Tinnitus

Search date November 2013

Julian Savage and Angus Waddell

ABSTRACT

INTRODUCTION: Up to 18% of people in industrialised societies are mildly affected by chronic tinnitus, and 0.5% report tinnitus having a severe effect on their daily life. Tinnitus can be associated with hearing loss, acoustic neuromas, drug toxicity, ear diseases, and depression. Tinnitus can last for many years, and can interfere with sleep and concentration. METHODS AND OUTCOMES: We conducted a systematic review and aimed to answer the following clinical question: What are the effects of treatments for chronic tinnitus? We searched: Medline, Embase, The Cochrane Library, and other important databases up to November 2013 (Clinical Evidence reviews are updated periodically; please check our website for the most up-to-date version of this review). We included harms alerts from relevant organisations such as the US Food and Drug Administration (FDA) and the UK Medicines and Healthcare products Regulatory Agency (MHRA). RESULTS: We found 33 studies that met our inclusion criteria. We performed a GRADE evaluation of the quality of evidence for interventions. CONCLUSIONS: In this systematic review, we present information relating to the effectiveness and safety of the following interventions: acamprosate, acupuncture, antidepressant drugs, benzodiazepines, carbamazepine, electromagnetic stimulation, ginkgo biloba, hearing aids, hypnosis, psychotherapy, tinnitus-masking devices, and cognitive behavioural therapy plus tinnitus-masking device (tinnitus retraining therapy).

QUESTIONS

INTERVENTIONS

Key points

- Up to 18% of people in industrialised societies are mildly affected by chronic tinnitus, and 0.5% report tinnitus having a severe effect on their daily life.

  Tinnitus can be associated with hearing loss, acoustic neuromas, drug toxicity, ear diseases, or depression.

  Tinnitus can last for many years, and can interfere with sleep and concentration.

- We found insufficient evidence to show that antidepressant drugs improve tinnitus symptoms.

  Antidepressant drugs can improve depression in people with tinnitus.

  Tricyclic antidepressants (TCAs) are associated with adverse effects such as dry mouth, blurred vision, and constipation.

- Psychotherapy (CBT) may be no more effective than placebo at reducing tinnitus loudness, but it may improve overall symptoms of tinnitus at 12 months.

  CBT may be more effective at improving anxiety, depression, quality of life, and annoyance scores for people with tinnitus.

  We don't know whether CBT plus a tinnitus masking device is more effective than waiting-list control at improving depression or tinnitus annoyance scores in people with tinnitus.

- We don't know whether benzodiazepines, acupuncture, hypnosis, electromagnetic stimulation, hearing aids, or tinnitus-masking devices are effective in people with tinnitus.

- Gingo biloba may be no more effective than placebo at improving overall symptoms of tinnitus at 3 months. However, evidence was limited and inconsistent.

- Acamprosate may be more effective than placebo at improving overall symptom scores at 3 months in people with tinnitus. However, evidence was weak, and it is unclear whether the improvement was clinically important.

- Carbamazepine may be no more effective than placebo at improving symptoms of tinnitus, and is associated with adverse effects such as dizziness, nausea, and headache.

DEFINITION

Tinnitus is the perception of sound in the ear or head that does not arise from the external environment, from within the body (e.g., vascular sounds), or from auditory hallucinations related to mental illness. This review is concerned with tinnitus for which tinnitus is the only, or the predominant, symptom in an affected person.

INCIDENCE/ PREVALENCE

Up to 18% of the general population in industrialised countries are mildly affected by chronic tinnitus, and 0.5% report tinnitus having a severe effect on their ability to lead a normal life. [1]

AETIOLOGY/ RISK FACTORS

Tinnitus can occur as an isolated idiopathic symptom, or in association with any type of hearing loss. Tinnitus can be a particular feature of presbycusis (age-related hearing loss), noise-induced hearing loss, Menière's disease (see review on Menière's disease), or the presence of an acoustic neuroma. In people with toxicity from aspirin or quinine, tinnitus can occur with hearing thresholds remaining normal. Tinnitus is also associated with depression, although it can be unclear whether the tinnitus is a manifestation of the depressive illness or a factor contributing to its development. [2] Studies involving people with tinnitus caused by Menière's disease, acoustic neuroma, chronic otitis media, head injury, barotraumas, or other clear pathology have been excluded from this review. This review is principally concerned with idiopathic tinnitus with or without degenerative sensorineural hearing loss.

PROGNOSIS

Tinnitus can have an insidious onset, with a long delay before clinical presentation. It can persist for many years or decades, particularly when associated with a sensorineural hearing loss. Tinnitus can cause disruption of sleep patterns, an inability to concentrate, and depression. [3]

AIMS OF INTERVENTION

To reduce the loudness and intrusiveness of the tinnitus, and to reduce its impact on daily life, with minimum adverse effects of treatment.

OUTCOMES

Resolution of tinnitus; **improvement in tinnitus** (includes tinnitus loudness [assessed by a visual analogue scale or symptom scores]); **impact of tinnitus on quality of life**, as measured by estimates of interference with activities of daily life or with emotional state; and **adverse effects**.

METHODS

Clinical Evidence search and appraisal November 2013. The following databases were used to identify studies for this systematic review: Medline 1966 to November 2013, Embase 1980 to November 2013, and The Cochrane Database of Systematic Reviews 2013, issue 11 (1966 to date of issue). Additional searches were carried out in the Database of Abstracts of Reviews of Effects (DARE) and Health Technology Assessment (HTA) database. We also searched for retractions of studies included in the review. Titles and abstracts identified by the initial search, run by an information specialist, were first assessed against predefined criteria by an evidence scanner. Full texts for potentially relevant studies were then assessed against predefined criteria by an evidence analyst. Studies selected for inclusion were discussed with an expert contributor. All data relevant to the review were then extracted by an evidence analyst. Study design criteria for inclusion in this review were: published RCTs and systematic reviews of RCTs in the English language, at least single-blinded, and containing at least 20 individuals, of whom at least 80% were followed up. There was no minimum length of follow-up required to include studies. We excluded all studies described as 'open', 'open label', or not blinded unless blinding was impossible. We included RCTs and systematic reviews of RCTs where harms of an included intervention were assessed, applying the same study design criteria for inclusion as we did for benefits. In addition, we use a regular surveillance protocol to capture harms alerts from organisations such as the FDA and the MHRA, which are added to the reviews as required. To aid readability of the numerical data in our reviews, we round many percentages to the nearest whole number. Readers should be aware of this when relating percentages to summary statistics such as relative risks (RRs) and odds ratios (ORs). We have performed a GRADE evaluation of the quality of evidence for interventions included in this review (see table, p 31). The categorisation of the quality of the evidence (high, moderate, low, or very low) reflects the quality of evidence available for our chosen outcomes in our defined populations of interest. These categorisations are not necessarily a reflection of the overall methodological quality of any individual study, because the Clinical Evidence population and outcome of choice may represent only a small subset of the total outcomes reported, and population included, in any individual trial. For further details of how we perform the GRADE evaluation and the scoring system we use, please see our website (www.clinicalevidence.com).

QUESTION What are the effects of treatments for chronic tinnitus?

OPTION ACAMPROSATE

- For GRADE evaluation of interventions for Tinnitus, see table, p 31 .

- Acamprosate may be more effective than placebo in improving overall symptom scores and tinnitus-specific quality of life after 3 months in people with tinnitus. However, evidence was weak, we don't know about tinnitus loudness, and the clinical importance of the improvement was unclear.

Benefits and harms

Acamprosate versus placebo:

We found one systematic review (search date 2012), [4] which included two RCTs comparing acamprosate with placebo. [5] [6] However, the methods of the review [4] were unclear, so we have reported the original RCT data here. [5] [6]

Improvement in tinnitus

Acamprosate compared with placebo Acamprosate may reduce the severity of tinnitus after 3 months, although the improvement may not be clinically important and the evidence was weak (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Tinnitus loudness					
[5] RCT **Crossover design**	40 people with tinnitus	**Mean subjective loudness (assessed using 10 cm visual analogue scale) , Day 45** 4.2 with acamprosate 6.3 with placebo Data reported prior to crossover	Significance not reported		
[5] RCT **Crossover design**	40 people with tinnitus	**Mean tinnitus matching (loudness assessed in decibels) , Day 45** 43 with acamprosate 49 with placebo Data reported prior to crossover	Significance not reported		
Overall symptoms of tinnitus					
[6] RCT	50 people with subjective tinnitus	**Proportion of people with improvement in tinnitus (measured on a tinnitus score [scale of 0–10]) , 3 months** 87% with acamprosate (3 times daily) 44% with placebo Absolute numbers not reported	P = 0.0004 It is unclear whether the difference in scores reflects a clinically important improvement in tinnitus People who withdrew from the RCT were not included in the data analysis, which would have affected the results	○○○	acamprosate

Resolution of tinnitus

No data from the following reference on this outcome. [5] [6]

Impact of tinnitus on quality of life

Acamprosate compared with placebo We don't know whether acamprosate improves tinnitus-specific quality of life scores after 3 months compared with placebo as the RCT did not test the significance of differences between groups (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Quality of life					
[5] RCT	40 people with tinnitus	**Mean quality of life (severity) , Day 45**	Signficance not reported		

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Crossover design		42.33 with acamprosate twice-daily for 45 days 67.19 with placebo Data reported prior to cross-over			

No data from the following reference on this outcome. [6]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[6] RCT	50 people with subjective tinnitus	**Proportion of people with an adverse effect , 3 months** 12% with acamprosate (3 times daily) 20% with placebo Absolute numbers not reported The RCT reported mild adverse effects with acamprosate, including epigastralgia, choking, and depression	P = 0.35 People who dropped out of the RCT were not included in the data analysis, which would have affected the results	⟷	Not significant

Comment: None.

