National Institute for Health and Care Excellence

Final

Tinnitus: assessment and management

[G] Evidence review for assessing quality of life

NICE guideline NG155

Intervention evidence review

March 2020

Final

This evidence review was developed by the National Guideline Centre

Disclaimer

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or service users. The recommendations in this guideline are not mandatory and the guideline does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and, where appropriate, their carer or guardian.

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.

NICE guidelines cover health and care in England. Decisions on how they apply in other UK countries are made by ministers in the Welsh Government, Scottish Government, and Northern Ireland Executive. All NICE guidance is subject to regular review and may be updated or withdrawn.

ISBN 978-1-4731-3711-0

Contents

1 Assessing quality of life

1.1 Review question: what is the most clinically and cost-effective method of assessing quality of life related to tinnitus?

1.2 Introduction

Tinnitus can have an important negative impact on a person's quality of life. It can affect how they go about their usual daily activities and impact on work, school, home and relationships as well as their mental health. The majority of tinnitus management strategies are focussed on improving the quality of life of the person living with tinnitus. Whilst the majority of management strategies available cannot permanently obliterate the tinnitus percept, they can increase acceptance of the tinnitus and improve quality of life. It is useful to assess quality of life to enable a management plan to be developed between the healthcare professional and the person with tinnitus.

This review considers the most clinically and cost-effective way to assess the impact tinnitus has on quality of life. These assessments would be followed up by appropriate interventions for tinnitus and the resulting patient outcomes assessed. These assessments can also be used to record and assess progress after using the interventions described in other reviews.

1.3 PICO table

For full details see the review protocol in appendix A.

Table 1: PICO characteristics of review question

Population	People presenting to a healthcare setting with tinnitus Strata: children/young people and adults
Intervention(s)	Adult questionnaires/interviews, e.g.: • Short Form 36 Health Survey Questionnaire (SF-36) • EuroQoL • Nottingham Health Profile (NHP) • Tinnitus Handicap Questionnaire • Tinnitus Reaction Questionnaire • Interviews • Likert scales • WHO-5 • Visual Analogue Scales Children's questionnaires: • CF-EQ-5D • Paediatric Quality of Life Questionnaire (PEDSQL) • Children's Auditory Performance Scale (CHAPS) – impact on schooling • Children's Auditory Performance Questionnaire • The Listening Inventory for Education Efficacy Tool (LIFE) • Screening Instrument for Targeting Educational Risk (SIFTER) • My World Tool (Ida Institute) • FISHER

	• LSQ • Interviews • Likert scales • Visual Analogue Scales
Comparison(s)	• Compared to each other • Compared to no questionnaire
Outcomes	• Tinnitus severity (critical) Impact of tinnitus (critical): • Tinnitus distress • Tinnitus annoyance Health related QoL(critical): • QoL (tinnitus) • QoL Tinnitus percept (important): • Tinnitus loudness Other co-occurring complaints (important): • Depression • Anxiety • Anxiety and depression • Sleep Adverse events (important): • Safety • Tolerability • Side effects
Study design	• Systematic review of RCTs • RCT • 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 tinnitus questionnaires with other tinnitus questionnaires or standard care (history and physical examination) were identified. Consequently, non-randomised comparative 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.

1.6 Evidence statements

1.6.1 Clinical evidence statements

- No clinical 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.

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

There was no outcome data for any of the 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 using questionnaires/interviews to assess the impact that tinnitus has on quality of life.

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 that matched the protocol were identified.

1.7.1.3 Benefits and harms

No evidence was identified that evaluated the clinical effectiveness of questionnaires and interviews to assess quality of life in people with tinnitus. The committee noted that whilst no

evidence was identified, the assessment of quality of life is a crucial part of the management pathway and therefore consensus recommendations were made.

The committee noted that an interview-style conversation about quality of life should be considered as an appropriate approach. This will ensure that tinnitus support can be tailored to the individual. The meaning of quality of life can be subjective and may have different meanings for different individuals. The assessment can include a discussion about different factors that contribute to quality of life such as work and functionality in everyday life. Asking these questions will allow management strategies to be tailored to the needs of the person and will allow some assessment of whether their outcomes have improved.

