Assessment of the feasibility and clinical value of further research to evaluate the management options for children with Down syndrome and otitis media with effusion: a feasibility study

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Scientific summary

Otitis media management in children with Down syndrome

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Scientific summary

Background

Otitis media with effusion (OME or glue ear) is a build-up of fluid in the middle ear and is the commonest cause of impaired hearing in children of > 6 months of age. The standard intervention to release the middle ear fluid is insertion of tympanostomy or ventilation tubes, more commonly known as grommets, and this is the most common surgical operation in children worldwide.

Down syndrome is the most common chromosomal disorder in the UK, with an incidence of 1 in 1000 live births. OME is almost universal in children with Down syndrome, begins at a younger age and persists to older ages than in children without Down syndrome.

Grommet insertion can be difficult or impossible in children with Down syndrome, as the morphological features include narrow ear canals. Amplification devices can be used to alleviate the hearing losses consequent upon the glue ear but conventional behind-the-ear hearing aids (HAs) are often not tolerated. Soft-band attachments for bone vibrators applied to the mastoid bone (BAHA [bone-anchored hearing aid] technology) may be tolerated better, although a controlled trial is lacking. Watchful waiting (WW) or active observation before determining definite need for intervention is accepted to be good practice in children who do not have Down syndrome but might be considered a lack of action in children with Down syndrome.

The National Institute for Care and Excellence (NICE) guidelines published in 2008 found only limited studies of OME in children with Down syndrome and reviewed just three studies in detail, concluding that existing studies evaluating effectiveness of interventions are of poor quality.

The NICE report recommended research projects to evaluate the acceptability, effectiveness and consequences of treatment strategies for children with Down syndrome who have glue ear. A randomised controlled trial (RCT) would assess both benefit and harm, and the resource costs and savings of all possible interventions, but any such trial requires the measurement of robust, relevant and measurable outcomes and, crucially, that parents and professionals would be willing to randomise the children. This study was undertaken to address questions of the feasibility and value of future research.

Objectives

1. To assess the level and practical effect of current uncertainty around treatment options for children with Down syndrome and OME.
2. To assess the feasibility of studying the options for management of OME in children with Down syndrome via a RCT or multicentre prospective cohort study.

    i. To evaluate the willingness of parents to agree to randomisation for their children.
    ii. To evaluate the willingness of clinicians to recruit participants to a definitive study.

3. To explore relevant and practically measurable outcome domains for use in a definitive study.
4. To assess the feasibility and practical requirements for collecting these outcome measures of the relevant type.
5. To undertake a value of information (VOI) analysis to assess the level and clinical impact of current uncertainty, and the likelihood of further research reducing that uncertainty and minimising its clinical impact.

Methods

Literature review

A targeted literature review was conducted to assess the current state of evidence and to feed into the economic model.

Parental opinions

Questionnaire survey

Parents of children with Down syndrome aged 1–11 years were identified by their paediatricians who sent a questionnaire, and a letter and information sheet explaining the project to each family. Questionnaires were returned directly to the research team.

Closed, forced-choice and open-ended questions concerned the experience of glue ear and general health of their child; the effects of glue ear experienced by the child; interventions and treatment received and the effects; circumstances that would encourage or discourage participation in research; views on the importance of various outcome domains for parents and the child; and demographic variables.

Interviews

Qualitative, semistructured interviews with a selected sample of parents who responded to the questionnaire were used to explore family experiences of treatment and attitudes towards future research in more detail and greater depth. Interviewees included parents with different experiences of treatment options with children of different ages. Some were positive about future research and others expressed concerns about research. Each interview was undertaken on a single occasion, face to face, and all but one were conducted in the family's home.

Focus groups

Focus groups enabled review and refinements of the findings from the questionnaires and interviews. A second purposively selected sample of parents was drawn from those previously involved in the project (both questionnaire and interview stages). Parents were encouraged to explore opinions and perspectives on treatment and clinical research including issues around randomisation.

Professional opinions

Online survey

Professionals with clinical/professional responsibility for children with Down syndrome and/or glue ear (ear, nose and throat surgeons, paediatricians, audiologists, speech and language therapists, and teachers) were contacted via regional and national professional organisations, and special interest groups. Details of the project and an invitation to complete an online questionnaire were distributed via e-mail lists, electronic and paper newsletters, online fora and social media sites.

