# Guided Internet-based versus face-to-face clinical care in the treatment of tinnitus: A multicentre randomized non-inferiority trial

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**KEY POINTS**

**Question** Is undertaking an Internet-based cognitive behavioural therapy programme as effective as undergoing individualized face-to-face care in reducing tinnitus distress?

**Findings** A randomized non-inferiority trial including 92 adults, undertaking Internet-based cognitive behavioural therapy led to similar outcomes when compared with a group undergoing individualized face-to-face tinnitus care.

**Meaning** Internet-based cognitive behavioural therapy has shown potential as an evidence-based tinnitus intervention that could increase access to tinnitus care access.

# ABSTRACT

**Importance** Accessible clinical care is not always available to those with distressing tinnitus. Internet-based cognitive behavioural therapy has potential to increase access to evidence-based tinnitus services. Research comparing the effectiveness of this intervention with face to face care is required.

**Objective** To evaluate whether an Internet-based cognitive behavioural therapy intervention is at least as effective as established individualized face-to-face care in reducing tinnitus distress and tinnitus-related difficulties.

**Design** A randomized, multi-centre, two-arm parallel group, non-inferiority trial with 2-month follow-up was run between October 2016 and July 2017. Participants were randomly assigned (1:1) to either intervention using variable permuted block sizes of four and six.

**Setting** The experimental group received the Internet-intervention online while the active control undertook the usual face-to-face tinnitus care at one of three UK-based National Health Service hospitals.

**Participants** Adults that had been referred to their local tinnitus clinics due to bothersome tinnitus, were invited to participate (n =374). 92 participants were randomized (experimental n = 46; control n= 46), of which 88 completed the immediate post-intervention assessment and 72 completed follow-up assessment measures.

**Interventions** Participants were randomized to receive either 8 weeks of guided Internet-based cognitive behavioural therapy or 2-3 individualized face-to-face appointments in a tinnitus clinic.

**Main Outcome measures** The primary outcome was a change in tinnitus distress (as assessed by the Tinnitus Functional Index). Secondary assessment measures were included for insomnia, anxiety, depression, hearing disability, hyperacusis, cognitive failures, and satisfaction with life.

**Results** The between-group difference in the Tinnitus Functional Index scores at post-intervention of 5.19 (95% CI -4.17 to 14.53) and 5.18 (95% CI -4.17 to 14.53) at follow-up, fell within the non-inferiority margin of 13 points for the lower 95% confidence interval. For the secondary outcomes, only outcomes for insomnia fell outside the non-inferiority margin, at both post-intervention and follow-up, favouring the iCBT group.

**Conclusions and Relevance** This is the first trial to compare an Internet-based intervention with standard individualized care for tinnitus. It demonstrates that both interventions were equally effective for reducing tinnitus distress and most tinnitus-related difficulties.

**Trial Registration** Clinicaltrials.gov: Identifier: NCT02665975

# INTRODUCTION

Tinnitus, described as the conscious perception of unwanted sounds in the absence of a corresponding external acoustic stimulus1, is a prevalent complaint and one of the most distressing audiological symptoms2. As no cure has been identified, treating tinnitus remains challenging and costly. The estimated healthcare cost of tinnitus is US$660 per patient per year in the USA,3 with an annual healthcare cost of £750 million, and resulting societal cost of £2.7 billion per year in the UK4. Tinnitus clinics are not always readily accessible due to service and geographical constraints5,6. Moreover, although various tinnitus management approaches exist, evidence for their eﬃcacy is scarce7. To date, cognitive behavioural therapy (CBT), has the most evidence of efficacy in reducing tinnitus distress8. Despite positive outcomes, there is limited accessibility to CBT for tinnitus, largely due to a shortage of suitably trained clinicians5. To improve access to evidence-based tinnitus care, an Internet-based cognitive behavioural therapy intervention (iCBT) tinnitus intervention was pioneered in Sweden9. An iCBT intervention aimed at a UK population was adapted 10 from previous versions of the Swedish program. Both feasibility11 and efficacy12 of the UK version of iCBT were found to be high. It is, however, not known how outcomes for tinnitus using iCBT compare with those of individualized face-to-face F2F care as is typically provided in the UK. Previous comparisons have used group-based CBT (GCBT) as the active control13-15.

