

**Long-term Efficacy of Audiologist-Guided Internet-Based
Cognitive Behaviour Therapy for Tinnitus in the United States: A
repeated-measures design**

Running Title: Long-term Efficacy of ICBT for Tinnitus

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ABSTRACT

Objectives: This study investigated the long-term outcomes 1-year after undertaking an Internet-based cognitive behavioural therapy (ICBT) for tinnitus distress in a US population. Secondary aims were to identify the effects on additional difficulties associate with tinnitus and any unwanted events related to ICBT for tinnitus.

Methods: A repeated-measures design with 4 time points was used. Participants previously undertaking two randomized ICBT efficacy trials for tinnitus in the US were invited to participate. Of the 200 invited, 132 (66%) completed the 1- year follow-up questionnaire. The primary outcome was a change in tinnitus distress from baseline at one year post-intervention, as assessed by the Tinnitus Functional Index. Secondary assessment measures were included for anxiety, depression, insomnia, hearing disability, hyperacusis, tinnitus cognitions and health-related quality of life.

Results: Undertaking ICBT for tinnitus led to significant improvements 1-year post-intervention for tinnitus severity, with a large effect size ($d = 1.06$; CI: 0.80 to 1.32). Medium effects were found for anxiety ($d = 0.54$; CI: 0.29 to 0.79), depression ($d = 0.46$; CI: 0.21 to 0.70), insomnia ($d = 0.47$; CI: 0.22 to 0.72), and tinnitus cognitions ($d = 0.43$, CI: 0.18 to 0.68). Small effect sizes were found for hearing disability, hyperacusis and health-related quality of life. Adverse events related to the intervention were only reported by 1 participant.

Conclusions: The benefits of audiologist-guided ICBT for tinnitus and tinnitus-related difficulties were maintained 1-year post-intervention with very few adverse events reported. Ways of disseminate evidence-based easily accessible interventions to the general population with bothersome tinnitus should be sought.

Keywords

Tinnitus, Internet-intervention, Digital therapeutics, Teleaudiology, Cognitive behavioural therapy, Long-term outcomes

1. Introduction

Tinnitus, the perception of sounds such as ringing or buzzing, generally in the ears or head, presents a major public health burden due to high prevalence rates of 10-20% of the global population.¹ The prevalence rate increases with age, which is of concern with an increasing aging population.² The majority of those with tinnitus manage to cope with it. However for about 1 in 10 (2-3% of the total population) tinnitus interferes with daily life.³ As no cure has been found for most cases of tinnitus, bothersome tinnitus is managed as a chronic condition, with the aim of reducing the tinnitus percept and the reactions towards it. As tinnitus is often accompanied by additional difficulties such as anxiety, depression and insomnia, there is a significant associated socioeconomic and healthcare economic burden.⁴ Seeking management approaches leading to long-term effects for tinnitus are important to reduce these burdens. Although various management strategies have evolved, many lack empirical support and few have demonstrated long-term outcomes. At present, psychological interventions, mainly cognitive behavioural therapy (CBT), currently has the most evidence of efficacy in reducing tinnitus distress.⁵ Despite this known efficacy, and that CBT is recommended in practice guidelines, it is rarely offered or available to those with distressing tinnitus.⁶

To make CBT for tinnitus more accessible, an internet-based treatment (ICBT) was developed⁷ and was subsequently adapted for various populations.⁸ To improve accessibility, the intervention was tested using guidance from audiologists instead of clinical psychologists, and efficacy for audiologist providing guidance was obtained.^{9,10}

A systematic review identified a medium effect size based on nine randomized control ICBT trials, demonstrating the efficacy of ICBT.¹¹ What was striking from this review was that

the trials had mostly been undertaken in Europe and the UK and that only a few of these monitored 1-year post-intervention outcomes.¹² As the efficacy of ICBT in the United States had not been determined, the intervention was translated into Spanish.^{13,14} Clinical trials supported the efficacy of the intervention in the United States¹⁵⁻¹⁷ and for Spanish speakers.¹⁸ Identifying whether these effects remain long-term is important to aid healthcare providers during decision making processes regarding which interventions to provide for those with tinnitus, they need evidence that intervention effects remain past the intervention period.

The aim of this study was to investigate the long-term outcomes 1-year after ICBT in a US tinnitus population. A single-group repeated-measures design was used, as all participant had had the intervention, so there was no control group at this point. The specific objectives were:

- i) To assess the stability of internet-based CBT in reducing tinnitus distress 1-year after the intervention.
- ii) To assess the stability of internet-based CBT in reducing comorbidities associated with tinnitus 1-year after the intervention.
- iii) To determine the extent of adverse effects of the intervention.