For children and young people, questions about the impact at school and home are important. When difficulties at school are raised it is helpful to ask more specifically about listening, listening effort, distractibility, concentration and focus, in noise or not in noise, with the teacher, with friends, in classrooms, during exams. Healthcare professionals can consider asking questions such as “do you avoid anything?”, “‘is it getting in the way of anything?” and “does it stop you enjoying things as much?”. Similar questions can be asked to adults with tinnitus.

The committee agreed that it is not current clinical practice to assess quality of life using questionnaires. With several other questionnaires being used to provide an overall assessment of the condition and specifically psychological impact, the committee did not want people with tinnitus to feel ‘over-whelmed’ by the quantity of questionnaires. The committee also noted some overlap in the domains of general tinnitus questionnaires such as the TFI, which assess components of quality of life (for example, enjoyment of social activities and relationships with family and friends). It was noted that currently quality of life questionnaires are predominantly used in research. The committee also noted that there are currently no quality of life questionnaires that are sensitive enough to assess or measure change in the impact of tinnitus on quality of life. It was decided that a recommendation encouraging the standard use of questionnaires was not necessary but asking people about their quality of life was good practice.

1.7.2 Cost effectiveness and resource use

There were no economic evaluations available for this question. The recommendation is not expected to require additional staff time. The committee noted that quality of life assessment tools are not widely used in practice and were mindful that people may be overwhelmed by the number of questionnaires they have to complete. As the committee were not advocating a change in practice and clinicians are already expected to ask people about the impact of tinnitus on quality of life, the committee did not consider that there were important economic considerations when forming their recommendation.

1.7.3 Other factors the committee took into account

Currently tinnitus related quality of life assessment is variable. The committee believed it to be an essential part of the management and development of a management plan across the care pathway. The committee wanted to recommend that the impact of tinnitus on quality of life is considered as standard practice and that this should be conducted using an interview style conversation.

There are some resources for assessment of quality of life within education usually used for children with hearing loss/ difficulties that can support this e.g. the LIFE, CHAPS and SIFTER.

References

1. Beukes EW, Manchaiah V, Valien TE, Baguley DM, Allen PM, Andersson G. Positive experiences related to living with tinnitus: A cross-sectional survey Clinical Otolaryngology. 2018; 43(2):489-495

2. El Refaie A, Davis A, Kayan A, Baskill J, Lovell E, Owen V. A questionnaire study of the quality of life and quality of family life of individuals complaining of tinnitus pre- and post-attendance at a tinnitus clinic. International Journal of Audiology. 2004; 43(7):410-416

3. Fackrell K, Hall DA, Barry JG, Hoare DJ. Performance of the Tinnitus Functional Index as a diagnostic instrument in a UK clinical population. Hearing Research. 2018; 358:74-85

4. Hebert S, Carrier J. Sleep complaints in elderly tinnitus patients: a controlled study. Ear and Hearing. 2007; 28(5):649-55

5. Karatas E, Deniz M. The comparison of acoustic and psychic parameters of subjective tinnitus. European Archives of Oto-Rhino-Laryngology. 2012; 269(2):441-7

6. Milerova J, Anders M, Dvorak T, Sand PG, Koniger S, Langguth B. The influence of psychological factors on tinnitus severity. General Hospital Psychiatry. 2013; 35(4):412-416

7. Moring J, Bowen A, Thomas J, Bira L. The emotional and functional impact of the type of tinnitus sensation. Journal of Clinical Psychology in Medical Settings. 2016; 23(3):310-318

8. Muluk NB. The SF-36 Health Survey in tinnitus patients with a high jugular bulb. Journal of Otolaryngology - Head and Neck Surgery. 2009; 38(2):166-171

9. National Institute for Health and Care Excellence. Developing NICE guidelines: the manual [Updated October 2018] London. National Institute for Health and Care Excellence, 2014. Available from: https://www.nice.org.uk/process/pmg20/chapter/introduction-and-overview

10. Newman CW, Wharton JA, Jacobson GP. Retest stability of the tinnitus handicap questionnaire. Annals of Otology, Rhinology and Laryngology. 1995; 104(9 Pt 1):718-23

11. Passi S, Ralli G, Capparelli E, Mammone A, Scacciatelli D, Cianfrone G. The THI questionnaire: Psychometric data for reliability and validity of the Italian version. International Tinnitus Journal. 2008; 14(1):26-33

12. Sanchez L, Stephens D. A Tinnitus problem questionnaire in a clinic population. Ear and Hearing. 1997; 18(3):210-217

13. Sourgen PM, Ross E. Perceptions of tinnitus in a group of senior citizens. South African Journal of Communication Disorders. 1998; 45:61-75

