Submitted manuscript

Audiologist Guided Internet-Based Cognitive Behaviour Therapy for Adults With Tinnitus in the United Kingdom: a Randomised Controlled Trial

Eldré W. Beukes,[1] David M. Baguley,[1,2] Peter M. Allen,[1,3] Vinaya Manchaiah,[4,5,6] and Gerhard Andersson[5,7]

1. Department of Vision and Hearing Sciences, Anglia Ruskin University, Cambridge, United Kingdom
2. National Institute for Health Research, Nottingham Hearing Biomedical Research Unit, Ropewalk House, 113 The Ropewalk, Nottingham, NG1 5DU
3. Vision and Eye Research Unit, Anglia Ruskin University, Cambridge, United Kingdom
4. Department of Speech and Hearing Sciences, Lamar University, Beaumont, Texas, USA
5. Department of Behavioral Sciences and Learning, Linköping University, Linköping, Sweden
6. Audiology India, Mysore, Karnataka, India
7. Department of Clinical Neuroscience, Division of Psychiatry, Karolinska Institute, Stockholm, Sweden

Address for correspondence:

Eldré W. Beukes, Department of Vision and Hearing Sciences, Faculty of Science and Technology, Anglia Ruskin University, Cambridge CB1 1PT, UK. E-mail: eldre.beukes@anglia.ac.uk

Keywords: Tinnitus, tinnitus treatment, e-Health, Internet-intervention, cognitive behavioural therapy

Conflicts of Interest and Financial disclosures: Anglia Ruskin and Linköping Universities supported the undertaking of this trial. No conflict of interest declared.

Abbreviations

ANCOVA: Analysis of covariance

CBT: Cognitive Behavioural Therapy

CFQ: Cognitive Failures Questionnaire

CONSORT: Consolidated Standards of Reporting Trials

GAD-7: Generalized Anxiety Disorder

GP: General Practitioner

HCPC: Health and Care Professions Council

HHIA-S: Hearing Handicap Inventory for Adults - Screening Version

HQ: Hyperacusis Questionnaire

NHS: National Health System

iCBT: Guided Internet-based Cognitive Behavioural Therapy Intervention

ISI: Insomnia Severity Index

PHQ-9: Patient Health Questionnaire

RCT: Randomized Control Trial

RCI: Reliable Change Index

SPIRIT: Standard Protocol Items, Recommendations for Interventional Trials

SPSS: Statistical Package for Social Sciences

SWLS: Satisfaction with Life Scales

TFI: Tinnitus Functional Index

THI-S: Tinnitus Handicap Inventory - Screening Version

UK: United Kingdom

WCI: Weekly Check-In Control Group

Abstract

Objectives

Specialist tinnitus services are in high demand due to the effects tinnitus may have on quality of life. Additional cost and clinically effective tinnitus management routes are imperative, due to constraints on current healthcare systems. One such route is providing Cognitive Behavioural Therapy for tinnitus via the Internet (iCBT). This study aimed to determine the efficacy of guided iCBT using Audiological support on tinnitus distress and tinnitus related comorbidities in the UK. Furthermore, it aimed to establish the stability of treatment effects two months postintervention. Lastly, the study aimed to identify for which populations of those with tinnitus this form of intervention may be most appropriate. The hypothesis was that iCBT for tinnitus would be more effective at reducing tinnitus distress than weekly monitoring.

Design

A randomised, delayed treatment efficacy trial, with a two-month follow-up was implemented to evaluate the efficacy of iCBT in the UK. After being stratified for tinnitus severity and age, adults experiencing tinnitus distress were randomly assigned to guided

iCBT (n = 73) or to a weekly check-in (WCI) group (n = 73). Once the iCBT group completed treatment, the WCI group underwent the same intervention. Standardised self-reported outcome measures for tinnitus distress, hearing handicap, insomnia, anxiety, depression, hyperacusis, cognitive failures and satisfaction with life were used to assess outcome. Outcome measures were completed immediately postintervention and two months posttreatment.

Results

Undertaking the iCBT intervention led to significant reduction in tinnitus distress, which were supported by medium effect sizes (Cohen's d = 0.69). This iCBT intervention was also effective at reducing insomnia, anxiety, depression, hyperacusis, cognitive failures and increasing life satisfaction, as supported by small to medium effect sizes (Cohen's d = 0.27-0.55). The only significant predictor of outcome was a higher initial tinnitus severity score. Treatment effects were stable two months posttreatment for tinnitus and related comorbidities.

Conclusions

Guided iCBT for tinnitus using Audiological support in the UK has shown to be effective at reducing tinnitus distress and associated symptoms, especially in those with higher tinnitus

severity scores. These effects remained stable two months postintervention. Further studies to determine the longer-term efficacy of iCBT and compare iCBT with standard clinical care in the UK are required.

Keywords

Tinnitus, tinnitus treatment, e-Health, internet-intervention, cognitive behavioural therapy

INTRODUCTION

Most healthcare in the United Kingdom is provided by publically funded National Health Service (NHS) systems and is largely free at the point of use. General Practitioners (GPs) provide primary healthcare and refer patients to specialist services as required. Recently the NHS has experienced challenges due to funding constraints together with an ever-growing demand for its services (Smith et al. 2014). This has led to an increase in appointment waiting times, which has been associated with poorer outcomes for a variety of health issues (e.g., Pizer & Prentice, 2011; Smith et al. 2014). For patients experiencing significant levels of health-related distress, such as those with chronic tinnitus, minimizing waiting times should be prioritized (Gander et al. 2011).

