BMJ Open

Does a brief, behavioural intervention, delivered by paediatricians or psychologists improve sleep problems for children with ADHD? A cluster-randomised, translational trial

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2016-014158
Article Type:	Protocol
Date Submitted by the Author:	05-Sep-2016
Complete List of Authors:	Sciberras, Emma; Murdoch Childrens Research Institute, Centre for Community Child Health Mulraney, Melissa; Murdoch Childrens Research Institute Heussler, Honey; Mater Medical Research Institute Rinehart, Nicole; Deakin University Schuster, Tibor; Murdoch Childrens Research Institute, Medical Statistics Gold, Lisa; Deakin University, Deakin Health Economics Hayes, Nicole; Mater Medical Research Institute Hiscock, Harriet; The Royal Children's Hospital, Centre for Community Child Health
Primary Subject Heading:	Mental health
Secondary Subject Heading:	Public health
Keywords:	attention deficit disorder with hyperactivity, randomised controlled trial, effectiveness, treatment, sleep, child

Does a brief, behavioural intervention, delivered by paediatricians or psychologists improve sleep problems for children with ADHD? A cluster-randomised, translational trial

Authors E Sciberras, DPsych,[1,2,3] M Mulraney, PhD,[2,3] H Heussler,[4] N Rinehart, PhD,[1] T Schuster,[2] L Gold PhD,[1,2] N Hayes PhD,[4] H Hiscock MD.[2,3,5]

Affiliations [1] Deakin University, Geelong, Vic Australia

[2] Murdoch Childrens Research Institute, Parkville, Vic Australia

[3] University of Melbourne, Department of Paediatrics, Parkville, Vic Australia

[4] Mater Research Institute-University of Queensland, South Brisbane, Qld Australia

[5] The Royal Children's Hospital, Parkville Vic Australia

Running title Behavioural sleep intervention for children with ADHD

Date 24th May 2016

Word count 3978 (Abstract 300)

Key words attention deficit disorder with hyperactivity, sleep, child, randomised controlled trial, effectiveness, treatment

Correspondence to

Dr Emma Sciberras

School of Psychology, Deakin University, Melbourne Burwood Campus, BC Building, Level 5, 221 Burwood Hwy, Burwood VIC 3125, AUSTRALIA

P +61 3 9251 7222 email emma.sciberras@deakin.edu.au

accepted) to be published in BMJ editions and any other BMJPG products and to exploit all subsidiary rights, as set out in our licence (http://resources.bmj.com/bmj/authors/checklists-forms/licence-for-publication)

Competing interests

All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare that they, their spouses, partners or children do not have any financial and non-financial relationships with companies that may be relevant to the submitted work to declare.

Author contribution

ES, HH, HH, NR and LG conceived the study. MM and NH coordinated the study. ES drafted the current manuscript. TS contributed to the design and analytic components of the study. All authors contributed, read and approved the final manuscript.

Funding source

This study is funded by the Australian National Health and Medical Research Council (NHMRC; project grant no. 1058827). Dr Sciberras' position is funded by an NHMRC Early Career Fellowship in Population Health 1037159 (2012–2015) and an NHMRC Career Development Fellowship 1110688 (2016-19). Professor Hiscock's position is funded by an NHMRC Career Development Fellowship 1068947 (2014-2017). This research was supported by the Victorian Government's Operational Infrastructure Support Program to the MCRI.

ABSTRACT

Introduction: Up to 70% of children with Attention-Deficit/Hyperactivity Disorder (ADHD) suffer from behavioural sleep problems. We have demonstrated the efficacy of a brief behavioural intervention in improving sleep for children with ADHD. We now aim to examine whether this intervention is effective in real-life clinical settings when delivered by paediatricians or psychologists in improving child sleep and child and family wellbeing. We will also assess the cost-effectiveness of the intervention.

Methods and analysis: Children aged 5-12 years with ADHD (n=320) are being recruited for this translational cluster randomised controlled trial (RCT) through paediatrician practices in Victoria and Queensland, Australia. Children are eligible if they meet DSM-5 criteria for ADHD, have a moderate/severe sleep problem, and meet American Academy of Sleep Medicine criteria for a behavioural sleep disorder. Clinicians are randomly allocated to either receive the sleep training or not. The behavioural intervention comprises two consultations covering sleep hygiene and standardized behavioural strategies. The primary outcome is change in the proportion of children with moderate/severe sleep problems from moderate/severe to no/mild by parent report at 3 months post-intervention. Secondary outcomes include a range of child (sleep severity, ADHD symptoms, quality of life, behaviour, working memory, executive functioning, learning, academic achievement, school attendance) and primary caregiver (mental health, parenting, work attendance) outcome domains. Analyses will address clustering at the level of the paediatrician using linear mixed effect models adjusting for potential a priori confounding variables.

Ethics and dissemination: Ethics approval has been granted. Findings will determine whether the benefits of an efficacy trial can be realised more broadly at the population level and will inform the development of clinical guidelines for managing sleep problems in this

population. We will seek to publish in leading international paediatric journals, present at major conferences and through established clinician networks.

Registration details: Current Controlled Trials ISRCTN50834814

Behavioural sleep problems are common and more persistent in children with ADHD, and associated with poorer child and family well-being.[1-4] Although randomised controlled trials (RCTs) have shown that melatonin is associated with improved sleep onset latency for children with ADHD,[5-7] broader benefits for daily functioning including ADHD symptom severity have yet to be shown. More recently, efficacy RCTs have shown that sleep problems are amenable to behavioural intervention in children with ADHD.[8-10] However, it is unknown whether the same benefits will be observed when such interventions are delivered by practitioners in 'real life' clinical settings. This article describes the protocol for the Sleeping Sound with ADHD Translational RCT, which aims to assess the effectiveness of a behavioural sleep intervention designed for children with ADHD, when delivered by psychologists or paediatricians in their daily clinical practice.

Sleep problems in children with ADHD

Up to 70% of children with ADHD experience sleep problems,[1,2] compared with 20-30% of children in the general population.[11] Sleep problems experienced by children with ADHD comprise difficulties initiating and/or maintaining sleep, with the most common sleep problems being difficulty falling asleep (reported by 84% of parents of children who report a sleep problem for their child with ADHD), bedtime resistance (68%), tiredness upon waking (62%) and difficulty waking in the morning (56%).[2] Medical conditions such as obstructive sleep apnoea (OSA) can also affect sleep in children with ADHD, although behavioural sleep problems appear more common.[12] Sleep problems have been associated with worse functioning for children with ADHD including poorer QoL, behaviour, daily functioning, and working memory, as well as increased school absenteeism.[2,4,13] They thus represent an important modifiable target for intervention.

A number of factors have been associated with sleep problems in children with ADHD. Insomnia can be a side-effect of stimulant medication,[1,14] although unmedicated

children with ADHD also experience higher rates of sleep problems relative to non-ADHD controls.[15] Comorbid externalising and internalising comorbidities are each associated with a 2-fold increase in moderate/severe sleep problems in children with ADHD, while co-occurring internalising and externalising comorbidities are associated with a 3-fold increase.[16] Parenting inconsistency in daily household routines has also been associated with increased bedtime resistance in this group.[17] Biologically, there is overlap in the brain regions and genetic factors (e.g., catecholaminergic system, CLOCK genes) associated with both ADHD and sleep disorders/arousal regulation.[1] ADHD is also a highly genetic condition and parents likely are affected by symptoms such as disorganisation and impulsivity, which may impact on child sleep.

Treating sleep problems in children with ADHD using behavioural strategies

We recently published our efficacy RCT evaluating the impact of a behavioural sleep program in children with ADHD and moderate/severe sleep problems (n=244 5-12 year old children with ADHD).[8] Children were recruited from 21 paediatric practices across Victoria, Australia and randomised to either a behavioural sleep intervention (n=122) or a usual care comparison group (n=122). Intervention families attended two x 50 minute individual sessions (held two weeks apart) with a trained clinician (psychologist or trainee paediatrician), comprising a standardised yet flexible intervention, tailored to the child's sleep problems and family preferences.

The intervention was associated with improved child outcomes at three and six months post-randomisation including improved parent-reported child sleep, ADHD symptom severity, QoL, daily functioning and behavior.[8] Intervention children also had improved teacher-reported classroom behavior, as well as improved school attendance and working memory assessed via blinded assessment.[8] There were small improvements in sleep duration for a subsample that completed actigraphy.[8] Although the intervention was associated with

improved caregiver work attendance and mental health three months later, these benefits were not observed at six months.[8]

Similarly, two additional randomised controlled trials have demonstrated the efficacy of improving sleep problems in children with ADHD. Keshavarzi et al. reported that a 12-week sleep-training program for children with ADHD aged 10 years (n=40) had beneficial effects for sleep and psychosocial functioning when compared to controls with ADHD who did not receive the intervention (n=20) and typically developing children (n=20).[9] Corkum and colleagues also recently reported the beneficial effects of their distance sleep intervention for childhood insomnia in a mixed sample of children with and without ADHD (n=61).[10] Improvements were identified at 2 and 6 months for sleep assessed using parent report as well as actigraphy, and benefits were also reported for broader child psychosocial health.[10]

Managing sleep problems in children with ADHD through existing clinical services

Although three trials have now shown that it is possible to improve sleep problems in children with ADHD using behavioural approaches, it remains to be seen whether it is possible to replicate such approaches and improve outcomes for children with ADHD in 'real life' clinical settings when delivered by clinicians rather than trained researchers. We are now testing the translation of this program at the population level by training community paediatricians and psychologists to deliver this sleep intervention to children with ADHD and sleep problems. If this intervention can be translated successfully to the population level within existing workforces, then this would have the real potential to improve outcomes for children with ADHD and their families. If cost-effective, it could be readily incorporated into the existing health system.

Paediatricians are the main care providers for ADHD in Australia.[18] The paediatrician's role includes both the assessment and treatment (behavioural and medication-based) of ADHD and associated comorbidities (including sleep problems, if identified).

Visits to a paediatrician are subsidised by Australia's Medicare scheme, however, families may experience out of pockets costs for these visits. Paediatricians (and general practitioners) may also refer children to a psychologist in the community to manage comorbid behaviours.[19] In Australia, this referral is facilitated by the Medicare Better Access to Mental Health Scheme, which provides subsidised access to up to 10 psychology sessions in a calendar year, provided the criteria for a DSM condition are met. We have deliberately designed our sleep intervention so that it is feasible for both paediatricians and psychologists to deliver within the Australian Medicare scheme and within their typical consultation durations.

Aims and hypotheses

Building on our efficacy trial, we aim to determine whether the Sleeping Sound with ADHD intervention, delivered by paediatricians or psychologists in their usual work setting can replicate the benefits of the efficacy trial. Therefore, in this translational, cluster-randomised trial we aim to determine whether a brief sleep intervention delivered by paediatricians or psychologists:

1. Decreases the proportion of children with moderate/severe sleep problems from moderate/severe to no/mild by parent report at 3 months post-intervention (**primary outcome**).
2. Improves child and family functioning at 3 and 6 months post-intervention **(secondary outcome)**.
3. Is cost-effective **(secondary outcome)**.

We hypothesise that, compared to the control children at 3 (primary outcome timepoint) and 6 months post-intervention, a brief behavioural sleep intervention will:

1. Decrease prevalence of child sleep problems from moderate/severe to no/mild;
2. Improve functioning in other child (sleep severity, ADHD symptoms, QoL, behaviour, working memory, executive functioning, learning, academic achievement,

school attendance) and primary caregiver (mental health, parenting, work attendance) outcome domains.

3. Be cost-effective.

Methods

Overall Study Design

This is a cluster RCT of a behavioural sleep intervention versus usual care conducted in Victoria and Queensland, Australia (see Figure 1). The trial will be reported according to Consolidated Standards of Reporting Trials guidelines and the extension report of non-pharmacological interventions.[20] This project has been funded by the National Health and Medical Research Council of Australia (1106427) and has been granted ethics approval from The Royal Children's Hospital (34072), University of Queensland (2014001555), Mater Hospital (RG-14-349), Deakin University (2015-211), Victorian Department of Education & Training (2014_002519), The Queensland Department of Education & Training (550/27/1570), and the Catholic Education Office (Ballarat; Brisbane; Melbourne; Toowoomba) Human Research Ethics Committees.

Participants

Participants include families of children aged 5-12 years at the time of recruitment with paediatrician-diagnosed and DSM-5 confirmed ADHD and a moderate to severe sleep problem as defined by the American Academy of Sleep Medicine diagnostic criteria[21]: chronic insomnia disorder, delayed sleep-wake phase disorder, or sleep related anxiety.

Recruitment of health professionals

Paediatricians are recruited via the Australian Paediatric Research Network or through clinical contacts.[18] Interested paediatricians are invited to attend a briefing session in which the study requirements and timetable is presented and clinicians have the opportunity to ask

questions. Interested paediatricians are sent a follow up email thanking them for their interest, asking them to sign an individual Memorandum of Understanding (MOU) if they consent to participation, and asking them to provide a list of psychologists to whom they refer patients. By signing the MOU, paediatricians agree to: (1) participate in training if randomised to the intervention arm; (2) deliver the sleep program to intervention families ***or*** refer the child to a psychologist to deliver the sleep program; (3) not share the intervention materials with control group paediatricians; and (4) allocate time for intervention session bookings.

Once paediatricians have been recruited, psychologists are invited to whom the paediatricians have indicated they refer patients. The research team then informs psychologists about the study via email or phone. The researchers then send psychologists who express interest in participating a follow up email thanking them for their interest and asking them to sign an individual MOU, agreeing to: (1) participate in training; (2) deliver the sleep program to intervention families referred by paediatricians; (3) use intervention materials only with children enrolled in the study; and (4) not share the intervention materials with any other families they see during the study period. This approach has worked well to minimise contamination in our previous RCTs.[22-24]

Screening children for sleep problems and recruiting families

This translational trial uses, where possible, the same procedures that were used in our efficacy trial.[8] Paediatricians pre-identify their patients with ADHD, aged between 5-12 years, seen within the last 12 months, either through their medical software or through case notes. Paediatricians then send a letter to the child's primary caregiver inviting them to take part. The letter advises families that the research team will ask them about their child's sleep and ADHD symptoms. An 'opt out' approach is used, whereby parents are asked to contact the paediatrician if they *do not* wish to learn more about the study. If parents do not opt out within a two-week period, the paediatrician provides the research team with the contact

details of the families. Only 9% of families opted out in our efficacy trial.[8] Paediatricians also have the option to use an active consent process. In these cases paediatricians send an 'opt in' version of the study invitation letter.

The research team then contacts interested (or not opted-out) families via telephone to ascertain if the child meets inclusion/exclusion criteria. Eligible families are sent a parent information statement and consent form and a baseline survey. Families have the option to complete hard copy surveys or online surveys (via REDCap - a secure, web-based application).[25] Surveys are completed by the child's primary caregiver. Parents have the option to consent to have their child's school teacher complete a survey about their child's behaviour. If consent is provided by the primary caregiver and school, a link to an online survey is sent to teachers. Parents also have the option to consent to being contacted for ethically approved future research, for the research team to keep their de-identified data to be shared with future ethically approved research, and to allow the research team to link with their child's *National Assessment Program – Literacy and Numeracy* (NAPLAN) results. NAPLAN is a national assessment of literacy and numeracy Australian children complete in Grades 3 and 5, and Years 7 and 9.[26]

Once caregivers provide consent, the research team contacts them to complete the Anxiety Disorders Interview Schedule for Children (ADIS-C) over the telephone to assess comorbid internalising and externalising diagnoses in children with ADHD.[27] To ensure we administer the telephone interviews consistently we are recording 10% of the sample to test inter-rater reliability.

Inclusion/exclusion criteria (all assessed via telephone)

Inclusion criteria

a. Child aged between 5-12 years at the time of the recruitment call.

b. Child's sleep is a moderate-severe problem for the caregiver ascertained using the following question: Has your child's sleep been a problem for you over the past 4 weeks?' If 'yes', they are asked to rate severity (mild, moderate or severe). This measure has been used in studies of children with and without ADHD and has good agreement with the Children's Sleep Habits Questionnaire.[2,28,29]

c. Child sleep problem meets the International Classification of Sleep Disorders – Third Edition criteria[21] for an eligible sleep disorder (chronic insomnia disorder, delayed sleep-wake phase disorder) or sleep-related anxiety assessed using study-designed questions.

d. Child meets DSM 5 criteria for ADHD assessed via the 18-item ADHD Rating Scale IV - a validated scale measuring the core symptoms of ADHD.[30] Caregivers need to rate at least 6 of 9 of the inattention and/or hyperactivity/impulsivity items as occurring 'often' or 'very often' in order to meet current symptom criteria. Caregivers are asked to rate symptoms off stimulant medication. Additional questions are then asked to ensure symptoms have been present for at least 6 months, contribute to cross-situational impairment and have age of onset prior to the age of 12.

Children are eligible to participate if they are taking melatonin or any other sleep inducing medication, as long as the inclusion criteria are still met despite medication use.

Exclusion criteria

a. Suspected OSA identified using three OSA items from the Children's Sleep Habits Questionnaire.[31] Paediatrician investigators Hiscock and Heussler telephone caregivers of children with suspected OSA to ask further about their symptoms and if OSA is suspected, these children are excluded and referred to appropriate clinical services as per usual clinical care (1% in our efficacy trial).[8]

b. No longer meeting criteria for ADHD at the time of recruitment.

c. Major illness or disability (e.g., intellectual disability). Common comorbidities including internalising/externalising disorder and autism spectrum disorder (ASD) are not excluded.

d. Parents with insufficient English language proficiency to complete study documentation and/or participate in the intervention.

e. Participated in our original efficacy trial.