The primary aim of this study was to evaluate whether iCBT for tinnitus is at least as effective as established F2F care in reducing tinnitus severity. The secondary objective was to compare the effects of these interventions for tinnitus-related difficulties, such as insomnia, depression and anxiety. A further objective was to assess the stability of results, two months post-intervention. The hypothesis was that iCBT is not inferior to F2F care.

# METHOD

## Trial design and participants

A randomized, multi-centre, two-arm parallel group, non-inferiority trial with a sequential adaptive design and 2-month follow-up period was used to compare the clinical effectiveness of iCBT with the usual tinnitus care. The recruitment and treatment sites for the control group were three UK based hospitals, namely, Norfolk and Norwich University Hospitals NHS Foundation Trust, Milton Keynes University Hospital NHS Foundation Trust, and Hinchingbrooke Health Care NHS Trust. Eligibility criteria included participants aged 18 years or older with regular computer and Internet access who did not report any major medical or psychiatric disorder and were not undergoing any tinnitus treatment. Participants were examined clinically (hearing test performed, ear examination, case history taken of symptoms) and had been referred to the local tinnitus clinic by an ENT Specialist and/or audiologist. As this was an effectiveness trial, the study was not advertised. ENT specialists/ nurses passed on details of the study to patients that met the inclusion criteria. Ethical approval was granted by the East of England-Cambridge South Research Ethics Committee and Health Research Authority. Individuals who wanted to participate provided informed consent online. The full study protocol has been published16 and no changes were made once the trial commenced.

## Interventions

The intervention groups ran in parallel with both receiving information about managing tinnitus by an audiological professional. Participants were provided with hearing aids or combination devices/s regardless of group allocation. The following interventions were provided:

***Guided iCBT intervention (experimental intervention)***

The iCBT intervention content was based on a CBT self-help programme originally developed in Swedish9 and adapted into an 8-week interactive e-learning version for a UK population consisting of 16 recommended modules and five optional modules10,17. To monitor progress and provide feedback on worksheets completed, a minimum of 10 minutes of asynchronous audiologist-guidance using an encrypted two-way messaging system was provided.

***Face-to-Face intervention (active control intervention)***

The F2F group received the usual information counselling approach generally followed in the management of tinnitus in the UK. The initial appointment (60 minutes) was used to provide explanations about tinnitus and provide some basic management strategies. Follow-up appointments provided additional strategies for tinnitus management including sleep hygiene, relaxation strategies and negative thought analysis.

## Randomisation and masking

Participants were randomly assigned (1:1) by an independent researcher to either treatment arm, using a randomisation sequence generated by computer algorithm and variable randomly permuted block sizes of four and six. To prevent a delay in providing the interventions, an adaptive design was followed to sequentially allocate groups of participants as they were recruited. Participants were stratified for tinnitus severity (score ≤ 50 or >50) using the Tinnitus Functional Index (TFI)18. Whilst a masked design would be optimal, in this context it was not feasible. Allocation was known to both participants and the clinicians. To minimize bias the data analysis was masked in terms of group allocation.

## Outcomes

Data were collected online at baseline (T0), at post-intervention (T1) and 2-month follow-up (T2). A demographical questionnaire was used to establish health-related and tinnitus specific information.

***Primary assessment measure***

The primary outcome was a change in tinnitus distress between the groups. The Tinnitus Functional Index (TFI) 18 was selected to measure tinnitus distress due to its validation for assessing intervention responsiveness. In addition, the Tinnitus Handicap Index (THI)19 was administered for comparative purposes, as this is the most commonly used tinnitus assessment measure within clinics globally20. Both questionnaires consist of 25 items, scored on a scale of 0–100 with lower scores indicating less distress.

### Secondary Assessment Measures

The following secondary measures were incorporated to assess commonly reported tinnitus-related difficulties:

1. The Insomnia Severity Index (ISI)21 assessed the presence of insomnia
2. The Generalized Anxiety Disorder-7 (GAD-7)22 which assessed symptoms of generalized anxiety disorder
3. The Patient Health Questionnaire-9 (PHQ-9)23 indicated symptoms of depression
4. The Hearing Handicap Inventory for Adults Screening version (HHIA-S)24 assessed difficulty in hearing
5. The Hyperacusis Questionnaire (HQ)25 was administered to assess the presence of reduced tolerance of everyday sounds
6. The Cognitive Failures Questionnaire (CFQ)26 was administered to assess cognitive functions
7. The Satisfaction with Life Scales (SWLS)27 was administered to assess life satisfaction

In addition, participants were monitored weekly using the Tinnitus Handicap Inventory-Screening version (THI-s)28.