2. Material and Methods

2.1 Study Design

A single-group repeated-measures design with 4 time points was used. The data were derived from two randomized clinical trials (RCTs) investigating the efficacy of ICBT.^{16,17} In both trials all participants had received the same intervention, but the control groups received this full intervention after a time delay. The outcomes at one-year post intervention were after participants completed the full intervention. Thus, a single group analysis was

conducted for the present study and there was no control group. Ethical approval was obtained (IRB-FY17-209 and IRB-FY20-200) and both trials were pre-registered at Clinicaltrials.gov (NCT04004260 and NCT04335812). Transparent Reporting of Evaluations with Nonrandomized Designs (TREND) checklist was used to report the trial. An independent data monitoring committee monitored the running of the trial.

2.1 The Intervention

An internet-based intervention was presented online consisting of 22 modules based on a CBT tinnitus program.¹⁹ To ensure suitability for a US population, the intervention was further modified with linguistic and cultural adaptations, such as lowering the readability to below the recommended 6th English reading grade level.^{13,14} The intervention was guided by an audiologist who monitored progress, provided feedback on worksheets completed, outlined the content of new modules, and answered questions.

2.2 Participants

All participants who undertook the ICBT intervention from the two clinical trials (RCT1, n =118¹⁶ and RCT2, n =82¹⁷ were invited to partake in the study. Participants who withdrew or never logged into the program (total n = 42) were excluded as they did not have any experience undertaking the intervention and provide informed consent. All eligible participants were invited to complete the 1-year post- intervention questionnaire. The original eligibility *inclusion criteria included*: aged 18 years and over; living in the US; the ability to read and type in English; access to a computer, the internet and the ability to email; experiencing tinnitus for a minimum period of three months with no major medical conditions that may prevent. The exclusion criteria were participants not completing the 1-year outcome measure.

2.3 Data collection

Data collection was online. The assessment timeline was as follows: T_0 =baseline; T_1 =post-intervention assessment; T_2 =2-months follow-up; and T_3 =1-year post-intervention follow-up for each group (see Figure 1). To minimise attrition, encouraging reminders were provided throughout for participants who had not completed questionnaires or worksheets on time. The primary outcome measure was the Tinnitus Functional Index as seen in Table 1. Secondary outcome measures were selected for generalized anxiety, depression, insomnia, tinnitus cognitions, health-related quality of life, hearing disability and hyperacusis. Table 1 provides detailed information about the outcome measures including the internal consistency, range of scores, and levels of significance.

2.4 Data Analysis

The Statistical Package for Social Sciences (SPSS) version 26.0 was used for statistical analysis. For all analyses, a more stringent two-tailed significance level of <0.001 was considered statistically significant, due to applying Bonferroni adjustments due to using multiple outcome measures. The primary study outcome was a change in the Tinnitus Functional Index (TFI) score at 1-year post-intervention (T_3). Secondary study outcomes were changes in the scores of secondary assessment measures at T_3 . Effect sizes, Linear Mixed Effects Models (LMM), and the Reliable Change Index (RCI) were used to assess the outcomes. The RCI was used as a standardized way of calculating clinical significance for the TFI as the primary outcome. This was calculated using the mean pretest-posttest score difference, the pretreatment standard deviation (20.7), and a test-retest reliability coefficient of 0.78, using the data from the TFI validation study. A reliable change criterion should be 1.96 times this which was 26.96. Effect sizes of Cohens's $d = 0.20$ represent small effect sizes; those of $d = 0.50$ represent medium effect sizes; and those equal or greater than $d = 0.80$ represent large effect sizes.

155

156 **2.5 Unwanted Events**

157 Both quantitative and qualitative methods of recording unwanted events were undertaken. As
158 recommended, probing for unwanted effects was undertaken by asking an open-ended question
159 as recommended by Rozental et al.²⁰. Additional follow up questions deemed to provide
160 important information were included as follows:

- 161 i) Did you experience any unwanted effects/events associated with the Internet
162 intervention you undertook? (yes/no)
- 163 ii) If yes, please list all the unwanted affects you experienced associated with undertaking
164 this intervention (open question)
- 165 iii) What was the negative impact of the event/s at the time of the event? (5 point Likert
166 scale from a range of minimal to very severe)
- 167 iv) What is the negative impact of the event/s at present? (i.e. 1 year post-intervention
168 (select on a 5-point Likert scale from a range of minimal to very severe))

169 **3. Results**

170 **3.1 Participant Characteristics**

171 Of the 200 invited, 132 (66%) completed the 1-year follow-up questionnaire as seen in Figure
172 1. From the cohort completing the long-term outcomes, the mean age was 56.33 years (SD:
173 12:84) with a range between 22 to 84 years (see Table 2). This is similar to the mean ages of
174 the original studies of 57 for RCT1 and 56 for RCT2. A slightly higher proportion of the
175 participants were female (56%). These differences were not seen in the original studies where
176 the ratios were 49% (males) and 51% (females). The average tinnitus duration was 11.64 (SD:
177 14:57) years which is lower than the 14-year average for RCT1 and 12 year average for RCT2.
178 There were no statistical differences between the demographic or clinical profiles of those
179 completing or not completing the outcomes at T3.

