Auto-titrating Continuous Positive Airway Pressure Treatment for Obstructive Sleep Apnoea after Acute Quadriplegia (COSAQ): study protocol for a randomized controlled trial

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Abstract

**Background:** Quadriplegia is a severe, catastrophic injury that predominantly affects people early in life resulting in lifelong physical disability. Obstructive sleep apnoea is a direct consequence of quadriplegia and is associated with neurocognitive deficits, sleepiness and reduced quality of life. The usual treatment for sleep apnoea is nasal continuous positive airway pressure (CPAP), however this is poorly tolerated in quadriplegia. If we are to encourage our patients to use this therapy, we have to demonstrate that the benefits outweigh the inconvenience. We therefore propose to perform a prospective, multi-national randomised controlled trial of three months of CPAP for obstructive sleep apnoea after acute quadriplegia.

**Methods/design:** Specialist spinal cord injury centres across Australia, New Zealand, the United Kingdom and Canada will recruit medically stable individuals who have sustained a (new) traumatic quadriplegia (complete or incomplete second cervical to first thoracic level lesions). Participants will be screened for the presence of obstructive sleep apnoea using full, portable sleep studies. Those with an apnoea hypopnoea index greater than 10 per hour will proceed to an initial three-night trial of CPAP. Those who can tolerate CPAP for at least four hours on at least one night of the initial trial, will be randomised to either usual care or a three month period of auto-titrating CPAP. The primary hypothesis is that nocturnal CPAP will improve neuropsychological functioning more than usual care alone. The secondary hypothesis is that the magnitude of improvement of neuropsychological function will be predicted by the severity of baseline sleepiness measures, sleep fragmentation and sleep apnoea. Neuropsychological tests and full polysomnography will be performed at baseline and 3 months with interim measures of sleepiness and symptoms of autonomic dysfunction measured weekly. Spirometry will be performed
monthly. Neuropsychological tests will be administered by blinded assessors. Recruitment commenced in July 2009.

**Discussion:** The results of this trial will demonstrate the effect of nocturnal CPAP treatment of obstructive sleep apnoea in acute quadriplegia. If CPAP can improve neurocognitive function after injury, it is likely that rehabilitation and subsequent community participation will be substantially improved for this group of predominantly young and severely physically disabled people.

**Trial Registration:** Australasian Clinical Trial Registry ACTRN12605000799651
Background

Spinal cord injury (SCI) is one of the most severe disabilities a person may sustain. The resultant loss of physical independence can lead to a significant requirement for assistance with personal care and activities of daily living, with consequent loss of privacy and compromised autonomy. The cost to the individual in terms of vocational opportunities and achievements can be extremely high. The cost to the community in terms of lost work capacity, reduced ability to utilise prior education and training and the financial costs of disability pensions, carer’s pensions, attendant care, respite care, equipment and environmental adaptations are associated with burden and reduced quality of life. In Australia, the annual incidence of SCI is approximately 15 per million,[1, 2]. Therefore, each year in Australia 260 people sustain a SCI and of these 57% will lose full function in their arms and legs (quadriplegia).

Quadriplegia affects 130-150 people per year in Australia.[3] The lifetime costs of the injury are substantial, even though the numbers affected are relatively small. In 2009, Access Economics estimated the lifetime health care cost of each incident case of quadriplegia in Australia to be $9.5 million, with the total cost of SCI estimated at $2.0 billion.[3] The majority of SCI patients sustain their injuries in their second or third decade of life. If those who do not survive the first year following injury are excluded from analysis, then life expectancy approaches that of the general population.[2] Thus, if any secondary disease or impairment were a direct consequence of the SCI, it would have a significant effect for many years. Obstructive Sleep Apnoea (OSA) is such a disease.

The prevalence of sleep disordered breathing (SDB), predominantly OSA, in quadriplegia is 2 to 5 times higher[4-11] than in the general population.[12] however the reasons for this
increased prevalence remain unclear. A prospective, longitudinal examination of the sleep and breathing of all new patients with acute quadriplegia who presented to a specialist spinal unit over an 18 month period found a prevalence of OSA of up to 83% in the first year after injury. [13] Sleep and respiratory studies were performed immediately after acute quadriplegia in 30 subjects (25 men) and at 2 weeks, 1, 3, 6 and 12 months post-injury. Three subjects (10%) had probable OSA before their injury. However, by 2 weeks after injury 60% had OSA, 83% at 3 months and 62% at 1 year. These findings have been confirmed in another centre. [14] It is thus apparent that the prevalence of OSA was extremely high in the first year after injury and that OSA is a direct consequence of acute quadriplegia.