## Statistical analysis

The CONSORT guidelines for non-inferiority randomized clinical trials were followed29 (eTable 1). Statistical analyses were performed using the Statistical Package for Social Sciences (SPSS) version 23.0.

***Sample size***

Sample size calculations were performed using the SampSize app30 for non-inferiority parallel groups. Alpha was 0.025, power 90% and the estimated standard deviation was 17 points, indicated by the preceding efficacy trial12. The non-inferiority margin was set to 13 points, as indicated during the validation of the TFI18 to be a clinically significant change in scores. This indicated that 39 participants were required for each arm. Each intervention arm was assigned 46 participants to allow for possible drop outs, estimated from previous effectiveness trials to be between 10–20%31,32.

### Group comparisons

Both intention-to-treat and per-protocol results were analyzed. Participants were per-protocol if they completed the post-intervention assessment measures at the time point under investigation (T1 or T2). As there were no differences in the results obtained, the per-protocol results are reported, in accordance with current guidelines for non-inferiority trials29.

Non-inferiority of iCBT, compared with F2F care for tinnitus distress, was established if the lower limit of the two-sided 95% confidence interval (CI) of the mean TFI difference between these two interventions was less than the non-inferiority margin of 13 points. For the secondary assessment measures non-inferiority was established if a marginal between-group effect size of less than Cohen’s *d* = 0.20 was found (Cohen, 1992).

Mixed 2x3 analyses of variance (ANOVA) for repeated measures with the between-subject factor of group and within-subject factor of time (T0, T1, T2) for each assessment measure were carried out. A Greenhouse-Geisser correction for non-sphericity was applied. For significant group by time interactions, the main effects were followed up by Bonferroni-corrected post-hoc testing. Effect sizes at post-intervention and follow-up were calculated, using Cohen’s *d* with Cohen’s *d* of 0.20 to 0.49 representing small effect sizes; those of *d* = 0.5 to 0.79 indicating medium effect sizes, and those equal to or greater than *d* = 0.80, large effect sizes 33. A sub-analysis was performed by comparing those in each group with and without amplification to determine the effect of amplification.

The Reliable Change Index (RCI)34 was used to determine clinical significance. The RCI criteria was calculated to be a 21-point difference score, using the baseline standard deviation and means, post-intervention means, and the test-retest reliability coefficient of 0.8 for the TFI18.

### Monitoring intervention effects Between T0–T1

A mixed 2x8 ANOVA for repeated measures was used to compare the weekly THI-S scores with the within-subject factor of time (weeks 1–8) and between-subject factor of group. The main effects were followed up by Bonferroni-corrected post-hoc testing.

# RESULTS

# Participant characteristics

The baseline assessment measures were completed by 92 participants who all met the eligibility criteria (Figure 1). The average age was 53 years (SD 12.07), with more male participants (60%). Hearing aids were fitted prior to or during the trial to 41% of participants (19 from each group). The groups were well matched, as there were no clinically meaningful imbalances between the groups at baseline (Table 1, 2).

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## Attrition

No participants withdrew during the study and no adverse events were reported. Assessment measures were completed by 96% at T1, and by 80% of the participants at T2, with no group differences.

Effectiveness of iCBT versus standard care for tinnitus distress

For both the iCBT and F2F group the within-group effect sizes for both tinnitus assessment measures (the TFI and THI) were large at T1 and T2 (Table 2).

For the iCBT group the T1 mean TFI scores were 26.27 (SD: 18.09) points lower than baseline. The T2 TFI scores were 27.49 (SD: 21.22) points lower than baseline.

For the F2F control group, the mean TFI scores at T1 and T2 were 21.69 (SD: 19.14) and 24.06 (SD: 22.37) points lower when compared with baseline.

The magnitude of the between-group difference was 5.18 points (95% CI: -4.17 to 14.53) at T1 and 5.52 points at T2 (95% CI: -4.60 to 15.61) favouring the iCBT group. The between-group T0–T1 and T0–T2 difference in TFI scores fell within the non-inferiority margin of 13 points for the lower 95% CI for both per-protocol and ITT analysis. Similar results were obtained for the THI (Figure 2).

