

Tinnitus: assessment and management

Sound therapy and amplification devices

NICE guideline

Intervention evidence review

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Draft for Consultation

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

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1 Sound therapy and amplification devices

2 1.1 Introduction

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

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

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

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

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

28 1.2 Review question: What is the clinical and cost 29 effectiveness of sound therapy and sound enrichment for 30 people with tinnitus?

31 1.3 PICO table

32 For full details see the review protocol in appendix A.

33 **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) | <ul style="list-style-type: none">• 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 |

| | |
|----------------------|--|
| | <ul style="list-style-type: none"> Masking |
| Comparison(s) | <ul style="list-style-type: none"> Interventions compared with each other “Tinnitus counselling” - education including coping strategies, provision of information and advice and relaxation Psychological therapy <ul style="list-style-type: none"> Cognitive Behavioural therapy (CBT) Mindfulness-based interventions e.g. Cognitive therapy and MBSR Brief solution focused therapy Narrative therapy Family therapy/Systemic therapy Acceptance and commitment therapy (ACT) EMDR Amplification devices for those with a hearing loss <ul style="list-style-type: none"> 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) |
| Outcomes | <ul style="list-style-type: none"> Tinnitus severity (critical) <p>Impact of tinnitus (critical):</p> <ul style="list-style-type: none"> Tinnitus distress Tinnitus annoyance <p>Health related QoL(critical):</p> <ul style="list-style-type: none"> QoL (tinnitus) QoL <p>Tinnitus percept (important):</p> <ul style="list-style-type: none"> Tinnitus loudness <p>Other co-occurring complaints (important):</p> <ul style="list-style-type: none"> Depression Anxiety Anxiety and depression Sleep <p>Adverse events (important):</p> <ul style="list-style-type: none"> Safety Tolerability Side effects (e.g. skin irritation and hyperacusis) |
| Study design | <ul style="list-style-type: none"> Systematic review of RCTs RCT If there is an inadequate amount of RCT data, non-randomised comparative studies will be considered. |

1 **1.4 Review question: What is the clinical and cost**
 2 **effectiveness of amplification devices for people with**
 3 **tinnitus who do not require an amplification device for a**
 4 **hearing loss alone?**

5 **1.5 PICO table**

6 For full details see the review protocol in appendix A.

7 **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) | <ul style="list-style-type: none"> • 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) | <ul style="list-style-type: none"> • Compared to each other • Control group/usual care |
| Outcomes | <ul style="list-style-type: none"> • Tinnitus severity (critical) <p>Impact of tinnitus (critical):</p> <ul style="list-style-type: none"> • Tinnitus distress • Tinnitus annoyance <p>Health related QoL(critical):</p> <ul style="list-style-type: none"> • QoL (tinnitus) • QoL <p>Tinnitus percept (important):</p> <ul style="list-style-type: none"> • Tinnitus loudness <p>Other co-occurring complaints (important):</p> <ul style="list-style-type: none"> • Depression • Anxiety • Anxiety and depression • Sleep <p>Adverse events (important):</p> <ul style="list-style-type: none"> • Safety • Tolerability • Side effects (e.g. skin irritation and hyperacusis) |
| Study design | <ul style="list-style-type: none"> • Systematic review of RCTs • RCT • If there is an inadequate amount of RCT data, non-randomised comparative studies will be considered. |

1 1.6 Clinical evidence

2 1.6.1 Included studies

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

5 A Cochrane review of sound therapy (using amplification devices and/or sound generators)
6 with 8 studies⁴⁴ was included in its entirety as it matched our protocols. The methods of data
7 analysis and quality assessment for this part of the review are therefore in accordance with
8 the methods described in the Cochrane review. Methods at the National Guideline Centre
9 includes the avoidance of an overall risk of bias assessment of “unclear” and the use of Peto
10 odds ratio analyses where there are zero events in either arm or a less than 1% event rate.
11 Cochrane methods include the use of “unclear” risk of bias ratings and the use of risk ratio
12 analyses where there are zero events in both arms of included studies.

13 Two further randomised controlled trials that were outside the scope of the Cochrane review
14 were also included in our review.^{26, 27} These compared customised sound therapy (pitch
15 matched) to non-customised sound therapy (broadband noise), and customised sound
16 therapy (altered music) to sound enrichment, respectively.

17 The included studies are summarised in Table 3 below.^{26, 27} Evidence from these studies is
18 summarised in the clinical evidence summaries below (Table 4, Table 5, Table 6 and Table
19 7).