OPTION ACUPUNCTURE

- For GRADE evaluation of interventions for Tinnitus, see table, p 31 .
- We don't know whether acupuncture is effective in people with tinnitus.

Benefits and harms

Acupuncture versus sham acupuncture:

We found one systematic review (search date 2012), [7] which included five RCTs, and one additional RCT [8] comparing acupuncture with sham acupuncture.

Improvement in tinnitus

Acupuncture compared with sham acupuncture We don't know whether acupuncture is more effective than sham acupuncture at reducing the severity of tinnitus at 3 weeks to 2 months (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Tinnitus loudness					
[7] Systematic review	54 people with chronic (at least 6 months) and severe tinnitus Data from 1 RCT	**Loudness (assessed using a visual analogue scale) , at 2 months** with acupuncture with sham acupuncture	MD –3.40 95% CI –16.66 to +9.86	⟷	Not significant

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
		Absolute numbers not reported			
[7] Systematic review	50 people with tinnitus Data from 1 RCT	**Tinnitus loudness , at 6 weeks** with acupuncture plus electroacupuncture with sham acupuncture Absolute numbers not reported	Reported as not significant P value not reported	⟷	Not significant
[8] RCT	54 people with chronic tinnitus	**Mean tinnitus loudness (assessed using the Tinnitus Loudness Questionnaire) , after 10 treatments** 5.3 with acupuncture 7.5 with sham acupuncture	P = 0.004 Similar significant results were observed after 5 treatment sessions in favour of acupuncture		acupuncture
Overall symptoms of tinnitus					
[7] Systematic review	54 people with chronic (at least 6 months) and severe tinnitus Data from 1 RCT	**Awareness (assessed using a visual analogue scale) , at 2 months** with acupuncture with placebo Absolute results not reported	MD –2.0 95% CI –18.5 to +14.5	⟷	Not significant
[7] Systematic review	50 people with tinnitus Data from 1 RCT 3-armed trial	**Tinnitus occurrence , at 6 weeks** with acupuncture with electro-acupuncture with sham acupuncture	Reported as not significant P value not reported	⟷	Not significant
[7] Systematic review	33 adults with chronic (at least 6 months) unilateral tinnitus, without moderate or severe hearing loss Data from 1 RCT	**Mean change in Tinnitus Handicap Inventory Score , 3 months** 24.2 with acupuncture 0.3 with sham acupuncture	MD –2.5. 95% CI –15.5 to +10.5 The review found similar findings immediately after treatment	⟷	Not significant
[8] RCT	54 people with chronic tinnitus	**Mean tinnitus severity index (assessed using Tinnitus Severity Index Questionnaire) , after 10 treatment sessions** 31.7 with acupuncture 42.9 with sham acupuncture	P = 0.001 Similar significant results were observed after 5 treatment sessions in favour of acupuncture See Further information on studies		Acupuncture

Impact of tinnitus on quality of life

Acupuncture compared with sham acupuncture We don't know whether acupuncture is more effective than sham acupuncture at reducing annoyance (as a result of tinnitus) or whether it improves the overall quality of life scores (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Quality of life					
[7] Systematic review	50 people with tinnitus Data from 1 RCT RCT was 3-armed	**Quality of life** with acupuncture with electro-acupuncture with sham acupuncture Absolute numbers not reported	Reported as not significant P values not reported	⟷	Not significant

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Annoyance					
[7] Systematic review	54 people with chronic (at least 6 months) and severe tinnitus Data from 1 RCT	**Annoyance (assessed using a visual analogue scale)** with acupuncture with sham acupuncture Absolute numbers not reported	MD –5.00 95% CI –21.26 to +11.26	⟷	Not significant

No data from the following reference on this outcome. [8]

Resolution of tinnitus

No data from the following reference on this outcome. [7] [8]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[8] RCT	54 people with chronic tinnitus	**Vasovagal shock** 1 with acupuncture 0 with sham acupuncture	Not reported		

No data from the following reference on this outcome. [7]

Further information on studies

[8] Before acupuncture was performed, patients were examined based on the diagnostic pattern of traditional Chinese medicine. Using this method, the acupoints for treatment were selected for each individual participant. The study had unclear randomisation and used a simple sampling method. Analysis of variance with repeated observations showed that, although the mean of the tinnitus severity index in the case group decreased significantly after treatment, the results were not significantly different from the control group by three-time assessments. The authors concluded that acupuncture is beneficial as a treatment modality for tinnitus, even though the effects may not last for a long period of time.

Comment: None.

OPTION ANTIDEPRESSANT DRUGS

- For GRADE evaluation of interventions for Tinnitus, see table, p 31 .
- We found no good evidence that antidepressant drugs improve tinnitus symptoms.
- Antidepressant drugs may improve depression and anxiety in people with tinnitus compared with placebo.
- Tricyclic antidepressants are associated with adverse effects such as dry mouth, blurred vision, and constipation.

Benefits and harms

Tricyclic antidepressants (TCAs) versus placebo:

We found three systematic reviews (search date 2010; [9] search date 2012 [10] [4]). The first review [9] identified one RCT [11] that compared TCAs with placebo; this RCT was also included in the second review. The second review [10] included four RCTs. [11] [12] [13] [14]) Since the review did not perform meta-analyses, the RCTs are reported individually. The methods of the third review [4] were unclear, so it has not been reported further here.

Improvement in tinnitus

Tricyclic antidepressants (TCAs) compared with placebo We don't know if TCA's are more effective than placebo at reducing the severity of tinnitus at 6–10 weeks (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Tinnitus loudness					
[13] RCT **Crossover design**	26 people In review [10]	**Improvement in subjective tinnitus loudness (mean subjective rating on a scale of 1–7) , 6 weeks** 4.3 with trimipramine 4.0 with placebo After initial treatment for 6 weeks, there was a 4-week rest period, followed by a further 6 weeks' treatment with all people crossed over to the other treatment	Reported as not significant P value not reported	⟷	Not significant
[14] RCT	225 people (123 people in this analysis) In review [10] 4-armed trial	**Proportion of people with improvement in subjective tinnitus loudness at rest** 28% (out of 83 people) with amitriptyline 5% (out of 40 people) with placebo Absolute numbers not reported The third and fourth arms assessed the effects of biofeedback and placebo biofeedback	P <0.011 (as reported in RCT) The review reported that results were presented as percentages, and further analysis is not possible	○○○	amitriptyline
Overall symptoms of tinnitus					
[12] RCT	37 people with no history of depression In review [10]	**Proportion of people with a decrease in subjective tinnitus , 6 weeks** 19/20 (95%) with amitriptyline 2/17 (12%) with placebo	Significance not assessed		
[13] RCT **Crossover design**	26 people In review [10]	**Proportion of people with worsening of tinnitus (mean subjective rating on a scale of 1–7) , 6 weeks** 7/19 (37%) with trimipramine 4/19 (21%) with placebo After initial treatment for 6 weeks, there was a 4-week rest period, followed by a further 6 weeks' treatment with all people crossed over to the other treatment	Significance not assessed		
[11] RCT	117 people; results are reported for the 92 people who completed the follow-up period	**Proportion of people reporting overall improvement in tinnitus severity (measured by asking "Has your tinnitus improved?") , 6 weeks**	Reported as not significant P value not reported	⟷	Not significant

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
	In review [10]	with nortriptyline (titrated to maintain therapeutic blood levels for depression) with placebo Absolute numbers not reported			

Impact of tinnitus on quality of life

Tricyclic antidepressants (TCAs) compared with placebo Nortriptyline may be more effective than placebo at improving symptoms of depression and anxiety at 6 weeks in people with tinnitus (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Depression					
[11] RCT	117 people; results are reported for the 92 people who completed the follow-up period In review [10]	**Hamilton Depression Rating Scale score , 6 weeks** 11 with nortriptyline 14 with placebo	P = 0.0001	○○○	nortriptyline
[11] RCT	117 people; results are reported for the 92 people who completed the follow-up period In review [10]	**Proportion of people reporting global satisfaction (measured by asking "Has the medication helped you in any way?") , 6 weeks** 33/49 (67%) with nortriptyline 17/43 (40%) with placebo	P <0.01	○○○	nortriptyline

No data from the following reference on this outcome. [12] [13] [14]

Resolution of tinnitus

No data from the following reference on this outcome. [11] [12] [13] [14]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[12] RCT	37 people with no history of depression In review [10]	**Adverse effects** with amitriptyline with placebo The RCT found that amitriptyline was associated with mild sedation and dryness of the mouth lasting for 1 to 2 weeks, but it reported no major adverse effects Other common adverse effects of TCAs include dry mouth, blurred vision, and constipation	Significance not assessed		

No data from the following reference on this outcome. [11] [13] [14]

Seretonin selective re-uptake inhibitors (SSRIs) versus placebo:

We found three systematic reviews (search date 2010; [9] search date 2012 [10] [4]). The first two reviews [9] [10] identified one RCT [15] comparing SSRIs with placebo. The third review [4] included three RCTs [15] [16] [17] comparing SSRIs versus placebo. The methods of the third review were unclear, so original RCT data have been reported for all three included trials.

