44.5 ) | 48.00% | 76.47% | 64.41% | 2.0400 | 0.6800 |
| ( >= 45 ) | 48.00% | 82.35% | 67.80% | 2.7200 | 0.6314 |
| ( >= 46 ) | 32.00% | 85.29% | 62.71% | 2.1760 | 0.7972 |
| ( >= 47 ) | 24.00% | 85.29% | 59.32% | 1.6320 | 0.8910 |
| ( >= 47.5 ) | 20.00% | 88.24% | 59.32% | 1.7000 | 0.9067 |
| ( >= 48 ) | 16.00% | 88.24% | 57.63% | 1.3600 | 0.9520 |
| ( >= 49 ) | 12.00% | 97.06% | 61.02% | 4.0800 | 0.9067 |
| ( >= 49.5 ) | 12.00% | 100.00% | 62.71% | | 0.8800 |
| ( >= 53 ) | 8.00% | 100.00% | 61.02% | | 0.9200 |
| ( >= 64 ) | 4.00% | 100.00% | 59.32% | | 0.9600 |
| ( > 64 ) | 0.00% | 100.00% | 57.63% | | 1.0000 |

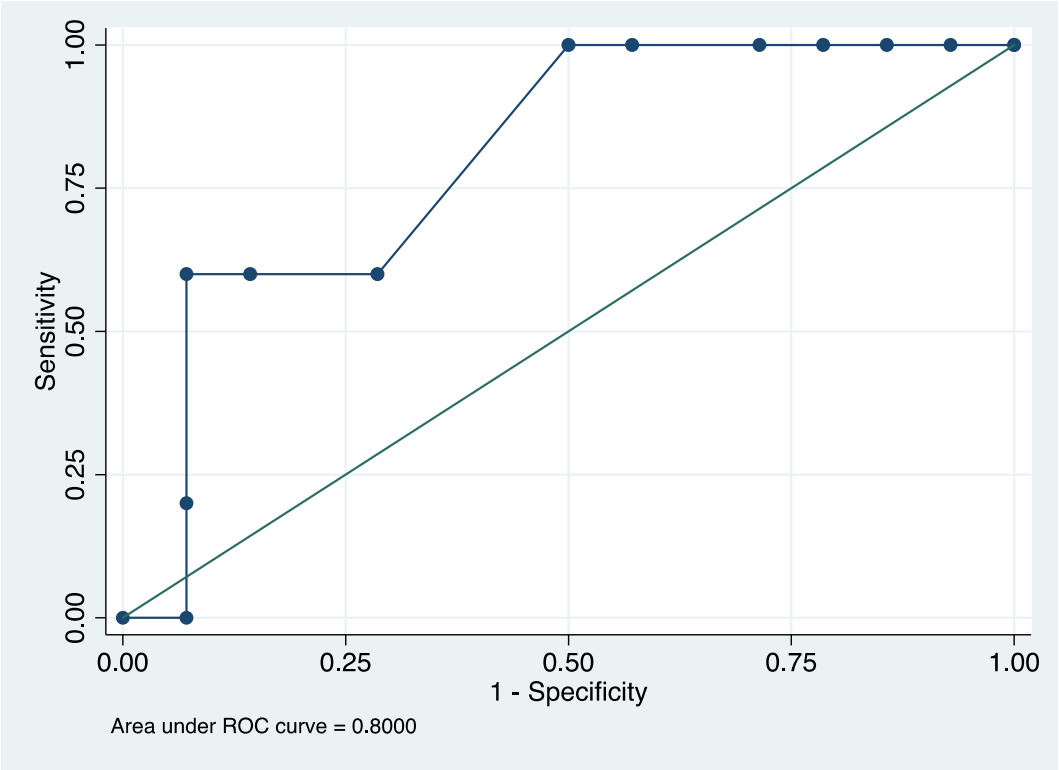


**Figure 8.6** **ROC curve showing performance of neck circumference (females) in discriminating moderate to severe OSA in people with tetraplegia.**

**Table 8.6** **Sensitivity and specificity at various neck circumference thresholds (females) for identifying moderate to severe OSA in people with tetraplegia**

| Cutpoint | Sensitivity | Specificity | Correctly Classified | LR+ | LR− |
|---|---|---|---|---|---|
| ( >= 30 ) | 100.00% | 0.00% | 26.32% | 1.0000 | |
| ( >= 31 ) | 100.00% | 7.14% | 31.58% | 1.0769 | 0.0000 |
| ( >= 32 ) | 100.00% | 14.29% | 36.84% | 1.1667 | 0.0000 |
| ( >= 32.5 ) | 100.00% | 21.43% | 42.11% | 1.2727 | 0.0000 |
| ( >= 33 ) | 100.00% | 28.57% | 47.37% | 1.4000 | 0.0000 |
| ( >= 34 ) | 100.00% | 42.86% | 57.89% | 1.7500 | 0.0000 |
| ( >= 35 ) | 100.00% | 50.00% | 63.16% | 2.0000 | 0.0000 |
| ( >= 36 ) | 60.00% | 71.43% | 68.42% | 2.1000 | 0.5600 |
| ( >= 37 ) | 60.00% | 85.71% | 78.95% | 4.2000 | 0.4667 |
| ( >= 38 ) | 60.00% | 92.86% | 84.21% | 8.4000 | 0.4308 |
| ( >= 41 ) | 20.00% | 92.86% | 73.68% | 2.8000 | 0.8615 |
| ( >= 43 ) | 0.00% | 92.86% | 68.42% | 0.0000 | 1.0769 |
| ( > 43 ) | 0.00% | 100.00% | 73.68% | | 1.0000 |

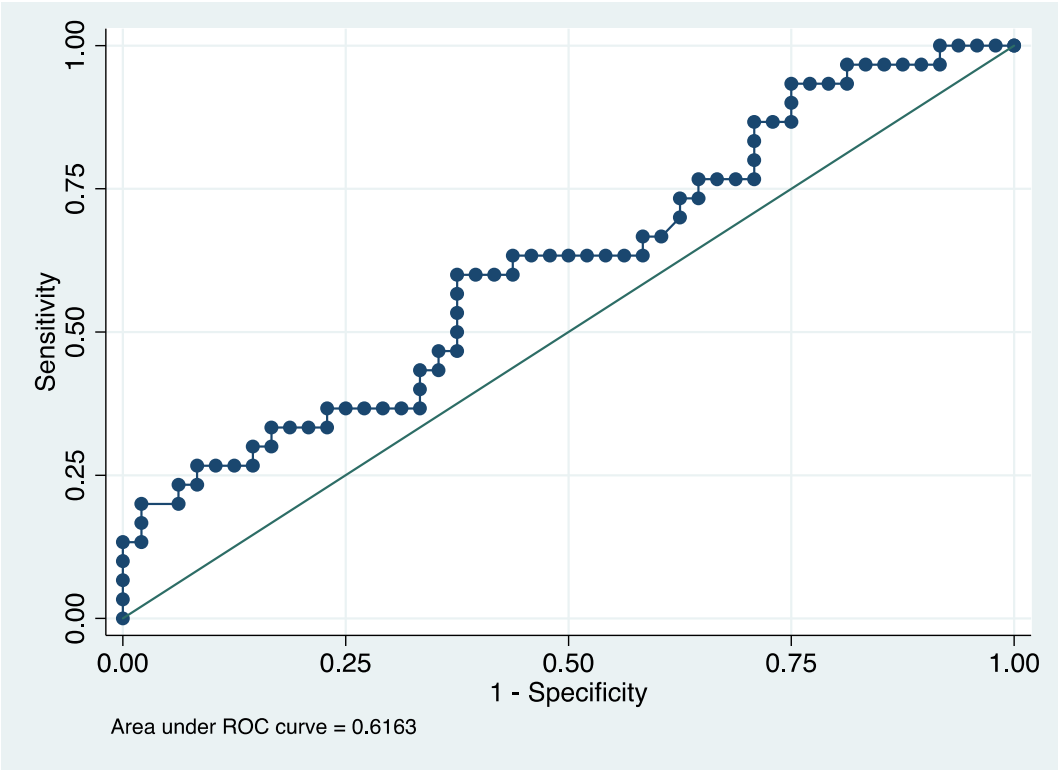


**Figure 8.7 ROC curve showing performance of BMI in discriminating moderate to severe OSA in people with tetraplegia.**

**Table 8.7 Sensitivity and specificity at various BMI thresholds for identifying moderate to severe OSA in people with tetraplegia**