[Insert Figure 1 and Table 2 around here]

3.2 Long-Term Effects for Tinnitus Distress

There was a significant T₃ TFI mean improvement of 24.3 (SD: 22.5) when compared to the pre-intervention mean (T₀) [T₀: 54.23, SD:20.7; T₃: 30.15; SD: 24.51]. This difference was statistically significant with a large effect size (Cohen's $d = 1.06$, CI: 0.80 to 1.32), as seen in Table 3. This was slightly smaller than the effect at T₂ of Cohen's $d = 1.23$, CI: 0.94 to 1.51. There was a clinically significant change for $n = 56$ (42%) of the participants using the reliable change criterion of 26.98 at T₃. There were no significant differences in the scores between T₂–T₃ indicating that scores had been maintained 1-year post-intervention, as seen in Figure 2. Comparison of the magnitude of the change between T₀–T₃ is shown in Figure 3. There were 12 participants whose pre-post TFI scores deteriorated (between 1-15 points) and variation of improvements scores were obtained from the other participants (up to 70 points) with more than 50% improving between 1-39 points.

[Insert Table 3, around here]

3.3 Long-Term Effects for Problems Associated with Tinnitus

The test of fixed effects (Table 4) indicated that the intercept and slope revealed significant changes in tinnitus severity. The model indicated an estimated baseline to post-intervention mean difference of 22 points (CI: 18 to 26) and follow-up and 1-year mean difference of 24 points (CI: 20 to 28) for both these time points. The estimated TFI score after undertaking the intervention was 32 (CI: 27 to 37).

203 The secondary tinnitus outcome, the THS tinnitus measure indicated a large effect size
204 at T3 (Cohen's $d = 0.89$, 0.63 to 1.15). The test of fixed effects (Table 4) indicated that the
205 intercept and slope had significant effects on the changes in tinnitus severity.

3.4 Long-Term Effects for Tinnitus-related Difficulties

There was a medium effect size for outcome measures for anxiety, depression, insomnia, tinnitus cognitions and small effect for hearing disability, hyperacusis, and health-related quality of life VAS score (see Table 3). The effect size at T2 was similar for anxiety, and larger for depression, insomnia, and quality of life. The test of fixed effects (Table 4) indicated that the intercept and slope revealed significant changes for all outcomes except for the EQ-5D-5L VAS. The estimated mean differences from baseline and pairwise comparisons are seen in Table 3.

[Insert Fig 2 & 3 around here]

3.5 Adverse Effects

Only 2 out of the 131 participants reported any adverse events. One of these reports were coded as related to the study (i.e., “Worried More often”; “Surveys TOO long”) and one was not related to the study (i.e., If I go to a tinnitus Facebook group it makes me feel more focused on it almost like it makes me feel like something is wrong with me and I don't want that mindset). The adverse effect was classified as prolongation of treatment using Linden³⁷ checklist for adverse events. The participant rated the severity of this unwanted effect as moderate.

4. Discussion

Due to the importance of ensuring lasting intervention effects, this study evaluated the efficacy of ICBT at 1-year follow-up and identify the nature of adverse events during the intervention period. This Discussion considers the results obtained for each objective.

4.1 Long-Term Efficacy of ICBT for Tinnitus Distress

This study found that the improvements obtained from ICBT at post-intervention were maintained at 1-year post-intervention as indicated by a large effect size of $d = 1.06$ for tinnitus distress. The improvement of 24.3 points was slightly smaller to that obtained at T2 (2 month follow-up) of $d = 1.23$, although this change was not significant. The results indicated a clinically significant change for 42% of the participants. The majority of the TFI scores improved between 0-39 points from baseline. These results contribute to the evidence regarding the stability of ICBT effects indicted by previous studies. The results are very similar to those obtained using the same intervention using a Swedish, German and UK population. The 1-year post-intervention effect size was $d = 1.04$ with 46% of UK-based participants indicating a clinically significant change.¹² In studies from the USA and UK, there was an expected distribution of improvements in the TFI scores post-intervention, with a few participants not improving, the majority indicating a 0-29 point improvement and a few with greater improvements. The results are also in line with those of Kaldo et al.²² and Hesser et al.,²³ using a Swedish population and Weise et al.²⁴ using a German population indicating stability of the results 1-year postintervention. When pooling the 1-year outcomes of these studies a small effect size ($d = 0.43$; CI: 0.27 to 0.59) was found for an earlier systematic review.¹¹ Further studies are required to determine the effects longer than 1-year post-intervention.

