National Institute for Health and Care Excellence

Final

# Tinnitus: assessment and management

## [J] Evidence review for imaging to investigate the cause of non-pulsatile tinnitus

*NICE guideline NG155*

*Diagnostic test and treat evidence review*

*March 2020*

*Final*

*This evidence review was developed by the National Guideline Centre*

**Disclaimer**

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Local commissioners and providers have a responsibility to enable the guideline to be applied when individual health professionals and their patients or service users wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with compliance with those duties.

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# Contents

# 1 Imaging to investigate the cause of non-pulsatile tinnitus

## 1.1 Review question: What is the most clinical and cost-effective imaging method to investigate the cause of non-pulsatile tinnitus?

## 1.2 Introduction

In certain groups of individuals with tinnitus, it is important to image the head and neck to exclude an organic cause for their symptoms. The role of imaging is to detect specific pathology that can be treated. A variety of imaging modalities may be considered depending on the type of tinnitus (pulsatile/non-pulsatile) and/or associated symptoms reported. Imaging modalities include ultrasound, computerised tomography and magnetic resonance imaging. A thorough history and clinical examination can direct the decision for imaging and the type of imaging.

Non-pulsatile tinnitus, which is heard as a continuous sound, is more common than pulsatile tinnitus. It can be idiopathic or associated with ontological, neurological or metabolic disorders. Unilateral or asymmetrical non-pulsatile tinnitus that is associated with neurological, audiological or head and neck signs and symptoms is more likely to indicate pathology than bilateral tinnitus or where there are no associated signs and symptoms. Following medical examination, healthcare professionals need to decide whether people with non-pulsatile tinnitus should be offered medical imaging, with options including CT scans, MRI and MRA. Scanning allows the diagnosis of significant and often treatable underlying diseases, for example a vestibular schwannoma which can cause tinnitus by compressing adjacent structures.

Whilst it is crucial not to miss significant pathology, it is also important not to scan people where significant pathology is unlikely. Not only is this cost unnecessary, it may be unpleasant and stressful for the person and possibly expose them to an unnecessary dose of ionising radiation.

## 1.3 PICO table

For full details see the review protocol in appendix A.

**Table 1: PICO characteristics of review question**

| | |
|---|---|
| **Population** | Children, young people and adults with non-pulsatile tinnitus.<br><br>Strata:<br>• People presenting with isolated non-pulsatile tinnitus<br>• People presenting with non-pulsatile tinnitus plus other conditions<br>• Somatic tinnitus<br>• Unilateral and bilateral |
| **Intervention(s)** | • CT scans<br>• MRI scans |
| **Comparison(s)** | • Compared to each other |

| | |
|---|---|
| | • No imaging |
| **Outcomes** | • Mortality (critical)<br><br>• Tinnitus severity (critical)<br><br>Impact of tinnitus (critical):<br>• Tinnitus distress<br>• Tinnitus annoyance<br><br>Health related QoL(critical):<br>• QoL (tinnitus)<br>• QoL<br><br>Tinnitus percept (important):<br>• Tinnitus loudness<br><br>Other co-occurring complaints (important):<br>• Depression<br>• Anxiety<br>• Anxiety and depression<br>• Sleep<br><br>Adverse events (important):<br>• Safety<br>• Tolerability<br>• Side effects |
| **Study design** | • Systematic review of RCTs<br>• RCT<br>• If there is an inadequate amount of RCT data, non-randomised comparative studies will be considered. |

# 1.4 Clinical evidence

## 1.4.1 Included studies

No relevant randomised controlled trial evidence comparing imaging methods with other imaging methods or with no imaging method were identified. Consequently, non-randomised comparative studies were also assessed. However, no relevant studies were identified for inclusion.

## 1.4.2 Excluded studies

See the excluded studies list in appendix I.

# 1.5 Economic evidence

## 1.5.1 Included studies

No relevant health economic studies were identified.

## 1.5.2 Excluded studies

No health economic studies that were relevant to this question were excluded due to assessment of limited applicability or methodological limitations.

See also the health economic study selection flow chart in appendix G.

## 1.5.3 Unit costs

**Table 2: UK costs of Imaging**

| Imaging Modality | Age | Contrast[(a)] | Number of areas[(b)] | Code | Costs |
|---|---|---|---|---|---|
| Computerised Tomography | 5 years and under | With Post-Contrast only | One area | RD21C | £152 |
| Computerised Tomography | Between 6 and 18 years | With Post-Contrast only | One area | RD21B | £135 |
| Computerised Tomography | 19 years and above | With Post-Contrast only | One area | RD21A | £106 |
| Magnetic Resonance Imaging | 5 years and under | Without Contrast | One area | RD01C | £138 |
| Magnetic Resonance Imaging | Between 6 and 18 years | Without Contrast | One area | RD01B | £142 |
| Magnetic Resonance Imaging | 19 years and above | Without Contrast | One area | RD01A | £144 |

(a) The committee provided the names of the key imaging techniques used for people with pulsatile tinnitus and the required contrast for each test. The costs were subsequently sourced from NHS reference costs.[9]

# 1.6 Evidence statements

## 1.6.1 Clinical evidence statements

- No relevant published evidence was identified.

## 1.6.2 Health economic evidence statements

- No relevant economic evaluations were identified.

# 1.7 The committee's discussion of the evidence

## 1.7.1 Interpreting the evidence

### 1.7.1.1 The outcomes that matter most

Tinnitus distress, annoyance and tinnitus severity were critical outcomes as they were thought to be common factors for people with tinnitus and impact their quality of life. Quality of life (tinnitus-related) and general quality of life were also critical outcomes due to their impact on the person with tinnitus. Mortality was also a critical outcome.