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There were no significant differences between the range of pre to post-intervention difference scores between the two groups [*F*(1,9) = 0.008, *P* = 0.93]. Clinical significance was achieved by 25 (57%) in the iCBT group, and 18 (41%) in the F2F group at T1, and for 20 (54%) of the iCBT group and 17 (46%) of the F2F group at T2. There were 23 (52%) from the iCBT group and 15 (34%) from the F2F group at T1 with TFI scores below the level of requiring intervention (less than a score of 25) who also had a reliable change of 21. There were no significant differences in post-intervention tinnitus distress when comparing only those using or not using hearing aids [*F*(2,57)= 1.20, *P* = 0.23].

### Monitoring intervention effects between T0 and T1

The iCBT group had greater weekly reductions in tinnitus distress (Figure 3), as evidenced by the significant between-group effects [time by group interaction: *F*(7, 524) = 2.80, *P* = 0.037]; and effect size of Cohen’s *d* = 0.57.Follow-up analysis indicated tinnitus distress was significantly lower in the iCBT group when compared with the F2F group between weeks 4 to 8.

<Insert Figure 3 around here>

### Effectiveness of iCBT versus standard care for tinnitus-related difficulties

The Cohen’s *d* within-group effect sizes for the ISI were medium to large for both groups. They were medium for the GAD and PHQ (except at T2 for the iCBT group where a large difference occurred). They were small for the other assessment measures. The T1 between-group effect sizes for the secondary assessment measures were within the non-inferiority margin (Cohen’s *d* < 0.20) for anxiety, depression, hearing disability, hyperacusis, and life satisfaction. They were outside this margin, favouring the iCBT group for insomnia and cognitive failures. At T2 they were outside this margin for insomnia, hearing handicap, and depression, again favouring the iCBT group.

### Treatment adherence and clinician resources

On average those in the F2F group received 2.28 (SD: 1.10) appointments (137 minutes) with a maximum of five appointments. Seven individuals did not attend their appointment. On average those in the iCBT group read 13 (SD: 8) of the 21 modules and 17 participants (37%) completed all the modules. Users sent an average of 7 messages (SD: 10), and the audiologist sent an average of 21 messages per iCBT participant, i.e. 64 minutes contact time per participant during the intervention period. When dividing the time spent with the average TFI score change (iCBT 64/26.27=2.44; F2F 137/21.69 = 6.32) it indicated that when only taking the audiologist’s time into account, iCBT was 2.59 times as time-effective as F2F.

# DISCUSSION

## Effectiveness of iCBT compared with F2F care for tinnitus

To our knowledge this is the first randomized effectiveness trial to compare the effects of iCBT for tinnitus with standard clinical care on a clinical population. The results indicated that undertaking either interventions was equally effective, within the boundaries of non-inferiority, for reducing tinnitus distress. The present trial is unique as it compared iCBT with individualized F2F clinical care, as opposed to GCBT used in previous efficacy studies, which also found no significant group differences between iCBT and GCBT13,15.

When monitoring the groups weekly during the first 8 weeks of the active treatment phase it was of interest that tinnitus distress in the iCBT group was rated significantly lower than that of the F2F group from week 4 onwards. This was possibly related to the differences in the intensive weekly input for the iCBT group as opposed to longer follow-up periods for the F2F group.

There have been two previous non-randomized iCBT for tinnitus effectiveness studies that were both run at the Uppsala Clinic in Sweden. The within-group effect sizes were smaller than the present study at *d* = 0.5631 and *d* = 0.5832. For the present study clinical significance was achieved by 54–57% from the iCBT group and 41–46% from the F2F group at T1 and T2. This is higher than the 27%13 and 38%32 reaching clinical significance in these previous studies. Differences in ways of calculating clinical significance (50% reduction in TRQ scores versus using a RCI criteria), may have contributed to these discrepancies.

Secondary intervention effects were largest for insomnia followed by anxiety and depression for both groups. The combined results across post-intervention and follow-up,indicated that undertaking either intervention was equally effective within the boundaries of non-inferiority for tinnitus-related difficulties, except for the results for insomnia, which favoured the iCBT group. In the preceding efficacy study12 intervention effects were also greatest for insomnia. This result is of interest as a previous meta-analyses8,35 and a Cochrane review36, largely based on F2F interventions, failed to show the effectiveness of CBT used with a tinnitus population for sleep problems. In the previous iCBT non-randomized effectiveness trials, significant pre-post intervention within-group differences for insomnia, anxiety and depression were found31,32. Further work is required to identify how tinnitus interventions can further improve the results for tinnitus-related problems.