4.2 Long-Term Efficacy of ICBT for Additional Problems Associated with Tinnitus

There was a significant improvement from baseline to 1-year follow-up for all secondary outcome measures except for the health-related quality of life. A medium effect size was seen for anxiety, depression, insomnia, and tinnitus cognitions. Compared with the 1-year post-

intervention effects from a UK population¹⁵ the effect sizes were improved for anxiety (US: $d = 0.54$; UK: $d = 0.32$), depression (US: $d = .46$; UK: $d = 0.21$) and slightly worse for insomnia (US $d = 0.47$; UK: $d = 0.55$). Kaldo et al.²² and Hesser et al.,²³ using a Swedish population and Weise et al.²⁴ b using a German population, reported stability (and improvements) of results 1-year after undertaking ICBT for the associated effects of anxiety and depression, but not for insomnia. An earlier systematic review pooling the results from previous studies indicated a small, pooled effect size for ICBT in improving additional difficulties ($d = 0.29$; CI: 0.21 to 0.36).¹¹ There was no significant effect for health-related quality of life. This finding may partly relate to the lack of appropriate quality of life measures for tinnitus, making valid measurements of this aspect difficult.

4.3 Adverse events

There was only one relevant adverse event reported regarding the questionnaires being too long. When investigating adverse effects at 1-year post-intervention after undertaking ICBT, from 104 participants there were 11 (11%) reporting adverse effects. These included worsening of symptoms, emergency of new symptoms, negative well-being and prolongation of treatment. Although these were not found for the present study, they are always plausible, and it is important to monitor for them. Awareness of these effects and attempting to minimise their impact when modifying the intervention¹³ may have contributed to the results be. There may be specific moderators associated with experiencing adverse effects.

4.4 Study Strengths, Limitations and Future Effects

Due to the limited number of studies within audiological interventions focusing on outcomes at periods longer than post-intervention, a strength of this study is adding to this body of evidence regarding the efficacy of ICBT 1-year post intervention. Having participants from two clinical trials is a further strength as it is more representative of the heterogeneity of the tinnitus population. Another study strength was that robust statistical measures were used to account for missing data and investigate the clinically significant effect of the intervention. There are, however, limitations and the results of this study need to be interpreted in the context of the findings. The results represent a within-group study design as randomization at 1 year-post intervention was not possible as all the participants had undertaken the same intervention at this point. This study design may inflate the results as there is no control comparison group. Completion of the post-intervention assessments may have been selectively done by those who obtained more benefit from the treatment, hence biasing the results. Future studies should include a control group for a more accurate comparison. Furthermore, some assessment measures (e.g., health-related quality of life) may not have been optimal for a tinnitus population and thus influenced the results. Further research is required to monitor the stability of outcomes longer term (e.g., 3-years post-intervention). Ways of engaging further participants and improving compliance in completing the outcome measure are furthermore important to reducing reporting bias. A further limitation was that self-reported outcome measures were used for purposes of this study due to a lack of acceptable and accessible objective outcomes measures are available for conditions such as tinnitus, anxiety and depression. Self-reported outcome measure due to their subjective nature may have biased the result obtained. A process evaluation undertaken confirmed that engagement in the intervention was not optimum²⁵ which may have affected the outcomes. Understanding the factors associated with poor engagement and experiencing adverse effects can help counteract these effects in future trials.

5. Conclusions

This study adds to the findings that results obtained from ICBT can be maintained longer term. As healthcare systems are under increasing pressure, innovative planning to manage the increasing demands is required. One way of relieving this pressure has been to increase the use of remote appointments and self-help interventions. The study provides evidence of long-term efficacy for an audiologist-guided tinnitus intervention. This intervention relies on minimal resources which can add to health economic benefits and benefits for individual patients. Identifying ways of making such interventions more accessible to the tinnitus population is important.

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Data Sharing and Data Availability

The data that support the findings of this study are openly available in Figshare at <http://dx.doi.org/10.6084/m9.figshare.19354781>

Conflict of interest disclosure

The authors report no conflicts of interest

Ethics approval statement

Ethical approval was obtained from the Institutional Review Board at Lamar University, Beaumont, Texas, US (IRB-FY17-209 and IRB-FY20-200).

Patient consent statement

Online informed consent was required to participate.

Permission to reproduce material from other sources

None required

Clinical trial registration

Clinicaltrials.gov (NCT04004260 and NCT04335812).