Tinnitus loudness, anxiety, depression, sleep, safety, tolerability and side effects were thought to be important outcomes.

The committee did not prioritise diagnostic accuracy outcomes such as sensitivity and specificity because they felt it was more useful to know about the effect on tinnitus outcomes and cost effectiveness of including these scans in the pathway compared to each other or no scanning.

There was no outcome data for any of the outcomes.

### 1.7.1.2 The quality of the evidence

Randomised controlled trials (RCTs) and systematic reviews of RCTs were searched for and assessed for eligibility but no relevant RCT evidence was identified which matched the review protocol. Consequently, non-randomised comparative studies were also searched for and assessed for eligibility. No relevant non-randomised comparative studies were identified.

### 1.7.1.3 Benefits and harms

The committee noted that whilst no evidence was identified, the use of imaging to investigate non-pulsatile tinnitus is a crucial part of the management pathway and therefore consensus recommendations were made.

The committee noted the importance of identifying and scanning the right people at the highest risk and not over scanning those at low risk. Scanning provides the opportunity to diagnose a significant and usually treatable disease such as a vestibular schwannoma compressing adjacent structures. However, the committee noted that most people once diagnosed with vestibular schwannoma are monitored unless neurological symptoms indicate treatment is required. Additionally, imaging non-pulsatile tinnitus can rule out vascular arteriovenous malformations, which could also be life-threatening.

Limiting scans to people with tinnitus and neurological, otological or head and neck signs (e.g. facial weakness, vertigo, asymmetric hearing loss) prevents unnecessary anxiety in people unlikely to have a significant pathology that needs treatment. Unilateral or asymmetrical non-pulsatile tinnitus that is associated with neurological, audiological or head and neck signs and symptoms is more likely to indicate pathology than bilateral tinnitus or where there are no associated signs and symptoms. Offering imaging of the internal auditory meati (IAM) to this population is also current practice.

Currently unnecessary scans are performed, where there is a low likelihood of any benefit to the person in terms of identification of findings that would change the management pathway. There is a risk of detecting sub-clinical findings which may never affect the person, but are likely to cause significant anxiety. In addition, it is very stressful for people and carers while waiting for their scans, having been told of the possibility that they may have a tumour. However, the committee noted that in some cases scanning can have an opposite effect by

reducing anxiety which can consequently improve tinnitus. Scans may be able to provide reassurance to concerned people who may want a tumour ruled out.

There are limited potential harms of not scanning everyone presenting with tinnitus in that there is a small probability of missing a serious condition such as a vestibular schwannoma. Two per 100,000 people per year in the UK present with vestibular schwannoma, 5% of this population present with normal hearing.[15] The committee noted that in clinical practice the incidence of vestibular schwannoma is very low in people with symmetrical/bilateral tinnitus.[6, 10]

If a person presents with unilateral non-pulsatile tinnitus and no associated symptoms or signs the incidence of pathology is low,[1, 2] and therefore clinicians should exercise caution in ordering scans of the IAM in these cases and consider the risks and benefits to the person.

Where a person presents with unilateral non-pulsatile tinnitus and neurological signs and symptoms then it is important to investigate further with a scan as there is a higher probability of a causative pathology, for example a space occupying lesion requiring treatment.

MRI scanning itself is very noisy and some people with tinnitus, and particularly those with hyperacusis, may find the scan very uncomfortable and may feel it exacerbates their condition. MRI may not be suitable for some people with metal implants or those unable to tolerate the confined space of the scan. In these cases, CT of the IAM is recommended, however this is associated with a risk from the dose of radiation received and risk of allergy to the contrast agent. It is for these reasons that the committee recommended MRI as the first option.

The recommendations apply equally to children, young people and adults.

### 1.7.2 Cost effectiveness and resource use

There were no economic evaluations available for this review question. The view of the committee was that in current practice, people with non-pulsatile unilateral tinnitus were in some cases being over tested. In the absence of clinical and economic evidence, the committee wanted to reduce the number of scans taking place by indicating that an MRI (or CT if MRI is contraindicated) of the internal auditory meati (IAM) be offered to adults, children and young people with non-pulsatile tinnitus only where there are neurological, otological or head and neck signs and symptoms. The rationale for this is that in these cases, the prevalence of a space occupying lesion that requires treatment is greater, and could result in high later expenditure if left untreated.

Where there are no such signs and symptoms, the committee made a weaker consensus recommendation that an MRI be ‘considered’ for people with unilateral or asymmetrical tinnitus as in these cases the prevalence of a significant pathology was expected to be lower and thereby an MRI would have a low positive predictive value (PPV). Finally, due to the low prevalence of significant pathology in those people with bilateral non-pulsatile tinnitus with no associated signs and symptoms, the committee agreed that testing these people would not be a cost-effective use of resources. This led them to make a negative recommendation.

These recommendations could reduce unnecessary testing and therefore there is a potential for modest savings for the NHS.

### 1.7.3 Other factors the committee took into account

Whilst some people may want a scan to rule out a tumour, the committee felt that in general people can be reassured by discussing this concern with and being fully informed by their doctor/audiologist. Many people will be anxious waiting of the results of the scans and the scans themselves can be uncomfortable, noisy and harmful in terms of radiation dose (CT).

Even if a vestibular schwannoma is found it can be slow to grow and only requires treatment if it starts to cause neurological symptoms. The committee concluded that many scans are unnecessary and have the potential to cause harm.