Tinnitus, being the sensation of sound in the absence of a corresponding external acoustic stimulus (Baguley et al. 2013), may be perceived on a spectrum from barely noticeable to debilitating (Brüggemann et al. 2016). For those who are severely affected, experiencing tinnitus may occur together with a wide range of associated symptoms such as sleep disturbance, concentration difficulties, irritation, frustration, anxiety and depression (Langguth et al. 2011). There are an estimated ¾ of a million people in England visiting their GPs each year with tinnitus as the primary complaint (El-Shunnar et al. 2011). Of these, only 37% on average are being referred for specialist services (El-Shunnar et al.

2011). In addition, those referred often have a substantial wait of up to 18 weeks before a treatment pathway, such as obtaining tinnitus counselling, commences (Department of Health, 2009). A further constraint in tinnitus management in the UK is that the treatment with the most evidence of efficacy, namely CBT (see Hesser et al. 2011) is not readily available for those with tinnitus, largely due to a shortage of trained specialists (Baguley et al. 2013). Moreover, specialist tinnitus services are not available in all NHS hospitals across the UK, leaving many with distressing tinnitus without any specialised treatment options (Hoare et al. 2015).

The need for widely available cost and clinically effective tinnitus treatments is evident worldwide, and not isolated to the UK (Andersson, 2016). To increase access to effective tinnitus treatments in Sweden, guided cognitive behavioural therapy is provided via the Internet (iCBT; Andersson, 2015). An important component of iCBT is that patients are supported by a therapist they can communicate with online. This therapeutic support has been provided by Clinical Psychologists, trained to provide CBT. As iCBT has been found to be effective at reducing tinnitus and associated problems (e.g., Andersson et al. 2002; Kaldo et al. 2008; Hesser et al. 2012; Kaldo et al. 2013), it has been incorporated into regular clinical care in Sweden (Kaldo-Sandström et al. 2004; Kaldo et al. 2013). Following the proven efficacy of iCBT in Sweden, efficacy was also demonstrated in clinical trials in

Germany (Nyenhuis et al. 2013, Jasper et al. 2014; Weise et al. 2016). In contrast to the success of iCBT in Sweden and Germany, no significant benefits were found when using the translated English iCBT version compared with an information-only control programme (without CBT content) on an industrial population in Australia (Abbott et al. 2009). Possible contributing factors for the lack of success included relatively low levels of baseline tinnitus distress and cultural attitude differences towards test-based Internet-based learning. Moreover, the intervention was offered from a commercial company website and not from a research or clinical facility.

Applying iCBT as an additional treatment route to complement existing tinnitus pathways for those with tinnitus in the UK has numerous potential benefits. These include improving access to CBT for tinnitus in a comprehensive evidence-based format. As there are fewer resources required, the burdens on specialist services can be reduced. Although there are advantages, further evidence is required regarding iCBT for tinnitus and who is most likely to respond to treatment for tinnitus via the Internet. To date there have been few consistent predictors of outcomes for Internet-interventions (Andersson & Herdman, 2013). Age, education, gender or level of computing skills have not been found to predict outcomes (Andersson et al. 2009). Kaldo-Sandström et al. (2004) found treatment compliance, external referral to the treatment and the number of earlier treatments for tinnitus were associated with

more positive outcomes for iCBT for tinnitus. Further exploring predictors of outcome is required if iCBT for tinnitus is to be considered as a treatment route in the UK.

There are, however, potential difficulties of using the Swedish iCBT programme in the UK. These include using Clinical Psychologists to provide therapeutic guidance, as this model would not fit in the UK where Audiologists play a significant role in tinnitus healthcare provision (Hoare et al. 2015). A further concern would be that a largely text-based intervention would not appeal to a UK population who are accustomed to face-to-face interventions. These potential barriers to usage would need to be minimised if iCBT is to be viewed as a credible treatment for tinnitus distress in the UK. With this in mind, a multi-professional collaboration with a broad skill set, consisting of the authors of this paper was formed to guide redeveloping iCBT for a UK population. The intervention was based on the CBT self-help programme designed by Kaldo et al. (2007). A comprehensive, user-friendly, tailored intervention was designed by Beukes et al. (2016a), using an interactive approach in which active involvement is encouraged. Following this development, the intervention underwent rigorous technical functionality and satisfaction testing. Results indicated that this version was highly rated for suitability, content, presentation, usability and exercises provided by both expert reviewers with an established background in tinnitus management and adults with significant levels of tinnitus distress. In addition, the feasibility of iCBT in

the UK in terms of recruitment, attrition and compliance rates was established using a single-group open trial design (Beukes et al. 2016b).

In a UK context, delivering iCBT guided by an Audiologist would be optimal, but the feasibility of iCBT by a non-Psychological professional is unproven. The clinical efficacy of this redeveloped iCBT intervention in the UK has also not yet been established. This trial set out to explore the use of iCBT in the UK with the following objectives:

1. To evaluate the efficacy of iCBT guided by an Audiologist, compared with that of a weekly check-in group (WCI) at reducing tinnitus distress and associated comorbidities
2. To determine iCBT treatment effects two months postintervention
3. To ascertain predictors of outcome for whom this iCBT intervention is a suitable intervention

MATERIALS AND METHODS

Study design

A randomised, delayed treatment efficacy trial, with a two-month follow-up was implemented to evaluate the efficacy of iCBT in the UK. The iCBT *Experimental Group* received treatment for 8 weeks, while the weekly check-in (WCI) *Control Group* were

monitored by means of the Tinnitus Handicap Inventory- Screening Version (THIs; Newman et al. 2008). Once the iCBT group completed treatment, the WCI group underwent the same intervention. The WCI group, thus, had a delay of 8 weeks before obtaining treatment. This delay is, however, less than the 18 weeks wait they may have if they were obtaining treatment within standard pathways on the NHS.

