Protocol Version 1

Pharmacological and non-pharmacological interventions for non-respiratory sleep disturbances in children with neurodevelopmental disorders: a systematic review

Sleep disturbances in children with neurodisabilities are more common and more severe compared to typically developing children (Tietze et al., 2012; Dorris et al., 2008). Whilst respiratory issues can cause sleep disturbance in this population, this only accounts for a relatively small proportion of cases. Non-respiratory causes of sleep disturbance among children with ND are wide-ranging and include: parents' practices around bedtime/settling and responding to night/early morning wakings; genetic, neurological or visual pathway damage/disorders affecting circadian rhythms, including melatonin release; hyper-arousal and sensory over-responsivity. Some of these causes are implicated in the initiation, scheduling *and* maintenance of sleep (e.g. parenting practices), whereas others are only associated with one particular type of sleep disturbance (e.g. the impact of visual impairment on sleep scheduling). The aetiology of an individual child's sleep disturbance may well be multifactorial (Grigg-Damberger and Ralls, 2013). Difficulties with sleep initiation (going to sleep), sleep maintenance (staying asleep) and sleep scheduling (when sleep takes place) result in disturbed sleep and sleep deprivation, not only for the child but often also other family members.

Child sleep problems are associated with poor outcome for parents (e.g. heightened levels of parental stress and irritability, Wiggs, 2007; Doo and Wing, 2006; Teitze et al., 2014) and children (e.g. poorer educational progress and daytime behaviour problems, Simola et al., 2014). These outcomes in themselves increase demands on statutory services as well as creating further, additional support needs, such as respite care (McConkey et al., 2011; Quach et al., 2013). The wider association between sleep quality and economic consequences have also been described (Colten, 2006; Hillman et al, 2006). Parents consistently highlight the need for support with their child's sleep problems (Beresford, 1995; Allard et al., 2014) although, historically, little time has been allocated to training the relevant professionals to provide this kind of support (Stores, 1999).

Given the various aetiologies of sleep disturbance in children with neurodisabilities, interventions to address sleep disturbance among children with neurodisabilities include both pharmacological and non-pharmacological approaches. However, whilst there have been some attempts to develop sleep management pathways within paediatrics, these have been restricted to particular types of sleep disturbance and/or sleep intervention and/or diagnostic groups where the evidence is more plentiful and/or of higher quality (e.g. RCPCH, 2009; Malow et al., 2012; NICE/SCIE, 2013). A robust evidence-base to inform the development of a paediatric neurodisabilities sleep management pathway for non-respiratory disturbance which integrates pharmacological and non-pharmacological interventions is clearly required.

This review has been commissioned by NIHR's Health Technology Assessment Programme.

AIMS AND OBJECTIVES

There are two over-arching objectives to this review: 1) if the quality of the evidence permits, to make recommendations about the management of non-respiratory sleep disturbance in children with neurodisability; and 2) to inform the focus and priorities of a future call by NIHR for primary research in this area. Unlike previous systematic reviews, it is seeking to be holistic in its approach,

both in terms of the population (all children with neurodisability) and the types of intervention (i.e. pharmacological and non-pharmacological).

We propose a broad systematic review of pharmacological and non-pharmacological interventions for non-respiratory sleep disturbance among children (0-18 years) with neurodisability which will:

- evaluate the effectiveness of sleep disturbance interventions for children with neurodisability with respect to child and parent/carer outcomes; and identify the impact of population and intervention related factors (identified *a priori*) on intervention effectiveness (addressing objective 1)
- review evidence related to the acceptability and feasibility of delivering these interventions within the NHS (addressing objectives 1 and 2);
- identify promising approaches which merit further primary research (addressing objective 2)

Specific aims are:

- To evaluate and compare the effectiveness of different intervention approaches to sleep disturbances for children with neurodevelopmental disabilities and, where possible, to:
    - examine whether intervention effectiveness differs between different types of neurodisability; different causes of sleep disturbance; and different types of sleep disturbance (i.e. sleep initiation, sleep maintenance and sleep scheduling),
    - to review and evaluate evidence regarding the use of more than one intervention approach, sequentially or in combination, to manage a specific cause of sleep disturbance;
    - to review and evaluate evidence regarding the impact of the setting and/or skills/qualifications of practitioners on intervention effectiveness;
- To describe and compare evidence regarding the acceptability and feasibility of sleep disturbance interventions;
- To describe the settings in which sleep disturbance interventions are being delivered, and by whom;
- Where appropriate, to make recommendations with respect to the management of sleep disturbance among children with neurodisability generally and/or with respect to particular neurodisabilities;
- To identify and describe interventions which look promising, and are of relevance and/or feasible to the NHS, but have not been robustly evaluated;
- To make recommendations regarding priorities for future primary research on this topic;
- To disseminate the findings in a timely and effective way.