The committee noted that MRI is loud and some people may find this noise can affect their tinnitus. Radiology departments provide earplugs if this is the case.

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# Appendices

# Appendix A: Review protocols

**Table 3: Review protocol: Imaging method to investigate the cause of non-pulsatile tinnitus**

| ID | Field | Content |
|---|---|---|
| 0. | PROSPERO registration number | Not registered |
| 1. | Review title | The most clinical and cost effective imaging method to investigate the cause of non-pulsatile tinnitus |
| 2. | Review question | What is the most clinical and cost effective imaging method to investigate the cause of non-pulsatile tinnitus? |
| 3. | Objective | People with non-pulsatile tinnitus will generally undergo medical imaging following a medical examination. The options are usually CT scans, MRI and MRA.<br><br>The objective of the review is to evaluate the clinical effectiveness and cost-effectiveness of different imaging methods to investigate the cause of non-pulsatile tinnitus. These imaging methods would be followed up by appropriate treatments for the cause of non-pulsatile tinnitus and the resulting patient outcomes assessed. |
| 4. | Searches | The following databases will be searched:<br>• Cochrane Central Register of Controlled Trials (CENTRAL)<br>• Cochrane Database of Systematic Reviews (CDSR)<br>• Embase<br>• MEDLINE<br>• CINAHL, Current Nursing and Allied |

| | | |
|---|---|---|
| | | Health Literature<br>•<br>Searches will be restricted by:<br>• English language<br>• Human studies<br>• Letters and comments are excluded.<br><br>Other searches:<br>• Inclusion lists of relevant systematic reviews will be checked by the reviewer.<br><br>The searches may be re-run 6 weeks before final committee meeting and further studies retrieved for inclusion if relevant.<br><br>The full search strategies will be published in the final review. |
| 5. | Condition or domain being studied | Tinnitus |
| 6. | Population | Inclusion:<br>Children, young people and adults with non-pulsatile tinnitus.<br><br>Strata:<br>• People presenting with isolated non-pulsatile tinnitus<br>• People presenting with non-pulsatile tinnitus plus other conditions<br>• Somatic tinnitus<br>• Unilateral and bilateral<br><br>Exclusion: None |
| 7. | Intervention/Exposure/Test | • CT scans<br>• MRI scans |

| | | |
|---|---|---|
| 8. | Comparator/Reference standard/Confounding factors | • Compared to each other<br>• No imaging |
| 9. | Types of study to be included | • Systematic reviews<br>• RCTs<br>• If there is an inadequate amount of RCT data, non-randomised comparative studies will be considered |
| 10. | Other exclusion criteria | • Non-English language studies<br>• Studies will only be included if they report one or more of the outcomes listed above.<br>• Descriptive (non-comparative) studies will be excluded |
| 11. | Context | N/A |
| 12. | Primary outcomes (critical outcomes) | • Mortality<br>• Tinnitus severity<br><br>Impact of tinnitus:<br>• Tinnitus distress<br>• Tinnitus annoyance<br><br>Health related QoL:<br>• QoL (tinnitus)<br>• QoL |
| 13. | Secondary outcomes (important outcomes) | Tinnitus percept:<br>• Tinnitus loudness<br><br>Other co-occurring complaints:<br>• Depression<br>• Anxiety<br>• Anxiety and depression<br>• Sleep<br><br>Adverse events:<br>• Safety<br>• Tolerability<br>• Side effects |
| 14. | Data extraction (selection and coding) | EndNote will be used for reference management, sifting, citations and bibliographies. Titles and/or abstracts of studies retrieved using the search strategy and those from additional sources will be screened for |

| | | |
|---|---|---|
| | | inclusion.<br><br>The full text of potentially eligible studies will be retrieved and will be assessed for eligibility in line with the criteria outlined above.<br><br>10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer.<br><br>An in-house developed database; EviBase, will be used for data extraction. A standardised form is followed to extract data from studies (see Developing NICE guidelines: the manual section 6.4) and for undertaking assessment of study quality. Summary evidence tables will be produced including information on: study setting; study population and participant demographics and baseline characteristics; details of the intervention and control interventions; study methodology' recruitment and missing data rates; outcomes and times of measurement; critical appraisal ratings.<br><br>A second reviewer will quality-assure the extracted data. Discrepancies will be identified and resolved through discussion (with a third reviewer where necessary). |
| 15. | Risk of bias (quality) assessment | Risk of bias will be assessed using the appropriate checklist as described in Developing NICE guidelines: the manual.<br><br>For Intervention reviews the following checklist will be used according to study design being assessed:<br><br>• Systematic reviews: Risk of Bias in Systematic Reviews (ROBIS)<br>• Randomised Controlled Trial: Cochrane RoB (2.0)<br><br>Disagreements between the review authors over the risk of bias in particular studies will be resolved by discussion, with involvement of a third review author where necessary. |
| 16. | Strategy for data synthesis | Where possible, data will be meta-analysed. Pairwise meta-analyses will be performed using Cochrane Review Manager (RevMan5) to |