14. Wakabayashi S, Saito H, Oishi N, Shinden S, Ogawa K. Effects of tinnitus treatments on sleep disorders in patients with tinnitus. International Journal of Audiology. 2018; 57(2):110-114

15. Weidt S, Delsignore A, Meyer M, Rufer M, Peter N, Drabe N et al. Which tinnitus-related characteristics affect current health-related quality of life and depression? A cross-sectional cohort study. Psychiatry Research. 2016; 237:114-121

Appendices

Appendix A: Review protocols

Table 2: Review protocol: What is the most clinically and cost-effective questionnaire to assess quality of life related to tinnitus?

ID	Field	Content
0.	PROSPERO registration number	Not registered
1.	Review title	Clinical and cost-effective methods of assessing the quality of life related to tinnitus
2.	Review question	What is the most clinically and cost-effective method of assessing quality of life related to tinnitus?
3.	Objective	The review aims to evaluate the clinical effectiveness and cost-effectiveness of different validated questionnaires and other methods that are utilised by different healthcare professionals for the assessment of tinnitus. These questionnaires/methods would be followed up by appropriate treatments for tinnitus and the resulting patient outcomes assessed. Quality of life is defined as relationships, ability to work for adults and concentration, listening for children.
4.	Searches	The following databases will be searched: • Cochrane Central Register of Controlled Trials (CENTRAL) • Cochrane Database of Systematic Reviews (CDSR) • Embase • MEDLINE • CINAHL, Current Nursing and Allied Health Literature • PsycINFO

		Searches will be restricted by: • English language • Human studies • Letters and comments are excluded. Other searches: • Inclusion lists of relevant systematic reviews will be checked by the reviewer. The searches may be re-run 6 weeks before final committee meeting and further studies retrieved for inclusion if relevant. The full search strategies will be published in the final review.
5.	Condition or domain being studied	Tinnitus
6.	Population	Inclusion: People presenting to a healthcare setting with tinnitus Strata: • Children/young people (up to 18 years) • Adults Exclusion: None
7.	Intervention/Exposure/Test	Questionnaires/interviews, e.g.: Adults: • Short Form 36 Health Survey Questionnaire (SF-36) • EuroQoL • Nottingham Health Profile (NHP) • Tinnitus Handicap Questionnaire • Tinnitus Reaction Questionnaire • Interviews • Likert scales

		• WHO-5 • Visual Analogue Scales Children/young people (up to 18 years): • CF-EQ-5D • Paediatric Quality of Life Questionnaire (PEDSQL) • Children's Auditory Performance Scale (CHAPS) – impact on schooling • Children's Auditory Performance Questionnaire • The Listening Inventory for Education Efficacy Tool (LIFE) • Screening Instrument for Targeting Educational Risk (SIFTER) • My World Tool (Ida Institute) • FISHER • LSQ • Interviews • Likert scales • Visual Analogue Scales
8.	Comparator/Reference standard/Confounding factors	• Compared to each other • Compared to no questionnaire
9.	Types of study to be included	• Systematic reviews • RCTs • If there is an inadequate amount of RCT data, non-randomised comparative studies will be considered
10.	Other exclusion criteria	• Non-English language studies • Studies will only be included if they report one or more of the outcomes listed above • Descriptive (non-comparative) studies will be excluded • Non-English version of questionnaires
11.	Context	N/A
12.	Primary outcomes (critical outcomes)	• Tinnitus severity Impact of tinnitus: • Tinnitus distress • Tinnitus annoyance

		Health related QoL: • QoL (tinnitus) • QoL
13.	Secondary outcomes (important outcomes)	Tinnitus percept: • Tinnitus loudness Other co-occurring complaints: • Depression • Anxiety • Anxiety and depression • Sleep Adverse events: • Safety • Tolerability • 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. The full text of potentially eligible studies will be retrieved and will be assessed for eligibility in line with the criteria outlined above. 10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer. 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. 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. For Intervention reviews the following checklist will be used according to study design being assessed: • Systematic reviews: Risk of Bias in Systematic Reviews (ROBIS) • Randomised Controlled Trial: Cochrane RoB (2.0) 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 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. 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. 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. Publication bias is tested for when there are