RESEARCH PLAN

A systematic review will be undertaken. The main components of the systematic review are outlined below.

Eligibility criteria

Studies will be assessed for eligibility based on the following criteria:

- *Population* – studies of children and young people with neurodevelopmental disorders experiencing non-respiratory sleep disturbances will be eligible for inclusion in the review.
    - Children and young people from 0 to 18 years old will be eligible for inclusion. We would not expect to find many studies targeted at very young infants. Some previous reviews have used a lower age cut-off of 3 months and others have not. Given the comprehensive nature of the review we will not use a lower age cut-off. Neurodevelopmental disorder will be defined according to the consensus definition developed by Morris et al. (2013): "congenital or acquired long-term conditions that are attributed to impairment of the brain and/or neuromuscular system and create functional limitations. A specific diagnosis may not be identified. Conditions may vary over time, occur alone or in combination, and include a broad range of severity and complexity. The impact may include difficulties with movement, cognition, hearing and vision, communication, emotion and behaviour" (p.3).
    - Non-respiratory *sleep disturbances* related to initiation, maintenance or scheduling of sleep, diagnosed by a healthcare professional based on parental/carer or child report or sleep observation will be eligible. Sleep disturbances of any duration will be included.
    - Non-respiratory sleep disorders which will be excluded are: central disorders of hypersomnolence (where daytime sleepiness is not caused by nocturnal sleep disturbance or misaligned circadian rhythms); and sleep-related movement disorders. We will exclude studies of respiratory related sleep disturbances. However, neurodevelopmental disorders are complex conditions and sleep disturbances may have multi-factorial causes. Therefore we will include studies where the respiratory related component is being controlled and the focus of the intervention is another cause of sleep disturbance. We will also exclude studies where the main focus of the intervention is not treatment of the sleep disturbance e.g. interventions to control seizures where sleep outcomes are also reported; and studies of mixed populations of children with and without neurodisability unless the results are reported separately for the two groups or the sample is predominantly neurodisability (>90%).
- *Intervention* – NHS relevant pharmacological and non-pharmacological interventions targeted at improving sleep initiation, maintenance, scheduling or sleep quality in any setting will be eligible for inclusion. For pharmacological studies NHS relevant is defined as drugs licensed for use for this indication in children or currently used for this purpose in the NHS. For non-pharmacological studies NHS relevant is defined as those meeting current practice standards, for example, behavioural interventions that use punishment will be excluded. Multi-component interventions will be eligible.
    - Relevant pharmacological interventions are melatonin, clonidine, and antihistamines.
    - Relevant non-pharmacological interventions include (but are not restricted to):
        - behavioural interventions delivered in a range of setting such as primary, secondary and tertiary; community, outpatient or inpatient; delivered in groups, to individual children/families by healthcare professionals;
        - self-help booklets; web-based packages and other online support.
        - behavioural / cognitive behavioural interventions: addressing behavioural aspects of sleep including parents' management of sleep behaviours and routines;
        - chronotherapy: intervening on the timing of sleep within the 24 hour cycle;
        - phototherapy (or 'bright light therapy'): using light exposure to effect changes in the circadian rhythm;

- dietary interventions: removing stimulants; restricting to hypoallergenic food
- sensory interventions including weighted blankets ; 'safe space' bed tents ;
- cranial osteopathy ;
- changing the bedroom environment such as removal of television or other stimulatory materials; adjusting heating and/or lighting;

- *Comparator* – studies using no intervention, waiting list control, placebo, or another NHS relevant intervention will be eligible for inclusion