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|---|---|---|
| | | combine the data given in all studies for each of the outcomes stated above. A fixed effect meta-analysis, with weighted mean differences for continuous outcomes and risk ratios for binary outcomes will be used, and 95% confidence intervals will be calculated for each outcome.<br><br>Heterogeneity between the studies in effect measures will be assessed using the $I^2$ statistic and visually inspected. We will consider an $I^2$ value greater than 50% indicative of substantial heterogeneity. Sensitivity analyses will be conducted based on pre-specified subgroups using stratified meta-analysis to explore the heterogeneity in effect estimates. If this does not explain the heterogeneity, the results will be presented using random-effects.<br><br>GRADE pro will be used to assess the quality of each outcome, taking into account individual study quality and the meta-analysis results. The 4 main quality elements (risk of bias, indirectness, inconsistency and imprecision) will be appraised for each outcome.<br><br>Publication bias is tested for when there are more than 5 studies for an outcome.<br>Other bias will only be taken into consideration in the quality assessment if it is apparent.<br><br>Where meta-analysis is not possible, data will be presented and quality assessed individually per outcome.<br><br>If sufficient data is available to make a network of treatments, WinBUGS will be used for network meta-analysis. |
| 17. | Analysis of sub-groups | • Sudden onset tinnitus<br>• Hearing loss<br>• Neurological features (e.g. double vision, dysarthria, ataxia, vertigo/dizziness, facial palsy)<br>• Vascular risks (e.g. hypertension and hypercholesterolaemia) |
| 18. | Type and method of review | ☐ Intervention<br>☐ Diagnostic<br>☐ Prognostic |

| | | | | |
|---|---|---|---|---|
| | | ☐ Qualitative<br>☐ Epidemiologic<br>☐ Service Delivery<br>☒ Other – diagnostic test and treat | | |
| 19. | Language | English | | |
| 20. | Country | England | | |
| 21. | Anticipated or actual start date | 27/06/18 | | |
| 22. | Anticipated completion date | 11/03/20 | | |
| 23. | Stage of review at time of this submission | Review stage | Started | Completed |
| | | Preliminary searches | ☐ | ☑ |
| | | Piloting of the study selection process | ☐ | ☑ |
| | | Formal screening of search results against eligibility criteria | ☐ | ☑ |
| | | Data extraction | ☐ | ☑ |
| | | Risk of bias (quality) assessment | ☐ | ☑ |
| | | Data analysis | ☐ | ☑ |
| 24. | Named contact | 5a. Named contact<br>National Guideline Centre | | |

| | | |
|---|---|---|
| | | 5b Named contact e-mail Tinnitus@nice.org.uk<br><br>5e Organisational affiliation of the review National Institute for Health and Care Excellence (NICE) and the National Guideline Centre |
| 25. | Review team members | From the National Guideline Centre:<br>• Dr Jennifer Hill [Guideline lead]<br>• Ms Sedina Lewis/Ms Julie Neilson [Senior systematic reviewers]<br>• Dr Richard Clubbe [Systematic reviewer]<br>• Mr David Wonderling [Health economist lead]<br>• Mr Emtiyaz Chowdhury [Health economist]<br>• Ms Jill Cobb [Information specialist]<br>• Dr Giulia Zuodar [Project manager] |
| 26. | Funding sources/sponsor | This systematic review is being completed by the National Guideline Centre which receives funding from NICE. |
| 27. | Conflicts of interest | All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline. |
| 28. | Collaborators | Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website: [NICE guideline webpage]. |
| 29. | Other registration details | N/A |

| | | |
|---|---|---|
| 30. | Reference/URL for published protocol | N/A |
| 31. | Dissemination plans | NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as:<br>• notifying registered stakeholders of publication<br>• publicising the guideline through NICE's newsletter and alerts<br>• issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE. |
| 32. | Keywords | Tinnitus, non-pulsatile tinnitus, imaging, MRI, CT, scans |
| 33. | Details of existing review of same topic by same authors | N/A |
| 34. | Current review status | ☐ Ongoing<br>☒ Completed but not published<br>☐ Completed and published<br>☐ Completed, published and being updated<br>☐ Discontinued |
| 35.. | Additional information | N/A |
| 36. | Details of final publication | www.nice.org.uk |

**Table 4: Health economic review protocol**

| Review question | All questions – health economic evidence |
|---|---|
| **Objectives** | To identify health economic studies relevant to any of the review questions. |
| **Search criteria** | • Populations, interventions and comparators must be as specified in the clinical review protocol above.<br>• Studies must be of a relevant health economic study design (cost–utility analysis, cost-effectiveness analysis, cost–benefit analysis, cost–consequences analysis, comparative cost analysis).<br>• Studies must not be a letter, editorial or commentary, or a review of health economic evaluations. (Recent reviews will be ordered although not reviewed. The bibliographies will be checked for relevant studies, which will then be ordered.) |

