

Tinnitus

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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 July 2011 (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 29 systematic reviews, RCTs, or observational 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, cinnarizine, electromagnetic stimulation, ginkgo biloba, hearing aids, hypnosis, psychotherapy, tinnitus-masking devices, and tinnitus retraining therapy.

QUESTIONS

What are the effects of treatments for chronic tinnitus? 2

INTERVENTIONS

TREATMENTS FOR CHRONIC TINNITUS		
?? Unknown effectiveness		
Acamprosate	2	Hearing aids 17
Acupuncture	3	Hypnosis 18
Antidepressant drugs	5	Psychotherapy 19
Benzodiazepines (alprazolam)	11	Tinnitus retraining therapy 22
Cinnarizine	13	Tinnitus-masking devices 21
Electromagnetic stimulation	14	
Ginkgo biloba	16	⬇️⬇️ Likely to be ineffective or harmful
		Carbamazepine 23

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.
- There is 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.
- **CBT** may be ineffective at reducing tinnitus loudness, but it may improve quality of life in people with tinnitus.
- We don't know whether **benzodiazepines, acupuncture, hypnosis, electromagnetic stimulation, hearing aids, tinnitus-masking devices, tinnitus retraining therapy, cinnarizine, ginkgo biloba, or acamprosate** are effective in people with tinnitus, as we found few studies.
- **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 of treatment**.

METHODS *Clinical Evidence* search and appraisal July 2011. The following databases were used to identify studies for this systematic review: Medline 1966 to July 2011, Embase 1980 to July 2011, and The Cochrane Database of Systematic Reviews 2011, Issue 2 (1966 to date of issue). An additional search within The Cochrane Library was carried out for the Database of Abstracts of Reviews of Effects (DARE) and Health Technology Assessment (HTA). We also searched for retractions of studies included in the review. Abstracts of the studies retrieved from the initial search were assessed by an information specialist. Selected studies were then sent to the contributor for additional assessment, using predetermined criteria to identify relevant studies. Study design criteria for inclusion in this review were: published systematic reviews of RCTs and RCTs in any language, at least single blinded, and containing >20 individuals of whom >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 systematic reviews of RCTs and RCTs where harms of an included intervention were studied applying the same study design criteria for inclusion as we did for benefits. In addition we did an observational harms search for specific harms as highlighted by the contributor, peer reviewer, and editor. 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 27). 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 27 .
- We don't know whether acamprosate is effective in people with tinnitus, as we found few studies.

Benefits and harms

Acamprosate versus placebo:

We found one RCT.^[4]

Improvement in tinnitus

Compared with placebo Acamprosate may reduce the severity of tinnitus after 3 months, although the improvement may not be clinically important (*low-quality evidence*).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Overall symptoms of tinnitus					
[4] RCT	50 people with subjective tinnitus	<p>Proportion of people with improvement in tinnitus (measured on a tinnitus score [scale of 0–10; increasing score is associated with increasing disturbance from tinnitus]) , 3 months</p> <p>87% with acamprosate 333 mg three times daily</p> <p>44% with placebo</p> <p>Absolute numbers not reported</p>	<p>P = 0.0004</p> <p>It is unclear whether the difference in scores reflects a clinically important improvement in tinnitus</p> <p>People who withdrew from the RCT were not included in the data analysis, which would have affected the results</p>	○ ○ ○	acamprosate

Resolution of tinnitus

No data from the following reference on this outcome. [4]

Impact of tinnitus on quality of life

No data from the following reference on this outcome. [4]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[4] RCT	50 people with subjective tinnitus	<p>Proportion of people with an adverse effect , 3 months</p> <p>12% with acamprosate 333 mg three times daily</p> <p>20% with placebo</p> <p>Absolute numbers not reported</p> <p>The RCT reported mild adverse effects with acamprosate, including epigastralgia, choking, and depression</p>	<p>P = 0.35</p> <p>People who dropped out of the RCT were not included in the data analysis, which would have affected the results</p>	↔	Not significant

Further information on studies

Comment: None.

OPTION ACUPUNCTURE

- For GRADE evaluation of interventions for Tinnitus, see table, p 27 .

- We don't know whether acupuncture is effective in people with tinnitus, as we found few studies.

