1 None declared

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

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Abbreviations

ANOVA: Analysis of variance

CBT: Cognitive Behavioural Therapy

CFQ: Cognitive Failures Questionnaire

CONSORT: Consolidated Standards of Reporting Trials

GAD-7: Generalized Anxiety Disorder

GP: General Practitioner

HHIA-S: Hearing Handicap Inventory for Adults - Screening

HQ: Hyperacusis Questionnaire

NHS: National Health System

iCBT: Guided Internet-based Cognitive Behavioural Therapy Intervention

ISI: Insomnia Severity Index

PHQ-9: Patient Health Questionnaire

RCI: Reliable Change Index

SPSS: Statistical Package for Social Sciences

SWLS: Satisfaction with Life Scales

TFI: Tinnitus Functional Index

THI-S: Tinnitus Handicap Inventory - Screening

UK: United Kingdom

ABSTRACT

Objectives

Specialist tinnitus services are in high demand as a result of the negative effect tinnitus may have on quality of life. Additional clinically and cost effective tinnitus management routes are needed. One potential 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. A further aim was to establish the stability of intervention effects 2-months post-intervention. The hypothesis was that iCBT for tinnitus would be more effective at reducing tinnitus distress than weekly monitoring.

Design

A randomised, delayed intervention efficacy trial, with a 2-month follow-up was implemented to evaluate the efficacy of iCBT in the UK. Participants were randomly assigned to the experimental (n=73) or weekly monitoring control group (n=73) after being stratified for tinnitus severity and age. After the experimental group completed the 8-week long iCBT intervention, the control group undertook the same intervention. Intervention

effects were, therefore, evaluated in two independent groups at two time points. The primary outcome was a change in tinnitus distress between the groups 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. These were completed at baseline, post-intervention and at a 2-month post-intervention follow-up.

Results

After undertaking the iCBT intervention, the experimental group had a greater reduction in tinnitus distress when compared with the control group. This reduction was statistically significant (Cohen's *d*= 0.7) and was clinically significant for 51% of the experimental group and 5% of the control group. This reduction was evident 4-weeks after commencing the iCBT intervention. Furthermore, the experimental group had a greater reduction in insomnia, depression, hyperacusis, cognitive failures and a greater improvement in quality of life, as evidenced by the significant differences in these assessment measures post-intervention. Results were maintained 2-months post-intervention.

Conclusions

Guided (using audiological support) iCBT for tinnitus resulted in statistically significant reductions in tinnitus distress and comorbidities (insomnia, depression, hyperacusis, cognitive failures and a significant increase in quality of life). These effects remained stable at 2-months post-intervention. Further trials to determine the longer-term efficacy of iCBT, to investigate predictors of outcome and to 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 the publically funded National Health Service (NHS) 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 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, minimising waiting times should be prioritised (Gander et al. 2011).

Tinnitus is defined as the sensation of sound in the absence of a corresponding external acoustic stimulus (Baguley et al. 2013). It may be perceived on a spectrum from barely noticeable to debilitating (Brüggemann et al. 2016). Experiencing tinnitus is often associated with a wide range of associated symptoms such as sleep disturbance, concentration difficulties, irritation, frustration, anxiety, and depression (Langguth et al. 2011). In England there are an estimated ¾ of a million people per year who visit their GP with tinnitus as the primary complaint (El-Shunnar et al. 2011). Of these, only 37% are referred for specialist services (El-Shunnar et al. 2011). In addition, those referred often have a substantial wait of up to 18-weeks before an intervention pathway, such as obtaining tinnitus counselling, commences (Department of Health, 2009). A further constraint in tinnitus management in the UK is that the intervention with the most evidence of efficacy, namely cognitive behavioural therapy (CBT, see Hesser et al. 2011) is not readily available for those with tinnitus. This is largely due to a shortage of trained specialists (Baguley et al. 2013). Moreover, specialist

tinnitus services are not offered in all NHS hospitals across the UK, leaving many with distressing tinnitus without any specialised intervention options (Hoare et al. 2015).

The need for widely available, cost and clinically effective, tinnitus management is evident worldwide, and not isolated to the UK (Andersson, 2016). To increase access to effective tinnitus intervention in Sweden, cognitive behavioural therapy is provided via the Internet (iCBT; Andersson, 2015). As iCBT has been found to be effective at reducing tinnitus and associated problems in clinical trials in Sweden and Germany (e.g., Andersson et al. 2002; Kaldo et al. 2008; Hesser et al. 2012; Nyenhuis et al. 2013, Jasper et al. 2014; Weise et al. 2016), it has been incorporated into regular clinical care in Sweden (Kaldo-Sandström et al. 2004; Kaldo et al. 2013). As iCBT could increase access to an evidence-based intervention in the UK a comprehensive, user-friendly, intervention tailored for a UK population was designed by Beukes et al. (2016). Feasibility of iCBT in the UK was established in terms of recruitment, attrition, and compliance (Beukes et al. 2017a). The clinical efficacy of this redeveloped iCBT intervention in the UK has not yet been established. In this context, delivering iCBT guided by an audiologist would be optimal, but the efficacy of iCBT by a non-psychological professional is unproven. This trial set out to explore the use of iCBT in the UK with the following objectives:

1. To evaluate the efficacy of audiology guided iCBT in reducing tinnitus distress compared with weekly monitoring.
2. To ascertain the efficacy of iCBT for comorbidities associated with tinnitus.
3. To assess the stability of iCBT intervention effects 2-months post-intervention.
4. To establish the on-going intervention effects during the course of iCBT.

The hypothesis was that iCBT for tinnitus would be more effective at reducing tinnitus distress and the associated comorbidities than weekly monitoring.

MATERIALS AND METHODS

Study design

A delayed intervention efficacy trial with a 2-month follow-up was implemented to evaluate the efficacy of iCBT in the UK. This prospective, two-arm, randomised control trial was registered with Clinical Trials.gov: NCT02370810 on 05/03/2015. The ***Experimental Group*** received the iCBT intervention for 8-weeks, while the ***Control Group*** were monitored weekly. Once the experimental group completed the intervention, the control group underwent the same iCBT intervention. This study design, therefore, provided the opportunity to evaluate the intervention effects in two independent groups at two time points. Although the control group had a delay of 8-weeks before undertaking this intervention, this may be less than the 18-weeks wait they may have on standard treatment pathways on the NHS.

The Consolidated Standards of Reporting Trials (CONSORT) eHealth guidelines (Eysenbach et al. 2011) were implemented to report the methods and results of this trial. For the full study protocol, see Beukes et al. (2015).