| | |
|---|---|
| | • Unpublished reports will not be considered unless submitted as part of a call for evidence.<br>• Studies must be in English. |
| **Search strategy** | A health economic study search will be undertaken using population-specific terms and a health economic study filter – see appendix B below. |
| **Review strategy** | Studies not meeting any of the search criteria above will be excluded. Studies published before 2003, abstract-only studies and studies from non-OECD countries or the USA will also be excluded.<br>Each remaining study will be assessed for applicability and methodological limitations using the NICE economic evaluation checklist which can be found in appendix H of Developing NICE guidelines: the manual (2014).[8]<br><br>**Inclusion and exclusion criteria**<br>• If a study is rated as both 'Directly applicable' and with 'Minor limitations' then it will be included in the guideline. A health economic evidence table will be completed and it will be included in the health economic evidence profile.<br>• If a study is rated as either 'Not applicable' or with 'Very serious limitations' then it will usually be excluded from the guideline. If it is excluded then a health economic evidence table will not be completed and it will not be included in the health economic evidence profile.<br>• If a study is rated as 'Partially applicable', with 'Potentially serious limitations' or both then there is discretion over whether it should be included.<br><br>**Where there is discretion**<br>The health economist will make a decision based on the relative applicability and quality of the available evidence for that question, in discussion with the guideline committee if required. The ultimate aim is to include health economic studies that are helpful for decision-making in the context of the guideline and the current NHS setting. If several studies are considered of sufficiently high applicability and methodological quality that they could all be included, then the health economist, in discussion with the committee if required, may decide to include only the most applicable studies and to selectively exclude the remaining studies. All studies excluded on the basis of applicability or methodological limitations will be listed with explanation in the excluded health economic studies appendix below.<br><br>The health economist will be guided by the following hierarchies.<br>*Setting:*<br>• UK NHS (most applicable).<br>• OECD countries with predominantly public health insurance systems (for example, France, Germany, Sweden).<br>• OECD countries with predominantly private health insurance systems (for example, Switzerland).<br>• Studies set in non-OECD countries or in the USA will be excluded before being assessed for applicability and methodological limitations.<br>*Health economic study type:*<br>• Cost–utility analysis (most applicable).<br>• Other type of full economic evaluation (cost–benefit analysis, cost-effectiveness analysis, cost–consequences analysis).<br>• Comparative cost analysis.<br>• Non-comparative cost analyses including cost-of-illness studies will be excluded before being assessed for applicability and methodological limitations.<br>*Year of analysis:*<br>• The more recent the study, the more applicable it will be.<br>• Studies published in 2003 or later but that depend on unit costs and resource data |

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|---|---|
| | entirely or predominantly from before 2003 will be rated as 'Not applicable'.<br>• Studies published before 2003 will be excluded before being assessed for applicability and methodological limitations.<br>*Quality and relevance of effectiveness data used in the health economic analysis:*<br>• The more closely the clinical effectiveness data used in the health economic analysis match with the outcomes of the studies included in the clinical review the more useful the analysis will be for decision-making in the guideline. |

# Appendix B: Literature search strategies

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual.[8]

*For more detailed information, please see the Methodology Review*.

## B.1 Clinical search literature search strategy

Searches were constructed using a PICO framework where population (P) terms were combined with Intervention (I) and in some cases Comparison (C) terms. Outcomes (O) are rarely used in search strategies for interventions as these concepts may not be well described in title, abstract or indexes and therefore difficult to retrieve. Search filters were applied to the search where appropriate.

**Table 5: Database date parameters and filters used**

| Database | Dates searched | Search filter used |
|---|---|---|
| Medline (OVID) | 1946 – 02 April 2019 | Exclusions |
| Embase (OVID) | 1974 – 02 April 2019 | Exclusions |
| The Cochrane Library (Wiley) | Cochrane Reviews to 2019 Issue 4 of 12<br>CENTRAL to 2019 Issue 4 of 12<br>DARE, and NHSEED to 2015 Issue 2 of 4<br>HTA to 2016 Issue 4 of 4 | None |
| CINAHL, Current Nursing and Allied Health Literature (EBSCO) | Inception – 02 April 2019 | Exclusions |

**Medline (Ovid) search terms**

| | |
|---|---|
| 1. | Tinnitus/ |
| 2. | tinnit*.ti,ab. |
| 3. | 1 or 2 |
| 4. | letter/ |
| 5. | editorial/ |
| 6. | news/ |
| 7. | exp historical article/ |
| 8. | Anecdotes as Topic/ |
| 9. | comment/ |
| 10. | case report/ |
| 11. | (letter or comment*).ti. |
| 12. | or/4-11 |
| 13. | randomized controlled trial/ or random*.ti,ab. |
| 14. | 12 not 13 |
| 15. | animals/ not humans/ |
| 16. | exp Animals, Laboratory/ |
| 17. | exp Animal Experimentation/ |
| 18. | exp Models, Animal/ |

| | |
|---|---|
| 19. | exp Rodentia/ |
| 20. | (rat or rats or mouse or mice).ti. |
| 21. | or/14-20 |
| 22. | 3 not 21 |
| 23. | limit 22 to English language |

**Embase (Ovid) search terms**

| | |
|---|---|
| 1. | tinnitus/ |
| 2. | tinnit*.ti,ab. |
| 3. | 1 or 2 |
| 4. | letter.pt. or letter/ |
| 5. | note.pt. |
| 6. | editorial.pt. |
| 7. | Case report/ or Case study/ |
| 8. | (letter or comment*).ti. |
| 9. | or/4-8 |
| 10. | randomized controlled trial/ or random*.ti,ab. |
| 11. | 9 not 10 |
| 12. | animal/ not human/ |
| 13. | Nonhuman/ |
| 14. | exp Animal Experiment/ |
| 15. | exp Experimental animal/ |
| 16. | Animal model/ |
| 17. | exp Rodent/ |
| 18. | (rat or rats or mouse or mice).ti. |
| 19. | or/11-18 |
| 20. | 3 not 19 |
| 21. | limit 20 to English language |

**Cochrane Library (Wiley) search terms**

| | |
|---|---|
| #1. | MeSH descriptor: [Tinnitus] explode all trees |
| #2. | tinnit*:ti,ab |
| #3. | #1 or #2 |