| Cutpoint | Sensitivity | Specificity | Correctly Classified | LR+ | LR− |
|---|---|---|---|---|---|
| ( >= 15.89.. ) | 100.00% | 0.00% | 38.46% | 1.0000 | |
| ( >= 16.28.. ) | 100.00% | 2.08% | 39.74% | 1.0213 | 0.0000 |
| ( >= 18.03.. ) | 100.00% | 4.17% | 41.03% | 1.0435 | 0.0000 |
| ( >= 18.36.. ) | 100.00% | 6.25% | 42.31% | 1.0667 | 0.0000 |
| ( >= 18.41.. ) | 100.00% | 8.33% | 43.59% | 1.0909 | 0.0000 |
| ( >= 18.51.. ) | 96.67% | 8.33% | 42.31% | 1.0545 | 0.4000 |
| ( >= 19.53.. ) | 96.67% | 10.42% | 43.59% | 1.0791 | 0.3200 |
| ( >= 19.72.. ) | 96.67% | 12.50% | 44.87% | 1.1048 | 0.2667 |
| ( >= 20.28.. ) | 96.67% | 14.58% | 46.15% | 1.1317 | 0.2286 |
| ( >= 20.2848 ) | 96.67% | 16.67% | 47.44% | 1.1600 | 0.2000 |
| ( >= 20.36.. ) | 96.67% | 18.75% | 48.72% | 1.1897 | 0.1778 |
| ( >= 20.44.. ) | 93.33% | 18.75% | 47.44% | 1.1487 | 0.3556 |
| ( >= 20.51.. ) | 93.33% | 20.83% | 48.72% | 1.1789 | 0.3200 |
| ( >= 20.62.. ) | 93.33% | 22.92% | 50.00% | 1.2108 | 0.2909 |
| ( >= 22.09.. ) | 93.33% | 25.00% | 51.28% | 1.2444 | 0.2667 |
| ( >= 22.40.. ) | 90.00% | 25.00% | 50.00% | 1.2000 | 0.4000 |
| ( >= 22.4438 ) | 86.67% | 25.00% | 48.72% | 1.1556 | 0.5333 |
| ( >= 22.54.. ) | 86.67% | 27.08% | 50.00% | 1.1886 | 0.4923 |
| ( >= 22.69.. ) | 86.67% | 29.17% | 51.28% | 1.2235 | 0.4571 |
| ( >= 22.78.. ) | 83.33% | 29.17% | 50.00% | 1.1765 | 0.5714 |
| ( >= 22.89.. ) | 80.00% | 29.17% | 48.72% | 1.1294 | 0.6857 |
| ( >= 23.41.. ) | 76.67% | 29.17% | 47.44% | 1.0824 | 0.8000 |
| ( >= 23.42.. ) | 76.67% | 31.25% | 48.72% | 1.1152 | 0.7467 |
| ( >= 23.45.. ) | 76.67% | 33.33% | 50.00% | 1.1500 | 0.7000 |
| ( >= 23.46.. ) | 76.67% | 35.42% | 51.28% | 1.1871 | 0.6588 |
| ( >= 23.49.. ) | 73.33% | 35.42% | 50.00% | 1.1355 | 0.7529 |
| ( >= 23.67.. ) | 73.33% | 37.50% | 51.28% | 1.1733 | 0.7111 |
| ( >= 23.72.. ) | 70.00% | 37.50% | 50.00% | 1.1200 | 0.8000 |
| ( >= 23.82.. ) | 66.67% | 39.58% | 50.00% | 1.1034 | 0.8421 |
| ( >= 23.95.. ) | 66.67% | 41.67% | 51.28% | 1.1429 | 0.8000 |
| ( >= 24.00.. ) | 63.33% | 41.67% | 50.00% | 1.0857 | 0.8800 |
| ( >= 24.21.. ) | 63.33% | 43.75% | 51.28% | 1.1259 | 0.8381 |
| ( >= 24.24.. ) | 63.33% | 45.83% | 52.56% | 1.1692 | 0.8000 |
| ( >= 24.30.. ) | 63.33% | 47.92% | 53.85% | 1.2160 | 0.7652 |
| ( >= 24.30.. ) | 63.33% | 50.00% | 55.13% | 1.2667 | 0.7333 |
| ( >= 24.41.. ) | 63.33% | 52.08% | 56.41% | 1.3217 | 0.7040 |
| ( >= 24.74.. ) | 63.33% | 54.17% | 57.69% | 1.3818 | 0.6769 |
| ( >= 24.80.. ) | 63.33% | 56.25% | 58.97% | 1.4476 | 0.6519 |
| ( >= 24.83.. ) | 60.00% | 56.25% | 57.69% | 1.3714 | 0.7111 |
| ( >= 24.93.. ) | 60.00% | 58.33% | 58.97% | 1.4400 | 0.6857 |
| ( >= 25.11.. ) | 60.00% | 60.42% | 60.26% | 1.5158 | 0.6621 |
| ( >= 25.18.. ) | 60.00% | 62.50% | 61.54% | 1.6000 | 0.6400 |
| ( >= 25.39.. ) | 56.67% | 62.50% | 60.26% | 1.5111 | 0.6933 |
| ( >= 25.39.. ) | 53.33% | 62.50% | 58.97% | 1.4222 | 0.7467 |
| ( >= 25.45.. ) | 50.00% | 62.50% | 57.69% | 1.3333 | 0.8000 |
| ( >= 25.54.. ) | 46.67% | 62.50% | 56.41% | 1.2444 | 0.8533 |
| ( >= 25.66.. ) | 46.67% | 64.58% | 57.69% | 1.3176 | 0.8258 |
| ( >= 25.68.. ) | 43.33% | 64.58% | 56.41% | 1.2235 | 0.8774 |
| ( >= 26.045 ) | 43.33% | 66.67% | 57.69% | 1.3000 | 0.8500 |
| ( >= 26.17.. ) | 40.00% | 66.67% | 56.41% | 1.2000 | 0.9000 |
| ( >= 26.21.. ) | 36.67% | 66.67% | 55.13% | 1.1000 | 0.9500 |
| ( >= 26.23.. ) | 36.67% | 68.75% | 56.41% | 1.1733 | 0.9212 |
| ( >= 26.83.. ) | 36.67% | 70.83% | 57.69% | 1.2571 | 0.8941 |
| ( >= 27.06.. ) | 36.67% | 72.92% | 58.97% | 1.3538 | 0.8686 |
| ( >= 27.08.. ) | 36.67% | 75.00% | 60.26% | 1.4667 | 0.8444 |
| ( >= 27.16.. ) | 36.67% | 77.08% | 61.54% | 1.6000 | 0.8216 |
| ( >= 27.16.. ) | 33.33% | 77.08% | 60.26% | 1.4545 | 0.8649 |
| ( >= 27.57.. ) | 33.33% | 79.17% | 61.54% | 1.6000 | 0.8421 |
| ( >= 27.62.. ) | 33.33% | 81.25% | 62.82% | 1.7778 | 0.8205 |
| ( >= 27.99.. ) | 33.33% | 83.33% | 64.10% | 2.0000 | 0.8000 |
| ( >= 28 ) | 30.00% | 83.33% | 62.82% | 1.8000 | 0.8400 |
| ( >= 28.07.. ) | 30.00% | 85.42% | 64.10% | 2.0571 | 0.8195 |
| ( >= 28.177 ) | 26.67% | 85.42% | 62.82% | 1.8286 | 0.8585 |
| ( >= 28.38.. ) | 26.67% | 87.50% | 64.10% | 2.1333 | 0.8381 |
| ( >= 29.06.. ) | 26.67% | 89.58% | 65.38% | 2.5600 | 0.8186 |
| ( >= 29.08.. ) | 26.67% | 91.67% | 66.67% | 3.2000 | 0.8000 |
| ( >= 29.15.. ) | 23.33% | 91.67% | 65.38% | 2.8000 | 0.8364 |
| ( >= 29.21.. ) | 23.33% | 93.75% | 66.67% | 3.7333 | 0.8178 |
| ( >= 29.38.. ) | 20.00% | 93.75% | 65.38% | 3.2000 | 0.8533 |
| ( >= 29.57.. ) | 20.00% | 97.92% | 67.95% | 9.6000 | 0.8170 |
| ( >= 30.61.. ) | 16.67% | 97.92% | 66.67% | 8.0000 | 0.8511 |
| ( >= 31.00.. ) | 13.33% | 97.92% | 65.38% | 6.4000 | 0.8851 |
| ( >= 31.22.. ) | 13.33% | 100.00% | 66.67% | | 0.8667 |
| ( >= 32.32.. ) | 10.00% | 100.00% | 65.38% | | 0.9000 |
| ( >= 34.90.. ) | 6.67% | 100.00% | 64.10% | | 0.9333 |
| ( >= 37.1001 ) | 3.33% | 100.00% | 62.82% | | 0.9667 |
| ( > 37.1001 ) | 0.00% | 100.00% | 61.54% | | 1.0000 |

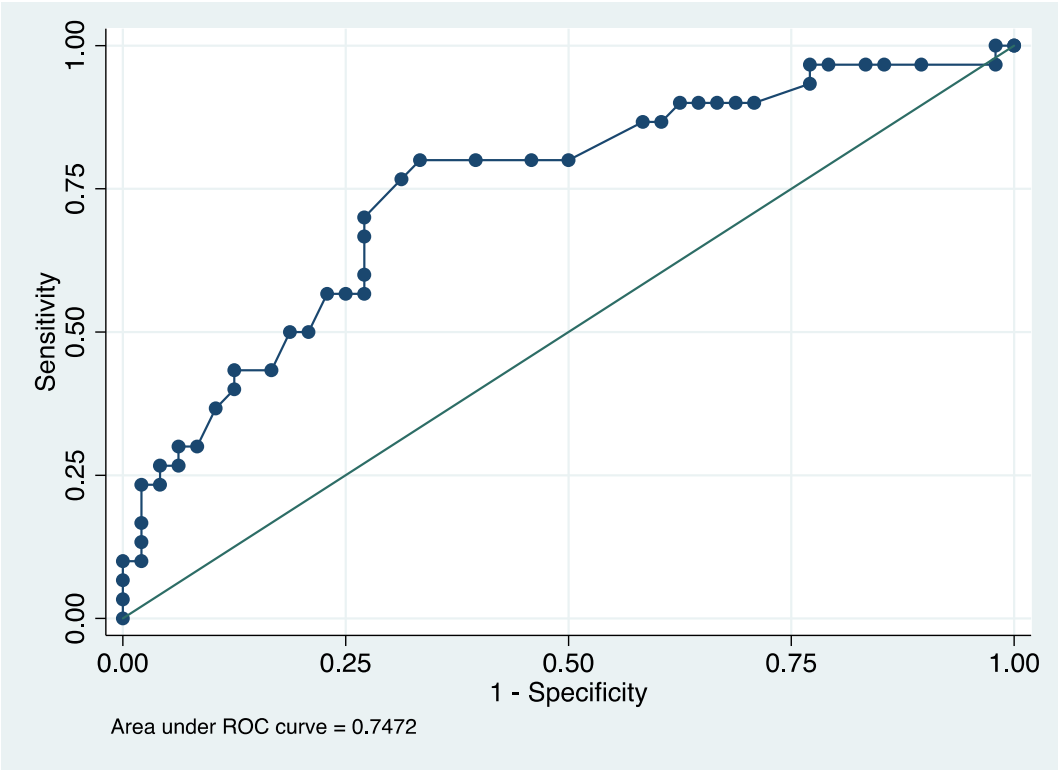


**Figure 8.8** **ROC curve showing performance of waist circumference in discriminating moderate to severe OSA in people with tetraplegia.**

**Table 8.8 Sensitivity and specificity at various waist circumference thresholds for identifying moderate to severe OSA in people with tetraplegia**

| Cutpoint | Sensitivity | Specificity | Correctly Classified | LR+ | LR− |
|---|---|---|---|---|---|
| ( >= 76 ) | 100.00% | 0.00% | 38.46% | 1.0000 | |
| ( >= 80 ) | 100.00% | 2.08% | 39.74% | 1.0213 | 0.0000 |
| ( >= 83 ) | 96.67% | 2.08% | 38.46% | 0.9872 | 1.6000 |
| ( >= 84 ) | 96.67% | 10.42% | 43.59% | 1.0791 | 0.3200 |
| ( >= 84.5 ) | 96.67% | 14.58% | 46.15% | 1.1317 | 0.2286 |
| ( >= 85 ) | 96.67% | 16.67% | 47.44% | 1.1600 | 0.2000 |
| ( >= 87 ) | 96.67% | 20.83% | 50.00% | 1.2211 | 0.1600 |
| ( >= 87.5 ) | 96.67% | 22.92% | 51.28% | 1.2541 | 0.1455 |
| ( >= 88 ) | 93.33% | 22.92% | 50.00% | 1.2108 | 0.2909 |
| ( >= 90 ) | 90.00% | 29.17% | 52.56% | 1.2706 | 0.3429 |
| ( >= 91 ) | 90.00% | 31.25% | 53.85% | 1.3091 | 0.3200 |
| ( >= 92 ) | 90.00% | 33.33% | 55.13% | 1.3500 | 0.3000 |
| ( >= 94 ) | 90.00% | 35.42% | 56.41% | 1.3935 | 0.2824 |
| ( >= 96 ) | 90.00% | 37.50% | 57.69% | 1.4400 | 0.2667 |
| ( >= 97 ) | 86.67% | 39.58% | 57.69% | 1.4345 | 0.3368 |
| ( >= 99 ) | 86.67% | 41.67% | 58.97% | 1.4857 | 0.3200 |
| ( >= 100 ) | 80.00% | 50.00% | 61.54% | 1.6000 | 0.4000 |
| ( >= 101 ) | 80.00% | 54.17% | 64.10% | 1.7455 | 0.3692 |
| ( >= 102 ) | 80.00% | 60.42% | 67.95% | 2.0211 | 0.3310 |
| ( >= 103 ) | 80.00% | 66.67% | 71.79% | 2.4000 | 0.3000 |
| ( >= 104 ) | 76.67% | 68.75% | 71.79% | 2.4533 | 0.3394 |
| ( >= 105 ) | 70.00% | 72.92% | 71.79% | 2.5846 | 0.4114 |
| ( >= 108 ) | 66.67% | 72.92% | 70.51% | 2.4615 | 0.4571 |
| ( >= 109 ) | 60.00% | 72.92% | 67.95% | 2.2154 | 0.5486 |
| ( >= 110 ) | 56.67% | 72.92% | 66.67% | 2.0923 | 0.5943 |
| ( >= 111 ) | 56.67% | 75.00% | 67.95% | 2.2667 | 0.5778 |
| ( >= 112 ) | 56.67% | 77.08% | 69.23% | 2.4727 | 0.5622 |
| ( >= 113 ) | 50.00% | 79.17% | 67.95% | 2.4000 | 0.6316 |
| ( >= 114 ) | 50.00% | 81.25% | 69.23% | 2.6667 | 0.6154 |
| ( >= 115 ) | 43.33% | 83.33% | 67.95% | 2.6000 | 0.6800 |
| ( >= 116 ) | 43.33% | 87.50% | 70.51% | 3.4667 | 0.6476 |
| ( >= 117 ) | 40.00% | 87.50% | 69.23% | 3.2000 | 0.6857 |
| ( >= 118 ) | 36.67% | 89.58% | 69.23% | 3.5200 | 0.7070 |
| ( >= 119 ) | 30.00% | 91.67% | 67.95% | 3.6000 | 0.7636 |
| ( >= 120 ) | 30.00% | 93.75% | 69.23% | 4.8000 | 0.7467 |
| ( >= 121 ) | 26.67% | 93.75% | 67.95% | 4.2667 | 0.7822 |
| ( >= 123 ) | 26.67% | 95.83% | 69.23% | 6.4000 | 0.7652 |
| ( >= 124 ) | 23.33% | 95.83% | 67.95% | 5.6000 | 0.8000 |
| ( >= 128 ) | 23.33% | 97.92% | 69.23% | 11.2000 | 0.7830 |
| ( >= 132 ) | 16.67% | 97.92% | 66.67% | 8.0000 | 0.8511 |
| ( >= 133 ) | 13.33% | 97.92% | 65.38% | 6.4000 | 0.8851 |
| ( >= 137 ) | 10.00% | 97.92% | 64.10% | 4.8000 | 0.9191 |
| ( >= 138 ) | 10.00% | 100.00% | 65.38% | | 0.9000 |
| ( >= 142 ) | 6.67% | 100.00% | 64.10% | | 0.9333 |
| ( >= 146 ) | 3.33% | 100.00% | 62.82% | | 0.9667 |
| ( > 146 ) | 0.00% | 100.00% | 61.54% | | 1.0000 |