Sample size

Sample size planning is based on the primary outcome, the proportion of children for whom parents no longer report moderate/severe sleep problems at 3 months. In the efficacy study, at 3 months, 56% and 30% of parents in the intervention and control group, respectively, reported that their child's sleep was still a moderate/severe problem i.e. a difference of 26%. We conservatively assume a smaller difference of 20%, i.e. 56% vs 36% to be observed in this trial. In order to have 80% power in detecting this difference at a two-sided type one error level of 5%, a group sample size of 107 individuals (total sample size n=214) is required. As this is a cluster controlled trial (clustered at the level of the paediatrician to minimise contamination), we will inflate our sample size by a design effect of 1.2 where the design effect = $1+(n-1)\cdot r$ with n=3 (the number of children seen by each paediatrician) and r=0.1 (the conservatively assumed intra-cluster correlation coefficient, based on our efficacy RCT). Allowing for 20% drop out to 3 months and accounting for clustering, we need to recruit 160 children in each study arm (total sample size n=320).

Randomisation

Paediatricians are randomly allocated to either receive the sleep training or not by an independent researcher, thereby avoiding potential contamination if all paediatricians were to

be trained in the program. Randomisation is based on a pre-generated group allocation sequence from the Murdoch Childrens Research Institute's Clinical Epidemiology and Biostatistics Unit and is stratified by location of the paediatrician (regional or metropolitan area). The randomisation is also stratified by the predicted number of enrolled patients (less than 10 and 10 or more). Paediatricians, families and researchers are blind to group allocation at the time of recruitment.

If the paediatrician is assigned to the intervention group and has more than four patients enrolled, families are randomised to receive the intervention from either the paediatrician or psychologist. This second step of randomisation takes place after family recruitment is complete. The research team then sends the paediatrician a letter informing them of whether they will be receiving the sleep training or not. In addition, participating families are also sent a letter informing them of whether they will be receiving the sleep intervention or not.

Families of children attending a paediatrician randomised to the control group receive 'usual care' which involves seeing their paediatrician as per usual regarding their child's ADHD. Our research has shown that this does not routinely include addressing sleep issues.[2] In Australia, paediatricians typically see children with ADHD every 6 months to check their height, weight, blood pressure and re-issue a script for medication (valid for 6 months), where necessary.

Intervention training

The intervention is designed to be feasible to deliver in paediatricians' and psychologists' practice. Intervention group paediatricians and all psychologists are trained to deliver the same program described for our efficacy trial[8] in one 3.5-hour session. Training occurs conjointly for paediatricians and psychologists, where possible, with investigators Hiscock, Sciberras and Heussler to maximise fidelity. Training addresses normal sleep

patterns in school-aged children and highlights the importance of sleep hygiene practices such as consistent bedtime routines and keeping bedrooms media-free. The intervention includes verbal and written information of standard sleep intervention strategies as recommended by the American Sleep Association[32] and addresses common behavioural sleep problems experienced at the beginning of, and during, the night. A summary of sleep problems addressed and management strategies are provided in Table 1. Training focuses on how these strategies can be individualised for families and includes evidence-based instructional strategies such as role play, feedback, modelling practice, and use of checklists. Training is supported by a manual and written parent education materials.

Prior to training, paediatricians and psychologists complete a "pre-quiz" to establish their baseline knowledge, skills and attitudes in relation to child sleep problems and their management. A "post-quiz" following training is used to assess changes in knowledge, confidence, and perceived competence in the management of child sleep problems.

Intervention delivery

Paediatricians and psychologists are sent an intervention package for each child allocated to them containing the child's contact details, a clinical checklist to complete after each appointment and parent education materials. Families contact the clinician to make an appointment (up to 30 minutes for paediatricians, up to 50 minutes for a psychologist) to discuss their child's sleep, with a follow-up session (up to 30 minutes for paediatricians, up to 50 minutes for a psychologist) approximately two weeks later and if needed, a final 15-20 minute phone call a further two weeks after that. Children are present at all face to face appointments. The first session focuses on an assessment of the child's sleep problem, providing information about normal sleep and sleep cycles, giving the family a sleep diary to complete, advice about sleep hygiene, and a plan specifically tailored to the child's particular sleep disorder. The second session and follow-up phone call include a review of the sleep

diary, re-enforcement/trouble shooting of existing strategies and the introduction of new strategies, where appropriate.

The research team contacts families within one month post-randomisation to ensure an appointment has been made with either their paediatrician or a psychologist and to encourage them to make the appointment if they have not yet done so.

Follow-up

We mail/email follow-up surveys to families and teachers at 3 and 6 months post-intervention (measured from first intended intervention session for intervention families with controls followed up at the median date of intervention follow-up) to determine both short and longer term changes in primary and secondary outcomes. Teachers are not informed of the child's intervention group status. For intervention families only, the 3 month survey also asks about the behavioural intervention components received, usefulness of the intervention, ease of use of strategies, and costs experienced by families in accessing the program. At 6 months a trained research assistant completes a blinded direct assessment of child executive functioning, learning, working memory, academic functioning, sleep and QoL via home visits (of 45 minutes duration).

Measures

All measures administered at baseline, 3 and 6 months are summarised in Table 2. The majority of measures were used in our efficacy trial. We now additionally measure academic functioning given that our efficacy trial showed a trend towards improvement in working memory, which is a key determinant of academic functioning. For similar reasons we also include a more detailed assessment of cognitive and executive functioning. The baseline questionnaire includes family (e.g., family composition, parental education and age, language spoken at home, annual household income) and child demographic and medical (e.g., medication, diagnosed comorbidities etc.) characteristics.

The research team prospectively records resources used to administer all program components to facilitate economic analyses. Families also report time, travel and out-of-pocket costs associated with visits as well as those costs associated with child ADHD medication/prescriptions.

Data analysis

Analyses will be based on the 'intention to treat' population at the level of the individual child and will adjust for clustering at the level of the paediatrician using a generalised linear mixed effect model (logit link function) for the binary outcome. In the primary efficacy analysis, the stratification variable *'location of study site (practice)'* as well as an indicator variable for the *type of health care professional* who delivered the intervention (paediatrician or psychologist) will be considered as adjustments variables. Model-based effect estimates (risk differences and risk ratios) will be reported along with 95% confidence intervals. Because of the range of outcomes and time-points, the results will be considered in their totality and interpreted with suitable caution regarding formal conclusions of "statistical significance". In order to reduce potential confounding bias due to differential patient-drop out over time, multiple imputation methodology will be applied to replace missing outcome data in the primary efficacy analysis. All secondary analyses will be adjusted for baseline scores and stratification variables wherever possible, in order to increase precision of comparisons.[33] We will present results of analyses both unadjusted and adjusted for further potential outcome predictor variables (child age, medication use, comorbidities, and family socio-demographic characteristics (Socioeconomic Index for Advantage linked to the family's postcode),[34] parent high school completion, and parent age). A comprehensive statistical analysis plan, finalized before database lock, will specify the details of the primary and secondary analyses.

Cost-effectiveness analyses

The economic analysis will first present cost-consequences analysis, then proceed to cost-effectiveness analysis against the primary outcome (*prevalence of sleep problems*) measure as the primary economic analysis. Secondary economic analyses will include cost-utility analysis against CHU9D-based QALYs.[35,36] These analyses will be conducted from both the health care and broader societal perspectives (as cost-effectiveness can vary significantly by perspective)[37] and will include extensive sensitivity analyses to test the impact of uncertainty in data and sensitivity to evaluation approach.

Dissemination

Findings will determine whether the benefits of an efficacy trial can be realised more broadly at the population level and whether it is cost-effective to do so. Findings will inform the development of clinical guidelines for managing sleep problems in this population. We will seek to publish in leading international paediatric journals, present at major conferences and disseminate findings through established clinician networks.

Discussion

ADHD affects approximately 5% of school-aged children[38] and is frequently associated with sleep problems, which worsen child and family outcomes.[2] The development of effective behavioural interventions that can be rolled out in routine clinical practice for children with ADHD and sleep problems may improve a host of child and family outcomes, as suggested by recent efficacy trials.[8-10]

It is essential to now take the next steps to translate these findings to everyday practice. To do this, we have deliberately designed our intervention so that it can be readily delivered by children's treating paediatricians or psychologists in the community. No such trial has been previously reported, either in Australia or internationally. If cost-effective, we expect the following outcomes: 1) the best evidence yet that addressing sleep problems

improves outcomes for children with ADHD; and 2) a ready-to-use intervention that is tailored to the Australian health system, and can be replicated internationally.

Article summary

Strengths and limitations

- First translational trial to determine whether a brief, behavioural sleep intervention has benefits for children with ADHD when delivered in 'real-life' clinical settings by paediatricians and psychologists.
- The inclusion of blinded teacher reports, as well as blinded direct assessment measures to minimise bias.
- Inclusion of economic analyses, which provide data on the cost-effectiveness of the program.
- Limited generalisability to non-English speaking families and children with ADHD presenting with serious medical conditions and/or intellectual disability.
- Sleep problems assessed using unblinded parent report as opposed to objective measures.

Table 1. Key behavioural sleep management strategies

Sleep disorder	Definition	Examples of behavioural strategies
Sleep onset association disorder	Child associates falling asleep with a person or object (e.g., television) and is unable to fall asleep without its presence.	• Adult fading (i.e. graduated extinction) using 'camping out' - gradual withdrawal of parental presence from the child's bedroom over 7-10 days. • 'Checking method' – parent checks on the child at regular time intervals (2, 5, or 10 minutes, with intervals increasing over time).
Delayed sleep phase	Shift in the child's sleep-wake cycle, in which the child cannot fall asleep until late and then wakes late in the morning.	• Bedtime fading - child's bedtime is temporarily set later to when they are usually falling asleep and gradually brought forward. The child is then woken at a pre-set time in the morning. • Early morning light exposure.
Limit setting sleep disorder	Child refusal to go to bed and general non-compliant behaviour at bedtime. Parent struggles to set appropriate and consistent bedtime limits.	• Parent management strategies - ignoring child protests, rewarding compliance with bedtime routines. A 'bedtime pass', whereby the child can only leave the bedroom one time before sleep, can be used to promote compliant behaviour. • Consideration of bedtime fading or the checking method.
Primary insomnia	Child has substantial difficulty initiating and/or maintaining sleep even if they go to bed at a later time.	• Visual imagery and relaxation. • Basic cognitive restructuring. • Restricting time in bed (e.g., temporarily setting the bedtime later as per delayed sleep phase or getting out of bed and doing a relaxing activity if the child cannot

		sleep).
Night time anxiety	Specific night time fears including fear of the dark and/or child worrying about other things while in bed.	• Visual imagery and relaxation training. • Discussing fears during the day rather than just before bedtime. • Rewarding brave behaviour. • Other - use of a security object, avoiding scary television shows, use of a book to record worries.

Table 2. Summary of measures

Construct	Measures	Source[a]	T1	T2	T3
Child Outcomes					
Sleep	**Sleep problem prevalence (primary outcome) -** Primary caregiver report of child sleep problem (none/mild vs moderate/severe).[2]	P	●	●	●
	Children's Sleep Habits Questionnaire (CSHQ) - 33-item validated measure of disorders of initiating and maintaining sleep.[31] Child Sleep Self Report collected at 6 months only.[15]	P	●	●	●
	Teacher Daytime Sleepiness Questionnaire - 10-item validated scale of daytime sleepiness at school.[39]	T	●	●	●
	Sleep Hygiene scale - 7-item measure assessing sleep hygiene.[24]	P	●		●
Comorbidity	**Anxiety Disorders Interview Schedule for DSM-IV (ADIS-C) -** diagnostic interview assessing mental health disorders according to DSM-IV criteria. This is completed with parents over the telephone and has been validated for this purpose.[27]	P	●		
ADHD	**ADHD Rating Scale IV** - 18-item validated scale measuring the core symptoms of ADHD.[30]	P, T	●	●	●
Behaviour	**Strengths and Difficulties Questionnaire** – 25 items assessing the following subscales: hyperactivity/inattention, conduct problems, emotional symptoms, peer relationship problems, and prosocial behavior.[40]	P, T	●	●	●
Irritability	**Affective reactivity index (ARI) -** 6-item validated measure assessing child irritability.[41]	P	●	●	●
School attendance	**School attendance** over the preceding 3 months.[2]	P	●	●	●
Quality of Life	**Child Health Utility-9D (CHU-9D)** - 9 item measure of child quality of life used to calculate quality adjusted life years. Child report is collected at the 6 month follow up only.[42]	P, C	●		●
	Pediatrics Quality of Life Inventory 4.0 – 23-item measure of child total, physical and psychosocial QoL.[43]	P	●		●

Memory	**Sleep Suite App** – An animated iPad application that includes a continuous performance test to measure sustained attention, and 2 tests of memory consolidation and learning.[44]	C			●
Working Memory	**Working Memory Test Battery for Children –** The Backward digit span recall subtest is administered as a measure of child working memory.[45]	C			●
Academic functioning	**Wide Range Achievement Test 4 (WRAT)** – word reading and math computation subtests.[46]	C			●
	NAPLAN – standardised academic tests of reading, writing, language conventions and numeracy. Results can be compared to National or State population results and against the national minimum standard.[26]	L			●
Autism	**Social Responsiveness Scale (SRS) Brief** – 16-item measure of autism spectrum disorder symptoms.[47]	P			●
Parent Outcomes					
Mental health	**Kessler 6 (K6) -** 6-item validated measure of adult psychological stress.[48]	P	●	●	●
Work attendance	**Work attendance** over the previous 3 months.[2]	P	●	●	●
Parenting	**Parenting -** validated scales developed for the Longitudinal Study of Australian Children assessing parenting consistency (6-items) and parental warmth (5-items).[49]	P	●		●
Family costs	**Service use and costs -** families report service use over previous 3 months as well as time, travel and out-of-pocket costs associated	P		●	●

[a] P = Parent-report, T = teacher-report, C = child-report, L = data linkage; T1 = baseline; T2 = 3 months post-intervention; T3 = 6 months post-intervention.

References

1. Cortese S, Brown TE, Corkum P, et al. Assessment and management of sleep problems in youths with attention-deficit/hyperactivity disorder. *J Am Acad Child Adolesc Psychiatry.* 2013;52(8):784-796.
2. Sung V, Hiscock H, Sciberras E, Efron D. Sleep problems in children with attention-deficit/hyperactivity disorder - Prevalence and the effect on the child and family. *Arch Pediatr Adolesc Med.* 2008;162(4):336-342.
3. Lycett K, Mensah F, Hiscock H, Sciberras E. A prospective study of sleep problems in children with ADHD. *Sleep Med.* 2014;15:1354–1361.
4. Hansen BH, Skirbekk B, Oerbeck B, Wentzel-Larsen T, H. K. Persistence of sleep problems in children with anxiety and attention deficit hyperactivity disorder. *Child Psychiatry Hum Dev.* 2013;44:290–304.
5. Weiss MD, Wasdell MB, Bomben MM, Rea KJ, Freeman RD. Sleep hygiene and melatonin treatment for children and adolescents with ADHD and initial insomnia. *J Am Acad Child Adolesc Psychiatry.* 2006;45(5):512-519.
6. Van Der Heijden KB, Smits MG, Van Someren EJW, Ridderinkhof R, Boudewijn Gunning W. Effect of melatonin on sleep, behavaiour, and cognition in ADHD and chronic sleep-onset insomnia. *J Am Acad Child Adolesc Psychiatry.* 2007;46:233-241.
7. Bendz LM, Scates AC. Melatonin treatment for insomnia in pediatric patients with Attention-Deficit/Hyperactivity Disorder. *Ann Pharmacother.* 2010;44(1):185-191.
8. Hiscock H, Sciberras E, Mensah F, et al. Impact of a behavioral sleep intervention on ADHD symptoms, child sleep and parent health: A randomized controlled trial. *BMJ.* 2015;350:h68.
9. Keshavarzi Z, Bajoghli H, Mohamadi MR, et al. In a randomized case-control trial with 10-years olds suffering from attention deficit/hyperactivity disorder (ADHD)

sleep and psychological functioning improved during a 12-week sleep-training program. *World J Biol Psychiatry.* 2014;15:609-619.

10. Corkum P, Lingley-Pottie P, Davidson F, et al. Better nights/better days—distance intervention for insomnia in school-aged children with/without ADHD: A randomized controlled trial. *J Pediatr Psychol.* 2016:1-13 doi: 10.1093/jpepsy/jsw1031.
11. Quach J, Hiscock H, Wake MA. Sleep problems and mental health in primary school new entrants: Cross-sectional community-based study. *J Paediatr Child Health.* 2012;48:1076-1081.
12. Bartholomew K, Owens J. Sleep and ADHD: a review. *Medicine and Health, Rhode Island.* 2006;89(3):91.
13. Sciberras E, DePetro A, Mensah F, Hiscock H. Association between sleep and working memory in children with ADHD: A cross sectional study. *Sleep Med.* 2015;10:1192-1197.
14. Kidwell KM, Van Dyk TR, Lundahl A, Nelson TD. Stimulant medications and sleep for youth with ADHD: A meta-analysis. *Pediatrics.* 2015;136:1144-1153.
15. Owens JA, Maxim R, Nobile C, McGuinn M, Msall M. Parental and self-report of sleep in children with attention-deficit/hyperactivity disorder. *Arch Pediatr Adolesc Med.* 2000;154(6):549-555.
16. Lycett K, Sciberras E, Mensah F, Hiscock H. Behavioural sleep problems and internalising and externalising comorbidities in children with attention-deficit/hyperactivity disorder (ADHD). *Europ Child Adolesc Psychiat.* 2013;24:31-40.
17. Noble GS, O'Laughlin L, Brubaker B. Attention deficit hyperactivity disorder and sleep disturbances: consideration of parental influence. *Behav Sleep Med.* 2012;10:41-53.