Benefits and harms

Acupuncture versus sham acupuncture:

We found one systematic review (search date 1998, 6 studies, 185 people).^[5] The review included one quasi-randomised RCT,^[6] two open RCTs,^[7] ^[8] two crossover RCTs,^[9] ^[10] and one blinded RCT.^[11] All studies were small and brief.

Improvement in tinnitus

Compared with sham acupuncture We don't know whether acupuncture is more effective at reducing the severity of tinnitus at 3 weeks to 2 months ([very low-quality evidence](#)).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Tinnitus loudness					
^[11] RCT	54 people In review ^[5]	Change in mean tinnitus loudness score (assessed using a pooled visual analogue score; change from baseline) From 78.5 to 74.1 with acupuncture (25 sessions of 30 minutes over 2 months) From 76.5 to 77.5 with sham acupuncture (superficial penetration at random, non-acupuncture points)	Reported as not significant P value not reported	↔	Not significant
Overall symptoms of tinnitus					
^[9] RCT Crossover design	14 people In review ^[5]	Proportion of people with subjective improvement in tinnitus (measured by verbal description, tinnitus matching, and visual analogue scale for tinnitus loudness) , after 1 session of treatment 5/14 (36%) with acupuncture 0/14 (0%) with sham acupuncture	P <0.05	○○○	acupuncture
^[10] RCT Crossover design	20 people In review ^[5]	Improvement in subjective tinnitus severity (measured using a pooled visual analogue score) , 3 weeks with acupuncture with placebo Absolute results not reported	P = 0.22	↔	Not significant
^[11] RCT	54 people In review ^[5]	Change in mean tinnitus awareness (assessed using a pooled visual analogue score; change from baseline) From 69.2 to 64.5 with acupuncture (25 sessions of 30 minutes over 2 months) From 65.1 to 66.5 with sham acupuncture (superficial penetration at random, non-acupuncture points)	Reported as not significant P value not reported	↔	Not significant

Impact of tinnitus on quality of life

Compared with sham acupuncture We don't know whether acupuncture is more effective at reducing annoyance as a result of tinnitus ([low-quality evidence](#)).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Annoyance					
[11] RCT	54 people In review [5]	Change in mean tinnitus annoyance score (assessed using a pooled visual analogue score; change from baseline) From 64.5 to 62.0 with acupuncture (25 sessions of 30 minutes over 2 months) From 67.1 to 67.0 with sham acupuncture (superficial penetration at random, non-acupuncture points)	Reported as not significant P value not reported	↔	Not significant

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

Resolution of tinnitus

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

Adverse effects

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

Further information on studies

Comment: None.

OPTION ANTIDEPRESSANT DRUGS

- For GRADE evaluation of interventions for Tinnitus, [see table, p 27](#).
- There is insufficient evidence to show that antidepressant drugs improve tinnitus symptoms.
- Antidepressant drugs can improve depression in people with tinnitus.
- 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 one systematic review^[12] (search date 2008, 4 RCTs, [13] [14] [15] [16]) comparing TCAs versus placebo. No meta-analysis was performed.

Improvement in tinnitus

Compared with placebo Tricyclic antidepressants seem no more effective at reducing the severity of tinnitus after 6 weeks ([moderate-quality evidence](#)).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Tinnitus loudness					
[14] RCT Crossover design	26 people In review [12]	Improvement in subjective tinnitus loudness (mean subjective rating on a scale of 1–7), 6 weeks 4.3 with trimipramine (150 mg/day for 6 weeks) 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
[15] RCT 4-armed trial	225 people In review [12] The third and fourth arms assessed the effects of biofeedback and placebo biofeedback	Proportion of people with improvement in subjective tinnitus loudness at rest 28% with amitriptyline (10 mg three times a day for 10 weeks) 5% with placebo Absolute numbers not reported 123 people in this analysis (83 people in amitriptyline group and 40 people in placebo group)	P <0.011 (as reported in RCT) The review reported that results were presented as percentages, and further analysis is not possible [12]	○○○	amitriptyline
Overall symptoms of tinnitus					
[13] RCT	37 people with no history of depression In review [12]	Proportion of people with a decrease in subjective tinnitus, 6 weeks 19/20 (95%) with amitriptyline (50 mg/night for 1 week followed by 100 mg/night for 5 weeks) 2/17 (12%) with placebo	Statistical analysis between groups not reported		
[14] RCT Crossover design	26 people In review [12]	Proportion of people with worsening of tinnitus (mean subjective rating on a scale of 1–7), 6 weeks 7/19 (37%) with trimipramine (150 mg/day for 6 weeks) 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		
[16] RCT	117 people; results are reported for the 92 people who completed the follow-up period In review [12]	Proportion of people reporting overall improvement in tinnitus severity (measured by asking "Has your tinnitus improved?"), 6 weeks with nortriptyline (titrated to maintain therapeutic blood levels for depression) with placebo Absolute numbers not reported	Reported as not significant P value not reported	↔	Not significant

