National Institute for Health and Care Excellence

Final

Tinnitus: assessment and management

[M] Evidence review for sound therapy and amplification devices

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 All NICE guidance is subject to regular review and may be updated or withdrawn.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 Sound therapy and amplification devices

1.1 Introduction

Hearing loss is a common factor underlying tinnitus, although some people with normal hearing also experience tinnitus. Loss of hearing is often an unnoticeable and gradual process and many people are surprised when they are told that they have a hearing loss. It is quite common for people to assume, incorrectly, that it is their tinnitus rather than their hearing loss that is causing hearing difficulties. Management of hearing loss in adults is covered by NICE guideline NG98. In this review we focus on only those people who have tinnitus.

Nationally, there are differences in how people with a hearing loss and tinnitus are treated. In some locations people with tinnitus and a measurable hearing loss are offered hearing aids to reduce the impact of their tinnitus.

People who have tinnitus often report that it is more noticeable and bothersome in a quiet environment, for example at night, and that listening to other sounds can make it less intrusive. The deliberate use of any sound to reduce tinnitus awareness or reduce the distress associated with it can be called *sound enrichment or sound therapy.* Sound therapy/ enrichment can be used as a self-help technique or as a component of a broader tinnitus management programme delivered with the support of a healthcare professional. Various types of sound are used including relaxing music, natural sounds such as waves and white noise.

Using sound to help manage tinnitus is common but practice varies across the country and may include hearing aids with a sound generator activated, wearable sound devices or other types of sound enrichment. Sound therapy/enrichment covers many different aspects from wearable devices, environmental sound, smart phone apps, bedside/ table top generators. The provision of sound therapy devices is inconsistent across the country.

The purpose of this review is to identify evidence as to whether hearing aids, sound therapy/ sound enrichment are a clinically and cost effective way of reducing the impact of tinnitus.

1.2 Review question: What is the clinical and cost effectiveness of sound therapy and sound enrichment for people with tinnitus?

1.3 PICO table

For full details see the review protocol in appendix A.

Table 1: PICO characteristics of sound therapy review question

Population	Children, young people and adults presenting with tinnitus Strata: Children/young people (up to 18 years) and adults
Intervention(s)	• Sound enrichment (e.g. environmental sound, a CD or mp3 download or the radio, a smartphone App, bedside/table-top sound generators, a wearable sound generator) • Combination hearing devices (hearing aid combined with sound generator) • Customised sound-based therapies, e.g. amplitude modulated tones, notched noise/music

	• Masking
Comparison(s)	• Interventions compared with each other • "Tinnitus counselling" - education including coping strategies, provision of information and advice and relaxation • Psychological therapy o Cognitive Behavioural therapy (CBT) o Mindfulness-based interventions e.g. Cognitive therapy and MBSR o Brief solution focused therapy o Narrative therapy o Family therapy/Systemic therapy o Acceptance and commitment therapy (ACT) o EMDR • Amplification devices for those with a hearing loss o Hearing aids o Implantable devices (including cochlear implants, bone-anchored hearing aids, bone-conduction hearing implants, bone-bridge/middle-ear devices) o Combination device (sound generator and hearing aids) • Control group (i.e. no sound therapy)
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 (e.g. skin irritation and hyperacusis)
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 Review question: What is the clinical and cost effectiveness of amplification devices for people with tinnitus who do not require an amplification device for a hearing loss alone?

1.5 PICO table

For full details see the review protocol in appendix A.

Table 2: PICO characteristics of amplification devices review question

Population	Children, young people and adults with tinnitus and hearing loss Strata: Children/young people (up to 18 years) and adults
Intervention(s)	• Hearing aids • Implantable devices (including cochlear implants, bone-anchored hearing aids, bone-conduction hearing implants, bone-bridge/middle-ear devices) • Combination device (sound generator and hearing aids)
Comparison(s)	• Compared to each other • Control group/usual care
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 (e.g. skin irritation and hyperacusis)
Study design	• Systematic review of RCTs • RCT • If there is an inadequate amount of RCT data, non-randomised comparative studies will be considered.

1.6 Clinical evidence

1.6.1 Included studies

The two review questions on sound therapy (including sound enrichment) and amplification devices were combined into a single evidence review.

A Cochrane review of sound therapy (using amplification devices and/or sound generators) with 8 studies[45] was included in its entirety as it matched our protocols. The methods of data analysis and quality assessment for this part of the review are therefore in accordance with the methods described in the Cochrane review.

NICE methods include the avoidance of an overall risk of bias assessment of "unclear", whilst Cochrane methods allow the use of "unclear". For the included Cochrane review, the Cochrane 'risk of bias' tool in Review Manager 5.3 was used for risk of bias assessments, whereas NICE methods include the use of Cochrane 'risk of bias' 2.0 tool. For data analysis, NICE methods consist of the use of Peto odds ratio analyses where there are zero events in either arm or a less than 1% event rate. Cochrane reviews however include the use of risk ratio analyses where there are zero events in both arms of included studies. Additionally, Cochrane selected different populations for potential subgroup analyses to investigate heterogeneity (see Appendix A: for our selected subgroup populations). The subgroups selected by Cochrane were: hearing loss, differing baseline tinnitus symptom severity and baseline anxiety or depression.

Two further randomised controlled trials that were outside the scope of the Cochrane review were also included in our review.[27, 28] These compared customised sound therapy (pitch matched) to non-customised sound therapy (broadband noise), and customised sound therapy (altered music) to sound enrichment, respectively.

The included studies are summarised in Table 3 below.[27, 28] Evidence from these studies is summarised in the clinical evidence summaries below (Table 4, Table 5, Table 6 and Table 7).

See also the study selection flow chart in appendix C, study evidence tables in appendix D, forest plots in appendix E and GRADE tables in appendix H.

1.6.2 Excluded studies

One Cochrane review was excluded (Hoare 2014[24] as it was superseded by the more recent Cochrane review).

See the excluded studies list in appendix H.

1.6.3 Summary of clinical studies included in the evidence review

Table 3: Summary of studies included in the evidence review

Study	Intervention and comparison	Population	Outcomes	Comments
Sereda 2018[45] (Systematic review including: Henry 2015[19], Erlandsson 1987[15], Stephens 1985[48], Melin 1987[32], Dos santos 2014[13], Parazzini 2011[39], Zhang 2013[53], Henry 2017[20])	Systematic review comparing amplification devices, sound generators and combination devices, with each other or with no device. Eight studies were included: Seven studies investigated the effects of hearing aids. Four studies investigated the effects of combination hearing devices (hearing aids combined with sound generators). Three studies investigated the effects of ear-level sound generator devices. Four studies included control arms with no amplification or sound generation device.	n=590 The review included studies of adults (≥ 18 years) with acute (≤ 3 months) or chronic (> 3 months) subjective idiopathic tinnitus. Age (range of means): 38.8 to 74.4 years. Gender: 44% female. Duration of tinnitus (range): 3 months to over 20 years. Various countries (USA, Brazil, Sweden, China, UK, Italy)	<u>Hearing aids versus sound generator (1 study):</u> Tinnitus severity (follow up: 3 months): measured using the Tinnitus Handicap Inventory (THI), scale range 0-100 Tinnitus severity (follow up: 6 months): measured using the Tinnitus Handicap Inventory (THI), scale range 0-100 Tinnitus severity (follow up: 12 months): measured using the Tinnitus Handicap Inventory (THI), scale range 0-100 <u>Hearing aids versus sound generator (3 studies):</u> Tinnitus severity (follow up: 3 – 5 months): various measures used, scale range 0-100	Most of the included studies did not report data for the outcomes specified in the protocol
Li 2016 [27]	Intervention (n=25) Customised sound-based therapy - participants were instructed to listen	n=50 People with unilateral or bilateral tinnitus for ≥12	Tinnitus distress (follow-up: 12 months): measured using the Tinnitus Handicap Inventory (THI), scale range 0-100	

Study	Intervention and comparison	Population	Outcomes	Comments
	to altered music at least 2 hours per day. Music was altered according to changes observed at the auditory cortex using proprietary software. For every participant, a music therapy package with 6 hours of altered music was created using the software. Comparison (n=25) Control group – sound enrichment without altered sounds, participants were instructed to listen to the music for at least 2 hours per day. No further details reported.	months Age (mean) : 55.5 years Gender (male to female ratio: 2:1 Duration of tinnitus: ≥10 years - 42% Canada	Tinnitus severity (follow-up: 12 months): measured using the Tinnitus Functional Index (TFI), scale range 0-100 Depression (follow-up: 12 months): measured using the Hospital Anxiety and Depression Scale (HADS) (depression sub-scale used), scale range 0-21 Anxiety (follow-up: 12 months): measured using the Hospital Anxiety and Depression Scale (HADS) (depression sub-scale used), scale range 0-21	
Mahboubi 2017[28] Crossover RCT	Intervention (n=23) Customised sound therapy where software pitch-matched the person's frequency and intra-aural and inter-frequency attenuation characteristics for tonal and non-tonal tinnitus to create a sound file that sounded similar to broadband noise but with less acoustic energy. This sound file was then mixed with 6 hours of classical music and uploaded onto an MP3 player and given to the subjects along with open ear headphones. Comparison (n=23)	n=23 People presenting with tinnitus (of 3 months or more) Age (mean): 53 (11) years Gender (male to female ratio): 12/6 (completers data provided only) Duration of tinnitus (mean): 118 +/- 9 months USA	Tinnitus loudness (follow-up: post-treatment 3 months): measured using a tinnitus loudness rating scale, scale range not reported Tinnitus depression (follow-u: post-treatment 3 months: measured using the Beck Depression Index, scale range 0-63 Tinnitus anxiety (follow-up: post-treatment 3 months): measured using the Beck Anxiety Inventory, scale range 0-63 Tinnitus severity (follow-up post-treatment 3 months): measured using	

Study	Intervention and comparison	Population	Outcomes	Comments
	The non-customised sound therapy involved the creation of a broadband noise with a spectral frequency of 1, meaning that equal proportions of all frequencies were present.		the Tinnitus Handicap Inventory, scale range 0-100	

See appendix D for full evidence tables.