Ethical considerations

Ethical approval was granted by the Faculty Research Ethics Panel of Anglia Ruskin University (FST/FREP/14/478). The trial was conducted in accordance with good clinical practice together with the ethical principles of the Declaration of Helsinki. A protocol was established to ensure the security of participants' confidentiality when using the web-portal,

complying with the following UK legislation: The Data Protection Act of 1998 and The Privacy and Electronic Communications (EC Directive) Regulations (Riach, 2003). There were no changes to the methods or assessment measures used after the trial commenced. No harms or unintended effects were reported.

Study population

Recruitment

Recruitment was UK wide for a period of two months 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 healthcare professionals (GP surgeries, audiologists).

Participants

Those interested in the study registered interest on the study website (www.tacklingtinnitus.co.uk). They were informed of their right to withdraw at any stage without penalty. Eligibility for the study was determined in a two-stage process. Initially, participants completed the baseline assessment 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) Experiencing tinnitus for a minimum duration of three months

v) A score of 25 or above on the Tinnitus Functional Index suggesting the need for tinnitus care (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 with partaking in this study

Assessment measures

A demographic questionnaire was used to obtain information related to gender, age, tinnitus duration, hearing aid use, medical examinations related to tinnitus, past or current tinnitus treatments, health and/or mental health conditions and employment. Self-reported assessment measures were selected to establish tinnitus distress and identify associated difficulties, as these are generally used in clinical practice. The following assessment measures were completed at baseline (T_0), at post-intervention (T_1) and follow-up (T_2) in both groups.

Primary assessment measure

The Tinnitus Functional Index (TFI; Meikle et al. 2012) was selected as the primary assessment measure to measure tinnitus distress. It was chosen above some other established tinnitus questionnaires, such as the Tinnitus Handicap Inventory (THI; Newman et al. 1996) because of its validation for assessing intervention responsiveness. It is a 25-item questionnaire, scored on a scale of 0-100. Scores less than 25 indicate mild tinnitus, with no need for intervention, whereas scores ranging from 25-50 signify significant tinnitus and the possible need for intervention. A score of 50 or greater demonstrates more severe tinnitus and indicates the need for more intensive intervention. A reduction in TFI scores shows improvement in tinnitus distress. Meikle et al. (2012) reported that meaningful changes occur when scores are reduced by 13 points or more. Due to regression to the mean artefacts, those with more severe scores are more likely to show significant changes on assessment measures than those reporting mild symptoms (Campbell & Kenny, 1999). The TFI has excellent psychometric properties with an internal consistency of 0.97 and test-retest reliability of 0.8 (Meikle et al. 2012).

Secondary assessment measures

The following secondary assessment measures were selected to identify difficulties that may be related to having tinnitus:

i) The Insomnia Severity Index (ISI; Bastien et al. 2001) was used to assess the presence of insomnia, as sleep difficulties are prevalent amongst those with tinnitus (Crönlein et al. 2016). The seven-item questionnaire is scored between 0-28 and has an acceptable internal consistency of 0.7 (Bastien et al. 2001).

ii) The Generalised Anxiety Disorder (GAD-7; Spitzer et al. 2006) was selected to quantify the level of anxiety, as the prevalence of anxiety is high in those with

severe tinnitus (Pinto et al. 2014). This seven-item questionnaire is scored between 0-21 and has an internal validity of 0.9 (Lowe et al. 2006).

iii) The Patient Health Questionnaire (PHQ-9; Spitzer et al. 1999) was chosen to assess symptoms of depression, as depression amongst those with severe tinnitus is often reported (Pinto et al. 2014). Scoring is between 0-28 on this nine-item questionnaire with an internal validity of 0.8 (Spitzer et al. 1999).

iv) The Hearing Handicap Inventory for Adults Screening version (HHIA-S; Newman et al. 1991) was administered to assess difficulty hearing, which in this context may be related to the penetrating nature of tinnitus or the presence of hearing loss, commonly found in those with tinnitus (Langguth et al. 2017). This measure consists of 10 items, scored between 0-40 and has a good internal consistency of 0.9 (Newman et al. 1991).

v) The Hyperacusis Questionnaire (HQ; Khalfa et al. 2002) was administered to assess the presence of reduced tolerance of everyday sounds, otherwise known as hyperacusis, as there is a large overlap in the prevalence of tinnitus and hyperacusis (Schecklmann et al. 2014). This 14-item questionnaire is scored between 0-42. Fackrell et al. (2015) evaluated the psychometric properties of the HQ in a large UK population of participants with tinnitus and found a high internal consistency of 0.9 but were unable to confirm the original three factor solution proposed by Khalfa et al. (2002) and therefore suggested cautious use of the HQ until an alternative has been developed. To date, a questionnaire has yet to be developed so the HQ was used as a measure of sound sensitivity.

vi) The Cognitive Failures Questionnaire (CFQ; Broadbent et al. 1982) was administered to assess cognitive functions, as tinnitus may impact the control of attention leading to cognitive slips and errors in task completion (Tegg-Quinn et al.

2016). This 25-item questionnaire is scored between 0-100 and has a good internal consistency of 0.9 (Broadbent et al. 1982).

vii) The Satisfaction with Life Scales (SWLS; Diener et al. 1985) was administered as a quality of life measure assessing global life satisfaction as opposed to quality of life measures often related to self-care and mobility. Scoring is between 0-35 for five-items and has an internal consistency is 0.9 (Dienter et al. 1985).

A low score signifies fewer problems than a high score and a reduction in score indicates improvement for all these measures except for the SWLS. For the SWLS a higher score shows more life satisfaction than a lower score and an increase in score reveals improved life satisfaction.

Weekly assessment measure

The Tinnitus Handicap Inventory Screening version (THI-S; Newman et al. 2008) was selected to monitor tinnitus severity in both groups on a weekly basis during the 8-week period between T_0 and T_1. This measure was selected instead of the TFI or THI due to its concise nature as it consists of only 10 questions. The scores obtained are comparable (r=0.9) with the full version of the THI (Newman et al. 2008) and good convergent validity (0.9) has been found between the TFI and THI (Meikle et al. 2012).

Data Collection

Data collection of the assessment measures was online throughout the trial for both groups. Results using an online format should be comparable to those using a paper presentation, as equivalent psychometric properties have been reported (Thoren et al. 2012). To minimise attrition post-intervention, reminder emails were sent to encourage participants to complete

the assessment measures. Assessment 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 ISI.