The Consolidated Standards of Reporting Trials (CONSORT) eHealth guidelines (Eysenbach et al. 2011) were used to report this study.

Ethical considerations

Ethical approval was granted by the Faculty Research Ethics Panel of Anglia Ruskin University (FST/FREP/14/478) and the study was registered with Clinical Trials.gov: NCT02370810, date 05/03/2015. It was conducted in accordance with good clinical practice together with the ethical principles of the Declaration of Helsinki. For the full study protocol, see Beukes et al. (2015). A protocol was established to ensure the security of participants' confidentiality when using the web-portal, complying with European guidelines for Internet studies. There were no changes to the methods or outcome measures used after trial commencement.

Study population

Recruitment

Recruitment was UK wide and targeted people from various demographical backgrounds with significant levels of tinnitus distress. Study information was available in various formats including: online (e.g., the NHS Choices and clinicaltrials.gov websites), Twitter (British Tinnitus Association), Facebook forums (e.g., Action on Hearing loss, Thyroid UK), Newspapers, and Magazines (e.g., Mature Times, People's Friend, Musicians Union bulletin, New Scientist, National Federation of Occupational Pensioners Magazine, Cambridge News), support groups (e.g., tinnitus, thyroid) and from professionals (GP surgeries, Audiologists).

Sample size

Sample size estimation was calculated using G*Power version 3.1.6 and based on achieving a clinically relevant change between baseline and postintervention using the primary outcome measure, the Tinnitus Functional Index (TFI; Meikle et al. 2012). Calculations based on pilot data indicated the need for fewer participants than calculations using the 13 point (SD 24.7) difference suggested during the development of the TFI. For the present study, estimates were based on these less conservative values. This indicated that 58 participants were required per group, with an allocation ratio of 1:1, to achieve a two-sided

significance level of 0.05 and a standardized mean difference effect size of 0.80. An additional 15 participants were allocated to each group to account for possible drop-outs. Therefore, 73 participants were recruited to each arm.

Strategies to minimise attrition rates were applied as recommended by Dziura et al. (2013). These included data collection not requiring face-to-face visits and regular contact with participants during the trial. Participants were informed of their right to withdraw at any stage without penalty.

Participants

Those interested in the study-registered interest on the study website (www.tacklingtinnitus.co.uk). When the recruitment commenced, they were invited to partake and this recruitment process lasted two weeks. Eligibility for the study was determined in a two-stage process. Initially, participants completed the baseline measurements online. Following completion, a telephonic screening was arranged, to ensure participants fulfilled the study requirements, which were as follows:

Inclusion Criteria

i) Aged 18 years and over living in the UK

ii) Computer and internet access and the ability to use these

iii) The ability to read and type in English

iv) Tinnitus for a minimum duration of 3 months

v) Tinnitus outcome measure scores indicating the need for tinnitus care (26 or above on the Tinnitus Functional Index (Meikle et al. 2012).

Exclusion Criteria

i) Reporting any major medical, psychiatric or mental disorder which may hamper commitment to the programme

ii) Reporting pulsatile, objective or unilateral tinnitus, which have not been investigated medically

iii) Tinnitus as a consequence of a medical disorder, still under investigation

iv) Undergoing any tinnitus therapy concurrently to partaking in this study

Enrolment and randomisation

Participants were randomly assigned and enrolled to either the control or experimental group at a 1:1 allocation by an independent researcher using a randomization sequence generated by computer algorithm (http://www.randomizer.org/). To prevent an unequal

distribution among groups, participants were prestratified on the factors of age (<= 60 or >60 years) and tinnitus severity (TFI <= 50 or >50). Block randomization, with blocks of four, were applied to ensure equal groups sizes within each stratum. Following allocation, participants were informed when their treatment would commence by the principle investigator, but not which group they had been assigned to. Due to the trial design the investigator was not masked to the assignment of interventions.

Study Outcomes

The self-reported study outcomes were carefully selected to evaluate the efficacy of iCBT on both tinnitus distress and associated difficulties such as insomnia, concentration problems, hearing disability, sound sensitivity, anxiety, depression, and quality of life, as shown in Table 1. Outcomes were completed online at baseline (T_0), posttreatment after the iCBT group completed their treatment and at follow-up (T_1) two months later after the control group undertook the treatment (T_2).

The TFI was selected as the main outcome measure, as it was designed to assess tinnitus severity and assess treatment responsiveness (Kamalski et al. 2010). As a secondary tinnitus measure, the screening version of the Tinnitus Handicap Inventory (THIs) was used, as scores are comparable (r=.90) with the full version of the THI (Newman et al. 2008). The

THIs was also used weekly during the active treatment phase to monitor levels of tinnitus severity of time. Outcome measures were used with permission of the copyright holders, and agreements were established for those that are not freely available to use, such as the TFI and Insomnia Severity Index (ISI). Online administration was used throughout the trial, as equivalent psychometric properties apply between computer and paper questionnaire delivery, with high test-retest reliability and completion rate on the internet (Thoren et al. 2012). To improve attrition rates at follow-up, reminder emails were sent to encourage participants to complete the questionnaires.