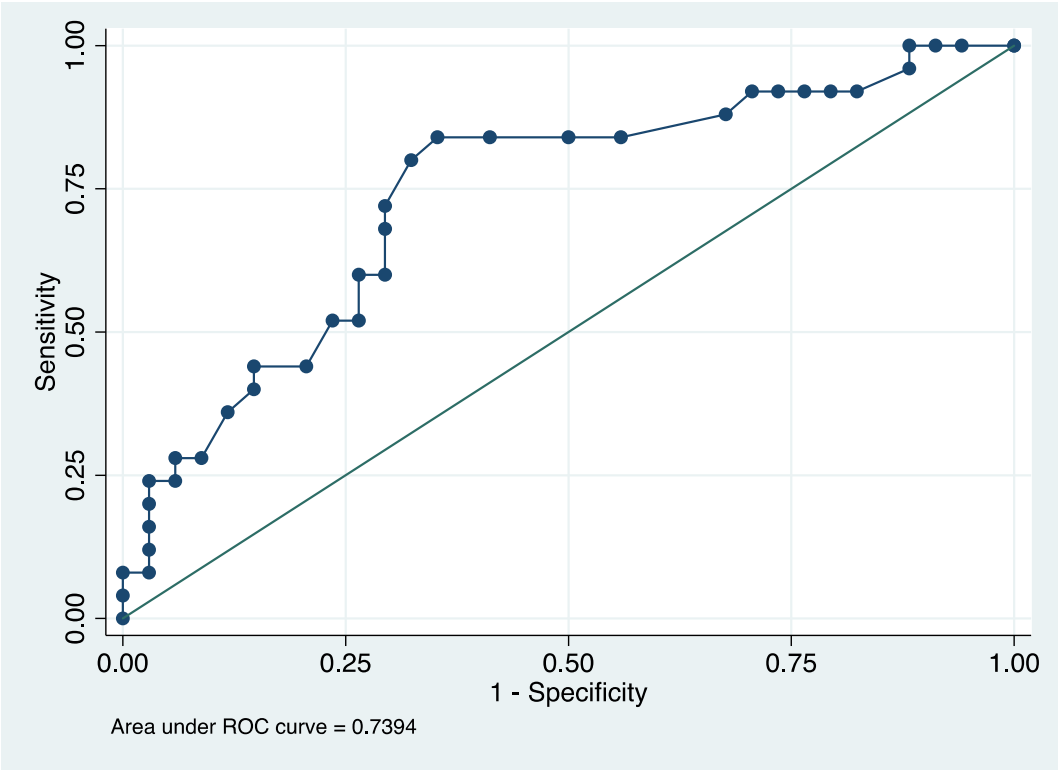


**Figure 8.9 ROC curve showing performance of waist circumference (males) in discriminating moderate to severe OSA in people with tetraplegia.**

**Table 8.9 Sensitivity and specificity at various waist circumference (males) thresholds for identifying moderate to severe OSA in people with tetraplegia**

| Cutpoint | Sensitivity | Specificity | Correctly Classified | LR+ | LR− |
|---|---|---|---|---|---|
| ( >= 83 ) | 100.00% | 0.00% | 42.37% | 1.0000 | |
| ( >= 84 ) | 100.00% | 5.88% | 45.76% | 1.0625 | 0.0000 |
| ( >= 85 ) | 100.00% | 8.82% | 47.46% | 1.0968 | 0.0000 |
| ( >= 87.5 ) | 100.00% | 11.76% | 49.15% | 1.1333 | 0.0000 |
| ( >= 88 ) | 96.00% | 11.76% | 47.46% | 1.0880 | 0.3400 |
| ( >= 90 ) | 92.00% | 17.65% | 49.15% | 1.1171 | 0.4533 |
| ( >= 91 ) | 92.00% | 20.59% | 50.85% | 1.1585 | 0.3886 |
| ( >= 92 ) | 92.00% | 23.53% | 52.54% | 1.2031 | 0.3400 |
| ( >= 94 ) | 92.00% | 26.47% | 54.24% | 1.2512 | 0.3022 |
| ( >= 96 ) | 92.00% | 29.41% | 55.93% | 1.3033 | 0.2720 |
| ( >= 99 ) | 88.00% | 32.35% | 55.93% | 1.3009 | 0.3709 |
| ( >= 100 ) | 84.00% | 44.12% | 61.02% | 1.5032 | 0.3627 |
| ( >= 101 ) | 84.00% | 50.00% | 64.41% | 1.6800 | 0.3200 |
| ( >= 102 ) | 84.00% | 58.82% | 69.49% | 2.0400 | 0.2720 |
| ( >= 103 ) | 84.00% | 64.71% | 72.88% | 2.3800 | 0.2473 |
| ( >= 104 ) | 80.00% | 67.65% | 72.88% | 2.4727 | 0.2957 |
| ( >= 105 ) | 72.00% | 70.59% | 71.19% | 2.4480 | 0.3967 |
| ( >= 108 ) | 68.00% | 70.59% | 69.49% | 2.3120 | 0.4533 |
| ( >= 111 ) | 60.00% | 70.59% | 66.10% | 2.0400 | 0.5667 |
| ( >= 112 ) | 60.00% | 73.53% | 67.80% | 2.2667 | 0.5440 |
| ( >= 113 ) | 52.00% | 73.53% | 64.41% | 1.9644 | 0.6528 |
| ( >= 114 ) | 52.00% | 76.47% | 66.10% | 2.2100 | 0.6277 |
| ( >= 115 ) | 44.00% | 79.41% | 64.41% | 2.1371 | 0.7052 |
| ( >= 116 ) | 44.00% | 85.29% | 67.80% | 2.9920 | 0.6566 |
| ( >= 117 ) | 40.00% | 85.29% | 66.10% | 2.7200 | 0.7034 |
| ( >= 118 ) | 36.00% | 88.24% | 66.10% | 3.0600 | 0.7253 |
| ( >= 119 ) | 28.00% | 91.18% | 64.41% | 3.1733 | 0.7897 |
| ( >= 120 ) | 28.00% | 94.12% | 66.10% | 4.7600 | 0.7650 |
| ( >= 121 ) | 24.00% | 94.12% | 64.41% | 4.0800 | 0.8075 |
| ( >= 123 ) | 24.00% | 97.06% | 66.10% | 8.1600 | 0.7830 |
| ( >= 128 ) | 20.00% | 97.06% | 64.41% | 6.8000 | 0.8242 |
| ( >= 132 ) | 16.00% | 97.06% | 62.71% | 5.4400 | 0.8655 |
| ( >= 133 ) | 12.00% | 97.06% | 61.02% | 4.0800 | 0.9067 |
| ( >= 137 ) | 8.00% | 97.06% | 59.32% | 2.7200 | 0.9479 |
| ( >= 142 ) | 8.00% | 100.00% | 61.02% | | 0.9200 |
| ( >= 146 ) | 4.00% | 100.00% | 59.32% | | 0.9600 |
| ( > 146 ) | 0.00% | 100.00% | 57.63% | | 1.0000 |

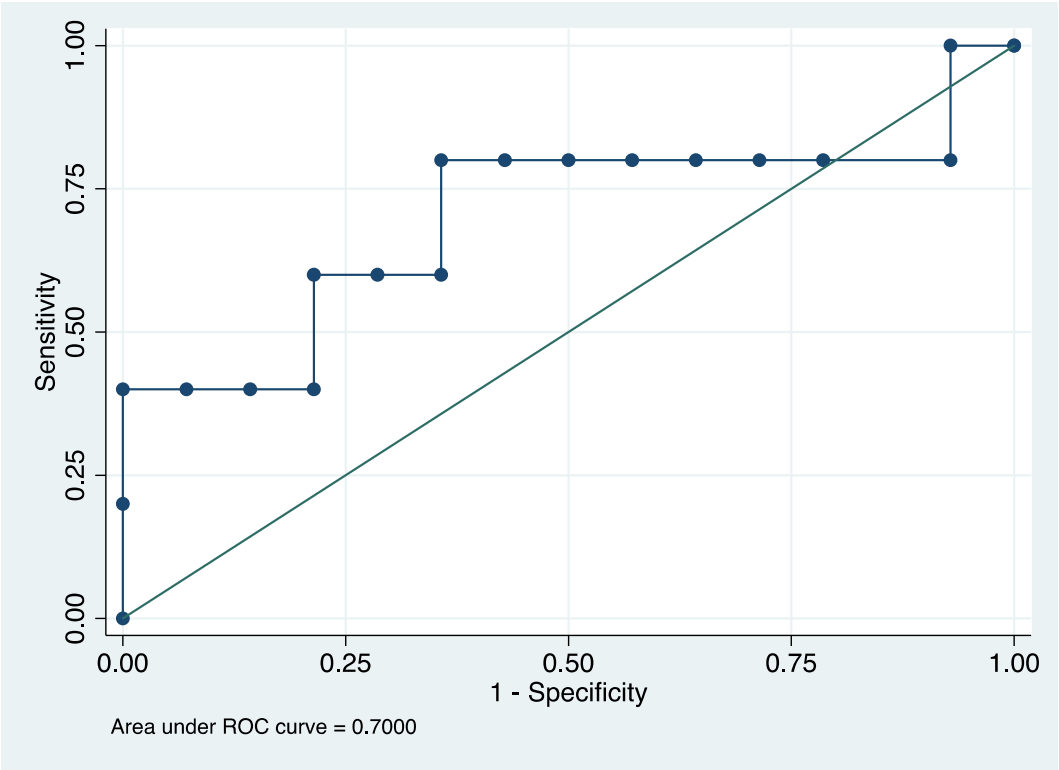


**Figure 8.10** **ROC curve showing performance of waist circumference (females) in discriminating moderate to severe OSA in people with tetraplegia.**