1.6.4 Quality assessment of clinical studies included in the evidence review

Table 4: Clinical evidence summary: Amplification (hearing aid) only versus ear-level sound generator only

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Sound generator only	Risk difference with Amplification only (95% CI)
Tinnitus symptom severity THI. Scale from: 0 to 100.	91 (1 study) 3 months	⨁⨁⊖⊖ LOW1,2 due to risk of bias, imprecision		The mean tinnitus symptom severity in the control groups was -20.2	The mean tinnitus symptom severity in the intervention groups was 1.3 higher (5.72 lower to 8.32 higher)
Tinnitus symptom severity at 6 months THI. Scale from: 0 to 100.	91 (1 study) 6 months	⨁⨁⊖⊖ LOW1,2 due to risk of bias, imprecision		The mean tinnitus symptom severity at 6 months in the control groups was -23.8	The mean tinnitus symptom severity in the intervention groups was 1.8 lower (8.82 lower to 5.22 higher)
Tinnitus symptom severity at 12 months THI. Scale from: 0 to 100.	91 (1 study) 12 months	⨁⨁⊖⊖ LOW1,2 due to risk of bias, imprecision		The mean tinnitus symptom severity at 12 months in the control groups was -29.2	The mean tinnitus symptom severity in the intervention groups was 0.9 lower (7.92 lower to 6.12 higher)

1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Sound generator only	Risk difference with Amplification only (95% CI)
at very high risk of bias 2 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs					

Table 5: Clinical evidence summary: Amplification and sound generator (combination hearing aid) versus amplification (hearing aid) only

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Hearing aid	Risk difference with Combination hearing aid (95% CI)
Tinnitus symptom severity at 3-5 months THI and TFI. Scale from: 0 to 100.	114 (3 studies) 3-5 months	⨁⨁⨀⨀ LOW1,2 due to risk of bias, imprecision		The mean tinnitus symptom severity in the control groups was -32.9	The mean tinnitus symptom severity in the intervention groups was 3.61 lower (11.4 lower to 4.17 higher)
1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias 2 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs					

Table 6: Clinical evidence summary: Customised sound therapy versus non-customised sound therapy (broadband noise)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Non-customised sound therapy (broadband noise)	Risk difference with Customised sound therapy (95% CI)
Loudness Tinnitus loudness rating scale	36 (1 study) 3 months	⨁⨀⨀⨀ VERY LOW1,2 due to risk of bias, imprecision		The mean loudness in the control groups was 6.1	The mean loudness in the intervention groups was 1.2 lower (2.58 lower to 0.18 higher)
Depression (BDI)	36	⨁⨀⨀⨀		The mean depression in the	The mean depression in the intervention groups was

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Non-customised sound therapy (broadband noise)	Risk difference with Customised sound therapy (95% CI)
BDI. Scale from: 0 to 63.	(1 study) 3 months	VERY LOW1,2 due to risk of bias, imprecision		control groups was 6.9	0.6 lower (6.12 lower to 4.92 higher)
Anxiety (BAI) BAI. Scale from: 0 to 63.	36 (1 study) 3 months	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean anxiety in the control groups was 7.9	The mean anxiety in the intervention groups was 0.4 higher (6.04 lower to 6.84 higher)
Severity (THI) THI Scale from 0 to 100	36 (1 study) 3 months	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean severity in the control group was 41	The mean severity in the intervention groups was 9.5 lower (22.8 lower to 3.8 higher)

1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
2 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 7: Clinical evidence summary: Customised sound therapy (altered music) versus sound enrichment

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Sound enrichment	Risk difference with Customised sound therapy (altered music) (95% CI)
Tinnitus distress (12 months) THI. Scale from: 0 to 100.	28 (1 study) 12 months	⊕⊕⊖⊖ LOW1,2 due to risk of bias, imprecision		The mean tinnitus distress in the control groups was 48.13	The mean tinnitus distress in the intervention groups was 18.46 lower (31.65 to 5.27 lower)
Tinnitus severity (12 months) TFI Scale from 0 to 100	28 (1 study) 12 months	⊕⊕⊖⊖ LOW1,2 due to risk of bias,		The mean tinnitus severity in the control groups was 52.03	The mean tinnitus severity in the intervention groups was 12.7 lower (29.47 lower to 4.07 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Sound enrichment	Risk difference with Customised sound therapy (altered music) (95% CI)
		imprecision			
Depression (12 months) HADS - depression. Scale from: 0 to 21.	28 (1 study) 12 months	⨁⨁⊖⊖ LOW1,2 due to risk of bias, imprecision		The mean depression in the control groups was 5.63	The mean depression in the intervention groups was 1.88 lower (4.89 lower to 1.13 higher)
Anxiety (12 months) HADS - anxiety. Scale from: 0 to 21.	28 (1 study) 12 months	⨁⨁⊖⊖ LOW1,2 due to risk of bias, imprecision		The mean anxiety in the control groups was 8.81	The mean anxiety in the intervention groups was 2.73 lower (6 lower to 0.54 higher)

1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
2 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

See appendix F for full GRADE tables.

1.7 Economic evidence

1.7.1 Included studies

No relevant health economic studies were identified.

1.7.2 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.

1.7.3 Unit costs

Table 8: UK costs of sound therapy and amplification

Procedure	National Average Unit Cost
Fitting of hearing aid or device for Tinnitus[(a)]	£117

(a) NHS reference cost[36]

1.8 Evidence statements

1.8.1 Clinical evidence statements

Amplification (hearing aid) only versus ear-level sound generator only

One study (n=91) were included in this comparison; no clinical evidence was reported for the critical outcomes: tinnitus distress, tinnitus annoyance, general quality of life and tinnitus-related quality of life. There was no clinical difference between amplification devices (hearing aid) and sound generators in terms of improving tinnitus severity. The overall quality of the evidence was low due to risk of bias and imprecision.

Amplification and ear-level sound generator (combination hearing aid) versus amplification (hearing aid) only

Three studies (n=114) were included in this comparison; no clinical evidence was reported for the critical outcomes: tinnitus distress, tinnitus annoyance, general quality of life and tinnitus-related quality of life. There was no clinical difference between combination hearing aids and hearing aids in terms of improving tinnitus severity. The overall quality of the evidence was Low due to risk of bias and imprecision.

Customised sound therapy versus non-customised sound therapy (broadband noise)

One study (n=36) was included in this comparison; no clinical evidence was reported for the critical outcomes: tinnitus distress, tinnitus annoyance, general quality of life and tinnitus-related quality of life. There was no clinical difference between customised sound therapy and non-customised sound therapy (broadband noise) in terms of improving depression, anxiety and tinnitus loudness. There was clinical benefit of customised sound therapy in terms of tinnitus severity. The overall quality of the evidence was Very Low due to risk of bias and imprecision.

Customised sound therapy (altered music) versus sound enrichment

One study (n=28) was included in this comparison; no clinical evidence was reported for the critical outcomes: tinnitus annoyance, general quality of life and tinnitus-related quality of life. There was a clinical benefit of customised sound therapy in terms of tinnitus distress and tinnitus severity. There was no clinical difference between altered music and sound enrichment for the outcomes of depression and anxiety. The overall quality of evidence was Low due to risk of bias and imprecision.

1.8.2 Health economic evidence statements

- No relevant economic evaluations were identified.

1.9 The committee's discussion of the evidence

1.9.1 Interpreting the evidence

1.9.1.1 The outcomes that matter most

Tinnitus distress, annoyance and tinnitus awareness 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.

1.9.1.2 The quality of the evidence

A Cochrane review was identified and was included in this review. The Cochrane review identified evidence for sound therapy (using amplification devices and/or sound generators) for the management of tinnitus. We included two additional studies on sound therapy.

Amplification devices

The Cochrane review identified studies which evaluated the use of hearing aids and combination hearing aids. One study evaluated the use of hearing aids compared to sound generators and reported outcome data for tinnitus severity at different time-points (3 months, 6 months and 12 months). Three studies were identified which compared combination hearing aids (amplification and sound generator) with a standard hearing aid. These three studies also reported outcome data for tinnitus severity. Overall, the evidence was low quality due to risk of bias and imprecision.

Sound therapy

Two randomised controlled trials (RCTs) relating to sound therapy were included in addition to the studies found in the relevant Cochrane Review. They were not included in the Cochrane Review as they compared one type of sound therapy to another. The Cochrane Review included studies that compared amplification devices, ear-level sound generators or combination devices to either placebo or education/information only with no device or in comparison to one another. The two trials evaluated customised sound therapy; the evidence was graded from very low to low for the various outcomes due to risk of bias and imprecision.

1.9.1.3 Benefits and harms

Amplification devices

The committee recommended amplification devices (hearing aids and combination devices) for those who present with tinnitus and have hearing loss. This was a strong recommendation and is in line with the NICE Hearing loss guideline (NG98) which

recommends offering hearing aids to those whose ability to communicate and hear is hampered by their hearing loss. The committee agreed that this should also apply to children and young people, although they are not covered by NG98.

For those with hearing loss but no self-perceived hearing difficulties the committee recommended that amplification devices should be considered. We did not find evidence for this population but the committee noted that sometimes those with a hearing loss but no self-perceived hearing difficulties may not always be offered a hearing aid for their hearing loss alone, but with co-occurring tinnitus they may experience a benefit for both their tinnitus and their hearing loss. The committee agreed to make a recommendation for further research to evaluate amplification devices for people with tinnitus who have hearing loss but no perceived hearing difficulties (see Appendix I:).

The committee also noted that there was no evidence for the use of amplification devices for people who are d/Deaf or who have a severe-to-profound hearing loss. Standard care for tinnitus in this population is not feasible, it is important that effective interventions are developed and investigated. The committee agreed that a research recommendation is made for the use of amplification devices for this population (see Appendix I:).

The committee recommended that people with tinnitus and normal hearing should not be offered amplification devices because there is unlikely to be an improvement to the impact of the tinnitus and amplification of sound where it is not required is inappropriate.

Sound therapies

With the limited evidence available for sound therapy as a sole intervention, the committee agreed that a recommendation cannot be made for its use in isolation. There are many different types of sound therapy and there was insufficient evidence for any particular type. The use of customised sound therapies is not part of current clinical practice in the UK. Two studies included in this review evaluated customised sound therapies. Whilst, these studies showed evidence of clinical benefit for customised sound therapies, the committee agreed that this evidence was insufficient for a practice recommendation at present. The evidence for sound therapy in combination with other interventions is discussed in evidence review P, where a research recommendation was made for the evaluation of sound therapy with tinnitus support.

Occasionally people report an increase or change in their tinnitus when using sound or hearing aids. While changes to the sound processing settings may help to alleviate this for some people, it is important to be alert to this possibility and include this in the discussion of the various management options.

1.9.2 Cost effectiveness and resource use

There were no economic evaluations available for this review question. The committee indicated that offering amplification devices (hearing aids) to people with tinnitus and hearing loss (that impacts their ability to communicate and hear) should be in line with NG98. However, the committee have also included children in their recommendation which is an extension to NG98 but as this recommendation is consistent with current practice it would not lead to added expenditure.

The committee indicated the existence of a subgroup of people who have a hearing loss (that they do not perceive to affect their ability to communicate and hear) alongside bothersome tinnitus that may also benefit from hearing aids. Due to the economic uncertainty and the potential for added expenditure, the committee concluded that this should be a ‘consider’ recommendation and be determined by clinicians on a case by case basis (as is current practice) as opposed to offering these devices routinely.