Study Intervention

The intervention 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 and engaging (Beukes et al. 2016). The web-based intervention platform used was designed in-house at Linköping University, Sweden and complied with a high level of data security and encrypted communications (Vlaescu et al. 2015). A responsive web design was implemented whereby the intervention content could be viewed on different sized platforms without losing any information. This ensured ease of access from various devices such as computers, tablets, and smartphones. The intervention ran over an 8-week period, during which 2-3 modules were released on a weekly basis. CBT principles such as goal setting, a clear structure, active participation, relapse prevention and setting a time-frame for completing the intervention were incorporated (Andersson, 2002). There were 16 recommended modules and five optional modules. Recommended modules included CBT content such as applied relaxation, thought analysis, cognitive restructuring, imagery and exposure techniques. Optional modules were available to add an element of tailoring, and participants could choose whether or not to do these modules. If initial baseline scores for the ISI indicated at least subthreshold insomnia (≥ 8) undertaking the optional sleep module was recommended. If the HHIA indicated a 50% probability of hearing disability (≥ 26) the hearing tactics module was suggested and if scores were ≥ 30 on the CFQ the module covering concentration guidelines was advised. The sound sensitivity module was recommended if scores were ≥ 28 on the HQ.

Guidance during the intervention

Internet interventions are either independent of professional support (unguided) or offer some form of support (guided). A key element of this intervention was that it was guided, as better outcomes are reported for guided interventions (Baumeister et al. 2014). To maintain consistency with the standard approach of tinnitus interventions being delivered within the audiology community in the UK, an experienced audiological scientist guided the intervention. The audiologist was registered with the Health and Care Professions Council and appropriately trained to Masters Level in Audiology. The audiologist was experienced in managing tinnitus patients both in a clinical setting and online and had a suitable understanding of CBT principles but no formal CBT training. Supervision was provided by a clinical psychologist (specialised in providing tinnitus intervention) throughout the duration of the trial. Having audiological support for an iCBT intervention is unique to this study, as psychologists have guided participants in previous trials. The audiologist's role was to conduct the telephone interviews, introduce weekly modules, provide feedback, answer queries, provide guidance, support and encourage engagement. A secure encrypted messaging system was available to enable this two-way communication. Communication included feedback on progress, encouragement, and information about the content of new modules. A minimum of 10 minutes per week was spent on each participant and more time if required.

Data Analysis

Sample Size

Sample size estimation was calculated using G*Power version 3.1.6 (Faul et al. 2007) and based on achieving a clinically relevant change between baseline and post-intervention using

the primary assessment measure, the TFI. Calculations using the 13-point difference suggested during the development of the TFI 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, with an effect size of 0.5 and 80% power. An additional 30 participants were recruited to ensure sufficient power during per-protocol analysis to account for possible dropouts. Therefore, 73 participants were recruited to each arm.

Enrolment and Randomisation

Participants meeting the inclusion criteria were randomly assigned in the ratio of 1:1 and enrolled to either the experimental or control group. Allocation was based on a randomisation sequence generated by computer algorithm (http://www.randomizer.org/) and done by an independent researcher. To prevent an unequal distribution among groups, participants were pre-stratified on the factors of age (<= 60 or >60 years) and tinnitus severity (TFI <= 50 or >50). Block randomisation, with blocks of four, were applied to ensure equal groups sizes within each stratum. Participants were informed when the intervention would commence by the principal investigator, but not which group they had been assigned to. The trial design resulted in the investigator not being masked to the assignment of interventions during the running of the trial. During the initial telephone screening, it was explained that the trial would start once registration was full and all participants were telephoned and randomised. Participants, therefore, expected a delay to the trial onset as no time-period was given. Participants may have realised their group assignment, but this was never explicitly stated.

Statistical Analysis

The Statistical Package for Social Sciences (SPSS) version 23.0 was used for statistical analysis and the data analyst was masked to the groups to minimise bias. For all analyses, a two-tailed significance level of <0.05 was considered statistically significant.

Missing Data Analysis

An intention-to-treat paradigm was used, as this analysis is less susceptible to bias than complete case analysis techniques. Missing value analysis was conducted to determine how to account for missing data. Little's missing completely at random test (Little, 1988), indicated that data were likely to be MCAR (missing completely at random; $\chi 2(55)= 42.4$, $p = 0.89$). This suggested that missing values were likely to be randomly distributed across all observations and that there was no systematic pattern to the missing data. Missing data could thus, be imputed through the multiple imputation procedure offered by SPSS using Markov Chain Monte Carlo method which uses five imputation runs (Asendorpf et al. 2014). All preintervention assessment measure results were used as predictors. These results were compared with those obtained with a per-protocol analysis. As there was no difference, the intention-to-treat results are reported. Results obtained by averaging the five imputation runs (pooled results) were used where available. For some of the statistics, a pooling algorithm is not yet available. When this was the case, the first imputed set of results was reported.

Study outcomes

The primary study outcome was a change in TFI score between the groups at post-intervention (T_1). Secondary study outcomes were changes in the scores of secondary assessment measures between groups at T_1. A difference in scores between T_1-T_2 for the experimental group was used to assess the stability of intervention effects.

Group differences and stability of intervention effects

A mixed 2x3 Analysis of variance (ANOVA) for repeated measures with the within-subject variable of time (T_0, T_1, T_2) and between-subject factor of group (experimental and control) was carried out to compare assessment measure results across the three-time points. Greenhouse-Geisser correction for non-sphericity was applied.

The main effects were followed up by paired samples *t*-tests to compare within-group differences at individual time points and independent sampled *t*-tests to compare results between the two groups at each time point.

Effect sizes

Effect sizes and the 95% confidence intervals at postintervention were calculated by dividing the mean differences by the pooled standard deviations. Effect sizes below d=0.5 represented small effect sizes; those of d=0.5- 0.79 medium effect sizes and those equal or greater than d=0.8, large effect sizes (Cohen, 1992).

Monitoring intervention effects Between T_0-T_1

A mixed 2x8 ANOVA for repeated measures was used to compare the results of the weekly THI-S scores with the within-subject variable of time (weeks 1-8) and between-subject factor of group (experimental and control). The main effects were followed up by paired samples *t*-tests to compare within-group differences at individual time points and independent sampled *t*-tests to compare results between the two groups at each time point.

Clinically significant Change

A statistical significance of differences in group means is the standard analysis of clinical trials. Supplementing these results with an evaluation to determine whether the change in score is clinically meaningful, is an indicator of the value of the intervention. The reliable change index (RCI; Jacobson & Truax, 1991) was used to determine clinical significance. It was calculated using the standard deviation and means at T_0, the means at T_1, and the test-retest reliability coefficient or Chronbach's alpha where this was not available.

Individual's mean difference scores for those completing the intervention (i.e. both groups) between T_0-T_1 were evaluated against the RCI criterion. Individual's mean difference scores for those completing the intervention from the control group between T_0-T_2 were also evaluated against the RCI criterion for the TFI.