**Table 8.10** **Sensitivity and specificity at various waist circumference (females) thresholds for identifying moderate to severe OSA in people with tetraplegia**

| Cutpoint | Sensitivity | Specificity | Correctly Classified | LR+ | LR− |
|---|---|---|---|---|---|
| ( >= 76 ) | 100.00% | 0.00% | 26.32% | 1.0000 | |
| ( >= 80 ) | 100.00% | 7.14% | 31.58% | 1.0769 | 0.0000 |
| ( >= 83 ) | 80.00% | 7.14% | 26.32% | 0.8615 | 2.8000 |
| ( >= 84 ) | 80.00% | 21.43% | 36.84% | 1.0182 | 0.9333 |
| ( >= 84.5 ) | 80.00% | 28.57% | 42.11% | 1.1200 | 0.7000 |
| ( >= 85 ) | 80.00% | 35.71% | 47.37% | 1.2444 | 0.5600 |
| ( >= 87 ) | 80.00% | 42.86% | 52.63% | 1.4000 | 0.4667 |
| ( >= 88 ) | 80.00% | 50.00% | 57.89% | 1.6000 | 0.4000 |
| ( >= 97 ) | 80.00% | 57.14% | 63.16% | 1.8667 | 0.3500 |
| ( >= 99 ) | 80.00% | 64.29% | 68.42% | 2.2400 | 0.3111 |
| ( >= 102 ) | 60.00% | 64.29% | 63.16% | 1.6800 | 0.6222 |
| ( >= 104 ) | 60.00% | 71.43% | 68.42% | 2.1000 | 0.5600 |
| ( >= 109 ) | 60.00% | 78.57% | 73.68% | 2.8000 | 0.5091 |
| ( >= 110 ) | 40.00% | 78.57% | 68.42% | 1.8667 | 0.7636 |
| ( >= 112 ) | 40.00% | 85.71% | 73.68% | 2.8000 | 0.7000 |
| ( >= 124 ) | 40.00% | 92.86% | 78.95% | 5.6000 | 0.6462 |
| ( >= 128 ) | 40.00% | 100.00% | 84.21% | | 0.6000 |
| ( >= 138 ) | 20.00% | 100.00% | 78.95% | | 0.8000 |
| ( > 138 ) | 0.00% | 100.00% | 73.68% | | 1.0000 |

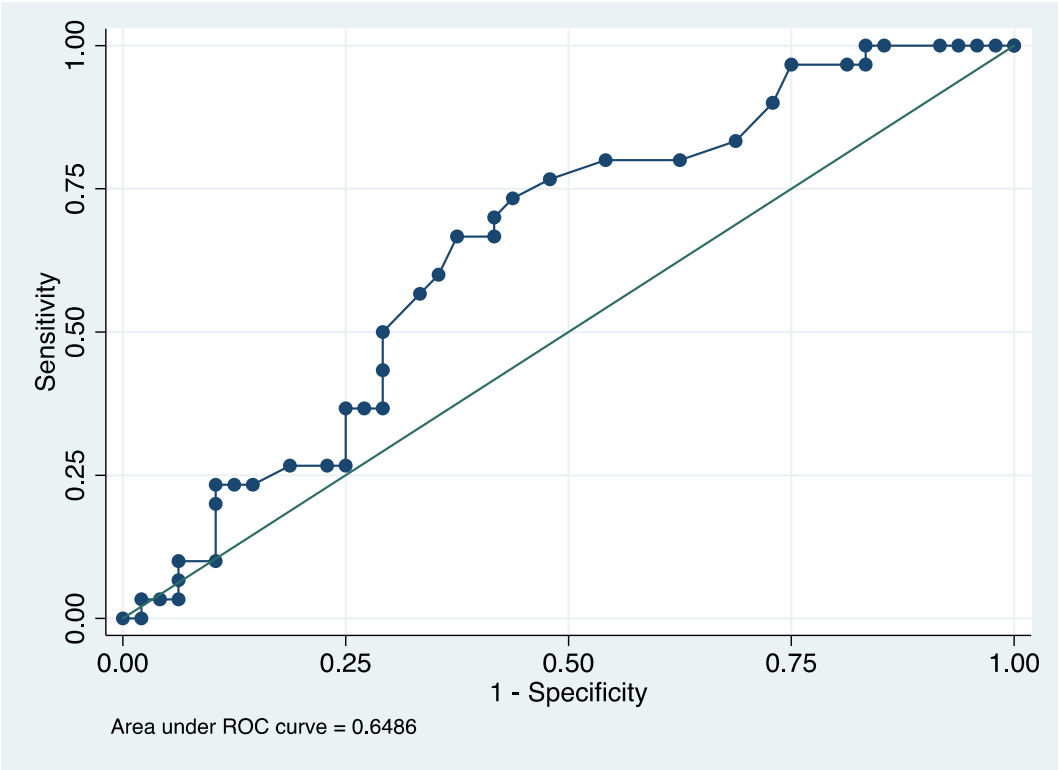


**Figure 8.11 ROC curve showing performance of age in discriminating moderate to severe OSA in people with tetraplegia.**

**Table 8.11 Sensitivity and specificity at various age thresholds for identifying moderate to severe OSA in people with tetraplegia**

| Cutpoint | Sensitivity | Specificity | Correctly Classified | LR+ | LR− |
|---|---|---|---|---|---|
| ( >= 20 ) | 100.00% | 0.00% | 38.46% | 1.0000 | |
| ( >= 23 ) | 100.00% | 2.08% | 39.74% | 1.0213 | 0.0000 |
| ( >= 24 ) | 100.00% | 4.17% | 41.03% | 1.0435 | 0.0000 |
| ( >= 25 ) | 100.00% | 6.25% | 42.31% | 1.0667 | 0.0000 |
| ( >= 27 ) | 100.00% | 8.33% | 43.59% | 1.0909 | 0.0000 |
| ( >= 28 ) | 100.00% | 14.58% | 47.44% | 1.1707 | 0.0000 |
| ( >= 30 ) | 100.00% | 16.67% | 48.72% | 1.2000 | 0.0000 |
| ( >= 31 ) | 96.67% | 16.67% | 47.44% | 1.1600 | 0.2000 |
| ( >= 32 ) | 96.67% | 18.75% | 48.72% | 1.1897 | 0.1778 |
| ( >= 33 ) | 96.67% | 25.00% | 52.56% | 1.2889 | 0.1333 |
| ( >= 34 ) | 90.00% | 27.08% | 51.28% | 1.2343 | 0.3692 |
| ( >= 35 ) | 83.33% | 31.25% | 51.28% | 1.2121 | 0.5333 |
| ( >= 36 ) | 80.00% | 37.50% | 53.85% | 1.2800 | 0.5333 |
| ( >= 38 ) | 80.00% | 45.83% | 58.97% | 1.4769 | 0.4364 |
| ( >= 39 ) | 76.67% | 52.08% | 61.54% | 1.6000 | 0.4480 |
| ( >= 40 ) | 73.33% | 56.25% | 62.82% | 1.6762 | 0.4741 |
| ( >= 42 ) | 70.00% | 58.33% | 62.82% | 1.6800 | 0.5143 |
| ( >= 43 ) | 66.67% | 58.33% | 61.54% | 1.6000 | 0.5714 |
| ( >= 44 ) | 66.67% | 62.50% | 64.10% | 1.7778 | 0.5333 |
| ( >= 45 ) | 60.00% | 64.58% | 62.82% | 1.6941 | 0.6194 |
| ( >= 46 ) | 56.67% | 66.67% | 62.82% | 1.7000 | 0.6500 |
| ( >= 48 ) | 50.00% | 70.83% | 62.82% | 1.7143 | 0.7059 |
| ( >= 49 ) | 43.33% | 70.83% | 60.26% | 1.4857 | 0.8000 |
| ( >= 51 ) | 36.67% | 70.83% | 57.69% | 1.2571 | 0.8941 |
| ( >= 52 ) | 36.67% | 72.92% | 58.97% | 1.3538 | 0.8686 |
| ( >= 53 ) | 36.67% | 75.00% | 60.26% | 1.4667 | 0.8444 |
| ( >= 54 ) | 26.67% | 75.00% | 56.41% | 1.0667 | 0.9778 |
| ( >= 55 ) | 26.67% | 77.08% | 57.69% | 1.1636 | 0.9514 |
| ( >= 56 ) | 26.67% | 81.25% | 60.26% | 1.4222 | 0.9026 |
| ( >= 57 ) | 23.33% | 85.42% | 61.54% | 1.6000 | 0.8976 |
| ( >= 58 ) | 23.33% | 87.50% | 62.82% | 1.8667 | 0.8762 |
| ( >= 59 ) | 23.33% | 89.58% | 64.10% | 2.2400 | 0.8558 |
| ( >= 60 ) | 20.00% | 89.58% | 62.82% | 1.9200 | 0.8930 |
| ( >= 61 ) | 10.00% | 89.58% | 58.97% | 0.9600 | 1.0047 |
| ( >= 62 ) | 10.00% | 93.75% | 61.54% | 1.6000 | 0.9600 |
| ( >= 66 ) | 6.67% | 93.75% | 60.26% | 1.0667 | 0.9956 |
| ( >= 67 ) | 3.33% | 93.75% | 58.97% | 0.5333 | 1.0311 |
| ( >= 68 ) | 3.33% | 95.83% | 60.26% | 0.8000 | 1.0087 |
| ( >= 69 ) | 3.33% | 97.92% | 61.54% | 1.6000 | 0.9872 |
| ( >= 70 ) | 0.00% | 97.92% | 60.26% | 0.0000 | 1.0213 |
| ( > 70 ) | 0.00% | 100.00% | 61.54% | | 1.0000 |

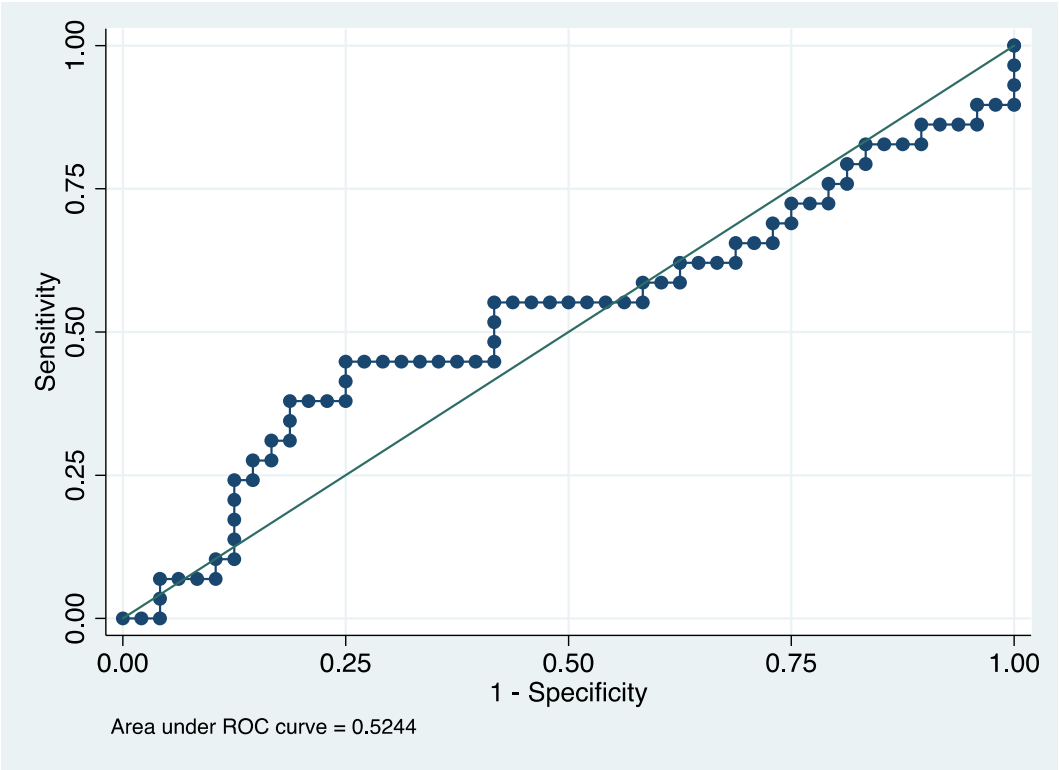


**Figure 8.12 ROC curve showing performance of years since injury in discriminating moderate to severe OSA in people with tetraplegia.**