The questionnaire explored the caseload of children with Down syndrome and the proportion who experience glue ear; approaches to clinical management; opinions on frequency and significance of the consequences of glue ear for this population; the importance of various outcomes; opinions of interventions and their role in future research; and views on health research and the facilitators and barriers to participation and recruitment in RCTs.

Delphi review

A multidisciplinary group of respondents to the survey questionnaire who indicated a willingness to take part in a Delphi review were invited to do so. This sought to establish consensus among an expert panel by using an iterative approach to scoring, revising and rescoring a series of structured statements until a designated level of agreement was reached or three scoring rounds had been completed. Participants were sent, via e-mail, a link to an electronic survey comprising a number of statements developed from the

responses to the preceding questionnaire and asked to provide an indication of the level of their agreement or disagreement with each statement on a five-point scale (strongly agree, agree, neutral, disagree, strongly disagree). All responses were anonymous. After each round the responses and opinions were summarised and returned to respondents. Any statements reaching a consensus level of $\geq 80\%$ were removed from further rounds.

Economic modelling

Value of information analyses were informed by deterministic cost–utility analyses in two settings: a clinical care pathways model and a hypothetical simple RCT model. In both cases an averaged cohort approach was taken. The economic models were constructed as probabilistic decision trees using TreeAge® (TreeAge Software, Inc., Williamstown, MA, USA), with costs and quality-adjusted life-year calculated in Microsoft Excel® (Microsoft Corporation, Redmond, WA, USA).

Results

Questionnaires were returned by 122 parents and 99 professionals. Interviews were held with 21 parents and focus groups with 11. Twenty-seven professionals responded to the Delphi review. This summary presents findings of the key themes of the research from the parent and professional perspective.

Glue ear and its consequences

Parent perspective:

- Sixty-eight per cent of parents reported that their child had difficulties with hearing and 56 per cent reported a diagnosis of glue ear.
- Difficulties of diagnosis, fluctuation in symptoms, uncertainty about treatment, and uncertainty about the impact of glue ear each contribute to a recognition that this is a difficult condition to manage.
- Hearing is perceived to be the primary symptom of glue ear but its greatest impact is on listening, understanding and using language.
- It is difficult to isolate the symptoms of glue ear from other aspects of Down syndrome. Hearing difficulties exacerbating developmental delay was considered an important reason for more effective management of glue ear.

Professional perspective:

- Glue ear is an important condition for this population owing to its prevalence and the implications it has for other behavioural/developmental difficulties.
- Difficulties hearing, listening and communicating were identified as the most frequent problems associated with glue ear in children with Down syndrome, and were also the problems that pose most difficulties for families. Difficulties with listening and communication were considered to be more challenging than reduced hearing level alone in terms of management of glue ear.

Glue ear and its treatment

Parent perspective:

- Air conduction HAs and grommets were the most commonly reported interventions received but other interventions (including antibiotics and WW) were also described.
- No single treatment option was universally favoured or universally rejected by parents, and no intervention was reported as generating improvements in all cases.
- There is inconsistent care with different interventions advocated by different clinicians, different interventions are available in different parts of the country, and unclear clinical pathways are based upon uncertain foundations and limited knowledge of glue ear in children with Down syndrome.

- WW was perceived to absolve clinicians of their responsibilities and to place additional pressure upon families to make 'clinical' decisions about their child's treatment.

Professional perspective:

- Treatment for glue ear in this population is challenging, and it is difficult to be entirely confident of effective treatment.
- Confidence in explaining the risks and benefits of different interventions for glue ear varied by profession. Respondents other than surgeons were least confident in explaining the risks and benefits of surgical intervention.
- Hearing level, speech production and parental concern were identified as the strongest influences on clinical decision-making, with hearing level as the most frequent single factor.
- HAs were presented as the most effective treatment, followed by BAHA technology and grommets.