**CINAHL (EBSCO) search terms**

| | |
|---|---|
| S1. | (MH "Tinnitus") |
| S2. | (MH "Tinnitus Retraining Therapy") |
| S3. | tinnit* |
| S4. | S1 OR S2 OR S3 |
| S5. | PT anecdote or PT audiovisual or PT bibliography or PT biography or PT book or PT book review or PT brief item or PT cartoon or PT commentary or PT computer program or PT editorial or PT games or PT glossary or PT historical material or PT interview or PT letter or PT listservs or PT masters thesis or PT obituary or PT pamphlet or PT pamphlet chapter or PT pictorial or PT poetry or PT proceedings or PT “questions and answers” or PT response or PT software or PT teaching materials or PT website |
| S6. | S4 NOT S5 |

## B.2 Health Economics literature search strategy

Health economic evidence was identified by conducting a broad search relating to the tinnitus population in NHS Economic Evaluation Database (NHS EED – this ceased to be updated after March 2015) and the Health Technology Assessment database (HTA) with no date restrictions. NHS EED and HTA databases are hosted by the Centre for Research and Dissemination (CRD). Additional searches were run on Medline and Embase for health economics and quality of life studies.

**Table 6: Database date parameters and filters used**

| Database | Dates searched | Search filter used |
|---|---|---|
| Medline | 2002 – 02 March 2019 | Exclusions<br>Health economics studies<br>Quality of life studies |
| Embase | 2002 – 02 March 2019 | Exclusions<br>Health economics studies<br>Quality of life studies |
| Centre for Research and Dissemination (CRD) | HTA - Inception – 31 Mar 2018<br>NHSEED - Inception to March 2015 | None |

**Medline (Ovid) search terms**

| | |
|---|---|
| 1. | Tinnitus/ |
| 2. | tinnit*.ti,ab. |
| 3. | 1 or 2 |
| 4. | letter/ |
| 5. | editorial/ |
| 6. | news/ |
| 7. | exp historical article/ |
| 8. | Anecdotes as Topic/ |
| 9. | comment/ |
| 10. | case report/ |
| 11. | (letter or comment*).ti. |
| 12. | or/4-11 |
| 13. | randomized controlled trial/ or random*.ti,ab. |
| 14. | 12 not 13 |
| 15. | animals/ not humans/ |
| 16. | exp Animals, Laboratory/ |
| 17. | exp Animal Experimentation/ |
| 18. | exp Models, Animal/ |
| 19. | exp Rodentia/ |
| 20. | (rat or rats or mouse or mice).ti. |
| 21. | or/14-20 |
| 22. | 3 not 21 |
| 23. | limit 22 to English language |
| 24. | Economics/ |
| 25. | Value of life/ |

| | |
|---|---|
| 26. | exp "Costs and Cost Analysis"/ |
| 27. | exp Economics, Hospital/ |
| 28. | exp Economics, Medical/ |
| 29. | Economics, Nursing/ |
| 30. | Economics, Pharmaceutical/ |
| 31. | exp "Fees and Charges"/ |
| 32. | exp Budgets/ |
| 33. | budget*.ti,ab. |
| 34. | cost*.ti. |
| 35. | (economic* or pharmaco?economic*).ti. |
| 36. | (price* or pricing*).ti,ab. |
| 37. | (cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab. |
| 38. | (financ* or fee or fees).ti,ab. |
| 39. | (value adj2 (money or monetary)).ti,ab. |
| 40. | or/24-39 |
| 41. | quality-adjusted life years/ |
| 42. | sickness impact profile/ |
| 43. | (quality adj2 (wellbeing or well being)).ti,ab. |
| 44. | sickness impact profile.ti,ab. |
| 45. | disability adjusted life.ti,ab. |
| 46. | (qal* or qtime* or qwb* or daly*).ti,ab. |
| 47. | (euroqol* or eq5d* or eq 5*).ti,ab. |
| 48. | (qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab. |
| 49. | (health utility* or utility score* or disutilit* or utility value*).ti,ab. |
| 50. | (hui or hui1 or hui2 or hui3).ti,ab. |
| 51. | (health* year* equivalent* or hye or hyes).ti,ab. |
| 52. | discrete choice*.ti,ab. |
| 53. | rosser.ti,ab. |
| 54. | (willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab. |
| 55. | (sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab. |
| 56. | (sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab. |
| 57. | (sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab. |
| 58. | (sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab. |
| 59. | (sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab. |
| 60. | or/41-59 |
| 61. | 23 and (40 or 60) |

**Embase (Ovid) search terms**

| | |
|---|---|
| 1. | tinnitus/ |
| 2. | tinnit*.ti,ab. |
| 3. | 1 or 2 |
| 4. | letter.pt. or letter/ |
| 5. | note.pt. |
| 6. | editorial.pt. |

| | |
|---|---|
| 7. | Case report/ or Case study/ |
| 8. | (letter or comment*).ti. |
| 9. | or/4-8 |
| 10. | randomized controlled trial/ or random*.ti,ab. |
| 11. | 9 not 10 |
| 12. | animal/ not human/ |
| 13. | Nonhuman/ |
| 14. | exp Animal Experiment/ |
| 15. | exp Experimental animal/ |
| 16. | Animal model/ |
| 17. | exp Rodent/ |
| 18. | (rat or rats or mouse or mice).ti. |
| 19. | or/11-18 |
| 20. | 3 not 19 |
| 21. | health economics/ |
| 22. | exp economic evaluation/ |
| 23. | exp health care cost/ |
| 24. | exp fee/ |
| 25. | budget/ |
| 26. | funding/ |
| 27. | budget*.ti,ab. |
| 28. | cost*.ti. |
| 29. | (economic* or pharmaco?economic*).ti. |
| 30. | (price* or pricing*).ti,ab. |
| 31. | (cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab. |
| 32. | (financ* or fee or fees).ti,ab. |
| 33. | (value adj2 (money or monetary)).ti,ab. |
| 34. | or/21-33 |
| 35. | quality adjusted life year/ |
| 36. | "quality of life index"/ |
| 37. | short form 12/ or short form 20/ or short form 36/ or short form 8/ |
| 38. | sickness impact profile/ |
| 39. | (quality adj2 (wellbeing or well being)).ti,ab. |
| 40. | sickness impact profile.ti,ab. |
| 41. | disability adjusted life.ti,ab. |
| 42. | (qal* or qtime* or qwb* or daly*).ti,ab. |
| 43. | (euroqol* or eq5d* or eq 5*).ti,ab. |
| 44. | (qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab. |
| 45. | (health utility* or utility score* or disutilit* or utility value*).ti,ab. |
| 46. | (hui or hui1 or hui2 or hui3).ti,ab. |