Improvement in tinnitus

SSRIs compared with placebo We don't know whether SSRIs are more effective than placebo at reducing the symptoms of tinnitus at up to 16 weeks (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Tinnitus loudness					
[15] RCT	120 people In review [10]	**Improvement in average pure tone** 1.8 dB with paroxetine 0.8 dB with placebo	P >0.05	⟷	Not significant
[16] RCT	76 people with tinnitus, considered to be at high risk of developing severe and disabling tinnitus	**Reduction in tinnitus loudness score (measured by visual analogue scale; scale of 0–100 mm) , 16 weeks** 15.21 with sertraline 3.21 with placebo People in both groups were also offered oxazepam during the first 2 weeks to alleviate distress; 3/29 (10%) in the sertraline group and 6/34 (18%) in the placebo group accepted oxazepam (significance not assessed)	P = 0.013 The RCT may have been underpowered to detect a clinically meaningful difference between groups	○○○	sertraline
Overall symptoms of tinnitus					
[16] RCT	76 people with tinnitus, considered to be at high risk of developing severe and disabling tinnitus	**Reduction in tinnitus severity questionnaire score (scale of 0–40) , 16 weeks** 4.69 with sertraline 2.12 with placebo People in both groups were also offered oxazepam during the first 2 weeks to alleviate distress; 3/29 (10%) in the sertraline group and 6/34 (18%) in the placebo group accepted oxazepam (significance not assessed)	P = 0.024 The RCT may have been underpowered to detect a clinically meaningful difference between groups	○○○	sertraline

No data from the following reference on this outcome. [17]

Impact of tinnitus on quality of life

SSRIs compared with placebo We don't know whether SSRIs are more effective than placebo at reducing annoyance, anxiety, sleep disturbance, and depression at 16 weeks in people with tinnitus as we were unable to draw robust conclusions (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
General well-being					
[17] RCT	75 people with tinnitus, considered to be at high risk of developing severe and disabling tinnitus Further report of reference [16]	**Change in Psychological General Well-Being Index (PGWB) , 16 weeks** 20.83 with sertraline 2.79 with placebo See Further information on studies for details of PGWB and further comment	P = 0.001 The RCT reported no significant correlation between visual analogue scale and tinnitus loudness The RCT may have been underpowered to detect a clinically meaningful difference between groups	○○○	sertraline
Annoyance					
[16] RCT	76 people with tinnitus, considered to be at high risk of developing severe and disabling tinnitus	**Reduction in tinnitus annoyance score (measured by visual analogue scale; scale of 0–100 mm) , 16 weeks** 15.76 with sertraline 5.15 with placebo People in both groups were also offered oxazepam during the first 2 weeks to alleviate distress; 3/29 (10%) in the sertraline group and 6/34 (18%) in the placebo group accepted oxazepam (significance not assessed)	Reported as not significant P value not reported The RCT may have been underpowered to detect a clinically meaningful difference between groups	⟷	Not significant
Anxiety					
[16] RCT	76 people with tinnitus, considered to be at high risk of developing severe and disabling tinnitus	**Reduction in clinician-rated anxiety score (measured by Hamilton Anxiety Rating Scale; scale of 0–56) , 16 weeks** 8.51 with sertraline 4.09 with placebo People in both groups were also offered oxazepam during the first 2 weeks to alleviate distress; 3/29 (10%) in the sertraline group and 6/34 (18%) in the placebo group accepted oxazepam (significance not assessed)	P = 0.037 The RCT may have been underpowered to detect a clinically meaningful difference between groups	○○○	sertraline
[16] RCT	76 people with tinnitus, considered to be at high risk of developing severe and disabling tinnitus	**Reduction in participant-rated anxiety score (measured by Comprehensive Psychopathological Rating Scale [CPRS-S-A] for anxiety; scale of 0–54) , 16 weeks** 4.38 with sertraline 0.73 with placebo People in both groups were also offered oxazepam during the first 2 weeks to alleviate distress; 3/29 (10%) in the sertraline group and 6/34 (18%) in the placebo group accepted oxazepam (significance not assessed)	P = 0.013 The RCT may have been underpowered to detect a clinically meaningful difference between groups	○○○	sertraline
Depression					
[16] RCT	76 people with tinnitus, considered to be at high risk of developing severe and disabling tinnitus	**Reduction in participant-rated depression score (measured by CPRS-S-A for depression; scale of 0–60) , 16 weeks** 5.93 with sertraline	P = 0.002 The RCT may have been underpowered to detect a clinically meaningful difference between groups	○○○	sertraline

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
		0.05 with placebo People in both groups were also offered oxazepam during the first 2 weeks to alleviate distress; 3/29 (10%) in the sertraline group and 6/34 (18%) in the placebo group accepted oxazepam (significance not assessed)			
[16] RCT	76 people with tinnitus, considered to be at high risk of developing severe and disabling tinnitus	**Reduction in clinician-rated depression score (measured by Hamilton Depression Rating Scale; scale 0–62) , 16 weeks** 9.79 with sertraline 5.87 with placebo People in both groups were also offered oxazepam during the first 2 weeks to alleviate distress; 3/29 (10%) in the sertraline group and 6/34 (18%) in the placebo group accepted oxazepam (significance not assessed)	Reported as not significant P value not reported The RCT may have been underpowered to detect a clinically meaningful difference between groups	⟷	Not significant

No data from the following reference on this outcome. [15]

Resolution of tinnitus

No data from the following reference on this outcome. [15] [16] [17]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[16] RCT	76 people with tinnitus, considered to be at high risk of developing severe and disabling tinnitus	**Adverse effects , 16 weeks** with sertraline with placebo See Further information on studies	The RCT may have been underpowered to detect a clinically meaningful difference between groups		

No data from the following reference on this outcome. [15] [17]

Serotonin antagonist and re-update inhibitor (SARI) versus placebo:

We found one systematic review (search date 2012), [10] which included one RCT. [18]

Improvement in tinnitus

SARI compared with placebo We don't know whether SARI's are more effective than placebo at reducing the symptoms of tinnitus at 8 weeks (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Tinnitus loudness					
[10] Systematic review	85 people with tinnitus Data from 1 RCT	**Mean tinnitus intensity (assessed using a 0–10 visual analogue scale) , 8 weeks** 5.86 with trazodone 5.62 with placebo	MD 0.24 95% CI –0.70 to +1.18 P = 0.62	⟷	Not significant
[10] Systematic review	85 people with tinnitus Data from 1 RCT	**Mean tinnitus discomfort (assessed using a 0–10 visual analogue scale) , 8 weeks** 5.91 with trazodone 5.10 with placebo	MD 0.81 95% CI –0.14 to +1.76 P = 0.096	⟷	Not significant

Impact of tinnitus on quality of life

SARIs compared with placebo We don't know whether SARIs are more effective than placebo at improving quality of life scores at 8 weeks in people with tinnitus (low quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Quality of life					
[10] Systematic review	885 people with tinnitus Data from 1 RCT	**Improvement in quality of life (assessed using a 0–10 visual analogue scale) , 8 weeks** with trazodone with placebo Absolute results not reported	Reported as not significant P values not reported	⟷	Not significant

Resolution of tinnitus

No data from the following reference on this outcome. [10]

Adverse effects

No data from the following reference on this outcome. [10]

Further information on studies

[16] The RCT found that 2/38 (5%) people in the placebo group had worsened psychiatric condition and were lost to follow-up, and 2/38 (5%) people in the sertraline group had adverse effects and were lost to follow-up (adverse effects not specified). People in both groups were also offered oxazepam during the first 2 weeks to alleviate distress; 3/29 (10%) in the sertraline group and 6/34 (18%) in the placebo group accepted oxazepam (significance not assessed).

[17] The Psychological General Well-Being Index (PGWB) provides an overall global score from six separate dimensions (anxiety, depressed mood, positive well-being, self-control, general health, and vitality). Maximum overall score 132 (optimal well-being) and minimum score 22. Pre-treatment scores were 86.8 (placebo) and 83.5 (sertraline). People in both groups were also offered oxazepam during the first 2 weeks to alleviate distress;

3/29 (10%) people in the sertraline group and 6/34 (18%) people in the placebo group accepted oxazepam (significance not assessed).

Comment: None.