		more than 5 studies for an outcome. Other bias will only be taken into consideration in the quality assessment if it is apparent. Where meta-analysis is not possible, data will be presented and quality assessed individually per outcome. If sufficient data is available to make a network of treatments, WinBUGS will be used for network meta-analysis.		
17.	Analysis of sub-groups	• People with learning disability or cognitive impairment • Visual impairment • Literacy level • Non English language speakers • Hearing loss • Mode of delivery		
18.	Type and method of review	☐ Intervention ☐ Diagnostic ☐ Prognostic ☐ Qualitative ☐ Epidemiologic ☐ Service Delivery ☒ 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 National Guideline Centre 5b Named contact e-mail Tinnitus@nice.org.uk 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: • Dr Jennifer Hill [Guideline lead] • Ms Sedina Lewis/Ms Julie Neilson [Senior systematic reviewers] • Dr Richard Clubbe [Systematic reviewer] • Mr David Wonderling [Health economist lead] • Mr Emtiyaz Chowdhury [Health economist] • Ms Jill Cobb [Information specialist] • 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: • notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts • 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, quality of life, questionnaires, interview
33.	Details of existing review of same topic by same authors	N/A
34.	Current review status	☐ Ongoing

		☒ Completed but not published ☐ Completed and published ☐ Completed, published and being updated ☐ Discontinued
35..	Additional information	N/A
36.	Details of final publication	www.nice.org.uk

Table 3: 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. • 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). • 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. • 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. 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).[9] **Inclusion and exclusion criteria** • 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. • 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. • If a study is rated as 'Partially applicable', with 'Potentially serious limitations' or both then there is discretion over whether it should be included. **Where there is discretion** 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.

The health economist will be guided by the following hierarchies.

Setting:

- UK NHS (most applicable).
- OECD countries with predominantly public health insurance systems (for example, France, Germany, Sweden).
- OECD countries with predominantly private health insurance systems (for example, Switzerland).
- Studies set in non-OECD countries or in the USA will be excluded before being assessed for applicability and methodological limitations.

Health economic study type:

- Cost–utility analysis (most applicable).
- Other type of full economic evaluation (cost–benefit analysis, cost-effectiveness analysis, cost–consequences analysis).
- Comparative cost analysis.
- Non-comparative cost analyses including cost-of-illness studies will be excluded before being assessed for applicability and methodological limitations.

Year of analysis:

- The more recent the study, the more applicable it will be.
- Studies published in 2003 or later but that depend on unit costs and resource data entirely or predominantly from before 2003 will be rated as ‘Not applicable’.
- Studies published before 2003 will be excluded before being assessed for applicability and methodological limitations.

Quality and relevance of effectiveness data used in the health economic analysis:

- 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.[9]

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 4: 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 CENTRAL to 2019 Issue 4 of 12 DARE, and NHSEED to 2015 Issue 2 of 4 HTA to 2016 Issue 4 of 4	None
CINAHL, Current Nursing and Allied Health Literature (EBSCO)	Inception – 02 April 2019	Exclusions
PsycINFO (ProQuest)	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

PsycINFO (ProQuest) search terms

1.	((MAINSUBJECT.EXACT.EXPLODE("Tinnitus") OR tinnit*) NOT (su.exact.explode("rodents") OR su.exact.explode("mice") OR (su.exact("animals") NOT (su.exact("human males") OR su.exact("human females"))) OR ti(rat OR rats OR mouse OR mice))) AND la.exact("ENG")Limits applied

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 5: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline	2002 – 02 March 2019	Exclusions Health economics studies Quality of life studies
Embase	2002 – 02 March 2019	Exclusions Health economics studies Quality of life studies
Centre for Research and Dissemination (CRD)	HTA - Inception – 31 Mar 2018 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.