**Table 8.12 Sensitivity and specificity at various years since injury thresholds for identifying moderate to severe OSA in people with tetraplegia**

| Cutpoint | Sensitivity | Specificity | Correctly Classified | LR+ | LR- |
|---|---|---|---|---|---|
| ( >= 1.295.. ) | 100.00% | 0.00% | 37.66% | 1.0000 | |
| ( >= 2.488.. ) | 96.55% | 0.00% | 36.36% | 0.9655 | |
| ( >= 2.642.. ) | 93.10% | 0.00% | 35.06% | 0.9310 | |
| ( >= 2.765.. ) | 89.66% | 0.00% | 33.77% | 0.8966 | |
| ( >= 2.778.. ) | 89.66% | 2.08% | 35.06% | 0.9156 | 4.9655 |
| ( >= 3.014.. ) | 89.66% | 4.17% | 36.36% | 0.9355 | 2.4828 |
| ( >= 3.019.. ) | 86.21% | 4.17% | 35.06% | 0.8996 | 3.3103 |
| ( >= 3.542.. ) | 86.21% | 6.25% | 36.36% | 0.9195 | 2.2069 |
| ( >= 3.611.. ) | 86.21% | 8.33% | 37.66% | 0.9404 | 1.6552 |
| ( >= 3.734.. ) | 86.21% | 10.42% | 38.96% | 0.9623 | 1.3241 |
| ( >= 3.748.. ) | 82.76% | 10.42% | 37.66% | 0.9238 | 1.6552 |
| ( >= 3.863.. ) | 82.76% | 12.50% | 38.96% | 0.9458 | 1.3793 |
| ( >= 4.188.. ) | 82.76% | 14.58% | 40.26% | 0.9689 | 1.1823 |
| ( >= 4.525.. ) | 82.76% | 16.67% | 41.56% | 0.9931 | 1.0345 |
| ( >= 4.70089 ) | 79.31% | 16.67% | 40.26% | 0.9517 | 1.2414 |
| ( >= 4.870.. ) | 79.31% | 18.75% | 41.56% | 0.9761 | 1.1034 |
| ( >= 4.977.. ) | 75.86% | 18.75% | 40.26% | 0.9337 | 1.2874 |
| ( >= 5.218.. ) | 75.86% | 20.83% | 41.56% | 0.9583 | 1.1586 |
| ( >= 5.68104 ) | 72.41% | 20.83% | 40.26% | 0.9147 | 1.3241 |
| ( >= 5.716.. ) | 72.41% | 22.92% | 41.56% | 0.9394 | 1.2038 |
| ( >= 5.765.. ) | 72.41% | 25.00% | 42.86% | 0.9655 | 1.1034 |
| ( >= 6.201.. ) | 68.97% | 25.00% | 41.56% | 0.9195 | 1.2414 |
| ( >= 6.275.. ) | 68.97% | 27.08% | 42.86% | 0.9458 | 1.1459 |
| ( >= 6.485.. ) | 65.52% | 27.08% | 41.56% | 0.8985 | 1.2732 |
| ( >= 6.524.. ) | 65.52% | 29.17% | 42.86% | 0.9249 | 1.1823 |
| ( >= 7.564.. ) | 65.52% | 31.25% | 44.16% | 0.9530 | 1.1034 |
| ( >= 8.002.. ) | 62.07% | 31.25% | 42.86% | 0.9028 | 1.2138 |
| ( >= 8.301.. ) | 62.07% | 33.33% | 44.16% | 0.9310 | 1.1379 |
| ( >= 8.459.. ) | 62.07% | 35.42% | 45.45% | 0.9611 | 1.0710 |
| ( >= 8.67625 ) | 62.07% | 37.50% | 46.75% | 0.9931 | 1.0115 |
| ( >= 8.698.. ) | 58.62% | 37.50% | 45.45% | 0.9379 | 1.1034 |
| ( >= 9.152.. ) | 58.62% | 39.58% | 46.75% | 0.9703 | 1.0454 |
| ( >= 9.188.. ) | 58.62% | 41.67% | 48.05% | 1.0049 | 0.9931 |
| ( >= 9.511.. ) | 55.17% | 41.67% | 46.75% | 0.9458 | 1.0759 |
| ( >= 9.689.. ) | 55.17% | 43.75% | 48.05% | 0.9808 | 1.0246 |
| ( >= 9.820.. ) | 55.17% | 45.83% | 49.35% | 1.0186 | 0.9781 |
| ( >= 9.823.. ) | 55.17% | 47.92% | 50.65% | 1.0593 | 0.9355 |
| ( >= 9.952.. ) | 55.17% | 50.00% | 51.95% | 1.1034 | 0.8966 |
| ( >= 9.976.. ) | 55.17% | 52.08% | 53.25% | 1.1514 | 0.8607 |
| ( >= 10.10.. ) | 55.17% | 54.17% | 54.55% | 1.2038 | 0.8276 |
| ( >= 10.25.. ) | 55.17% | 56.25% | 55.84% | 1.2611 | 0.7969 |
| ( >= 10.31.. ) | 55.17% | 58.33% | 57.14% | 1.3241 | 0.7685 |
| ( >= 10.57.. ) | 51.72% | 58.33% | 55.84% | 1.2414 | 0.8276 |
| ( >= 12.21.. ) | 48.28% | 58.33% | 54.55% | 1.1586 | 0.8867 |
| ( >= 12.37.. ) | 44.83% | 58.33% | 53.25% | 1.0759 | 0.9458 |
| ( >= 13.26.. ) | 44.83% | 60.42% | 54.55% | 1.1325 | 0.9132 |
| ( >= 13.89.. ) | 44.83% | 62.50% | 55.84% | 1.1954 | 0.8828 |
| ( >= 14.13.. ) | 44.83% | 64.58% | 57.14% | 1.2657 | 0.8543 |
| ( >= 14.75.. ) | 44.83% | 66.67% | 58.44% | 1.3448 | 0.8276 |
| ( >= 15.01.. ) | 44.83% | 68.75% | 59.74% | 1.4345 | 0.8025 |
| ( >= 15.11.. ) | 44.83% | 70.83% | 61.04% | 1.5369 | 0.7789 |
| ( >= 15.24.. ) | 44.83% | 72.92% | 62.34% | 1.6552 | 0.7567 |
| ( >= 15.36.. ) | 44.83% | 75.00% | 63.64% | 1.7931 | 0.7356 |
| ( >= 15.57.. ) | 41.38% | 75.00% | 62.34% | 1.6552 | 0.7816 |
| ( >= 15.61.. ) | 37.93% | 75.00% | 61.04% | 1.5172 | 0.8276 |
| ( >= 16.19.. ) | 37.93% | 77.08% | 62.34% | 1.6552 | 0.8052 |
| ( >= 16.62.. ) | 37.93% | 79.17% | 63.64% | 1.8207 | 0.7840 |
| ( >= 16.72.. ) | 37.93% | 81.25% | 64.94% | 2.0230 | 0.7639 |
| ( >= 18.32.. ) | 34.48% | 81.25% | 63.64% | 1.8391 | 0.8064 |
| ( >= 19.25.. ) | 31.03% | 81.25% | 62.34% | 1.6552 | 0.8488 |
| ( >= 19.64.. ) | 31.03% | 83.33% | 63.64% | 1.8621 | 0.8276 |
| ( >= 19.76.. ) | 27.59% | 83.33% | 62.34% | 1.6552 | 0.8690 |
| ( >= 19.82.. ) | 27.59% | 85.42% | 63.64% | 1.8916 | 0.8478 |
| ( >= 19.84.. ) | 24.14% | 85.42% | 62.34% | 1.6552 | 0.8881 |
| ( >= 20.69.. ) | 24.14% | 87.50% | 63.64% | 1.9310 | 0.8670 |
| ( >= 21.54.. ) | 20.69% | 87.50% | 62.34% | 1.6552 | 0.9064 |
| ( >= 21.99.. ) | 17.24% | 87.50% | 61.04% | 1.3793 | 0.9458 |
| ( >= 22.02.. ) | 13.79% | 87.50% | 59.74% | 1.1034 | 0.9852 |
| ( >= 22.16.. ) | 10.34% | 87.50% | 58.44% | 0.8276 | 1.0246 |
| ( >= 22.5462 ) | 10.34% | 89.58% | 59.74% | 0.9931 | 1.0008 |
| ( >= 22.70.. ) | 6.90% | 89.58% | 58.44% | 0.6621 | 1.0393 |
| ( >= 23.19.. ) | 6.90% | 91.67% | 59.74% | 0.8276 | 1.0157 |
| ( >= 23.46.. ) | 6.90% | 93.75% | 61.04% | 1.1034 | 0.9931 |
| ( >= 23.61.. ) | 6.90% | 95.83% | 62.34% | 1.6552 | 0.9715 |
| ( >= 27.96.. ) | 3.45% | 95.83% | 61.04% | 0.8276 | 1.0075 |
| ( >= 36.08.. ) | 0.00% | 95.83% | 59.74% | 0.0000 | 1.0435 |
| ( >= 37.96.. ) | 0.00% | 97.92% | 61.04% | 0.0000 | 1.0213 |
| ( > 37.96.. ) | 0.00% | 100.00% | 62.34% | | 1.0000 |

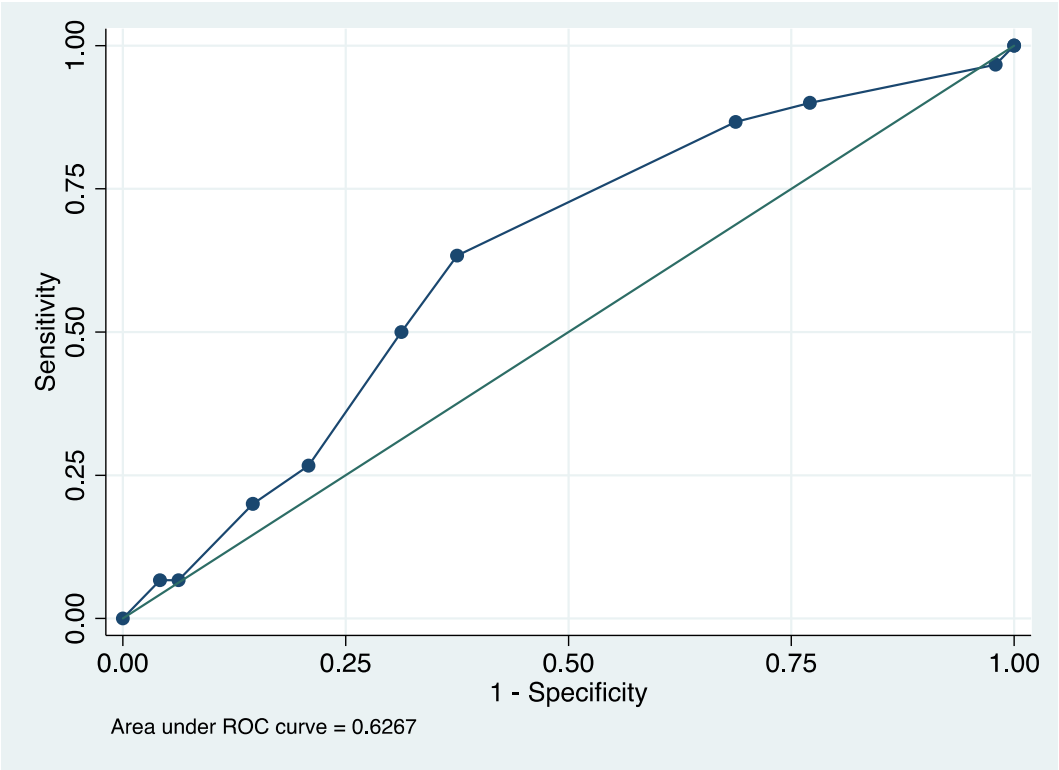


**Figure 8.13 ROC curve showing performance of KSS in discriminating moderate to severe OSA in people with tetraplegia.**