Authorship

EB, GA, VM designed the work; EB acquired and analysed data; EB drafted, EB, GA, VM revised and approved the manuscript; EB, GA, VM agree to be accountable for all aspects of the work

References

1. Biswas R, Lugo A, Akeroyd MA, Schlee W, Gallus S, Hall DA. Tinnitus prevalence in Europe: a multi-country cross-sectional population study. *The Lancet Regional Health - Europe* [Internet]. 2022 Jan [cited 2022 Mar 21];12:100250. Available from: <https://doi.org/10.1016/j.lanepe.2021.100250>
2. Oosterloo BC, Croll PH, Baatenburg de Jong RJ, Ikram MK, Goedegebure A. Prevalence of tinnitus in an aging population and its relation to age and hearing loss. *Otolaryngol Head Neck Surg.* 2021 [cited 2022 Mar 21];164(4):859–68. Available from: <https://doi.org/10.1177/0194599820957296>
3. Kleinjung T, Langguth B. Avenue for future tinnitus treatments. *Otolaryngologic Clinics of North America* [Internet]. 2020 Aug [cited 2022 Mar 21];53(4):667–83. Available from: <https://doi.org/10.1016/j.otc.2020.03.013>
4. Trochidis I, Lugo A, Borroni E, Cederroth CR, Cima R, Kikidis D, et al. Systematic review on healthcare and societal costs of tinnitus. *Int J Environ Res Public Health.* 2021 Jun [cited 2022 Mar 21];18(13):6881. Available from: <https://doi.org/10.3390/ijerph18136881>
5. Fuller T, Cima R, Langguth B, Mazurek B, Vlaeyen JW, Hoare DJ. Cognitive behavioural therapy for tinnitus. *Cochrane Database Syst Rev.* 2020 Jan [cited 2022 Mar 21];1:CD012614. Available from: <https://doi.org/10.1002/14651858.CD012614.pub2>
6. McKenna L, Vogt F, Marks E. Current validated medical treatments for tinnitus: cognitive behavioral therapy. *Otolaryngol Clin North Am.* 2020 Aug [cited 2022 Mar 21];53(4):605–15. <https://doi.org/10.1016/j.otc.2020.03.007>
7. Andersson G, Kaldö V. Internet-based cognitive behavioral therapy for tinnitus. *J Clin Psychol.* 2004 Feb Aug [cited 2022 Mar 21]

8. Beukes EW, Vlaescu G, Manchaiah V, Baguley DM, Allen PM, Kaldo V, et al.
Development and technical functionality of an Internet-based intervention for tinnitus in the UK. *Internet Interv.* 2016 Nov [cited 2022 Mar 21];6:6–15. Available from: <https://doi.org/10.1016/j.invent.2016.08.002>
9. Beukes EW, Baguley DM, Allen PM, Manchaiah V, Andersson G. Audiologist-guided internet-based cognitive behavior therapy for adults with tinnitus in the United Kingdom: a randomized controlled trial. *Ear Hear.* 2018 Jun [cited 2022 Mar 21];39(3):423–33. Available from: <https://doi.org/10.1097/AUD.0000000000000505>
10. Beukes EW, Andersson G, Allen PM, Manchaiah V, Baguley DM. Effectiveness of guided internet-based cognitive behavioral therapy vs face-to-face clinical care for treatment of tinnitus: a randomized clinical trial. *JAMA Otolaryngol Head Neck Surg* [Internet]. 2018 Dec 1 [cited 2022 Mar 21];144(12):1126. Available from: <https://doi.org/10.1001/jamaoto.2018.2238>
11. Beukes EW, Manchaiah V, Allen PM, Baguley DM, Andersson G. Internet-based interventions for adults with hearing loss, tinnitus, and vestibular disorders: a systematic review and meta-analysis. *Trends in Hearing* [Internet]. 2019 Jan [cited 2022 Mar 21];23:233121651985174. Available from: <http://journals.sagepub.com/doi/10.1177/2331216519851749>
12. Beukes EW, Allen PM, Baguley DM, Manchaiah V, Andersson G. Long-term efficacy of audiologist-guided internet-based cognitive behavior therapy for tinnitus. *American Journal of Audiology* [Internet]. 2018 Nov [cited 2022 Mar 21];27(3S):431–47. Available from: https://pubs.asha.org/doi/10.1044/2018_AJA-IMIA3-18-0004
13. Beukes EW, Fagelson M, Aronson EP, Munoz MF, Andersson G, Manchaiah V. Readability following cultural and linguistic adaptations of an internet-based

- intervention for tinnitus for use in the United States. *Am J Audiol*. 2020 Jun [cited 2022 Mar 21];29(2):97–109. Available from: https://doi.org/10.1044/2019_AJA-19-00014
14. Manchaiah V, Vlaescu G, Varadaraj S, Aronson EP, Fagelson MA, Munoz MF, et al. Features, functionality, and acceptability of internet-based cognitive behavioral therapy for tinnitus in the United States. *Am J Audiol* [Internet]. 2020 Sep [cited 2022 Mar 21];29(3):476–90. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7842846/>
 15. Beukes EW, Andersson G, Fagelson M, Manchaiah V. Audiologist-supported internet-based cognitive behavioral therapy for tinnitus in the United States: a pilot trial. *Am J Audiol*. 2021 Sep [cited 2022 Mar 21];30(3):717–29. Available from: https://doi.org/10.1044/2021_AJA-20-00222
 16. Beukes EW, Andersson G, Fagelson M, Manchaiah V. Internet-based audiologist-guided cognitive behavioral therapy for tinnitus: randomized controlled trial. *J Med Internet Res* [Internet]. 2022 Feb [cited 2022 Mar 21];24(2):e27584. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8887633/>
 17. Beukes EW, Andersson G, Fagelson MA, Manchaiah V. Dismantling internet-based cognitive behavioral therapy for tinnitus. The contribution of applied relaxation: A randomized controlled trial. *Internet Interv* [Internet]. 2021 May [cited 2022 Mar 21];25:100402. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8141772/>
 18. Beukes EW, Munzo MF, Andersson G, Manchaiah V. Internet-based cognitive behavioural therapy for tinnitus in Spanish: a global feasibility trial. *International Journal of Audiology* [Internet]. 2021 Sep [cited 2022 Mar 21];0(0):1–10. Available from: <https://doi.org/10.1080/14992027.2021.1971780>