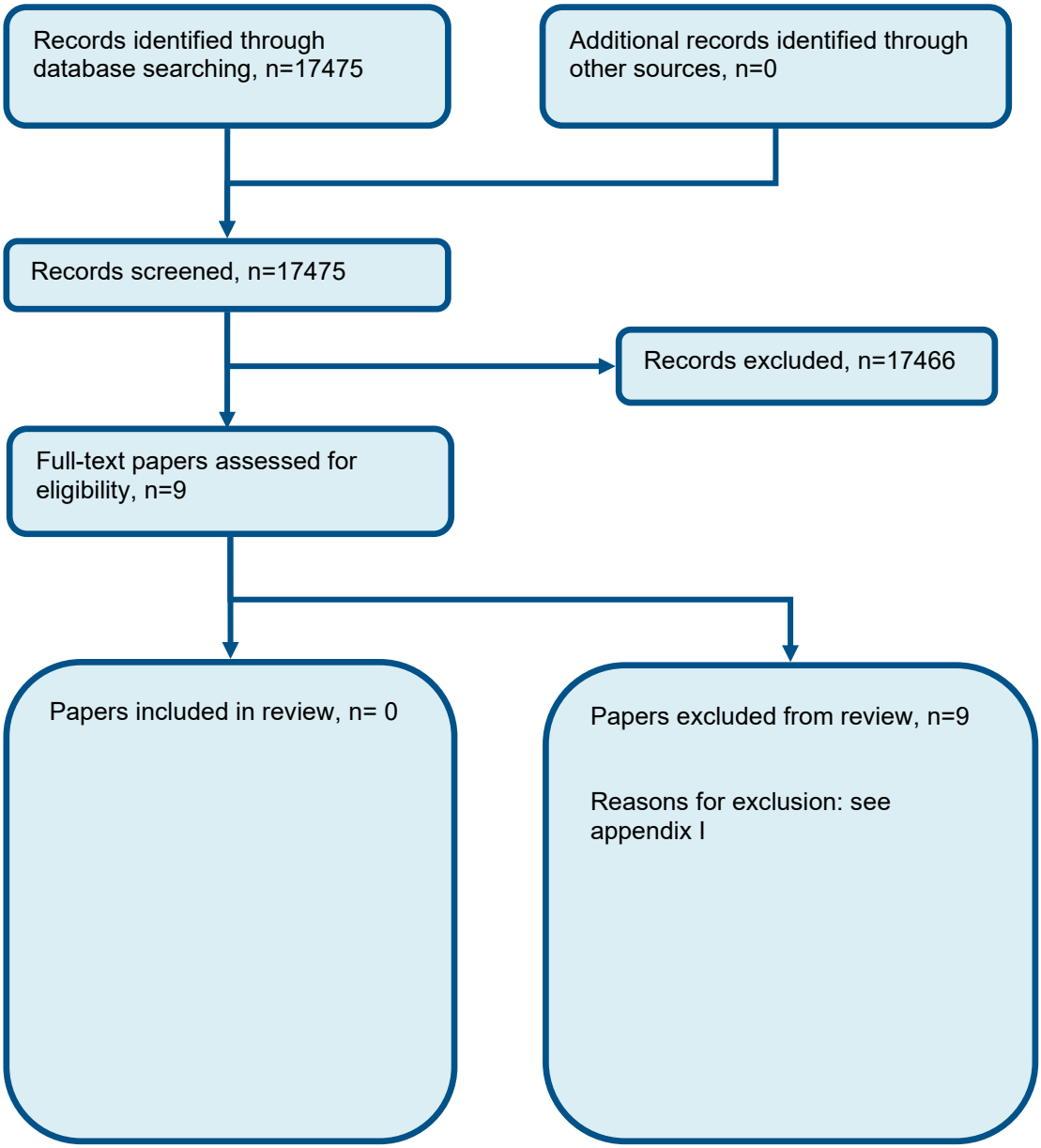
| | |
|---|---|
| 47. | (health* year* equivalent* or hye or hyes).ti,ab. |
| 48. | discrete choice*.ti,ab. |
| 49. | rosser.ti,ab. |
| 50. | (willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab. |
| 51. | (sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab. |
| 52. | (sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab. |
| 53. | (sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab. |
| 54. | (sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab. |
| 55. | (sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab. |
| 56. | or/35-55 |
| 57. | 20 and (34 or 56) |
| 58. | limit 57 to English language |

**NHS EED and HTA (CRD) search terms**

| | |
|---|---|
| #1. | MeSH DESCRIPTOR Tinnitus EXPLODE ALL TREES |
| #2. | (tinnit*) |
| #3. | #1 OR #2 |

# Appendix C: Clinical evidence selection

**Figure 1: Flow chart of clinical study selection for the review of imaging method to investigate the cause of non-pulsatile tinnitus**



# Appendix D: Clinical evidence tables

No evidence identified.