Untreated OSA is a significant issue for those with quadriplegia. Previous authors have demonstrated that OSA in quadriplegia results in significant neurocognitive deficits. [15] Sajkov et al demonstrated that hypoxia during sleep in subjects with quadriplegia and untreated OSA was associated with deficits in attention, concentration, memory and learning. Further, the neurocognitive impairments were both statistically and clinically significant in the people with both quadriplegia and OSA, when compared with normal population values. These deficits are likely to substantially prolong rehabilitation, reduce future independence and limit vocational outcomes following injury.

The usual treatment for OSA is Continuous Positive Airway Pressure (CPAP) which corrects sleep hypoxia, improves neurocognitive performance [16] and nocturnal blood pressure control [17] in the able bodied with OSA. Reports of CPAP treatment in quadriplegia in uncontrolled studies are disappointing with low levels of compliance with therapy reported. Stockhammer et al found 31 cases of SDB after screening 50 subjects with quadriplegia. [10] Only 16 of the 31 had used CPAP in the past, with 11 (35%)
continuing to use the device for at least a few weeks. Burns et al undertook a cross-sectional postal survey of patients of a US Veterans Affairs Spinal Cord Service whose record indicated diagnosis or treatment for OSA.[18] Of those identified, only 39% were currently using CPAP and an additional 27% had used CPAP, but discontinued therapy due to intolerance. In our previously described cohort study,[13] five of the subjects were suspected clinically of having OSA and treatment with CPAP was offered. Only one of the subjects continued with CPAP for more than a few days, and that subject only did so after a period of respiratory failure. The reasons for this poor adherence are multi-factorial, but the most common reported complaints are nasal congestion, an inability to fall asleep with the mask on and no perceived benefit or noticeable change in symptoms.

In summary, it is known that OSA is a direct consequence of acute quadriplegia and that it is associated with cognitive deficits likely to impair rehabilitation after injury. Additionally, although CPAP is the usual treatment for OSA, it is poorly tolerated in quadriplegia. If the detection, treatment and adherence to CPAP therapy are to be improved in these patients, further research is vital. We propose to perform a prospective, multi-centre randomised controlled trial of CPAP for OSA after acute quadriplegia.

In preparation for this trial, the Melbourne research team completed a one year feasibility study of this project.[19] The primary aim of the feasibility study was to determine the feasibility of CPAP treatment for OSA following acute quadriplegia. All patients (n=44) with new quadriplegia who presented to the Austin hospital during the nine months of study recruitment were eligible for study inclusion. Participants were tested for OSA with the Somte PSG (Compumedics, Abbotsford Australia) and those with OSA were offered treatment with an auto-titrating CPAP device for three months. Rates of patient accrual, enrolment and OSA that were experienced during the study accurately reflected initial
estimates. The feasibility study findings suggested that this current trial would confirm that OSA is associated with significant sub-acute morbidity and that CPAP treatment will be associated with an improvement in clinical outcomes.

The specific aim of the COSAQ study is to determine the effect of nocturnal auto-titrating CPAP treatment on neuropsychological function, quality of life, autonomic dysfunction and breathing in people with acute quadriplegia and OSA. To address this aim, one primary and two secondary hypotheses were developed and will be tested. The primary hypothesis is that usual care and nocturnal CPAP treatment will improve neuropsychological functioning more than usual care alone; specifically working memory as tested on the PASAT. The first secondary hypothesis is that the magnitude of improvement in neuropsychological function will be predicted by the severity of baseline sleepiness (KSS), sleep fragmentation (Sleep Efficiency, Arousal Index) and sleep apnoea (Apnoea Hypopnoea Index (AHI), %total sleep time with SpO₂ < 90%). The second secondary hypothesis is that usual care and nocturnal CPAP will improve the following parameters more than usual care alone;

1. Sleepiness and symptoms: Karolinska Sleepiness Scale (KSS) and the Basci Nordic Sleep Questionnaire (BNSQ)
2. Lung Function: Spirometry
3. Quality of life: Assessment of Quality of life (AQoL)
4. Autonomic dysfunction: Event diary and heart rate variability
5. Health utility; AQoL derived change in utility and associated Quality Adjusted Life-Years (QALY)
6. Depression and anxiety: Hospital Anxiety and Depression Scale (HADS) and the Profile of Mood States (POMS)
Methods/Design

Funding
The trial is funded by the Transport Accident Commission of Victoria. The COSAQ study is an element of the “Sleep Health in Quadriplegia” five year program grant.