- *Outcomes* – The following outcomes will be assessed:
  - Primary outcomes:
    - Child's sleep related outcomes - parent/carer and child reported outcomes related to initiation, maintenance, scheduling or quality of sleep (using measures such as sleep diaries; standardised scales e.g. the Composite Sleep Disturbance Index, Epworth Sleepiness Scale) and objective measures such as actigraphy (used to calculate outcomes such as total sleep duration, time taken to fall asleep, sleep efficiency);
    - parent sleep-related outcomes - quality of sleep;
    - measures of perceived parenting confidence and/or efficacy and/or understanding of sleep/sleep management (particularly relevant for parent training/behavioural interventions which seek to change the way parents manage sleep disturbance)
  - Secondary outcomes:
    - Child-related quality of life, daytime behaviour and cognition;
    - Parent/carer quality of life and well-being (including global quality of life (e.g. SF36) and more specific outcomes such as physical well-being, mental well-being, mental health (e.g. stress, depression);
    - Family functioning;
    - Adverse events, including side effects from medication;
  - Data on uptake of the intervention, retention and intervention adherence: these will be used as indicators of the acceptability and feasibility of the intervention. Quantitative or qualitative data on:
    - parents'/children's experiences of receiving a sleep disturbance intervention including
    - the acceptability and feasibility of the intervention
    - other experiences of receiving the intervention,
    - satisfaction with intervention outcomes and 'fit' with their priorities with regard to their child's sleep disturbances
    - views/perspectives on the mechanisms by which outcomes were achieved.

- *Study design* – RCTs and non-randomised controlled studies such as controlled before and after studies and cohort studies with a control group will be included. Both parallel and cross-over RCTs will be eligible for inclusion. Concerns have been expressed by others that a cross-over design may be inappropriate due to uncertainty about the duration of the effect of interventions on sleep patterns and circadian rhythm and therefore the most appropriate duration for the washout period (Appleton 2012). We agree with these concerns. However, given that a broad

review has been requested and there are few RCTs likely to be available we propose to include crossover studies. These will be handled carefully in the quality assessment and synthesis according to established methods (Curtin 2002; Elbourne 2002).

In order to achieve the second objective of the review, studies without a control group will be included in the absence of controlled studies i.e. cohort studies and before and after studies. This is because they may include potentially promising interventions that are at an early stage of evaluation. Case studies will not be eligible for inclusion.

Qualitative and quantitative studies will also be included if they report data on parents'/children's experiences of receiving a sleep disturbance intervention (including intervention acceptability) and the process of receiving the sleep intervention, satisfaction with intervention outcomes and 'fit' with their priorities with regard to their child's sleep disturbances, and views/perspectives on the mechanisms by which outcomes were achieved. Some of this data may be reported as part of studies of effectiveness, and some may be reported in studies that sought only to examine research questions on experiences and satisfaction.

A summary of the inclusion and exclusion criteria is summarised in table 1.

Table 1. Summary of inclusion/exclusion criteria

	Included	Excluded
Population	- Children aged 0-18 years - Neuro-developmental disorders - Non-respiratory sleep disturbances of any duration related to initiation, maintenance or scheduling of sleep, diagnosed by a healthcare professional based on parental/carer or child report or sleep observation	- Respiratory sleep disturbances (except where studies control for this AND the focus of the intervention is another cause of sleep disturbance) - Studies of mixed populations of children with and without neurodisability unless the results are reported separately for the two groups or the sample is predominantly neurodisability (>90%)
Intervention	- NHS relevant pharmacological and non-pharmacological interventions targeted at improving sleep initiation, maintenance, scheduling or sleep quality in any setting	- Main focus of the intervention is not treatment of the sleep disturbance
Comparator	- No intervention - Waiting list control - Placebo - Another NHS relevant intervention	
Outcomes	- Primary: Child's sleep related outcomes, both parent/child reported and objective measures; parent-sleep	

	related outcomes (e.g. quality of parent sleep) - Secondary: Child-related quality of life, daytime behaviour and cognition; parent/carer quality of life and well-being; family functioning; for behavioural interventions which seek to change the way parents' manage sleep disturbance, perceived parenting confidence and/or efficacy; adverse events, including side effects from medication; data on uptake of the intervention, retention and intervention adherence; quantitative or qualitative data on: parents'/ children's experiences of receiving a sleep disturbance intervention including intervention acceptability; experiences of the process of receiving the intervention; perceived outcomes; views/perspectives on the mechanisms by which outcomes were achieved.	
Study Design	- RCTs - Non-randomised controlled studies - Studies without a control group in the absence of controlled studies - Studies reporting qualitative and/or quantitative data about parents/children's experiences of sleep interventions	Case studies

English and non-English language controlled studies will be eligible for inclusion. Where uncontrolled studies are included, these will be English language only.