Impact of tinnitus on quality of life

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

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Depression					
[16] RCT	117 people; results are reported for the 92 people who completed the follow-up period In review [12]	Hamilton Depression Rating Scale score , 6 weeks 11 with nortriptyline (titrated to maintain therapeutic blood levels for depression) 14 with placebo	P = 0.0001	○○○	nortriptyline
[16] RCT	117 people; results are reported for the 92 people who completed the follow-up period In review [12]	Proportion of people reporting global satisfaction (measured by asking "Has the medication helped you in any way?") , 6 weeks 33/49 (67%) with nortriptyline (titrated to maintain therapeutic blood levels for depression) 17/43 (40%) with placebo	P <0.01	○○○	nortriptyline

No data from the following reference on this outcome. [13] [14] [15]

Resolution of tinnitus

No data from the following reference on this outcome. [13] [14] [15] [16]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[13] RCT	37 people with no history of depression In review [12]	Adverse effects with amitriptyline (50 mg/night for 1 week followed by 100 mg/night for 5 weeks) 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 (see harms of antidepressants in the Depression in adults: drug and physical treatments review)	Statistical analysis between groups not reported		

No data from the following reference on this outcome. [14] [15] [16]

SSRIs versus placebo:

We found one systematic review (search date 2008, 1 RCT, [17] 120 people), [12] one additional RCT, [18] and one subsequent RCT [19] comparing SSRIs versus placebo.

Improvement in tinnitus

Compared with placebo We don't know whether SSRIs are more effective at reducing the symptoms of tinnitus after 14 to 16 weeks (*low-quality evidence*).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Tinnitus loudness					
[17] RCT	120 people In review [12]	Improvement in average pure tone 1.8 dB with paroxetine (10 mg/day, increased to maximum 50 mg/day for 100 days) 0.8 dB with placebo	P > 0.05		Not significant
[18] 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; higher score denotes louder levels of tinnitus), 16 weeks 15.21 with sertraline (25 mg/day for 1 week followed by 50 mg/day for 15 weeks) 3.21 with placebo People in both groups were also offered oxazepam 10 mg 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					
[18] 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; higher scores denote more severe tinnitus), 16 weeks 4.69 with sertraline (25 mg/day for 1 week followed by 50 mg/day for 15 weeks) 2.12 with placebo People in both groups were also offered oxazepam 10 mg 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. [19]