Results for both groups indicated stability of results at 2-month follow-up for both tinnitus-distress and the secondary assessment measures. Stability of results have been reported for longer follow-up periods of 6 months15, and 1 year13 when comparing iCBT with GCBT for tinnitus distress. Further studies with longer follow-up periods are required to establish the longer-term effects of these interventions.

## Intervention adherence and clinician resources

Completion rates of assessment measures (96% at T1 and 78% at T2) were equal in both groups, regardless of allocation. No demographic or clinical differences were identified between those completing assessment measures and those who did not complete these measures in the present study unlike Kaldo and colleagues32 who found that younger participants were more likely to dropout. Studies with larger sample sizes are required to further investigate these effects.

When assessing the resources required, iCBT was 2.59 times more time-effective than individualized care, when taking only clinician time into account (assuming equality of grading of the audiological professionals involved). Kaldo and colleagues13, reported that in comparison with iCBT, the therapist time was twice as long for the GCBT sessions. These sessions consisted of seven participants per group attending 120-minute group sessions. Therefore, iCBT was 1.7 times more time-effective when compared with GCBT in terms of staff time. In contrast, Jasper and colleagues15 found no difference in therapist time, largely due to more participants being included per GCBT group (10 participants) with shorter 90 minute sessions and more therapist time for the iCBT group with an average of 14 minutes per week.

### Study limitations

Running this trial led to many challenges such as difficulty recruiting a sufficient number of participants. Understandably, after following a long pathway to reach ENT and audiology services, some may have wanted to continue on this pathway and not take part in a research study. Implementing more effective recruitment strategies will be required for future effectiveness trials. The low ratio of those participating in comparison to those invited was a potential source of bias. In addition, the non-uniform nature of the clinical care received from the different study centres may have attributed to the variability found. Interpretation is limited to participants with similar demographical and clinical profiles and further generalisability of the results to other populations is not possible without further systematic replication in other settings. Moreover, some of the outcome measures selected may not have been optimal for a tinnitus population. Although the GAD-7 can identify generalized anxiety disorder, other anxiety symptoms more specific to a tinnitus population may be missed.

**Future research**

The present study focused on clinical effectiveness. More work is required to determine cost effectiveness as this information is required by stakeholders4,37. A lexicon of assessment and outcome measures for tele-mental health has been developed as a resource for the evaluation of these services38. Evaluation metrics include treatment utilisation, travel costs, stigma, anxiety, waiting times, training, and motivational readiness. Future research can use these domains to standardize approaches, to determine cost effectiveness and provide a more comprehensive comparison of services.

Although further work is required to differentiate which patients are best suited for iCBT or F2F interventions and whether including low-intensity interventions would be cost- and clinically effective, this study adds to the evidence of effectiveness of iCBT for tinnitus.

# REFERENCES

1. Baguley D, McFerran D, Hall D. Tinnitus. *The Lancet*. 2013;382(9904):1600-1607.

2. Cima RF, Vlaeyen JW, Maes IH, Joore MA, Anteunis LJ. Tinnitus interferes with daily life activities: A psychometric examination of the tinnitus disability index. *Ear Hear*. 2011;32(5):623-633. doi: 10.1097/AUD.0b013e31820dd411.

3. Goldstein E, Ho C, Hanna R, et al. Cost of care for subjective tinnitus in relation to patient satisfaction. *Otolaryngology–Head and Neck Surgery*. 2015;152(3):518-523..

4. Stockdale D, McFerran D, Brazier P, et al. An economic evaluation of the healthcare cost of tinnitus management in the UK. *BMC Health Services Research*. 2017;17(1):577.

5. Hoare DJ, Broomhead E, Stockdale D, Kennedy V. Equity and person-centeredness in provision of tinnitus services in UK national health service audiology departments. *European Journal for Person Centered Healthcare*. 2015;3(3):318-326.

6. Gander PE, Hoare DJ, Collins L, Smith S, Hall DA. Tinnitus referral pathways within the national health service in england: A survey of their perceived effectiveness among audiology staff. *BMC Health Serv Res*. 2011;11:162-6963-11-162. doi: 10.1186/1472-6963-11-162.

7. Hoare DJ, Kowalkowski VL, Kang S, Hall DA. Systematic review and meta‐analyses of randomized controlled trials examining tinnitus management. *Laryngoscope*. 2011;121(7):1555-1564.

8. Hesser H, Weise C, Westin VZ, Andersson G. A systematic review and meta-analysis of randomized controlled trials of cognitive–behavioral therapy for tinnitus distress. *Clin Psychol Rev*. 2011;31(4):545-553.