Finally, the committee provided a negative recommendation for the provision of hearing aids in the absence of hearing loss (as there is potential for harm) which has the potential to generate modest cost savings.

Sound therapy and sound enrichment devices are widely used in the NHS and the committee highlighted that from their clinical experience people with tinnitus do benefit from the use of these interventions. However, a concern raised by the committee was the existence of many different variants of sound therapy from environmental sounds (i.e. windows open) or audio generated from one's mobile phone (which would not incur cost for the NHS) to expensive sound masking and customisable devices where the sounds generated are tuned specifically for a person's tinnitus. As there is a lack of clarity on which of these variants would be most clinically effective and cost-effective, the committee opted to form a research recommendation to explore this question further.

1.9.3 Other factors the committee took into account

Whilst people with tinnitus and a hearing loss that affects their ability to communicate are covered by NICE guideline NG98 (recommendation 1.6.1) and they should be receiving hearing aids currently, there are a group with hearing loss (but no self- perceived hearing difficulties) where practice is more variable. Some units may need to review their local guidelines for these people and amplification devices will need to be considered on a case by case basis. The person's choice is important as different management strategies will suit people differently. These strategies should be offered with a discussion of the possible benefits and the alternatives available. The rationale for using hearing aids should be clearly explained as some people find it confusing that adding sound can help.

Lay members reported that there is a lack of knowledge in the general population about how hearing aids may help them cope with their tinnitus. This, coupled with the belief that 'nothing can be done about tinnitus', means that many people with hearing difficulties but who do not have hearing aids do not consult their GP about their tinnitus. Some who have hearing difficulties do not report having tinnitus. This may mean they are referred inappropriately and do not receive the tinnitus support they need. There are some people who have chosen not to accept hearing aids for their hearing difficulties but have welcomed them when they learn it may also help with their tinnitus.

References

1. Arfeller C, Vonthein R, Plontke SK, Plewnia C. Efficacy and safety of bilateral continuous theta burst stimulation (cTBS) for the treatment of chronic tinnitus: design of a three-armed randomized controlled trial. Trials. 2009; 10:74

2. Argstatter H, Grapp M, Hutter E, Plinkert PK, Bolay HV. The effectiveness of neuro-music therapy according to the Heidelberg model compared to a single session of educational counseling as treatment for tinnitus: a controlled trial. Journal of Psychosomatic Research. 2015; 78(3):285-292

3. Argstatter H, Grapp M, Plinkert PK, Bolay HV. Heidelberg Neuro-Music Therapy for chronic-tonal tinnitus-treatment outline and psychometric evaluation. International Tinnitus Journal. 2012; 17(1):31-41

4. Argstatter H, Krick C, Plinkert P, Bolay HV. Music therapy for noisiform tinnitus. Concept development and evaluation. HNO. 2010; 58(11):1085-1093

5. Argstatter H, Plinkert P, Bolay HV. Music therapy for tinnitus patients: an interdisciplinary pilot study of the Heidelberg Model. HNO. 2007; 55(5):375-383

6. Arndt S, Aschendorff A, Laszig R, Beck R, Schild C, Kroeger S et al. Comparison of pseudobinaural hearing to real binaural hearing rehabilitation after cochlear implantation in patients with unilateral deafness and tinnitus. Otology & Neurotology. 2011; 32(1):39-47

7. Arts RA, George EL, Janssen M, Griessner A, Zierhofer C, Stokroos RJ. Tinnitus suppression by intracochlear electrical stimulation in single sided deafness - a prospective clinical trial: Follow-up. PloS One. 2016; 11(4):e0153131

8. Basile CE, Fournier P, Hutchins S, Hebert S. Psychoacoustic assessment to improve tinnitus diagnosis. PloS One. 2013; 8(12):e82995

9. Blasco MA, Redleaf MI. Cochlear implantation in unilateral sudden deafness improves tinnitus and speech comprehension: meta-analysis and systematic review. Otology & Neurotology. 2014; 35(8):1426-1432

10. Davis PB, Paki B, Hanley PJ. Neuromonics tinnitus treatment: Third clinical trial. Ear and Hearing. 2007; 28(2):242-259

11. Del Bo L, Ambrosetti U. Hearing aids for the treatment of tinnitus. Progress in Brain Research. 2007; 166:341-5

12. Derks LS, Wegner I, Smit AL, Thomeer HG, Topsakal V, Grolman W. Effect of day-case unilateral cochlear implantation in adults on general and disease-specific quality of life, postoperative complications and hearing results, tinnitus, vertigo and cost-effectiveness: protocol for a randomised controlled trial. BMJ Open. 2016; 6(10):e012219

13. dos Santos GM, Bento RF, de Medeiros IR, Oiticcica J, da Silva EC, Penteado S. The influence of sound generator associated with conventional amplification for tinnitus control: randomized blind clinical trial. Trends in hearing. 2014; 18:1-9

14. dos Santos GM, Silva EM, Penteado S, Bento RF. The use of hearing aids generic sound generator with integrated control of tinnitus-pilot study. International Archives of Otorhinolaryngology. 2012; 16(Suppl 1):26

15. Erlandsson S, Ringdahl A, Hutchins T, Carlsson SG. Treatment of tinnitus: a controlled comparison of masking and placebo. British Journal of Audiology. 1987; 21(1):37-44

16. Ferrari GMS, Sanchez TG. The influence of BTE hearing aid earmold ventilation on tinnitus control: crossover blind randomized clinical trial. XVIII World Congress of the International Federation of Oto-Rhino-Laryngological Societies Rome, Italy, 25-30 June, 2005. 2005:Abstract No. F74

17. Heijneman KM, Kleine E, Dijk P. A randomized double-blind crossover study of phase-shift sound therapy for tinnitus. Otolaryngology - Head & Neck Surgery. 2012; 147(2):308-315

18. Henry JA, Frederick M, Sell S, Griest S, Abrams H. Validation of a novel combination hearing aid and tinnitus therapy device. Ear and Hearing. 2015; 36(1):42-52

19. Henry JA, McMillan G, Dann S, Bennett K, Griest S, Theodoroff S et al. Tinnitus management: Randomized controlled trial comparing extended-wear hearing aids, conventional hearing aids, and combination instruments. Journal of the American Academy of Audiology. 2017; 28(6):546-561

20. Herraiz C, Diges I, Cobo P, Aparicio JM, Toledano A. Auditory discrimination training for tinnitus treatment: the effect of different paradigms. European Archives of Oto-Rhino-Laryngology. 2010; 267(7):1067-1074

21. Hesser H, Pereswetoff-Morath CE, Andersson G. Consequences of controlling background sounds: the effect of experiential avoidance on tinnitus interference. Rehabilitation Psychology. 2009; 54(4):381-389

22. Hiller W, Haerkotter C. Does sound stimulation have additive effects on cognitive-behavioral treatment of chronic tinnitus? Behaviour Research and Therapy. 2005; 43(5):595-612

23. Hoare DJ, Edmondson-Jones M, Sereda M, Akeroyd MA, Hall D. Amplification with hearing aids for patients with tinnitus and co-existing hearing loss. Cochrane Database of Systematic Reviews 2014, Issue 1. Art. No.: CD010151. DOI: 10.1002/14651858.CD010151.pub2.

24. Hoare DJ, Kowalkowski VL, Hall DA. Effects of frequency discrimination training on tinnitus: results from two randomised controlled trials. Journal of the Association for Research in Otolaryngology. 2012; 13(4):543-559

25. Hodgson SA, Herdering R, Singh Shekhawat G, Searchfield GD. A crossover trial comparing wide dynamic range compression and frequency compression in hearing aids for tinnitus therapy. Disability & Rehabilitation Assistive Technology. 2017; 12(1):97-103

26. Li SA, Bao L, Chrostowski M. Investigating the effects of a personalized, spectrally altered music-based sound therapy on treating tinnitus: A blinded, randomized controlled trial. Audiology and Neuro-Otology. 2016; 21(5):296-304

27. Mahboubi H, Haidar YM, Kiumehr S, Ziai K, Djalilian HR. Customized versus noncustomized sound therapy for treatment of tinnitus: A randomized crossover clinical trial. Annals of Otology, Rhinology and Laryngology. 2017; 126(10):681-687

28. Mahboubi H, Ziai K, Brunworth J, Djalilian HR. Accuracy of tinnitus pitch matching using a web-based protocol. Annals of Otology, Rhinology and Laryngology. 2012; 121(10):671-674

29. Mahboubi H, Ziai K, Djalilian HR. Customized web-based sound therapy for tinnitus. International Tinnitus Journal. 2012; 17(1):26-30

30. Mei ZG, Yang SB, Cai SJ, Lei HP, Zhou C, Guo YH et al. Treatment of tinnitus with electrical stimulation on acupoint in the distribution area of ear vagus nerve combining with sound masking: randomized controlled trial. World Journal of Acupuncture - Moxibustion. 2014; 24(2):30-35

31. Melin L, Scott B, Lindberg P, Lyttkens L. Hearing aids and tinnitus--an experimental group study. British Journal of Audiology. 1987; 21(2):91-97

32. Munhoes dos Santos Ferrari G, Sanchez TG, Bovino Pedalini ME. The efficacy of open molds in controlling tinnitus. Brazilian Journal of Otorhinolaryngology. 2007; 73(3):370-377

33. 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

34. Newman CW, Sandridge SA. A comparison of benefit and economic value between two sound therapy tinnitus management options. Journal of the American Academy of Audiology. 2012; 23(2):126-138

35. NHS Improvement. NHS reference costs 2017-18. 2017. Available from: https://improvement.nhs.uk/resources/reference-costs/#rc1718 Last accessed: 29/05/19

36. Oz I, Arslan F, Hizal E, Erbek SH, Eryaman E, Senkal OA et al. Effectiveness of the combined hearing and masking devices on the severity and perception of tinnitus: a randomized, controlled, double-blind study. journal of oto-rhino-laryngology and its related specialties. 2013; 75(4):211-220

37. Pantev C, Rudack C, Stein A, Wunderlich R, Engell A, Lau P et al. Study protocol: Munster tinnitus randomized controlled clinical trial-2013 based on tailor-made notched music training (TMNMT). BMC Neurology. 2014; 14:40

38. Parazzini M, Bo L, Jastreboff M, Tognola G, Ravazzani P. Open ear hearing aids in tinnitus therapy: an efficacy comparison with sound generators. International Journal of Audiology. 2011; 50(8):548-553

39. Ramakers GGJ, Kraaijenga VJC, Smulders YE, van Zon A, Stegeman I, Stokroos RJ et al. Tinnitus after simultaneous and sequential bilateral cochlear implantation. Frontiers in Surgery. 2017; 4:65

40. Ramakers GGJ, Van Zon A, Stegeman I, Grolman W. The effect of cochlear implantation on tinnitus in patients with bilateral hearing loss: A systematic review. Laryngoscope. 2015; 125(11):2584-2592

41. Schad ML, McMillan GP, Thielman EJ, Groon K, Morse-Fortier C, Martin JL et al. Comparison of acoustic therapies for tinnitus suppression: a preliminary trial. International Journal of Audiology. 2018; 57(2):143-149

42. Schilder AG, Burton MJ, Eby TL, Rosenfeld RM. Cochrane corner: Amplification with hearing aids for patients with tinnitus and co-existing hearing loss. Otolaryngology - Head & Neck Surgery. 2014; 150(6):915-8

43. Searchfield GD, Kobayashi K, Hodgson SA, Hodgson C, Tevoitdale H, Irving S. Spatial masking: Development and testing of a new tinnitus assistive technology. Assistive Technology. 2016; 28(2):115-125

44. Sereda M, Xia J, El RA, Hall D, Hoare D. Sound therapy (using amplification devices and/or sound generators) for tinnitus. Cochrane Database of Systematic Reviews 2018, Issue 12. Art. No.: CD013094. DOI: 10.1002/14651858.CD013094.pub2.