Search strategy

A literature search to identify the available evidence will be conducted by carrying out systematic searches of electronic databases, consulting with experts in the field, and reference checking. The searches will be undertaken by an experienced information specialist and the search strategy will be peer reviewed by a second information specialist.

A range of databases will be searched to ensure coverage from the fields of health, nursing & allied health, and social care. These will include the following: Applied Social Science Abstracts & Indexes (ASSIA); The Cochrane Central Register of Controlled Trials (CENTRAL); Cochrane Database of Systematic Reviews (CDSR); Cumulative Index to Nursing & Allied Health (CINAHL); Database of Abstracts of Reviews of Effects (DARE); Embase; Health Management Information Consortium

(HMIC); MEDLINE; MEDLINE In-Process; PsycINFO; Science Citation Index; Social Care Online; Social Policy & Practice; and Conference Proceedings Citation Index. The Social Care Online, Social Policy & Practice, HMIC, Conference Proceedings Citation Index and PsycINFO all provide some coverage of reports and other unpublished documents so the available grey literature will be represented. In addition, Clinical-Trials.gov, WHO International Clinical Trials Registry Platform (ICTRP), NIHR, and UK Clinical Trials Gateway will be searched for ongoing trials.

The reference lists of all included studies, any related systematic reviews and key background papers will also be checked.

Qualitative evidence related to parents'/children's experiences of receiving a sleep intervention disturbance may have been collected and reported by effectiveness studies identified by our searches. In addition, we will conduct a second, specific search of relevant databases to identify papers reporting qualitative evidence on:

- parents'/children's experiences of receiving a sleep disturbance intervention including intervention acceptability,
- experiences of the process of receiving the intervention,
- perceived outcomes,
- views/perspectives on the mechanisms by which outcomes were achieved.

Screening of searches

The records identified by all the database searches will be managed using Endnote bibliographic software. Screening of the records generated by the searches will take place over three stages.

1. Early work on the search strategy indicates that a larger than expected volume of records generated through the searches[1]. There will be an initial stage of screening *titles only* to exclude papers irrelevant to the review. Two researchers will do this independently for 200 records and compare decisions for consistency. The remaining record titles will then be screened by one researcher.
2. After excluding records from Stage 1, all remaining titles *and* abstracts will be screened independently by two researchers for relevance and full papers of potentially relevant articles retrieved.
3. Full papers will then be screened by two researchers independently against the inclusion and exclusion criteria.

Disagreements will be resolved by consensus and where relevant through discussion with a third team member.

Data extraction

[1] Searches conducted to inform the early development of the protocol were restricted to MEDLINE and PubMED and indicated that 5-6000 records would be identified. However, preliminary searches of EMBASE have generated almost doubled this number. Examination of a small sample of records suggests that the main reason for this is because sleep disturbance can be a side effect of pharmacological interventions used with children with neurodisabilities to manage non-sleep related symptoms/conditions such as epilepsy

A data extraction form will be developed, piloted on a small selection of studies and adjusted as necessary. Data will be extracted by one researcher and checked by a second. Examples of the data that will be extracted are:

- Study methods including study design, inclusion criteria, method of recruitment and selection of participants;
- Country; setting (tertiary/secondary clinic, community, home-based or mix); type of service (health, social care or third sector);
- Participant characteristics e.g. age, nature of sleeping disturbance, nature of neurodevelopmental disorder, method of assessment/identification of sleeping disorder, details of any previous interventions, baseline characteristics;
- Intervention e.g. dose, formulation, and duration for pharmacological; theoretical underpinning, content, duration, intensity and how delivered for non-pharmacological; practitioners involved in delivering the intervention; 'position' of the intervention on a wider sleep management pathway, (including where possible the nature of that previous intervention and the period of time which has elapsed since the intervention).
- Comparator (as above);
- Outcome measures;
- Study flow data including number randomised, number included in analyses, drop out and loss to follow-up;