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

22 1.6.2 Excluded studies

23 One Cochrane review was excluded (Hoare 2014²³ as it was superseded by the more recent
24 Cochrane review).

25 See the excluded studies list in appendix I.

26

1 1.6.3 Summary of clinical studies included in the evidence review

2 **Table 3: Summary of studies included in the evidence review**

| Study | Intervention and comparison | Population | Outcomes | Comments |
|---|--|--|---|---|
| Sereda 2018 ⁴⁴ (Systematic review including: Henry 2015 ¹⁸ , Erlandsson 1987 ¹⁵ , Stephens 1985 ⁴⁷ , Melin 1987 ³¹ , Dos santos 2014 ¹³ , Parazzini 2011 ³⁸ , Zhang 2013 ⁵² , Henry 2017 ¹⁹) | <p>Systematic review comparing amplification devices, sound generators and combination devices, with each other or with no device.</p> <p>Eight studies were included:</p> <p>Seven studies investigated the effects of hearing aids.</p> <p>Four studies investigated the effects of combination hearing devices (hearing aids combined with sound generators).</p> <p>Three studies investigated the effects of ear-level sound generator devices.</p> <p>Four studies included control arms with no amplification or sound generation device.</p> | <p>n=590</p> <p>The review included studies of adults (≥ 18 years) with acute (≤ 3 months) or chronic (> 3 months) subjective idiopathic tinnitus.</p> <p>Age (range of means): 38.8 to 74.4 years. Gender: 44% female. Duration of tinnitus (range): 3 months to over 20 years.</p> <p>Various countries (USA, Brazil, Sweden, China, UK, Italy)</p> | <p><u>Hearing aids versus sound generator (1 study):</u></p> <p>Tinnitus severity (follow up: 3 months): measured using the Tinnitus Handicap Inventory (THI), scale range 0-100</p> <p>Tinnitus severity (follow up: 6 months): measured using the Tinnitus Handicap Inventory (THI), scale range 0-100</p> <p>Tinnitus severity (follow up: 12 months): measured using the Tinnitus Handicap Inventory (THI), scale range 0-100</p> <p><u>Hearing aids versus sound generator (3 studies):</u></p> <p>Tinnitus severity (follow up: 3 – 5 months): various measures used, scale range 0-100</p> | Most of the included studies did not report data for the outcomes specified in the protocol |
| Li 2016 ²⁶ | <p>Intervention (n=25)</p> <p>Customised sound-based therapy - participants were instructed to listen</p> | <p>n=50</p> <p>People with unilateral or bilateral tinnitus for ≥12</p> | <p>Tinnitus distress (follow-up: 12 months): measured using the Tinnitus Handicap Inventory (THI), scale range 0-100</p> | |

| Study | Intervention and comparison | Population | Outcomes | Comments |
|--|---|--|--|----------|
| | <p>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.</p> <p>Comparison (n=25)</p> <p>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.</p> | <p>months</p> <p>Age (mean) : 55.5 years Gender (male to female ratio: 2:1 Duration of tinnitus: ≥10 years - 42%</p> <p>Canada</p> | <p>Tinnitus severity (follow-up: 12 months): measured using the Tinnitus Functional Index (TFI), scale range 0-100</p> <p>Depression (follow-up: 12 months): measured using the Hospital Anxiety and Depression Scale (HADS) (depression sub-scale used), scale range 0-21</p> <p>Anxiety (follow-up: 12 months): measured using the Hospital Anxiety and Depression Scale (HADS) (depression sub-scale used), scale range 0-21</p> | |
| <p>Mahboubi 2017²⁷</p> <p>Crossover RCT</p> | <p>Intervention (n=23)</p> <p>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.</p> <p>Comparison (n=23)</p> | <p>n=23</p> <p>People presenting with tinnitus (of 3 months or more)</p> <p>Age (mean): 53 (11) years Gender (male to female ratio): 12/6 (completers data provided only) Duration of tinnitus (mean): 118 +/- 9 months</p> <p>USA</p> | <p>Tinnitus loudness (follow-up: post-treatment 3 months): measured using a tinnitus loudness rating scale, scale range not reported</p> <p>Tinnitus depression (follow-u: post-treatment 3 months): measured using the Beck Depression Index, scale range 0-63</p> <p>Tinnitus anxiety (follow-up: post-treatment 3 months): measured using the Beck Anxiety Inventory, scale range 0-63</p> <p>Tinnitus severity (follow-up post-treatment 3 months): measured using</p> | |

| 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 | |

1 See appendix D for full evidence tables.

1.6.4.2 Quality assessment of clinical studies included in the evidence review

3 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 | | | | | |

1 **Table 5: Clinical evidence summary: Amplification and sound generator (combination hearing aid) versus amplification (hearing aid) only**
2

| 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 | | | | | |

3 **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 LOW ^{1,2} 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 LOW ^{1,2} 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 LOW ^{1,2} 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

1 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 | ⊕⊕⊖⊖ LOW ^{1,2} 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) |

| 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 severity (12 months) TFI Scale from 0 to 100 | 28 (1 study) 12 months | ⊕⊕⊖⊖ LOW ^{1,2} due to risk of bias, imprecision | | 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) |
| Depression (12 months) HADS - depression. Scale from: 0 to 21. | 28 (1 study) 12 months | ⊕⊕⊖⊖ LOW ^{1,2} 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 | ⊕⊕⊖⊖ LOW ^{1,2} 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) |
| <p>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</p> <p>2 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs</p> | | | | | |

1 See appendix F for full GRADE tables.

2

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 cost³⁵

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

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

7 **1.8.2 Health economic evidence statements**

- 8 • No relevant economic evaluations were identified.

9 **1.9 The committee's discussion of the evidence**

10 **1.9.1 Interpreting the evidence**

11 **1.9.1.1 The outcomes that matter most**

12 Tinnitus distress, annoyance and tinnitus awareness were critical outcomes as they were
13 thought to be common complaints for those with tinnitus and impact their quality of life.
14 Quality of life (tinnitus-related) and general quality of life were also critical outcomes due to
15 their impact on the person with tinnitus.

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

18 **1.9.1.2 The quality of the evidence**

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

22 *Amplification devices*

23 The Cochrane review identified studies which evaluated the use of hearing aids and
24 combination hearing aids. One study evaluated the use of hearing aids compared to sound
25 generators and reported outcome data for tinnitus severity at different time-points (3 months,
26 6 months and 12 months). Three studies were identified which compared combination
27 hearing aids (amplification and sound generator) with a standard hearing aid. These three
28 studies also reported outcome data for tinnitus severity. Overall, the evidence was low quality
29 due to risk of bias and imprecision.

30 *Sound therapy*

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

38 **1.9.1.3 Benefits and harms**

39 *Amplification devices*

40 The committee recommended amplification devices for those who present with tinnitus and
41 have hearing loss. This was a strong recommendation and is in line with the NICE Hearing
42 loss guideline (NG98) which recommends offering hearing aids to those whose ability to

1 communicate and hear is hampered by their hearing loss. The committee agreed that this
2 should also apply to children and young people, although they are not covered by NG98.