Design
A prospective multi-centre randomised controlled trial will be undertaken. The control group will receive usual care and the experimental group will receive 3 months of nocturnal CPAP using an autotitrating CPAP device. The trial is being conducted in 10 specialist SCI units in Australia, New Zealand, the U.K. and Canada. Ethical approval has been obtained for the Human Research Ethics Committee at each site and the Austin Hospital (EC00204). Informed consent will be provided prior to recruitment and participation. Subject recruitment commenced at Austin Health in July 2009 and subsequently at the other sites as they achieved readiness. Recruitment is scheduled to finish mid 2015.

Participants
Participants will be recruited from consecutive admissions at the trial sites.

Inclusion criteria

- Acute, traumatic quadriplegia (T1 or higher lesion, complete or incomplete).
- Aged greater than 18.

Exclusion criteria

- Successful CPAP therapy for OSA prior to injury
• Significant head injury (Glasgow Coma Score < 8 at first assessment)
• Ongoing hypercapnic ventilatory failure (PaCO$_2$ > 45 mmHg at time of consent)
• Likely inability to be followed up until three months
• Condition likely to significantly limit CPAP use (eg major psychoses, facial or base of skull fractures, etc)

**General testing procedures**

All testing will be performed at the participants’ bedside. The respiratory function, questionnaires and other subjective data are collected at the same time in the mid afternoon for each subject to control for possible circadian influences. Sleep studies will commence at the subject’s usual bed time. Figure 1 illustrates the study recruitment and data collection flowchart.

**Post-enrolment data collection**

The following information is collected at baseline following witnessed, informed consent. Human ethics approval has been provided for witnessed verbal consent to be obtained where impaired upper limb function limits the ability of potential participants to provide written consent.

  a) Demographic information (age at injury, sex, date of injury)
  b) Time and date of assessment
  c) Current lesion level and completeness (AIS score)
  d) Medical history
  e) Height and weight
  f) Current medications
  g) Whether the subject was suffering from any intercurrent illness
  h) Likelihood of undiagnosed, pre-existing OSA (Multivariate Apnoea Prediction Index (MAPI))[20]
i) Abdominal girth at end-expiration and neck circumference

j) Sleep studies

The presence of OSA will be assessed using a portable sleep monitoring device which comprehensively measures respiratory and sleep variables. (Compumedics™ SomtePSG, Abbotsford, Australia). All studies will be sleep staged and respiratory scored by an independent, trained sleep scientist. Sleep will be staged in 30 second epochs, arousals marked and respiratory events scored according to international standard criteria.[21] Summary indices and statistics will be calculated. Heart rate variability will be calculated from the ECG trace taken during quite resting (prior to sleep onset)

All participants with an apnoea hypopnoea index (AHI) $> 10$ will be considered as positive OSA cases and will proceed to have baseline measures (below) taken.

### Baseline measures

These tests are all made prior to the trial of CPAP and randomisation.

a) Cognitive test battery

- Rey Auditory Verbal Learning Test
- Digit Span sub-test of the Wechsler Adult Intelligence Scale Revised
- Paced Auditory Serial Addition Test (PASAT)
- Symbol Digit Modalities Test
- National Adult Reading Test

These tests have been previously employed to show neuro-cognitive limitation in those with quadriplegia and OSA.[15] All these test are administered verbally so that written replies or motor responses are not required. This battery of tests takes approximately 40 minutes for subjects to complete and measures function in the
following areas: Short-term memory, attention/concentration, immediate memory span, cognitive flexibility, internal scanning, working memory, visual perception, visual attention and concentration. Previous authors have found that patients with quadriplegia and OSA had deficits in attention, concentration, memory and learning skills.[15] The significance of poor function in these areas is greater in the quadriplegic population due to their limited physical functioning. As a result, cognition becomes even more important for optimal participation in rehabilitation and society. Additionally, it is anticipated that performance on these tests will be improved by CPAP treatment.