**Table 8.13 Sensitivity and specificity at various KSS thresholds for identifying moderate to severe OSA in people with tetraplegia**

Detailed report of sensitivity and specificity

| Cutpoint | Sensitivity | Specificity | Correctly Classified | LR+ | LR− |
|---|---|---|---|---|---|
| ( >= 0 ) | 100.00% | 0.00% | 38.46% | 1.0000 | |
| ( >= 1 ) | 96.67% | 2.08% | 38.46% | 0.9872 | 1.6000 |
| ( >= 2 ) | 90.00% | 22.92% | 48.72% | 1.1676 | 0.4364 |
| ( >= 3 ) | 86.67% | 31.25% | 52.56% | 1.2606 | 0.4267 |
| ( >= 4 ) | 63.33% | 62.50% | 62.82% | 1.6889 | 0.5867 |
| ( >= 5 ) | 50.00% | 68.75% | 61.54% | 1.6000 | 0.7273 |
| ( >= 6 ) | 26.67% | 79.17% | 58.97% | 1.2800 | 0.9263 |
| ( >= 7 ) | 20.00% | 85.42% | 60.26% | 1.3714 | 0.9366 |
| ( >= 8 ) | 6.67% | 93.75% | 60.26% | 1.0667 | 0.9956 |
| ( >= 9 ) | 6.67% | 95.83% | 61.54% | 1.6000 | 0.9739 |
| ( > 9 ) | 0.00% | 100.00% | 61.54% | | 1.0000 |

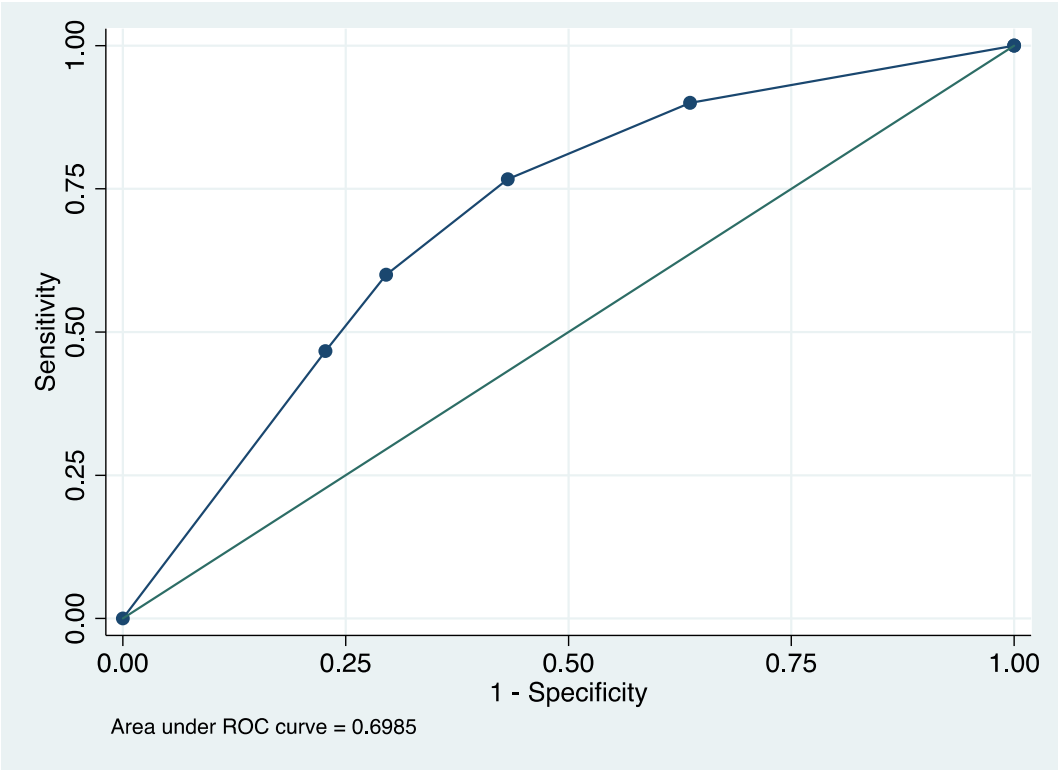


**Figure 8.14 ROC curve showing performance of self-reported snoring in discriminating moderate to severe OSA in people with tetraplegia.**

**Table 8.14 Sensitivity and specificity at various self-reported snoring thresholds for identifying moderate to severe OSA in people with tetraplegia**

| Cutpoint | Sensitivity | Specificity | Correctly Classified | LR+ | LR− |
|---|---|---|---|---|---|
| ( >= 1 ) | 100.00% | 0.00% | 40.54% | 1.0000 | |
| ( >= 2 ) | 90.00% | 36.36% | 58.11% | 1.4143 | 0.2750 |
| ( >= 3 ) | 76.67% | 56.82% | 64.86% | 1.7754 | 0.4107 |
| ( >= 4 ) | 60.00% | 70.45% | 66.22% | 2.0308 | 0.5677 |
| ( >= 5 ) | 46.67% | 77.27% | 64.86% | 2.0533 | 0.6902 |
| ( > 5 ) | 0.00% | 100.00% | 59.46% | | 1.0000 |

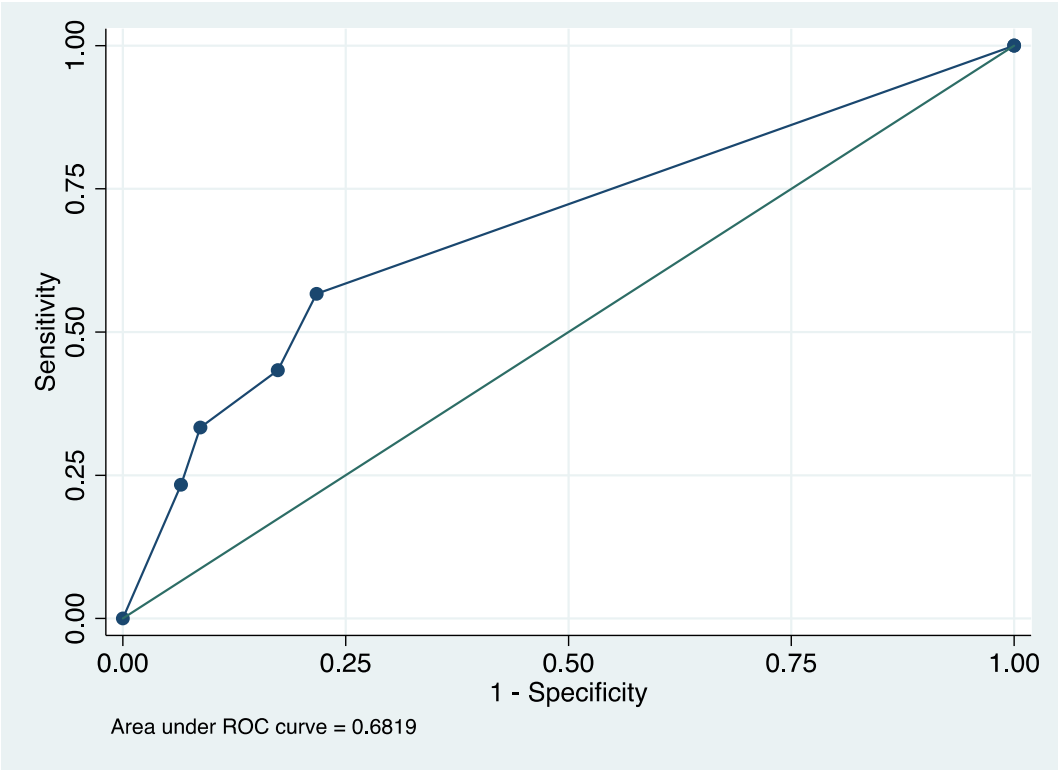


**Figure 8.15** **ROC curve showing performance of self-reported apnoeas in discriminating moderate to severe OSA in people with tetraplegia.**

**Table 8.15** **Sensitivity and specificity at various self-reported apnoea thresholds for identifying moderate to severe OSA in people with tetraplegia**

| Cutpoint | Sensitivity | Specificity | Correctly Classified | LR+ | LR− |
|---|---|---|---|---|---|
| ( >= 1 ) | 100.00% | 0.00% | 39.47% | 1.0000 | |
| ( >= 2 ) | 56.67% | 78.26% | 69.74% | 2.6067 | 0.5537 |
| ( >= 3 ) | 43.33% | 82.61% | 67.11% | 2.4917 | 0.6860 |
| ( >= 4 ) | 33.33% | 91.30% | 68.42% | 3.8333 | 0.7302 |
| ( >= 5 ) | 23.33% | 93.48% | 65.79% | 3.5778 | 0.8202 |
| ( > 5 ) | 0.00% | 100.00% | 60.53% | | 1.0000 |

## 8.4 Sensitivity and specificity tables of questionnaires and ODI for classifying MS-OSA

**Table 8.16 Sensitivity and specificity at various OSA50 thresholds for identifying moderate to severe OSA in people with tetraplegia.**

| Cutpoint | Sensitivity | Specificity | Correctly Classified | LR+ | LR− |
|---|---|---|---|---|---|
| ( >= 0 ) | 100.00% | 0.00% | 38.46% | 1.0000 | |
| ( >= 2 ) | 100.00% | 18.75% | 50.00% | 1.2308 | 0.0000 |
| ( >= 3 ) | 100.00% | 29.17% | 56.41% | 1.4118 | 0.0000 |
| ( >= 4 ) | 90.00% | 52.08% | 66.67% | 1.8783 | 0.1920 |
| ( >= 5 ) | 86.67% | 52.08% | 65.38% | 1.8087 | 0.2560 |
| ( >= 6 ) | 80.00% | 66.67% | 71.79% | 2.4000 | 0.3000 |
| ( >= 7 ) | 66.67% | 83.33% | 76.92% | 4.0000 | 0.4000 |
| ( >= 8 ) | 63.33% | 89.58% | 79.49% | 6.0800 | 0.4093 |
| ( >= 10 ) | 10.00% | 97.92% | 64.10% | 4.8000 | 0.9191 |
| ( > 10 ) | 0.00% | 100.00% | 61.54% | | 1.0000 |

**Table 8.17 Sensitivity and specificity at various SOSAT thresholds for identifying moderate to severe OSA in people with tetraplegia**

| Cutpoint | Sensitivity | Specificity | Correctly Classified | LR+ | LR− |
|---|---|---|---|---|---|
| ( >= 2 ) | 100.00% | 0.00% | 38.46% | 1.0000 | |
| ( >= 3 ) | 100.00% | 16.67% | 48.72% | 1.2000 | 0.0000 |
| ( >= 4 ) | 100.00% | 25.00% | 53.85% | 1.3333 | 0.0000 |
| ( >= 5 ) | 100.00% | 27.08% | 55.13% | 1.3714 | 0.0000 |
| ( >= 6 ) | 90.00% | 56.25% | 69.23% | 2.0571 | 0.1778 |
| ( >= 7 ) | 83.33% | 75.00% | 78.21% | 3.3333 | 0.2222 |
| ( >= 8 ) | 73.33% | 87.50% | 82.05% | 5.8667 | 0.3048 |
| ( >= 10 ) | 40.00% | 97.92% | 75.64% | 19.2000 | 0.6128 |
| ( > 10 ) | 0.00% | 100.00% | 61.54% | | 1.0000 |