18. Hiscock H, Roberts G, Efron D, et al. Children Attending Paediatricians Study: a national prospective audit of outpatient practice from the Australian Paediatric Research Network. *MJA.* 2011;194:392-397.

19. Efron D, Davies S, Sciberras E. Current Australian paediatric practice in the assessment and treatment of Attention Deficit Hyperactivity Disorder: A survey and practice audit. Royal Australasian College of Physicians; 2012; Brisbane.

20. Schulz KF, Altman DG, Moher D. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. *BMC medicine.* 2010;8(1):18.

21. American Academy of Sleep Medicine. *International Classification of Sleep Disorders.* 3rd ed. Darien, IL: American Academy of Sleep Medicine; 2014.

22. Hiscock H, Bayer J, Price A, Ukoumunne OC, Rogers S, Wake M. A universal parenting program to prevent early child behaviour problems: cluster randomised trial. *BMJ.* 2008;336:318–321.

23. Hiscock H, Bayer J, Gold L, Hampton A, Ukoumunne OC, Wake M. Improving infant sleep and maternal mental health: a cluster randomised trial. *Arch Dis Child.* 2007;92:952-958.

24. Quach J, Gold L, Arnup S, Sia KL, Wake M, Hiscock H. Sleep well-be well study: improving school transition by improving child sleep: a translational randomised trial. *BMJ Open.* 2013;3:e004009.

25. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap) - A metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform.* 2009;42:377-381.

26. Australian Curriculum Assessment and Reporting Authority. NAPLAN Website http://www.nap.edu.au/. 2016. Accessed 12 August 2016.

27. Lyneham HJ, Rapee RMJ. Agreement Between Telephone and In-Person Delivery of a Structured Interview for Anxiety Disorders in Children. *J Am Acad Child Adolesc Psychiatry.* 2005;44:274-282.

28. Quach J, Hiscock H, Canterford L, Wake MA. Outcomes of child sleep problems over the school-transition period: Australian population longitudinal study. *Pediatrics.* 2009;123:1287-1292.

29. Lycett K, Mensah F, Hiscock H, Sciberras E. The validity of a global measure of sleep problem severity in children with ADHD: a cross-sectional comparison with a validated multi-dimensional measure and sleep log. . *Sleep Med.* 2015;16:1377-1380.

30. DuPaul GJ, Power TJ, Anastopoulos AD, Reid R. *ADHD Rating Scale IV: Checklists, Norms, and Clinical Interpretation.* New York, NY: The Guilford Publications Inc; 1998.

31. Owens J, Spirito A, McGuinn M. The Children's Sleep Habits Questionnaire (CSHQ): Psychometric properties of a survey instrument for school aged children. *Sleep.* 2000;23:1043-1051.

32. Mindell JA, Owen J. *A Clinical Guide to Pediatric Sleep: Diagnosis and Management of Sleep Problems in Children and Adolescents. 2nd ed.* 2nd ed. Philadelphia, PA: Lippincott Williams & Wilkins 2010.

33. Barnett AG, van der Pols JC, Dobson AJ. Regression to the mean: what it is and how to deal with it. *Int J Epidemiol.* 2005;34:215-220.

34. Australian Bureau of Statistics. *Socio-Economic Indexes for Areas (SEIFA) - Technical Paper.* Canberra: ABS; 2006.

35. Coast J. Is economic evaluation in touch with society's health values? *BMJ.* 2004;329:1233-1236.

36. Drummond M, Sculpher M, Torrance G, O'Brien B, G. S. *Methods for the economic evaluation of health care programs. 3rd ed.* Oxford: Oxford University Press; 2005.

37. Gibbard D, Coglan L, MacDonald J. Cost-effectiveness analysis of current practice and parent intervention for children under 3 years presenting with expressive language delay. *Int J Lang Comm.* 2004;39:229-244.

38. Polanczyk GV, Willcutt EG, Salum GA, Kieling C, Rohde LA. ADHD prevalence estimates across three decades: an updated systematic review and meta-regression analysis. *Int J Epidemiol.* 2014;43:434-442.

39. Owen JA, Spirito A, McGuinn M, Nobile C. Sleep habits and sleep disturbance in elementary school-aged children. *J Dev Behav Pediatr.* 2000;21:27-36.

40. Goodman R. Psychometric properties of the Strengths and Difficulties Questionnaire. *J Am Acad Child Adolesc Psychiatry.* 2001;40:1337-1345.

41. Stingaris A, Goodman R, Ferdinando S, et al. The Affective Reactivity Index: a concise irritability scale for clinical and research settings. *J Child Psychol Psychiatry.* 2012;53:1109-1117.

42. Stevens K. Valuation of the Child Health Utility 9D Index. *Pharmacoeconomics* 2012;30:729-747.

43. Varni JW, Limbers CA, Burwinkle TM. Parent proxy-report of their children's health-related quality of life: an analysis of 13,878 parents' reliability and validity across age subgroups using the PedsQL™ 4.0 Generic Core Scales. *Health Qual Life Out.* 2007;5:1043-1051.

44. Colonna A, Smith AB, Pal DK and Gringras P. Novel mechanisms, treatments, and outcome measures in childhood sleep. *Front Psychol* 2015;6:602. doi: 10.3389/fpsyg.2015.00602

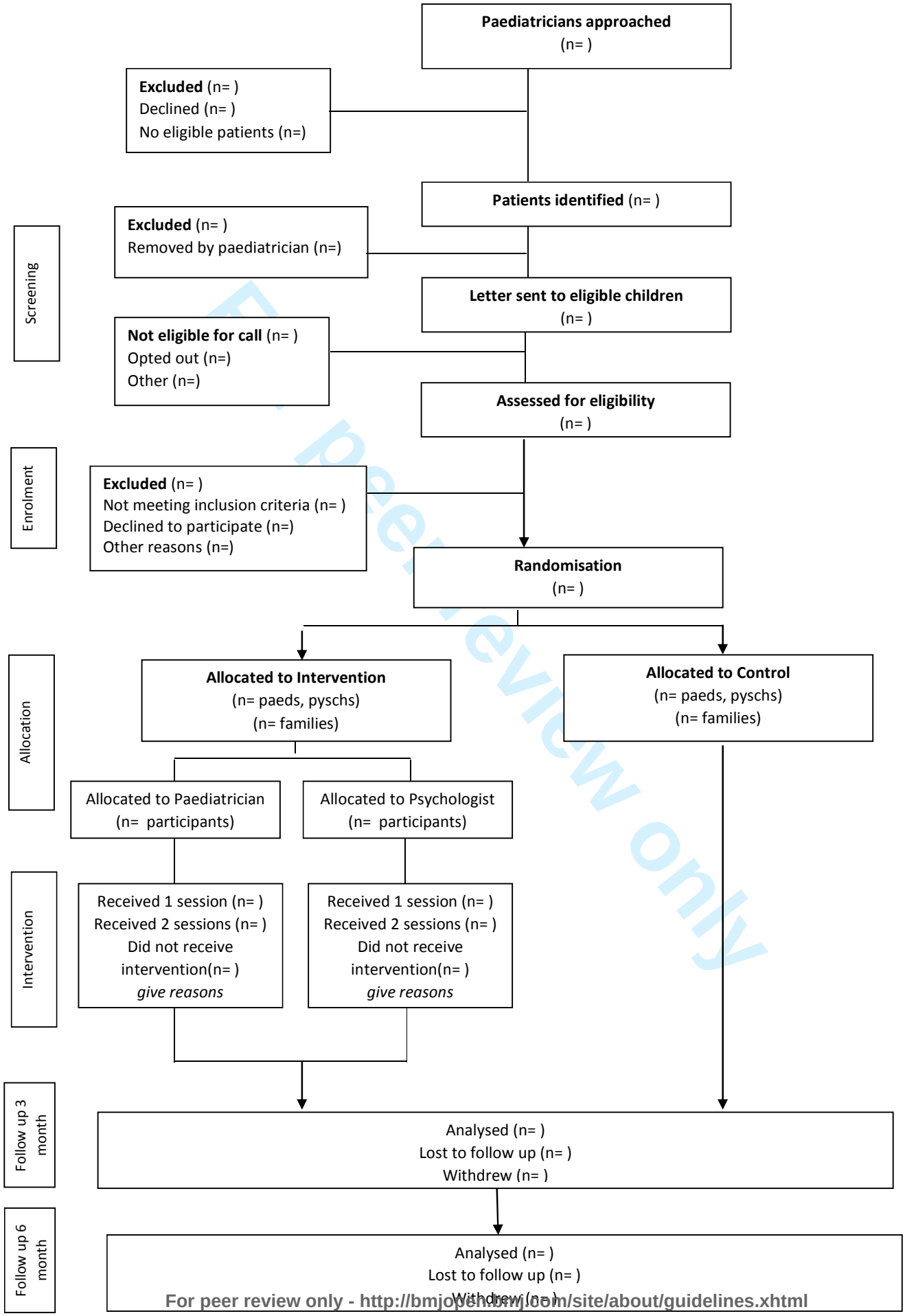
45. Pickering S, Gathercole S. *Working Memory Test Battery for Children (WMTB-C).* London: Pearson Education Ltd; 2001.

46. Wilkinson GS, Robertson GJ. *Wide Range Achievement Test 4 (WRAT 4).* Lutz, FL: Psychological Assessment Resources; 2006.

47. Moul C, Cauchi A, Hawes DJ, Brennan J, Dadds MR. Differentiating autism spectrum disorder and overlapping psychopathology with a brief version of the social responsiveness scale. *Child Psychiatry Hum Dev.* 2015;46:108-117.

48. Furukawa TA, Kessler RC, Slade T, Andrews G. The performance of the K6 and K10 screening scales for psychological distress in the Australian National Survey of Mental Health and Well-Being. *Psychol Med.* 2003;33:357-362.

49. Zubrick SR, Lucas N, Westrupp EM, Nicholson JM. *Parenting measures in the Longitudinal Study of Australian Children: Construct validity and measurment quality Waves 1 to 4.* Canberra, Australia: Department of Social Services; 2014.



BMJ Open

Does a brief, behavioural intervention, delivered by paediatricians or psychologists improve sleep problems for children with ADHD? Protocol for a cluster-randomised, translational trial

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2016-014158.R1
Article Type:	Protocol
Date Submitted by the Author:	01-Dec-2016
Complete List of Authors:	Sciberras, Emma; Murdoch Childrens Research Institute, Centre for Community Child Health Mulraney, Melissa; Murdoch Childrens Research Institute Heussler, Honey; Mater Medical Research Institute Rinehart, Nicole; Deakin University Schuster, Tibor; Murdoch Childrens Research Institute, Medical Statistics Gold, Lisa; Deakin University, Deakin Health Economics Hayes, Nicole; Mater Medical Research Institute Hiscock, Harriet; The Royal Children's Hospital, Centre for Community Child Health
Primary Subject Heading:	Mental health
Secondary Subject Heading:	Public health
Keywords:	attention deficit disorder with hyperactivity, randomised controlled trial, effectiveness, treatment, sleep, child

Does a brief, behavioural intervention, delivered by paediatricians or psychologists improve sleep problems for children with ADHD? Protocol for a cluster-randomised, translational trial

Authors E Sciberras, DPsych,[1,2,3] M Mulraney, PhD,[2,3] H Heussler,[4] N Rinehart, PhD,[1] T Schuster,[2] L Gold PhD,[1,2] N Hayes PhD,[4] H Hiscock MD.[2,3,5]

Affiliations [1] Deakin University, Geelong, Vic Australia

[2] Murdoch Childrens Research Institute, Parkville, Vic Australia

[3] University of Melbourne, Department of Paediatrics, Parkville, Vic Australia

[4] Mater Research Institute-University of Queensland, South Brisbane, Qld Australia

[5] The Royal Children's Hospital, Parkville Vic Australia

Running title Behavioural sleep intervention for children with ADHD

Key words attention deficit disorder with hyperactivity, sleep, child, randomised controlled trial, effectiveness, treatment

Correspondence to

Dr Emma Sciberras

School of Psychology, Deakin University, Melbourne Burwood Campus, BC Building, Level 5, 221 Burwood Hwy, Burwood VIC 3125, AUSTRALIA

P +61 3 9251 7222 email emma.sciberras@deakin.edu.au

ABSTRACT

Introduction: Up to 70% of children with Attention-Deficit/Hyperactivity Disorder (ADHD) experience sleep problems. We have demonstrated the efficacy of a brief behavioural intervention for children with ADHD in a large randomised controlled trial (RCT) and now aim to examine whether this intervention is effective in real-life clinical settings when delivered by paediatricians or psychologists. We will also assess the cost-effectiveness of the intervention.

Methods and analysis: Children aged 5-12 years with ADHD (n=320) are being recruited for this translational cluster RCT through paediatrician practices in Victoria and Queensland, Australia. Children are eligible if they meet criteria for ADHD, have a moderate/severe sleep problem, and meet American Academy of Sleep Medicine criteria for either chronic insomnia disorder or delayed sleep-wake phase disorder; or are experiencing sleep-related anxiety. Clinicians are randomly allocated at the level of the paediatrician to either receive the sleep training or not. The behavioural intervention comprises two consultations covering sleep hygiene and standardized behavioural strategies. The primary outcome is change in the proportion of children with moderate/severe sleep problems from moderate/severe to no/mild by parent report at 3 months post-intervention. Secondary outcomes include a range of child (e.g., sleep severity, ADHD symptoms, quality of life, behaviour, working memory, executive functioning, learning, academic achievement) and primary caregiver (mental health, parenting, work attendance) measures. Analyses will address clustering at the level of the paediatrician using linear mixed effect models adjusting for potential a priori confounding variables.

Ethics and dissemination: Ethics approval has been granted. Findings will determine whether the benefits of an efficacy trial can be realised more broadly at the population level and will inform the development of clinical guidelines for managing sleep problems in this

population. We will seek to publish in leading international paediatric journals, present at major conferences and through established clinician networks.

Registration details: Current Controlled Trials ISRCTN50834814

Article summary

Strengths and limitations

- First translational trial to determine whether a brief, behavioural sleep intervention has benefits for children with ADHD when delivered in 'real-life' clinical settings by paediatricians and psychologists.
- The inclusion of blinded teacher reports, as well as blinded direct assessment measures to minimise bias.
- Inclusion of economic analyses, which provide data on the cost-effectiveness of the program.
- Limited generalisability to non-English speaking families and children with ADHD presenting with serious medical conditions and/or intellectual disability.
- Sleep problems assessed using unblinded parent report as opposed to objective measures.

INTRODUCTION

Sleep problems are common and more persistent in children with ADHD, and associated with poorer child and family well-being.[1-4] Efficacy Randomised Controlled Trials (RCTs) have shown that sleep problems are amenable to intervention[5-10] in children with ADHD, particularly behavioural interventions.[8-10] However, it is unknown whether the same benefits will be observed when such interventions are delivered by practitioners in 'real life' clinical settings. This article describes the protocol for the Sleeping Sound with ADHD Translational RCT, which aims to assess the effectiveness of a behavioural sleep intervention designed for children with ADHD, when delivered by psychologists or paediatricians in their daily clinical practice.

Sleep problems in children with ADHD

Up to 70% of children with ADHD experience sleep problems,[1,2] compared with 20-30% of children in the general population.[11] Sleep problems experienced by children with ADHD are largely comprise difficulties initiating and/or maintaining sleep, with the most common sleep problems being difficulty falling asleep (reported by 84% of parents of children who report a sleep problem for their child with ADHD), bedtime resistance (68%), tiredness upon waking (62%) and difficulty waking in the morning (56%).[2] Medical conditions such as obstructive sleep apnoea (OSA) can also affect sleep in children with ADHD, although behavioural sleep problems appear more common.[12] In this study we use the term sleep problems to denote those difficulties that can be addressed using behavioural intervention. Sleep problems have been associated with worse functioning for children with ADHD including poorer quality of life (QoL), behaviour, daily functioning, and working memory, as well as increased school absenteeism.[2,4,13] They thus represent an important modifiable target for intervention.

A number of factors have been associated with sleep problems in children with ADHD and it is possible that biological sleep problems such as restless legs syndrome,

obstructive sleep apnoea and narcolepsy can lead to continued sleep disruptions.[12] Insomnia can be a side-effect of stimulant medication,[1,14] although unmedicated children with ADHD also experience higher rates of sleep problems relative to non-ADHD controls.[15] Comorbid externalising and internalising comorbidities are each associated with a 2-fold increase in moderate/severe sleep problems in children with ADHD, while co-occurring internalising and externalising comorbidities are associated with a 3-fold increase.[16] Parenting inconsistency in daily household routines has also been associated with increased bedtime resistance in this group.[17] Biologically, there is overlap in the brain regions and genetic factors (e.g., catecholaminergic system, CLOCK genes) associated with both ADHD and sleep disorders/arousal regulation.[1] ADHD is also a highly genetic condition and parents likely are affected by symptoms such as disorganisation and impulsivity, which may impact on child sleep.

Treating sleep problems in children with ADHD using behavioural strategies

We recently published our efficacy RCT evaluating the impact of a behavioural sleep program in children with ADHD and moderate/severe sleep problems (n=244 5-12 year old children with ADHD).[8] Children were recruited from 21 paediatric practices across Victoria, Australia and randomised to either a behavioural sleep intervention (n=122) or a usual care comparison group (n=122). Intervention families attended two x 50 minute individual sessions (held two weeks apart) with a clinician trained in the intervention (psychologist or trainee paediatrician), comprising a standardised yet flexible intervention, tailored to the child's sleep problems and family preferences.