OPTION BENZODIAZEPINES

- For GRADE evaluation of interventions for Tinnitus, see table, p 31 .
- We don't know whether benzodiazepines are effective in people with tinnitus.
- Long-term use of benzodiazepines can lead to dependence.

Benefits and harms

Benzodiazepines versus placebo:

We found two systematic reviews (search date 1995; [19] search date 2010 [4]) which identified one RCT. [20] The methods of the second review [4] were unclear, so it has not been reported further here. We also found one subsequent RCT. [21]

Improvement in tinnitus

Benzodiazepines compared with placebo We don't know whether benzodiazepines are more effective than placebo at improving symptoms of tinnitus after 12 to 18 weeks (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Tinnitus loudness					
[20] RCT	40 people In review [19]	**Proportion of people with improvement in tinnitus (measured by tinnitus synthesiser and visual analogue scale [scale of 0–10; increasing score is associated with increasing loudness]) , 12 weeks** 13/17 (77%) with alprazolam 1/19 (5%) with placebo	Significance not assessed The RCT used dose adjustment of alprazolam but no dose adjustment of placebo, potentially biasing the results because of a difference in the attention given to people in the 2 groups		
[21] RCT **Crossover design**	36 people	**Proportion of people with improvement in tinnitus (measured by tinnitus matching and reported as a change in dB sensation level) , 18 weeks** From 8.7 to 8.6 (–0.1) with alprazolam (3 times daily, on escalating scale to minimise adverse effects) From 8.4 to 8.4 (0) with placebo Crossover design: 2 8-week treatment periods separated by a 2-week washout period Per-protocol analysis: 30/36 (83%) people completed the trial and were included in the analysis	P value not reported Reported as not significant	⟷	Not significant
General tinnitus symptoms					
[21] RCT **Crossover design**	36 people	**Mean change in Tinnitus Handicap Injury (THI) score , 18 weeks** From 43.9 to 42.8 (–1.1) with alprazolam (3 times daily, on escalating scale to minimise adverse effects)	P value not reported Reported as not significant	⟷	Not significant

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
		From 49.6 to 49.2 (–0.4) with placebo Crossover design: 2 8-week treatment periods separated by a 2-week washout period Per-protocol analysis: 30/36 (83%) people completed the trial and were included in the analysis			
[21] RCT **Crossover design**	36 people	**Proportion of people with improvement in tinnitus (visual analogue scale 1–100, higher score = more severe) , 18 weeks** From 76.0 to 55.1 (–20.9) with alprazolam (3 times daily, on escalating scale to minimise adverse effects) From 70.1 to 68.6 (–1.5) with placebo Crossover design: 2 8-week treatment periods separated by a 2-week washout period Per-protocol analysis: 30/36 (83%) people completed the trial and were included in the analysis	P <0.001	○○○	alprazolam

Resolution of tinnitus

No data from the following reference on this outcome. [20] [21]

Impact of tinnitus on quality of life

No data from the following reference on this outcome. [20] [21]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[20] RCT	40 people In review [19]	**Adverse effects** with alprazolam with placebo The RCT reported that 2 (10%) people receiving alprazolam withdrew from the RCT because of excessive drowsiness Long-term use of benzodiazepines can lead to dependence (see Generalised anxiety disorders review)	The RCT used dose adjustment of alprazolam but no dose adjustment of placebo, potentially biasing the results because of a difference in the attention given to people in the 2 groups		
[21]	36 people	**Proportion of people who withdrew from treatment**	Significance not assessed		

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
RCT **Crossover design**		2 with alprazolam three times daily (on escalating scale to minimise adverse effects) 4 with placebo Long-term use of benzodiazepines can lead to dependence (see Generalised anxiety disorders review) Placebo was chlorpheniramine maleate, used to create a similar sedative effect to alprazolam to aid in the blinding process			

Comment: None.

OPTION ELECTROMAGNETIC STIMULATION

- For GRADE evaluation of interventions for Tinnitus, see table, p 31 .
- We don't know whether electromagnetic stimulation is effective in people with tinnitus, as we found few studies.

Benefits and harms

Electromagnetic stimulation versus placebo:

We found three systematic reviews (search date 2011; [22] search date 2012 [23] [4]) comparing electromagnetic stimulation with placebo. The first and second reviews identified nine RCTs between them. However, as the reviews included unique RCTs and have reported different data on different outcomes, both have been reported below. The methods of the third review were unclear, so it has not been reported further here. We also found one crossover RCT. [24]

Improvement in tinnitus

Electromagnetic stimulation compared with placebo We don't know how electromagnetic stimulation compares with placebo at improving symptoms of tinnitus (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Tinnitus loudness					
[22] Systematic review	89 people with tinnitus 2 RCTs in this analysis	**Proportion of people reporting improvement in tinnitus loudness** 16/49 (33%) with repetitive transcranial magnetic stimulation (rTMS) 3/40 (8%) with sham rTMS	RR 1.54 95% CI 1.3 to 13.40 P = 0.016	●●○	magnetic stimulation
Overall symptoms of tinnitus					
[22] Systematic review	153 people with tinnitus 3 RCTs in this analysis	**Proportion of people reporting worsening of tinnitus** 11/94 (12%) with repetitive transcranial magnetic stimulation (rTMS) 5/59 (8%) with sham rTMS	RR 1.54 95% CI 0.50 to 4.74 P = 0.46 The RCT reported that 4/58 (7%) people withdrew from the trial, and that the analysis was not by intention to treat	⟷	Not significant

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
[23] Systematic review	66 people with tinnitus Data from 1 RCT	**Duration of residual inhibition** with left temporoparietal cortex repetitive transcranial magnetic stimulation (rTMS) with sham stimulation (occipital) Absolute results not reported	It was reported that residual inhibition increased significantly more after rTMS than with sham stimulation		
[24] RCT **Crossover design**	20 people	**Proportion of people who had improved tinnitus (tinnitus severity measured on a scale of 0–7)** 2/20 (10%) with electrical suppression 3/20 (15%) with placebo device	Significance not assessed		

Resolution of tinnitus

No data from the following reference on this outcome. [22] [23] [24]

Impact of tinnitus on quality of life

Electromagnetic stimulation compared with placebo We don't know whether electromagnetic stimulation improves quality of life scores in people with tinnitus at 2 weeks (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Annoyance					
[23] Systematic review	66 people with tinnitus Data from 1 RCT	**Annoyance ratings , 2 weeks** with left temoroparietal cortex repetitive transcranial magnetic stimulation (rTMS) with sham stimulation Absolute results not reported	It was reported that improvement in annoyance ratings were greater with rTMS than with sham stimulation		

No data from the following reference on this outcome. [22] [24]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[25] RCT	58 people In review [22]	**Adverse effects** with electromagnetic stimulation (15 minutes/day) with placebo device The RCT reported no adverse effects associated with electromagnetic stimulation			
[24] RCT	20 people	**Adverse effects** with electrical suppression			

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Crossover design		with placebo device The RCT reported no adverse effects associated with electrical suppression			

Comment: None.

OPTION GINKGO BILOBA

- For GRADE evaluation of interventions for Tinnitus, see table, p 31 .
- Ginkgo biloba may be no more effective than placebo at improving symtoms of tinnitus at 3 months.
- However, evidence was limited, and results inconsistent.

Benefits and harms

Ginkgo biloba versus placebo:

We found two systematic review (search date 2012) [26] [27] comparing ginkgo biloba versus placebo. The reviews reported four RCTs between them. [28] [29] [30] [31] The reviews did not perform a meta-analysis; the explicit reasoning was not specified, but the authors of the review noted that most RCTs were of poor quality. [26] We have not reported one of the RCTs because of poor methods (pseudo-randomisation, unblinded assessors, selection of participants by previous positive response to ginkgo biloba), or high withdrawal rate. [28]

Improvement in tinnitus

Ginkgo biloba compared with placebo Ginkgo biloba may be no more effective than placebo at improving the symptoms of tinnitus at up to 3 months. However, evidence was limited and results inconsistent (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Overall symptoms of tinnitus					
[26] Systematic review	978 people with tinnitus Data from 1 RCT	**Improvement in tinnitus, post-treatment , 12 weeks** 13.6% with ginkgo biloba 12.4% with placebo Absolute numbers not reported	Reported as not significant The review reported that there were no significant between-group differences in mean scores for tinnitus loudness, awareness, or impact	⟷	Not significant
[27] RCT	66 people Data from 1 RCT	**Change in tinnitus intensity (scale of 0–3) , 3 months** –1.00 with ginkgo biloba –0.67 with placebo	P = 0.03		ginkgo biloba
[30] RCT	66 people In review [26]	**Mean change in Tinnitus Handicap Inventory score (scale of 1–100; increasing score is associated with increasing severity of handicap) , 12 weeks** –4.7 with ginkgo biloba –2.2 with placebo	P = 0.51	⟷	Not significant
[27] Systematic review	100 people with tinnitus (mean duration 134 days)	**Global rating of change (much improved) , 3 months** 40% with ginkgo biloba	P = 0.05		ginkgo biloba

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
	Data from 1 RCT	24% with placebo Absolute numbers not reported			

Resolution of tinnitus

No data from the following reference on this outcome. [29] [30] [31]

Impact of tinnitus on quality of life

Ginkgo biloba compared with placebo We don't know whether ginkgo biloba improves the quality of life in people with tinnitus at 3 months (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Annoyance					
[27] Systematic review	100 people with tinnitus (mean duration 134 days) Data from 1 RCT	**Change in nuisance (scale 0–3), 3 months** –0.84 with ginkgo biloba –0.59 with placebo	P = 0.08	⟷	Not significant

No data from the following reference on this outcome. [29] [30]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[30] RCT	66 people In review [26]	**Proportion of people with diarrhoea , 12 weeks** 3% with ginkgo biloba 6% with placebo Absolute numbers not reported	Significance not assessed		
[30] RCT	66 people In review [26]	**Proportion of people with headache , 12 weeks** 3% with ginkgo biloba 3% with placebo Absolute numbers not reported	Significance not assessed		

Comment: None.