45. Shekhawat GS, Searchfield GD, Stinear CM. Role of hearing aids in tinnitus intervention: A scoping review. Journal of the American Academy of Audiology. 2013; 24(8):747-762

46. Stein A, Wunderlich R, Lau P, Engell A, Wollbrink A, Shaykevich A et al. Clinical trial on tonal tinnitus with tailor-made notched music training. BMC Neurology. 2016; 16:17

47. Stephens SD, Corcoran AL. A controlled study of tinnitus masking. British Journal of Audiology. 1985; 19(2):159-167

48. Tao Y, Chang X, Ye S, Chu G, Guan T, Wang J et al. Multiple-frequency matching treatment strategy for tinnitus. Journal of International Advanced Otology. 2017; 13(2):221-225

49. Theodoroff SM, McMillan GP, Zaugg TL, Cheslock M, Roberts C, Henry JA. Randomized controlled trial of a novel device for tinnitus sound therapy during sleep. American Journal of Audiology. 2017; 26(4):543-554

50. Tian RR, Diao MF, Tian FJ, Sun JJ, Lin X. Preliminary analysis of the effects of tailor-made notched music therapy on chronic idiopathic tinnitus. Chinese Journal of Otorhinolaryngology, Head, and Neck Surgery. 2017; 52(5):343-348

51. Vanneste S, Dongen M, Vree B, Hiseni S, Velden E, Strydis C et al. Does enriched acoustic environment in humans abolish chronic tinnitus clinically and electrophysiologically? A double blind placebo controlled study. Hearing Research. 2013; 296:141-148

52. Zhang M, Zhou H, Zhang J, Guo Y, Wang X, Wang N. Evaluating the effects of hearing aids combined with psychological counseling on tinnitus in patients with deafness. Journal of Clinical Otorhinolaryngology, Head and Neck Surgery. 2013; 27(10):461-464

53. Zon A, Smulders YE, Ramakers GG, Stegeman I, Smit AL, Zanten GA et al. Effect of unilateral and simultaneous bilateral cochlear implantation on tinnitus: A prospective study. Laryngoscope. 2016; 126(4):956-961

Appendices

Appendix A: Review protocols

Table 9: Review protocol: Sound therapy and sound enrichment

ID	Field	Content
0.	PROSPERO registration number	Not registered
1.	Review title	The clinical and cost effectiveness of sound therapy and sound enrichment
2.	Review question	What is the clinical and cost effectiveness of sound therapy and sound enrichment?
3.	Objective	Sound therapy and sound enrichment can either act as a psychological distraction or to change a person's sensitivity to the tinnitus or help in relaxation. The review aims to evaluate sound therapies in comparison or combination with each other, with other management strategies or to no sound therapy for clinical and cost-effective outcomes. Recommendations might cover the inclusion of sound therapy or sound enrichment as part of a package of care for people with tinnitus.
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

		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: Children, young people and adults presenting with tinnitus Strata: • Children/young people (up to 18 years) • Adults Exclusion: None
7.	Intervention/Exposure/Test	• Sound enrichment (e.g. environmental sound, a CD or mp3 download or the radio, a smartphone App, bedside/table-top sound generators, a wearable sound generator) • Combination hearing devices (hearing aid combined with sound generator) • Customised sound-based therapies, e.g. amplitude modulated tones and notched noise/music • Masking

8.	Comparator/Reference standard/Confounding factors	• Interventions compared with each other
		• "Tinnitus counselling"- education including coping strategies, provision of information and advice and relaxation
		• Psychological therapy
		  ○ Cognitive Behavioural therapy (CBT)
		  ○ Mindfulness-based interventions e.g. Cognitive therapy and MBSR
		  ○ Brief solution focused therapy
		  ○ Narrative therapy (children)
		  ○ Family therapy/Systemic therapy
		  ○ Acceptance and commitment therapy (ACT)
		  ○ EMDR
		• Amplification devices for those with hearing loss
		  ○ Hearing aids
		  ○ Implantable devices (including cochlear implants, bone-anchored hearing aids, bone-conduction hearing implants, bone-bridge/middle-ear devices)
		  ○ Combination device (sound generator and hearing aids)
		• Control group (i.e. no sound therapy)

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
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 (e.g. skin irritation, hyperacusis)
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	• Profoundly deaf • People with hyperacusis • People with learning disability or cognitive impairment • Mild hearing loss		
18.	Type and method of review	☒ Intervention ☐ Diagnostic ☐ Prognostic ☐ Qualitative ☐ Epidemiologic ☐ Service Delivery ☐ Other (please specify)		
19.	Language	English		
20.	Country	England		
21.	Anticipated or actual start date	29/05/18		
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, sound therapy
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 10: Review protocol: Amplification devices

ID	Field	Content
0.	PROSPERO registration number	Not registered
1.	Review title	The clinical and cost effectiveness of amplification devices for people with tinnitus who do not require an amplification device for a hearing loss alone
2.	Review question	What is the clinical and cost effectiveness of amplification devices for people with tinnitus who do not require an amplification device for a hearing loss alone?
3.	Objective	Amplification devices will be studied in relation to those with tinnitus who have a hearing loss but who are not offered amplification devices for their hearing loss alone or those with amplification devices where a combination device is being assessed (sound generator with a hearing aid). The review aims to evaluate amplification devices or no amplification devices for those who have a hearing loss but who are not offered amplification devices for their hearing loss for clinical and cost-effective outcomes. Recommendations might cover the inclusion of amplification devices as part of a package of care for people with tinnitus and hearing loss.
4.	Searches	The following databases will be searched:

		• Cochrane Central Register of Controlled Trials (CENTRAL) • Cochrane Database of Systematic Reviews (CDSR) • Embase • MEDLINE • Cinahl 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 submission of the review and further studies retrieved for inclusion if relevant. The full search strategies for MEDLINE database will be published in the final review.
5.	Condition or domain being studied	Tinnitus
6.	Population	Inclusion: Children, young people and adults with tinnitus and hearing loss Strata: • Children/young people (up to 18 years) • Adults Exclusion: None
7.	Intervention/Exposure/Test	• Hearing aids • Implantable devices (including cochlear

		implants, bone-anchored hearing aids, bone-conduction hearing implants, bone-bridge/middle-ear devices) • Combination device (sound generator and hearing aids)
8.	Comparator/Reference standard/Confounding factors	• Compared to each other • Control group/usual care
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
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 (e.g. skin irritation, hyperacusis)

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 profound deafness • People with mild hearing loss • People with tinnitus and hearing loss who use one (monaural) rather two (binaural) amplification devices

		• People with hyperacusis • Open fit/ear mould • People with learning disability or cognitive impairment		
18.	Type and method of review	☒ Intervention ☐ Diagnostic ☐ Prognostic ☐ Qualitative ☐ Epidemiologic ☐ Service Delivery ☐ Other (please specify)		
19.	Language	English		
20.	Country	England		
21.	Anticipated or actual start date	29/05/18		
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 Jenny 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, amplification devices, hearing loss
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 11: 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).[34] **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.[34]

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 12: 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

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 13: 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.

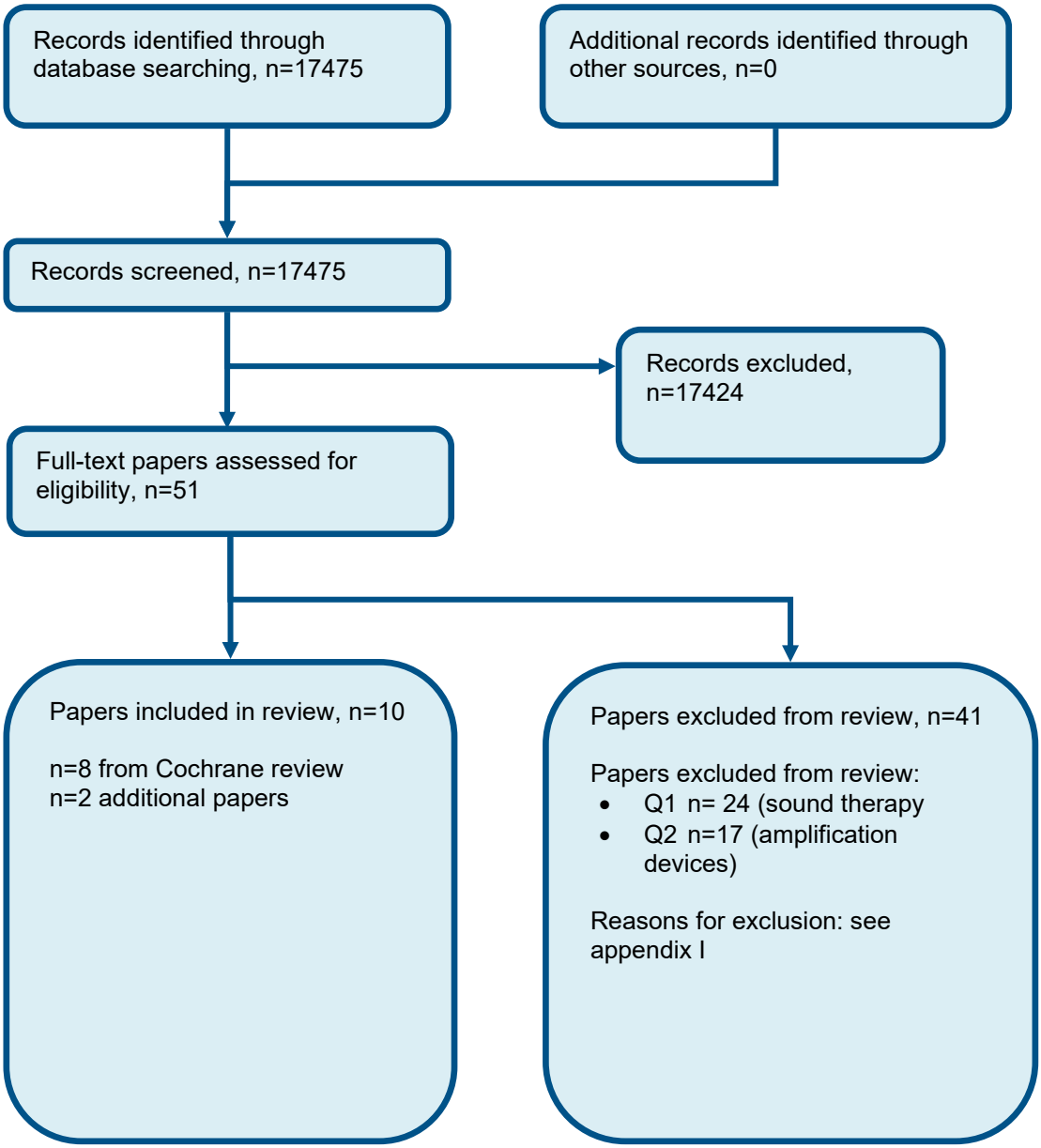
32.	(financ* or fee or fees).ti,ab.
33.	(value adj2 (money or monetary)).ti,ab.
34.	or/21-33
35.	quality adjusted life year/
36.	"quality of life index"/
37.	short form 12/ or short form 20/ or short form 36/ or short form 8/
38.	sickness impact profile/
39.	(quality adj2 (wellbeing or well being)).ti,ab.
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 sound therapy and amplification devices



