Tinnitus represents a major burden of disability, yet there is scant evidence for effective management strategies and a lack of clinical trials to formally test even some of the most commonly used drugs and medical devices. The James Lind Alliance gives a voice to patients and clinicians to identify and prioritize important clinical research questions concerning treatment uncertainties. This article describes the initiative conducted by the Tinnitus Priority Setting Partnership; how it was set up, what the consultation process was, and how the top ten research priorities were identified. For each priority, we recommend a research strategy; either calling for a systematic review or appropriate clinical study. We promote these as topics for commissioned research and as priority areas to encourage researcher-led funding applications.

Keywords: assessment • clinical trials • diagnosis • James Lind Alliance • research • tinnitus • treatment

Tinnitus describes a ringing or hissing sound that is perceived in the ears or head, without an identifiable physical noise source. It remains one of the most common chronic hearing-related conditions in the western world with a prevalence of 10.2% in the total adult population, rising to 14.2% in those aged over 50 years of age [1]. There are no effective cures for the condition, with current treatments targeting the symptoms of tinnitus (either the effects of the condition on emotions and mood or associated hearing loss), or seeking to reduce the persons’ awareness of the tinnitus sound. A majority of treatments have little or no evidence for their efficacy [2,101]. The heterogeneity of tinnitus with respect to its etiology, pathophysiology and clinical characteristics most likely exacerbates the variable individual response to tinnitus management [2–4].

Clinical research is traditionally led by scientists, clinical professionals or commercial interest and the government and charity research agendas are somewhat biased towards underpinning research and etiology (69% of total spend), with only 8% spent on evaluating treatments and therapeutic interventions [102]. To make best use of the government increase in support for clinical research, Chalmers and Glasziou, among others, have argued strongly for a more efficient research culture in which scientists study health conditions that are not only the greatest burden on the population, but also address questions about interventions and outcomes that patients and clinicians consider to be the most important [5]. This argument is highly relevant to the field of tinnitus research, which is rather patchy in terms of which key questions are driving current research programs, with considerable focus on animal models and underpinning neurophysiological mechanisms.
Patient and public involvement has become an important theme in health and social care research. In particular, a recent UK Clinical Research Collaboration report identifies evidence for a role in making research more relevant and appropriate for users [6]. The James Lind Alliance (JLA) supports the growing role for patients, the public and clinicians in research activity in the form of Priority Setting Partnerships (PSPs) (Table 1) [103]. The purpose of this article is to describe the Tinnitus PSP in providing a platform for patients and clinicians to collaborate to identify and prioritize uncertainties or ‘unanswered questions’ that they agree are the most important supporting clinical research.

The JLA
The JLA was established in 2004 in the UK. It is an independent, not-for-profit initiative that is principally funded by the National Institute for Health Research (NIHR). The JLA aims to raise awareness among those who fund health research about what matters to both patients and clinicians, so that clinical research is relevant and beneficial to end users. The process starts off by defining unanswered questions about the effects of treatment – questions that cannot be adequately answered by existing research evidence, such as a reliable, up-to-date systematic reviews – and then prioritizes them according to which are the most important. The JLA provides independent facilitation and guidance to the process of identification and prioritization. This input significantly increases the effectiveness of the PSP and the Steering Group in ensuring credible and useful outcomes.

The partnership between the British Thoracic Society and Asthma UK was the first formal PSP to complete the JLA process [7]. There have since been eight further completed PSPs, with the Ear, Nose and Throat specialty contributing two completed partnerships (balance and tinnitus).

Establishing a working partnership
The JLA Tinnitus partnership began in October 2011. Its founders were the British Tinnitus Association (BTA) – the only UK-based charity dedicated to supporting people with tinnitus and funding research in this field – the NIHR Nottingham Hearing Biomedical Research Unit and the Judi Meadows Memorial Fund. The Steering Group was key to the success of the project. Its role was to oversee and drive the progress of categorizing and prioritizing identified tinnitus uncertainties. Membership of the Steering Group provided a broad representation of people from the field of tinnitus in the UK, including professional bodies, charities and advocates for people with tinnitus. The wider working partnership included 56 major UK stakeholders including individual advocates for people with tinnitus, support groups, hospital centers and commercial organizations.