The intervention was associated with improved child outcomes at three and six months post-randomisation including improved parent-reported child sleep, ADHD symptom severity, QoL, daily functioning and behavior.[8] Intervention children also had improved teacher-reported classroom behavior, as well as improved school attendance and working

memory assessed via blinded assessment.[8] There were small improvements in sleep duration for a subsample that completed actigraphy.[8] Although the intervention was associated with improved caregiver work attendance and mental health three months later, these benefits were not observed at six months.[8]

Similarly, two additional randomised controlled trials have demonstrated the efficacy of improving sleep problems in children with ADHD. Keshavarzi et al. reported that a 12-week sleep-training program for children with ADHD aged 10 years (n=40) had beneficial effects for sleep and psychosocial functioning when compared to controls with ADHD who did not receive the intervention (n=20) and typically developing children (n=20).[9] However the professional group responsible for delivering the intervention was not reported. Corkum and colleagues also recently reported the beneficial effects of their distance sleep intervention delivered by paraprofessionals for childhood insomnia in a mixed sample of children with and without ADHD (n=61).[10] Improvements were identified at 2 and 6 months for sleep assessed using parent report as well as actigraphy, and benefits were also reported for broader child psychosocial health.[10]

Although RCTs have shown that melatonin is associated with improved sleep onset latency for children with ADHD,[5-7] broader benefits for daily functioning including ADHD symptom severity have yet to be shown.

Managing sleep problems in children with ADHD through existing clinical services

Although three trials have now shown that it is possible to improve sleep problems in children with ADHD using behavioural approaches, it remains to be seen whether it is possible to replicate such approaches and improve outcomes for children with ADHD in 'real life' clinical settings when delivered by their treating clinicians (e.g., community paediatricians or psychologists) rather than by clinicians hired to deliver interventions in tightly controlled research trials. We are now testing the translation of this program at the

population level by training community paediatricians and psychologists to deliver this sleep intervention to children with ADHD and sleep problems. If this intervention can be translated successfully to the population level within existing workforces, then this would have the real potential to improve outcomes for children with ADHD and their families. If cost-effective, it could be readily incorporated into the existing health system.

Paediatricians are the main care providers for ADHD in Australia.[18] The paediatrician's role includes both the assessment and treatment (behavioural and medication-based) of ADHD and associated comorbidities (including sleep problems, if identified). Visits to a paediatrician are subsidised by Australia's Medicare scheme, however, families may experience out of pockets costs for these visits. Paediatricians (and general practitioners) may also refer children to a psychologist in the community to manage comorbid behaviours.[19] In Australia, this referral is facilitated by the Medicare Better Access to Mental Health Scheme, which provides subsidised access to up to 10 psychology sessions in a calendar year, provided the criteria for a DSM condition are met. We have deliberately designed our sleep intervention so that it is feasible for both paediatricians and psychologists to deliver within the Australian Medicare scheme and within their typical consultation durations.

Aims and hypotheses

Building on our efficacy trial, we aim to determine whether the Sleeping Sound with ADHD intervention, delivered by paediatricians or psychologists in their usual work setting can replicate the benefits of the efficacy trial. Therefore, in this translational, cluster-randomised trial we aim to determine whether a brief sleep intervention delivered by paediatricians or psychologists:

1. Decreases the proportion of children with moderate/severe sleep problems from moderate/severe to no/mild by parent report at 3 months post-intervention (**primary outcome**).

2. Improves child and family functioning at 3 and 6 months post-intervention **(secondary outcome)**.
3. Is cost-effective **(secondary outcome)**.

We hypothesise that, compared to the control children at 3 (primary outcome timepoint) and 6 months post-intervention, a brief behavioural sleep intervention will:

1. Decrease prevalence of child sleep problems from moderate/severe to no/mild;
2. Improve functioning in other child (sleep severity, ADHD symptoms, QoL, behaviour, working memory, executive functioning, learning, academic achievement, school attendance) and primary caregiver (mental health, parenting, work attendance) outcome domains.
3. Be cost-effective.

METHODS AND ANALYSIS

Overall Study Design

This is a cluster RCT of a behavioural sleep intervention versus usual care conducted in Victoria and Queensland, Australia (see Figure 1). The trial will be reported according to Consolidated Standards of Reporting Trials guidelines and the extension report of non-pharmacological interventions.[20]

Participants

Participants include parents of children aged 5-12 years at the time of recruitment with paediatrician-diagnosed and DSM-5 confirmed ADHD and a moderate to severe sleep problem as defined by the American Academy of Sleep Medicine diagnostic criteria[21]: chronic insomnia disorder, delayed sleep-wake phase disorder, or sleep related anxiety.

Recruitment of health professionals

Given that paediatricians are the main healthcare provider for children with ADHD, recruitment and randomisation occurs at the level of the paediatrician. Paediatricians are recruited via the Australian Paediatric Research Network or through clinical contacts.[18] Interested paediatricians are invited to attend a briefing session in which the study requirements and timetable is presented and paediatricians have the opportunity to ask questions. Interested paediatricians are sent a follow up email thanking them for their interest, asking them to sign an individual Memorandum of Understanding (MOU) if they consent to participation, and asking them to provide a list of psychologists to whom they refer patients. By signing the MOU, paediatricians agree to: (1) participate in training if randomised to the intervention arm; (2) deliver the sleep program to intervention families ***or*** refer the child to a psychologist to deliver the sleep program; (3) not share the intervention materials with control group paediatricians; and (4) allocate time for intervention session bookings.

Once paediatricians have been recruited, psychologists are invited to whom the paediatricians have indicated they refer patients. Psychologists are only recruited for the intervention arm of the project and have no contact with control participants. The research team then informs psychologists about the study via email or phone. The researchers then send psychologists who express interest in participating a follow up email thanking them for their interest and asking them to sign an individual MOU, agreeing to: (1) participate in training; (2) deliver the sleep program to intervention families referred by paediatricians; (3) use intervention materials only with children enrolled in the study; and (4) not share the intervention materials with any other families they see during the study period. This approach has worked well to minimise contamination in our previous RCTs.[22-24]

Screening children for sleep problems and recruiting families

This translational trial uses, where possible, the same procedures that were used in our efficacy trial.[8] Paediatricians pre-identify their patients with ADHD, aged between 5-12

years, seen within the last 12 months, either through their medical software or through case notes. Paediatricians then send a letter to the child's primary caregiver inviting them to take part. The letter advises families that the research team will ask them about their child's sleep and ADHD symptoms. An 'opt out' approach is used, whereby parents are asked to contact the paediatrician if they *do not* wish to learn more about the study. If parents do not opt out within a two-week period, the paediatrician provides the research team with the contact details of the families. Only 9% of families opted out in our efficacy trial.[8] Paediatricians also have the option to use an active consent process. In these cases paediatricians send an 'opt in' version of the study invitation letter.

The research team then contacts interested (or not opted-out) families via telephone to ascertain if the child meets inclusion/exclusion criteria. Eligible families are sent a parent information statement and consent form and a baseline survey. Families have the option to complete hard copy surveys or online surveys (via REDCap - a secure, web-based application).[25] Surveys are completed by the child's primary caregiver. Parents have the option to consent to have their child's school teacher complete a survey about their child's behaviour. If consent is provided by the primary caregiver and school, a link to an online survey is sent to teachers. Parents also have the option to consent to being contacted for ethically approved future research, for the research team to keep their de-identified data to be shared with future ethically approved research, and to allow the research team to link with their child's *National Assessment Program – Literacy and Numeracy* (NAPLAN) results. NAPLAN is a national assessment of literacy and numeracy Australian children complete in Grades 3 and 5, and Years 7 and 9.[26]

Once caregivers provide written consent, the research team contacts them to complete the Anxiety Disorders Interview Schedule for Children (ADIS-C) over the telephone to assess comorbid internalising and externalising diagnoses in children with ADHD.[27] To ensure we

administer the telephone interviews consistently we are recording 10% of the sample to test inter-rater reliability.

Inclusion/exclusion criteria (all assessed via telephone)

Inclusion criteria

a. Child aged between 5-12 years at the time of the recruitment call.

b. Child's sleep is a moderate-severe problem for the caregiver ascertained using the following question: Has your child's sleep been a problem for you over the past 4 weeks?' If 'yes', they are asked to rate severity (mild, moderate or severe). This measure has been used in studies of children with and without ADHD and has good agreement with the Children's Sleep Habits Questionnaire.[2,28,29]

c. Child sleep problem meets the International Classification of Sleep Disorders – Third Edition criteria[21] for an eligible sleep disorder (chronic insomnia disorder, delayed sleep-wake phase disorder) or sleep-related anxiety assessed using study-designed questions. To meet criteria for *chronic insomnia disorder* in this study children needed to meet criterion A (one or more of the following: difficulty initiating sleep, difficulty maintaining sleep, waking earlier than desired, resistance going to bed, difficulty sleeping without a caregiver), B (evidence of impairments related to the sleep difficulty such as daytime sleepiness, impaired social, family, or academic performance etc), C (sleep problem not be explained by inadequate sleep opportunity or circumstances) and D and E (symptoms and associated impairment must have been present 3 times a week or more for at least 3 months) needed to be met.[21] To meet criteria for *delayed sleep-wake phase disorder* in this study, criterion A (significant phase delay as shown by difficulty initiating sleep and awakening at a required time), B (delayed sleep-wake phase must have been present for at least 3 months), and C (improved sleep quality and duration when allowed to choose their own schedule)

needed to be satisfied.[21] Children were accepted into the study on the basis of experiencing sleep-related anxiety if the caregiver endorses significant difficulty falling asleep at night, in addition to anxious behaviour at bedtime (e.g., fearful behaviours such as crying, asking for reassurance or lying in bed worrying).

d. Child meets DSM 5 criteria for ADHD assessed via the 18-item ADHD Rating Scale IV - a validated scale measuring the core symptoms of ADHD.[30] Caregivers need to rate at least 6 of 9 of the inattention and/or hyperactivity/impulsivity items as occurring 'often' or 'very often' in order to meet current symptom criteria. Caregivers are asked to rate symptoms off stimulant medication. Additional questions are then asked to ensure symptoms have been present for at least 6 months ('Did your child have these symptoms for at least 6 months before being diagnosed with ADHD?), and contribute to cross-situational impairment ('Are these symptoms present at home, school and/or when out socially?) Given the included age range all participants met age of onset criteria. We did not assess whether the symptoms were not better explained by another mental disorder.

Children are eligible to participate if they are taking melatonin or any other sleep inducing medication, as long as the inclusion criteria are still met despite medication use.

Exclusion criteria

a. Suspected OSA identified using three OSA items from the Children's Sleep Habits Questionnaire.[31] Paediatrician investigators Hiscock and Heussler telephone caregivers of children with suspected OSA to ask further about their symptoms and if OSA is suspected, these children are excluded and referred to appropriate clinical services as per usual clinical care (1% in our efficacy trial).[8]

b. No longer meeting criteria for ADHD at the time of recruitment.

c. Major illness or disability (e.g., intellectual disability). Parents are asked if their child has ever been diagnosed with an intellectual disability or serious medical condition. If yes, parents are asked to provide further details (e.g., IQ score, diagnosis). If clarification is needed permission is sought to recontact the paediatrician to obtain relevant information from the child's medical record. Common comorbidities including internalising/externalising disorder and autism spectrum disorder (ASD) are not excluded.

d. Parents with insufficient English language proficiency to complete study documentation and/or participate in the intervention.

e. Participated in our original efficacy trial.

Sample size

Sample size planning is based on the primary outcome, the proportion of children for whom parents no longer report moderate/severe sleep problems at 3 months. In the efficacy study, at 3 months, 56% and 30% of parents in the intervention and control group, respectively, reported that their child's sleep was still a moderate/severe problem i.e. a difference of 26%. We conservatively assume a smaller difference of 20%, i.e. 56% vs 36% to be observed in this trial. In order to have 80% power in detecting this difference at a two-sided type one error level of 5%, a group sample size of 107 individuals (total sample size n=214) is required. As this is a cluster controlled trial (clustered at the level of the paediatrician to minimise contamination), we will inflate our sample size by a design effect of 1.2 where the design effect = $1+(n-1)\cdot r$ with n=3 (the number of children seen by each paediatrician) and r=0.1 (the conservatively assumed intra-cluster correlation coefficient, based on our efficacy RCT). Allowing for 20% drop out to 3 months and accounting for clustering, we need to recruit 160 children in each study arm (total sample size n=320). All recruitment procedures described have been used in our previous trials to achieve similar recruitment numbers.

Randomisation

Randomisation occurs at the level of the paediatrician. Paediatricians are randomly allocated to either receive the sleep training or not by an independent researcher, thereby avoiding potential contamination if all paediatricians were to be trained in the program. Randomisation is based on a pre-generated group allocation sequence from the Murdoch Childrens Research Institute's Clinical Epidemiology and Biostatistics Unit and is stratified by location of the paediatrician (regional or metropolitan area). The randomisation is also stratified by the predicted number of enrolled patients (less than 10 and 10 or more). Paediatricians, families and researchers are blind to group allocation at the time of recruitment.

If the paediatrician is assigned to the intervention group and has more than four patients enrolled, families are randomised to receive the intervention from either the paediatrician or psychologist. This second step of randomisation takes place after family recruitment is complete. The research team then sends the paediatrician a letter informing them of whether they will be receiving the sleep training or not. In addition, participating families are also sent a letter informing them of whether they will be receiving the sleep intervention or not.

Families of children attending a paediatrician randomised to the control group receive 'usual care' which involves seeing their paediatrician as per usual regarding their child's ADHD. Our research has shown that this does not routinely include addressing sleep issues.[2] In Australia, paediatricians typically see children with ADHD every 6 months to check their height, weight, blood pressure and re-issue a script for medication (valid for 6 months), where necessary.

Intervention training

The intervention is designed to be feasible to deliver in paediatricians' and psychologists' practice. Intervention group paediatricians and psychologists are trained to deliver the same program described for our efficacy trial[8] in one 3.5-hour session. Training occurs conjointly for paediatricians and psychologists, where possible, with investigators Hiscock, Sciberras and Heussler to maximise fidelity. Training addresses normal sleep patterns in school-aged children and highlights the importance of sleep hygiene practices such as consistent bedtime routines and keeping bedrooms media-free. The intervention includes verbal and written information of standard sleep intervention strategies as recommended by the American Sleep Association[32] and addresses common sleep problems experienced at the beginning of, and during, the night. A summary of sleep problems addressed and management strategies are provided in Table 1. Training focuses on how these strategies can be individualised for families and includes evidence-based instructional strategies such as role play, feedback, modelling practice, and use of checklists. Training is supported by a manual and written parent education materials.

Prior to training, paediatricians and psychologists complete a "pre-quiz" to establish their baseline knowledge, skills and attitudes in relation to child sleep problems and their management. A "post-quiz" following training is used to assess changes in knowledge, confidence, and perceived competence in the management of child sleep problems.

Intervention delivery

Paediatricians and psychologists are sent an intervention package for each child allocated to them containing the child's contact details, a clinical checklist to complete after each appointment and parent education materials. Families contact the clinician they have been allocated to make an appointment (up to 30 minutes for paediatricians, up to 50 minutes for a psychologist) to discuss their child's sleep, with a follow-up session (up to 30 minutes for paediatricians, up to 50 minutes for a psychologist) approximately two weeks later and if

needed, a final 15-20 minute phone call a further two weeks after that. The differences in consultation duration reflect real life clinical practice. We record the actual duration of all consultations, which will enable us to examine the relationship between intervention dose and outcomes. Children are present at all face to face appointments. The first session focuses on an assessment of the child's sleep problem, providing information about normal sleep and sleep cycles, giving the family a sleep diary to complete, advice about sleep hygiene, and a plan specifically tailored to the child's particular sleep disorder. The second session and follow-up phone call include a review of the sleep diary, re-enforcement/trouble shooting of existing strategies and the introduction of new strategies, where appropriate.

The research team contacts families within one month post-randomisation to ensure an appointment has been made with either their paediatrician or a psychologist and to encourage them to make the appointment if they have not yet done so.

Follow-up

We mail/email follow-up surveys to families and teachers at 3 and 6 months post-intervention (measured from first intended intervention session for intervention families with controls followed up at the median date of intervention follow-up) to determine both short and longer term changes in primary and secondary outcomes. Teachers are not informed of the child's intervention group status. For intervention families only, the 3 month survey also asks about the behavioural intervention components received, usefulness of the intervention, ease of use of strategies, and costs experienced by families in accessing the program. At 6 months a trained research assistant completes a blinded direct assessment of child executive functioning, learning, working memory, academic functioning, sleep and QoL via home visits (of 45 minutes duration).

Measures

All measures administered at baseline, 3 and 6 months are summarised in Table 2. The majority of measures were used in our efficacy trial. We now additionally measure academic functioning given that our efficacy trial showed a trend towards improvement in working memory, which is a key determinant of academic functioning. For similar reasons we also include a more detailed assessment of cognitive and executive functioning. The baseline questionnaire includes family (e.g., family composition, parental education and age, language spoken at home, annual household income) and child demographic and medical (e.g., medication, diagnosed comorbidities etc.) characteristics.

The research team prospectively records resources used to administer all program components to facilitate economic analyses. Families also report time, travel and out-of-pocket costs associated with visits as well as those costs associated with child ADHD medication/prescriptions.