Study Intervention

The treatment was based on a self-help programme originally developed by Andersson and Kaldo (2004). This content was redeveloped into an interactive e-learning version, to ensure it was visually stimulating, engaging and responsive to both computer and mobile devices (Beukes et al. 2016a). The web-based treatment platform used was designed in-house at Linköping University, Sweden, complying with a high level of data security and encrypted communications (Vlaescu et al. 2015). The treatment ran over an eight-week period, during which 2-3 modules were released on a weekly basis. These included key CBT techniques such as an applied relaxation programme, thought analysis, cognitive restructuring, imagery and exposure techniques. Audiological principles found to be effective for tinnitus such as

sound enrichment, hearing tactics and advice for sound sensitivity were also included. The treatment was tailored so that participants could select from additional option modules including concentration tips and sleep management, if they were having difficulties in the areas covered by these modules. If initial baseline scores were significant in areas covered by these optional modules, the clinician recommended going through these modules. CBT principles such as goal setting, a clear structure, active participation, relapse prevention and setting a time-frame for the therapy were incorporated (Beck, 2011). Each module accommodated a variety of learning styles by including written information, diagrams, pictures, videos, frequently asked questions, step-by-step guides, quizzes, worksheets to keep track of progress and suggested techniques to apply in daily life. Each module could be read online, downloaded to read offline or printed. A key element was a secure messaging system, enabling participants to ask questions and allow the therapist to provide feedback.

Therapist

As this was a guided intervention, participants had access to an Audiologist throughout the programme. The therapist's role was to conduct the telephone interviews, introduce weekly modules, provide feedback, answer queries, provide guidance, support and encourage engagement. To maintain consistency with the standard approach of tinnitus therapy being

delivered within the audiology community in the UK, an experienced Audiological Scientist, registered with the Health and Care Professions Council (HCPC), and appropriately trained to Masters Level in Audiology, undertook the role of supporting the participants. The therapist was experienced in managing tinnitus patients both in a clinical setting and online and had a suitable understanding of CBT principles. Feedback was provided using an encrypted messaging system within the intervention and by telephone when required.

Data Analysis

The Statistical Package for Social Sciences (SPSS) version 23.0 was used and the data analyst was masked to the groups, to minimise bias. An intention-to-treat paradigm was used, as this analysis is less susceptible to bias than complete case analysis techniques. Missing follow-up data were analyzed using Little's missing completely at random test (Little, 1988).

For all analyses, a two-tailed significance level of < 0.05 was considered statistically significant. One-way analysis of covariance (ANCOVA) was conducted for this study, to support analysis of pooled imputed data and controls for the effect of covariates that may affect the outcomes (Vickers & Altman, 2001). The independent variable, baseline TFI

scores as well as age were included as covariates for the various dependent variables. Effect sizes (Cohen's *d*) were calculated by dividing the mean differences by the pooled standard deviations.

One way repeated measures ANOVAs were used to determine the effects of the intervention over time for within-subject variables. Chi-Squared tests were used to evaluate the relationship between categorical variables. The Wilcoxon-Mann-Whitney test was used to determine if there was a difference between groups when non-parametric data were analyzed.

Partial correlations were performed, to determine the relationship between posttreatment scores while controlling the effects of additional variables. The reliable change index (RCI; Jacobson & Truax, 1991) was used as a means of calculating clinical significance for the TFI. This was calculated using the pretreatment standard deviation, and a test-retest reliability coefficient of 0.78, as reported in the validation study (Meikle et al. 2012). The internal data monitoring committee had access to the data and ensured correct interpretation and analysis thereof.

RESULTS

Participant Characteristics

There were 244 people registered on the study waiting list, which had been activated two months prior to the study starting. Of these 169 completed the screening questionnaire, within two weeks of the study commencing. Not all persons interested in the study met the inclusion criteria, in most instances due to their TFI score being below 26. A total of 146 participants were eligible for the study and were randomly assigned to the iCBT (n = 73) and WCI groups (n = 73) as shown in the CONSORT diagram (Fig. 1). Baseline demographical and clinical characteristics of the participants are shown in Table 2. This demographic profile demonstrated that the groups were well matched, with more male participants overall and an average age of 55.6 years (SD 12.9). A range of participants with different educational and employment backgrounds, as well as varying tinnitus experiences were drawn to the study. ANCOVAs revealed that there were no significant differences in clinical variables for any of the outcome measurement between the two groups and Chi-Square tests indicated that there were also no baseline differences between demographical variables between the two groups regarding gender, age, education, employment or tinnitus duration variables.

Attrition and missing data

Missing data analysis indicated that data were missing 'completely at random' [$\chi 2(55) = 42.4$, $p = 0.89$], demonstrating that there was no relationship between missing and observed data. Missing data were imputed through the multiple imputation procedure offered by SPSS using Markov Chain Monte Carlo method using five imputation runs. These results were compared with those obtained with a per-protocol analysis. As there were no difference, the intention-to-treat results are reported. Pooled results are discussed where available, otherwise, the first imputed set of results are reported.

Completion rates for the postintervention and follow-up questionnaires are seen in Table 3. Significant between-group difference were found in completion rates at postintervention (T1; after the iCBT group completed treatment, prior to the WCI group commencing treatment). More participants from the WCI group completed the questionnaire compared with the iCBT group. In contrast, there was no significant differences in completion rates at the follow-up assessment (T2) after both groups received the treatment.