3 For those with hearing loss but no self-perceived hearing difficulties the committee
4 recommended that amplification devices should be considered. We did not find evidence for
5 this population but the committee noted that sometimes those with a hearing loss but no self-
6 perceived hearing difficulties may not always be offered a hearing aid for their hearing loss
7 alone, but with co-occurring tinnitus they may experience a benefit for both their tinnitus and
8 their hearing loss.

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

12 *Sound therapies*

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

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

27 **1.9.2 Cost effectiveness and resource use**

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

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

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

43 Sound therapy and sound enrichment devices are widely used in the NHS and the committee
44 highlighted that from their clinical experience people with tinnitus do benefit from the use of
45 these interventions. However, a concern raised by the committee was the existence of many
46 different variants of sound therapy from environmental sounds (i.e. windows open) or audio
47 generated from one's mobile phone (which would not incur cost for the NHS) to expensive
48 sound masking and customisable devices where the sounds generated are tuned specifically

1 for a person's tinnitus. As there is a lack of clarity on which of these variants would be most
2 clinically effective and cost-effective, the committee opted to form a research
3 recommendation to explore this question further.

4 **1.9.3 Other factors the committee took into account**

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

14 Lay members reported that there is a lack of knowledge in the general population about how
15 hearing aids may help them cope with their tinnitus. This, coupled with the belief that 'nothing
16 can be done about tinnitus', means that many people with hearing difficulties but who do not
17 have hearing aids do not consult their GP about their tinnitus. Some who have hearing
18 difficulties do not report having tinnitus. This may mean they are referred inappropriately and
19 do not receive the tinnitus support they need. There are some people who have chosen not
20 to accept hearing aids for their hearing difficulties but have welcomed them when they learn
21 it may also help with their tinnitus.
22

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- 32

1

Appendices

2

Appendix A: Review protocols

3

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 | <p>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.</p> <p>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.</p> |
| 4. | Searches | <p>The following databases will be searched:</p> <ul style="list-style-type: none">• Cochrane Central Register of Controlled Trials (CENTRAL)• Cochrane Database of Systematic Reviews (CDSR)• Embase• MEDLINE• CINAHL, Current Nursing and Allied Health Literature |

| | | |
|----|-----------------------------------|--|
| | | <p>Searches will be restricted by:</p> <ul style="list-style-type: none"> • English language • Human studies • Letters and comments are excluded. <p>Other searches:</p> <ul style="list-style-type: none"> • Inclusion lists of relevant systematic reviews will be checked by the reviewer. <p>The searches may be re-run 6 weeks before final committee meeting and further studies retrieved for inclusion if relevant.</p> <p>The full search strategies will be published in the final review.</p> |
| 5. | Condition or domain being studied | Tinnitus |
| 6. | Population | <p>Inclusion:</p> <p>Children, young people and adults presenting with tinnitus</p> <p>Strata:</p> <ul style="list-style-type: none"> • Children/young people (up to 18 years) • Adults <p>Exclusion: None</p> |
| 7. | Intervention/Exposure/Test | <ul style="list-style-type: none"> • 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 | <ul style="list-style-type: none"> • Interventions compared with each other • “Tinnitus counselling”- education including coping strategies, provision of information and advice and relaxation • Psychological therapy <ul style="list-style-type: none"> ○ 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 <ul style="list-style-type: none"> ○ 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 | <ul style="list-style-type: none"> • Systematic reviews • RCTs • If there is an inadequate amount of RCT data, non-randomised comparative studies will be considered |
| 10. | Other exclusion criteria | <ul style="list-style-type: none"> • 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) | <ul style="list-style-type: none"> • Tinnitus severity <p>Impact of tinnitus:</p> <ul style="list-style-type: none"> • Tinnitus distress • Tinnitus annoyance <p>Health related QoL:</p> <ul style="list-style-type: none"> • QoL (tinnitus) • QoL |

| | | |
|-----|---|---|
| 13. | Secondary outcomes (important outcomes) | <p>Tinnitus percept:</p> <ul style="list-style-type: none"> • Tinnitus loudness <p>Other co-occurring complaints:</p> <ul style="list-style-type: none"> • Depression • Anxiety • Anxiety and depression • Sleep <p>Adverse events:</p> <ul style="list-style-type: none"> • Safety • Tolerability • Side effects (e.g. skin irritation, hyperacusis) |
| 14. | Data extraction (selection and coding) | <p>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.</p> <p>The full text of potentially eligible studies will be retrieved and will be assessed for eligibility in line with the criteria outlined above.</p> <p>10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer.</p> <p>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.</p> <p>A second reviewer will quality assure the extracted data. Discrepancies will be identified and resolved through discussion (with a third reviewer where necessary).</p> |

| | | |
|-----|-----------------------------------|--|
| 15. | Risk of bias (quality) assessment | <p>Risk of bias will be assessed using the appropriate checklist as described in Developing NICE guidelines: the manual.</p> <p><u>For Intervention reviews the following checklist will be used according to study design being assessed:</u></p> <ul style="list-style-type: none"> • <u>Systematic reviews: Risk of Bias in Systematic Reviews (ROBIS)</u> • <u>Randomised Controlled Trial: Cochrane RoB (2.0)</u> <p>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.</p> |
| 16. | Strategy for data synthesis | <p>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.</p> <p>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.</p> <p>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.</p> <p>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.</p> |

| | | | | |
|-----|--|--|--------------------------|-------------------------------------|
| | | <p>Where meta-analysis is not possible, data will be presented and quality assessed individually per outcome.</p> <p>If sufficient data is available to make a network of treatments, WinBUGS will be used for network meta-analysis.</p> | | |
| 17. | Analysis of sub-groups | <ul style="list-style-type: none"> • Profoundly deaf • People with hyperacusis • People with learning disability or cognitive impairment • Mild hearing loss | | |
| 18. | Type and method of review | <input checked="" type="checkbox"/> Intervention <input type="checkbox"/> Diagnostic <input type="checkbox"/> Prognostic <input type="checkbox"/> Qualitative <input type="checkbox"/> Epidemiologic <input type="checkbox"/> Service Delivery <input type="checkbox"/> 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 | <input type="checkbox"/> | <input checked="" type="checkbox"/> |
| | | Piloting of the study selection process | <input type="checkbox"/> | <input checked="" type="checkbox"/> |
| | | Formal screening of search results against | <input type="checkbox"/> | <input checked="" type="checkbox"/> |