RESULTS

Participant Characteristics

The baseline assessment measures were completed by 169 of the 244 adults on the trial waiting list. A total of 146 adults met the eligibility criteria and were randomly assigned to the experimental (n=73) and control groups (n=73) as shown in the CONSORT diagram (Figure 1). The mean age was 55.6 years (SD 12.9) and there were more male participants overall (57%). The groups were well matched, as there were no clinically meaningful differences as seen in Table 1.

Attrition

There were 4 participants (5%) from the experimental group and 3 participants (4%) from the control group who withdrew whilst undertaking iCBT, generally due to time pressures or health problems. Significantly more participants [$\chi^2(1,n = 146) = 5.8$, $p = 0.02$] from the

control group (99%) completed the assessment measures at T_1 compared with those from the experimental group (73%). There was no significant difference [$\chi^2(1,n = 146) = 2.1$, $p = 0.16$] in completion rates at T_2 with 73% from the experimental group and 82% from the control group completing these assessment measures.

No significant baseline differences in terms of age, gender, employment status and level of education, tinnitus severity, insomnia, anxiety or depression were found between those who completed the assessment measures and those who choose not to complete them.

Efficacy of iCBT versus weekly monitoring for tinnitus distress

Differences between the treatment arms were not constant over time (Table 2). Pre-intervention (T_0) means were similar. At post-intervention (T_1) the mean TFI score was 21 points lower (SD 14.9) compared with baseline among those in the experimental group. For the control group, the mean TFI score was 5 points lower (SD 3.9) when compared with baseline. Although both groups exhibited reduced mean scores, the magnitude of the reduction in mean score in the experimental group was greater than in the control group and this difference was statistically significant (Cohen's d=0.7) as seen in Table 2.

Figure 3 shows that the majority of the experimental group had a T_0-T_1 difference score reduction of between 10-40 points, with a maximum reduction of 81 points. In comparison, the majority of the control group had smaller improvements with a T_0-T_1 difference score higher than baseline or up to 20 points reduced. The maximum improvement for the control group was 29 points. Both groups had similar means at follow-up (T_2), indicating that the control group improved further after completing the intervention as summarised in Table 2.

Using the reliable change criterion of 23.3 in TFI score (i.e. 1.96 times the standard error of 11.9), clinical significance was achieved by 51% of the experimental group and 5% of the control group at T_1. A clinically significant change was found for 47% of the control group at T_2 after they undertook the intervention. At T_1, there was 41% of the experimental group and 1% of the control group with TFI scores below the level requiring intervention (<25) who also had a reliable change of 23.3 after they completed the intervention. This was achieved by 38% of the control group at T_2.

Efficacy of iCBT versus weekly monitoring for comorbidities associated with tinnitus

Differences between the secondary assessment measures were not constant over time for the treatment arms (Table 2). Pre-intervention (T_0) means were similar. At post-intervention (T_1) the experimental group had a significantly greater reduction in insomnia, depression, hyperacusis, cognitive failures and improvement in the quality of life in comparison with the control group. For anxiety and hearing disability, significant within group differences were found post-intervention, but no significant interaction between time and group was seen.

For the assessment measures that were statistically significant, they were only clinically significant for a few participants at T_1. Clinical significance (score change >9.8) was reached by 22% of the experimental group and 4% of the control group for the ISI. For the PHQ-9, this was reached by 16% of the experimental group and 4% of the control group (score change of 6.4). For the HQ clinical significance (score change of 14.3) was reached by 11% of the experimental group and 4% of the control group. For the CFQ it was 18% and 5% of the groups respectively (score change of 14.1) whereas it was reached by 14% and 3% of the respective groups for the SWLS (score change of 6.3). The ISI had the highest percentage of

participants having a clinically significant change amongst the secondary assessment measures.

Both groups had similar means at follow-up (T_2), indicating that the control group had improved to the level of the experimental group after completing the intervention as summarised in Table 2.

Stability of intervention effects

There was no significant difference in the TFI scores between T_1-T_2 for the experimental group, as seen in Figure 2. Likewise, improvements were maintained for all secondary assessment measures as no statistically significant differences were found. Intervention effects were, therefore, maintained 2-months postintervention for the experimental group.

Monitoring intervention effects between T_0 and T_1

Differences between the intervention arms were not constant across the 8-time points between T_0 and T_1. The experimental group had a greater weekly reduction in tinnitus distress, as evidenced by the significant interaction [$F(7, 1008)=19.5$, $p=0.001$*; Cohen's $d=0.9$].

Follow-up analysis examining this main effect week-by-week indicated no group differences in weeks 1-3 of this period. From week 4 to 8 there were significant differences, as the experimental group's tinnitus distress was rated significantly lower than that of the control group who were not undergoing the intervention, as seen in Figure 4.

DISCUSSION

This randomised trial found that iCBT guided by an audiologist was effective in reducing tinnitus distress. The symptoms of several tinnitus comorbidities, such as insomnia, depression, hyperacusis, and cognitive failures were also reduced and an increase in life satisfaction was found. Results were stable 2-months post-intervention. This discussion highlights the implications of the finding for each of the four research objectives.

Effects of iCBT for tinnitus distress

The main outcome measure for this trial was a change in tinnitus distress as measured by the TFI. Undertaking iCBT led to significantly greater improvements in tinnitus distress, compared with weekly monitoring. The small improvement found in the control group (5 points) at T_1 may have been related to the positive effects of being included on an intervention pathway, despite not yet starting the intervention. The mean score reduction of 21 between T_0-T_1 in the experimental group in the present study is comparable to the findings in the initial feasibility study with a mean difference of 19 points (Beukes et al. 2017). The TFI score improvements found in the experimental group were greater than those occurring in the control group.

To relate these findings to clinical significance, the RCI was calculated. Results indicated that a change of 23.3 on the TFI score was regarded as clinically significant. This was similar to the change of 23.9 found in the initial feasibility trial. At T_1 clinical significance was reached by 51% of the experimental group and 5% of the control group. Earlier iCBT for tinnitus trials found that a clinically significant change was reached by 29-52% of participants (Andersson et al. 2002, Kaldo et al. 2008, Nyenhuis et al. 2013 and Jasper et al. 2014). A more recent study by Weise et al. (2016) reported that a higher proportion (73-81%)

reached clinical significance following undertaking iCBT for tinnitus. Andersson et al. (2002) and Kaldo et al. (2008) reported finding 4-5% of a waiting-list control group achieved clinical significance, in line with the results of the present study. Discrepancies between different trials may be partly related to the differences in assessment measures used. Previous iCBT trials have used varying tinnitus assessment measures such as the THI, the Tinnitus Reactions Questionnaire (TRQ; Wilson et al. 1991), or the Tinnitus Questionnaire (TQ; Hiller et al. 1994) with various study designs, thereby making direct comparisons difficult. Andersson, (2015) reported that 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= 0.6, although a later study by Weise et al. (2016) was not included. Weise et al. (2016) found an effect size of Hedge's g= 0.8 for tinnitus distress postintervention when using the THI. The medium effect size found of Cohen's d = 0.7 (Hedge's g= 0.7) for the present study is, therefore, between the values of previous iCBT tinnitus trials. This provides encouragement that the results of this study are consistent with those of previous iCBT trials.