OPTION HEARING AIDS

- For GRADE evaluation of interventions for Tinnitus, see table, p 31 .
- We don't know whether hearing aids are effective in people with tinnitus because we found very few RCTs.

Benefits and harms

Hearing aids versus waiting list control:

We found no systematic review. We found one RCT comparing hearing aids versus a waiting list control in people who were having hearing aids fitted primarily for hearing loss, and who also had tinnitus. [32]

Improvement in tinnitus

Hearing aids compared with waiting list control Hearing aids may be no more effective at reducing the severity of tinnitus after 6 weeks than being on a waiting list in people with hearing loss and tinnitus. However, evidence was very limited (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Tinnitus intensity					
[32] RCT	39 people	**Perceived tinnitus intensity (measured on a 10-cm visual analogue scale) , 6 weeks** with hearing aid (worn for 6 weeks) with waiting list control Absolute results not reported	Reported as not significant P value not reported	⟷	Not significant

Resolution of tinnitus

No data from the following reference on this outcome. [32]

Impact of tinnitus on quality of life

No data from the following reference on this outcome. [32]

Adverse effects

No data from the following reference on this outcome. [32]

Comment: None.

OPTION HYPNOSIS

- For GRADE evaluation of interventions for Tinnitus, see table, p 31 .
- We don't know whether hypnosis is effective in people with tinnitus, as we found few studies.

Benefits and harms

Hypnosis versus counselling:

We found one systematic review (search date 1995) [19] and one additional RCT. [33] The review found no RCTs that met its inclusion criteria. [19]

Improvement in tinnitus

Hypnosis compared with counselling We don't know whether self-hypnosis training is more effective than a single counselling session at reducing the severity of tinnitus after 3 months (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Overall symptoms (other than loudness) of tinnitus					
[33] RCT	92 people pre-selected to be suggestible to hypnosis	**Proportion of people who had improved symptom severity scores , 3 months** 24/44 (54.5%) with hypnosis (3 sessions teaching self-hypnosis) 23/42 (54.8%) with counselling (single session)	Reported as not significant P value not reported	⟷	Not significant
[33] RCT	92 people pre-selected to be suggestible to hypnosis	**Proportion of people reporting worsened tinnitus , 3 months** 14/44 (32%) with hypnosis (3 sessions teaching self-hypnosis) 11/42 (26%) with counselling (single session)	Reported as not significant P value not reported	⟷	Not significant

Resolution of tinnitus

No data from the following reference on this outcome. [33]

Impact of tinnitus on quality of life

No data from the following reference on this outcome. [33]

Adverse effects

No data from the following reference on this outcome. [33]

Comment: None.

OPTION PSYCHOTHERAPY

- For GRADE evaluation of interventions for Tinnitus, see table, p 31 .
- We don't know whether cognitive behavioural therapy (CBT) is more effective than placebo at reducing the loudness of tinnitus, but CBT may be more effective at reducing the overall symptoms of tinnitus at 12 months.
- CBT may be more effective than placebo at improving anxiety, depression, quality of life, and tinnitus annoyance scores in people with tinnitus.
- We don't know whether acceptance commitment therapy (ACT) is more effective than waiting-list control at improving depression or tinnitus annoyance scores in people with tinnitus.

Benefits and harms

CBT versus placebo:

We found four systematic review (search date 1998; [34] search date 2009; [35] search date 2010; [36] search date 2012 [4]), which assessed the effects of different psychotherapeutic approaches. The methods of the fourth review [4] were unclear, so it has not been reported further here. The one RCT [37] included in the fourth review has been reported using original RCT data. All of the other three reviews included different RCTs, and presented results for outcomes in different ways. Therefore, all three reviews are reported below.

Improvement in tinnitus

CBT compared with placebo We don't know whether CBT is more effective than placebo at reducing the loudness of tinnitus, but CBT may be more effective at reducing the overall symptoms of tinnitus at 12 months (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Tinnitus loudness					
[36] Systematic review	164 people 4 RCTs in this analysis	**Reduction of subjective tinnitus loudness** with CBT with alternative intervention (yoga, education, minimal contact-education) Absolute results not reported	SMD +0.1 95% CI –0.22 to +0.42 P = 0.56	⟷	Not significant
[36] Systematic review	354 people 6 RCTs in this analysis	**Reduction of subjective tinnitus loudness** with CBT with waiting-list control Absolute results not reported	SMD +0.24 95% CI –0.02 to +0.51 P = 0.075	⟷	Not significant
[34] Systematic review	269 people 8 RCTs in this analysis	**Reduction in subjective tinnitus loudness , 3 months or more post treatment** with CBT (combination of different psychotherapeutic approaches) with placebo Absolute results not reported	SMD 0.68 95% CI 0.62 to 0.74 The review had important flaws in its methods, compromising its validity (see Further information on studies for more details)	○○○	CBT
Overall symptoms of tinnitus					
[37] RCT	492 people with tinnitus	**Tinnitus severity (assessed using Tinnitus Questionnaire) , 12 months** with CBT with usual care Absolute results not reported	Difference –8.062 95% CI –10.829 to –5.295		CBT
[37] RCT	492 people with tinnitus	**Tinnitus impairment (assessed using Tinnitus Handicap Inventory) , 12 months** with CBT with usual care Absolute results not reported	Difference –7.506 95% CI –10.661 to –4.352 P <0.0001		CBT

Impact of tinnitus on quality of life

CBT compared with placebo CBT may more effective than placebo at improving anxiety, depression, quality of life, and tinnitus annoyance scores in people with tinnitus (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Anxiety					
[37] RCT	492 people with tinnitus	**Tinnitus catastrophising (assessed using Tinnitus Catastrophising Scale) , 12 months** with CBT with usual care Absolute results not reported	Difference –3.830 99% CI –6.185 to –1.475 The review found similar significant results between groups at 8 months		CBT
[37] RCT	492 people with tinnitus	**Tinnitus-related fear (assessed using Fear of Tinnitus Questionnaire) , 12 months** with CBT with usual care Absolute results not reported	Difference –1.502 99% CI –2.317 to –0.688 The review found similar significant results between groups at 8 months		CBT
Depression					
[36] Systematic review	117 people 3 RCTs in this analysis	**Symptoms of depression** with CBT with alternative intervention (yoga, education, minimal contact-education) Absolute results not reported	SMD +0.01 95% CI –0.43 to +0.45	⟷	Not significant
[36] Systematic review	335 people 6 RCTs in this analysis	**Symptoms of depression** with CBT with waiting-list control Absolute results not reported	SMD 0.37 95% CI 0.15 to 0.59 P = 0.001	○○○	CBT
[35] Systematic review	99 people with tinnitus Data from 1 RCT	**Mood (assessed using the Hospital Anxiety and Depression Scale)** with CBT with waiting list Absolute results not reported	Effect size 0.47 95% CI 0 to 0.9	⟷	Not significant
[35] Systematic review	112 people with tinnitus Data from 1 RCT	**Mood (assessed using General Depression Scale)** with CBT with waiting list Absolute results not reported	Effect size 0.34 95% CI –0.1 to +0.8	⟷	Not significant
[37] RCT	492 people with tinnitus	**Negative affect (assessed using Hospital and Anxiety Depression Scale) , 12 months** with CBT with usual care Absolute results not reported	Difference –1.507 99% CI –2.867 to –0.148 P = 0.004 The review found similar significant results between groups at 8 months		CBT
Quality of life					
[36] Systematic review	146 people 3 RCTs in this analysis	**Quality-of-life scores** with CBT with alternative intervention (yoga, education, minimal contact-education) Absolute results not reported	SMD 0.64 95% CI 0.29 to 1.00 P <0.0004	○○○	CBT