- Results: Intervention effectiveness data will be extracted to allow calculation of between group differences and 95% confidence intervals as appropriate for the specific outcome measure (relative risk, hazard ratio, mean difference). Where SD values are not available for continuous data, standard data imputation methods will be used (Higgins & Green, 2011). For continuous data, the post-intervention (final value) mean and SD will be extracted as first preference, then change scores (the difference between baseline and follow-up) and SD for each group. The preferred choice for use in the synthesis is endpoint data but the final choice will also be determined by what data can be extracted from the primary studies.

  To maximise the possibility of between study comparisons the standardised mean difference will be used where appropriate. For cross-over trials paired data will be extracted where available, otherwise data from the first sequence of the crossover trial will be extracted and treated as data from a parallel trial (Curtin 2002; Elbourne 2002).

  Where adjusted and unadjusted data are reported preference will be given to extracting adjusted data. Unadjusted data will be used if a covariate analysis for the mixed treatment comparison is feasible.

  Depending on the data available, for studies without a control group, data will be extracted to calculate change from baseline and associated 95% confidence intervals.

- Results: Quantitative and quantitative data on parents' and/or children's satisfaction, take up, retention and adherence to the intervention will also be extracted.

- Results: Qualitative data on experience of the intervention (including satisfaction, acceptability and feasibility) will be extracted using a thematic approach. Papers will be read and analytical

notes made of topic areas covered and themes within each topic area. Two members of the team will work on this task independently and then meet to discuss and develop a thematic framework (themes, sub-themes); that is, the structure within which the data will be organised and summarised. For each study, findings are summarised according to the thematic framework using a series of tabulated pro-formas with each study occupying the same row of every table. The columns allow each theme to be broken into sub-themes. One researcher will extract the data onto the pro-formas. This will then be checked by a second researcher.

Assessment of risk of bias

The Cochrane Risk of Bias Tool (Higgins et al., 2011) will used to assess the quality of RCTs and the newly developed tool ACROBAT-NRSI will be used to assess the non-randomised studies (Sterne 2014). Risk of bias will be independently assessed by two researchers. Disagreements will be resolved through consensus and through discussion with a third researcher if necessary. In addition, for cross-over trials we will assess whether an appropriate analysis using paired data was conducted and whether there was a treatment by period interaction, as undertaken in a previous systematic review including cross-over studies (McDaid 2009).

For studies containing qualitative and quantitative data on parents' and/or children's satisfaction with the intervention, take up, retention and adherence to the intervention, and experiences of the intervention, the quality of studies taken forward to data extraction will be assessed and reported using Hawker et al's (2002) quality appraisal checklist.

Synthesis

The synthesis will aim to assess (i) the clinical effectiveness of the interventions for sleep disturbance, in particular interventions that may work across conditions and (ii) inform future research by identifying gaps in the evidence and identifying interventions which are the most promising front runners that could be considered for future primary research.

First a narrative and tabular summary of key study characteristics will be undertaken. This will include baseline population details (e.g. type of ND, nature and severity of sleep disturbance, cause of disturbance) intervention and comparator; study methods (e.g. study design, how outcomes were measured, length of follow-up); and risk of bias. This will allow a mapping of which interventions have been investigated for which neurodisability and for which type of sleep disturbance (e.g. sleep initiation) in order to identify interventions which have been investigated across conditions. We will also map information on the feasibility and acceptability of each of the interventions.

Synthesis will involve narrative synthesis, paired meta-analyses and/or mixed treatment comparisons depending on the data available.

Meta-analyses

Meta-analyses will be undertaken where appropriate based on clinical and statistical heterogeneity following guidance in the Cochrane Handbook. Individual study results will be combined in a series of pairwise meta-analyses stratified by type of intervention and comparator. It is likely that studies will report different durations of follow-up but the extent of variation is unknown until completion of data extraction. Prior to undertaking analysis a decision will be made about how to group studies

by length of follow-up. A random effects model will be used. Heterogeneity will be assessed using chi-squared test and quantified using the I^2 statistic. An I^2 value >50% will be taken to indicate substantial statistical heterogeneity.