Impact of tinnitus on quality of life

Compared with placebo We don't know whether SSRIs are more effective at reducing annoyance, anxiety, and depression at 16 weeks in people with tinnitus (*very low-quality evidence*).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
General well-being					
[19] RCT	75 people with tinnitus, considered to be at high risk of developing severe and disabling tinnitus Further report of reference [18]	Change in Psychological General Well-Being Index (PGWB) , 16 weeks +20.83 with sertraline 50 mg daily +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 50 mg daily
Annoyance					
[18] 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; higher score denotes higher level of annoyance) , 16 weeks 15.76 with sertraline (25 mg/day for 1 week followed by 50 mg/day for 15 weeks) 5.15 with placebo People in both groups were also offered oxazepam 10 mg 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					
[18] 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; higher score denotes higher level of anxiety) , 16 weeks 8.51 with sertraline (25 mg/day for 1 week followed by 50 mg/day for 15 weeks) 4.09 with placebo People in both groups were also offered oxazepam 10 mg 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
[18] 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; higher score denotes higher level of anxiety) , 16 weeks 4.38 with sertraline (25 mg/day for 1 week followed by 50 mg/day for 15 weeks) 0.73 with placebo People in both groups were also offered oxazepam 10 mg during the first 2 weeks to alleviate distress; 3/29 (10%) in the sertraline	P = 0.013 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
		group and 6/34 (18%) in the placebo group accepted oxazepam (significance not assessed)			
Depression					
[18] RCT	76 people with tinnitus, considered to be at high risk of developing severe and disabling tinnitus	<p>Reduction in participant-rated depression score (measured by CPRS-S-A for depression; scale of 0–60; higher score denotes higher level of depression) , 16 weeks</p> <p>5.93 with sertraline (25 mg/day for 1 week followed by 50 mg/day for 15 weeks)</p> <p>0.05 with placebo</p> <p>People in both groups were also offered oxazepam 10 mg 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>	<p>P = 0.002</p> <p>The RCT may have been underpowered to detect a clinically meaningful difference between groups</p>	○ ○ ○ ○	sertraline
[18] RCT	76 people with tinnitus, considered to be at high risk of developing severe and disabling tinnitus	<p>Reduction in clinician-rated depression score (measured by Hamilton Depression Rating Scale; scale 0–62; higher score denotes higher level of depression) , 16 weeks</p> <p>9.79 with sertraline (25 mg/day for 1 week followed by 50 mg/day for 15 weeks)</p> <p>5.87 with placebo</p> <p>People in both groups were also offered oxazepam 10 mg 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>	<p>Reported as not significant</p> <p>P value not reported</p> <p>The RCT may have been underpowered to detect a clinically meaningful difference between groups</p>	↔	Not significant

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

Resolution of tinnitus

No data from the following reference on this outcome. [17] [18] [19]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[18] RCT	76 people with tinnitus, considered to be at high risk of developing severe and disabling tinnitus	<p>Adverse effects , 16 weeks</p> <p>with sertraline (25 mg/day for 1 week followed by 50 mg/day for 15 weeks)</p> <p>with placebo</p> <p>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)</p> <p>People in both groups were also offered oxazepam 10 mg 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>	The RCT may have been under-powered to detect a clinically meaningful difference between groups		

No data from the following reference on this outcome. [12] [17] [19]

Further information on studies

[19] The Psychological General Well-Being Index (PGWB) provides an overall global score from 6 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 10 mg 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 27 .
- We don't know whether benzodiazepines are effective in people with tinnitus, as we found few studies.
- Long-term use of benzodiazepines can lead to dependence.

Benefits and harms

Benzodiazepines versus placebo:

We found one systematic review (search date 1995), [20] which identified one RCT. [21] We found one subsequent RCT. [22]

Improvement in tinnitus

Compared with placebo Benzodiazepines may reduce some measures of tinnitus severity after 8 to 12 weeks (*very low-quality evidence*).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Tinnitus loudness					
[21] RCT	40 people In review [20]	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 (initially 0.5 mg/night) 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		
[22] 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 0.5 mg three times daily (on escalating scale to minimise adverse effects) From 8.4 to 8.4 (0) with placebo Crossover design: two 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					
[22] 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 0.5 mg three times daily (on escalating scale to minimise adverse effects) From 49.6 to 49.2 (–0.4) with placebo Crossover design: two 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
[22] 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 0.5 mg three times daily (on escalating scale to minimise adverse effects) From 70.1 to 68.6 (–1.5) with placebo Crossover design: two 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. ^[21] ^[22]

Impact of tinnitus on quality of life

No data from the following reference on this outcome. ^[21] ^[22]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
^[21] RCT	40 people In review ^[20]	<p>Adverse effects</p> <p>with alprazolam (initially 0.5 mg/night)</p> <p>with placebo</p> <p>The RCT reported that 2 (10%) people receiving alprazolam withdrew from the RCT because of excessive drowsiness</p> <p>Long-term use of benzodiazepines can lead to dependence (see Generalised anxiety disorders review)</p>	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		
^[22] RCT Crossover design	36 people	<p>Proportion of people who withdrew from treatment</p> <p>2 with alprazolam 0.5 mg three times daily (on escalating scale to minimise adverse effects)</p> <p>4 with placebo</p> <p>Long-term use of benzodiazepines can lead to dependence (see Generalised anxiety disorders review)</p> <p>Placebo was chlorpheniramine maleate, used to create a similar sedative effect to alprazolam to aid in the blinding process</p>	Significance not assessed		

Further information on studies

Comment: None.