b) Sleep symptoms and functional consequences of sleepiness

The Basic Nordic Sleep Questionnaire (BNSQ)[22] has been validated in a spinal population and will provide additional information about sleep quality.

c) Quality of life and health utility values

The Assessment of Quality of Life (AQoL)[23] is a generic quality of life instrument and has tested as good or better than instruments commonly used in measuring outcomes in stroke, co-ordinated care, influenza, cochlear implants, population monitoring and elderly groups. The AQoL provides both health related quality of life information in the domains of “Illness”, “Independent Living”, “Social relationships”, “Physical senses”, “Psychological wellbeing” and a total AQoL value. In addition to these outcomes, the AQoL may be summarised to generate utility values, thereby enabling the generation of Quality Adjusted Life Years (QALY) and facilitating economic analyses.

d) The Hospital Anxiety and Depression Scale (HADS)

e) The Profile of Mood States (POMS)

Pre-randomisation procedure
All subjects who fulfil the inclusion, exclusion criteria, consent to participate and who are classified as positive OSA cases will be trialled on auto titrating CPAP (Resmed Autoset, San Diego USA) for up to three nights.

Subjects who are able to use the CPAP for at least four hours on any night, will then be randomised as soon as they do so, into either the treatment or usual care group. If four hours are tolerated on the first night, they will be randomised at this time. Those who do not use the CPAP for four hours on any of the three nights will cease participation in the trial. The four-hour cut off was derived from the feasibility trial where those who were unable to achieve this time were not likely to be compliant in an ongoing way.

The decision to only randomize those who are likely to be adherent with CPAP was the most significant study design modification to arise from the feasibility study. A rate of non-adherence of 50%, as was observed in the feasibility study, would render this study unfeasible. Pre-randomization selection potentially limits the study generalisability to those who are tolerant of CPAP, although it accurately reflects clinical practice (you would never “force” a patient to use a therapy they did not accept), was strongly supported by the Australasian Sleep Trials Network (see below), is a similar protocol to that employed in the multi-national The Sleep Apnoea cardio Vascular Endpoints (SAVE) study [http://www.savetrial.org/index.htm](http://www.savetrial.org/index.htm) and significantly increases the project feasibility by reducing the numbers of subjects, the timeframe and the associated staff cost.

**Randomization**

Randomization will be performed centrally using the research study database ([www.shiq.com.au](http://www.shiq.com.au)). A blocked, randomization sequence was generated using [www.randomization.com](http://www.randomization.com) and loaded into the online database by an independent member.
of the research unit prior to trial commencement. Allocation concealment is assured through the site design that requires subject enrolment be completed prior to randomization becoming possible. Additionally the randomized group is only revealed after a commitment to randomization is both made and confirmed.

**Weekly measures**

The following measures will be made at baseline and then weekly upon review

a) Time and date of assessment  
b) Current medications  
c) Any intercurrent illness  
d) Sleepiness, using the Karolinska Sleepiness Scale (KSS),[24] a ten item scale which describes current (state) sleepiness  
e) Machine usage data in the CPAP treatment group will be downloaded weekly.  
f) Clinical review / Autonomic dysfunction / troubleshooting  
   All participants will be provided with an Autonomic Dysfunction Symptom Diary. The diary will record the number, nature and treatment of symptoms typically related to AD (Table 1)  
h) Additionally, those subjects in the CPAP treatment group will be reviewed with respect to any machine usage / masking issues.

**Monthly measures**

The following measures will be made at baseline and then monthly upon review

a) Respiratory function  
   All testing will be performed in the supine position. Simple spirometry will be used to obtain vital capacity and forced expiratory volume in 1 second. All tests of respiratory function will be performed without an abdominal binder and in accordance with the performance limitations imposed by quadriplegia.[25]
End study (three months or hospital discharge) data collection

The baseline testing battery will be repeated in the same manner with the exception of the MAPI. Following the completion of all testing procedures, a semi-structured subject interview will be held in a subset of the trial participants to examine their experience of the trial and to explore themes related to adherence. The sleep study will be repeated, with the subjects using their CPAP (or not) as randomised. At this time participants will be provided with full details of their physiological tests and referred for ongoing clinical management of any OSA if they wish.