Gathering suggestions for research on the assessment, diagnosis & treatment of tinnitus
A questionnaire was used to gather suggestions for clinical research from as many representatives of people with tinnitus, clinicians and scientists as possible. The survey was publicized at the London (UK) launch meeting in December 2011 and widely disseminated through our working partnership and on the BTA and JLA websites. The BTA played a major role in dissemination by posting the questionnaire in their members’ magazine (Quiet, Winter 2011) with a circulation of 4500. Over a 2.5-month period, an incredible 2483 responses were submitted by 835 people (Figure 1).

Checking & categorizing submitted uncertainties
The purpose of collation was to reduce the initial list to a shorter one that would go forward to the prioritization

<table>
<thead>
<tr>
<th>Table 1. Steering Group of the James Lind Alliance Tinnitus Priority Setting Partnership.</th>
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<tbody>
<tr>
<td><strong>Steering Group members</strong></td>
</tr>
<tr>
<td>Lester Firkins</td>
</tr>
<tr>
<td>David Stockdale and Emily Broomhead</td>
</tr>
<tr>
<td>Deborah Hall and Najibah Mohamad</td>
</tr>
<tr>
<td>Tim Husband</td>
</tr>
<tr>
<td>Don McFerran</td>
</tr>
<tr>
<td>Christopher Dowrick</td>
</tr>
<tr>
<td>Emma Harrison</td>
</tr>
<tr>
<td>Philip Nash</td>
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<tr>
<td>Mark Fenton</td>
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</tbody>
</table>

ENT UK: Ear, Nose and Throat UK; NIHR: National Institute for Health Research.
stage. Details of the process are given in Figure 1. Almost a third were removed either because there was no specific suggestion for research (classified as 'void'; e.g., ‘Can I have any information about your tinnitus survey?’) or it was unrelated to the assessment, diagnosis and treatment of tinnitus. Qualitative research methods were used to identify, analyze and report themes within the remaining data [8]. The unprecedented number of submitted responses meant that this was one of the most time-consuming steps in the project. For each uncertainty, we required a consensus in thematic categorization across three independent raters, sought iterative input from the Steering Group and verified each uncertainty against published evidence such as the Cochrane Database of Systematic Reviews [106] and the Database of Abstracts of Reviews of Effects [107]. At the end of this process, in May 2012, we had generated a second questionnaire listing 170 distinct questions for tinnitus research spanning 36 themes.

### Prioritizing the uncertainties

This questionnaire asked people to select and then rank their top ten personal 'most important uncertainties'.

**Figure 1.** The key steps within the stages of consultation, collation and prioritization, with contributions from the Steering Group. The final uncertainties edited into appropriate ‘PICO’ format. PICO describes the core elements of a well-formed clinical question: Patient, Intervention, Comparator and Outcome.

BRU: Biomedical research unit; NIHR: National Institute for Health Research; PICO: Patient, Intervention, Comparator and Outcome.

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1. **Public consultation and data analysis**
   - 2483 suggestions for research received
     - Respondents: 638 tinnitus sufferers; 159 clinicians; 28 unknown
     - Mode of response: 131 postal; 697 website; seven e-mail

2. **Steering group contributions**
   - Design and dissemination of the questionnaire to harvest uncertainties about tinnitus assessment, diagnosis and treatment
   - Reach consensus on which responses were outside the scope of the survey
   - Thematic analysis led by Hall and Mohamad with colleagues from NIHR Nottingham Hearing BRU
   - Approve the thematic structure
   - Approve the pooling process and ensure edited uncertainties were written in ‘PICO’ format and lay terms, seeking external opinion from audiologist

3. **Consultation**
   - Weighting process led by Stockdale, with colleagues from British Tinnitus Association, and approved by Steering Group
   - Reviewed the list of ranks and agreed a consensus on 25 to go forward to the priority setting workshop

4. **Collation**
   - Design and dissemination of the questionnaire for ranking
   - Ranking of personal ‘top tens’
     - Respondents: 550 tinnitus sufferers; nine patient representatives; 71 clinicians
     - Mode of response: postal 153; e-mail 477
     - Scores weighted so that both groups contributed equal weighting to scores 40 uncertainties selected