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
[36] Systematic review	309 people 5 RCTs in this analysis	**Quality-of-life scores** with CBT with waiting-list control Absolute results not reported	SMD 0.91 95% CI 0.50 to 1.32 P <0.0001	○○○	CBT
[37] RCT	492 people with tinnitus	**Health-related quality of life (assessed using the Health Utilities Index) , 12 months** with CBT with usual care Absolute results not reported	Difference 0.059 95% CI 0.025 to 0.094 P = 0.001 The review found similar significant results between groups at 8 months		CBT
Tinnitus annoyance					
[34] Systematic review	269 people 8 RCTs in this analysis	**Reduction in subjective tinnitus annoyance , 3 months or more post treatment** with CBT (combination of different psychotherapeutic approaches) with placebo Absolute results not reported	SMD 0.83 95% CI 0.82 to 0.84 The review had important flaws in its methods, compromising its validity (see Further information on studies for more details)	○○○	CBT
[35] Systematic review	99 people with tinnitus Data from 1 RCT	**Tinnitus distress (assessed using the Tinnitus Handicap Inventory)** with CBT with waiting list Absolute results not reported	Effect size 0.6 95% CI 0.1 to 1.1		CBT
[35] Systematic review	112 people with tinnitus Data from 1 RCT	**Tinnitus distress (assessed using the Tinnitus Questionnaire)** with CBT with waiting list Absolute results not reported	Effect size 0.74 95% CI 0.3 to 1.2		CBT

Resolution of tinnitus

No data from the following reference on this outcome. [34] [35] [36] [37]

Adverse effects

No data from the following reference on this outcome. [34] [35] [36] [37]

Acceptance and commitment therapy (ACT) versus waiting-list control:

We found two systematic reviews (search date 2009; [35] search date 2012 [4]), which assessed the effects of different psychotherapeutic approaches. The methods of the second review [4] were unclear, therefore, the review has not been reported further here.

Improvement in tinnitus

No data from the following reference on this outcome. [35]

Impact of tinnitus on quality of life

ACT compared with waiting-list control We don't know whether ACT is more effective than waiting-list control at improving depression or tinnitus annoyance in people with tinnitus as we were unable to draw robust conclusions (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Depression					
[35] Systematic review	99 people with tinnitus Data from 1 RCT	**Mood (assessed using the Hospital Anxiety and Depression Scale)** with ACT with waiting-list control Absolute results not reported	Effect size 0.61 95% CI 0.7 to 1.7		ACT
Tinnitus annoyance					
[35] Systematic review	99 people with tinnitus Data from 1 RCT	**Tinnitus distress** with ACT with waiting-list control Absolute results not reported	Effect size is 1.20 95% CI 0.7 to 1.7		ACT

Resolution of tinnitus

No data from the following reference on this outcome. [35]

Adverse effects

No data from the following reference on this outcome. [35]

Further information on studies

[34] The review pooled study results across arms of trials, losing the benefits of randomisation and increasing the risk of bias. In addition, pre-treatment to post-treatment effect sizes do not allow comparison of psychotherapy with no treatment or any other treatment. The review also did not report which interventions were used as controls in the RCTs.

Comment: Despite many studies on psychotherapeutic measures to treat tinnitus, the evidence for benefit remains limited. Many of the RCTs suffer from less reliable methods, high withdrawal rates, and pooled or surrogate outcome measures. The revised Cochrane meta-analysis on CBT [36] resulted in the authors changing their conclusions. While there remains no evidence of an effect of CBT in the improvement of subjective loudness of tinnitus, it does now seem effective for improving de-

pression associated with tinnitus compared with placebo (in addition to its effectiveness in improving overall quality of life compared with placebo or an alternative intervention).

OPTION TINNITUS-MASKING DEVICES

- For GRADE evaluation of interventions for Tinnitus, see table, p 31 .
- We don't know whether tinnitus-masking devices are more effective than placebo in people with tinnitus.

Benefits and harms

Tinnitus-masking devices versus placebo:

We found one systematic review (search date 1998, 2 RCTs). [38] One RCT was of insufficient quality to include in this review: the RCT had a high withdrawal rate (67%) and was unblinded. [39]

Improvement in tinnitus

Tinnitus-masking device compared with placebo We don't know whether tinnitus-masking devices are more effective at reducing the severity of tinnitus (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Overall symptoms (other than loudness) of tinnitus					
[40] RCT **Crossover design**	21 people In review [38]	**Proportion of people with a significant improvement from baseline in intensity of tinnitus symptoms (assessed using tinnitus intensity rating [scale of 0–10])** 7/17 (41%) with tinnitus-masking device 5/17 (29%) with placebo	Significance not assessed Reported results were post-crossover; post-crossover results are difficult to interpret because of the possibility of a persistence of treatment effect after crossover Data were omitted for 4/21 (19%) people for inadequate use of the tinnitus rating scale		

Resolution of tinnitus

No data from the following reference on this outcome. [40]

Impact of tinnitus on quality of life

No data from the following reference on this outcome. [40]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[40] RCT **Crossover design**	21 people In review [38]	**Adverse effects** with tinnitus-masking device with placebo The RCT found that 2/21 (10%) people reported worsened tinnitus with a masking device			

Comment: None.

OPTION COGNITIVE BEHAVIOURAL THERAPY (CBT) PLUS TINNITUS-MASKING DEVICE (TINNITUS RETRAINING THERAPY)

- For GRADE evaluation of interventions for Tinnitus, see table, p 31 .
- We don't know whether CBT plus a tinnitus-masking device (tinnitus retraining therapy) is more effective than waiting-list control at improving depression or tinnitus annoyance in people with tinnitus.

Benefits and harms

CBT plus a tinnitus-masking device versus waiting-list control:

We found two systematic review (search date 2009; [35] search date 2012 [4]) comparing CBT plus a tinnitus-masking device with waiting-list control. The methods of the second review [4] were unclear, therefore, it has not been reported here further.

Improvement in tinnitus

No data from the following reference on this outcome. [35]

Impact on quality of life

CBT plus tinnitus-masking device versus waiting-list control We don't know whether CBT plus a tinnitus-masking device is more effective than waiting-list control at improving depression or tinnitus annoyance in people with tinnitus (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Depression					
[35] Systematic review	90 people with tinnitus Data from 1 RCT	**Mood (assessed using the General Depression Scale)** with enhanced psychological CBT plus tinnitus-masking device with waiting list Absolute results not reported	Effect size 0.42 95% CI 0 to 0.5	⟷	Not significant
Tinnitus annoyance					
[35] Systematic review	90 people with tinnitus Data from 1 RCT	**Tinnitus distress (assessed using the Tinnitus Questionnaire)** with enhanced psychological CBT plus tinnitus-masking device with waiting list Absolute results not reported	Effect size 0.55 95% CI 0.1 to 1.0		CBT plus tinnitus masking device

Resolution of tinnitus

No data from the following reference on this outcome. [35]

Adverse effects

No data from the following reference on this outcome. [35]

Comment: None.

OPTION CARBAMAZEPINE

- For GRADE evaluation of interventions for Tinnitus, see table, p 31 .
- We don't know whether carbamazepine is more effective than placebo at reducing the severity of tinnitus, and is associated with adverse effects such as dizziness, nausea, and headache.

Benefits and harms

Carbamazepine versus placebo:

We found two systematic reviews (search date 1998; [38] search date 2010 [41]), which both identified one RCT [42] comparing carbamazepine with placebo in people with tinnitus.

Improvement in tinnitus

Carbamazepine compared with placebo We don't know whether carbamazepine is more effective than placebo at reducing the severity of tinnitus (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Overall symptoms of tinnitus					
[41] Systematic review	48 people with 'annoying tinnitus' Data from 1 RCT	**Near or total eradication of tinnitus , 30 days** 2/24 (8%) with carbamazepine 3/24 (13%) with placebo	RD –0.04 95% CI –0.21 to +0.13 P value not reported	⟷	Not significant

Resolution of tinnitus

No data from the following reference on this outcome. [41]

Impact of tinnitus on quality of life

No data from the following reference on this outcome. [41]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[42] RCT	48 people with 'annoying tinnitus' In review [38]	**Proportion of people with dizziness , 30 days** 8/24 (33%) with carbamazepine 0/24 (0%) with placebo In the carbamazepine group, 10 people (40%) withdrew from the trial because of adverse effects; the RCT did not report on withdrawals in the placebo group	Significance not assessed		
[42] RCT	48 people with 'annoying tinnitus' In review [38]	**Proportion of people with nausea , 30 days** 8/24 (33%) with carbamazepine 0/24 (0%) with placebo In the carbamazepine group, 10 people (40%) withdrew from the trial because of adverse effects; the RCT did not report on withdrawals in the placebo group	Significance not assessed		
[42] RCT	48 people with 'annoying tinnitus' In review [38]	**Proportion of people with headache , 30 days** 4/24 (17%) with carbamazepine 1/24 (4%) with placebo In the carbamazepine group, 10 people (40%) withdrew from the trial because of adverse effects; the RCT did not report on withdrawals in the placebo group	Significance not assessed		
[42] RCT	48 people with 'annoying tinnitus' In review [38]	**Proportion of people reporting tiredness , 30 days** 2/24 (8%) with carbamazepine 0/24 (0%) with placebo In the carbamazepine group, 10 people (40%) withdrew from the trial because of adverse effects; the RCT did not report on withdrawals in the placebo group	Significance not assessed		
[42] RCT	48 people with 'annoying tinnitus' In review [38]	**Proportion of people with vomiting , 30 days** 2/24 (8%) with carbamazepine 0/24 (0%) with placebo In the carbamazepine group, 10 people (40%) withdrew from the trial because of adverse effects; the RCT did not report on withdrawals in the placebo group	Significance not assessed		
[42] RCT	48 people with 'annoying tinnitus' In review [38]	**Proportion of people with diarrhoea , 30 days** 1/24 (4%) with carbamazepine 0/24 (0%) with placebo In the carbamazepine group, 10 people (40%) withdrew from the trial because of adverse effects; the RCT did not report on withdrawals in the placebo group	Significance not assessed		

Further information on studies

Comment: None.