OPTION CINNARIZINE

- For GRADE evaluation of interventions for Tinnitus, see table, p 27 .

- We don't know whether cinnarizine is effective in people with tinnitus, as we found few studies.

Benefits and harms

Cinnarizine versus placebo:

We found one systematic review (search date 1998), ^[23] which identified one RCT. ^[7]

Improvement in tinnitus

Compared with placebo Cinnarizine may be no more effective at reducing the severity of tinnitus after 10 weeks (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Overall symptoms of tinnitus					
^[7] RCT	30 people In review ^[23]	Proportion of people with subjective improvement of tinnitus (self-reported; severity measured on 5-point scale) , 10 weeks 1/10 (10%) with cinnarizine (25 mg three times/day for 10 weeks) 1/20 (5%) with placebo	Reported as not significant P value not reported The RCT did not specify the follow-up period, and might have lacked power to detect a clinically important effect	↔	Not significant

Resolution of tinnitus

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

Impact of tinnitus on quality of life

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

Adverse effects

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

Further information on studies

Comment: None.

OPTION ELECTROMAGNETIC STIMULATION

- For GRADE evaluation of interventions for Tinnitus, see table, p 27 .
- 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 no systematic review, but found two small RCTs comparing electromagnetic stimulation versus placebo. ^[24] ^[25]

Improvement in tinnitus

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
Overall symptoms of tinnitus					
^[24] RCT	58 people	Proportion of people who had improved tinnitus (assessed using a subjective response assessed by 4-point questionnaire — tinnitus worse, same, improved, or abolished) , 1 week 14/31 (45%) with electromagnetic stimulation (15 minutes/day) 2/23 (9%) with placebo device	P = 0.0013 The RCT reported that 4/58 (7%) people withdrew from the trial, and that the analysis was not by intention to treat	○○○	electromagnetic stimulation
^[25] 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. ^[24] ^[25]

Impact of tinnitus on quality of life

No data from the following reference on this outcome. ^[24] ^[25]

Adverse effects

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

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

Further information on studies

Comment: None.

OPTION	GINKGO BILOBA
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- For GRADE evaluation of interventions for Tinnitus, see table, p 27 .
- We don't know whether ginkgo biloba is effective in people with tinnitus, as we found few RCTs.

Benefits and harms

Ginkgo biloba versus placebo:

We found one systematic review^[26] (search date 2009, 3 RCTs,^[27] ^[28] ^[29] 1143 adults with tinnitus) comparing ginkgo biloba versus placebo. The review 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 two 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.^[27] ^[28]

Improvement in tinnitus

Compared with placebo Ginkgo biloba seems no more effective at reducing the severity of tinnitus after 12 weeks (moderate-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Overall symptoms of tinnitus					
^[29] 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 (120 mg/day) –2.2 with placebo	P = 0.51	↔	Not significant

Resolution of tinnitus

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

Impact of tinnitus on quality of life

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

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
^[29] RCT	66 people In review ^[26]	Proportion of people with diarrhoea , 12 weeks 3% with ginkgo biloba (120 mg/day) 6% with placebo Absolute numbers not reported	Significance not assessed		
^[29] RCT	66 people In review ^[26]	Proportion of people with headache , 12 weeks 3% with ginkgo biloba (120 mg/day) 3% with placebo Absolute numbers not reported	Significance not assessed		

Further information on studies

Comment: None.

OPTION HEARING AIDS

- For GRADE evaluation of interventions for Tinnitus, see table, p 27 .
- 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. ^[30]

Improvement in tinnitus

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 (*low-quality evidence*).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Tinnitus intensity					
^[30] RCT	39 people	Perceived tinnitus intensity (measured on a 10-cm visual analogue scale) , 6 weeks with hearing aid (worn for 6 weeks)	Reported as not significant P value not reported	↔	Not significant

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
		with waiting list control Absolute results not reported			

Resolution of tinnitus

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

Impact of tinnitus on quality of life

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

Adverse effects

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

Further information on studies

Comment: None.