When comparing baseline demographical characteristic of age, gender, employment status and level of education and clinical characteristics from the baseline measurements, there

were no significant differences between completers and non-completers. No harms or unintended effects evident from any participants.

Analysis of efficacy of iCBT versus weekly monitoring

Descriptive statistics based on imputed data for all outcome measures together with the level of significance and effect size are shown in Table 4. When performing ANCOVAs on all outcome measures the assumptions that the covariate did not differ between the two groups as well as the assumption of homogeneity between the groups and independent variables was met.

When comparing posttreatment scores between groups, there was a significant effect after controlling for age and pretreatment scores for all outcome measure except the HHIA-S. After completing the iCBT treatment, significant improvements were evident for tinnitus distress and associated problems, when compared with that of the WCI group who had not undergone the intervention. These findings were supported by medium between-group effect sizes for both tinnitus questionnaires and the ISI. Small effect sizes were seen for anxiety, depression, SWLS, Hyperacusis and CFQ questionnaires.

For the main outcome measure, there was a mean difference of 21.12 in the prepost scores for the TFI. The RCI indicated that a change of 23.34 in the TFI score was required postintervention to be considered clinically significant. For those completing the intervention, this was reached by 50.79% of participants (n = 32/63) of the experimental group posttreatment. There were 41.27% (26/63) participants with postintervention TFI scores below the level of requiring intervention (< 26) and who had a reliable change of 23.34.

ANCOVA results indicated that there were no between-group differences once both groups had undergone iCBT, at the follow-up assessment, except for ISI [$F(1,144) = 4.34$; $p = 0.04$], with Cohen's d showing a small effect size of 0.36. This indicated that both groups showed equal levels of improvement once they had both undertaken the treatment, except for the ISI scores, which continued to show further improvements over time for the group who had iCBT first.

One way repeated measures indicated that there was a significant treatment effect for all outcome measures, including the HHIA-S for the WCI group after undergoing the intervention [$F(1,72) = 11.44$, $p = 0.001$]. The HHIA-S was not significant for the iCBT group at posttreatment.

Stability of treatment effects

One way repeated measures indicated that there was no significant difference in the TFI scores between the postassessment and follow-up assessment for the iCBT group, indicating that treatment effects were maintained over a 2 month period as seen in Figure 2. Likewise, improvements were maintained for secondary outcomes measures, as illustrated in Figure 3 for the anxiety and depression outcome measures. At the follow-up assessment, scores for the ISI had further improved between posttreatment and the follow-up assessment. [$F(1,72) = 31.17$, $p = 0.0001$].

Weekly monitoring

The THI-S was used to monitor both groups during the first 8 weeks of the active treatment phase. No differences between these scores were found between the groups during the first three weeks of the intervention. For weeks 4-8 there were significant between-group differences, with the iCBT group indicating significantly lower levels of tinnitus severity [e.g., week 8: $F(1,145) = 24.56$, $p = 0.0001$] as seen in Figure 4. This indicated that after undergoing the iCBT intervention for 4 weeks, tinnitus severity had decreased significantly for the iCBT group.

Possible outcome predictors

Partial correlations were calculated to aid determining which preintervention factors may indicate possible outcome predictors for the favourable posttreatment TFI results. There was a significant positive correlation between pre- and postintervention TFI score [$r(31) = .533$, $p = 0.001$], whilst controlling for the effects of additional variables such as age, gender, tinnitus duration, educational level, and employment status. A higher level of tinnitus severity preintervention was considered a possible predictor of outcome. There were no significant correlations found between the final TFI score and level of education, employment status, and duration of having tinnitus, age or gender, whiles controlling for the effects of additional variables.

Discussion

Treatment effects

The aim of this randomised control trial was to evaluate the efficacy of guided iCBT for tinnitus in a UK population using Audiological support. Results show that iCBT led to significantly greater improvements in tinnitus distress, compared with a WCI group. This result is supported by medium between-group effect sizes and the finding of 50.79% of participants meeting the criteria for reliable change for the TFI. These results are comparable to the findings in the initial feasibility study, indicating a similar mean

difference of 19.04 points (present trial 21.12 points) in the pre-post treatment TFI scores and RCI of 23.96 (present trial 23.34).

Previous studies of iCBT have used varying tinnitus outcome measures such as the Tinnitus Reactions Questionnaire (TRQ; Wilson et al. 1991), Tinnitus Handicap Inventory (Newman, Jacobson, & Spitzer, 1996) or Tinnitus Questionnaire (TQ; Hiller et al. 1994) with various study designs, thereby making direct comparisons difficult. The pooled effect size of previous iCBT control studies (Andersson et al. 2002; Abbot et al. 2009; Hesser et al. 2012; Nyenhuis et al. 2013; Jasper et al. 2014) was Hedges $g = 0.58$, although a later study by Weise et al. (2016) was not included. Weise et al. (2016) found an effect size of Hedge's $g = 0.83$ for tinnitus distress postintervention when using the THI. The medium effect size found of Hedge's $g = 0.68$ for the present study is, therefore, between the values of previous iCBT studies for tinnitus. This provides encouraging evidence that using an Audiologist to provide iCBT is an effective means of delivering iCBT. Internet-based studies for depression, anxiety and social phobia have also found comparable results, regardless of whether the therapist was a clinician or a technical assistant (Titov et al. 2009; Robinson et al. 2010; Titov et al. 2010). It appears as though there are other factors unrelated to the therapist that affect intervention outcomes. These factors need further exploration in future research studies.