19. Beukes E, Andersson G, Manchaiah V, Kaldo V. Cognitive behavioral therapy for tinnitus. San Diego, USA: Plural Publishing Inc; 2021.
20. Rozental A, Andersson G, Boettcher J, Ebert DD, Cuijpers P, Knaevelsrud C, et al. Consensus statement on defining and measuring negative effects of Internet interventions. *Internet Interventions* [Internet]. 2014 Mar 1 [cited 2022 Mar 24];1(1):12–9. Available from: <https://doi.org/10.1016/j.invent.2014.02.001>
21. Linden M. How to define, find and classify side effects in psychotherapy: from unwanted events to adverse treatment reactions. *Clin Psychol Psychother*. 2013 Aug [cited 2022 Mar 21];20(4):286–96. Available from: <https://doi.org/10.1002/cpp.1765>
22. Kaldo V, Levin S, Widarsson J, Buhrman M, Larsen H-C, Andersson G. Internet versus group cognitive-behavioral treatment of distress associated with tinnitus: a randomized controlled trial. *Behav Ther*. 2008 Dec [cited 2022 Mar 21];39(4):348–59. <https://doi.org/10.1016/j.beth.2007.10.003>
23. Hesser H, Gustafsson T, Lundén C, Henrikson O, Fattahi K, Johnsson E, et al. A randomized controlled trial of internet-delivered cognitive behavior therapy and acceptance and commitment therapy in the treatment of tinnitus. *Journal of Consulting and Clinical Psychology* [Internet]. 2012 Aug [cited 2022 Mar 24];80(4):649–61. Available from: <https://doi.org/10.1037/a0027021>
24. Weise C, Kleinstäuber M, Andersson G. Internet-delivered cognitive-behavior therapy for tinnitus: a randomized controlled trial. *Psychosomatic Medicine* [Internet]. 2016 May [cited 2022 Mar 24];78(4):501–10. Available from: <https://doi.org/10.1097/PSY.0000000000000310>
25. Beukes EW, Andersson G, Manchaiah V. Patient uptake, experiences, and process evaluation of a randomized controlled trial of internet-based cognitive behavioral

therapy for tinnitus in the United States. Front Med [Internet]. 2021 Nov 17 [cited 2022 Mar 24];8:771646. Available from: <https://doi.org/10.3389/fmed.2021.771646>

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Figure 1. The study profile

Figure 2 Change in tinnitus distress over time as measured by the Tinnitus Functional Index (TFI) at baseline (T_0), after intervention (T_2) and 1-year post-intervention (T_3). T_1 was not included as the control group had not received the intervention at this time point. Error bars represent standard error of the mean.

Figure 3 Distribution of Tinnitus Functional Index change from baseline to 1-year postintervention..

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Dimension	Outcome Measures	Internal consistency	Range of scores	Levels of significance
Primary outcome measure				
Tinnitus distress	Tinnitus Functional Index (TFI; 42)	.97	0-100 A reduction of scores indicates improvement	>25= mild (no need for intervention) 26-50= significant (possible need for intervention) 50+ =severe (need for a more intense intervention)
Secondary outcome measures				
Generalized Anxiety	Generalized Anxiety Disorder (GAD-7, 44)	.89	0-21 A reduction of scores indicates improvement	0-4= minimal anxiety 5-9= mild anxiety 10-14= moderate anxiety 15-21= severe anxiety
Depression	Patient Health Questionnaire (PHQ-9; 45)	.83	0-27 A reduction of scores indicates improvement	5-9=mild depression 10-14=moderate 15-19=moderately severe 20-27= severe depression
Insomnia	Insomnia Severity Index (ISI; 46)	.74	0-28 A reduction of scores indicates improvement	0–7 = Not clinically significant 8–14 = Subthreshold insomnia 15–21 = Clinical insomnia (moderate severity) 22–28 = Clinical insomnia (severe degree)
Tinnitus Cognitions	Tinnitus Cognitions Questionnaire (TCQ; 47)	.91	0-104 A reduction of scores indicates improvement	Higher scores indicate a greater tendency to engage in negative cognitions in response to tinnitus