OPTION HYPNOSIS

- For GRADE evaluation of interventions for Tinnitus, [see table, p 27](#) .
- 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) ^[20] and one additional RCT. ^[31] The review found no RCTs that met its inclusion criteria. ^[20]

Improvement in tinnitus

Compared with counselling Self-hypnosis training may be no 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					
^[31] 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)	Reported as not significant P value not reported	↔	Not significant

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
		23/42 (54.8%) with counselling (single session)			
[31] 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. [31]

Impact of tinnitus on quality of life

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

Adverse effects

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

Further information on studies

Comment: None.

OPTION PSYCHOTHERAPY

- For GRADE evaluation of interventions for Tinnitus, see table, p 27 .
- CBT may be ineffective at reducing tinnitus loudness, but it may improve quality of life in people with tinnitus.

Benefits and harms

CBT versus placebo:

We found two systematic reviews. [32] [33] The first review (search date 2010) [32] assessed CBT in patients with tinnitus. The second review (search date 1998) [33] assessed different psychotherapeutic approaches (CBT, relaxation therapy, education/information, biofeedback).

Improvement in tinnitus

Compared with placebo CBT seems no more effective at reducing the severity of tinnitus (*moderate-quality evidence*).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Tinnitus loudness					
[32] 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
[32] 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
[33] 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

Impact of tinnitus on quality of life

Compared with placebo CBT seems more effective at improving quality of life and tinnitus annoyance scores, but we don't know whether it is more effective at improving symptoms of depression ([moderate-quality evidence](#)).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Depression					
[32] 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
[32] 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 = 0.0009	○○○	CBT
Quality of life					
[32] 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
[32] 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

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Tinnitus annoyance					
[33] 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

Resolution of tinnitus

No data from the following reference on this outcome. [32] [33]

Adverse effects

No data from the following reference on this outcome. [32] [33]

Further information on studies

[33] 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 [32] 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 depression 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 27 .
- We don't know whether tinnitus-masking devices are effective in people with tinnitus, as we found few studies.

Benefits and harms

Tinnitus-masking devices versus placebo:

We found one systematic review (search date 1998, 2 RCTs). [23] One RCT was of insufficient quality to include in this review: the RCT had a high withdrawal rate (67%) and was unblinded. [34]

Improvement in tinnitus

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					
^[35] RCT Crossover design	21 people In review ^[23]	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. ^[35]

Impact of tinnitus on quality of life

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

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
^[35] RCT Crossover design	21 people In review ^[23]	Adverse effects with tinnitus-masking device with placebo The RCT found that 2/21 (10%) people reported worsened tinnitus with a masking device			

Further information on studies

Comment: None.

OPTION TINNITUS RETRAINING THERAPY

- For GRADE evaluation of interventions for Tinnitus, [see table, p 27](#) .
- We don't know whether tinnitus retraining therapy is effective in people with tinnitus.

- We found no clinically important results from RCTs about the effects of tinnitus retraining therapy in people with chronic tinnitus.

Benefits and harms

Tinnitus retraining therapy:

We found no systematic review or RCTs of [tinnitus retraining therapy](#) in people with chronic tinnitus.

Further information on studies

Comment: None.

OPTION CARBAMAZEPINE

- For GRADE evaluation of interventions for Tinnitus, [see table, p 27](#) .
- 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.

Benefits and harms

Carbamazepine versus placebo:

We found one systematic review (search date 1998), ^[23] which identified one RCT. ^[36]

Improvement in tinnitus

Compared with placebo Carbamazepine may be no more effective at reducing the severity of tinnitus after 30 days (*low-quality evidence*).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Overall symptoms of tinnitus					
^[36] RCT	48 people with "annoying tinnitus" In review ^[23]	Proportion of people with an improvement in tinnitus severity (assessed by people stating that "tinnitus was no longer annoying") , 30 days 2/24 (8%) with carbamazepine (150 mg three times/day for 30 days) 3/24 (13%) with placebo	Significance not assessed		

Resolution of tinnitus

No data from the following reference on this outcome. ^[36]