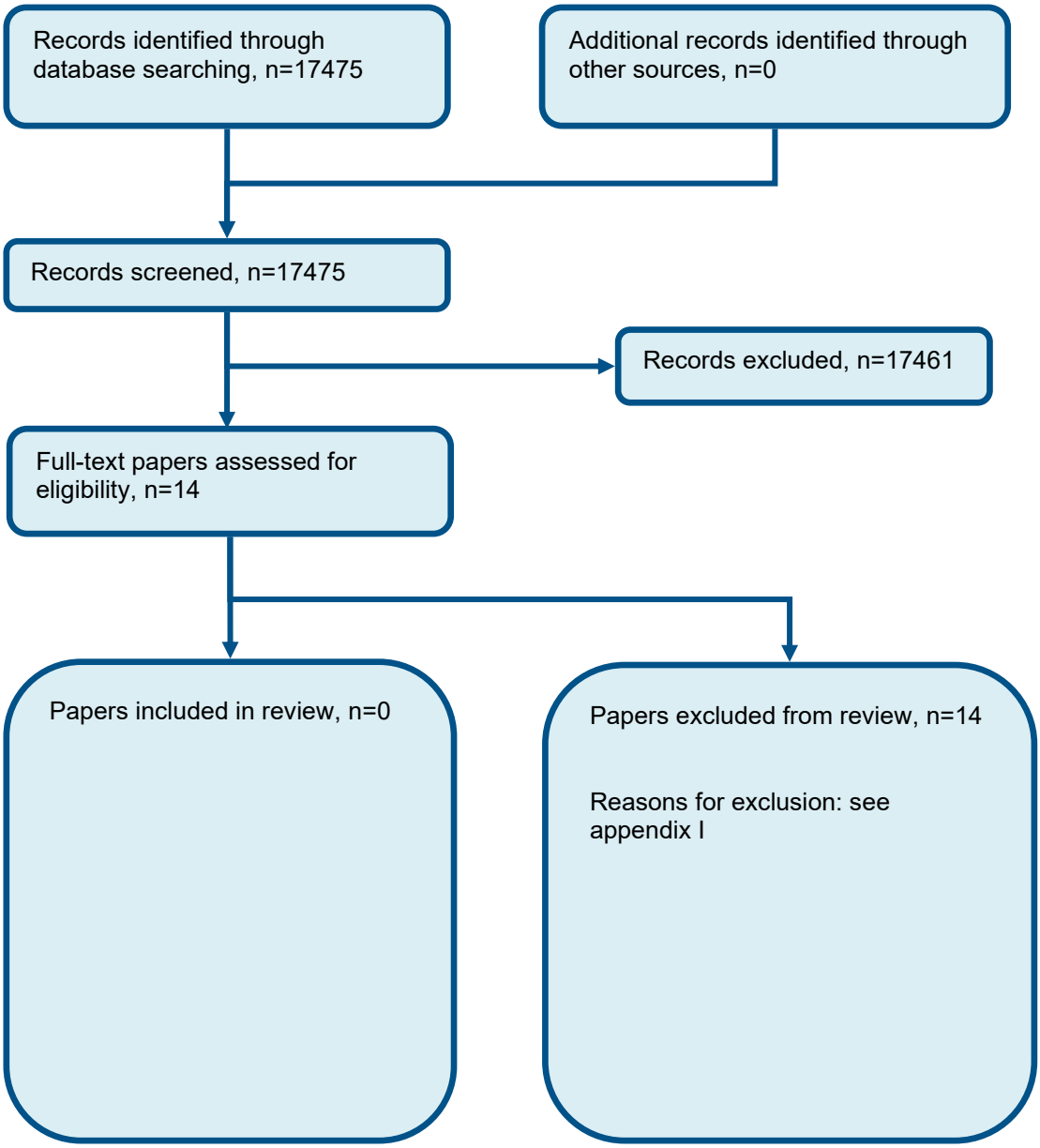
43.	(euroqol* or eq5d* or eq 5*).ti,ab.
44.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
45.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
46.	(hui or hui1 or hui2 or hui3).ti,ab.
47.	(health* year* equivalent* or hye or hyes).ti,ab.
48.	discrete choice*.ti,ab.
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



Appendix D: Clinical evidence tables

No evidence identified.