**Table 8.18 Sensitivity and specificity of various 3%ODI thresholds for identifying moderate to severe OSA**

| Cutpoint | Sensitivity | Specificity | Correctly Classified | LR+ | LR− |
|---|---|---|---|---|---|
| ( >= .9 ) | 100.00% | 0.00% | 38.46% | 1.0000 | |
| ( >= 1.3 ) | 100.00% | 2.08% | 39.74% | 1.0213 | 0.0000 |
| ( >= 1.7 ) | 100.00% | 4.17% | 41.03% | 1.0435 | 0.0000 |
| ( >= 1.8 ) | 100.00% | 8.33% | 43.59% | 1.0909 | 0.0000 |
| ( >= 2.2 ) | 100.00% | 10.42% | 44.87% | 1.1163 | 0.0000 |
| ( >= 2.3 ) | 100.00% | 14.58% | 47.44% | 1.1707 | 0.0000 |
| ( >= 2.6 ) | 100.00% | 16.67% | 48.72% | 1.2000 | 0.0000 |
| ( >= 2.8 ) | 100.00% | 18.75% | 50.00% | 1.2308 | 0.0000 |
| ( >= 2.9 ) | 100.00% | 20.83% | 51.28% | 1.2632 | 0.0000 |
| ( >= 3.1 ) | 100.00% | 22.92% | 52.56% | 1.2973 | 0.0000 |
| ( >= 3.2 ) | 100.00% | 25.00% | 53.85% | 1.3333 | 0.0000 |
| ( >= 3.4 ) | 100.00% | 27.08% | 55.13% | 1.3714 | 0.0000 |
| ( >= 3.5 ) | 100.00% | 29.17% | 56.41% | 1.4118 | 0.0000 |
| ( >= 3.6 ) | 100.00% | 31.25% | 57.69% | 1.4545 | 0.0000 |
| ( >= 4 ) | 100.00% | 35.42% | 60.26% | 1.5484 | 0.0000 |
| ( >= 4.3 ) | 100.00% | 37.50% | 61.54% | 1.6000 | 0.0000 |
| ( >= 4.5 ) | 100.00% | 39.58% | 62.82% | 1.6552 | 0.0000 |
| ( >= 4.6 ) | 100.00% | 43.75% | 65.38% | 1.7778 | 0.0000 |
| ( >= 5 ) | 100.00% | 45.83% | 66.67% | 1.8462 | 0.0000 |
| ( >= 5.2 ) | 100.00% | 47.92% | 67.95% | 1.9200 | 0.0000 |
| ( >= 5.3 ) | 96.67% | 50.00% | 67.95% | 1.9333 | 0.0667 |
| ( >= 5.7 ) | 96.67% | 52.08% | 69.23% | 2.0174 | 0.0640 |
| ( >= 5.9 ) | 96.67% | 54.17% | 70.51% | 2.1091 | 0.0615 |
| ( >= 6 ) | 96.67% | 56.25% | 71.79% | 2.2095 | 0.0593 |
| ( >= 6.1 ) | 96.67% | 58.33% | 73.08% | 2.3200 | 0.0571 |
| ( >= 6.6 ) | 96.67% | 60.42% | 74.36% | 2.4421 | 0.0552 |
| ( >= 6.7 ) | 93.33% | 60.42% | 73.08% | 2.3579 | 0.1103 |
| ( >= 7.1 ) | 93.33% | 64.58% | 75.64% | 2.6353 | 0.1032 |
| ( >= 7.6 ) | 93.33% | 66.67% | 76.92% | 2.8000 | 0.1000 |
| ( >= 8.4 ) | 93.33% | 68.75% | 78.21% | 2.9867 | 0.0970 |
| ( >= 9 ) | 90.00% | 70.83% | 78.21% | 3.0857 | 0.1412 |
| ( >= 9.3 ) | 90.00% | 72.92% | 79.49% | 3.3231 | 0.1371 |
| ( >= 9.4 ) | 90.00% | 75.00% | 80.77% | 3.6000 | 0.1333 |
| ( >= 9.5 ) | 90.00% | 77.08% | 82.05% | 3.9273 | 0.1297 |
| ( >= 10.8 ) | 86.67% | 77.08% | 80.77% | 3.7818 | 0.1730 |
| ( >= 11.3 ) | 86.67% | 79.17% | 82.05% | 4.1600 | 0.1684 |
| ( >= 12.3 ) | 86.67% | 81.25% | 83.33% | 4.6222 | 0.1641 |
| ( >= 12.7 ) | 86.67% | 83.33% | 84.62% | 5.2000 | 0.1600 |
| ( >= 13.1 ) | 83.33% | 83.33% | 83.33% | 5.0000 | 0.2000 |
| ( >= 13.9 ) | 80.00% | 83.33% | 82.05% | 4.8000 | 0.2400 |
| ( >= 15.4 ) | 80.00% | 85.42% | 83.33% | 5.4857 | 0.2341 |
| ( >= 16 ) | 80.00% | 87.50% | 84.62% | 6.4000 | 0.2286 |
| ( >= 16.7 ) | 80.00% | 89.58% | 85.90% | 7.6800 | 0.2233 |
| ( >= 18.5 ) | 76.67% | 91.67% | 85.90% | 9.2000 | 0.2545 |
| ( >= 21.1 ) | 73.33% | 91.67% | 84.62% | 8.8000 | 0.2909 |
| ( >= 21.5 ) | 73.33% | 93.75% | 85.90% | 11.7333 | 0.2844 |
| ( >= 22.2 ) | 73.33% | 95.83% | 87.18% | 17.6000 | 0.2783 |
| ( >= 23.4 ) | 66.67% | 95.83% | 84.62% | 16.0000 | 0.3478 |
| ( >= 23.9 ) | 63.33% | 95.83% | 83.33% | 15.2000 | 0.3826 |
| ( >= 24.1 ) | 63.33% | 97.92% | 84.62% | 30.4001 | 0.3745 |
| ( >= 26.6 ) | 60.00% | 97.92% | 83.33% | 28.8001 | 0.4085 |
| ( >= 30.3 ) | 56.67% | 97.92% | 82.05% | 27.2001 | 0.4426 |
| ( >= 31.7 ) | 53.33% | 97.92% | 80.77% | 25.6001 | 0.4766 |
| ( >= 32.9 ) | 50.00% | 97.92% | 79.49% | 24.0001 | 0.5106 |
| ( >= 33 ) | 46.67% | 97.92% | 78.21% | 22.4001 | 0.5447 |
| ( >= 36.8 ) | 43.33% | 97.92% | 76.92% | 20.8001 | 0.5787 |
| ( >= 37.6 ) | 40.00% | 97.92% | 75.64% | 19.2000 | 0.6128 |
| ( >= 38.2 ) | 36.67% | 97.92% | 74.36% | 17.6000 | 0.6468 |
| ( >= 39.6 ) | 33.33% | 97.92% | 73.08% | 16.0000 | 0.6809 |
| ( >= 45.3 ) | 33.33% | 100.00% | 74.36% | | 0.6667 |
| ( >= 45.7 ) | 30.00% | 100.00% | 73.08% | | 0.7000 |
| ( >= 48.2 ) | 26.67% | 100.00% | 71.79% | | 0.7333 |
| ( >= 49.1 ) | 23.33% | 100.00% | 70.51% | | 0.7667 |
| ( >= 50 ) | 20.00% | 100.00% | 69.23% | | 0.8000 |
| ( >= 51.1 ) | 16.67% | 100.00% | 67.95% | | 0.8333 |
| ( >= 52.3 ) | 13.33% | 100.00% | 66.67% | | 0.8667 |
| ( >= 61.8 ) | 10.00% | 100.00% | 65.38% | | 0.9000 |
| ( >= 64.9 ) | 6.67% | 100.00% | 64.10% | | 0.9333 |
| ( >= 68 ) | 3.33% | 100.00% | 62.82% | | 0.9667 |
| ( > 68 ) | 0.00% | 100.00% | 61.54% | | 1.0000 |

## 8.5 Interview guide for Spinal Physicians managing patients with chronic tetraplegia.

**Introduction**

As outlined in the participant information sheet, this study aims to identify and explore the factors that influence the management of tetraplegic patients with obstructive sleep apnoea.

You do not have to answer every question and can cease the interview at any time. If you need to attend to an urgent matter we can stop the interview and recommence it later.

We will talk about your spinal unit, how you screen patients for obstructive sleep apnoea, how you manage patients with suspected or confirmed obstructive sleep apnoea, and the factors that influence this management. We are interviewing spinal physicians from around the world, and in different sized units, with and without access to specialist sleep services so that we get a broad view. Interviews will be audio-taped and you will be provided with a copy of the transcript and invited to provide feedback on the accuracy of the information. All information will be treated as strictly confidential.

Before we start do you have any questions?

**Background information**

Can you describe your spinal unit, its clientele and the services it offers?

Prompt questions

How many years of experience do you have working as a spinal physician?

How many inpatient beds do you have?

What is the mix of traumatic vs non-traumatic injuries?

How many new patients do you admit per year?

What outpatient/ outreach services do you have?

How big is the hospital?

Emergency department? Trauma services?

How would you describe the socio-economic status of your patient population?

Is there a sleep laboratory in the hospital? What sleep services do they offer? If not, where are the nearest specialist sleep services? Is there a waiting list for services?

Now I am going to ask you questions about how you manage OSA in your SCI patients, and what factors influence your clinical practice. First I will ask how and why you screen for and diagnose OSA in both the inpatient and outpatient units, and then we will ask about how and why you manage a positive diagnosis of OSA.

## Screening for and diagnosing obstructive sleep apnoea

### Understanding clinical practice

Can you talk me through the various steps in how you screen patients for obstructive sleep apnoea in:

- The inpatient unit
- The outpatient clinic

Prompt questions:

- Do you screen patients for signs and symptoms of OSA?
    - If so, how do you screen? What questions do you ask? Which signs and symptoms alert you to possible OSA?
    - Are there any particular clinical signs or symptoms that you would consider as high risk? How would you measure these?
    - Who does the screening?
    - Do you routinely screen everyone? If not, who do you (not) screen?
    - When do you screen? At what time point post injury? Roughly what proportion of your SCI outpatients do you screen for signs and symptoms? Is this different for paraplegia/quadriplegia?
- Do you order diagnostic tests for suspected OSA?
    - If so, what tests do you order? If more than one type, how would you decide which test?
    - Who orders the testing?
    - Who performs the testing?
    - Which patients do you test for OSA?
    - Roughly what proportion of your SCI outpatients do you refer for testing for OSA? Is this different for paraplegia/quadriplegia?
    - Where are the results of the assessments/tests recorded? (and by who?)
    - How are the results used? (and by who?)
    - How do you determine whether a patient has a diagnosis of OSA?
    - Do you know roughly how long your patients wait for diagnostic test?

**Factors influencing practice**

Now I want to ask you about what influences your OSA screening practices. I am using a framework called the Theoretical Domains Framework, which is a set of 12 domains that are known to influence clinical behaviours. Some of the questions will seem more relevant than others.

Firstly, before I prompt with specific questions about potential factors that are known to influence clinical practice, can I first ask you tell me what you think are the biggest influences on your decision to screen/not screen your patients for OSA in both the inpatient and outpatient settings?