An adverse event audit will be performed at study conclusion. This process will be auspiced by an independent outcomes committee comprised of two sleep and/or spinal specialist clinicians. The patient medical record will be audited for all adverse events defined by the outcomes committee. The blinded assessor at each site will perform the audit. The outcomes committee review the standardised audit report and will classify any defined event by severity and as likely or not to have been associated with study treatment or assessment procedures. These classified event reports will be passed to the independent Data Monitoring and Review Committee for review.

Treatment device

Intervention cases will be fitted with a nasal or face mask and head gear. The choice of patient interface will be made locally by each of the treating teams. The CPAP will be delivered by an auto titrating device (Resmed Autoset, San Diego USA). These devices automatically set the level of delivered pressure to ensure upper airway patency, thereby eliminating the need for a pressure titration sleep study to be performed in the sleep laboratory. In addition, if, as was observed in the pilot study, effective CPAP alters over the
trial period,[19] the device will alter the delivered pressure accordingly to maintain airway patency.

The autoset devices record the number and type of respiratory events detected, the pressure delivered in response to these events and the amount of time that the machine was on and delivering pressure to a patient. If the machine is running, but has been removed from the face, this time does not contribute to the measure of CPAP compliance.

**Feasibility, safety and efficacy**

The research team have completed a one year study examining the feasibility and safety of the planned protocol. No major adverse events were observed, in particular no episodes of excess, uncontrolled flow such that exhalation was impeded by the auto titrating CPAP were observed.[19] One device was found to be faulty and exchanged. This fault did not affect any participant. All minor adverse events (mask irritation, nasal stuffiness) related to acclimatisation to CPAP and are common to all new CPAP users.

**Implementation**

A member of the research team will instruct the patients, their families and the ward staff in the use of the CPAP. These staff will introduce, apply and adjust the mask for comfort, until the participants are satisfied. The research staff will also review the subjects each morning to identify any barriers to use and to address any difficulties. The feasibility study suggested that CPAP adherence could be maximized through early and careful attention to any difficulties.

**Treatment duration**
In the able-bodied with OSA, a minimum of 6 weeks of treatment is required to establish CPAP adherence and to observe changes in neuropsychological functioning outcomes. Three months of therapy has been demonstrated as sufficient to improve neurocognitive functioning, specifically improved memory, in the able-bodied with OSA.[26] Other cardiovascular changes occur more slowly, however improvements would be evident after three months of therapy. We propose to treat people for three months or until hospital discharge.

**Data analysis**

All analyses will be performed on an intention to treat basis. This presents particular challenges in a clinical trial such as this where effective clinician and patient blinding of treatment allocation is impossible.

**Blinding of assessments**

In a trial of a physical device such as this, patient and clinical blinding is impossible. We therefore propose to perform blinded assessment of the maximum proportion of the outcome measures. The following measures will be blinded to group allocation:

1. All initial, baseline data, including PSG staging and scoring
2. Cognitive test battery
3. Spirometry
4. Quality of life and sleep questionnaires
The clinical scenarios outlined below will be managed in the following fashion. Both of the first two scenarios occurred during the feasibility trial.

1. Unable to continue with CPAP. Should any participant choose to cease CPAP treatment, they will remain in the study until 3 months. The test collection battery will proceed as planned.

2. Hospital discharge prior to end of treatment period. To continue the proposed RCT in the home is beyond the scope of the study, therefore the treatment period will cease at hospital discharge. The end study data collection battery will be performed in the week prior to discharge and all obtained results will be treated as “last observation carried forward”.

3. Randomized group cross-over. Should a patient with OSA who is randomized to usual care proceed to be treated with CPAP or non-invasive ventilatory support, they will remain in their allocated group for primary analysis purposes.