Appendix D: Clinical evidence tables

Study	**Li 2016[27]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=50)
Countries and setting	Conducted in Canada; Setting:
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 12 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Adults
Subgroup analysis within study	Not applicable
Inclusion criteria	(a) presence of unilateral or bilateral tinnitus ≥12 months; (b) agreement to participate for 12 months; (c) agreement to ≥2 hour of daily music listening; (d) fluency to read, understand and communicate in English (e) ≥18 years old
Exclusion criteria	(a) history of neurological/psychiatric disorders; (b) presence of hyperacusis or Meniere's disease; (c) expectation to take ototoxic medication during study (participants were asked to confer with their physician about ototoxicity of prescribed medications); (d) expectation to experience constant exposure to loud noise during the study (i.e. constant exposure in a regular work environment or via regular recreational exposure); (e) Tinnitus Handicap Inventory (THI) score <26' and (f) absolute hearing thresholds > 70 dB HL for any corresponding frequencies (below 8 kHz) in left and right

	ears.
Recruitment/selection of patients	Participants were recruited from the Hamilton region, a mid-sized urban city, via online advertisement and audiology clinics.
Age, gender and ethnicity	Age - Mean (SD): 55.5 years. Gender (M:F): 2/1. Ethnicity: Not reported
Further population details	1. People with hyperacusis: Not stated / Unclear 2. People with learning disability or cognitive impairment: Not stated / Unclear 3. People with mild hearing loss: Not stated / Unclear 4. Profoundly deaf: Not stated / Unclear
Extra comments	Tinnitus for ≥10 years: 42% (Intervention group 36%; Comparison group 48%).
Indirectness of population	No indirectness
Interventions	(n=25) Intervention 1: Customised sound-based therapies - Notched noise/music. The intervention is a personalised, spectrally altered music-based sound therapy developed by proprietary software that takes into account changes observed at the auditory cortex. For every participant, a music therapy package with 6 hours of altered music was created using a software developed by Sounds Options Tinnitus Treatments. The software employs a proprietary computational model that uses each individual's auditory thresholds and self-assessed tinnitus characteristics to predict changes in neural connectivity and activity that may have developed to cause tinnitus. Classical music was selected as the delivery mode. Participants selected either around-the-ear headphones or in-ear ear-buds. They were instructed to listen to the music within a comfortable volume range in a quiet environment for at least 2 hours per day. While listening, participants could engage in other activities that did not interfere with music listening.. Duration 12 months. Concurrent medication/care: The music tracks were the same for both groups with the only difference with the treatment group receiving music tracks that had been spectrally altered. Participants with hearing aids were instructed to remove the hearing aids while listening to the music.. Indirectness: No indirectness (n=25) Intervention 2: Sound enrichment - CD or MP3 download or the radio. Unaltered music therapy - participants were provided with MP3 players with classical music. Participants selected either around-the-ear headphones or in-ear ear-buds. They were instructed to listen to the music within a comfortable volume range in a quiet environment for at least 2 hours per day. While

	listening, participants could engage in other activities that did not interfere with music listening.. Duration 12 months. Concurrent medication/care: The music tracks were the same for both groups with the only difference with the treatment group receiving music tracks that had been spectrally altered. Participants with hearing aids were instructed to remove the hearing aids while listening to the music.. Indirectness: No indirectness
Funding	Study funded by industry (Funding from the Ontario Brain Institute)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ALTERED MUSIC-SOUND THERAPY versus CD OR MP3 DOWNLOAD OR THE RADIO

Protocol outcome 1: Tinnitus distress
- Actual outcome for Adults: Tinnitus distress at 12 months; Group 1: mean 29.67 (SD 15.49); n=12, Group 2: mean 48.13 (SD 20.11); n=16; Tinnitus Handicap Inventory (THI) 0-100 Top=High is poor outcome
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 13, Reason: Lost to follow-up (declined to participate), did not listen to music, did not complete listening report, listened to music in noisy environment; Group 2 Number missing: 9, Reason: Lost to follow-up (declined to participate), did not listen to music, did not complete listening report

Protocol outcome 2: Depression
- Actual outcome for Adults: Depression at 12 months; Group 1: mean 3.75 (SD 4.33); n=12, Group 2: mean 5.63 (SD 3.58); n=16; Hospital Anxiety and Depression Scale (HADS) - depression subscale 0-21 Top=High is poor outcome
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 13, Reason: Lost to follow-up (declined to participate), did not listen to music, did not complete listening report, listened to music in noisy environment; Group 2 Number missing: 9, Reason: Lost to follow-up (declined to participate), did not listen to music, did not complete listening report

Protocol outcome 3: Anxiety
- Actual outcome for Adults: Anxiety at 12 months; Group 1: mean 6.08 (SD 4.38); n=12, Group 2: mean 8.81 (SD 4.35); n=16; Hospital Anxiety and Depression Scale (HADS) - anxiety subscale 0-21 Top=High is poor outcome
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 13, Reason: Lost to follow-up (declined to participate), did not listen to music, did not complete listening report, listened to music in noisy environment; Group 2 Number missing: 9,

Reason: Lost to follow-up (declined to participate), did not listen to music, did not complete listening report Protocol outcome 4: Severity - Actual outcome for Adults: Tinnitus severity at 12 months; Group 1: mean 39.33 (SD 22.36); n=12, Group 2: mean 52.03 (SD 22.48); n=16; Tinnitus Functional Index 0-100 Top=High is poor outcome Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 13, Reason: Lost to follow-up (declined to participate), did not listen to music, did not complete listening report, listened to music in noisy environment; Group 2 Number missing: 9, Reason: Lost to follow-up (declined to participate), did not listen to music, did not complete listening report	
Protocol outcomes not reported by the study	Tinnitus loudness; Tinnitus annoyance; Anxiety and depression; Sleep; Quality of life; Adverse events

Study	Mahboubi 2017[28]
Study type	RCT (Patient randomised; Crossover: 1 month)
Number of studies (number of participants)	1 (n=23)
Countries and setting	Conducted in USA; Setting: Clinic in USA.
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 3 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Asked about tinnitus characteristics and rated loudness on VAS and completed THI. Pre-treatment standard audiometry, and a consultation with an otolaryngologist to determine that there is no treatable cause of the tinnitus and tinnitus pitch was matched.
Stratum	Overall: Not applicable
Subgroup analysis within study	Not applicable
Inclusion criteria	Age greater than or equal to 18 years of age and presence of tinnitus for at least 3 months or more.
Exclusion criteria	Patients with abnormalities of the ear canal, active illicit drug use or alcohol dependence, active ear infections, history of psychosis, pulsatile tinnitus, and those currently under another sound or masking therapy for tinnitus.
Recruitment/selection of patients	Enrolled through clinic and included interested subjects from the affiliated VA hospital.
Age, gender and ethnicity	Age - Mean (SD): 53 (11) years. Gender (M:F): 12/6 (completers only). Ethnicity: Not reported
Further population details	1. People with hyperacusis: Not applicable 2. People with learning disability or cognitive impairment:

	Not applicable 3. People with mild hearing loss: Not applicable 4. Profoundly deaf: Not applicable
Extra comments	Mean tinnitus duration 118 +/- 9 months
Indirectness of population	No indirectness
Interventions	(n=23) Intervention 1: Customised sound-based therapies - Notched noise/music. Created using a type of software (see Mahboubi 2012) which pitch-matched using pure tones for tonal/ringing tinnitus and narrowband noise stimuli for non-tonal tinnitus. The software took into account the subject's tinnitus pitch-matched frequency along with the intra-aural and inter-frequency attenuation characteristics and created a sound file that was composed of a series of narrow-band noise peaks centred on the pitch-matched frequency and its first and fourth subharmonics. The width of these bands was one-half octave of the centre frequency. The result was a file that sounded similar to broadband noise but with less acoustic energy. This sound file was then mixed with 6 hours of classical music and uploaded onto an MP3 player and given to the subjects along with open ear headphones. . Duration Use the MP3 player for at least 2 hours per day every day. Concurrent medication/care: Not reported (n=23) Intervention 2: Masking. Created a broadband noise for the non-customised sound therapy with a spectral frequency of 1, meaning that equal proportions of all frequencies were present. . Duration At least 2 hours per day every day for duration of study. Concurrent medication/care: Not reported. Indirectness: No indirectness
Funding	Academic or government funding (National Institute of Health, National Research Service Award 1T32DC010775-01 from the University of California, Irvine.)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CUSTOMISED SOUND THERAPY USING SOFTWARE PITCH MATCHING versus MASKING

Protocol outcome 1: Tinnitus loudness
- Actual outcome: Loudness rating at post-treatment (3 months); Group 1: mean 4.9 Not applicable (SD 1.9); n=18, Group 2: mean 6.1 Not applicable (SD 2.3); n=18; Loudness rating Not reported Top=High is poor outcome

Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - High, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness ; Baseline details: Crossover study ; Group 1 Number missing: 5, Reason: non-compliant with treatment or lost to follow-up; Group 2 Number missing: 5, Reason: non-compliant with treatment or lost to follow-up Protocol outcome 2: Depression at 3 months - Actual outcome: BDI at post-treatment (3 months); Group 1: mean 6.3 Not applicable (SD 8.6); n=18, Group 2: mean 6.9 Not applicable (SD 8.3); n=18; BDI 0-63 Top=High is poor outcome Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness ; Baseline details: Crossover study ; Group 1 Number missing: 5, Reason: non-compliant with treatment or lost to follow-up; Group 2 Number missing: 5, Reason: non-compliant with treatment or lost to follow-up Protocol outcome 3: Anxiety - Actual outcome: BAI at post-treatment (3 months); Group 1: mean 8.3 Not applicable (SD 9.9); n=18, Group 2: mean 7.9 Not applicable (SD 9.8); n=18; BAI 0-63 Top=High is poor outcome Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness ; Baseline details: Crossover study ; Group 1 Number missing: 5, Reason: non-compliant with treatment or lost to follow-up; Group 2 Number missing: 5, Reason: non-compliant with treatment or lost to follow-up Protocol outcome 4: Severity - Actual outcome: THI at post-treatment (3 months); Group 1: mean 31.5 Not applicable (SD 20.3); n=18, Group 2: mean 41 Not applicable (SD 20.4); n=18; THI 0-100 Top=High is poor outcome Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness ; Baseline details: Crossover study ; Group 1 Number missing: 5, Reason: non-compliant with treatment or lost to follow-up; Group 2 Number missing: 5, Reason: non-compliant with treatment or lost to follow-up	
Protocol outcomes not reported by the study	Tinnitus distress; Tinnitus annoyance; Anxiety and depression; Sleep; Quality of life; Adverse events

Study (subsidiary papers)	**Sereda 2018[45] (Henry 2015[19], Erlandsson 1987[15], Stephens 1985[48], Melin 1987[32], Dos santos 2014[13], Parazzini 2011[39], Zhang 2013[53], Henry 2017[20])**
Study type	Systematic Review
Number of studies (number of participants)	8 (n=590)
Countries and setting	Conducted in Multiple countries; Setting: Two studies were set in Veterans Affairs clinics in the USA (Henry 2015; Henry 2017), three in university hospital clinics in Brazil, Sweden and China (dos Santos 2014; Melin 1987; Zhang 2013), one in a hospital ENT department in the UK (Stephens 1985), one in a hospital audiology department in Sweden (Erlandsson 1987), and one in two tinnitus clinics in Italy and USA (Parazzini 2011).
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 6 weeks - 12 months
Method of assessment of guideline condition	Systematic review: method of assessment mixed
Stratum	Adults
Subgroup analysis within study	Systematic review – pre-specified in protocol: Authors planned to carry out subgroup analyses to explore the potential effect modifiers of hearing loss, baseline tinnitus symptom severity and baseline anxiety or depression. However, insufficient data were available.
Inclusion criteria	Type of studies: RCTs. No restriction on language, year of publication or publication status. Type of participants: Adults (≥ 18 years) with acute (≤ 3 months) or chronic (> 3 months) subjective idiopathic tinnitus.

	Type of interventions: amplification-only devices, sound generators and combination devices (compared with each other or with no device).
Exclusion criteria	Type of studies: quasi-RCTs Types of interventions: - complex interventions, including sound therapy and other non-sound components (e.g. psychotherapy) as part of a programme (e.g. Neuromonics). - neuromodulation (desynchronisation) devices.
Recruitment/selection of patients	Not specified
Age, gender and ethnicity	Age - Range of means: 38.8 to 74.4 years. Gender (M:F): 44% female. Ethnicity: NR
Further population details	1. People with hyperacusis: Not stated / Unclear (Not reported). 2. People with learning disability or cognitive impairment: Not stated / Unclear (Not reported). 3. People with mild hearing loss: Systematic review: mixed (Mixed populations re: degree of hearing loss). 4. People with tinnitus and hearing loss: Not stated / Unclear (Not reported). 5. Profoundly deaf: Not stated / Unclear (Not reported).
Extra comments	All studies recruited patients with hearing loss and/or perceived hearing difficulties; with Stephens 1985 recruiting an additional group of participants without perceived hearing difficulties (the actual hearing status of that group was not reported). The extent of the hearing loss of the included participants varied between studies. Individual tinnitus duration ranged from three months to over 20 years. Tinnitus duration was not reported in Henry 2017. Most studies specified an inclusion criterion that considered tinnitus symptom severity. Baseline anxiety and/or depression scores were not reported in any of the included studies. Four studies had eligibility criteria regarding mental and emotional state.
Indirectness of population	No indirectness

Interventions	(n=236) Intervention 1: Hearing aids. Seven studies investigated the effects of hearing aids. The hearing aids used varied between the studies. Henry 2017 included two hearing aid arms (conventional and extended wear). Only the data from the conventional arm was included in the analysis as the extended wear arm was considered not comparable to the other hearing aids used in the included studies.. Duration 6 weeks - 12 months. Concurrent medication/care: Varied across studies. . Indirectness: No indirectness Further details: 1. Open fit/ear mould: Systematic review: mixed (n=81) Intervention 2: Combination hearing devices - Hearing aid combined with sound generator. Four studies investigated the effects of combination hearing devices (hearing aids combined with sound generators). . Duration 3 months - 6 months. Concurrent medication/care: Varied between studies. Indirectness: No indirectness Further details: 1. Open fit/ear mould: Systematic review: mixed (n=126) Intervention 3: Sound enrichment - Wearable sound generator. Three studies investigated the effects of sound generator devices. Two studies used Viennatone devices, one of which had a second sound generator arm using an A&M device. The third study used a device constructed specifically for the study. All delivered sound simulation unilaterally. Duration 6 weeks - 12 months. Concurrent medication/care: Varied between studies. Indirectness: No indirectness Further details: 1. Open fit/ear mould: Not applicable (n=123) Intervention 4: Control group - Usual care. Four studies included control arms with no amplification or sound generation device. In one study the control arm used a placebo device, one utilised a waiting list control, one utilised "limited counselling", and the final study used relaxation. . Duration 6 weeks - 12 months. Concurrent medication/care: Varied between studies. Indirectness: No indirectness Further details: 1. Open fit/ear mould: Not applicable
Funding	Academic or government funding (National Institute for Health Research, UK)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: HEARING AIDS versus SOUND GENERATOR Protocol outcome 1: Severity	

- Actual outcome for Adults: Tinnitus symptom severity (Tinnitus Handicap Inventory) at 3 months; MD; 1.30 (95%CI -5.72 to 8.32) 0-100 Top=High is poor outcome; Risk of bias: All domain - High, Selection - Unclear, Blinding - High, Incomplete outcome data - Unclear, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for Adults: Tinnitus symptom severity (Tinnitus Handicap Inventory) at 6 months; MD; -1.80 (95%CI -8.82 to 5.22) 0-100 Top=High is poor outcome; Risk of bias: All domain - High, Selection - Unclear, Blinding - High, Incomplete outcome data - Unclear, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for Adults: Tinnitus symptom severity (Tinnitus Handicap Inventory) at 12 months; MD; -0.90 (95%CI -7.92 to 6.12) 0-100 Top=High is poor outcome; Risk of bias: All domain - High, Selection - Unclear, Blinding - High, Incomplete outcome data - Unclear, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: HEARING AID COMBINED WITH SOUND GENERATOR versus HEARING AIDS Protocol outcome 1: Severity - Actual outcome for Adults: Tinnitus symptom severity (various measures) at 3-5 months; MD; -3.61 (95%CI -11.4 to 4.17) 0-100 Top=High is poor outcome; Risk of bias: All domain - High, Selection - Unclear, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:
Protocol outcomes not reported by the study	Tinnitus loudness; Tinnitus distress; Tinnitus annoyance; Depression; Anxiety; Anxiety and; Sleep; Quality of life; Adverse events

Appendix E: Forest plots

E.1 Amplification devices

E.1.1 Amplification devices (hearing aids) versus ear-level sound enrichment (sound generator)

Figure 2: Tinnitus severity at 3 months; scale 0-100

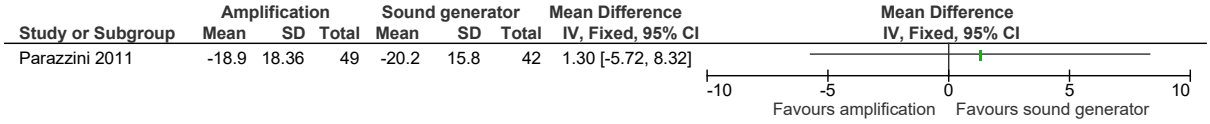


Figure 3: Tinnitus severity at 6 months; scale 0-100

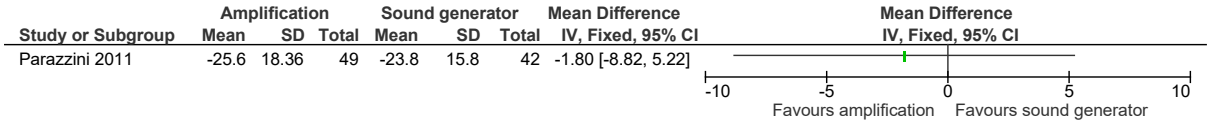
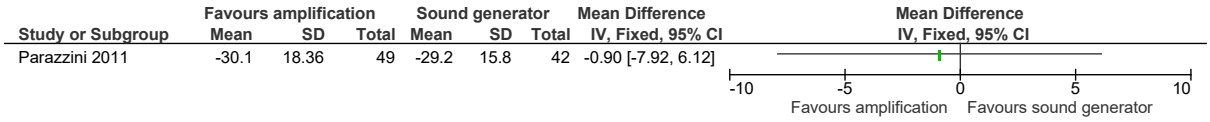
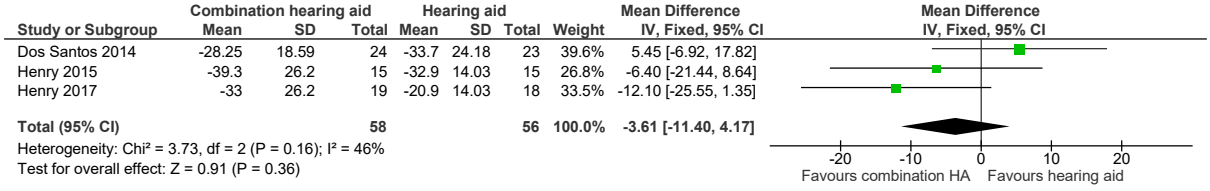


Figure 4: Tinnitus severity at 12 months; scale 0-100



E.1.2 Amplification and sound generator (combination hearing aid) versus amplification (hearing aid)

Figure 5: Tinnitus severity at 3-5 months; scale 0-100



E.2 Sound therapies

E.2.1 Customised sound therapy versus non-customised sound therapy (broadband noise)