Prompt questions to explore factors influencing practice (grouped by TDF domains).

| **TDF Domains** | **TDF Definitions [Constructs]** | **Prompt questions (if required)** |
|---|---|---|
| Knowledge | An awareness of the existence of something. [Knowledge including knowledge of condition/scientific rationale. Procedural knowledge. Knowledge of task environment.] | Are you aware of any clinical practice guidelines recommending screening for OSA?<br><br>What do you think is best practice in management of OSA in tetraplegia?<br><br>Are you aware of any research about the prevalence and impact of OSA in SCI?<br><br>Are you familiar with any risk assessment tools? |
| Skills | An ability or proficiency acquired through practice. [Skills<br>Skills development<br>Competence<br>Ability<br>Interpersonal skills<br>Practice<br>Skill assessment] | What skills are needed?<br><br>Do you know how to order a diagnostic test for OSA?<br><br>Do you know how to interpret results of screening and diagnostic tests for OSA? |
| Social professional role and identity | A coherent set of behaviors and displayed personal qualities of an individual in a social or work setting. [Professional identity | Do you think screening/diagnosing OSA is part of your role as physician? If not, whose role is it?<br><br>Is there a commitment from your organization to manage OSA in |

| | | |
|---|---|---|
| | Professional role<br>Social identity<br>Identity<br>Professional boundaries<br>Professional confidence<br>Group identity<br>Leadership<br>Organizational commitment] | tetraplegia? |
| Beliefs about capabilities | Acceptance of the truth, reality, or validity about an ability, talent, or facility that a person can put to constructive use.<br>[Self-confidence<br>Perceived competence<br>Self-efficacy<br>Perceived behavioral control<br>Beliefs<br>Self-esteem<br>Empowerment<br>Professional confidence] | Any difficulties in assessing signs and symptoms of OSA?<br><br>Any challenges in determining presence of OSA in general and using/ordering different tests/tools in particular?<br><br>What would help you to identify your patients with OSA?<br><br>How confident are you that you can identify OSA in your patients? |
| Beliefs about consequences | Acceptance of the truth, reality, or validity about outcomes of a behaviour in a given situation.<br>[Beliefs<br>Outcome expectancies<br>Characteristics of outcome expectancies<br>Anticipated regret<br>Consequences] | What do you think are the benefits and costs of screening for OSA in people with tetraplegia? (for your patients, you, your colleagues and the organization)<br><br>What are the benefits and costs of not screening for OSA? (for your patients, you, your colleagues and the organization)<br><br>What will happen if you don't routinely screen?<br><br>Do the benefits outweigh the costs?<br><br>Does the evidence suggest that screening is worthwhile? |
| Motivation and goals | A conscious decision to perform a behavior or resolve to act in a certain | Are there incentives to screen for OSA?<br>Do you feel you have to? |

| | | |
|---|---|---|
| | way.<br>Mental representations of outcomes or end states that an individual wants to achieve.<br>[Stability of intentions<br>Stages of change model<br>Transtheoretical model and stages of change<br>Goals (distal/proximal)<br>Goal priority<br>Goal/target setting<br>Goals (autonomous/controlled)<br>Action planning<br>Implementation intention] | Are there other aspects of your role that interfere with screening for OSA? |
| Memory, attention and decision processes | The ability to retain information, focus selectively on aspects of the environment and choose between two or more alternatives.<br>[Memory<br>Attention<br>Attention control<br>Decision making<br>Cognitive overload/tiredness] | Are there any reminders in place to prompt you to do any of the relevant tests? If no, do you think these would be helpful?'<br><br>Is it something you do routinely?<br><br>Is screening for OSA something you do if you have time? |
| Environmental context and resources | Any circumstance of a person's situation or environment that discourages or encourages the development of skills and abilities, independence, social competence, and adaptive behavior.<br>[Environmental stressors<br>Resources/material resources<br>Organizational culture/climate<br>Salient events/critical | Do resources influence whether you assess these patients for OSA?<br><br>Are there sufficient human resources?<br><br>Are there sufficient physical resources?<br><br>Do you have enough time/do you have competing demands?<br><br>Does the working environment in inpatient/ outpatients have an effect?<br><br>Are there environmental stressors that impact on your ability to screen for OSA? |

| | | |
|---|---|---|
| | incidents<br>Person x environment interaction<br>Barriers and facilitators] | Do rules/regulations from compensation bodies ever influence your decisions about screening/diagnosing OSA? |
| Social influences | Those interpersonal processes that can cause individuals to change their thoughts, feelings, or behaviors.<br>[Social pressure<br>Social norms<br>Group conformity<br>Social comparisons<br>Group norms<br>Social support<br>Power<br>Intergroup conflict<br>Alienation<br>Group identity<br>Modeling] | Do you seek opinions of colleagues in whether to screen for OSA/ interpreting test results?<br><br>What are the views of your colleagues re: screening for OSA?<br><br>Do you observe others screening patients for OSA? |
| Emotion | A complex reaction pattern, involving experiential, behavioral, and psychological elements, by which an individual attempts to deal with a personally significant matter or event.<br>[Fear<br>Anxiety<br>Affect<br>Stress<br>Depression<br>Positive/negative effect<br>Burn-out] | Is there anything about screening for OSA that evokes an emotional response? If so, what? Does this alter your clinical management decisions? |
| Behavioral regulation | Anything aimed at managing or changing objectively observed or measured actions.<br>[Self-monitoring<br>Breaking habit<br>Action planning] | Are there any protocols or referral pathways that facilitate screening for OSA? |

**Treatment of obstructive sleep apnoea**

**Understanding clinical practice**

Can you talk me through the various steps in how you treat patients with a diagnosis of obstructive sleep apnoea in both the inpatient and outpatient units?

Prompt questions

- Are all patients diagnosed with OSA offered treatment?
    - If not, under what circumstances would they not be referred for treatment?
- Who provides the treatment?
- What is the process for referring a person with OSA for treatment?
- Where is the referral for treatment recorded?
- What treatment/s are offered to patients with OSA?
- How is the decision to offer a particular treatment made?
- Would you/others involve the patient in the decision? If so, how?
- Where are the details of the treatment prescribed and the outcome of the treatment recorded?
- If a particular treatment is not successful (ie not accepted by the patient), what happens next? Are they referred for an alternative treatment?
- Do you know roughly how long your patients wait for treatment?

**Factors influencing practice**

Now I want to ask you about what influences your OSA treatment practices. Firstly, before I prompt with specific questions about potential factors that are known to influence clinical practice, can I first ask you tell me what you think are the biggest influences on your decisions to treat your patients for OSA in both the inpatient and outpatient settings?

Prompt questions to explore factors influencing practice (grouped by TDF domains).

| **TDF Domains** | **TDF Definitions [Constructs][234]** | **Prompt questions (if required)** |
|---|---|---|
| Knowledge | An awareness of the existence of something. [Knowledge including knowledge of condition/scientific rationale. Procedural knowledge. | Are you aware of any clinical practice recommendations regarding treatment of OSA in tetraplegia?<br><br>What do you think is best practice in management of OSA in tetraplegia? |

| | | |
|---|---|---|
| | Knowledge of task environment.] | Are you aware of any research about the effectiveness of OSA treatments in SCI? |
| Skills | An ability or proficiency acquired through practice.<br>[Skills<br>Skills development<br>Competence<br>Ability<br>Interpersonal skills<br>Practice<br>Skill assessment] | What skills are needed to treat OSA?<br><br>Do you know how to prescribe treatment for OSA?<br><br>Do you know how to initiate treatment for OSA? |
| Social professional role and identity | A coherent set of behaviors and displayed personal qualities of an individual in a social or work setting.<br>[Professional identity<br>Professional role<br>Social identity<br>Identity<br>Professional boundaries<br>Professional confidence<br>Group identity<br>Leadership<br>Organizational commitment] | Do you think prescribing treatment for OSA is part of your role as spinal physician? If not, whose role is it?<br><br>Do you think it would ever be feasible for OSA treatment to become the role of the spinal physician or spinal unit? If not, why?<br><br>Is there a commitment from your organization to manage OSA in tetraplegia? |
| Beliefs about capabilities | Acceptance of the truth, reality, or validity about an ability, talent, or facility that a person can put to constructive use.<br>[Self-confidence<br>Perceived competence<br>Self-efficacy<br>Perceived behavioral control<br>Beliefs<br>Self-esteem<br>Empowerment<br>Professional confidence] | Any difficulties in prescribing treatment for OSA?<br><br>What would help you to effectively treat your patients with OSA?<br><br>How confident are you that you can effectively treat OSA in your patients? |
| Beliefs about consequences | Acceptance of the truth, reality, or validity about | What are the benefits and costs of treating OSA in people with tetraplegia? (for your |

| | | |
|---|---|---|
| | outcomes of a behaviour in a given situation.<br>[Beliefs<br>Outcome expectancies<br>Characteristics of outcome expectancies<br>Anticipated regret<br>Consequences] | patients, you, your colleagues and the organization)<br><br>What are the benefits and costs of not treating OSA? (for your patients, you, your colleagues and the organization)<br><br>What will happen if you don't prescribe treatment?<br><br>Do the benefits outweigh the costs?<br><br>Does the evidence suggest that treatment for OSA is worthwhile? |
| Motivation and goals | A conscious decision to perform a behavior or resolve to act in a certain way.<br>Mental representations of outcomes or end states that an individual wants to achieve.<br>[Stability of intentions<br>Stages of change model<br>Transtheoretical model and stages of change<br>Goals (distal/proximal)<br>Goal priority<br>Goal/target setting<br>Goals (autonomous/controlled)<br>Action planning<br>Implementation intention] | Are there incentives to treat OSA?<br><br>Do you feel you have to?<br><br>Are there other aspects of your role that interfere with treating OSA? |
| Memory, attention and decision processes | The ability to retain information, focus selectively on aspects of the environment and choose between two or more alternatives.<br>[Memory<br>Attention<br>Attention control<br>Decision making | Are there any reminders in place to prompt you to prescribe/refer for treatment? If no, do you think these would be helpful?'<br><br>Is it something you do routinely? |

| | | |
|---|---|---|
| | Cognitive overload/tiredness] | |
| Environmental context and resources | Any circumstance of a person's situation or environment that discourages or encourages the development of skills and abilities, independence, social competence, and adaptive behavior.<br>[Environmental stressors<br>Resources/material resources<br>Organizational culture/climate<br>Salient events/critical incidents<br>Person x environment interaction<br>Barriers and facilitators] | Do resources influence whether you prescribe/refer patients for OSA treatment?<br><br>Are there sufficient human resources?<br><br>Are there clear communication channels?<br><br>Are there sufficient physical resources?<br><br>Do you have enough time/do you have competing demands?<br><br>Does the working environment in outpatients have an effect?<br><br>Are there environmental stressors that impact on your ability to treat OSA? |
| Social influences | Those interpersonal processes that can cause individuals to change their thoughts, feelings, or behaviors.<br>[Social pressure<br>Social norms<br>Group conformity<br>Social comparisons<br>Group norms<br>Social support<br>Power<br>Intergroup conflict<br>Alienation<br>Group identity<br>Modeling] | Do you seek opinions of colleagues in whether/how to treat OSA?<br><br>What are the views of your colleagues re: OSA treatment?<br><br>Do you observe others treating patients for OSA? |
| Emotion | A complex reaction pattern, involving experiential, behavioral, and psychological elements, by which an individual attempts to | Is there anything about prescribing/referring for OSA treatment that evokes an emotional response? If so, what? Does this alter your clinical management decisions? |

| | | |
|---|---|---|
| | deal with a personally significant matter or event.<br>[Fear<br>Anxiety<br>Affect<br>Stress<br>Depression<br>Positive/negative effect<br>Burn-out] | |
| Behavioral regulation | Anything aimed at managing or changing objectively observed or measured actions.<br>[Self-monitoring<br>Breaking habit<br>Action planning] | Are there any protocols or referral pathways that facilitate OSA treatment? |

If time permits and only if these items have not yet been covered:

- What do you think are the key actions/decisions when managing a patient with OSA that maximize the beneficial outcomes for the patient?
- Is there an aspect of the patient pathway we should pay more attention to in future interviews?
- If there was one thing you could change in your spinal unit to improve the management of OSA in people with tetraplegia, what would you change?
- Do you think it would ever be feasible for your spinal unit to take on the diagnosis and treatment of non-complicated? If yes, what would be required to do this? If not, why?

Final questions:

- Is there anything else about the management of patients with OSA that you would like to mention that is not already covered?
- Do you have any additional comments on the content of the interview or feedback on how the interview went?

**THANK YOU VERY MUCH FOR YOUR TIME**