| | | | | |
|-----|-------------------------|---|--------------------------|-------------------------------------|
| | | eligibility criteria | | |
| | | Data extraction | <input type="checkbox"/> | <input checked="" type="checkbox"/> |
| | | Risk of bias (quality) assessment | <input type="checkbox"/> | <input checked="" type="checkbox"/> |
| | | Data analysis | <input type="checkbox"/> | <input checked="" type="checkbox"/> |
| 24. | Named contact | <p>5a. Named contact National Guideline Centre</p> <p>5b Named contact e-mail Tinnitus@nice.org.uk</p> <p>5e Organisational affiliation of the review National Institute for Health and Care Excellence (NICE) and the National Guideline Centre</p> | | |
| 25. | Review team members | <p>From the National Guideline Centre:</p> <ul style="list-style-type: none"> • 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 | <p>This systematic review is being completed by the National Guideline Centre which receives funding from NICE.</p> | | |
| 27. | Conflicts of interest | <p>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</p> | | |

| | | |
|-----|--|---|
| | | 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 | <p>NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as:</p> <ul style="list-style-type: none"> • 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 | <input type="checkbox"/> Ongoing <input checked="" type="checkbox"/> Completed but not published <input type="checkbox"/> Completed and published <input type="checkbox"/> Completed, published and being updated |

| | | |
|-----|------------------------------|--|
| | | <input type="checkbox"/> Discontinued |
| 35. | Additional information | N/A |
| 36. | Details of final publication | www.nice.org.uk |

1

2

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 | <p>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).</p> <p>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.</p> |
| 4. | Searches | The following databases will be searched: |

| | | |
|----|-----------------------------------|--|
| | | <ul style="list-style-type: none"> • Cochrane Central Register of Controlled Trials (CENTRAL) • Cochrane Database of Systematic Reviews (CDSR) • Embase • MEDLINE • Cinahl <p>Searches will be restricted by:</p> <ul style="list-style-type: none"> • English language • Human studies • Letters and comments are excluded. <p>Other searches:</p> <ul style="list-style-type: none"> • Inclusion lists of relevant systematic reviews will be checked by the reviewer. <p>The searches may be re-run 6 weeks before final submission of the review and further studies retrieved for inclusion if relevant.</p> <p>The full search strategies for MEDLINE database will be published in the final review.</p> |
| 5. | Condition or domain being studied | Tinnitus |
| 6. | Population | <p>Inclusion:</p> <p>Children, young people and adults with tinnitus and hearing loss</p> <p>Strata:</p> <ul style="list-style-type: none"> • Children/young people (up to 18 years) • Adults <p>Exclusion: None</p> |
| 7. | Intervention/Exposure/Test | <ul style="list-style-type: none"> • Hearing aids • Implantable devices (including cochlear |

| | | |
|-----|---|---|
| | | <p>implants, bone-anchored hearing aids, bone-conduction hearing implants, bone-bridge/middle-ear devices)</p> <ul style="list-style-type: none"> • Combination device (sound generator and hearing aids) |
| 8. | Comparator/Reference standard/Confounding factors | <ul style="list-style-type: none"> • Compared to each other • Control group/usual care |
| 9. | Types of study to be included | <ul style="list-style-type: none"> • Systematic reviews • RCTs • If there is an inadequate amount of RCT data, non-randomised comparative studies will be considered |
| 10. | Other exclusion criteria | <ul style="list-style-type: none"> • 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) | <ul style="list-style-type: none"> • Tinnitus severity <p>Impact of tinnitus:</p> <ul style="list-style-type: none"> • Tinnitus distress • Tinnitus annoyance <p>Health related QoL:</p> <ul style="list-style-type: none"> • QoL (tinnitus) • QoL |
| 13. | Secondary outcomes (important outcomes) | <p>Tinnitus percept:</p> <ul style="list-style-type: none"> • Tinnitus loudness <p>Other co-occurring complaints:</p> <ul style="list-style-type: none"> • Depression • Anxiety • Anxiety and depression • Sleep <p>Adverse events:</p> <ul style="list-style-type: none"> • Safety • Tolerability • Side effects (e.g. skin irritation, hyperacusis) |

| | | |
|-----|--|---|
| 14. | Data extraction (selection and coding) | <p>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.</p> <p>The full text of potentially eligible studies will be retrieved and will be assessed for eligibility in line with the criteria outlined above.</p> <p>10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer.</p> <p>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.</p> <p>A second reviewer will quality assure the extracted data. Discrepancies will be identified and resolved through discussion (with a third reviewer where necessary).</p> |
| 15. | Risk of bias (quality) assessment | <p>Risk of bias will be assessed using the appropriate checklist as described in Developing NICE guidelines: the manual.</p> <p><u>For Intervention reviews the following checklist will be used according to study design being assessed:</u></p> <ul style="list-style-type: none"> • <u>Systematic reviews: Risk of Bias in Systematic Reviews (ROBIS)</u> • <u>Randomised Controlled Trial: Cochrane RoB (2.0)</u> <p>Disagreements between the review authors</p> |

| | | |
|-----|-----------------------------|--|
| | | <p>over the risk of bias in particular studies will be resolved by discussion, with involvement of a third review author where necessary.</p> |
| 16. | Strategy for data synthesis | <p>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.</p> <p>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.</p> <p>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.</p> <p>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.</p> <p>Where meta-analysis is not possible, data will be presented and quality assessed individually per outcome.</p> <p>If sufficient data is available to make a network of treatments, WinBUGS will be used for network meta-analysis.</p> |
| 17. | Analysis of sub-groups | <ul style="list-style-type: none"> • People with profound deafness • People with mild hearing loss • People with tinnitus and hearing loss who use one (monaural) rather two (binaural) amplification devices |