In previous clinical trials, the intervention was guided by clinical psychologists trained in the provision of CBT. This trial is unique in providing this guidance using an audiologist, in line with tinnitus healthcare provision in the UK. Results indicate the efficacy of audiologist-guided iCBT to reduce tinnitus distress. Previous Internet-based trials for depression, anxiety, and social phobia have found comparable results, regardless of whether a clinician or an appropriately trained technical assistant guided the intervention (Titov et al. 2009; Robinson et al. 2010; Titov et al. 2010).

Effects of iCBT for comorbidities associated with tinnitus

Significant improvements for insomnia, depression, hyperacusis, cognitive failures and satisfaction with life were evident. Each group significantly improved in terms of anxiety and hearing disability following the completion of the iCBT intervention, but no main effect for the interaction between time and group was seen for these assessment measures. This may be related to the large variability in scores for these assessment measures between the groups over time. Low baseline scores were also evident for the anxiety assessment measure (7 points, SD: 0.3), which may have contributed to the non-significant interaction found. To relate these findings to clinical significance, the RCI was calculated for each secondary assessment measure at T_1. For the ISI, 22% of the experimental group had a clinically significant change, compared with 4% of the control group. The range of clinical significance for the other secondary assessment measures were 11-18% of the experimental group and 3-5% of the control group. The proportions of those with clinically significant improvements with regards to the secondary assessment measures are, therefore, lower than was found for the TFI.

Previous trials of iCBT for tinnitus have used secondary outcome measures for insomnia (using the ISI), anxiety and depression (using the Hospital Anxiety and Depression scale; Zigmond et al. 1983). Significant intervention effects have been reported for these tinnitus associated comorbidities (Kaldo-Sandström et al. 2004; Kaldo et al. 2008; Jasper et al. 2014; Weise et al. 2016). These studies have not reported whether these results were clinically significant as they focused on statistical significance. Effect sizes in the present study for anxiety and depression (d=0.3) were lower than those reported by Jasper et al. (2014) and Weise et al. (2016) of d=0.5. This difference may partly be attributed to the difference in assessment measures used in these trials compared with the present trial. The result for

insomnia for the present study was similar to that of Jasper et al. (2014) of *d*=0.6 and lower than that reported by Weise et al. (2016) of *g*=0.7.

Stability of intervention effects

Maintaining intervention effects is an important aspect of the efficacy of an intervention. It was found that the intervention effects were stable 2-months post-intervention (T_2) for both tinnitus severity and the secondary assessment measures in the experimental group. Stability of iCBT intervention effects have also been found in previous trials that monitored these effects over a longer period. Jasper et al. (2014) reported stability 6-months after completing iCBT for tinnitus severity, anxiety, depression, and insomnia. Kaldo et al. (2008) using a Swedish population and Weise et al. (2015) using a German population, found results were maintained 1-year after undertaking iCBT for tinnitus severity, anxiety, depression, and insomnia.

Intervention effects during iCBT

A further objective of this trial was determining when intervention effects can be expected. Participant's tinnitus severity was, therefore, monitored on a weekly basis by means of the THI-S. After the experimental group completed 4-weeks of the iCBT intervention they had significantly lower tinnitus severity scores than those not undergoing the intervention. The likely delay in intervention effects are important to convey to future participants to adjust their expectations.

Study limitations and further research

This study is not without limitations, which have implications for result interpretation. Firstly, the participants were recruited from the general public due to interest in undertaking

an Internet-intervention and not from a clinical setting. Therefore, these results may not be the same in a clinical sample. The demographical distribution of the participants in the present study showed more male participants, a slightly higher mean age distribution and longer tinnitus duration than those reported by previous iCBT trials on tinnitus (e.g. Andersson et al. 2002, Kaldo et al. 2007, Weise et al. 2016). This should be considered when assessing the generalisability of the results. Secondly, the likelihood of Type I errors cannot be excluded due to multiplicity of testing. Thirdly, not all participants completed the outcome measures at T_1 and T_2. Ways of encouraging more participants to complete these questionnaires and minimise attrition is required. A deeper understanding of factors affecting adherence is thus needed. The fourth limitation involves the assessment measures used. The HQ was used despite concerns raised regarding its psychometric properties (Fackrell et al. 2015) because of a lack of a better measure for hyperacusis. The TFI was selected as it was developed to evaluate intervention effects. There are, however, limitations in selecting this outcome measure as it has only been recently developed and further psychometric evaluations are required. Fackrell et al. (2016) raised concerns regarding substantial floor effects on many items and concluded that it may not be good at detecting treatment-related benefits in a research population. It may, therefore, have been a suboptimal assessment measure for a research volunteer population as used in the present trial. Lastly, data were not collected on treatment credibility which is an important consideration regarding evaluating a new intervention.

Further research is required to gain more insights into iCBT for tinnitus. This includes determining the longer-term results and participant's experiences regarding this version of iCBT used and using an audiologist to guide the intervention. In addition, determining moderators and mediators of outcome (Hesser et al. 2014) and which specific aspects of

iCBT result in positive outcomes, needs further exploration. Comparing intervention effects when guidance is provided by an audiologist versus a psychologist is required to determine the efficacy of using an audiologist for iCBT. Comparing these results with existing tinnitus clinical care is also required. A further RCT is therefore underway to compare iCBT with individualised face-to-face clinical care for tinnitus in the UK (Beukes et al. 2017b).

Conclusions

Guided iCBT for tinnitus using audiological support resulted in statistically significant reductions in tinnitus distress and comorbidities (insomnia, depression, hyperacusis, cognitive failures and quality of life). A clinically significant reduction in tinnitus distress was achieved by 51% of the experimental group compared with 5% of the control group. Including iCBT as an additional tinnitus intervention could be a cost-effective way of increasing access to CBT for tinnitus.