5. **Prioritization**
   - Ten uncertainties about assessment, diagnosis and treatment chosen during the priority setting workshop. Attendees: Nine patient representatives, nine clinicians, three facilitators, five observers
Again, the working partnership played a major role in distributing the questionnaire, with a hard copy being posted out with the Spring 2012 issue of the BTA’s Quiet magazine. Over a 6-week period, 630 responses were received. Quantitative research methods were used to produce a final weighted rank for each uncertainty that gave equal significance to votes from members of the public and healthcare professionals. Considering this list of weighted ranks, the Steering Group agreed on a final set of 26 important uncertainties to be considered at the final prioritizing meeting. Although this final step was primarily an objective, quantitative process, the Steering Group promoted several questions on ‘Cinderella’ topics that members considered to be particularly under-represented in the tinnitus research field.

**Developing consensus**

The London priority setting workshop in July 2012 was the most exciting part of the project and the culmination of months of hard work. Its purpose was to agree on a ‘top-ten’ list of tinnitus uncertainties through facilitated discussion between equal numbers of patient representatives and clinicians. Extensive debates within two parallel groups containing a mixture of patients and clinicians generated independent ranked lists that were then pooled together to produce a combined version. This version initiated a second conversation amongst the whole group. Lively debate focused around a small number of questions that were particularly challenging for the group to reach a consensus.

**Top ten clinical research questions**

The final top ten demonstrate the breadth of research required to identify mechanisms and models of tinnitus, the need for a cure and the requirement to better understand and demonstrate the efficacy of existing treatments (Table 2, column 1). It is particularly reassuring to see questions focusing on minority issues such as pediatric tinnitus and Deaf people with tinnitus. Some of the underpinning evidence supporting each uncertainty is given in column 2, with particular emphasis on those studies outside of the Cochrane Collaboration.

**Recommendations for future research strategy**

In consultation with the Professional Advisors’ Committee of the BTA, the Steering Group formulated ideas for future research strategies to address each uncertainty (Table 2, column 3). For so many questions there is a paucity of evidence and several of the questions in the top ten immediately lend themselves to systematic review, preferably within the Cochrane Collaboration since these are internationally recognized as the highest standard in evidence-based healthcare.

The Steering Group strongly supports general improvements in methodology and reporting in clinical trials for tinnitus. These have historically been rather low in quality [2,3] and several authors have already called for methodological standards in tinnitus trials, such as developing standards for tinnitus and tinnitus-related quality of life outcome measures in clinical studies that appropriately separate the effects of tinnitus from other treatment-related improvements (generalized anxiety, depression, hearing loss and so forth) [2,4,9]. International guidelines for good clinical practice and reporting should also be used. For example, the CONSORT statement provides guidance for randomized controlled trials [108], but has rarely been adopted in tinnitus research.

**Notable strengths & weaknesses**

The high response rate from members of the public has enabled a voice that is rarely given an opportunity to input into tinnitus research. Anecdotal comments from a small number of basic scientists indicate some unease in this process, implying that ‘patients might not sufficiently understand the condition to identify important and valid research questions’. Certainly the concept of a tinnitus uncertainty was challenging for some, with many responses being written as personal stories rather than specific questions for research. We would argue that those experiences are nevertheless extremely valuable and informative. The data management group, comprising members of the Steering Group, the JLA and the UK Database of Uncertainties about the Effects of Treatments (DUETs), used Patient, Intervention, Comparator and Outcome to identify active treatment components of the submission from the narrative text.

The implementation of the JLA Tinnitus PSP explored a novel cost-effective model involving minimal face-to-face contact with the JLA facilitator (at the launch and the priority setting workshop only) and a greater reliance on e-mail communication and teleconferencing between members of the Steering Group (five teleconferences, mostly at the collation and prioritization stages). The project was completed with a contribution of GB£6900 from the Judi Meadows Memorial Fund, with in-kind donations of staff time from the BTA and the NIHR Nottingham Hearing Biomedical Research Unit. Timescales for the project were negotiated within the partnership and carefully planned to minimize the overall duration of the project – just 11 months for the five stages of initiation, consultation, collation, prioritization and reporting. The collation stage was the most time-consuming and resource intensive because there was no way to have predicted the sheer volume of individual submissions. The Steering Group was also somewhat ill-prepared for submitting the uncertainties to the
Table 2. Top ten research suggestions identified by the James Lind Alliance Tinnitus Priority Setting Partnership.