| | | | | |
|-----|--|--|--------------------------|-------------------------------------|
| | | <ul style="list-style-type: none"> • People with hyperacusis • Open fit/ear mould • People with learning disability or cognitive impairment | | |
| 18. | Type and method of review | <input checked="" type="checkbox"/> Intervention <input type="checkbox"/> Diagnostic <input type="checkbox"/> Prognostic <input type="checkbox"/> Qualitative <input type="checkbox"/> Epidemiologic <input type="checkbox"/> Service Delivery <input type="checkbox"/> 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 | <input type="checkbox"/> | <input checked="" type="checkbox"/> |
| | | Piloting of the study selection process | <input type="checkbox"/> | <input checked="" type="checkbox"/> |
| | | Formal screening of search results against eligibility criteria | <input type="checkbox"/> | <input checked="" type="checkbox"/> |
| | | Data extraction | <input type="checkbox"/> | <input checked="" type="checkbox"/> |

| | | | | |
|-----|-------------------------|---|--------------------------|-------------------------------------|
| | | Risk of bias (quality) assessment | <input type="checkbox"/> | <input checked="" type="checkbox"/> |
| | | Data analysis | <input type="checkbox"/> | <input checked="" type="checkbox"/> |
| 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: <ul style="list-style-type: none"> • 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 | <p>NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as:</p> <ul style="list-style-type: none"> • 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 | <input type="checkbox"/> Ongoing <input checked="" type="checkbox"/> Completed but not published <input type="checkbox"/> Completed and published <input type="checkbox"/> Completed, published and being updated <input type="checkbox"/> Discontinued |
| 35.. | Additional information | N/A |
| 36. | Details of final publication | www.nice.org.uk |

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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 | <ul style="list-style-type: none"> • 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 | <p>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.</p> <p>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).³³</p> <p>Inclusion and exclusion criteria</p> <ul style="list-style-type: none"> • 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. <p>Where there is discretion</p> <p>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.</p> <p>The health economist will be guided by the following hierarchies.</p> <p><i>Setting:</i></p> <ul style="list-style-type: none"> • 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). |

| |
|--|
| <ul style="list-style-type: none"> • Studies set in non-OECD countries or in the USA will be excluded before being assessed for applicability and methodological limitations. <p><i>Health economic study type:</i></p> <ul style="list-style-type: none"> • 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. <p><i>Year of analysis:</i></p> <ul style="list-style-type: none"> • 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. <p><i>Quality and relevance of effectiveness data used in the health economic analysis:</i></p> <ul style="list-style-type: none"> • 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.³³