Data analysis

Analyses will be based on the 'intention to treat' population at the level of the individual child and will adjust for clustering at the level of the paediatrician using a generalised linear mixed effect model (logit link function) for the binary outcome. In the primary efficacy analysis, the stratification variable *'location of study site (practice)'* as well as an indicator variable for the *type of health care professional* who delivered the intervention (paediatrician or psychologist) will be considered as adjustments variables. Model-based effect estimates (risk differences and risk ratios) will be reported along with 95% confidence intervals. Because of the range of outcomes and time-points, the results will be considered in their totality and interpreted with suitable caution regarding formal conclusions of "statistical significance". In order to reduce potential confounding bias due to differential patient-drop out over time, multiple imputation methodology will be applied to replace missing outcome data in the primary efficacy analysis. All secondary analyses will be adjusted for baseline

scores and stratification variables wherever possible, in order to increase precision of comparisons.[33] We will present results of analyses both unadjusted and adjusted for further potential outcome predictor variables (child age, medication use, comorbidities, and family socio-demographic characteristics (Socioeconomic Index for Advantage linked to the family's postcode),[34] parent high school completion, and parent age). A comprehensive statistical analysis plan, finalized before database lock, will specify the details of the primary and secondary analyses.

Cost-effectiveness analyses

The economic analysis will first present cost-consequences analysis, then proceed to cost-effectiveness analysis against the primary outcome (*prevalence of sleep problems*) measure as the primary economic analysis. Secondary economic analyses will include cost-utility analysis against CHU9D-based QALYs.[35,36] These analyses will be conducted from both the health care and broader societal perspectives (as cost-effectiveness can vary significantly by perspective)[37] and will include extensive sensitivity analyses to test the impact of uncertainty in data and sensitivity to evaluation approach.

ETHICS AND DISSEMINATION

ADHD affects approximately 5% of school-aged children[38] and is frequently associated with sleep problems, which worsen child and family outcomes.[2] Findings will determine whether the benefits of an efficacy trial can be realised more broadly at the population level and whether it is cost-effective to do so. If cost-effective, we expect the following outcomes: 1) the best evidence yet that addressing sleep problems improves outcomes for children with ADHD; and 2) a ready-to-use intervention that is tailored to the Australian health system, and can be replicated internationally. Findings will inform the development of clinical guidelines for managing sleep problems in this population. We will seek to publish in leading

international paediatric journals, present at major conferences and disseminate findings through established clinician networks.

This project has been funded by the National Health and Medical Research Council of Australia (1106427) and has been granted ethics approval from The Royal Children's Hospital (34072), University of Queensland (2014001555), Mater Hospital (RG-14-349), Deakin University (2015-211), Victorian Department of Education & Training (2014_002519), The Queensland Department of Education & Training (550/27/1570), and the Catholic Education Office (Ballarat; Brisbane; Melbourne; Toowoomba) Human Research Ethics Committees.

Table 1. Key behavioural sleep management strategies

Sleep disorder	Definition	Examples of behavioural strategies
Sleep onset association disorder	Child associates falling asleep with a person or object (e.g., television) and is unable to fall asleep without its presence.	• Adult fading (i.e. graduated extinction) using 'camping out' - gradual withdrawal of parental presence from the child's bedroom over 7-10 days. • 'Checking method' – parent checks on the child at regular time intervals (2, 5, or 10 minutes, with intervals increasing over time).
Delayed sleep phase	Shift in the child's sleep-wake cycle, in which the child cannot fall asleep until late and then wakes late in the morning.	• Bedtime fading - child's bedtime is temporarily set later to when they are usually falling asleep and gradually brought forward. The child is then woken at a pre-set time in the morning. • Early morning light exposure.
Limit setting sleep disorder	Child refusal to go to bed and general non-compliant behaviour at bedtime. Parent struggles to set appropriate and consistent bedtime limits.	• Parent management strategies - ignoring child protests, rewarding compliance with bedtime routines. A 'bedtime pass', whereby the child can only leave the bedroom one time before sleep, can be used to promote compliant behaviour. • Consideration of bedtime fading or the checking method.
Primary insomnia	Child has substantial difficulty initiating and/or maintaining sleep even if they go to bed at a later time.	• Visual imagery and relaxation. • Basic cognitive restructuring. • Restricting time in bed (e.g., temporarily setting the bedtime later as per delayed sleep phase or getting out of bed and doing a relaxing activity if the child cannot

		sleep).
Night time anxiety	Specific night time fears including fear of the dark and/or child worrying about other things while in bed.	• Visual imagery and relaxation training. • Discussing fears during the day rather than just before bedtime. • Rewarding brave behaviour. • Other - use of a security object, avoiding scary television shows, use of a book to record worries.

Table 2. Summary of measures

Construct	Measures	Source[a]	T1	T2	T3
Child Outcomes					
Sleep	**Sleep problem prevalence (primary outcome) -** Primary caregiver report of child sleep problem (none/mild vs moderate/severe).[2]	P	●	●	●
	Children's Sleep Habits Questionnaire (CSHQ) - 33-item validated measure of disorders of initiating and maintaining sleep.[31] Child Sleep Self Report collected at 6 months only.[15]	P	●	●	●
	Teacher Daytime Sleepiness Questionnaire - 10-item validated scale of daytime sleepiness at school.[39]	T	●	●	●
	Sleep Hygiene scale - 7-item measure assessing sleep hygiene.[24]	P	●		●
Comorbidity	**Anxiety Disorders Interview Schedule for DSM-IV (ADIS-C) -** diagnostic interview assessing mental health disorders according to DSM-IV criteria. This is completed with parents over the telephone and has been validated for this purpose.[27]	P	●		
ADHD	**ADHD Rating Scale IV** - 18-item validated scale measuring the core symptoms of ADHD.[30]	P, T	●	●	●
Behaviour	**Strengths and Difficulties Questionnaire** – 25 items assessing the following subscales: hyperactivity/inattention, conduct problems, emotional symptoms, peer relationship problems, and prosocial behavior.[40]	P, T	●	●	●
Irritability	**Affective reactivity index (ARI) -** 6-item validated measure assessing child irritability.[41]	P	●	●	●
School attendance	**School attendance** over the preceding 3 months.[2]	P	●	●	●
Quality of Life	**Child Health Utility-9D (CHU-9D)** - 9 item measure of child quality of life used to calculate quality adjusted life years. Child report is collected at the 6 month follow up only.[42]	P, C	●		●
	Pediatrics Quality of Life Inventory 4.0 – 23-item measure of child total, physical and psychosocial QoL.[43]	P	●		●

Memory	**Sleep Suite App** – An animated iPad application that includes a continuous performance test to measure sustained attention, and 2 tests of memory consolidation and learning.[44]	C			●
Working Memory	**Working Memory Test Battery for Children –** The Backward digit span recall subtest is administered as a measure of child working memory.[45]	C			●
Academic functioning	**Wide Range Achievement Test 4 (WRAT)** – word reading and math computation subtests.[46]	C			●
	NAPLAN – standardised academic tests of reading, writing, language conventions and numeracy. Results can be compared to National or State population results and against the national minimum standard.[26]	L			●
Autism	**Social Responsiveness Scale (SRS) Brief** – 16-item measure of autism spectrum disorder symptoms.[47]	P			●
Parent Outcomes					
Mental health	**Kessler 6 (K6) -** 6-item validated measure of adult psychological stress.[48]	P	●	●	●
Work attendance	**Work attendance** over the previous 3 months.[2]	P	●	●	●
Parenting	**Parenting -** validated scales developed for the Longitudinal Study of Australian Children assessing parenting consistency (6-items) and parental warmth (5-items).[49]	P	●		●
Family costs	**Service use and costs -** families report service use over previous 3 months as well as time, travel and out-of-pocket costs associated	P		●	●

[a] P = Parent-report, T = teacher-report, C = child-report, L = data linkage; T1 = baseline; T2 = 3 months post-intervention; T3 = 6 months post-intervention.

REFERENCES

1. Cortese S, Brown TE, Corkum P, et al. Assessment and management of sleep problems in youths with attention-deficit/hyperactivity disorder. *J Am Acad Child Adolesc Psychiatry.* 2013;52(8):784-796.
2. Sung V, Hiscock H, Sciberras E, Efron D. Sleep problems in children with attention-deficit/hyperactivity disorder - Prevalence and the effect on the child and family. *Arch Pediatr Adolesc Med.* 2008;162(4):336-342.
3. Lycett K, Mensah F, Hiscock H, Sciberras E. A prospective study of sleep problems in children with ADHD. *Sleep Med.* 2014;15:1354–1361.
4. Hansen BH, Skirbekk B, Oerbeck B, Wentzel-Larsen T, H. K. Persistence of sleep problems in children with anxiety and attention deficit hyperactivity disorder. *Child Psychiatry Hum Dev.* 2013;44:290–304.
5. Weiss MD, Wasdell MB, Bomben MM, Rea KJ, Freeman RD. Sleep hygiene and melatonin treatment for children and adolescents with ADHD and initial insomnia. *J Am Acad Child Adolesc Psychiatry.* 2006;45(5):512-519.
6. Van Der Heijden KB, Smits MG, Van Someren EJW, Ridderinkhof R, Boudewijn Gunning W. Effect of melatonin on sleep, behavaiour, and cognition in ADHD and chronic sleep-onset insomnia. *J Am Acad Child Adolesc Psychiatry.* 2007;46:233-241.
7. Bendz LM, Scates AC. Melatonin treatment for insomnia in pediatric patients with Attention-Deficit/Hyperactivity Disorder. *Ann Pharmacother.* 2010;44(1):185-191.
8. Hiscock H, Sciberras E, Mensah F, et al. Impact of a behavioral sleep intervention on ADHD symptoms, child sleep and parent health: A randomized controlled trial. *BMJ.* 2015;350:h68.
9. Keshavarzi Z, Bajoghli H, Mohamadi MR, et al. In a randomized case-control trial with 10-years olds suffering from attention deficit/hyperactivity disorder (ADHD)

sleep and psychological functioning improved during a 12-week sleep-training program. *World J Biol Psychiatry.* 2014;15:609-619.

10. Corkum P, Lingley-Pottie P, Davidson F, et al. Better nights/better days—distance intervention for insomnia in school-aged children with/without ADHD: A randomized controlled trial. *J Pediatr Psychol.* 2016:1-13 doi: 10.1093/jpepsy/jsw1031.
11. Quach J, Hiscock H, Wake MA. Sleep problems and mental health in primary school new entrants: Cross-sectional community-based study. *J Paediatr Child Health.* 2012;48:1076-1081.
12. Bartholomew K, Owens J. Sleep and ADHD: a review. *Medicine and Health, Rhode Island.* 2006;89(3):91.
13. Sciberras E, DePetro A, Mensah F, Hiscock H. Association between sleep and working memory in children with ADHD: A cross sectional study. *Sleep Med.* 2015;10:1192-1197.
14. Kidwell KM, Van Dyk TR, Lundahl A, Nelson TD. Stimulant medications and sleep for youth with ADHD: A meta-analysis. *Pediatrics.* 2015;136:1144-1153.
15. Owens JA, Maxim R, Nobile C, McGuinn M, Msall M. Parental and self-report of sleep in children with attention-deficit/hyperactivity disorder. *Arch Pediatr Adolesc Med.* 2000;154(6):549-555.
16. Lycett K, Sciberras E, Mensah F, Hiscock H. Behavioural sleep problems and internalising and externalising comorbidities in children with attention-deficit/hyperactivity disorder (ADHD). *Europ Child Adolesc Psychiat.* 2013;24:31-40.
17. Noble GS, O'Laughlin L, Brubaker B. Attention deficit hyperactivity disorder and sleep disturbances: consideration of parental influence. *Behav Sleep Med.* 2012;10:41-53.

18. Hiscock H, Roberts G, Efron D, et al. Children Attending Paediatricians Study: a national prospective audit of outpatient practice from the Australian Paediatric Research Network. *MJA.* 2011;194:392-397.

19. Efron D, Davies S, Sciberras E. Current Australian paediatric practice in the assessment and treatment of Attention Deficit Hyperactivity Disorder: A survey and practice audit. Royal Australasian College of Physicians; 2012; Brisbane.

20. Schulz KF, Altman DG, Moher D. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. *BMC medicine.* 2010;8(1):18.

21. American Academy of Sleep Medicine. *International Classification of Sleep Disorders.* 3rd ed. Darien, IL: American Academy of Sleep Medicine; 2014.

22. Hiscock H, Bayer J, Price A, Ukoumunne OC, Rogers S, Wake M. A universal parenting program to prevent early child behaviour problems: cluster randomised trial. *BMJ.* 2008;336:318–321.

23. Hiscock H, Bayer J, Gold L, Hampton A, Ukoumunne OC, Wake M. Improving infant sleep and maternal mental health: a cluster randomised trial. *Arch Dis Child.* 2007;92:952-958.

24. Quach J, Gold L, Arnup S, Sia KL, Wake M, Hiscock H. Sleep well-be well study: improving school transition by improving child sleep: a translational randomised trial. *BMJ Open.* 2013;3:e004009.

25. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap) - A metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform.* 2009;42:377-381.

26. Australian Curriculum Assessment and Reporting Authority. NAPLAN Website http://www.nap.edu.au/. 2016. Accessed 12 August 2016.

27. Lyneham HJ, Rapee RMJ. Agreement Between Telephone and In-Person Delivery of a Structured Interview for Anxiety Disorders in Children. *J Am Acad Child Adolesc Psychiatry.* 2005;44:274-282.

28. Quach J, Hiscock H, Canterford L, Wake MA. Outcomes of child sleep problems over the school-transition period: Australian population longitudinal study. *Pediatrics.* 2009;123:1287-1292.

29. Lycett K, Mensah F, Hiscock H, Sciberras E. The validity of a global measure of sleep problem severity in children with ADHD: a cross-sectional comparison with a validated multi-dimensional measure and sleep log. . *Sleep Med.* 2015;16:1377-1380.

30. DuPaul GJ, Power TJ, Anastopoulos AD, Reid R. *ADHD Rating Scale IV: Checklists, Norms, and Clinical Interpretation.* New York, NY: The Guilford Publications Inc; 1998.

31. Owens J, Spirito A, McGuinn M. The Children's Sleep Habits Questionnaire (CSHQ): Psychometric properties of a survey instrument for school aged children. *Sleep.* 2000;23:1043-1051.

32. Mindell JA, Owen J. *A Clinical Guide to Pediatric Sleep: Diagnosis and Management of Sleep Problems in Children and Adolescents. 2nd ed.* 2nd ed. Philadelphia, PA: Lippincott Williams & Wilkins 2010.

33. Barnett AG, van der Pols JC, Dobson AJ. Regression to the mean: what it is and how to deal with it. *Int J Epidemiol.* 2005;34:215-220.

34. Australian Bureau of Statistics. *Socio-Economic Indexes for Areas (SEIFA) - Technical Paper.* Canberra: ABS; 2006.

35. Coast J. Is economic evaluation in touch with society's health values? *BMJ.* 2004;329:1233-1236.

36. Drummond M, Sculpher M, Torrance G, O'Brien B, G. S. *Methods for the economic evaluation of health care programs. 3rd ed.* Oxford: Oxford University Press; 2005.

37. Gibbard D, Coglan L, MacDonald J. Cost-effectiveness analysis of current practice and parent intervention for children under 3 years presenting with expressive language delay. *Int J Lang Comm.* 2004;39:229-244.

38. Polanczyk GV, Willcutt EG, Salum GA, Kieling C, Rohde LA. ADHD prevalence estimates across three decades: an updated systematic review and meta-regression analysis. *Int J Epidemiol.* 2014;43:434-442.

39. Owen JA, Spirito A, McGuinn M, Nobile C. Sleep habits and sleep disturbance in elementary school-aged children. *J Dev Behav Pediatr.* 2000;21:27-36.

40. Goodman R. Psychometric properties of the Strengths and Difficulties Questionnaire. *J Am Acad Child Adolesc Psychiatry.* 2001;40:1337-1345.

41. Stingaris A, Goodman R, Ferdinando S, et al. The Affective Reactivity Index: a concise irritability scale for clinical and research settings. *J Child Psychol Psychiatry.* 2012;53:1109-1117.

42. Stevens K. Valuation of the Child Health Utility 9D Index. *Pharmacoeconomics* 2012;30:729-747.

43. Varni JW, Limbers CA, Burwinkle TM. Parent proxy-report of their children's health-related quality of life: an analysis of 13,878 parents' reliability and validity across age subgroups using the PedsQL™ 4.0 Generic Core Scales. *Health Qual Life Out.* 2007;5:1043-1051.

44. Colonna A, Smith AB, Pal DK and Gringras P. Novel mechanisms, treatments, and outcome measures in childhood sleep. *Front Psychol* 2015;6:602. doi: 10.3389/fpsyg.2015.00602

45. Pickering S, Gathercole S. *Working Memory Test Battery for Children (WMTB-C).* London: Pearson Education Ltd; 2001.

46. Wilkinson GS, Robertson GJ. *Wide Range Achievement Test 4 (WRAT 4).* Lutz, FL: Psychological Assessment Resources; 2006.

47. Moul C, Cauchi A, Hawes DJ, Brennan J, Dadds MR. Differentiating autism spectrum disorder and overlapping psychopathology with a brief version of the social responsiveness scale. *Child Psychiatry Hum Dev.* 2015;46:108-117.

48. Furukawa TA, Kessler RC, Slade T, Andrews G. The performance of the K6 and K10 screening scales for psychological distress in the Australian National Survey of Mental Health and Well-Being. *Psychol Med.* 2003;33:357-362.

49. Zubrick SR, Lucas N, Westrupp EM, Nicholson JM. *Parenting measures in the Longitudinal Study of Australian Children: Construct validity and measurment quality Waves 1 to 4.* Canberra, Australia: Department of Social Services; 2014.

AUTHORS' CONTRIBUTIONS:

ES, HH, HH, NR and LG conceived the study. MM and NH coordinated the study. ES drafted the current manuscript. TS contributed to the design and analytic components of the study. All authors contributed, read and approved the final manuscript.