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<thead>
<tr>
<th>Uncertainty in the diagnosis and assessment of treatment of tinnitus</th>
<th>Underpinning evidence</th>
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<tr>
<td>What management strategies are more effective than a usual model of audiological care in improving outcomes for people with tinnitus?</td>
<td>Cochrane Database of Systematic Reviews [106]</td>
<td>Step 1 – Studies comparing effects of different management strategies in reducing the functional impact of subjective idiopathic tinnitus and improving quality of life Proceeding to Step 2 – timely systematic review of the evidence from clinical trials</td>
</tr>
<tr>
<td>Is CBT/psychological therapy, delivered by audiology professionals, effective for people with tinnitus? Here comparisons might be with usual audiological care or CBT delivered by a psychologist</td>
<td>Cochrane Database of Systematic Reviews [106] Hesser et al. [10] Cima et al. [11]</td>
<td>Step 1 – Studies evaluating CBT and/or other psychological counselling approaches delivered by appropriately trained audiology professionals</td>
</tr>
<tr>
<td>What management strategies are more effective for improving tinnitus-related insomnia than a usual model of care?</td>
<td>Cochrane Database of Systematic Reviews [106] McKenna and Daniel [12] Edinger et al. [13]</td>
<td>Step 1 – A study comparing the effects of different management strategies specifically aimed at improving sleep for patients with tinnitus and insomnia, including CBT as one arm of the research design</td>
</tr>
<tr>
<td>Do any of the various available complementary therapies provide improved outcome for people with tinnitus compared with a usual model of care?</td>
<td>Cochrane Database of Systematic Reviews [106] Park et al. [14] Meehan et al. [15]</td>
<td>Step 1 – Studies comparing different complementary therapies for improving functional outcomes for people with subjective idiopathic tinnitus and compared with the usual model of care. Studies should consider those complementary therapies that have been shown to be beneficial in treating other chronic health conditions Proceeding to Step 2 – Timely systematic review of the evidence from clinical trials</td>
</tr>
<tr>
<td>What type of digital hearing aid or amplification strategy provides the most effective tinnitus relief?</td>
<td>None found</td>
<td>Step 1 – Studies to determine whether digital hearing aids are effective in reducing the functional impact of subjective idiopathic tinnitus. Proceeding if necessary to Step 2 – Parallel activities comprising: i) Studies evaluating the effects of different amplification strategies for people with subjective idiopathic tinnitus ii) Studies evaluating the effects of different hearing-aid devices, including digital combination devices (hearing aid and sound masker) as one arm of the trial iii) Timely systematic review of the evidence from clinical trials</td>
</tr>
<tr>
<td>What is the optimal set of guidelines for assessing children with tinnitus?</td>
<td>Shetye and Kennedy [16] Savastano [17,18]</td>
<td>Step 1 – Parallel activities comprising: i) A systematic approach to gain consensus among a multidisciplinary panel of experts about the most appropriate assessment methods and diagnostic criteria for children with tinnitus ii) Development of an evidence-based algorithm/pathway to aid clinical diagnosis based on existing research iii) Development of a systematic form of national data collection from existing services to provide an evidence base that would inform development of guidelines</td>
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CBT: Cognitive Behavior Therapy.
Table 2. Top ten research suggestions identified by the James Lind Alliance Tinnitus Priority Setting Partnership (cont.).