Sub-group analyses will be restricted to a small number of potentially important characteristics that may reasonably be expected to modify the effect of the intervention. This will focus on type of sleep disturbance, and causes and type of neurodevelopmental disorder in order to address the focus in the commissioning brief on identifying interventions that may work across conditions. If sufficient data are available, other factors that will be considered for sub-group analysis are age of child, previous interventions, whether the intervention is 'single' (or 'stand-alone') (e.g. melatonin), combined (e.g. melatonin + behavioural) or sequential (e.g. behavioural followed by melatonin for those with ongoing sleep disturbance, as in the Appleton et al (2012) trial), and, for non-pharmacological interventions, setting, practitioner or family characteristics. Sub-group analyses will be interpreted cautiously due to the limitations of meta-analyses to explore sub-group effects.

Given the range of interventions being considered, a mixed treatment comparison (MTC), could permit ranking of the benefits and harms of the different treatment options (Caldwell 2005). This statistical method is an extension of a traditional meta-analysis. Whereas a traditional meta-analysis includes only trials making direct comparisons between an intervention and comparator, a mixed treatment comparison overcomes the limitations of the traditional approach in cases where there are no or limited trials making the relevant head-to-head comparison, also using indirect comparisons. This is of particular value where several treatment options are under consideration, as in the proposed systematic review. However, the appropriateness of such an approach depends on the principle of exchangeability, i.e. that there are no systematic differences between the trials that evaluate particular types of intervention. There is a strong possibility that the included studies may not meet the exchangeability assumption, for example children in the trials of specific pharmacological interventions may have different sleep problems to children in trials of behavioural interventions or have had a different pathway of previous treatments. However, the feasibility and appropriateness of an MTC will be explored and undertaken if appropriate (Ades 2003). Current guidance on good practice will be followed (Dias 2014). Should data permit a similar approach will be taken to subgroups as outlined above. Within our meta-analyses we will also look for opportunities to investigate the impact of single, combined, and sequential intervention on effectiveness by appropriate stratification.

Narrative synthesis

Narrative synthesis will be undertaken where quantitative synthesis is not appropriate or there are insufficient data. We will attempt to display outcomes in a forest plot even where studies are not statistically pooled to aid exploration of study results. Where feasible we will investigate the subgroup characteristics outlined above. Studies will be grouped by type of intervention (e.g. behavioural approach or medicinal product, and whether it is single, combined, sequential), and comparator if heterogeneous. If feasible we will also group studies by type of sleep disturbance and neurodevelopmental disorder. We will explore outcomes by type of sleep disturbance with the aim of identifying effects that may be transferable to other neurodevelopmental disorders. Results will be discussed in the context of risk of bias in the individual studies.

In terms of the qualitative data analysis, the topic areas which will be subject to review are well-defined (see above) and we will therefore adopt a thematic approach to data extraction, analysis

and synthesis (Thomas and Harden, 2008; Centre for Reviews and Dissemination, 2009). To start, studies will be grouped into pharmacological, behavioural and other non-pharmacological studies. For each, a descriptive report of relevant studies, and topic areas covered, will be produced. The tabulated data will then scrutinised and analytical notes made summarising findings across studies with respect to the topic areas set out above. Part of this process involves testing for contradictions in the evidence (Booth et al., 2013).

Factors taken into consideration in identifying promising interventions include feasibility of delivery of the intervention in a NHS setting, acceptability to children and families, evidence of effectiveness or in the direction of effectiveness based on confidence intervals (taking into consideration the clinical significance of the estimates). Many of the included studies are likely to be evaluating complex interventions. There is currently no widely accepted guidance on the synthesis of data on complex interventions in systematic reviews, though these are currently being developed by the Cochrane collaboration. There is general agreement that the consideration of the mechanism of action and developing an understanding of what drives variations in outcomes is a critical aspect. The synthesis will interrogate such data, where available, to assist in identifying interventions which may be generalisable across conditions and those which are condition specific (Anderson 2013; Burford 2013).

Table 2 summarises the main components of the review.