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 |

1

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 |

1 **Cochrane Library (Wiley) search terms**

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

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 |

3 **B.2 Health Economics literature search strategy**

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

10 **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 |

11 **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) |

1

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 |

1

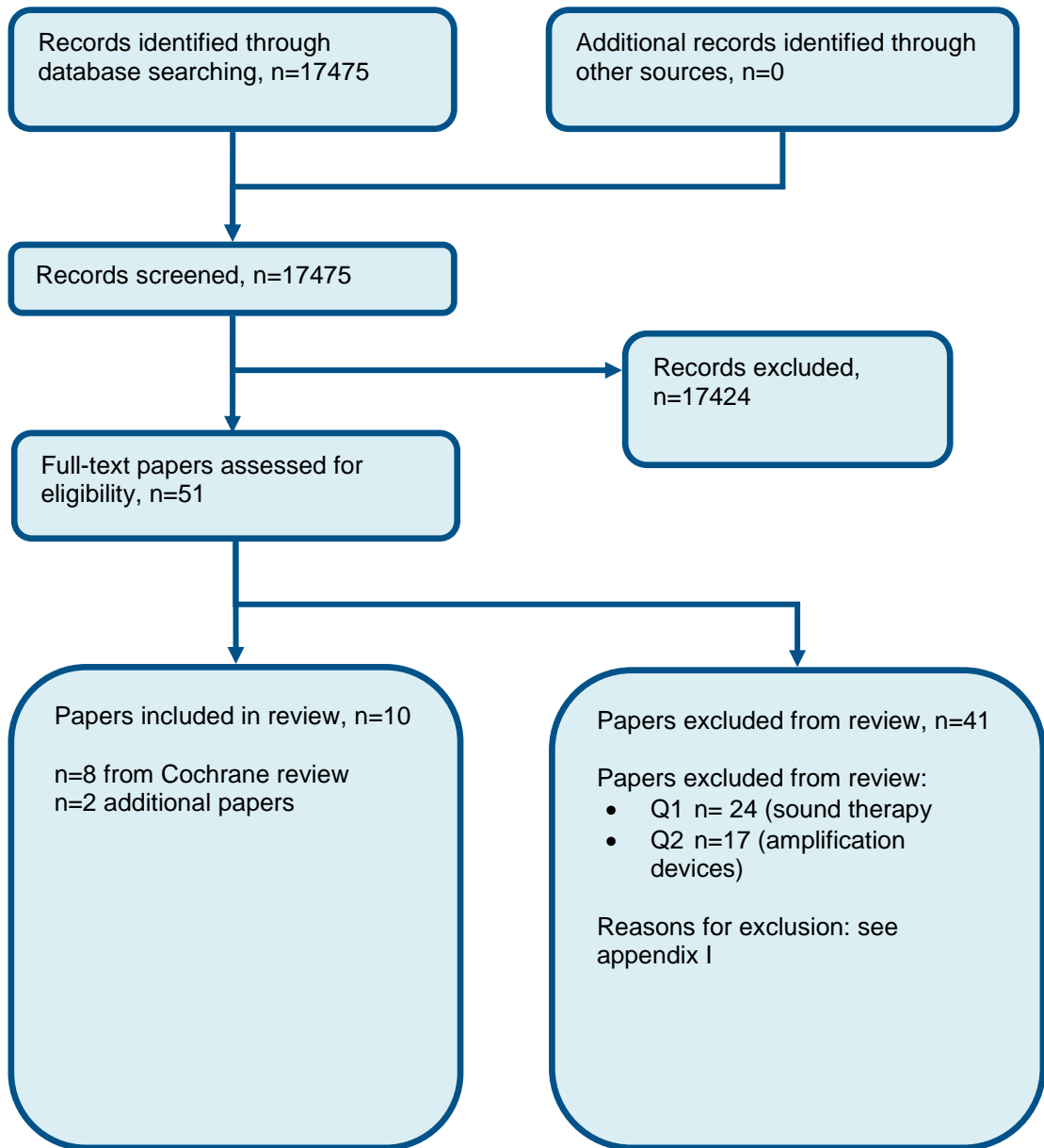
NHS EED and HTA (CRD) search terms

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

1

Appendix C: Clinical evidence selection

Figure 1: Flow chart of clinical study selection for the review of sound therapy and amplification devices



2

1 Appendix D: Clinical evidence tables

| Study | Li 2016 ²⁶ |
|---|---|
| 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 | <p>(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</p> <p>(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</p> |

| | |
|--|--|
| | <p>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</p> |
| <p>Funding</p> | <p>Study funded by industry (Funding from the Ontario Brain Institute)</p> |
| <p>RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ALTERED MUSIC-SOUND THERAPY versus CD OR MP3 DOWNLOAD OR THE RADIO</p> <p>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</p> <p>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</p> <p>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</p> | |

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 ²⁷ |
|---|---|
| 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 | <p>(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</p> <p>(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</p> |
| 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 2018⁴⁴ (Henry 2015¹⁸, Erlandsson 1987¹⁵, Stephens 1985⁴⁷, Melin 1987³¹, Dos santos

| | |
|---|--|
| | 2014¹³, Parazzini 2011³⁸, Zhang 2013⁵², Henry 2017¹⁹) |
| 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 | <p>(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</p> <p>(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</p> <p>(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</p> <p>(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</p> |
| 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

1 Appendix E: Forest plots

E.1.2 Amplification devices

E.1.13 Amplification devices (hearing aids) versus ear-level sound enrichment (sound generator)

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

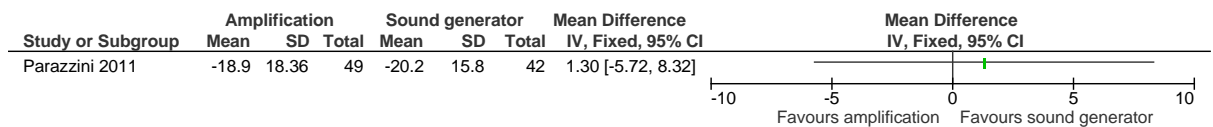


Figure 3: Tinnitus severity at 6 months; scale 0-100

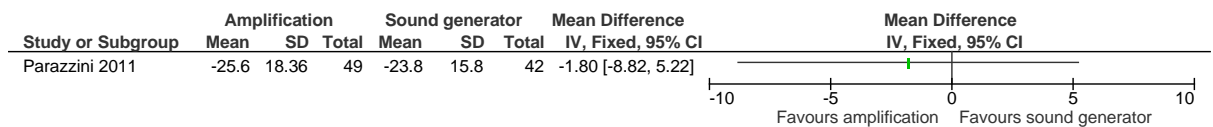
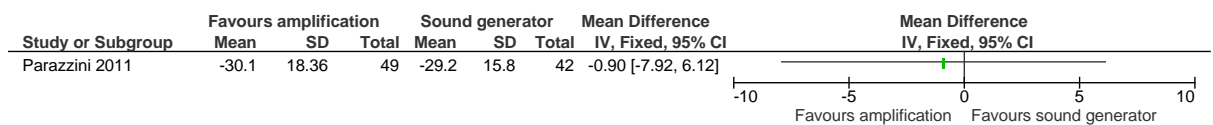
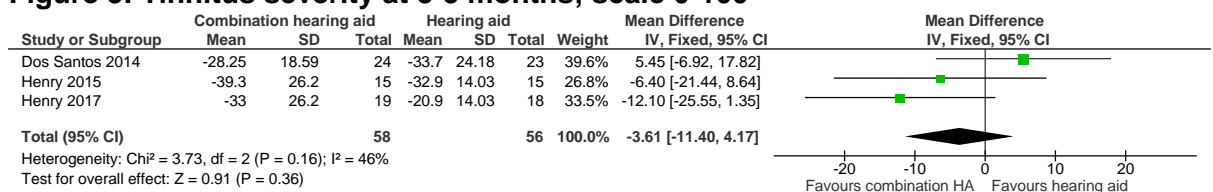


Figure 4: Tinnitus severity at 12 months; scale 0-100



E.1.25 Amplification and sound generator (combination hearing aid) versus amplification (hearing aid)

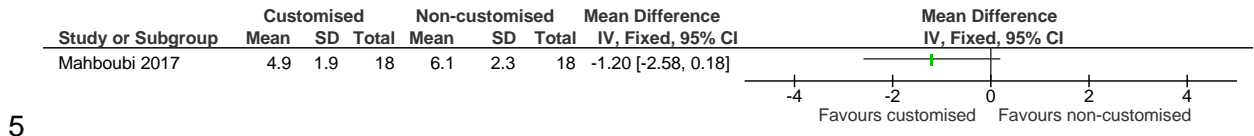
Figure 5: Tinnitus severity at 3-5 months; scale 0-100



E.2.1 Sound therapies

E.2.1.2 Customised sound therapy versus non-customised sound therapy (broadband noise)