**Trial data management**

Each site will be responsible for local storage of hard-copy data, which will be entered online into a centralized database. Automated, digital data capture methods will be used wherever possible. Sleep studies will be performed locally and data transferred electronically to the coordinating centre for analyses. This process has been successfully used by the research team in a previous, inter-laboratory concordance trial.[27]

**Estimated subject numbers**

This is a three month treatment trial at a time where there is profound disruption in the life of the study participants. Over this acute period direct measurements of quality of life and performance in rehabilitation will not demonstrate the efficacy or otherwise of CPAP. The feasibility study clearly demonstrated that there was substantial variability in quality of life
post-injury unrelated to OSA or CPAP, thus rendering these outcomes unsuitable for
demonstrating short-term improvement in a study sample of constrained size. We
therefore are basing our sample size calculations on neurocognitive performance, a
number of measures of which form our test battery. The specific neurocognitive test in the
test battery, which is best characterized in both the spinal population and OSA, is the
PASAT. Lower (worse) PASAT scores correlate with sleep fragmentation severity in the
able-bodied[28] and OSA severity in quadriplegia.[15] Lower PASAT scores are also
associated with diminished frontal lobe function assessed by functional magnetic
resonance imaging[29] and a mean difference in PASAT scores of seven discriminates
between those with and without cognitive impairment in multiple sclerosis.[30] In the able-
bodied with OSA, those adherent to CPAP over three months have an 18 unit (standard
device of 33) higher PASAT score than those who are not.[31]

Assuming a mean difference between the study arms of 18,[31] a standard deviation of 33,
a power of 0.8, an alpha of 0.05 and a non-adherence to CPAP rate of 15%, 150 subjects
will be randomized. To ensure that 150 participants complete the study, approximately 820
admission with quadriplegia are estimated to be required across our collaborating centres
(at least 8 of 44 admissions will fulfil inclusion/exclusion, agree to participate, have OSA
and tolerate CPAP) This sample is also adequate to detect any true difference between
secondary outcomes such as sleepiness (KSS number required = 44).

**Adherence with therapy**

All usage data collected by the treatment devices will be downloaded weekly and analysed
fully. Previous research in the able-bodied population with OSA improvements in memory,
sleepiness and daily function may be observed if CPAP is used for 4 hours per night for 5
out of every 7 days.[32, 33] Those subjects who use CPAP for at least this amount will be classified as “adherent” for each week of the study.

**Statistical analyses**

Usage data from the CPAP devices will be described and subjects classified as adherent as described above. The proportion of subjects continuing to use CPAP over the three months of treatment will be plotted and examined using survival (Kaplan-Meier) analyses. Statistics describing the distribution of CPAP usage, average numbers of hours used per night, etc will be calculated.

Changes in neurocognitive performance, AQiL, BNSQ and KSS will be examined with paired t-tests, repeated measures analysis of variance and generalized linear mixed models as appropriate. The rate of AD and the time course of development will be compared with Chi squared and mixed model regression modelling as appropriate. Exploratory linear and logistic regression modelling will be performed to determine if the average number of hours used or the likelihood of adherence can be predicted by any of the groups’ baseline characteristics.

**Project governance and administrative support**

The Chief Investigator (Dr Berlowitz) will be responsible for overall project management, but is assisted and advised by a project steering committee comprised of the collaborating researchers and administrative support from the administering, coordinating institution. Additional support and membership has been seconded from the partner organisations. The project steering committee will meet regularly and all agendas and minutes circulated to all stakeholders. Funding agreements will be entered into between all collaborating
agencies and the administering institution. The project will be supported by a part-time project manager.

An outcomes committee will be established as detailed above and an independent Data Monitoring Committee will be externally appointed by the Australasian Clinical Trials Network.

**Follow up at trial completion**

Participants in the treatment group will be given their mask and CPAP device at the end of the 3 months to enable them to continue treatment of their OSA. Those randomised to the control group will be fully supported to commence CPAP treatment and also be offered a mask and CPAP device for ongoing use. All participants will be referred to their local Respiratory or Sleep Clinic as appropriate for ongoing management of their OSA.

**Discussion**

This trial will determine the effectiveness of nocturnal CPAP in the acute quadriplegic population. In particular, improvement in cognitive performance in this group may improve their ability to engage with the rehabilitation process and allow them to participate more fully in life following the initial rehabilitation phase. The profound reduction in physical functioning that characterises quadriplegia means a greater reliance on cognitive functioning for work and participation in family and community life post injury. Any therapy that optimises cognitive function is potentially of great significance to those with quadriplegia, their families, friends and colleagues.
**Trial Status**

The trial commenced recruitment in July 2009. Recruitment will cease when 150 trial participants have been randomised. It is anticipated that this target will be reached by mid 2015.