Health-related quality of life	EQ-5D-5L (48)	.7-.85	0-15 A reduction of scores indicates improvement	Measures 5 dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/ depression
Health-related quality of life	EQ-5D-5L Visual Analogue Scale (VAS; 48)	.7-.85	0-100 Higher scores indicates improved health	VAS for overall health.
Short measure for tinnitus, hearing disability and hyperacusis	Tinnitus and Hearing Survey (THS; 49)	.86-.94	Subscale for Tinnitus: 0-16 Hearing: 0-16 Sound tolerance: 0-8	

Table 2 Baseline demographical and clinical characteristics of the participants

Category	Description	Participants at 1-year post-intervention (n = 131)
Gender	Male	56 (44%)
	Female	74 (56%)
Age	Mean years (SD)	56.33 (SD: 12:84)
	Range	22–84 years
Tinnitus duration	Mean years (SD)	11.64 (SD: 14.57)
	Range	0.3 to 70 years
Tinnitus location	Right	21 (16%)
	Left	17 (13%)
	Both ears	76 (57%)
	In the head	18 (14%)
Ethnicity	Hispanic/Latino	20 (15%)
	Not-Hispanic/Latino	112 (85%)
Race	American Indian / Alaska Native	3 (2%)
	Asian	2 (2%)
	Black or African American	1 (1%)
	White	123 (93%)

	More than One Race	3 (2%)
Highest educational level	High School	12 (9%)
	College/ vocational training	31 (24%)
	University degree	89 (67%)
Employment	Entry-level or unskilled work	3 (2%)
	Skilled or professional	78 (59%)
	Retired	22 (32%)
	Not working	9 (7%)

Table 3 Within-group comparisons of the assessment measures over time

Outcome measure and	T0: Pre-treatment (baseline)	T1: Post-intervention	T2: 2 month follow-up	T3: one-year outcome	Within-group Cohen's <i>d</i> (95% confidence intervals)
Tinnitus Functional Index (TFI)	54.23 (20.7)	30.20 (23.32)	27.66 (22.84)	30.15 (24.51)	T0 to T1: 1.09 (0.82 to 1.36) T0 to T2: 1.23 (0.94 to 1.51) T0 to T3: 1.06 (0.80 to 1.32)
Anxiety (GAD-7)	7.25 (5.39)	4.21 (4.3)	4.48 (4.68)	4.46 (4.90)	T0 to T1: 0.62 (0.36 to 0.87) T1 to T2: 0.54 (0.27 to 0.81) T2 to T3: 0.54 (0.29 to 0.79)
Depression (PHQ-9)	7.09 (5.52)	4.16 (4.5)	4.02 (4.92)	4.60 (5.40)	T0 to T1: 0.58 (0.32 to 0.84) T1 to T2: 0.59 (0.33 to 0.84) T2 to T3: 0.46 (0.21 to 0.70)
Insomnia (ISI)	11.13 (6.67)	7.00 (5.86)	6.68 (6.57)	7.96 (6.76)	T0 to T1: 0.66 (0.39 to 0.91) T1 to T2: 0.67 (0.41 to 0.93) T2 to T3: 0.47 (0.22 to 0.72)
Health-related quality of	7.79 (2.75)	7.11 (2.00)	6.86 (1.70)	7.20 (2.09)	T0 to T1: 0.28 (0.03 to 0.53) T1 to T2: 0.4 (0.14 to 0.66)

life (EQ-5D-5L)					T2 to T3: 0.24 (-0.01 to 0.49)
Health-related quality of life (EQ-5D-5L) VAS scores	76.76 (16.46)	78.36 (16.05)	80.15 (15.53)	77.22 (15.18)	T0 to T1: 0.10 (0.03 to 0.16) T1 to T2: 0.21 (0.04 to 0.46) T2 to T3: 0.03 (0.22 to 0.27)
Tinnitus score from THS	6.3 (4.18)	2.97 (3.12)	2.87 (3.70)	3.45 (4.15)	T0 to T1: 0.89 (0.63 to 1.15) T1 to T2: 0.86 (0.58 to 1.14) T2 to T3: 0.68 (0.43 to 0.93)
Hearing disability (THS)	6.45 (4.85)	4.23 (3.83)	3.56 (3.34)	5.02 (4.28)	T0 to T1: 0.50 (0.25 to 0.76) T1 to T2: 0.69 (0.44 to 0.94) T2 to T3: 0.31 (0.07 to 0.56)
Hyperacusis (THS)	1.17 (1.34)	.86 (1.20)	.75 (1.00)	.83 (1.24)	T0 to T1: 0.24 (0.00 to 0.49) T1 to T2: 0.35 (0.08 to 0.61) T2 to T3: 0.26 (0.02 to 0.51)
Tinnitus cognitions (TCQ)	40.86 (17.56)	27.54 (18.34)	28.13 (18.46)	32.69 (20.44)	T0 to T1: 0.74 (0.48 to 1.00) T1 to T2: 0.71 (0.45 to 0.96) T2 to T3: 0.43 (0.18 to 0.68)