In addition to iCBT reducing tinnitus distress, significant improvements were found for anxiety, depression, insomnia, cognitive failures, hyperacusis and satisfaction with life. For the iCBT experimental group, there was no difference found in hearing handicap, however, there were significant differences postintervention after the WCI control group completed the treatment. Further trials will be required to fully investigate the intervention effects on hearing handicap. This study has assessed those with tinnitus in a more holistic nature, as previous studies have focused on sleep, anxiety, and depression. These studies have also indicated that iCBT reduced these associated effects (Kaldo-Sandström et al. 2004; Kaldo et al. 2008; Jasper et al. 2014; Weise et al. 2016).

Stability of treatment effects

A further aim of the study was to examine the stability of treatment effects following iCBT. It was encouraging that treatment effects were stable two months postintervention for both tinnitus and secondary effects. With regards to the ISI, further improvements were evident two months after the intervention was completed, indicating that over time quality of sleep continued to improve. Determining longer-term effects of the intervention will be required to further monitor intervention outcomes.

When comparing participants on a weekly basis, it was found that once they were half way through the intervention (i.e., week 4-8), those receiving treatment had significantly lower tinnitus severity scores than those not undergoing the intervention. Communicating this with prospective participants is important so that they do not expect immediate improvements.

Outcome predictors

An important aim of this study is to determine for which patient profiles, iCBT may be a suitable form of intervention. From this present study, the only predictor of outcome was the baseline TFI score, with a higher initial baseline score indicating a greater drop in TFI score posttreatment. This is interesting, as it may be predicted that those with very severe tinnitus would need to be seen for face-to-face therapy instead, however, at present, the study suggest that a higher TFI score does not exclude participants from this form of treatment, in fact they may be the most suitable. Previous iCBT trials have not investigated the impact of tinnitus severity on outcomes. Finding related to severity for other Internet interventions have been mixed as higher baseline symptom levels was shown to led to better treatment adherence for depression prevention intervention (Calear et al. 2013), whilst lower severity of social anxiety disorder was associated with better post-treatment outcomes (Nordgreen et al. 2011).

It may also have been predicted that certain age groups would have better outcomes as they either have more time to do the intervention or have better computing skills. Again, this was not found to be the case, as has been reported previously by Andersson et al. (2009). This indicating that this intervention is applicable to most adults experiencing tinnitus. Identifying moderators and mediators of outcome for iCBT requires further exploration. Lindner et al. (2016) investigated whether greater cognitive flexibility (the ability to simultaneously consider several concepts and tasks and switch effortlessly between them) would result in greater treatment gains. Findings suggested that iCBT outcome was not influenced by cognitive flexibility. A high level of motivation and the ability to work independently may, however, be a factor (Macea et al. 2010), and should be further explored in subsequent studies.

More males than females partook in this study, which is of interest as tinnitus annoyance is greater in women (Seydel et al. 2013). An internet-based intervention may be particularly appealing to men who may prefer the flexibility provided by iCBT. Furthermore, they may place more value on the ability to working independently.

Study implications

Guided iCBT for tinnitus using Audiological support in the UK has shown to be effective at reducing tinnitus distress and associated symptoms, especially in those with higher tinnitus severity scores. Including guided iCBT as a treatment route to complement existing treatment pathways, should be considered. This could have numerous advantages, such as including access to CBT for tinnitus, which is not readily available in clinics (Hoare et al. 2015). Significant cost saving can be made, as fewer resources and less therapeutic time is required for treatment via the Internet. Referrals can be streamlined to ensure that those in most need of face-to-face interventions are seen in a timelier manner. For those who find traveling difficult or have difficulty taking time off work for hospital appointments, an Internet Intervention may be more convenient, flexible and accessible. Using Audiologists to guide participants also creates consistency between those receiving hospital-based and Internet-based treatment.

Strengths and limitations of the study

Guided iCBT for tinnitus using Audiological support in the UK has shown to be effective at reducing tinnitus distress and associated symptoms, especially in those with higher tinnitus severity scores. These effects remained stable two months postintervention.

This study has been of great value in indicating the efficacy of iCBT for those experiencing tinnitus in the UK. It indicated that iCBT using Audiological support is a viable option to

reduce tinnitus severity. The use of sound methodological principles and holistic approach to evaluate the effects of iCBT not only on tinnitus, but also other comorbid factors, adds further value to this study.

Although attrition rates were lower than rates during the initial feasibility study, these can be further improved. It was evident that those who had undergone the treatment did not always see the need to complete the outcome questionnaires. Suggestions to reduce attrition include more encouragement and motivation throughout the programme to participants. Ensuring participants are aware that treatment results are generally not evident until at least half of the treatment is completed, may be helpful in guiding expectation levels for future participants and consequently reduce attrition.

Future directions

This study has provided encouraging results regarding the efficacy of iCBT in the UK. Further research is required to determine the longer-term effects of this intervention as well as participant's experiences of this form of treatment. Further trials should focus on comparing this intervention to standard clinical care for tinnitus in the UK. Determining moderators and mediators of outcome (Hesser et al. 2014) and which specific aspects of iCBT result in positive outcomes, need to be further explored.

CONCLUSIONS

In this trial iCBT has reduced both tinnitus severity and the effects of associated problems for those with significant levels of tinnitus in the UK. Further research is required to compare this intervention with standard clinical care for tinnitus in the UK. Determining the longer-term outcomes and participant experiences of iCBT is also important.