Table 2. Review components

Objective	Type of evidence considered	Review:
To review and evaluate the effectiveness of sleep disturbance interventions for children with neurodisability	Outcomes of effectiveness from RCTs, non-randomised controlled studies and studies without a control group in the absence of controlled studies	1
To review evidence related to the acceptability and feasibility of delivering sleep interventions within the NHS	Quantitative and qualitative evidence from the effectiveness studies identified for review 1 and qualitative and quantitative evidence from studies focusing solely on these questions/issues.	2
To identify promising approaches which merit further primary research	Drawing upon evidence from review 1 and 2.	3

DISSEMINATION AND PROJECTED OUTPUTS

A detailed dissemination strategy will be produced at an early stage. The clinician/practitioner members of the research team will play an important role in devising this strategy to ensure all relevant audiences are identified and an effective means of disseminating to these various audiences are identified.

Key project outputs will be a research report, short non-technical summary (giving brief background details, information about the quality of evidence, the results and clinical implications), and a PowerPoint presentation with audio narration which can be viewed on-line and/or downloaded. The non-technical summary will include a detachable, A3 size poster. Downloadable, electronic and hard copies of the non-technical summary will be produced. A hard copy will be sent to all community paediatric and paediatric neurology services, specialist sleep services, CAMHS LD teams, paediatric leads in clinical commissioning groups and voluntary sector organisations which support families with disabled children. An email alert notifying recipients of the publication of the report and summary will also be sent to these groups as well as other relevant children's health services. Twitter, blogposts and press releases will be used to announce publication more widely.

A paper will be submitted to Developmental Medicine and Child Neurology (0pen Access) and a second paper submitted to Child: Care, Health and Development (key multi-disciplinary journal for practitioners working with children with neurodisabilities). We will also submit abstracts for oral presentations at the annual scientific meetings of the European Academy of Childhood Disability (costs included in project budget), the British Association for Community Child Health, Royal College of Paediatrics and Child Health.

PLAN OF INVESTIGATION AND TIMETABLE

Key milestone	**Month**
Project Meeting (see project management section below)	*1*
Protocol development	1
Registration of protocol on PROSPERO	1
Literature searches	1-2
Screening and study selection	2-3
Project Meeting	*3*
Data extraction, quality assessment, checking	3-5
Data synthesis	6-9
Project Meeting	*7*
Project Meeting	*10*
Draft report	10-12
Drafting of summary, journal publications and other activities to underpin dissemination	10-12

PROJECT MANAGEMENT

Bryony Beresford will provide overall management for the project and will input into all aspects of the review and will ensure the quality of the work, achievement of project milestones and the delivery of the project. She will also lead on liaison and consultation with the senior healthcare practitioners on the research team, and will chair the research team meetings.

The entire research team (York-based staff and healthcare practitioners) will convene for a project start-up meeting plus three 1 - 2 day meetings over the course of the project. Three parent advisors will attend for part of these '**Project Meetings'**. Outside of these meetings, senior clinicians/practitioners will contribute to, and be consulted about, the project via telephone/Skype calls and email.

The academic members of the research team (BB, CM, CH, GS and KB) are all based at the University of York and will meet regularly (‘**Team Meetings’**, approximately 2 weekly) to discuss the work of the project and to review progress against project milestones. Smaller ‘**Task Meetings**’ between a senior member of the team and junior staff, and pertaining to a specific activity, will also take place to ensure all aspects of the project are closely monitored and junior staff properly supervised.

ETHICAL ARRANGEMENTS

The systematic review will not involve patients or identifiable patient data and so no ethical arrangements are required.

PATIENT AND PUBLIC INVOLVEMENT

The lead applicant directs a research team which, for the past 12 years, has had in place an active and highly committed parents’ consultation group, comprised of parents of children with a range of disabilities and ages, including neurodevelopmental disorders (http://www.york.ac.uk/inst/spru/research/childconsult.html). The research team meets with this group approximately three times a year. Around 15 parents belong to the group with, on average, 10-12 parents attending each meeting. The team use this group to ground their research in the everyday of lives of families with a disabled child, and to guide future research activities.

Some of the key areas where parents’ input will be extremely valuable include issues related to feasibility and acceptability of interventions; issues of clinical significance, specifically, parents’ views on minimum improvements required to make an intervention worthwhile; and the identification of potentially promising interventions.

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