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LIST OF FIGURES

LIST OF TABLES

AUTHOR'S CONTRIBUTION

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 PRESENTATION

1 None declared

Figure 1

Click here to download Figure Fig 1 RCT.tif

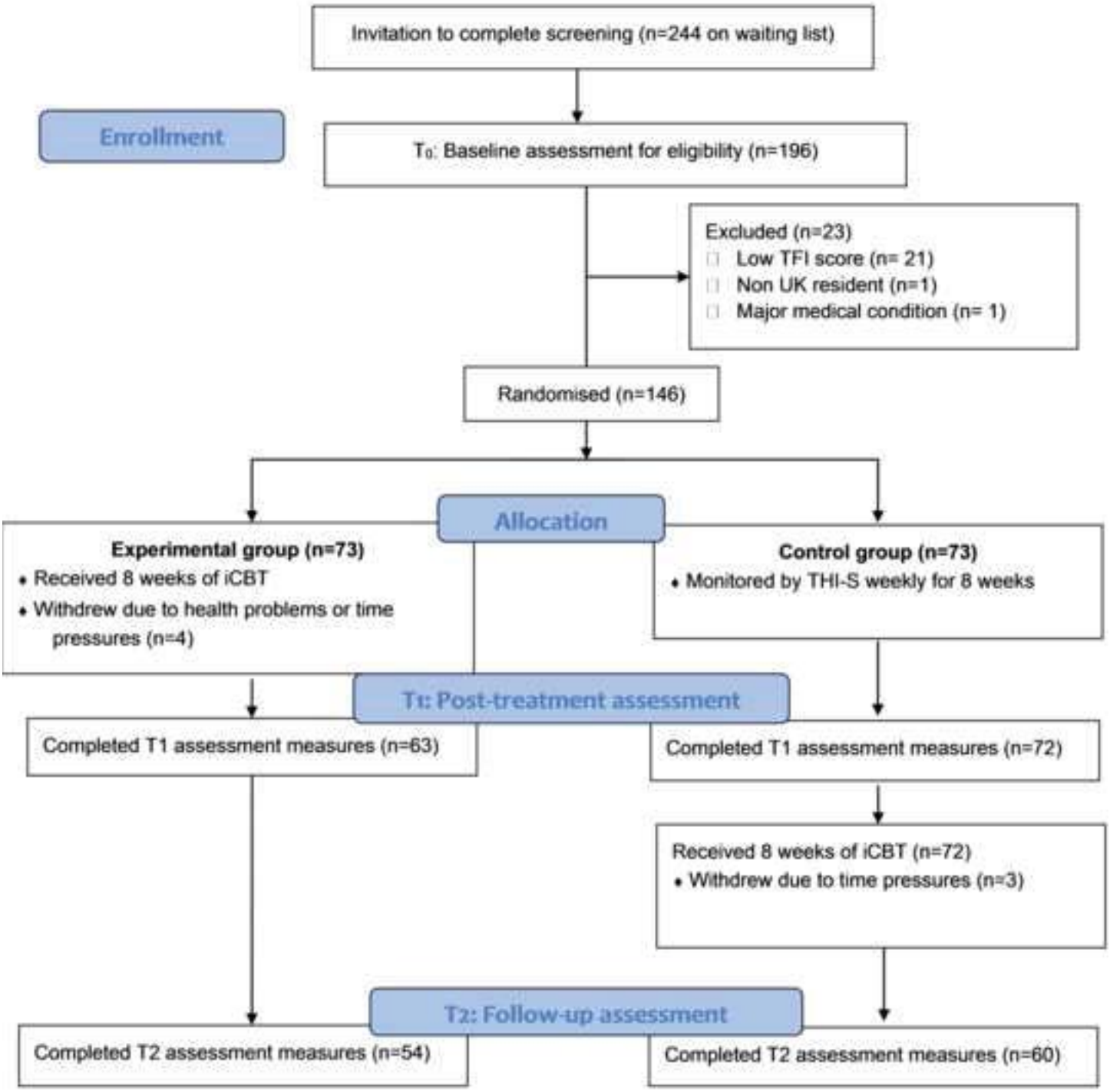

Figure 2

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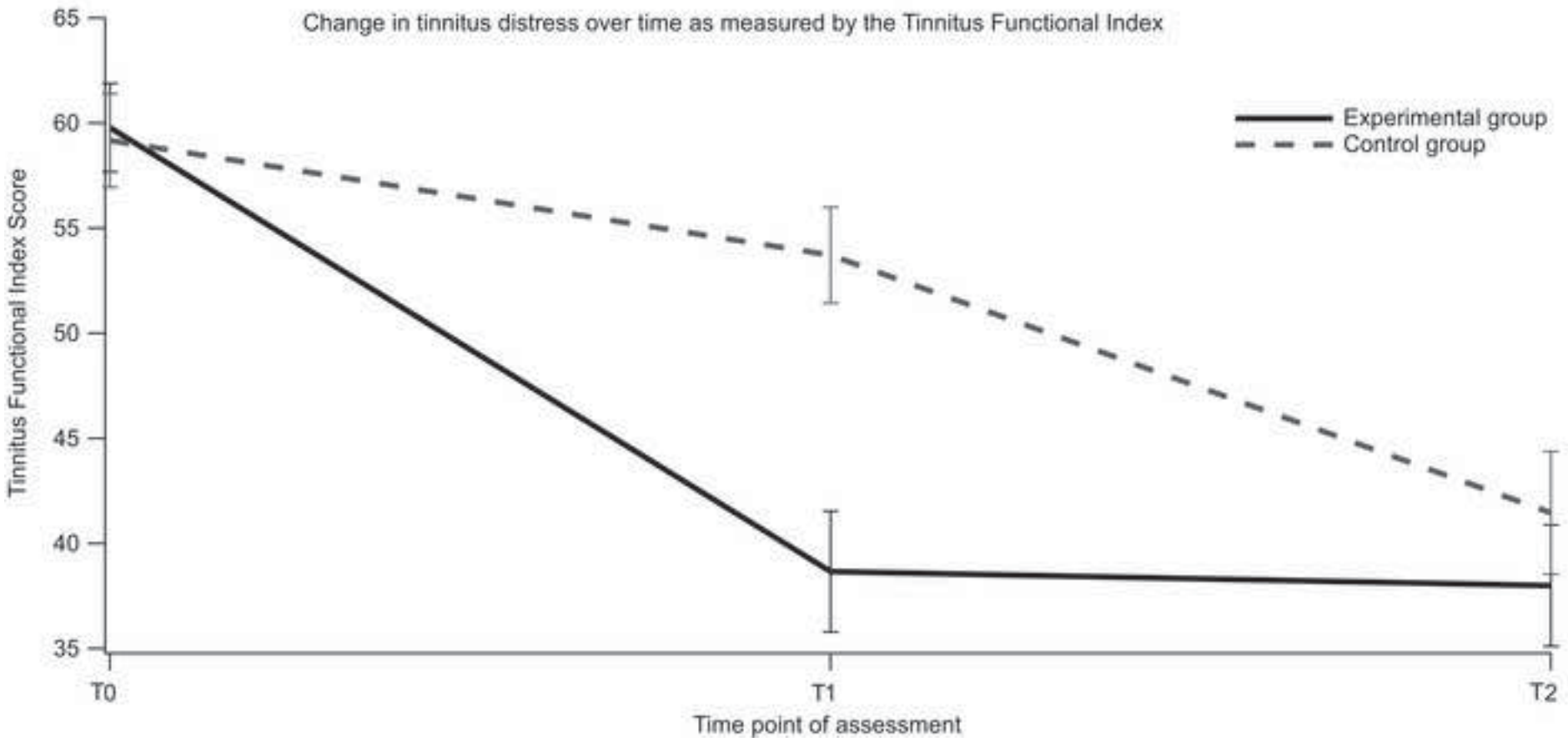