GLOSSARY

Tinnitus Handicap Inventory A questionnaire assessing the impact of tinnitus on the subject's quality of life.

Tinnitus retraining therapy A combination of cognitive behavioural therapy and tinnitus masking, highly tailored to individual people.

Low-quality evidence Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Masking device A small device similar to a behind-the-ear hearing aid that produces a broad frequency noise. It is thought to hide the noise of the tinnitus.

Menière's disease A condition characterised by episodic vertigo, tinnitus, and sensorineural hearing loss.

Presbycusis Age-related hearing loss.

Very low-quality evidence Any estimate of effect is very uncertain.

SUBSTANTIVE CHANGES

Acamprosate One systematic review [4] and one RCT added. [5] Categorisation unchanged (unknown effectiveness).

Acupuncture One systematic review added, [7] and one additional RCT. [8] Categorisation unchanged (unknown effectiveness).

Antidepressant drugs One review updated, [10] and two reviews added. [4] [9] Categorisation unchanged (unknown effectiveness), as there remains insufficient evidence to judge the effectiveness of this intervention.

Benzodiazepines One systematic review added. [4] Categorisation unchanged (unknown effectiveness).

CBT plus tinnitus-masking device Two systematic reviews added. [4] [35] Categorisation unchanged (unknown effectiveness).

Carbamazepine One new systematic review added. [41] Categorisation unchanged (likely to be ineffective or harmful).

Electromagnetic stimulation Three new reviews added. [4] [22] [23] Categorisation unchanged (unknown effectiveness).

Psychotherapy Two systematic reviews added. [4] [35] Categorisation unchanged (unknown effectiveness).

Ginkgo biloba One review updated, [26] one review added. [27] Categorisation changed from unknown effectiveness to unlikely to be beneficial.

REFERENCES

1. Coles RR. Epidemiology of tinnitus: (1) prevalence. *J Laryngol Otol* 1984;9(suppl):7–15.[PubMed]
2. Sullivan MD, Katon W, Dobie R, et al. Disabling tinnitus: association with affective disorder. *Gen Hosp Psychiatry* 1988;10:285–291.[PubMed]
3. Zoger S, Svedlund J, Holgers KM. Psychiatric disorders in tinnitus patients without severe hearing impairment: 24 month follow-up of patients at an audiological clinic. *Audiology* 2001;40:133–140.[PubMed]
4. Pichora-Fuller MK, Santaguida P, Hammill A, et al; Agency for Healthcare Research and Quality. Evaluation and treatment of tinnitus: comparative effectiveness. August 2013. Available at http://effectivehealthcare.ahrq.gov/search-for-guides-reviews-and-reports/?pageaction=displayproduct&productid=1650 (accessed on 25 July 2014).[PubMed]
5. Sharma DK, Kaur S, Singh J, et al. Role of acamprosate in sensorineural tinnitus. *Ind J Pharmacol* 2012;44:93–96.[PubMed]
6. Azevedo AA, Figueiredo RR. Tinnitus treatment with acamprosate: double-blind study. *Rev Bras Otorhinolaringol* 2005;71:618–623.
7. Kim JI, Choi JY, Lee DH, et al. Acupuncture for the treatment of tinnitus: a systematic review of randomized clinical trials. *BMC Complement Altern Med* 2012;12:97. Search date 2012.[PubMed]
8. Rogha M, Rezvani M, Khodami AR. The effects of acupuncture on the inner ear originated tinnitus. *J Res Med Sci* 2011;16:1217–1223.[PubMed]
9. Hoare DJ, Kowalkowski VL, Kang S, et al. Systematic review and meta-analyses of randomized controlled trials examining tinnitus management. Laryngoscope 2011;121:1555–1564. Search date 2010.[PubMed]
10. Baldo P, Doree C, Molin P, et al. Antidepressants for patients with tinnitus. In: The Cochrane Library, Issue 11; 2013. Chichester, UK: John Wiley & Sons, Ltd. Search date 2012.[PubMed]
11. Sullivan M, Katon W, Russo J, et al. A randomised trial of nortriptyline for severe chronic tinnitus. *Arch Intern Med* 1993;153:2251–2259.[PubMed]
12. Bayar N, Boke B, Turan E, et al. Efficacy of amitriptyline in the treatment of subjective tinnitus. *J Otolaryngol* 2001;30:300–303.[PubMed]
13. Mihail RC, Crowley JM, Walden BE, et al. The tricyclic trimipramine in the treatment of subjective tinnitus. *Ann Otolo Rhinol Laryngol* 1988;97:120–123.[PubMed]
14. Podoshin L, Ben-David Y, Fradis M, et al. Idiopathic subjective tinnitus treated by amitryptiline hydrochloride/biofeedback. *Int Tinnitus J* 1995;1:54–60.[PubMed]
15. Robinson SK, Viirre ES, Bailey KA, et al. Randomised placebo-controlled trial of a selective serotonin reuptake inhibitor in the treatment of nondepressed tinnitus subjects. *Psychosom Med* 2005;67:981–988.[PubMed]
16. Zoger S, Svedlund J, Holgers KM. The effects of sertraline on severe tinnitus suffering - a randomized, double-blind, placebo-controlled study. *J Clin Psychopharmacol* 2006;26:32–39.[PubMed]
17. Holgers KM, Zoger S, Svedlund J. The impact of sertraline on health-related quality of life in severe refractory tinnitus: a double-blind, randomized, placebo-controlled study. *Audiol Med* 2011;9:67–72.
18. Dib GC, Kasse CA, ves de Andrade T, et al. Tinnitus treatment with Trazodone. *Brasileira J Otorrinolaringologia* 2007;73:390–397.[PubMed]

19. Schilter B, Jager B, Heerman R, et al. Pharmacological and psychological treatment options in chronic subjective tinnitus: a meta-analysis of effective treatments. *HNO* 2000;48:589–597. Search date 1995.[PubMed]
20. Johnson RM, Brummett R, Schleuning A. Use of alprazolam for relief of tinnitus. A double-blind study. *Arch Otolaryngol Head Neck Surg* 1993;119:842–845.[PubMed]
21. Jalali MM, Kousha A, Naghavi SE, et al. The effects of alprazolam on tinnitus: a cross-over randomized clinical trial. *Med Sci Monit* 2009;15:I55–I60.[PubMed]
22. Meng Z, Liu S, Zheng Y, et al. Repetitive transcranial magnetic stimulation for tinnitus. In: The Cochrane Library, Issue 11, 2013. Chichester, UK: John Wiley & Sons, Ltd. Search date May 2011.[PubMed]
23. Peng Z, Chen XQ, Gong SS. Effectiveness of repetitive transcranial magnetic stimulation for chronic tinnitus: a systematic review. *Otolaryngol Head Neck Surg* (US) 2012;147:817–825. Search date 2012.[PubMed]
24. Dobie RA, Hoberg KE, Rees TS. Electrical tinnitus suppression: a double-blind crossover study. *Otolaryngol Head Neck Surg* 1986;95:319–333. [PubMed]
25. Roland NJ, Hughes JB, Daley MB, et al. Electromagnetic stimulation as a treatment of tinnitus: a pilot study. *Clin Otolaryngol* 1993;18:278–281.[PubMed]
26. Hilton M, Zimmerman EF, Hunt WT. Ginkgo biloba for tinnitus. In: The Cochrane Library, Issue 11, 2013. Chichester, UK: John Wiley & Sons, Ltd. Search date 2012.[PubMed]
27. von Boetticher A. Ginkgo biloba extract in the treatment of tinnitus: a systematic review. *Neuropsychiatr Dis Treat* 2011;7:441–447. Search date 2012.[PubMed]
28. Morgenstern C, Biermann E. Long-term treatment of tinnitus with the special gingko extract, Egb 761. *Fortschr Med* 1997;115:57–58. [In German]
29. Drew S, Davies E. Effectiveness of ginkgo biloba in treating tinnitus: double blind, placebo controlled trial. *BMJ* 2001;322:73–75.[PubMed]
30. Rejali D, Sivakumar A, Balaji N. Ginkgo biloba does not benefit patients with tinnitus: a randomized placebo-controlled double-blind trial and meta-analysis of randomized trials. *Clin Otolaryngol Allied Sci* 2004;29:226–231.[PubMed]
31. Meyer B. A multicentre, randomized, double-blind drug versus placebo study of Ginkgo biloba extract in the tratment of tinnitus. *Presse Med* 1986;15:1562–1564. [In French][PubMed]
32. Melin L, Scott B, Lindberg P, et al. Hearing aids and tinnitus – an experimental group study. *Br J Audiol* 1987;21:91–97.[PubMed]
33. Mason JD, Rogerson DR, Butler JD. Client centred hypnotherapy in the management of tinnitus — is it better than counselling? *J Laryngol Otol* 1996;110:117–120.[PubMed]
34. Andersson G, Lyttkens L. A meta-analytic review of psychological treatments for tinnitus. *Br J Audiol* 1999;33:201–210. Search date 1998.[PubMed]
35. Hesser H, Weise C, Westin VZ, et al. A systematic review and meta-analysis of randomized controlled trials of cognitive-behavioral therapy for tinnitus distress. *Clin Psychol Rev* 2011;31:545–553. Search date 2009.[PubMed]
36. Martinez Devesa P, Waddell A, Perera R, et al. Cognitive behavioural therapy for tinnitus. In: The Cochrane Library, Issue 11, 2013. Chichester, UK: John Wiley & Sons, Ltd. Search date 2010.[PubMed]
37. Cima RF, Maes IH, Joore MA, et al. Specialised treatment based on cognitive behaviour therapy versus usual care for tinnitus: a randomised controlled trial. *Lancet* 2012;379:1951–1959.[PubMed]
38. Dobie RA. A review of randomized clinical trials in tinnitus. *Laryngoscope* 1999;109:1202–1211. Search date 1998.[PubMed]
39. Stephens SDG, Corcoran AL. A controlled study of tinnitus masking. *Br J Audiol* 1985;19:159–167.[PubMed]
40. Erlandsson S, Ringdahl A, Hutchins T, et al. Treatment of tinnitus: a controlled comparison of masking and placebo. *Br J Audiol* 1987;21:37–44.[PubMed]
41. Hoekstra CEL, Rynja SP, van Zanten GA, et al. Anticonvulsants for tinnitus. In: The Cochrane Library, Issue 11, 2013. Chichester, UK: John Wiley & Sons, Ltd. Search date 2010.[PubMed]
42. Hulshof JH, Vermeij P. The value of carbamazepine in the treatment of tinnitus. *ORL J Otorhinolaryngol Relat Spec* 1985;47:262–266.[PubMed]