FUNDING STATEMENT:

This study is funded by the Australian National Health and Medical Research Council (NHMRC; project grant no. 1058827). Dr Sciberras' position is funded by an NHMRC Early Career Fellowship in Population Health 1037159 (2012–2015) and an NHMRC Career Development Fellowship 1110688 (2016-19). Professor Hiscock's position is funded by an NHMRC Career Development Fellowship 1068947 (2014-2017). This research was supported by the Victorian Government's Operational Infrastructure Support Program to the MCRI.

COMPETING INTERESTS STATEMENT:

All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare that they, their spouses, partners or children do not have any financial and non-financial relationships with companies that may be relevant to the submitted work to declare.

Figure 1:

Participant Flow

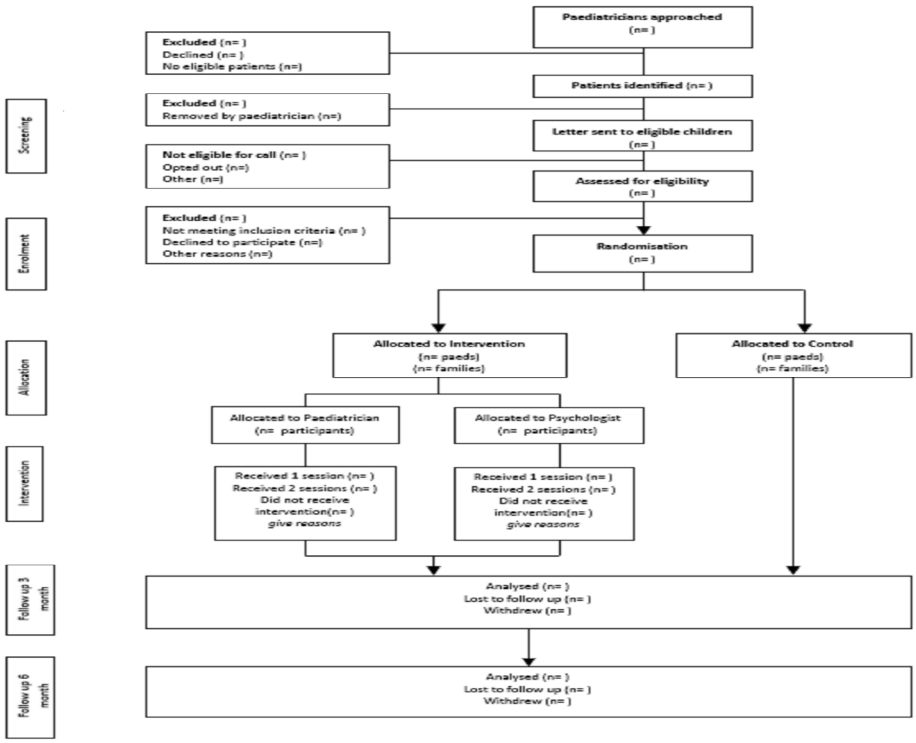


Figure 1: Participant Flow

219x165mm (300 x 300 DPI)

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description
Administrative information		
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym PAGE 1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry PAGE 3
	2b	All items from the World Health Organization Trial Registration Data Set PAGE 3 + YES SEE TRIAL REGISTRY
Protocol version	3	Date and version identifier PAGE 3 + YES SEE TRIAL REGISTRY
Funding	4	Sources and types of financial, material, and other support PAGE 18, 29
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors PAGE 1, 29
	5b	Name and contact information for the trial sponsor NA
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities NA
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee) NA
Introduction		
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention PAGE 4-8
	6b	Explanation for choice of comparators PAGE 13-14
Objectives	7	Specific objectives or hypotheses PAGE 7-8
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory) PAGE 8

Methods: Participants, interventions, and outcomes

Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained PAGE 8
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists) PAGE 11-13
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered PAGE 14-16, 20-21
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease) NA
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests) NA
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial PAGE 14
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended PAGE 16-17, 22-23
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure) PAGE 8-10, 14-16
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations PAGE 13
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size PAGE 13

Methods: Assignment of interventions (for controlled trials)

Allocation:

Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions PAGE 14

Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned PAGE 14
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions PAGE 14
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how PAGE 14, 16
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial NA
Methods: Data collection, management, and analysis		
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol PAGE 16-17, 22-23
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols PAGE 13, 16-17, 22-23
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol PAGE 17
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol PAGE 17-18
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses) PAGE 17-18
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation) PAGE 17-18
Methods: Monitoring		
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed NA

	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial NA
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct PAGE 16
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor NA

Ethics and dissemination

Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval PAGE 18
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators) NA
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32) PAGE 16
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable PAGE 16
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial PAGE 16
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site PAGE 29
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators SEE TRIAL REGISTRY
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation NA
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions PAGE 18
	31b	Authorship eligibility guidelines and any intended use of professional writers NA
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code SEE TRIAL REGISTRY

Appendices

Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates SEE TRIAL REGISTRY
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable N/A

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

BMJ Open

Does a brief, behavioural intervention, delivered by paediatricians or psychologists improve sleep problems for children with ADHD? Protocol for a cluster-randomised, translational trial

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2016-014158.R2
Article Type:	Protocol
Date Submitted by the Author:	26-Jan-2017
Complete List of Authors:	Sciberras, Emma; Murdoch Childrens Research Institute, Centre for Community Child Health Mulraney, Melissa; Murdoch Childrens Research Institute Heussler, Honey; Mater Medical Research Institute Rinehart, Nicole; Deakin University Schuster, Tibor; Murdoch Childrens Research Institute, Medical Statistics Gold, Lisa; Deakin University, Deakin Health Economics Hayes, Nicole; Mater Medical Research Institute Hiscock, Harriet; The Royal Children's Hospital, Centre for Community Child Health
Primary Subject Heading:	Mental health
Secondary Subject Heading:	Public health
Keywords:	attention deficit disorder with hyperactivity, randomised controlled trial, effectiveness, treatment, sleep, child

Does a brief, behavioural intervention, delivered by paediatricians or psychologists improve sleep problems for children with ADHD? Protocol for a cluster-randomised, translational trial

Authors E Sciberras, DPsych,[1,2,3] M Mulraney, PhD,[2,3] H Heussler,[4] N Rinehart, PhD,[1] T Schuster,[2] L Gold PhD,[1,2] N Hayes PhD,[4] H Hiscock MD.[2,3,5]

Affiliations [1] Deakin University, Geelong, Vic Australia

[2] Murdoch Childrens Research Institute, Parkville, Vic Australia

[3] University of Melbourne, Department of Paediatrics, Parkville, Vic Australia

[4] Mater Research Institute-University of Queensland, South Brisbane, Qld Australia

[5] The Royal Children's Hospital, Parkville Vic Australia

Running title Behavioural sleep intervention for children with ADHD

Key words attention deficit disorder with hyperactivity, sleep, child, randomised controlled trial, effectiveness, treatment

Correspondence to

Dr Emma Sciberras

School of Psychology, Deakin University, Melbourne Burwood Campus, BC Building, Level 5, 221 Burwood Hwy, Burwood VIC 3125, AUSTRALIA

P +61 3 9251 7222 email emma.sciberras@deakin.edu.au

ABSTRACT

Introduction: Up to 70% of children with Attention-Deficit/Hyperactivity Disorder (ADHD) experience sleep problems. We have demonstrated the efficacy of a brief behavioural intervention for children with ADHD in a large randomised controlled trial (RCT) and now aim to examine whether this intervention is effective in real-life clinical settings when delivered by paediatricians or psychologists. We will also assess the cost-effectiveness of the intervention.

Methods and analysis: Children aged 5-12 years with ADHD (n=320) are being recruited for this translational cluster RCT through paediatrician practices in Victoria and Queensland, Australia. Children are eligible if they meet criteria for ADHD, have a moderate/severe sleep problem, and meet American Academy of Sleep Medicine criteria for either chronic insomnia disorder or delayed sleep-wake phase disorder; or are experiencing sleep-related anxiety. Clinicians are randomly allocated at the level of the paediatrician to either receive the sleep training or not. The behavioural intervention comprises two consultations covering sleep hygiene and standardized behavioural strategies. The primary outcome is change in the proportion of children with moderate/severe sleep problems from moderate/severe to no/mild by parent report at 3 months post-intervention. Secondary outcomes include a range of child (e.g., sleep severity, ADHD symptoms, quality of life, behaviour, working memory, executive functioning, learning, academic achievement) and primary caregiver (mental health, parenting, work attendance) measures. Analyses will address clustering at the level of the paediatrician using linear mixed effect models adjusting for potential a priori confounding variables.

Ethics and dissemination: Ethics approval has been granted. Findings will determine whether the benefits of an efficacy trial can be realised more broadly at the population level and will inform the development of clinical guidelines for managing sleep problems in this

population. We will seek to publish in leading international paediatric journals, present at major conferences and through established clinician networks.

Registration details: Current Controlled Trials ISRCTN50834814

Article summary

Strengths and limitations

- First translational trial to determine whether a brief, behavioural sleep intervention has benefits for children with ADHD when delivered in 'real-life' clinical settings by paediatricians and psychologists.
- The inclusion of blinded teacher reports, as well as blinded direct assessment measures to minimise bias.
- Inclusion of economic analyses, which provide data on the cost-effectiveness of the program.
- Limited generalisability to non-English speaking families and children with ADHD presenting with serious medical conditions and/or intellectual disability.
- Sleep problems assessed using unblinded parent report as opposed to objective measures.

INTRODUCTION

Sleep problems are common and more persistent in children with ADHD, and associated with poorer child and family well-being.[1-4] Efficacy Randomised Controlled Trials (RCTs) have shown that sleep problems are amenable to intervention[5-10] in children with ADHD, particularly behavioural interventions.[8-10] However, it is unknown whether the same benefits will be observed when such interventions are delivered by practitioners in 'real life' clinical settings. This article describes the protocol for the Sleeping Sound with ADHD Translational RCT, which aims to assess the effectiveness of a behavioural sleep intervention designed for children with ADHD, when delivered by psychologists or paediatricians in their daily clinical practice.

Sleep problems in children with ADHD

Up to 70% of children with ADHD experience sleep problems,[1,2] compared with 20-30% of children in the general population.[11] Sleep problems experienced by children with ADHD largely comprise difficulties initiating and/or maintaining sleep, with the most common sleep problems being difficulty falling asleep (reported by 84% of parents of children who report a sleep problem for their child with ADHD), bedtime resistance (68%), tiredness upon waking (62%) and difficulty waking in the morning (56%).[2] Medical conditions such as obstructive sleep apnoea (OSA) can also affect sleep in children with ADHD, although behavioural sleep problems appear more common.[12] In this study we use the term sleep problems to denote those difficulties that can be addressed using behavioural intervention. Sleep problems have been associated with worse functioning for children with ADHD including poorer quality of life (QoL), behaviour, daily functioning, and working memory, as well as increased school absenteeism.[2,4,13] They thus represent an important modifiable target for intervention.

A number of factors have been associated with sleep problems in children with ADHD and it is possible that biological sleep problems such as restless legs syndrome,

obstructive sleep apnoea and narcolepsy can lead to continued sleep disruptions.[12] Insomnia can be a side-effect of stimulant medication,[1,14] although unmedicated children with ADHD also experience higher rates of sleep problems relative to non-ADHD controls.[15] Comorbid externalising and internalising comorbidities are each associated with a 2-fold increase in moderate/severe sleep problems in children with ADHD, while co-occurring internalising and externalising comorbidities are associated with a 3-fold increase.[16] Parenting inconsistency in daily household routines has also been associated with increased bedtime resistance in this group.[17] Biologically, there is overlap in the brain regions and genetic factors (e.g., catecholaminergic system, CLOCK genes) associated with both ADHD and sleep disorders/arousal regulation.[1] ADHD is also a highly genetic condition and parents likely are affected by symptoms such as disorganisation and impulsivity, which may impact on child sleep.

Treating sleep problems in children with ADHD using behavioural strategies

We recently published our efficacy RCT evaluating the impact of a behavioural sleep program in children with ADHD and moderate/severe sleep problems (n=244 5-12 year old children with ADHD).[8] Children were recruited from 21 paediatric practices across Victoria, Australia and randomised to either a behavioural sleep intervention (n=122) or a usual care comparison group (n=122). Intervention families attended two x 50 minute individual sessions (held two weeks apart) with a clinician trained in the intervention (psychologist or trainee paediatrician), comprising a standardised yet flexible intervention, tailored to the child's sleep problems and family preferences.

The intervention was associated with improved child outcomes at three and six months post-randomisation including improved parent-reported child sleep, ADHD symptom severity, QoL, daily functioning and behavior.[8] Intervention children also had improved teacher-reported classroom behavior, as well as improved school attendance and working

memory assessed via blinded assessment.[8] There were small improvements in sleep duration for a subsample that completed actigraphy.[8] Although the intervention was associated with improved caregiver work attendance and mental health three months later, these benefits were not observed at six months.[8]

Similarly, two additional randomised controlled trials have demonstrated the efficacy of improving sleep problems in children with ADHD. Keshavarzi et al. reported that a 12-week sleep-training program for children with ADHD aged 10 years (n=40) had beneficial effects for sleep and psychosocial functioning when compared to controls with ADHD who did not receive the intervention (n=20) and typically developing children (n=20).[9] However the professional group responsible for delivering the intervention was not reported. Corkum and colleagues also recently reported the beneficial effects of their distance sleep intervention delivered by paraprofessionals for childhood insomnia in a mixed sample of children with and without ADHD (n=61).[10] Improvements were identified at 2 and 6 months for sleep assessed using parent report as well as actigraphy, and benefits were also reported for broader child psychosocial health.[10]

Although RCTs have shown that melatonin is associated with improved sleep onset latency for children with ADHD,[5-7] broader benefits for daily functioning including ADHD symptom severity have yet to be shown.

Managing sleep problems in children with ADHD through existing clinical services

Although three trials have now shown that it is possible to improve sleep problems in children with ADHD using behavioural approaches, it remains to be seen whether it is possible to replicate such approaches and improve outcomes for children with ADHD in 'real life' clinical settings when delivered by their treating clinicians (e.g., community paediatricians or psychologists) rather than by clinicians hired to deliver interventions in tightly controlled research trials. We are now testing the translation of this program at the

population level by training community paediatricians and psychologists to deliver this sleep intervention to children with ADHD and sleep problems. If this intervention can be translated successfully to the population level within existing workforces, then this would have the real potential to improve outcomes for children with ADHD and their families. If cost-effective, it could be readily incorporated into the existing health system.

Paediatricians are the main care providers for ADHD in Australia.[18] The paediatrician's role includes both the assessment and treatment (behavioural and medication-based) of ADHD and associated comorbidities (including sleep problems, if identified). Visits to a paediatrician are subsidised by Australia's Medicare scheme, however, families may experience out of pocket costs for these visits. Paediatricians (and general practitioners) may also refer children to a psychologist in the community to manage comorbid behaviours.[19] In Australia, this referral is facilitated by the Medicare Better Access to Mental Health Scheme, which provides subsidised access to up to 10 psychology sessions in a calendar year, provided the criteria for a DSM condition are met. We have deliberately designed our sleep intervention so that it is feasible for both paediatricians and psychologists to deliver within the Australian Medicare scheme and within their typical consultation durations.

Aims and hypotheses

Building on our efficacy trial, we aim to determine whether the Sleeping Sound with ADHD intervention, delivered by paediatricians or psychologists in their usual work setting can replicate the benefits of the efficacy trial. Therefore, in this translational, cluster-randomised trial we aim to determine whether a brief sleep intervention delivered by paediatricians or psychologists:

1. Decreases the prevalence of children with moderate/severe sleep problems from moderate/severe to no/mild by parent report at 3 months post-intervention (**primary outcome**).

2. Improves child and family functioning at 3 and 6 months post-intervention **(secondary outcome)**.
3. Is cost-effective **(secondary outcome)**.

We hypothesise that, compared to the control children at 3 (primary outcome timepoint) and 6 months post-intervention, a brief behavioural sleep intervention will:

1. Decrease prevalence of child sleep problems from moderate/severe to no/mild;
2. Improve functioning in other child (sleep severity, ADHD symptoms, QoL, behaviour, working memory, executive functioning, learning, academic achievement, school attendance) and primary caregiver (mental health, parenting, work attendance) outcome domains.
3. Be cost-effective.

METHODS AND ANALYSIS

Overall Study Design

This is a cluster RCT of a behavioural sleep intervention versus usual care conducted in Victoria and Queensland, Australia (see Figure 1). The trial will be reported according to Consolidated Standards of Reporting Trials guidelines and the extension report of non-pharmacological interventions.[20]

Participants

Participants are parents of children aged 5-12 years at the time of recruitment with paediatrician-diagnosed and DSM-5 confirmed ADHD and a moderate to severe sleep problem as defined by the American Academy of Sleep Medicine diagnostic criteria[21]: chronic insomnia disorder, delayed sleep-wake phase disorder, or sleep related anxiety.

Recruitment of health professionals

Given that paediatricians are the main healthcare provider for children with ADHD, recruitment and randomisation occurs at the level of the paediatrician. Paediatricians are recruited via the Australian Paediatric Research Network or through clinical contacts.[18] Interested paediatricians are invited to attend a briefing session in which the study requirements and timetable is presented and paediatricians have the opportunity to ask questions. Interested paediatricians are sent a follow up email thanking them for their interest, asking them to sign an individual Memorandum of Understanding (MOU) if they consent to participation, and asking them to provide a list of psychologists to whom they refer patients. By signing the MOU, paediatricians agree to: (1) participate in training if randomised to the intervention arm; (2) deliver the sleep program to intervention families ***or*** refer the child to a psychologist to deliver the sleep program if allocated to the intervention; (3) not share the intervention materials with control group paediatricians if allocated to the intervention; and (4) allocate time for intervention session bookings.