Figure 3

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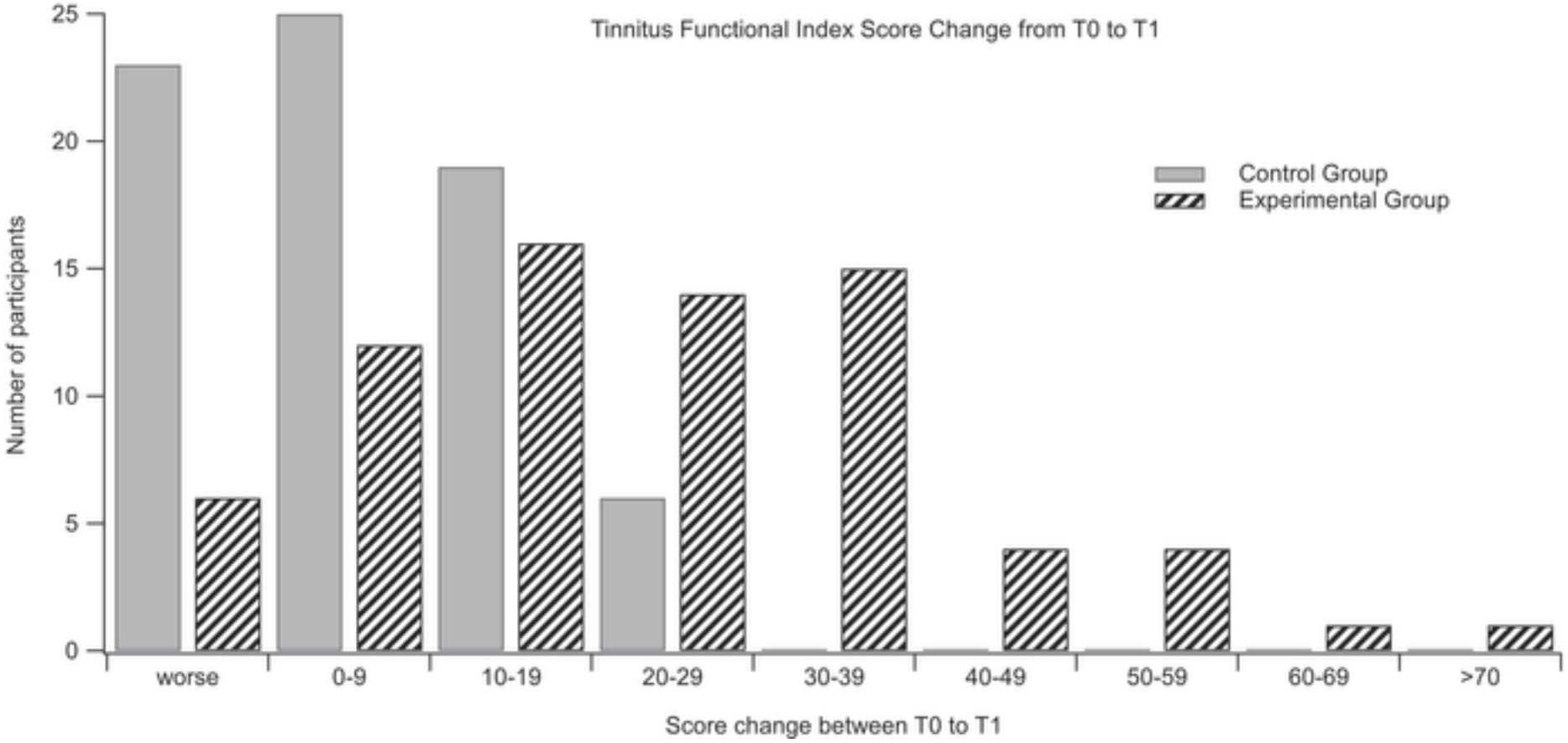

Figure 4

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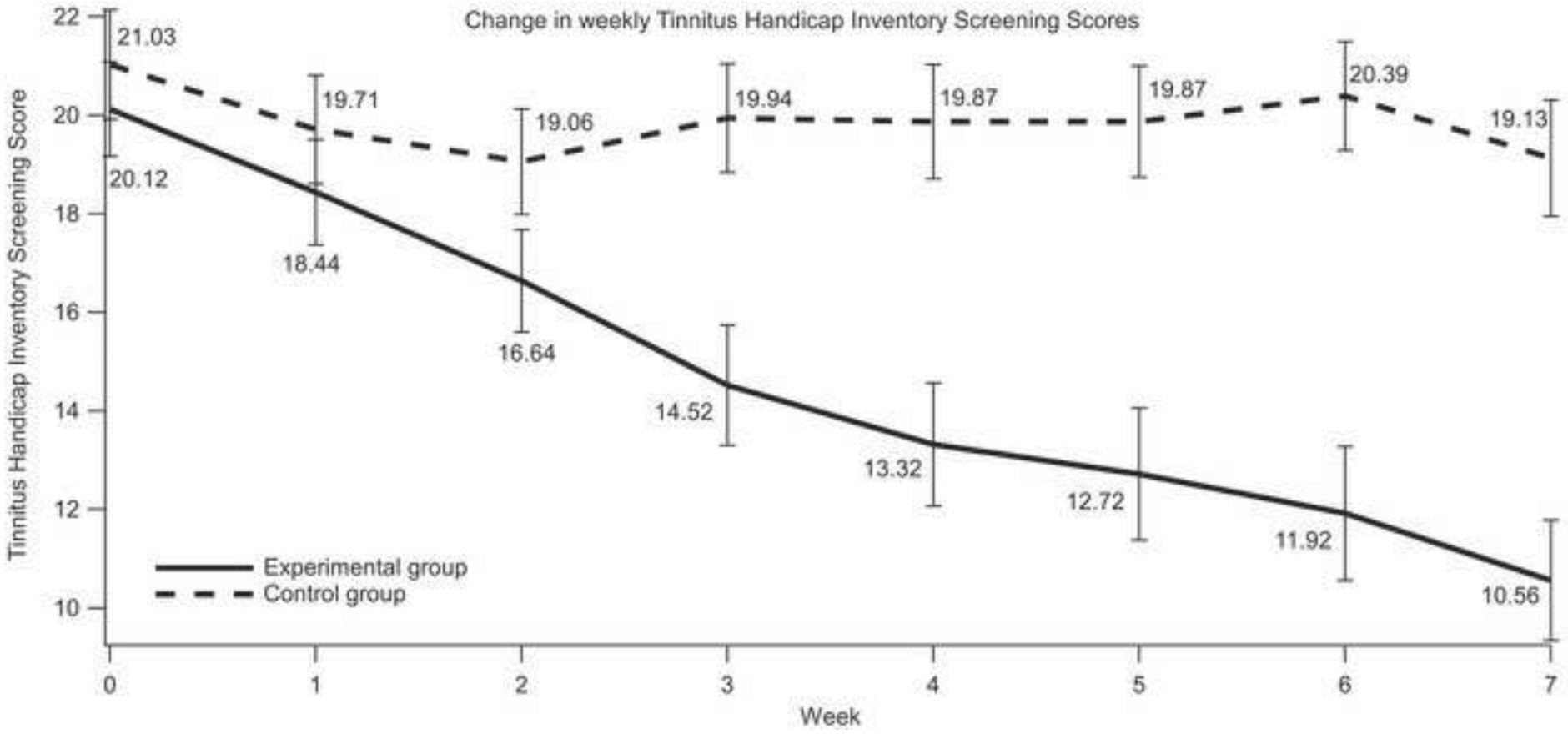