Impact of tinnitus on quality of life

No data from the following reference on this outcome. ^[36]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[36] RCT	48 people with "annoying tinnitus" In review [23]	Proportion of people with dizziness , 30 days 8/24 (33%) with carbamazepine (150 mg three times/day for 30 days) 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		
[36] RCT	48 people with "annoying tinnitus" In review [23]	Proportion of people with nausea , 30 days 8/24 (33%) with carbamazepine (150 mg three times/day for 30 days) 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		
[36] RCT	48 people with "annoying tinnitus" In review [23]	Proportion of people with headache , 30 days 4/24 (17%) with carbamazepine (150 mg three times/day for 30 days) 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		
[36] RCT	48 people with "annoying tinnitus" In review [23]	Proportion of people reporting tiredness , 30 days 2/24 (8%) with carbamazepine (150 mg three times/day for 30 days) 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		
[36] RCT	48 people with "annoying tinnitus" In review [23]	Proportion of people with vomiting , 30 days 2/24 (8%) with carbamazepine (150 mg three times/day for 30 days) 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		

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
[36] RCT	48 people with "annoying tinnitus" In review [23]	Proportion of people with diarrhoea , 30 days 1/24 (4%) with carbamazepine (150 mg three times/day for 30 days) 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.

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

Presbycusis Age-related hearing loss.

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

SUBSTANTIVE CHANGES

Antidepressant drugs for tinnitus New evidence added. [19] Categorisation unchanged (Unknown effectiveness), as there remains insufficient evidence to judge the effectiveness of this intervention.

Benzodiazepines New evidence added. [22] Categorisation unchanged (Unknown effectiveness), as there remains insufficient evidence to judge the effectiveness of this intervention.

Ginkgo biloba One systematic review updated, [26] no new data added. Categorisation unchanged (Unknown effectiveness), as there remains insufficient evidence to judge the effectiveness of this intervention.

Psychotherapy One Cochrane systematic review updated, new data added. [32] Categorisation unchanged (Unknown effectiveness), as there remains insufficient evidence to judge the effectiveness of this intervention.

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GRADE Evaluation of interventions for Tinnitus.

Important outcomes	Impact of tinnitus on quality of life, Improvement in tinnitus, Resolution of tinnitus									
	Studies (Participants)	Outcome	Comparison	Type of evidence	Quality	Consistency	Directness	Effect size	GRADE	Comment
<i>What are the effects of treatments for chronic tinnitus?</i>										
	1 (50) ^[4]	Improvement in tinnitus	Acamprosate versus placebo	4	-2	0	0	0	Low	Quality points deducted for sparse data and no intention-to-treat analysis
	3 (122) ^{[9] [10] [11]}	Improvement in tinnitus	Acupuncture versus sham acupuncture	4	-2	-1	0	0	Very low	Quality points deducted for sparse data and incomplete reporting of results. Consistency point deducted for conflicting results
	1 (54) ^[11]	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 (405) ^{[13] [14] [15] [16]}	Improvement in tinnitus	Tricyclic antidepressants (TCAs) versus placebo	4	-1	0	0	0	Moderate	Quality point deducted for incomplete reporting of results
	1 (117) ^[16]	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) ^{[17] [18]}	Improvement in tinnitus	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) ^[18]	Impact of tinnitus on quality of life	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)
	2 (70) ^{[21] [22]}	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
	1 (30) ^[7]	Improvement in tinnitus	Cinnarizine versus placebo	4	-3	0	0	0	Very low	Quality points deducted for sparse data, incomplete reporting of results, and uncertain follow-up
	2 (78) ^{[24] [25]}	Improvement in tinnitus	Electromagnetic stimulation versus placebo	4	-3	-1	0	0	Very low	Quality points deducted for sparse data, incomplete reporting of results, and other methodological flaws. Consistency point deducted for conflicting results
	1 (66) ^[29]	Improvement in tinnitus	Ginkgo biloba versus placebo	4	-1	0	0	0	Moderate	Quality point deducted for sparse data
	1 (39) ^[30]	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) ^[31]	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
	18 (787) ^{[32] [33]}	Improvement in tinnitus	CBT versus placebo	4	-1	0	0	0	Moderate	Quality point deducted for methodological flaws of 1 review
	at least 9 (at least 455) ^{[32] [33]}	Impact of tinnitus on quality of life	CBT versus placebo	4	-1	0	0	0	Moderate	Quality point deducted for methodological flaws of 1 review

Important outcomes		Impact of tinnitus 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 (21) ^[35]	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 (48) ^[36]	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.