Once paediatricians have been recruited, psychologists are invited to whom the paediatricians have indicated they refer patients. Psychologists are only recruited for the intervention arm of the project and have no contact with control participants. The research team then informs psychologists about the study via email or phone. The researchers then send psychologists who express interest in participating a follow up email thanking them for their interest and asking them to sign an individual MOU, agreeing to: (1) participate in training; (2) deliver the sleep program to intervention families referred by paediatricians; (3) use intervention materials only with children enrolled in the study; and (4) not share the intervention materials with any other families they see during the study period. This approach has worked well to minimise contamination in our previous RCTs.[22-24]

Screening children for sleep problems and recruiting families

This translational trial uses, where possible, the same procedures that were used in our efficacy trial.[8] Paediatricians pre-identify their patients with ADHD, aged between 5-12 years, seen within the last 12 months, either through their medical software or through case notes. Paediatricians then send a letter to the child's primary caregiver inviting them to take part. The letter advises families that the research team will ask them about their child's sleep and ADHD symptoms. An 'opt out' approach is used, whereby parents are asked to contact the paediatrician if they *do not* wish to learn more about the study. If parents do not opt out within a two-week period, the paediatrician provides the research team with the contact details of the families. Only 9% of families opted out in our efficacy trial.[8] Paediatricians also have the option to use an active consent process. In these cases paediatricians send an 'opt in' version of the study invitation letter.

The research team then contacts interested (or not opted-out) families via telephone to ascertain if the child meets inclusion/exclusion criteria. Eligible families are sent a parent information statement and consent form (to participate in the RCT and for optional consents outlined below) as and a baseline survey. Families have the option to complete hard copy surveys or online surveys (via REDCap - a secure, web-based application).[25] Surveys are completed by the child's primary caregiver. Parents have the option to consent to have their child's school teacher complete a survey about their child's behaviour. If consent is provided by the primary caregiver and school, a link to an online survey is sent to teachers. Parents also have the option to consent to being contacted for ethically approved future research, for the research team to keep their de-identified data to be shared with future ethically approved research, and to allow the research team to link with their child's *National Assessment Program – Literacy and Numeracy* (NAPLAN) results. NAPLAN is a national assessment of literacy and numeracy Australian children complete in Grades 3 and 5, and Years 7 and 9.[26]

Once caregivers provide written consent, the research team contacts them to complete the Anxiety Disorders Interview Schedule for Children (ADIS-C) over the telephone to assess comorbid internalising and externalising diagnoses in children with ADHD.[27] To ensure we administer the telephone interviews consistently we are recording 10% of the sample to test inter-rater reliability.

Inclusion/exclusion criteria (all assessed via telephone)

Inclusion criteria

a. Child aged between 5-12 years at the time of the recruitment call.

b. Child's sleep is a moderate-severe problem for the caregiver ascertained using the following question: Has your child's sleep been a problem for you over the past 4 weeks?' If 'yes', they are asked to rate severity (mild, moderate or severe). This measure has been used in studies of children with and without ADHD and has good agreement with the Children's Sleep Habits Questionnaire.[2,28,29]

c. Child sleep problem meets the International Classification of Sleep Disorders – Third Edition criteria[21] for an eligible sleep disorder (chronic insomnia disorder, delayed sleep-wake phase disorder) or sleep-related anxiety assessed using study-designed questions. To meet criteria for *chronic insomnia disorder* in this study children need to meet criterion A (one or more of the following: difficulty initiating sleep, difficulty maintaining sleep, waking earlier than desired, resistance going to bed, difficulty sleeping without a caregiver), B (evidence of impairments related to the sleep difficulty such as daytime sleepiness, impaired social, family, or academic performance etc.), C (sleep problem not be explained by inadequate sleep opportunity or circumstances) and D and E (symptoms and associated impairment must have been present 3 times a week or more for at least 3 months).[21] To meet criteria for *delayed sleep-wake phase disorder* in this study, criterion A (significant phase delay as shown

by difficulty initiating sleep and awakening at a required time), B (delayed sleep-wake phase must have been present for at least 3 months), and C (improved sleep quality and duration when allowed to choose their own schedule) need to be satisfied.[21] Children were accepted into the study on the basis of experiencing sleep-related anxiety if the caregiver endorses significant difficulty falling asleep at night, in addition to anxious behaviour at bedtime (e.g., fearful behaviours such as crying, asking for reassurance or lying in bed worrying).

d. Child meets DSM 5 criteria for ADHD assessed via the 18-item ADHD Rating Scale IV - a validated scale measuring the core symptoms of ADHD.[30] Caregivers need to rate at least 6 of 9 of the inattention and/or hyperactivity/impulsivity items as occurring 'often' or 'very often' in order to meet current symptom criteria. Caregivers are asked to rate symptoms off stimulant medication. Additional questions are then asked to ensure symptoms have been present for at least 6 months ('Did your child have these symptoms for at least 6 months before being diagnosed with ADHD?), and contribute to cross-situational impairment ('Are these symptoms present at home, school and/or when out socially?) Given the target age range all participants will meet age of onset criteria. We do not assess whether the symptoms were better explained by another mental disorder.

Children are eligible to participate if they are taking melatonin or any other sleep inducing medication, as long as the inclusion criteria are still met despite medication use.

Exclusion criteria

a. Suspected OSA identified using three OSA items from the Children's Sleep Habits Questionnaire.[31] Paediatrician investigators Hiscock and Heussler telephone caregivers of children with suspected OSA to ask further about their symptoms and if

OSA is suspected, these children are excluded and referred to appropriate clinical services as per usual clinical care (1% in our efficacy trial).[8]

b. No longer meeting criteria for ADHD at the time of recruitment.

c. Major illness or disability (e.g., intellectual disability). Parents are asked if their child has ever been diagnosed with an intellectual disability or serious medical condition. If yes, parents are asked to provide further details (e.g., IQ score, diagnosis). If clarification is needed permission is sought to recontact the paediatrician to obtain relevant information from the child's medical record. Common comorbidities including internalising/externalising disorder and autism spectrum disorder (ASD) are not excluded.

d. Parents with insufficient English language proficiency to complete study documentation and/or participate in the intervention.

e. Participated in our original efficacy trial.

Sample size

Sample size planning is based on the primary outcome, the proportion of children for whom parents no longer report moderate/severe sleep problems at 3 months. In the efficacy study, at 3 months, 56% and 30% of parents in the intervention and control group, respectively, reported that their child's sleep was still a moderate/severe problem i.e. a difference of 26%. We conservatively assume a smaller difference of 20%, i.e. 56% vs 36% to be observed in this trial. In order to have 80% power in detecting this difference at a two-sided type one error level of 5%, a group sample size of 107 individuals (total sample size n=214) is required. As this is a cluster controlled trial (clustered at the level of the paediatrician to minimise contamination), we will inflate our sample size by a design effect of 1.2 where the design effect = $1+(n-1)\cdot r$ with n=3 (the number of children seen by each paediatrician) and

r=0.1 (the conservatively assumed intra-cluster correlation coefficient, based on our efficacy RCT). Allowing for 20% drop out to 3 months and accounting for clustering, we need to recruit 160 children in each study arm (total sample size n=320). All recruitment procedures described have been used in our previous trials to achieve similar recruitment numbers.

Randomisation

Randomisation occurs at the level of the paediatrician. Paediatricians are randomly allocated to either receive the sleep training or not by an independent researcher, thereby avoiding potential contamination if all paediatricians were to be trained in the program. Randomisation is based on a pre-generated group allocation sequence from the Murdoch Childrens Research Institute's Clinical Epidemiology and Biostatistics Unit and is stratified by location of the paediatrician (regional or metropolitan area). The randomisation is also stratified by the predicted number of enrolled patients (less than 10 and 10 or more). Paediatricians, families and researchers are blind to group allocation at the time of recruitment.

If the paediatrician is assigned to the intervention group and has more than four patients enrolled, families are randomised to receive the intervention from either the paediatrician or psychologist. This second step of randomisation takes place after family recruitment is complete. The research team then sends the paediatrician a letter informing them of whether they will be receiving the sleep training or not. In addition, participating families are also sent a letter informing them of whether they will be receiving the sleep intervention or not.

Families of children attending a paediatrician randomised to the control group receive 'usual care' which involves seeing their paediatrician as per usual regarding their child's ADHD. Our research has shown that this does not routinely include addressing sleep issues.[2] In Australia, paediatricians typically see children with ADHD every 6 months to check their

height, weight, blood pressure and re-issue a script for medication (valid for 6 months), where necessary.

Intervention training

The intervention is designed to be feasible to deliver in paediatricians' and psychologists' practice. Intervention group paediatricians and psychologists are trained to deliver the same program described for our efficacy trial[8] in one 3.5-hour session. Training occurs conjointly for paediatricians and psychologists, where possible, with investigators Hiscock, Sciberras and Heussler to maximise fidelity. Training addresses normal sleep patterns in school-aged children and highlights the importance of sleep hygiene practices such as consistent bedtime routines and keeping bedrooms media-free. The intervention includes verbal and written information of standard sleep intervention strategies as recommended by the American Sleep Association[32] and addresses common sleep problems experienced at the beginning of, and during, the night. A summary of sleep problems addressed and management strategies are provided in Table 1. Training focuses on how these strategies can be individualised for families and includes evidence-based instructional strategies such as role play, feedback, modelling practice, and use of checklists. Training is supported by a manual and written parent education materials.

Prior to training, paediatricians and psychologists complete a "pre-quiz" to establish their baseline knowledge, skills and attitudes in relation to child sleep problems and their management. A "post-quiz" following training is used to assess changes in knowledge, confidence, and perceived competence in the management of child sleep problems.

Intervention delivery

Paediatricians and psychologists are sent an intervention package for each child allocated to them containing the child's contact details, a clinical checklist to complete after each appointment and parent education materials. Families contact the clinician they have been

allocated to make an appointment (up to 30 minutes for paediatricians, up to 50 minutes for a psychologist) to discuss their child's sleep, with a follow-up session (up to 30 minutes for paediatricians, up to 50 minutes for a psychologist) approximately two weeks later and if needed, a final 15-20 minute phone call a further two weeks after that. The differences in consultation duration reflect real life clinical practice. We record the actual duration of all consultations, which will enable us to examine the relationship between intervention dose and outcomes. Children are present at all face to face appointments. The first session focuses on an assessment of the child's sleep problem, providing information about normal sleep and sleep cycles, giving the family a sleep diary to complete, advice about sleep hygiene, and a plan specifically tailored to the child's particular sleep disorder. The second session and follow-up phone call include a review of the sleep diary, re-enforcement/trouble shooting of existing strategies and the introduction of new strategies, where appropriate.

The research team contacts families within one month post-randomisation to ensure an appointment has been made with either their paediatrician or a psychologist and to encourage them to make the appointment if they have not yet done so.

Follow-up

We mail/email follow-up surveys to families and teachers at 3 and 6 months post-intervention (measured from first intended intervention session for intervention families with controls followed up at the median date of intervention follow-up) to determine both short and longer term changes in primary and secondary outcomes. Teachers are not informed of the child's intervention group status. For intervention families only, the 3 month survey also asks about the behavioural intervention components received, usefulness of the intervention, ease of use of strategies, costs experienced by families in accessing the program and any negative events/experienced. At 6 months a trained research assistant completes a blinded direct

assessment of child executive functioning, learning, working memory, academic functioning, sleep and QoL via home visits (of 45 minutes duration).

Measures

All measures administered at baseline, 3 and 6 months are summarised in Table 2. The majority of measures were used in our efficacy trial. We now additionally measure academic functioning given that our efficacy trial showed a trend towards improvement in working memory, which is a key determinant of academic functioning. For similar reasons we also include a more detailed assessment of cognitive and executive functioning. The baseline questionnaire includes family (e.g., family composition, parental education and age, language spoken at home, annual household income) and child demographic and medical (e.g., medication, diagnosed comorbidities etc.) characteristics.

The research team prospectively records resources used to administer all program components to facilitate economic analyses. Families also report time, travel and out-of-pocket costs associated with visits as well as those costs associated with child ADHD medication/prescriptions.

Data analysis

Primary (aim 1) and secondary (aim 2) analyses will be based on the 'intention to treat' population at the level of the individual child and will adjust for clustering at the level of the paediatrician using a generalised linear mixed effect model (logit link function) for the binary primary outcome (proportion of children with moderate/severe sleep problems). For primary and secondary analyses, the stratification variable *'location of study site (practice)'* as well as an indicator variable for the *type of health care professional* who delivered the intervention (paediatrician or psychologist) will be considered as adjustments variables. For all analyses model-based effect estimates (risk differences and risk ratios) will be reported along with 95% confidence intervals. Because of the range of outcomes and time-points, the results will

be considered in their totality and interpreted with suitable caution regarding formal conclusions of "statistical significance". In order to reduce potential confounding bias due to differential patient-drop out over time, multiple imputation methodology will be considered to replace missing outcome data in the primary efficacy analysis. All secondary analyses (aim 2) will be adjusted for baseline scores and stratification variables wherever possible, in order to increase precision of comparisons.[33] For primary and secondary analyses, we will present results of analyses both unadjusted and adjusted for further potential outcome predictor variables (child age, medication use, comorbidities, and family socio-demographic characteristics (Socioeconomic Index for Advantage linked to the family's postcode),[34] parent high school completion, and parent age). Syntax will be written before database lock, which will cover the primary and secondary analyses. Participant level data is available on request.

Cost-effectiveness analyses

The economic analysis (aim 3) will first present cost-consequences analysis, then proceed to cost-effectiveness analysis against the primary outcome (*prevalence of sleep problems*) measure as the primary economic analysis. Secondary economic analyses will include cost-utility analysis against CHU9D-based QALYs.[35,36] These analyses will be conducted from both the health care and broader societal perspectives (as cost-effectiveness can vary significantly by perspective)[37] and will include extensive sensitivity analyses to test the impact of uncertainty in data and sensitivity to evaluation approach.

ETHICS AND DISSEMINATION

ADHD affects approximately 5% of school-aged children[38] and is frequently associated with sleep problems, which worsen child and family outcomes.[2] Findings will determine whether the benefits of an efficacy trial can be realised more broadly at the population level and whether it is cost-effective to do so. If cost-effective, we expect the following outcomes: 1)

the best evidence yet that addressing sleep problems improves outcomes for children with ADHD; and 2) a ready-to-use intervention that is tailored to the Australian health system, and can be replicated internationally. Findings will inform the development of clinical guidelines for managing sleep problems in this population. We will seek to publish in leading international paediatric journals, present at major conferences and disseminate findings through established clinician networks.

This project has been funded by the National Health and Medical Research Council of Australia (1106427) and has been granted ethics approval from The Royal Children's Hospital (34072), University of Queensland (2014001555), Mater Hospital (RG-14-349), Deakin University (2015-211), Victorian Department of Education & Training (2014_002519), The Queensland Department of Education & Training (550/27/1570), and the Catholic Education Office (Ballarat; Brisbane; Melbourne; Toowoomba) Human Research Ethics Committees.

Table 1. Key behavioural sleep management strategies

Sleep disorder	Definition	Examples of behavioural strategies
Sleep onset association disorder	Child associates falling asleep with a person or object (e.g., television) and is unable to fall asleep without its presence.	• Adult fading (i.e. graduated extinction) using 'camping out' - gradual withdrawal of parental presence from the child's bedroom over 7-10 days. • 'Checking method' – parent checks on the child at regular time intervals (2, 5, or 10 minutes, with intervals increasing over time).
Delayed sleep phase	Shift in the child's sleep-wake cycle, in which the child cannot fall asleep until late and then wakes late in the morning.	• Bedtime fading - child's bedtime is temporarily set later to when they are usually falling asleep and gradually brought forward. The child is then woken at a pre-set time in the morning. • Early morning light exposure.
Limit setting sleep disorder	Child refusal to go to bed and general non-compliant behaviour at bedtime. Parent struggles to set appropriate and consistent bedtime limits.	• Parent management strategies - ignoring child protests, rewarding compliance with bedtime routines. A 'bedtime pass', whereby the child can only leave the bedroom one time before sleep, can be used to promote compliant behaviour. • Consideration of bedtime fading or the checking method.
Primary insomnia	Child has substantial difficulty initiating and/or maintaining sleep even if they go to bed at a later time.	• Visual imagery and relaxation. • Basic cognitive restructuring. • Restricting time in bed (e.g., temporarily setting the bedtime later as per delayed sleep phase or getting out of bed and doing a relaxing activity if the child cannot

		sleep).
Night time anxiety	Specific night time fears including fear of the dark and/or child worrying about other things while in bed.	• Visual imagery and relaxation training. • Discussing fears during the day rather than just before bedtime. • Rewarding brave behaviour. • Other - use of a security object, avoiding scary television shows, use of a book to record worries.