ACKNOWLEDGEMENTS

The authors wish to thank all participants and organisations that promoted and supported this study. We would also like to thank Linköping University for hosting the web portal and their webmaster, George Vlaescu, for technical assistance provided.

REFERENCES

Abbott, J. M., Kaldo, V., Klein, B., et al. (2009). A cluster randomised trial of an internet-based intervention program for tinnitus distress in an industrial setting. *Cogn Behav Ther, 38*(3), 162-173.

Andersson, G. (2014). *The internet and CBT: A clinical guide*. Boca Raton: CRC Press.

Andersson, G. (2015). Clinician-supported Internet-delivered psychological treatment of tinnitus. *Am J Audiol, 24*(3), 299-301.

Andersson, G. (2016). Internet-delivered psychological treatments. *Annu Rev Clin Psychol*, 12,157-179.

Andersson, G., Kaldo, V. (2004). *Internet- based cognitive behavioral therapy for tinnitus* doi:10.1002/jclp.10243

Andersson, G., Stromgren, T., Strom, L., et al. (2002). Randomized controlled trial of internet-based cognitive behavior therapy for distress associated with tinnitus. *Psychosom Med, 64*(5), 810-816.

Baguley, D.M., Andersson, G., McKenna, L. (2013). Tinnitus: A Multidisciplinary Approach. 2nd ed. Chichester: Wiley-Blackwell.

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

Bartels, H., Middel, B. L., van der Laan, B. F., et al. (2008). The additive effect of co-occurring anxiety and depression on health status, quality of life and coping strategies in help-seeking tinnitus sufferers. *Ear Hear, 29*(6), 947-956. doi:10.1097/AUD.0b013e3181888f83 [doi].

Bastien, C. H., Vallières, A., Morin, C. M. (2001). Validation of the insomnia severity index as an outcome measure for insomnia research. *Sleep Med, 2*(4), 297-307.

Beukes, E.W. Allen, P.M., Manchaiah, V., et al. (2016b). Internet-based intervention for tinnitus: Outcome of a single-group open trial. *J Am Acad Audiol*, accepted.

Beukes, E. W., Manchaiah, V., Allen, P. M., et al. (2015). Internet-based cognitive behavioural therapy for adults with tinnitus in the UK: Study protocol for a randomised controlled trial. *BMJ Open, 5*(9), e008241-2015-008241. doi:10.1136/bmjopen-2015-008241 [doi].

Beukes, E.W., Vlaescu, G., Manchaiah, V., et al. (2016a). Development and technical functionality of an internet-based intervention for tinnitus in the UK. *Internet Interv, doi:10.1016/j.invent.2016.08.002.*

Broadbent, D. E., Cooper, P. F., FitzGerald, P., et al. (1982). The cognitive failures questionnaire (CFQ) and its correlates. *Br J Clin Psychol, 21*(1), 1-16.

Diener, E., Emmons, R. A., Larsen, R. J., et al. (1985). The satisfaction with life scale. *J Pers Assess, 49*(1), 71-75. doi:10.1207/s15327752jpa4901_13.

Brüggemann, P., Szczepek, A. J., Rose, M., et al. (2016). Impact of Multiple Factors on the Degree of Tinnitus Distress. *Front Hum Neurosci*, *10*.

Dziura, J. D., Post, L. A., Zhao, Q., et al. (2013). Strategies for dealing with missing data in clinical trials: From design to analysis. *Yale J Biol Med, 86*(3), 343-358.

El-Shunnar, S. K., Hoare, D. J., Smith, S., et al. (2011). Primary care for tinnitus: Practice and opinion among GPs in England. *J Eval Clin Pract, 17*(4), 684-692.

Eysenbach, G. (2011). CONSORT-EHEALTH: Improving and standardizing evaluation reports of web-based and mobile health interventions. *J Med Internet Res, 13*(4), e126.

Gander, P. E., Hoare, D. J., Collins, L., et al. (2011). Tinnitus referral pathways within the national health service in england: A survey of their perceived effectiveness among audiology staff. *BMC Health Serv Res*, *11*(1), 1.

Hesser, H., Weise, C., Westin, V. Z., et al. (2011). A systematic review and meta-analysis of randomized controlled trials of cognitive–behavioral therapy for tinnitus distress. *Clin Psychol Rev, 31*(4), 545-553.

Hesser, H., Westin, V. Z., Andersson, G. (2014). Acceptance as a mediator in internet-delivered acceptance and commitment therapy and cognitive behavior therapy for tinnitus. *J Behav Med, 37*(4), 756-767.

Hesser, H., Gustafsson, T., Lunden, C., et al. (2012). A randomized controlled trial of internet-delivered cognitive behavior therapy and acceptance and commitment therapy

in the treatment of tinnitus. *J Consult Clin Psychol, 80*(4), 649-661. doi:10.1037/a0027021.

Hoare, D. J., Broomhead, E., Stockdale, D., et al. (2015). Equity and person-centeredness in provision of tinnitus services in UK National Health Service Audiology departments. *EJPCH, 3*(3), 318-326.

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

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

Kaldo, V., Cars, S., Rahnert, M., et al. (2007). Use of a self-help book with weekly therapist contact to reduce tinnitus distress: A randomized controlled trial. *J Psychosom Res, 63*(2), 195-202.