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



5

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

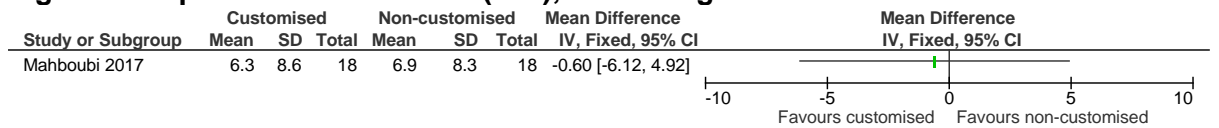


Figure 8: Anxiety at 3 months (BAI), scale range 0-63

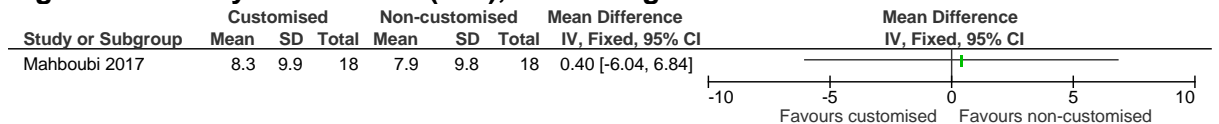
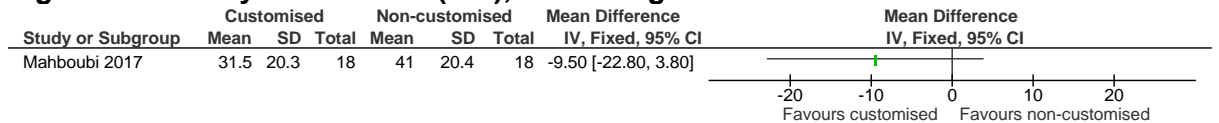


Figure 9: Severity at 3 months (THI), scale range 0-100



E.2.2.6 Customised sound therapy (altered music) versus sound enrichment

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

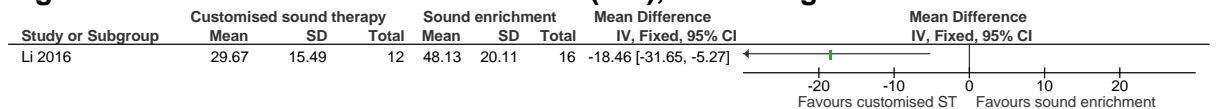


Figure 11: Tinnitus severity at 12 months (TFI), scale range 0-100

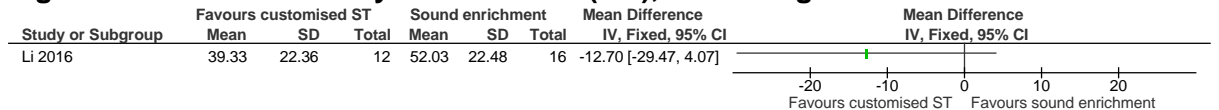


Figure 12: Depression at 12 months (HADS), scale range 0-21

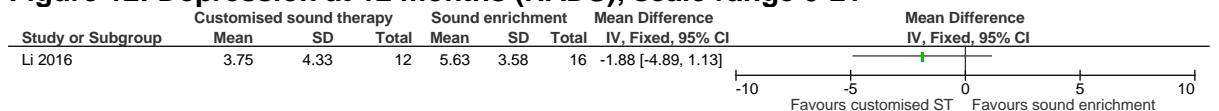
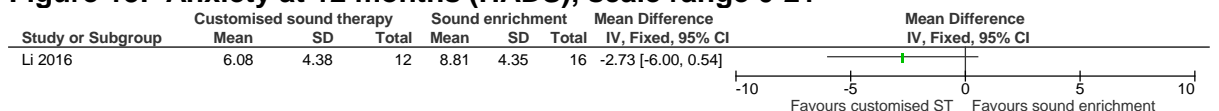


Figure 13: Anxiety at 12 months (HADS), scale range 0-21



1

1 Appendix F: GRADE tables

2 **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) | ⊕⊕⊕⊕ 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) | ⊕⊕⊕⊕ 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) | ⊕⊕⊕⊕ LOW | CRITICAL |

3 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

4 ² Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

5 **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 | Design | Risk of | Inconsistency | Indirectness | Imprecision | Other | Combination | Hearing | Relative | Absolute | | |

| studies | | bias | | | | considerations | hearing aid | aid | (95% CI) | | | |
|---|-------------------|----------------------|--------------------------|-------------------------|----------------------|----------------|-------------|-----|----------|---|---------|----------|
| 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) | ⊕⊕⊕ LOW | CRITICAL |

- 1 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 ² Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

3 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) | ⊕⊕⊕ 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) | ⊕⊕⊕ 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) | ⊕⊕⊕ 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) | ⊕○○○ VERY LOW | CRITICAL |

- 1 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 ² Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

3 **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) | ⊕⊕○○ 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) | ⊕⊕○○ 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) | ⊕⊕○○ 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 | ⊕⊕○○ | IMPORTANT |