9. Andersson G, Strömgren T, Ström L, Lyttkens L. Randomized controlled trial of internet-based cognitive behavior therapy for distress associated with tinnitus. *Psychosom Med*. 2002;64(5):810-816.

10. Beukes EW, Vlaescu G, Manchaiah V, et al. Development and technical functionality of an internet-based intervention for tinnitus in the UK. *Internet Interventions*. 2016;6:6-15.

11. Beukes EW, Allen PM, Manchaiah V, Baguley DM, Andersson G. Internet-based intervention for tinnitus: Outcome of a single-group open trial. *J Am Acad Audiol*. 2017;28(4):340-351.

12. 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*. 2017.

13. Kaldo V, Levin S, Widarsson J, Buhrman M, Larsen H, Andersson G. Internet versus group cognitive-behavioral treatment of distress associated with tinnitus: A randomized controlled trial. *Behavior Therapy*. 2008;39(4):348-359.

14. Nyenhuis N, Kröner-Herwig B, Zastrutzki S, Jäger B. An internet- based cognitive- behavioural training for acute tinnitus: Secondary analysis of acceptance in terms of satisfaction, trial attrition and non-usage attrition. *Cognitive Behaviour Therapy*. 2013;42(2):139-145. doi: 10.1080/16506073.2012.724081.

15. Jasper K, Weise C, Conrad I, Andersson G, Hiller W, Kleinstaeuber M. Internet- based guided self-help versus group cognitive behavioral therapy for chronic tinnitus: A randomized controlled trial. *Psychother Psychosom*. 2014;83(4):234-246. doi: 10.1159/000360705.

16. Beukes EW, Baguley DM, Allen PM, Manchaiah V, Andersson G. Guided internet-based versus face-to-face clinical care in the management of tinnitus: Study protocol for a multi-centre randomised controlled trial. *Trials*. 2017;18(1):186.

17. Vlaescu G, Carlbring P, Lunner T, Andersson G. An e-platform for rehabilitation of persons with hearing problems. *Am J Audiol*. 2015;24(3):271-275.

18. Meikle MB, Henry JA, Griest SE, et al. The tinnitus functional index: Development of a new clinical measure for chronic, intrusive tinnitus. *Ear Hear*. 2012;33(2):153-176. doi: 10.1097/AUD.0b013e31822f67c0.

19. Newman CW, Jacobson GP, Spitzer JB. Development of the tinnitus handicap inventory. *Archives of Otolaryngology–Head & Neck Surgery*. 1996;122(2):143-148.

20. Hall DA, Haider H, Szczepek AJ, et al. Systematic review of outcome domains and instruments used in clinical trials of tinnitus treatments in adults. *Trials*. 2016;17(1):270.

21. Bastien CH, Vallières A, Morin CM. Validation of the insomnia severity index as an outcome measure for insomnia research. *Sleep Med*. 2001;2(4):297-307.

22. Spitzer RL, Kroenke K, Williams JB, Löwe B. A brief measure for assessing generalized anxiety disorder: The GAD-7. *Arch Intern Med*. 2006;166(10):1092-1097.

23. Spitzer RL, Kroenke K, Williams JB, Patient Health Questionnaire Primary Care Study Group. Validation and utility of a self-report version of PRIME-MD: The PHQ primary care study. *JAMA*. 1999;282(18):1737-1744.

24. Newman CW, Weinstein BE, Jacobson GP, Hug GA. Test-retest reliability of the hearing handicap inventory for adults. *Ear Hear*. 1991;12(5):355-357.

25. Khalfa S, Dubal S, Veuillet E, Perez-Diaz F, Jouvent R, Collet L. Psychometric normalization of a hyperacusis questionnaire. *ORL J Otorhinolaryngol Relat Spec*. 2002;64(6):436-442. doi: 67570 [pii].

26. Broadbent DE, Cooper PF, FitzGerald P, Parkes KR. The cognitive failures questionnaire (CFQ) and its correlates. *British Journal of Clinical Psychology*. 1982;21(1):1-16.

27. Diener E, Emmons RA, Larsen RJ, Griffin S. The satisfaction with life scale. *J Pers Assess*. 1985;49(1):71-75. [doi.org/10.1207/s15327752jpa4901\_13](http://dx.doi.org/10.1207/s15327752jpa4901_13).