Table 1: Baseline demographical and clinical characteristics of the participants

Category	Description	Experimental group (n=73)	Control group (n=73)	Overall (n=146)
Gender	Male	43 (59%)	40 (55%)	83 (57%)
	Female	30 (41%)	33 (45%)	63 (43%)
Age	Mean years (SD)	56.8 (12.2)	54.3 (13.5)	55.6 (12.9)
	Range	24-79 years	22-83 years	22-83 years
Tinnitus duration	Mean years (SD)	11.1 (11.5)	12.4 (12.2)	11.7 (11.9)
	Range	0.3– 52 years	0.3-56 years	0.3-56 years
Using hearing aids	No	46 (63%)	46 (63%)	92 (63%)
	Yes	27 (37%)	27 (37%)	54 (37%)
Employment status	Retired/unemployed	30 (41%)	32 (44%)	62 (44%)
	Professional	18 (25%)	23 (32%)	41 (28%)
	Service occupation	9 (12%)	6 (8%)	15 (10%)
	Administrative/sales	8 (11%)	9 (12%)	17 (12%)
	Technical	8 (11%)	3 (4%)	11 (8%)
TFI score		59.8 (18.0)	59.2 (19.0)	59.5 (18.4)

Acronyms: TFI= Tinnitus Functional Index; SD= standard deviation

Table 2

Table 2: Within and between group comparisons of the assessment measures over time.

Assessment Measure	Control vs Experimental group mean difference at each time point (SD)			Group comparison: *F*-Statistic[a]			Follow-up analysis: *t*-statistic	Cohen's *d* (95% Confidence interval)
	T_0	T_1	T_2	Time by group interaction	Within group time effect	Between group effect	Between group at T_1	Between group at T_1
TFI	-0.6 (0.4)	15.1 (10.6)	3.5 (2.5)	15.8, $p<0.001$*	97.5, $p< 0.001$*	3.9, $p= 0.05$*	4.3, $p<0.001$*	0.7 (0.4-1.0)
ISI	1.2 (0.8)	3.8 (2.7)	2.5 (1.7)	5.3, $p=0.006$*	47.6, $p <0.001$*	5.4, $p=0.02$*	3.3, $p<0.001$*	0.6 (0.2-0.9)
GAD-7	-0.4 (0.3)	1.4 (1.0)	0.4 (0.3)	3.1, $p=0.05$	11.6, $p <0.001$*	0.5, $p=0.55$	1.8, $p=0.07$	0.3 (0.1-0.6)
PHQ-9	0.2 (0.2)	1.9 (1.3)	0.4 (0.3)	3.7, $p=0.03$*	17.8, $p <0.001$*	1.1, $p=0.31$	2.1, $p=0.04$*	0.3 (0.0-0.7)
HHIA-S	1.2 (0.8)	2.6 (1.8)	0.6 (0.4)	1.7, $p=0.18$	12.2, $p <0.001$*	0.7, $p=0.42$	0.6, $p=0.53$	0.2 (0.1-0.6)
HQ	0.2 (0.2)	3.2 (2.3)	1.4 (1.0)	3.1, $p= 0.04$*	5.9, $p =0.003$*	1.2, $p=0.27$	2.1, $p=0.04$*	0.3 (0.0-0.7)
CFQ	1.3 (0.9)	6.5 (4.6)	3.6 (2.5)	4.2, $p= 0.01$*	1.1, $p=0.32$	1.8, $p=0.18$	2.2, $p=0.03$*	0.4 (0.0-0.7)
SWLS	-0.4 (0.3)	-2.2 (1.5)	-0.6 (0.4)	3.1, $p=0.04$*	12.0, $p <0.001$*	1.4, $p=0.24$	2.3, $p=0.02$*	0.3 (0.0-0.7)

*=significance at < 0.05

Acronyms: SD= Standard Deviation, T_0= preintervention, T_1= postintervention, T_2= 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

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	P1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	P3-4
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	P6-7
	2b	Specific objectives or hypotheses	P7
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	P8
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	P9
Participants	4a	Eligibility criteria for participants	P10
	4b	Settings and locations where the data were collected	P13
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	P14 -15
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	P11-13
	6b	Any changes to trial outcomes after the trial commenced, with reasons	P9
Sample size	7a	How sample size was determined	P16
	7b	When applicable, explanation of any interim analyses and stopping guidelines	NA
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	P16
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	P16
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	P16
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	P16
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those	P16

		assessing outcomes) and how	
	11b	If relevant, description of the similarity of interventions	P14
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	P17-19
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	P18
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	Fig 1, P19
	13b	For each group, losses and exclusions after randomisation, together with reasons	Fig 1, P19-20
Recruitment	14a	Dates defining the periods of recruitment and follow-up	P10
	14b	Why the trial ended or was stopped	NA
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Table 1
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	Fig 1
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	Table 2
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	NA
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	NA
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	P9
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	P26-27
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	P27
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	P27
Other information			
Registration	23	Registration number and name of trial registry	P8
Protocol	24	Where the full trial protocol can be accessed, if available	P8
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	P2

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.