Kaldo, V., Haak, T., Buhrman, M., et al. (2013). Internet-based cognitive behaviour therapy for tinnitus patients delivered in a regular clinical setting: Outcome and analysis of treatment dropout. *Cogn Behav Ther, 42*(2), 146-158.

Kaldo, V., Levin, S., Widarsson, J., et al. (2008). Internet versus group cognitive-behavioral treatment of distress associated with tinnitus: A randomized controlled trial. *Behav Ther, 39*(4), 348-359.

Kaldo-Sandström, V., Larsen, H. C., Andersson, G. (2004). Internet- based cognitive-behavioral self-help treatment of tinnitus: Clinical effectiveness and predictors of outcome. *Am J Audiol, 13*(2), 185-192. doi:10.1044/1059-0889(2004/023)

Langguth, B. (2011). A review of tinnitus symptoms beyond 'ringing in the ears': A call to action. *Curr Med Res Opin, 27*(8), 1635-1643.

Lindner, P., Carlbring, P., Flodman, E., et al. (2016). Does cognitive flexibility predict treatment gains in internet-delivered psychological treatment of social anxiety disorder, depression, or tinnitus? *PeerJ, 4*, e1934.

Little, R. J. (1988). A test of missing completely at random for multivariate data with missing values. *J Am Stat Assoc, 83*(404), 1198-1202.

Meikle, M. B., Henry, J. A., Griest, S. E., et al. (2012). The tinnitus functional index: Development of a new clinical measure for chronic, intrusive tinnitus. *Ear Hear, 33*(2), 153-176. doi:10.1097/AUD.0b013e31822f67c0 [doi].

Newman, C. W., Jacobson, G. P., Spitzer, J. B. (1996). Development of the tinnitus handicap inventory. *Arch Otolaryngol Head Neck Surg, 122*(2), 143-148.

Newman, C. W., Sandridge, S. A., Bolek, L. (2008). Development and psychometric adequacy of the screening version of the tinnitus handicap inventory. *Otol Neurotol, 29*(3), 276-281.

Newman, C. W., Weinstein, B. E., Jacobson, G. P., et al. (1991). Test-retest reliability of the hearing handicap inventory for adults. *Ear Hear, 12*(5), 355-357.

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

Pizer, S. D., Prentice, J. C. (2011). What are the consequences of waiting for health care in the veteran population?. *J Gen Intern Med*, *26*(2), 676-682.

Robinson, E., Titov, N., Andrews, G., et al. (2010). Internet treatment for generalized anxiety disorder: A randomized controlled trial comparing clinician vs. technician assistance. *PloS One, 5*(6), e10942.

Seydel, C., Haupt, H., Olze, H., et al. (2013). Gender and chronic tinnitus: Differences in tinnitus-related distress depend on age and duration of tinnitus. *Ear Hear, 34*(5), 661-672. doi:10.1097/AUD.0b013e31828149f2

Smith, P., McKeon, A., Blunt, I., et al. (2014). NHS hospitals under pressure: Trends in acute activity up to 2022. *London, UK: Nuffield Trust,*

Spitzer, R. L., Kroenke, K., Williams, J. B., et al. (2006). A brief measure for assessing generalized anxiety disorder: The GAD-7. *Arch Intern Med, 166*(10), 1092-1097.

Spitzer, R. L., Kroenke, K., Williams, J. B., et al. (1999). Validation and utility of a self-report version of PRIME-MD: The PHQ primary care study. *Jama, 282*(18), 1737-1744.

Titov, N., Andrews, G., Davies, M., et al. (2010). Internet treatment for depression: A randomized controlled trial comparing clinician vs. technician assistance. *PloS One, 5*(6), e10939.

Titov, N., Andrews, G., Schwencke, G., et al. (2009). An RCT comparing effect of two types of support on severity of symptoms for people completing internet-based cognitive behaviour therapy for social phobia. *Aust NZ J Psychiatry, 43*(10), 920-926.

Thorén, E. S., Andersson, G., Lunner, T. (2012). The use of research questionnaires with hearing impaired adults: online vs. paper-and-pencil administration. *BMC Ear Nose Throat Disord*, *12*(1), 1.

Vernon, J. A. (1987). Pathophysiology of tinnitus: A special case--hyperacusis and a proposed treatment. *Am J Otol, 8*(3), 201-202.

Vickers, A. J., Altman, D. G. (2001). Statistics notes: Analysing controlled trials with baseline and follow up measurements. *BMJ (Clin Resear Ed.), 323*(7321), 1123-1124.

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

Weise, C., Kleinstauber, M., Andersson, G. (2016). Internet-delivered cognitive-behavior therapy for tinnitus: A randomized controlled trial. *Psychosomatic Medicine, 78*(4), 501-510. doi:10.1097/PSY.0000000000000310 [doi].

List of figure legends

Figure 1: The CONSORT study profile

Figure 2: Change in tinnitus outcome measures over time

Figure 3: Change in Anxiety and Depression Outcome Measures over time

Figure 4: Change in THIs scores during the active treatment phase

List of table legends

Table 1. Primary and secondary outcome measures used

Table 2: Demographics characteristics of the participants

Table 3: Completion rates for postintervention and follow-up outcome measures

Table 4: Mean changes and statistical analysis of outcome measures over time

Author's contributions

All authors conceived and designed this study. GA developed the Swedish original iCBT intervention for tinnitus together with Viktor Kaldo, EB developed this version for a UK population, carried out the study, and analyzed the data. The manuscript was drafted by EB and critically revised and approved by all authors.

Previous presentations: none declared