Julian Savage
Assistant Professor
Université de Sherbrooke
Québec
Canada

Angus Waddell
Consultant Otolaryngologist
Great Western Hospital
Swindon
UK

Competing interests: JS and AW declare that they have no competing interests.
JS and AW would like to acknowledge Stephanie Cook, the previous contributor of this review.

Disclaimer

GRADE **Evaluation of interventions for Tinnitus.**

Important outcomes	Impact of tinnitus on quality of life, Impact on quality of life, Improvement in tinnitus, Resolution of tinnitus								
Studies (Participants)	Outcome	Comparison	Type of evidence	Quality	Consistency	Directness	Effect size	GRADE	Comment
What are the effects of treatments for chronic tinnitus?									
2 (90) [5] [6]	Improvement in tinnitus	Acamprosate versus placebo	4	–2	0	–1	0	Very low	Quality points deducted for sparse data and no intention-to-treat analysis; directness point deducted for no statistical analysis between groups in one RCT
1 (40) [5]	Impact of tinnitus on quality of life	Acamprosate versus placebo	4	–2	0	0	0	Low	Quality points deducted for sparse data and incomplete reporting of results
6 (222) [7] [8]	Improvement in tinnitus	Acupuncture versus sham acupuncture	4	–1	–1	0	0	Low	Quality points deducted for incomplete reporting of results; consistency point deducted for conflicting results
2 (104) [7]	Impact of tinnitus on quality of life	Acupuncture versus sham acupuncture	4	–2	0	0	0	Low	Quality points deducted for sparse data and incomplete reporting of results
4 (278) [12] [13] [14] [11]	Improvement in tinnitus	Tricyclic antidepressants (TCAs) versus placebo	4	–1	0	–1	0	Low	Quality point deducted for incomplete reporting of results; directness point deducted for no statistical analysis between groups in one RCT
1 (117) [11]	Impact of tinnitus on quality of life	Tricyclic antidepressants (TCAs) versus placebo	4	–2	0	0	0	Low	Quality points deducted for sparse data and incomplete reporting of results
2 (196) [15] [16]	Improvement in tinnitus	Seretonin selective re-uptake inhibitors (SSRIs) versus placebo	4	–1	0	–1	0	Low	Quality point deducted for sparse data; directness point deducted for inclusion of a co-intervention in 1 RCT (oxazepam)
1 (76) [16]	Impact of tinnitus on quality of life	Seretonin selective re-uptake inhibitors (SSRIs) versus placebo	4	–2	0	–1	0	Very low	Quality points deducted for sparse data and RCT being underpowered to detect a clinically meaningful difference between groups; directness point deducted for inclusion of a co-intervention (oxazepam)
1 (85)	Improvement in tinnitus	Serotonin antagonist and reupdate inhibitor (SARI) versus placebo	4	–2	0	0	0	Low	Quality points deducted for sparse data and incomplete reporting of results
1 (85) [10]	Impact of tinnitus on quality of life	Serotonin antagonist and reupdate inhibitor (SARI) versus placebo	4	–2	0	0	0	Low	Quality points deducted for sparse data and incomplete reporting of results
2 (70) [20] [21]	Improvement in tinnitus	Benzodiazepines versus placebo	4	–3	0	–1	0	Very low	Quality points deducted for sparse data, incomplete reporting of results, and flaws with blinding in 1 RCT; directness point deducted for lack of inert placebo in crossover RCT
5 (271) [22] [23] [24]	Improvement in tinnitus	Electromagnetic stimulation versus placebo	4	–2	–1	0	0	Very low	Quality points deducted for incomplete reporting of results, and other methodological flaws; consistency point deducted for conflicting results

Important outcomes	Impact of tinnitus on quality of life, Impact on quality of life, Improvement in tinnitus, Resolution of tinnitus								
Studies (Participants)	Outcome	Comparison	Type of evidence	Quality	Consistency	Directness	Effect size	GRADE	Comment
1 (66) [23]	Impact of tinnitus on quality of life	Electromagnetic stimulation versus placebo	4	–2	0	–1	0	Very low	Quality points deducted for sparse data and incomplete reporting of results; directness point deducted for no statistical analysis between groups
3 (1144) [29] [30] [31]	Improvement in tinnitus	Ginkgo biloba versus placebo	4	–2	–1	0	0	Very low	Quality points deducted for incomplete reporting of results and other methodological flaws; consistency point deducted for conflicting results
1 (100) [31]	Impact of tinnitus on quality of life	Ginkgo biloba versus placebo	4	–2	0	0	0	Low	Quality points deducted for sparse data and incomplete reporting of results
1 (39) [32]	Improvement in tinnitus	Hearing aids versus waiting list control	4	–2	0	0	0	Low	Quality points deducted for sparse data and incomplete reporting of results
1 (92) [33]	Improvement in tinnitus	Hypnosis versus counselling	4	–2	0	–1	0	Very low	Quality points deducted for sparse data and incomplete reporting of results; directness point deducted for inclusion of only those who were suggestible to hypnosis
19 (1279) [34] [35] [36] [37]	Improvement in tinnitus	CBT versus placebo	4	–2	0	0	0	Low	Quality point deducted for methodological flaws of one review and incomplete reporting of results
at least 12 (at least 1158) [34] [35] [36] [37]	Impact of tinnitus on quality of life	CBT versus placebo	4	–2	0	0	0	Low	Quality points deducted for incomplete reporting of results and methodological flaws of one review
1 (99) [35]	Impact of tinnitus on quality of life	Acceptance and commitment therapy (ACT) versus waiting-list control	4	–2	0	0	0	Low	Quality points deducted for sparse data and incomple reporting of results
1 (21) [40]	Improvement in tinnitus	Tinnitus-masking devices versus placebo	4	–3	0	0	0	Very low	Quality points deducted for sparse data, no blinding, incomplete reporting of results, and other methodological flaws (reporting of post-crossover results)
1 (90) [35]	Impact on quality of life	CBT plus a tinnitus-masking device versus waiting-list control	4	–2	0	–1	0	Very low	Quality points deducted for sparse data and incomplete reporting of results; directness point deducted for the addition of CBT in the control group at 10 months
1 (48) [41]	Improvement in tinnitus	Carbamazepine versus placebo	4	–2	0	0	0	Low	Quality points deducted for sparse data and incomplete reporting of results

We initially allocate 4 points to evidence from RCTs, and 2 points to evidence from observational studies. To attain the final GRADE score for a given comparison, points are deducted or added from this initial score based on preset criteria relating to the categories of quality, directness, consistency, and effect size. Quality: based on issues affecting methodological rigour (e.g., incomplete reporting of results, quasi-randomisation, sparse data [<200 people in the analysis]). Consistency: based on similarity of results across studies. Directness: based on generalisability of population or outcomes. Effect size: based on magnitude of effect as measured by statistics such as relative risk, odds ratio, or hazard ratio.