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<td>How can tinnitus be effectively managed in people who are deaf or have profound hearing loss?</td>
<td>None found</td>
<td>Step 1 – Parallel activities comprising: i) Studies to evaluate the effects of non-audiological tinnitus interventions in reducing tinnitus symptoms for people with profound hearing loss and tinnitus ii) A systematic review of the effects of multichannel intra-cochlear cochlear implants to suppress tinnitus Proceeding if necessary to Step 2 – Development of new treatment approaches for people with profound hearing loss or deafness and tinnitus</td>
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<td>Are there different types of tinnitus and can they be explained by different mechanisms in the ear or brain?</td>
<td>None found</td>
<td>Step 1 – Identification of (i) meaningful criteria for tinnitus subtyping; (ii) the underpinnings of the different tinnitus subtypes in humans in terms of inner ear pathology and neurobiology and (iii) their relevance for response to various treatments Proceeding if necessary to Step 2 – Development of an evidence-based algorithm/pathway to guide patient assessment, diagnosis and management</td>
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<td>What is the link between tinnitus and hyperacusis (over-sensitivity to sounds)?</td>
<td>Nelson and Chen [19]</td>
<td>Step 1 – A systematic review of the association between tinnitus and hyperacusis, including epidemiological data. Proceeding if necessary to Step 2 – Understanding of the underpinnings of tinnitus and hyperacusis in terms of inner ear pathology and neurobiology</td>
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<td>Which medications have proven to be effective in tinnitus management compared with placebo?</td>
<td>Cochrane Database of Systematic Reviews [106], Schilter et al. [20]</td>
<td>Step 1 – Systematic reviews of the other classes of drugs that are prescribed to alleviate tinnitus and/or associated symptoms. Proceeding if necessary to Step 2 – Studies of drug treatments for reducing tinnitus symptoms, including reduced perception of the tinnitus sound</td>
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**Future perspective**

The JLA Tinnitus PSP most successfully engaged the public and healthcare professionals in raising the profile of the unmet patient needs. In identifying what the most important questions for research are that will make a difference to people’s well being, it is our sincere hope that a greater proportion of tinnitus research undertaken will be directly relevant to patient and clinician priorities. The NIHR Evaluation Trials and Studies Coordinating Centre (NIHR NETSCC) will continue to manage the work of the JLA. This organizational restructure brings exciting opportunities for new research and activities.

**Communicating the outcome**

The main legacy of the project has been its contribution to the UK DUETs. This web-based public information repository sits within NHS Evidence and is managed by the NICE. Its purpose is to make uncertainties explicit primarily to help those prioritizing research in the UK to take into account the information needs of patients, carers and clinicians. Each record within DUETs contains information about the source of the uncertainty; evidence about why it is an uncertainty; references to any reliable up-to-date systematic reviews, information on uncertainty; references to any reliable up-to-date systematic reviews, information on need for new research and details of what is needed from new research and data. The intention is to publish all 390 ‘true’ uncertainties, although this will need to be implemented gradually, due to limited resources. The DUETs website continues to provide unrestricted access to the prioritized uncertainties, which are available in this database.

To raise awareness amongst key stakeholders, the top ten uncertainties have been widely disseminated to the public and hearing healthcare professionals in various membership magazines and annual meetings.

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**CBT: Cognitive Behavior Therapy.**
The James Lind Alliance Tinnitus Priority Setting Partnership

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No writing assistance was used in the production of the manuscript.

References
Papers of special note have been highlighted as:
■ of interest
■■ of considerable interest
■■ Up-to-date systematic review of the peer-reviewed literature, critically evaluating and conducting meta-analyses on the existing level of evidence for tinnitus management strategies identified within the UK Department of Health’s Good Practice Guideline (see [101]).
■■ Highlights the most important aspects of trial design in clinical studies in tinnitus and makes suggestions for an international methodological standard in tinnitus trials.
■■ Important strategic paper examining the ‘avoidable waste in research’ and makes a persuasive argument for involving clinicians and patients in setting research questions.
Research Update  Hall, Mohamad, Firkins, Fenton & Stockdale


Websites


104  British Tinnitus Association, James Lind Alliance Tinnitus Priority Setting Partnership. www.tinnitus.org.uk/JLA


106  Cochrane Database of Systematic Reviews on tinnitus. www.thecochranelibrary.com/details/browseReviews/579549/Tinnitus.html

107  Database of Abstracts of Reviews of Effects. www.crd.york.ac.uk/CRDWeb/AboutDare.asp

108  Consolidated Standards of Reporting Trials statement. www.consort-statement.org/home

109  NHS Evidence – UK Database of Uncertainties about the Effects of Treatments. www.library.nhs.uk/DUETs

107  Records the 26 priority tinnitus uncertainties with information about the source of the uncertainty, evidence for why it is an uncertainty, references to any reliable up-to-date systematic reviews, information on any reviews that need updating or extending and any in preparation, what is needed from new research, and details of any ongoing controlled trials.