**List of abbreviations**

- **AD**: Autonomic dysreflexia
- **AQoL**: Assessment of quality of life
- **BNSQ**: Basic Nordic sleep questionnaire
- **CPAP**: Continuous positive airway pressure
- **HADS**: Hospital depression and anxiety scale
- **KSS**: Karolinska sleepiness scale
- **OSA**: Obstructive sleep apnoea
- **PASAT**: Paced auditory serial addition task
- **SCI**: Spinal cord injury
- **QALY**: Quality adjusted life years

**Competing Interests**

David J Berlowitz (DJB)

DJB has received competitive research funding support from the ResMed Foundation in the USA. Additionally, he has received competitive research support from the Transport Accident Commission to perform research examining other aspects of sleep and respiratory disorders in spinal cord injury. DJB declares he has no other financial or non-financial competing interests.
Najib Ayas (NA)
NA declares no competing interests.

Maree Barnes (MB)
MB declares no competing interests.

Douglas J Brown (DJBa)
DJBa has received competitive research support from the Transport Accident Commission to perform research in spinal cord injury. DJBa declares he has no other financial or non-financial competing interests.

Peter A. Cistulli
PAC has received research support from ResMed Inc (CPAP) and SomnoMed Ltd (oral appliances) for investigator-initiated studies in obstructive sleep apnoea. He has served on SomnoMed's medical advisory board and has an ongoing pecuniary interest in the company. He is currently a medical advisor to Exploramed (a medical device incubator).

Tim Geraghty (TG)
TG declares no competing interests.

Alison Graham (AG)
AG declares no competing interests.

Bonne B Lee (BBL)
AG declares no competing interests.

Meg Morris (MM)
MM declares no competing interests

Fergal O'Donoghue (FOD)
FOD has received competitive research support from the Transport Accident Commission to perform research examining other aspects of sleep and respiratory disorders in spinal cord injury. FOD declares he has no other competing financial or non-financial competing interests.

Peter D Rochford (PDR)
PDR declares no competing interests.

Jack Ross (JR)
JR declares no competing interests.

Raj Singhal (RS)
RS declares no competing interests.

Jo Spong (JS)
JS declares no competing interests.

Brooke Wadsworth (BW)
BW declares no competing interests.
Robert J Pierce (RJP)

*Please note that RJP has passed away since protocol development.

Author’s contributions

The trial protocol was developed by all authors during a two-day workshop in Melbourne, Australia during June 2008 from an original idea developed by DJB, DJBa and RJP. DJB and JR were responsible for initial manuscript preparation and all authors reviewed the final version prior to submission.

Acknowledgments

Trial funding was obtained from the Transport Accident Commission through the Victorian Neurotrauma Initiative.

Resmed San Diego USA will provide all the auto titrating CPAP machines, integrated humidifiers and masks used in the trial at no cost. The company had no input into the design of the trial, nor will they be involved in data interpretation or result publication.

References


Figure Legends

Figure 1.

Flowchart of COSAQ study participant flow.
Table Legends

Table 1. Autonomic dysreflexia diary

In the last week, have you experienced any of the following symptoms, and if so, were they treated?
COSAQ FLOWCHART

1. Screening Inclusion/Exclusion

2. Recruitment

3. Pre-sleep study Assessment Including PaCO₂

4. Sleep Study

5. OSA AHI<10

6. CPAP Trial 3 nights

7. Randomisation

8. Weekly Ax

9. Monthly Ax

10. 3 month (final) assessment

11. 3 month Sleep study

12. Adverse Events Assessment

13. Ongoing Referral for monitoring of OSA + CPAP treatment

A. Incident Quadriplegic Admitted

A. Not Eligible Excluded

A. Not tolerated Excluded

A. No Consent Excluded

A. Hypercapnic Excluded

A. No OSA Excluded

Figure 1
Additional files provided with this submission:

Additional file 1: Table 1.docx, 39K
http://www.trialsjournal.com/imedia/3414755985256890/supp1.docx