2 **Table 4.** The test of fixed effects for the primary and secondary outcome measures

Outcome predictor	Tinnitus	Anxiety	Depression	Insomnia	EQ-5D-VAS	THS: Tinnitus	THS: Hearing disability	THS: Hyperacusis	Tinnitus cognitions
Intercept:	$F(1,137.022)$ = 421.134, p < .001*	$F(1,126.627)$ = 205.544, p < .001*	$F(1,122.355)$ = 163.897, p < .001*	$F(1,264.249)$ = 264.249, p < .001*	$F(1,69.852)$ = 4691.500, p < .001*	$F(1,152.436)$ = 194.739, p < .001*	$F(1,140.048)$ = 249.649, p < .001*	$F(1,131.703)$ = 114.610, p < .001*	$F(1,128.960)$ = 549.290, p < .001*
Time	$F(3,125.613)$ = 52.994, p < .001*	$F(3, 111.325)$ = 17.04, p < .001*	$F(3,113.533)$ = 12.293, p < 0.001*	$F(3,108.620)$ = 19.17, p < .001*	$F(1,26.112)$ = .47, p < .71	$F(3,119.336)$ = 37.408, p < .001*	$F(3,113.593)$ = 12.152, p < .001*	$F(3,113.490)$ = 5.18, p = .002	$F(3,110.614)$ = 19.627, p < .001*
Estimated means T0	54.2 (CI: 50.6 to 57.8)			11.2 (10.0 to 12.3)	76.72 (73.9 to 79.6)	6.3 (5.6 to 7.0)	6.3 (5.6 to 7.2)	1.2 (.9 to 1.4)	40.8 (37.7 to 43.9)

T1	32.0 (27.8 to	7.3 (6.4 to	7.1 (6.2 to	7.3 (6.2 to	77.6 (74.7	3.2 (2.6 to	4.4 (3.7 to	.9 (.7 to 1.2)	29.7 (25.4 to
T2	36.2)	8.2)	8.1)	8.4)	to 80.6)	3.7)	5.1)	.8 (.6 to 1.0)	32.1)
T3	30.2 (26 to	4.5 (3.7 to	4.5 (3.6 to	7.1 (5.8 to	77.6 (74.7	3.2 (2.5 to	4.2 (3.5 to	.8 (.6 to 1.0)	32.6 (29.0 to
	34)	5.2)	5.3)	8.4)	to 80.6)	3.8)	4.8)		36.2)
	30.1 (26.0 to	4.8 (3.9 to	4.4 (3.5 to	8.0 (6.8 to	78.7 (75.6	3.5 (2.8 to	4.9 (4.2 to		
	34.4)	5.7)	5.3)	9.2)	to 81.9)	4.2)	5.7)		
		4.5 (3.7 to			77.1 (74.5				
		5.4)			to 79.8)				
Estimated mean difference from baseline T1	22.3 (18 to	2.8 (1.0 to	2.7 (1.8 to	3.8 (2.7 to	.5 (.4 to .6)	3.1 (2.5 to	2.0 (1.2 to	.3 (0.0 to .5)	12.1 (8.8 to
	26)	3.7)	3.6)	4.9)	.5 (.43	3.7)	2.7)	.4 (.2 to .6)	15.4)
				4.0 (2.9 to	to .47)	3.2 (2.5 to	2.2 (1.5 to	.3 (.1 to .6)	11.6 (8.1 to
				5.2)		3.8)	3.0)		15.1)

T2	24.1 (20 to	2.6 (1.6 to	2.8 (1.8 to	3.2 (2.2 to	.5 (.47	2.8 (2.2 to	1.5 (.8 to 2.1)		8.2 (4.5 to
T3	28)	3.4)	3.7)	4.2)	to .57)	3.5)			11.9)
	24.4 (20 to	2.8 (1.0 to	2.5 (1.6 to						
	28)	3.7)	3.4)						
Pairwise comparisons	24 (20 to 28)	2.8 (2.0 to	2.5 (1.6 to	3.2 (2.2 to	.45 (2.0 to	2.8 (2.2 to	1.5 (.8 to 2.1)	.3 (.1 to .6)	8.2 (4.5 to
T0-T3	2 (0.5 to 4)	3.6)	2.4)	4.2)	2.9)	3.5)	.78 (.3 to 1.2)	.06 (.15	12.0)
T2-T3		-.2.9 (.4 to	0.35 (.35	.8 (.01 to 1.7)	1.6 (1.7 to			to .27)	3.4 (.8 to 6.0)
		1.0)	to .86)		4.8)	.32 (-.08			
						to .7)			

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