28. Newman CW, Sandridge SA, Bolek L. Development and psychometric adequacy of the screening version of the tinnitus handicap inventory. *Otology & Neurotology*. 2008;29(3):276-281.

29. Piaggio G, Elbourne DR, Pocock SJ, Evans SJ, Altman DG, ConsoRt Group. Reporting of noninferiority and equivalence randomized trials: Extension of the CONSORT 2010 statement. *JAMA*. 2012;308(24):2594-2604.

30. Flight L, Julious SA. Practical guide to sample size calculations: An introduction. *Pharmaceutical statistics*. 2016;15(1):68-74.

31. Kaldo-Sandström V, Larsen HC, Andersson G. Internet-based Cognitive—Behavioral self-help treatment of tinnitus: Clinical effectiveness and predictors of outcome. *Am J Audiol*. 2004;13(2):185-192.

32. Kaldo V, Haak T, Buhrman M, Alfonsson S, Larsen H, Andersson G. Internet-based cognitive behaviour therapy for tinnitus patients delivered in a regular clinical setting: Outcome and analysis of treatment dropout. *Cognitive behaviour therapy*. 2013;42(2):146-158.

33. Cohen J. A power primer. *Psychol Bull*. 1992;112(1):155.

34. Jacobson NS, Truax P. Clinical significance: A statistical approach to defining meaningful change in psychotherapy research. *J Consult Clin Psychol*. 1991;59(1):12.

35. Andersson G, Lyttkens L. A meta-analytic review of psychological treatments for tinnitus. *Br J Audiol*. 1999;33(4):201-210.

36. Martinez‐Devesa P, Perera R, Theodoulou M, Waddell A. Cognitive behavioural therapy for tinnitus. *The Cochrane Library*. 2010.

37. Cima R, Joore M, Maes I, et al. Cost-effectiveness of multidisciplinary management of tinnitus at a specialized tinnitus centre. *BMC health services research*. 2009;9(1):29.

38. Shore JH, Mishkind MC, Bernard J, et al. A lexicon of assessment and outcome measures for telemental health. *Telemedicine and e-Health*. 2014;20(3):282-292.

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Figure 3: Weekly Tinnitus Handicap Inventory-screening scores for each group across the first 8 week period intervention period between T0 and T1. Error bars represent the ±1 standard error of the mean.

**Online-Only supplements**

eTable 1: The CONSORT Checklist for non-inferiority trials

**Table 1 Demographical characteristics of the participants**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Category | Description | Experimental group (n = 46)  | Control group (n = 46)  | Overall (n = 92) |
| Sex | No. Male (%) No. Female (%) | 29 (63)17 (37) | 26 (57)20 (44) | 55 (60)37 (40) |
| Age  | Mean years(SD)Range in years | 50.65 (12.19)26–79  |  55.26 (11.62)29–76  | 52.96 (12.07)26–79  |
| Tinnitus duration | Mean years (SD)Range in years | 5.23 (9.01)0.4–40  | 7.85 (9.62)0.4–50  | 6.54 (9.25)0.4–50  |
| Using hearing aids  | No. Not using (%)No. Using (%) | 27 (5)19 (41) | 27 (59)19 (41) | 54 (59)38 (41) |