# Appendix E: Forest plots

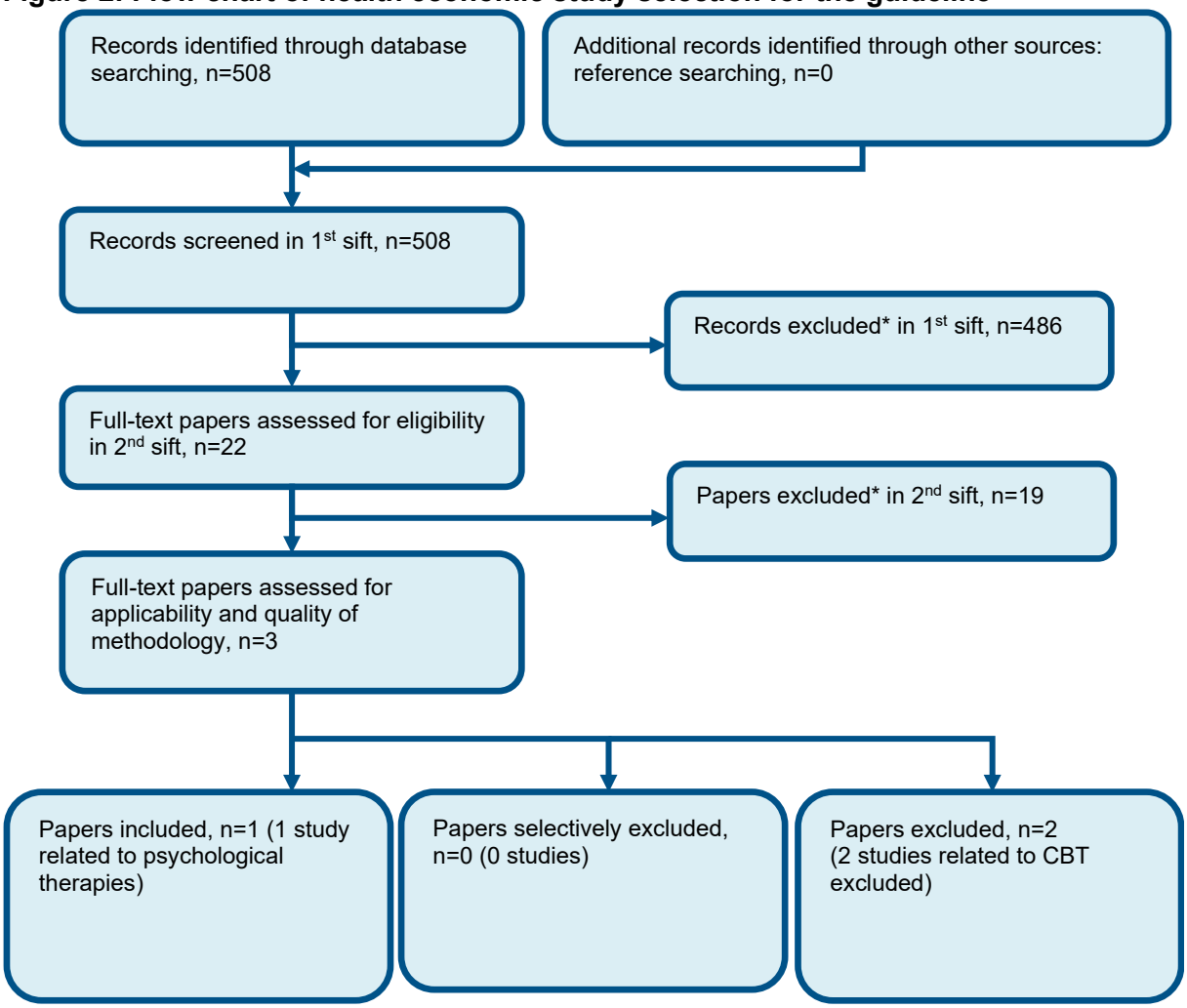
No evidence identified.

# Appendix F: GRADE tables

No evidence identified.

# Appendix G: Health economic evidence selection

**Figure 2: Flow chart of health economic study selection for the guideline**




* Non-relevant population, intervention, comparison, design or setting; non-English language

# Health economic evidence tables

None.

# Appendix H: Excluded studies

## H.1 Excluded clinical studies

**Table 7: Studies excluded from the clinical review**

| Reference | Reason for exclusion |
|---|---|
| Dawes 1999[3] | No relevant outcomes (details of diagnoses reported) |
| De Ridder 2005[4] | Incorrect comparison (MRI for pulsatile versus non-pulsatile tinnitus); no relevant outcomes |
| Fortnum 2009[5] | Systematic review of non-RCTs |
| Mundada 2015[7] | No relevant outcomes (details of diagnoses reported) |
| Remley 1990[11] | No relevant outcomes (details of diagnoses reported) |
| Seemann 2005[12] | No relevant outcomes (details of diagnoses reported) |
| Simonetti 2015[13] | Systematic review; incorrect comparisons (functional studies comparing people with tinnitus versus people without tinnitus) |
| Song 2012[14] | Meta-analysis; incorrect comparison (people with tinnitus versus people without tinnitus) |
| Waldvogel 1998[16] | No relevant outcomes (details of diagnoses reported) |

## H.2 Excluded health economic studies

None.