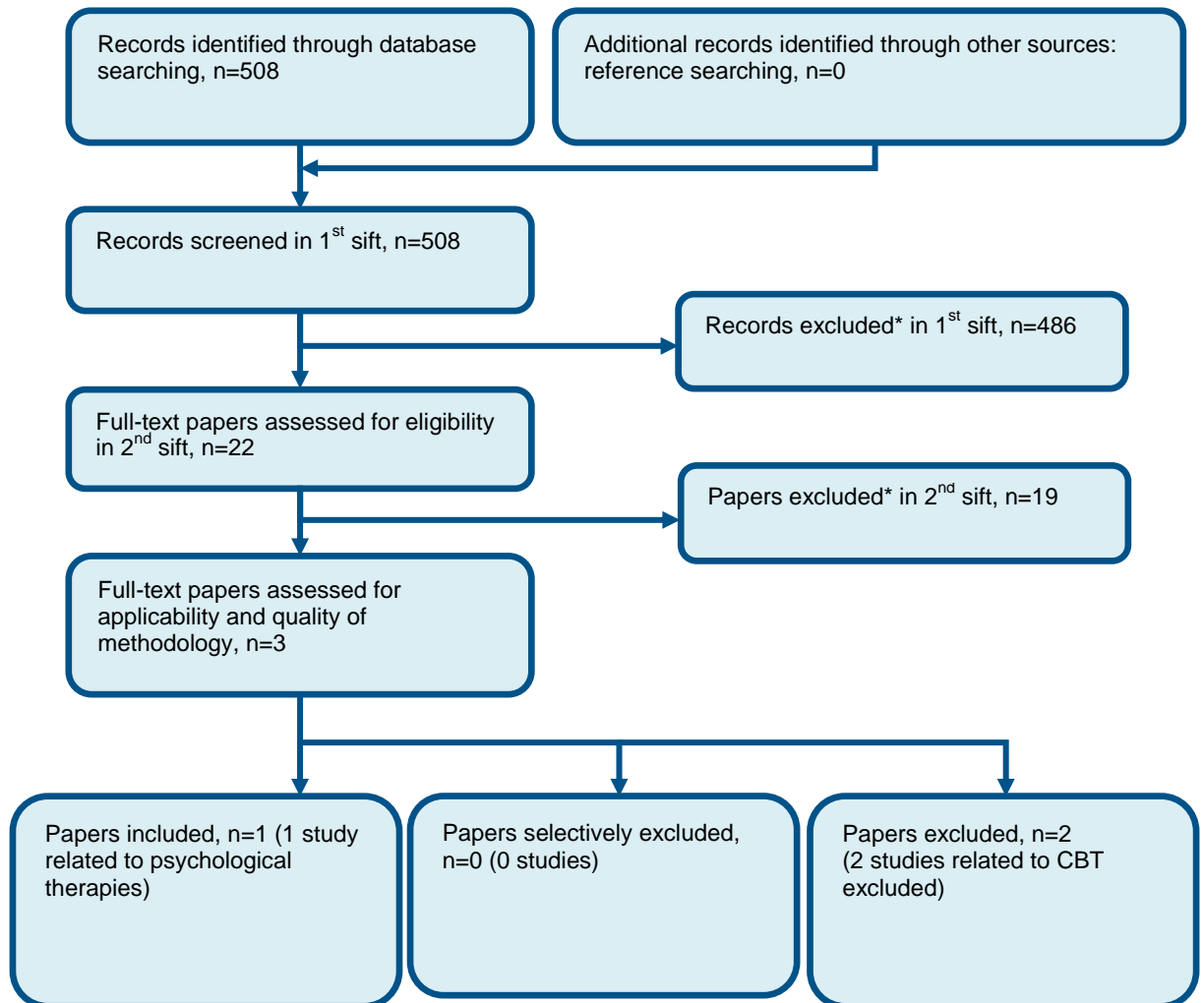
| | | | | | | | | | | | | |
|--|--------|--|---------------|--------------|--|--|--|--|--|-----------------------|-----|--|
| | trials | | inconsistency | indirectness | | | | | | lower to 0.54 higher) | LOW | |
|--|--------|--|---------------|--------------|--|--|--|--|--|-----------------------|-----|--|

- 1 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 ² Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

3

1 Appendix G: Health economic evidence selection

3 Figure 14: Flow chart of health economic study selection for the guideline



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

4
5

1 Appendix H: Excluded studies

H.1.2 Excluded clinical studies

3 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 ¹⁷ | Incorrect interventions (pure tone versus pure tone + phase shifting) |
| Herraiz 2010 ²⁰ | No extractable data |
| Hesser 2009 ²¹ | Incorrect interventions (control of sounds versus no control of sounds) |
| Hiller 2005 ²² | Included in combination review |
| Hoare 2012 ²⁴ | Incorrect study design (results from two RCTs) |
| Mahboubi 2012 ²⁸ | Incorrect interventions (tinnitus pitch matching) |
| Mahboubi 2012 ²⁹ | Incorrect study design (non-randomised study) |
| Mei 2014 ³⁰ | Incorrect interventions (electrical stimulation) |
| Newman 2012 ³⁴ | Incorrect study design (non-randomised study) |
| Pantev 2014 ³⁷ | Inappropriate study design (protocol) |
| Schad 2018 ⁴¹ | No extractable data |
| Searchfield 2016 ⁴³ | Incorrect interventions. More relevant to combination review. No relevant outcome data reported |
| Stein 2016 ⁴⁶ | No extractable data |
| Tao 2017 ⁴⁸ | Incorrect interventions (multiple-frequency matching versus traditional masking therapy) |
| Theodoroff 2017 ⁴⁹ | No extractable data |
| Tian 2017 ⁵⁰ | Not English language |
| Vanneste 2013 ⁵¹ | No extractable data |

4 Review: What is the clinical and cost effectiveness of amplification devices for people with tinnitus 5 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 ¹⁶ | Inappropriate study design (abstract) |
| Hoare 2014 ²³ | Cochrane review but includes one study and in process of being updated |
| Hodgson 2017 ²⁵ | No extractable data |
| Munhoes dos Santos Ferrari 2007 ³² | Incorrect interventions (hearing aid ear molds) |
| Oz 2013 ³⁶ | Incorrect interventions (compares betahistine plus combined hearing aid or sound generator versus betahistine) |
| Ramakers 2015 ⁴⁰ | Inappropriate study design (systematic review of case series studies) |
| Ramakers 2017 ³⁹ | Inappropriate study design (secondary analysis of an RCT) |
| Schilder 2014 ⁴² | Inappropriate study design (abstract) |
| Shekhawat 2013 ⁴⁵ | Inappropriate study design (scoping review of study designs) |
| Zhang 2013 ⁵² | Not English language |
| Zon 2016 ⁵³ | No extractable data (results were combined) |

H.2₁ Excluded health economic studies

2 None.

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