The value of future research

Parent perspective:

- Applied health research (AHR) was perceived positively. The need for further research into the management of glue ear in children with Down syndrome was supported, although parents identified barriers that would prevent them from participating in any such study including lack of time and uncertainty about the treatment that would be offered.
- The benefits of future research might include addressing difficulties with current clinical pathways and bringing about improved clinical and developmental outcomes for children with Down syndrome.

Professional perspective:

- The value of AHR was recognised and there was strong support for further research in this area, indicating in the main that it might generate evidence to inform/change guidelines and practice.
- The complexity of the condition and the challenges of working with this population were not considered a sufficient barrier to prevent research.

The form of future research

Parent perspective:

- No study design (i.e. RCT or observational study) was automatically dismissed by parents.
- Research should seek improvements in a child's speech, language and communication, rather than a focus on hearing in isolation.
- Understanding of research processes varied widely and often included inaccurate assumptions.
- Randomisation and treatment allocation by chance is a significant barrier that might prevent parents from consenting to a research study.
- Observational research involving treatment actively allocated by a clinician would make this type of research more acceptable.
- The risks associated with surgery and anaesthetic would discourage parents from involvement in a study including a surgical option. Inclusion of WW would also discourage their involvement for fear of not receiving treatment and disadvantaging their child.
- Decisions about involving their child in research are influenced by parents' experiences. Well-managed symptoms, previously tried treatment options, experience of previous treatments, etc. will all influence a parent's decision.

Professional perspective:

- Future research should seek improvements in hearing and communication.
- If comparing only two treatment options then these should be BAHA technology and grommets.
- Clinicians expressed no difficulty in explaining either a RCT or observational study design to parents.
- Randomisation was identified as a potential barrier to recruitment and clinicians were more likely to indicate a willingness to recruit families to an observational study than to a RCT.

Facilitators and barriers to randomised controlled trial participation

Parent perspective:

- Appointments at convenient times and places, being knowledgeable about the process, and opportunities to try otherwise unavailable treatments were seen as facilitators.
- Lack of time, the need for more appointments, disruption to routine and the possibility of receiving an unwanted treatment were seen as barriers.

Professional perspective:

- Practical factors for the families (e.g. having all out-of-pocket expenses reimbursed, time to take part and minimal inconvenience) would encourage professionals to recruit a parent and his/her child with Down syndrome to take part in research or to advise them to do so.
- The existence of clinical equipoise, having confidence in explaining the study and taking consent, contributing to determining the best treatment efficacy and minimal disruption to clinical commitments would encourage professionals to recruit patients to a RCT.
- Improvements to a curriculum vitae, loss of autonomy in treatment decision making, lack of research experience or receiving a personal financial reward for research participation were viewed as having low importance.

Economic modelling

- In clinical management the most cost-effective strategy for a child with Down syndrome experiencing OME-induced hearing loss is WW, followed by symptom management using hearing aids in those who tolerate them.
- If further research using RCTs into new OME recovery-improved surgical interventions are to be conducted then to mitigate uncertainty at conventional incremental cost-effectiveness ratio threshold levels economic benefit can be derived, provided that costs do not exceed £650,000.

Recommendations for research

- To maximise recruitment and retention, future research of the cost-effectiveness and clinical effectiveness of interventions for glue ear in children with Down syndrome should be based on an observational cohort study design rather than a RCT.
- There is a possible role for small in-depth studies in particular subgroups of children, as it is unlikely that one approach will address all issues.
- If a RCT design is proposed all professionals involved must be trained in the methodology and confident in their explanation to parents about clinical equipoise surrounding all interventions including, if appropriate, WW. If a RCT design is proposed, researchers should be aware of parental concerns expressed in this report and design any trial to maximise participation.
- If comparing only two treatment options then these should be BAHA technology and grommets.
- Future research should consider within-subject measures of developmental outcomes. If a standardised assessment tool is not available, appropriate tools will need to be developed.

- Although improved hearing levels might be seen as the primary outcome measure owing to the ease of measurement and an obvious link with intervention; speech, language and communication are considered to be equally, if not more, important domains by both parents and professionals.
- If question-based outcome measures are to be used, resources should be available to support all parents to access and complete them.
- In order to be cost-effective, research costs should be < £650,000.

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