Table 2. Summary of measures

Construct	Measures	Source[a]	T1	T2	T3
Child Outcomes					
Sleep	**Sleep problem prevalence (primary outcome) -** Primary caregiver report of child sleep problem (none/mild vs moderate/severe).[2]	P	●	●	●
	Children's Sleep Habits Questionnaire (CSHQ) - 33-item validated measure of disorders of initiating and maintaining sleep.[31] Child Sleep Self Report collected at 6 months only.[15]	P	●	●	●
	Teacher Daytime Sleepiness Questionnaire - 10-item validated scale of daytime sleepiness at school.[39]	T	●	●	●
	Sleep Hygiene scale - 7-item measure assessing sleep hygiene.[24]	P	●		●
Comorbidity	**Anxiety Disorders Interview Schedule for DSM-IV (ADIS-C) -** diagnostic interview assessing mental health disorders according to DSM-IV criteria. This is completed with parents over the telephone and has been validated for this purpose.[27]	P	●		
ADHD	**ADHD Rating Scale IV** - 18-item validated scale measuring the core symptoms of ADHD.[30]	P, T	●	●	●
Behaviour	**Strengths and Difficulties Questionnaire** – 25 items assessing the following subscales: hyperactivity/inattention, conduct problems, emotional symptoms, peer relationship problems, and prosocial behavior.[40]	P, T	●	●	●
Irritability	**Affective reactivity index (ARI) -** 6-item validated measure assessing child irritability.[41]	P	●	●	●
School attendance	**School attendance** over the preceding 3 months.[2]	P	●	●	●
Quality of Life	**Child Health Utility-9D (CHU-9D)** - 9 item measure of child quality of life used to calculate quality adjusted life years. Child report is collected at the 6 month follow up only.[42]	P, C	●		●
	Pediatrics Quality of Life Inventory 4.0 – 23-item measure of child total, physical and psychosocial QoL.[43]	P	●		●

Memory	**Sleep Suite App** – An animated iPad application that includes a continuous performance test to measure sustained attention, and 2 tests of memory consolidation and learning.[44]	C			●
Working Memory	**Working Memory Test Battery for Children –** The Backward digit span recall subtest is administered as a measure of child working memory.[45]	C			●
Academic functioning	**Wide Range Achievement Test 4 (WRAT)** – word reading and math computation subtests.[46]	C			●
	NAPLAN – standardised academic tests of reading, writing, language conventions and numeracy. Results can be compared to National or State population results and against the national minimum standard.[26]	L			●
Autism	**Social Responsiveness Scale (SRS) Brief** – 16-item measure of autism spectrum disorder symptoms.[47]	P			●
Parent Outcomes					
Mental health	**Kessler 6 (K6) -** 6-item validated measure of adult psychological stress.[48]	P	●	●	●
Work attendance	**Work attendance** over the previous 3 months.[2]	P	●	●	●
Parenting	**Parenting -** validated scales developed for the Longitudinal Study of Australian Children assessing parenting consistency (6-items) and parental warmth (5-items).[49]	P	●		●
Family costs	**Service use and costs -** families report service use over previous 3 months as well as time, travel and out-of-pocket costs associated	P		●	●

[a] P = Parent-report, T = teacher-report, C = child-report, L = data linkage; T1 = baseline; T2 = 3 months post-intervention; T3 = 6 months post-intervention.

REFERENCES

1. Cortese S, Brown TE, Corkum P, et al. Assessment and management of sleep problems in youths with attention-deficit/hyperactivity disorder. *J Am Acad Child Adolesc Psychiatry.* 2013;52(8):784-796.
2. Sung V, Hiscock H, Sciberras E, Efron D. Sleep problems in children with attention-deficit/hyperactivity disorder - Prevalence and the effect on the child and family. *Arch Pediatr Adolesc Med.* 2008;162(4):336-342.
3. Lycett K, Mensah F, Hiscock H, Sciberras E. A prospective study of sleep problems in children with ADHD. *Sleep Med.* 2014;15:1354–1361.
4. Hansen BH, Skirbekk B, Oerbeck B, Wentzel-Larsen T, H. K. Persistence of sleep problems in children with anxiety and attention deficit hyperactivity disorder. *Child Psychiatry Hum Dev.* 2013;44:290–304.
5. Weiss MD, Wasdell MB, Bomben MM, Rea KJ, Freeman RD. Sleep hygiene and melatonin treatment for children and adolescents with ADHD and initial insomnia. *J Am Acad Child Adolesc Psychiatry.* 2006;45(5):512-519.
6. Van Der Heijden KB, Smits MG, Van Someren EJW, Ridderinkhof R, Boudewijn Gunning W. Effect of melatonin on sleep, behavaiour, and cognition in ADHD and chronic sleep-onset insomnia. *J Am Acad Child Adolesc Psychiatry.* 2007;46:233-241.
7. Bendz LM, Scates AC. Melatonin treatment for insomnia in pediatric patients with Attention-Deficit/Hyperactivity Disorder. *Ann Pharmacother.* 2010;44(1):185-191.
8. Hiscock H, Sciberras E, Mensah F, et al. Impact of a behavioral sleep intervention on ADHD symptoms, child sleep and parent health: A randomized controlled trial. *BMJ.* 2015;350:h68.
9. Keshavarzi Z, Bajoghli H, Mohamadi MR, et al. In a randomized case-control trial with 10-years olds suffering from attention deficit/hyperactivity disorder (ADHD)

sleep and psychological functioning improved during a 12-week sleep-training program. *World J Biol Psychiatry.* 2014;15:609-619.

10. Corkum P, Lingley-Pottie P, Davidson F, et al. Better nights/better days—distance intervention for insomnia in school-aged children with/without ADHD: A randomized controlled trial. *J Pediatr Psychol.* 2016:1-13 doi: 10.1093/jpepsy/jsw1031.
11. Quach J, Hiscock H, Wake MA. Sleep problems and mental health in primary school new entrants: Cross-sectional community-based study. *J Paediatr Child Health.* 2012;48:1076-1081.
12. Bartholomew K, Owens J. Sleep and ADHD: a review. *Medicine and Health, Rhode Island.* 2006;89(3):91.
13. Sciberras E, DePetro A, Mensah F, Hiscock H. Association between sleep and working memory in children with ADHD: A cross sectional study. *Sleep Med.* 2015;10:1192-1197.
14. Kidwell KM, Van Dyk TR, Lundahl A, Nelson TD. Stimulant medications and sleep for youth with ADHD: A meta-analysis. *Pediatrics.* 2015;136:1144-1153.
15. Owens JA, Maxim R, Nobile C, McGuinn M, Msall M. Parental and self-report of sleep in children with attention-deficit/hyperactivity disorder. *Arch Pediatr Adolesc Med.* 2000;154(6):549-555.
16. Lycett K, Sciberras E, Mensah F, Hiscock H. Behavioural sleep problems and internalising and externalising comorbidities in children with attention-deficit/hyperactivity disorder (ADHD). *Europ Child Adolesc Psychiat.* 2013;24:31-40.
17. Noble GS, O'Laughlin L, Brubaker B. Attention deficit hyperactivity disorder and sleep disturbances: consideration of parental influence. *Behav Sleep Med.* 2012;10:41-53.

18. Hiscock H, Roberts G, Efron D, et al. Children Attending Paediatricians Study: a national prospective audit of outpatient practice from the Australian Paediatric Research Network. *MJA.* 2011;194:392-397.

19. Efron D, Davies S, Sciberras E. Current Australian paediatric practice in the assessment and treatment of Attention Deficit Hyperactivity Disorder: A survey and practice audit. Royal Australasian College of Physicians; 2012; Brisbane.

20. Schulz KF, Altman DG, Moher D. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. *BMC medicine.* 2010;8(1):18.

21. American Academy of Sleep Medicine. *International Classification of Sleep Disorders.* 3rd ed. Darien, IL: American Academy of Sleep Medicine; 2014.

22. Hiscock H, Bayer J, Price A, Ukoumunne OC, Rogers S, Wake M. A universal parenting program to prevent early child behaviour problems: cluster randomised trial. *BMJ.* 2008;336:318–321.

23. Hiscock H, Bayer J, Gold L, Hampton A, Ukoumunne OC, Wake M. Improving infant sleep and maternal mental health: a cluster randomised trial. *Arch Dis Child.* 2007;92:952-958.

24. Quach J, Gold L, Arnup S, Sia KL, Wake M, Hiscock H. Sleep well-be well study: improving school transition by improving child sleep: a translational randomised trial. *BMJ Open.* 2013;3:e004009.

25. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap) - A metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform.* 2009;42:377-381.

26. Australian Curriculum Assessment and Reporting Authority. NAPLAN Website http://www.nap.edu.au/. 2016. Accessed 12 August 2016.

27. Lyneham HJ, Rapee RMJ. Agreement Between Telephone and In-Person Delivery of a Structured Interview for Anxiety Disorders in Children. *J Am Acad Child Adolesc Psychiatry.* 2005;44:274-282.

28. Quach J, Hiscock H, Canterford L, Wake MA. Outcomes of child sleep problems over the school-transition period: Australian population longitudinal study. *Pediatrics.* 2009;123:1287-1292.

29. Lycett K, Mensah F, Hiscock H, Sciberras E. The validity of a global measure of sleep problem severity in children with ADHD: a cross-sectional comparison with a validated multi-dimensional measure and sleep log. . *Sleep Med.* 2015;16:1377-1380.

30. DuPaul GJ, Power TJ, Anastopoulos AD, Reid R. *ADHD Rating Scale IV: Checklists, Norms, and Clinical Interpretation.* New York, NY: The Guilford Publications Inc; 1998.

31. Owens J, Spirito A, McGuinn M. The Children's Sleep Habits Questionnaire (CSHQ): Psychometric properties of a survey instrument for school aged children. *Sleep.* 2000;23:1043-1051.

32. Mindell JA, Owen J. *A Clinical Guide to Pediatric Sleep: Diagnosis and Management of Sleep Problems in Children and Adolescents. 2nd ed.* 2nd ed. Philadelphia, PA: Lippincott Williams & Wilkins 2010.

33. Barnett AG, van der Pols JC, Dobson AJ. Regression to the mean: what it is and how to deal with it. *Int J Epidemiol.* 2005;34:215-220.

34. Australian Bureau of Statistics. *Socio-Economic Indexes for Areas (SEIFA) - Technical Paper.* Canberra: ABS; 2006.

35. Coast J. Is economic evaluation in touch with society's health values? *BMJ.* 2004;329:1233-1236.

36. Drummond M, Sculpher M, Torrance G, O'Brien B, G. S. *Methods for the economic evaluation of health care programs. 3rd ed.* Oxford: Oxford University Press; 2005.

37. Gibbard D, Coglan L, MacDonald J. Cost-effectiveness analysis of current practice and parent intervention for children under 3 years presenting with expressive language delay. *Int J Lang Comm.* 2004;39:229-244.

38. Polanczyk GV, Willcutt EG, Salum GA, Kieling C, Rohde LA. ADHD prevalence estimates across three decades: an updated systematic review and meta-regression analysis. *Int J Epidemiol.* 2014;43:434-442.

39. Owen JA, Spirito A, McGuinn M, Nobile C. Sleep habits and sleep disturbance in elementary school-aged children. *J Dev Behav Pediatr.* 2000;21:27-36.

40. Goodman R. Psychometric properties of the Strengths and Difficulties Questionnaire. *J Am Acad Child Adolesc Psychiatry.* 2001;40:1337-1345.

41. Stingaris A, Goodman R, Ferdinando S, et al. The Affective Reactivity Index: a concise irritability scale for clinical and research settings. *J Child Psychol Psychiatry.* 2012;53:1109-1117.

42. Stevens K. Valuation of the Child Health Utility 9D Index. *Pharmacoeconomics* 2012;30:729-747.

43. Varni JW, Limbers CA, Burwinkle TM. Parent proxy-report of their children's health-related quality of life: an analysis of 13,878 parents' reliability and validity across age subgroups using the PedsQL™ 4.0 Generic Core Scales. *Health Qual Life Out.* 2007;5:1043-1051.

44. Colonna A, Smith AB, Pal DK and Gringras P. Novel mechanisms, treatments, and outcome measures in childhood sleep. *Front Psychol* 2015;6:602. doi: 10.3389/fpsyg.2015.00602

45. Pickering S, Gathercole S. *Working Memory Test Battery for Children (WMTB-C).* London: Pearson Education Ltd; 2001.

46. Wilkinson GS, Robertson GJ. *Wide Range Achievement Test 4 (WRAT 4).* Lutz, FL: Psychological Assessment Resources; 2006.

47. Moul C, Cauchi A, Hawes DJ, Brennan J, Dadds MR. Differentiating autism spectrum disorder and overlapping psychopathology with a brief version of the social responsiveness scale. *Child Psychiatry Hum Dev.* 2015;46:108-117.

48. Furukawa TA, Kessler RC, Slade T, Andrews G. The performance of the K6 and K10 screening scales for psychological distress in the Australian National Survey of Mental Health and Well-Being. *Psychol Med.* 2003;33:357-362.

49. Zubrick SR, Lucas N, Westrupp EM, Nicholson JM. *Parenting measures in the Longitudinal Study of Australian Children: Construct validity and measurment quality Waves 1 to 4.* Canberra, Australia: Department of Social Services; 2014.

AUTHORS' CONTRIBUTIONS:

ES, HH, HH, NR and LG conceived the study. MM and NH coordinated the study. ES drafted the current manuscript. TS contributed to the design and analytic components of the study. All authors contributed, read and approved the final manuscript.

FUNDING STATEMENT:

This study is funded by the Australian National Health and Medical Research Council (NHMRC; project grant no. 1058827). Dr Sciberras' position is funded by an NHMRC Early Career Fellowship in Population Health 1037159 (2012–2015) and an NHMRC Career Development Fellowship 1110688 (2016-19). Professor Hiscock's position is funded by an NHMRC Career Development Fellowship 1068947 (2014-2017). This research was supported by the Victorian Government's Operational Infrastructure Support Program to the MCRI.

COMPETING INTERESTS STATEMENT:

All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare that they, their spouses, partners or children do not have any financial and non-financial relationships with companies that may be relevant to the submitted work to declare.

Figure 1:

Participant Flow

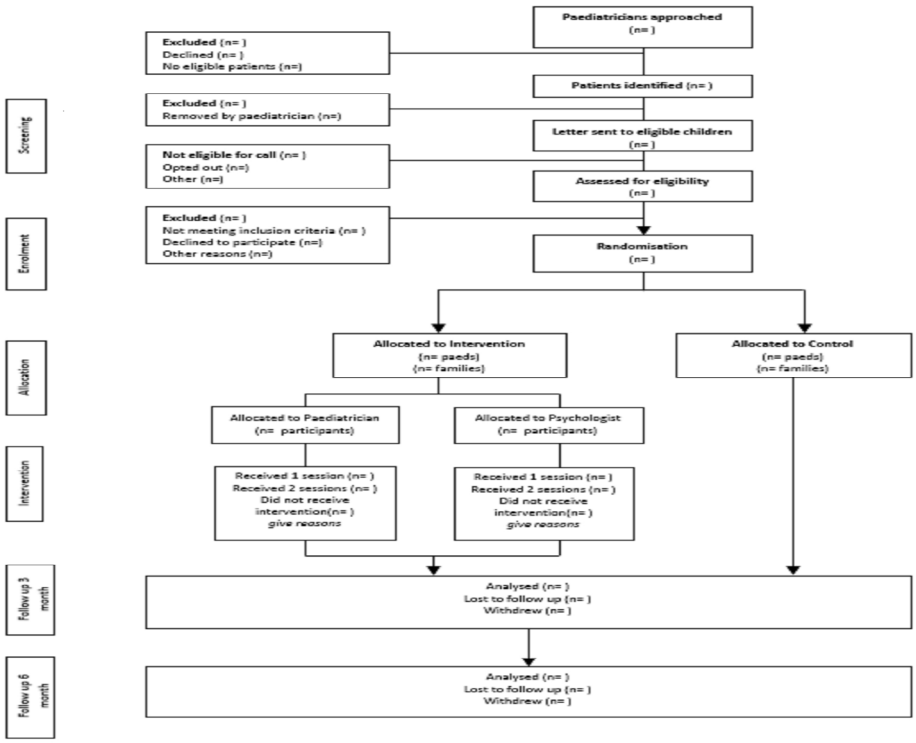


Figure 1: Participant Flow

219x165mm (300 x 300 DPI)

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description
Administrative information		
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym PAGE 1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry PAGE 3
	2b	All items from the World Health Organization Trial Registration Data Set PAGE 3 + YES SEE TRIAL REGISTRY
Protocol version	3	Date and version identifier PAGE 3 + YES SEE TRIAL REGISTRY
Funding	4	Sources and types of financial, material, and other support PAGE 16, 29
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors PAGE 1, 29
	5b	Name and contact information for the trial sponsor NA
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities NA
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee) NA
Introduction		
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention PAGE 4-8
	6b	Explanation for choice of comparators PAGE 13-14
Objectives	7	Specific objectives or hypotheses PAGE 7-8
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory) PAGE 8

Methods: Participants, interventions, and outcomes

Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained PAGE 8
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists) PAGE 11-13
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered PAGE 14-16, 20-21
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease) NA
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests) NA
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial PAGE 14
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended PAGE 16-17, 22-23
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure) PAGE 8-10, 14-16
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations PAGE 13
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size PAGE 13

Methods: Assignment of interventions (for controlled trials)

Allocation:

Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions PAGE 14

Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned PAGE 14
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions PAGE 14
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how PAGE 14, 16
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial NA

Methods: Data collection, management, and analysis

Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol PAGE 16-17, 22-23
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols PAGE 13, 16-17, 22-23
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol PAGE 17
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol PAGE 17-18
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses) PAGE 17-18
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation) PAGE 17-18

Methods: Monitoring

Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed NA

	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial NA.
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct PAGE 16
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor NA

Ethics and dissemination

Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval PAGE 18
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators) NA
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32) PAGE 16
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable PAGE 16
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial PAGE 9-10
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site PAGE 29
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators ~~SEE TRIAL REGISTRY~~ PAGE 18
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation NA
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions PAGE 18
	31b	Authorship eligibility guidelines and any intended use of professional writers NA
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code SEE TRIAL REGISTRY

Appendices

Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates SEE TRIAL REGISTRY
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable N/A

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.