Figure 6: Tinnitus loudness at 3 months; scale range not reported

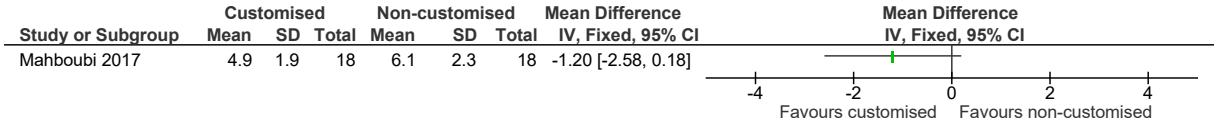


Figure 7: Depression at 3 months (BDI), scale range 0-63

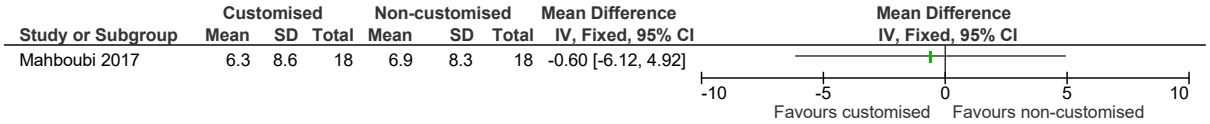


Figure 8: Anxiety at 3 months (BAI), scale range 0-63

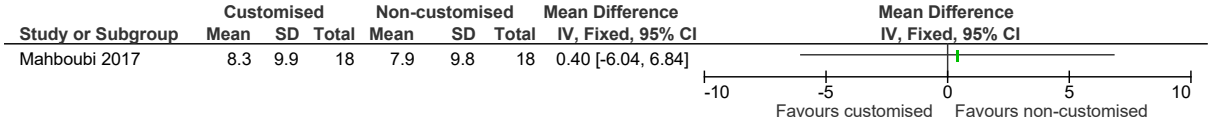
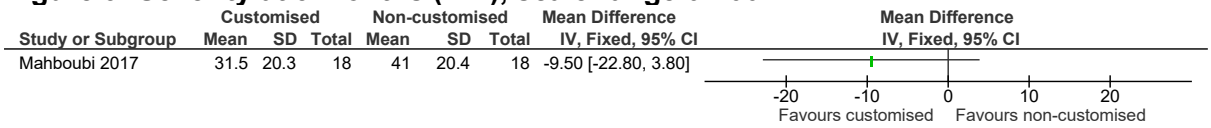


Figure 9: Severity at 3 months (THI), scale range 0-100



E.2.2 Customised sound therapy (altered music) versus sound enrichment

Figure 10: Tinnitus distress at 12 months (THI), scale range 0-100

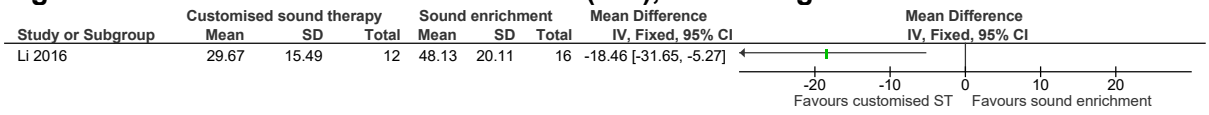


Figure 11: Tinnitus severity at 12 months (TFI), scale range 0-100

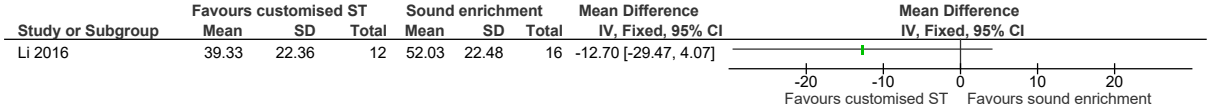


Figure 12: Depression at 12 months (HADS), scale range 0-21

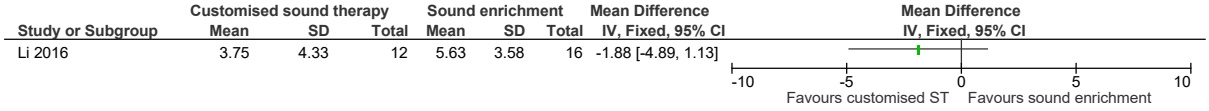
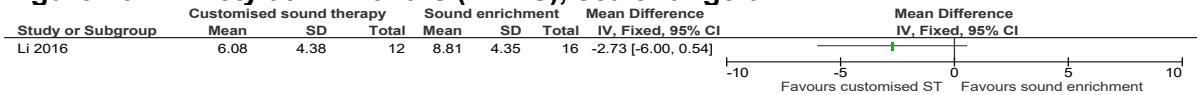


Figure 13: Anxiety at 12 months (HADS), scale range 0-21



Appendix F: GRADE tables

Table 14: Clinical evidence profile: Amplification (hearing aid) only versus sound generator only

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Amplification only	Sound generator only	Relative (95% CI)	Absolute		
Tinnitus symptom severity at 3 months (follow-up mean 3 months; measured with: THI; range of scores: 0-100; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	49	42	-	MD 1.3 higher (5.72 lower to 8.32 higher)	⊕⊕OO LOW	CRITICAL
Tinnitus symptom severity at 6 months (follow-up mean 6 months; measured with: THI; range of scores: 0-100; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	49	42	-	MD 1.8 lower (8.82 lower to 5.22 higher)	⊕⊕OO LOW	CRITICAL
Tinnitus symptom severity at 12 months (follow-up mean 12 months; measured with: THI; range of scores: 0-100; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	49	42	-	MD 0.9 lower (7.92 lower to 6.12 higher)	⊕⊕OO LOW	CRITICAL

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 15: Clinical evidence profile: Amplification and sound generator (combination hearing aid) versus amplification (hearing aid) only

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Combination hearing aid	Hearing aid	Relative (95% CI)	Absolute		
Tinnitus symptom severity at 3-5 months (follow up 3-5 months; measured with: THI and TFI; range of scores: 0-100; Better indicated by lower values)												
3	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	58	56	-	MD 3.61 lower (11.4 lower to 4.17 higher)	⊕⊕OO LOW	CRITICAL

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 16: Clinical evidence profile: Customised sound therapy versus non-customised sound therapy (broadband noise)

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Customised sound therapy	Non-customised sound therapy (broadband noise)	Relative (95% CI)	Absolute		
Loudness (follow-up mean 3 months; measured with: Tinnitus loudness rating scale; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	18	18	-	MD 1.2 lower (2.58 lower to 0.18 higher)	⊕OOO VERY LOW	IMPORTANT
Depression (BDI) (follow-up mean 3 months; measured with: BDI; range of scores: 0-63; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	18	18	-	MD 0.6 lower (6.12 lower to 4.92 higher)	⊕OOO VERY LOW	IMPORTANT
Anxiety (BAI) (follow-up mean 3 months; measured with: BAI; range of scores: 0-63; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	18	18	-	MD 0.4 higher (6.04 lower to 6.84 higher)	⊕OOO VERY LOW	IMPORTANT
Severity (THI) (follow-up mean 3 months; measured with: THI; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	18	18	-	MD 9.5 lower (22.8 lower to 3.8 higher)	⊕OOO VERY LOW	CRITICAL

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

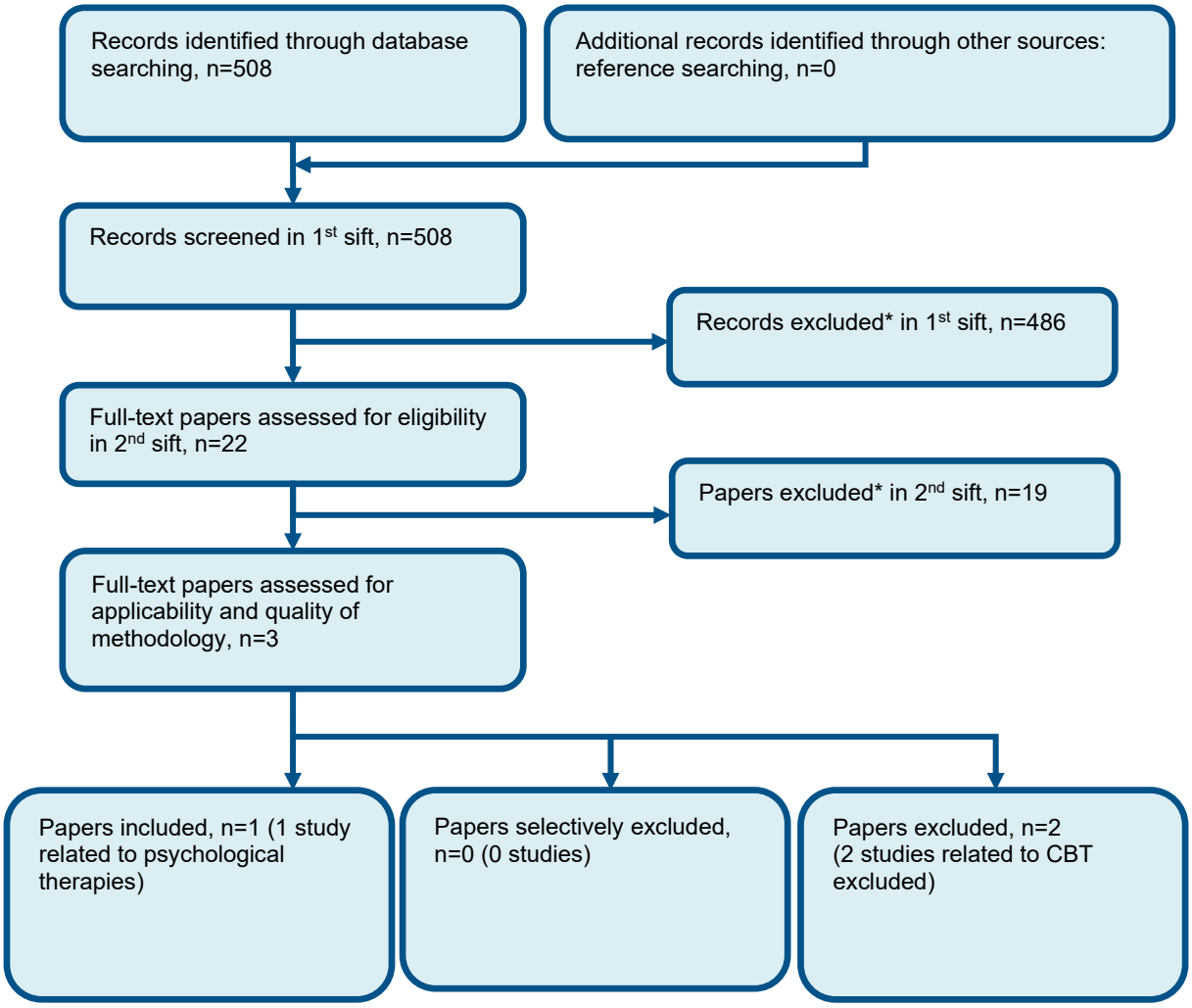
Table 17: Clinical evidence profile: Customised sound therapy (altered music) versus sound enrichment

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Customised sound therapy (altered music)	Sound enrichment	Relative (95% CI)	Absolute		
Tinnitus distress (12 months) (follow-up mean 12 months; measured with: THI; range of scores: 0-100; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	12	16	-	MD 18.46 lower (31.65 to 5.27 lower)	⊕⊕OO LOW	CRITICAL
Tinnitus severity (12 months) (follow-up mean 12 months; measured with: TFI; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	12	16	-	MD 12.7 lower (29.47 lower to 4.07 higher)	⊕⊕OO LOW	CRITICAL
Depression (12 months) (follow-up mean 12 months; measured with: HADS - depression; range of scores: 0-21; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	12	16	-	MD 1.88 lower (4.89 lower to 1.13 higher)	⊕⊕OO LOW	IMPORTANT
Anxiety (12 months) (follow-up mean 12 months; measured with: HADS - anxiety; range of scores: 0-21; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	12	16	-	MD 2.73 lower (6 lower to 0.54 higher)	⊕⊕OO LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Appendix G: Health economic evidence selection

Figure 14: 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 18: Studies excluded from the clinical review

Review: What is the clinical and cost effectiveness of sound therapy and sound enrichment?