Appendix E: Forest plots

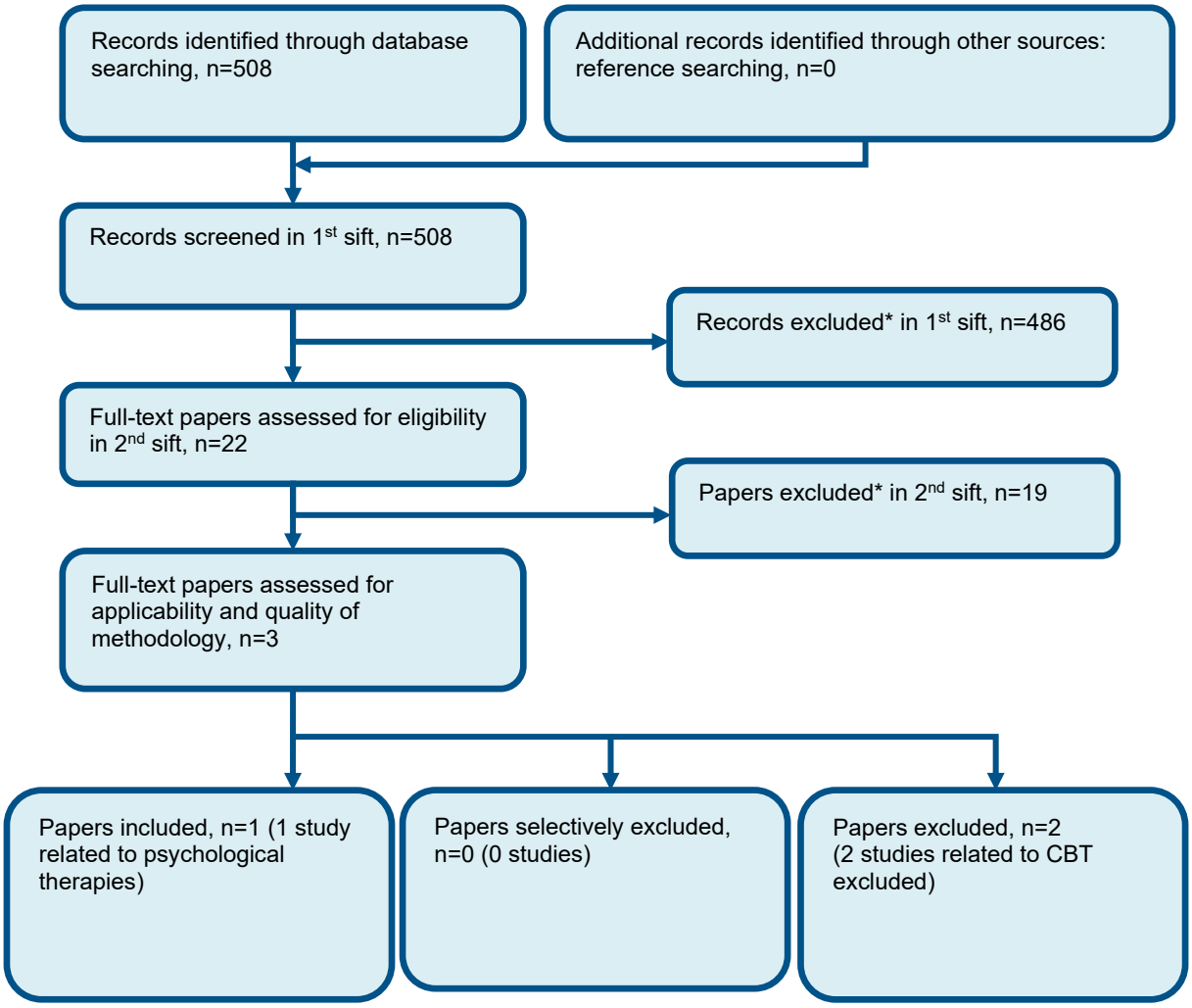
No evidence identified.

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

Appendix H: Excluded studies

H.1 Excluded clinical studies

Table 6: Studies excluded from the clinical review

Reference	Reason for exclusion
Beukes 2018[1]	No relevant outcome data
El Refaie 2004[2]	Incorrect comparison (all participants received one type of questionnaire)
Fackrell 2018[3]	No relevant outcome data
Hebert 2007[4]	Incorrect comparison (tinnitus patients versus non-tinnitus patients)
Karatas 2012[5]	No relevant outcome data
Milerova 2013[6]	No relevant outcome data
Moring 2016[7]	No relevant outcome data
Muluk 2009[8]	Incorrect comparison (tinnitus patients versus non-tinnitus patients)
Newman 1995[10]	No relevant outcome data
Passi 2008[11]	incorrect intervention (validation of Italian questionnaire)
Sanchez 1997[12]	No relevant outcome data
Sourgen 1998[13]	No relevant outcome data
Wakabayashi 2018[14]	Incorrect comparison (all participants received one type of questionnaire)
Weidt 2016[15]	No relevant outcome data

H.2 Excluded health economic studies

None.