**Table 2 Group comparisons over time**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Measure | Group | Means (Standard deviation) | Group comparison, *P* value\* | Within-group analysis |
|  | **T0**  | **T1** | **T2** | **Time by group interaction** | **Within-group time effect** | **Between-group effect** | **T0**–**T1****Cohen’s *d*** **(95% CI)** | **T0**–**T2****Cohen’s *d* (95% CI)** |
| TFI | **iCBT** | 55.01 (21.58)  | 27.88 (20.84) | 22.85 (19.26) | *P* = 0.36 | *P* < 0.001\* | *P* = 0.072 | 1.28 (0.81-1.72) | 1.56 (1.06–2.04) |
| **F2F** | 56.57 (20.61) | 34.88 (24.91) | 32.51 (23.28) | 0.95 (0.51–1.38) | 1.10 (0.63–1.56) |
| THI | **iCBT** | 44.57 (23.40) | 22.33 (19.63) | 17.78 (14.77) | *P* = 0.38 | *P* < 0.001\* | *P*=0.022\* | 1.08 (0.63–1.51) | 1.28 (0.80–1.74) |
| **F2F** | 47.13 (20.31) | 28.74 (20.07) | 27.11 (21.62) | 0.96 (0.55–1.38) | 1.05 (0.58–1.50) |
| ISI | **iCBT** | 11.43 (6.36) | 6.71 (6.20) | 5.69 (4.64) | *P* = 0.33 | *P* < 0.001\* | *P* = 002\* | 0.75 (0.32–1.17) | 1.01 (0.55–1.46) |
| **F2F** | 13.65 (6.62) | 9.55 (6.15) | 10.03 (6.88) | 0.65 (0.21–1.06) | 0.54 (0.09–0.97) |
| GAD-7 | **iCBT** | 6.43 (5.64) | 3.45 (3.66) | 3.33 (3.21) | *P* = 0.56 | *P* < 0.001\* | *P* = 0.67 | 0.62 (0.20–1.04) | 0.66 (0.21–1.09) |
| **F2F** | 6.78 (5.54) | 3.33 (3.78) | 3.42 (3.60) | 0.72 (0.29–1.14) | 0.70 (0.25–1.14) |
| PHQ-9 | **iCBT** | 6.50 (5.48) | 3.67 (3.64) | 2.78 (3.02) | *P* = 0.55 | *P* < 0.001\* | *P* = 0.042 | 0.61 (0.18–1.02) | 0.82 (0.36–1.26) |
| **F2F** | 7.98 (6.05) | 4.19 (4.08) | 4.97 (4.54) | 0.73 (0.30–1.15) | 0.55 (0.11–0.99) |
| HHIA-S | **iCBT** | 11.74 (10.66) | 10.10 (10.82) | 9.11 (11.59) | *P* = 0.98 | *P* = 0.006\* | *P* = 0.23 | 0.15 (-0.26–0.57) | 0.24 (-0.20–0.67) |
| **F2F** | 14.30 (11.58) | 12.14 (10.71) | 12.00 (9.56) | 0.19 (-0.22–0.61) | 0.21 (-0.22–0.65) |
| HQ | **iCBT** | 15.65 (9.06) | 12.24 (7.61) | 12.51 (9.01) | *P* = 0.94 | *P* < 0.001\* | *P* = 0.68 | 0.41 (-0.01–0.82) | 0.35 (-0.09–0.78) |
| **F2F** | 16.54 (7.42) | 13.40 (7.29) | 12.94 (7.51) | 0.43 (0.01–0.84) | 0.48 (0.04–0.92) |
| CFQ | **iCBT** | 34.93 (14.38) | 30.83 (12.14) | 30.06 (12.89) | *P* = 0.91 | *P* = 0.009\* | *P* = 0.32 | 0.31 (-0.11– 0.72) | 0.35 (-0.08–0.79) |
| **F2F** | 39.65 (19.31) | 35.56 (19.23) | 33.06 (19.24) | 0.21 (-0.20– 0.62) | 0.34 (-0.10–0.77) |
| SWLS | **iCBT** | 18.70 (5.73) | 20.10 (4.96) | 21.00 (5.05) | *P* = 0.44 | *P* = 0.04\* | *P* = 0.61 | 0.26 (-0.16– 0.67) | 0.43 (0.00–0.84) |
| **F2F** | 19.48 (5.54) | 20.05 (5.61) | 20.50 (4.95) | 0.10 (-0.31–0.51) | 0.19 (-0.24–0.62) |

Acronyms: CI: confidence interval, T0: pre-intervention, T1: post-intervention, T2: follow-up, TFI: Tinnitus Functional Index, ISI: Insomnia Severity Index, GAD: Generalised Anxiety Disorder, PHQ: Patient Health Questionnaire, HHIA-S: Hearing Handicap Inventory for Adults-screening version, HQ: Hyperacusis Questionnaire, CFQ: Cognitive Failures Questionnaire, SWLS= Satisfaction with Life Scales



Figure 1: CONSORT Study profile



Figure 2: Mean between-group difference in scores between baseline and follow-up for each assessment measure with the 95% confidence interval. The between-group effect size (Cohen’s *d*) and the 95% confidence intervals (CI) are provide on the right side of the graph.



Figure 3: Weekly Tinnitus Handicap Inventory-screening scores for each group across the first 8 week period intervention period between T0 and T1. Error bars represent the ±1 standard error of the mean.

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## Author Contributions

All authors participated in the design for this clinical trial. EB was the study investigator and collected and analysed the data. EB drafted the manuscript and all other authors critically reviewed and approved the manuscript for submission.

## Conflict of Interest Disclosures

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