Study	Exclusion reason
Arfeller 2009[1]	Incorrect interventions (theta burst stimulation rTMS)
Argstatter 2007[5]	Incorrect study design (non-randomised study). Study not available
Argstatter 2010[4]	Incorrect study design (non-randomised study). Study not available
Argstatter 2012[3]	Incorrect study design (non-randomised study)
Argstatter 2015[2]	Incorrect study design (non-randomised study)
Basile 2013[8]	Incorrect study design (non-randomised study). Incorrect interventions (tinnitus pitch matching)
Davis 2007[10]	Incorrect interventions (neuromonics one stage versus two stage)
Heijneman 2012[18]	Incorrect interventions (pure tone versus pure tone + phase shifting)
Herraiz 2010[21]	No extractable data
Hesser 2009[22]	Incorrect interventions (control of sounds versus no control of sounds)
Hiller 2005[23]	Included in combination review
Hoare 2012[25]	Incorrect study design (results from two RCTs)
Mahboubi 2012[29]	Incorrect interventions (tinnitus pitch matching)
Mahboubi 2012[30]	Incorrect study design (non-randomised study)
Mei 2014[31]	Incorrect interventions (electrical stimulation)
Newman 2012[35]	Incorrect study design (non-randomised study)
Pantev 2014[38]	Inappropriate study design (protocol)
Schad 2018[42]	No extractable data
Searchfield 2016[44]	Incorrect interventions. More relevant to combination review. No relevant outcome data reported
Stein 2016 [47]	No extractable data
Tao 2017[49]	Incorrect interventions (multiple-frequency matching versus traditional masking therapy)
Theodoroff 2017[50]	No extractable data
Tian 2017[51]	Not English language
Vanneste 2013[52]	No extractable data

Review: What is the clinical and cost effectiveness of amplification devices for people with tinnitus who do not require an amplification device for a hearing loss alone?

Study	Exclusion reason
Arndt 2011[6]	Incorrect study design (non-randomised study)
Arts 2016[7]	Incorrect interventions (electrical stimulation)

Blasco 2014[9]	Inappropriate study design (systematic review and meta-analysis of case studies)
Del Bo 2007[11]	Inappropriate study design (narrative)
Derks 2016[12]	Inappropriate study design (protocol)
Dos Santos 2012[14]	Inappropriate study design (abstract)
Ferrari 2005[17]	Inappropriate study design (abstract)
Hoare 2014[24]	Cochrane review but includes one study and in process of being updated
Hodgson 2017[26]	No extractable data
Munhoes dos Santos Ferrari 2007[33]	Incorrect interventions (hearing aid ear molds)
Oz 2013[37]	Incorrect interventions (compares betahistine plus combined hearing aid or sound generator versus betahistine)
Ramakers 2015[41]	Inappropriate study design (systematic review of case series studies)
Ramakers 2017[40]	Inappropriate study design (secondary analysis of an RCT)
Schilder 2014[43]	Inappropriate study design (abstract)
Shekhawat 2013[46]	Inappropriate study design (scoping review of study designs)
Zhang 2013[53]	Not English language
Zon 2016[54]	No extractable data (results were combined)

H.2 Excluded health economic studies

None.

Appendix I: Research recommendations

I.1 Amplification devices for people who are d/Deaf or who have a severe-to-profound hearing loss

Research question: What is the clinical and cost effectiveness of amplification devices for people who are d/Deaf or who have a severe-to-profound hearing loss?

Why this is important:

Improving access to sound can be beneficial for those with tinnitus and hearing loss. There is no current evidence regarding the effectiveness of amplification, hearing aids or implant devices, for managing tinnitus in those who may only receive limited hearing benefit from the amplification. However it may be that even some hearing benefit from amplification may improve perception of tinnitus.

Criteria for selecting high-priority research recommendations:

PICO question	**Population:** Children, young people and adults presenting with tinnitus who are d/Deaf or who have a severe-to-profound hearing loss
	
	Intervention(s):
	• Amplification devices for those with hearing loss
	  ○ Implantable devices (including cochlear implants, bone-anchored hearing aids, bone-conduction hearing implants, bone-bridge/middle-ear devices)
	  ○ Combination device (sound generator and hearing aids)
	  ○ Hearing aids
	
	Comparison:
	• Waiting-list control
	• Interventions compared with each other
	
	Outcome(s):
	• Tinnitus severity (critical)
	
	Impact of tinnitus:(critical)
	• Tinnitus Distress
	• Tinnitus Annoyance
	
	Health related QoL (critical):
	• QoL (EQ-5D)
	
	Tinnitus percept:
	• Tinnitus Loudness (important)
	
	Other co-occurring complaints (important)
	• Depression
	• Anxiety
	• Anxiety and depression

	• Sleep
Importance to patients or the population	There is currently very limited research regarding how to manage tinnitus in patients who are D/deaf or who have a severe-to-profound hearing loss. Therefore there is no clinical evidence or guidance on how to manage this important group of people. Tinnitus often coexists alongside hearing loss, so understanding how to manage tinnitus within this population should be a priority, as standard care is not feasible for people who are D/deaf or who have a severe-to-profound hearing loss.
Relevance to NICE guidance	It would help to ensure future guidance is relevant to a key group for whom tinnitus is an issue and who are identified as such within the equality impact assessment.
Relevance to the NHS	This may impact on strategic delivery or service delivery depending on findings. In the SignHealth Report of 2014, 'Sick of it: how the health service is failing deaf people'(https://www.signhealth.org.uk/health-information/sick-of-it-report/), it was pointed out that deaf people have worse health and lower life expectancy than people who are not deaf. It is important to find evidence to help reduce this inequality.
National priorities	N/A
Current evidence base	No evidence was identified that evaluated amplification in people presenting with tinnitus who are d/Deaf or who have a severe-to-profound hearing loss
Equality	This research recommendation addresses people with who are d/Deaf or who have a severe-to-profound hearing loss, a group that needs special consideration.
Study design	Randomised controlled trial or well-designed prospective or retrospective cohort study.
Feasibility	N/A
Other comments	N/A
Importance	Low: the research is of interest and will fill existing evidence gaps.

I.2 Amplification devices for people with tinnitus who have hearing loss but no perceived hearing difficulties

Research question: What is the clinical and cost effectiveness of fitting amplification devices in people with tinnitus who have hearing loss but no perceived hearing difficulties?

Why this is important:

People with mild hearing loss do not always report difficulty with hearing and/or communication, but may present in the tinnitus clinic because they have noticed tinnitus and upon testing their hearing, an underling hearing loss is detected. Amplification devices (e.g. hearing aids) should be available for people with hearing loss who present with hearing difficulties and have been recommended for people with hearing loss and tinnitus in order to manage tinnitus. For those who do not experience hearing and/or communication difficulties, it is uncertain whether or not hearing aids may be of benefit for managing tinnitus.

PICO question	**Population:** Children, young people and adults presenting with tinnitus-

who have a hearing loss but no perceived hearing and/or communication difficulties

Intervention(s):

- Amplification devices for those with hearing loss
    - Hearing aids
    - Implantable devices (including cochlear implants, bone-anchored hearing aids, bone-conduction hearing implants, bone-bridge/middle-ear devices)
    - Combination device (sound generator and hearing aids)

Comparison:

- Interventions compared with each other
- Interventions in combination with each other
- Waiting-list control
- Sound therapy and sound enrichment
    - sound enrichment (e.g. environmental sound, a CD or mp3 download or the radio, a smartphone App, bedside/table-top sound generators, a wearable sound generator)
    - Customised sound-based therapies
    - Masking
- Tinnitus support, intervention involving the following components:
    - Discussion of experience of tinnitus, including any concerns and its impact with individuals presenting with tinnitus. This discussion occurs between the person with tinnitus or their family members or carers and healthcare professional.
    - A management plan is also developed to include information and opportunities for discussion about different management options
- Psychological therapies
    - Cognitive Behavioural therapy (CBT)
    - Mindfulness-based interventions e.g. Cognitive therapy and MBSR
    - Brief solution focused therapy
    - Narrative therapy
    - Family therapy/Systemic therapy

Outcome(s):

- Tinnitus severity (critical)

Impact of tinnitus:(critical)

- Tinnitus Distress
- Tinnitus Annoyance

Health related QoL (critical):

- QoL (EQ-5D)

Tinnitus percept:

- Tinnitus Loudness (important)

Other co-occurring complaints (important)

- Depression
- Anxiety
- Anxiety and depression

	• Sleep
Importance to patients or the population	Practice is varied across the country in terms of fitting hearing aids for mild hearing loss when there is tinnitus but no perceived hearing and/or communication difficulty. Evidence would improve the health-related quality of life and would allow patients to make decisions based on evidence instead of the opinion of their clinician.
Relevance to NICE guidance	There is currently low quality evidence of hearing aids and tinnitus and no evidence regarding the effectiveness of hearing aids in people with mild hearing loss who do not seek help for hearing loss. Future NICE guidance would be able to include or exclude this group of people from the current recommendation to fit hearing aids.
Relevance to the NHS	There may be an increase in hearing aid fittings for people who have milder hearing loss.
National priorities	N/A
Current evidence base	No evidence was identified that evaluated hearing aids in people with tinnitus who have hearing loss but no perceived hearing difficulties.
Equality	The research recommendation should include people who have additional needs, e.g. learning disability.
Study design	Randomised controlled trial or well-designed prospective or retrospective cohort study.
Feasibility	N/A.
Other comments	There is a risk of bias if hearing aid manufacturers fund research in this area.
Importance	Low: the research is of interest and will fill existing evidence gaps.