PROTOCOL:

Internet-based intervention versus face-to-face clinical care for tinnitus: A randomized control trial

Title: internet-based intervention versus face-to-face clinical care for tinnitus: A randomized control trial

Clinical Trials registration number: NCT02665975

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Ethical approval: Cambridge South Research Ethics Committee, under the REC reference number: 16/EE/0148. The IRAS project identification number is 195565

Sponsor: Anglia Ruskin University

Clinical Sites: Norfolk and Norwich University Hospitals NHS Foundation Trust

Hinchingbrooke Health Care HNS Trust

Milton Keynes University Hospital NHS Foundation Trust

Intervention: Internet-based cognitive behavioural therapy intervention for tinnitus (iCBT)

INTRODUCTION

Experiencing tinnitus may be very distressing, due to hearing unwanted subjective auditory sensations, such as ringing or buzzing. Many aspects of daily life, such as sleep, mood and concentration may be affected as a result of having tinnitus. Ensuring readily accessible specialist tinnitus clinical services throughout the country is desirable, but difficult to implement, due to the burdens on the current health care system. Innovative ways of helping those with tinnitus, as well as manage the related health care burden, is required. An alternative tinnitus management approach was therefore developed in the form of an internet-delivered cognitive behavioural intervention (iCBT), based on previous research in Europe that showed promising results. A protocol to assess the effectiveness of an internet-based intervention in the UK was published and initial clinical trials are underway. To ensure the gold standard for testing a new intervention is followed, it needs to be compared to standard clinical care. The aim of this research is, therefore, to evaluate the effectiveness of internet-delivered treatment for tinnitus, to that of face-to-face clinical care provided in Tinnitus Clinics. This study is important as it is actively looking at improving patient experiences by developing additional accessible services and excellence in care for adults with tinnitus.

The internet-based intervention is based on cognitive behavioural therapy principles and will be referred to as iCBT in this protocol.

OBJECTIVES

1. To compare the effectiveness of iCBT to that of standard face-to-face clinical care, in reducing the impact of tinnitus, for adults in the East of England
2. To ascertain predictors of outcome for whom this iCBT intervention is a suitable intervention

3. To determine the longer-term effects of both interventions, 2 months post-intervention

STUDY DESIGN

This study is designed to let the public, clinician's and researchers work together in creating an opportunity for a new scientific and clinical intervention. Involvement from a service public-patient partnership is included in this study. A multicentre intervention study is proposed at three sites in the East of England (EOE), namely Norfolk and Norwich Universities Hospitals Trust, Milton Keynes University Hospital NHS Foundation Trust and Hinchingbrooke Health Care NHS Trust, which all have reputable clinical tinnitus services.

The study is a non-inferiority two-armed randomized control trial (RCT), with a two-month follow-up, to evaluate the longer term effectiveness of iCBT on tinnitus distress. The experimental group will receive eight weeks of guided internet-delivered treatment (iCBT). The control group will receive a standard tinnitus audiological appointment and follow-ups. A randomised trial design, regarding centres as blocks will be used.

PARTICIPANTS

Sample size

Sample size calculations have indicated that 46 participants are required per group.

Estimated recruitment is 36 participants from both Norfolk and Norwich University Hospital and Hinchingbrookes Hospital and 20 from Milton Keynes University Hospital.

ENROLLMENT

All adult patients referred to the Tinnitus Clinic by ENT consultants and Audiologists at the clinical sites during the recruitment period who meet inclusion criteria will be invited to participate. The invitation will be made according to standard appointment approaches for each site, by giving the PIS at this stage. Those interested can find out more about the study from the PI or public-patient partnership and register for the study on the study website (www.tackingtinnitus.co.uk).

It is estimated that recruitment will last over a 5 month period.

Inclusion Criteria

1. Referred by an ENT Consultant or Audiologist for tinnitus intervention

2. The ability to read and type in English

3. No barriers to using a computer (e.g. significant fine motor control or visual problems)

4. Internet and e-mail access, and the ability to use these

5. Commitment to completing the programme

6. Completion of the online screening and outcome questionnaires

7. Agreeing to participate in either group and be randomized to one of these groups

8. Understanding and working towards the end goal of reducing the impact and distress of tinnitus, although the strength of the tinnitus may remain the same

9. Availability for 2 months after starting the study to complete an online follow-up questionnaire

Exclusion Criteria

1. Reporting any major medical or psychiatric conditions

2. Undergoing any tinnitus therapy concurrently to partaking in this study

Withdrawal

Participants will be informed of the right to withdraw without penalty. Statistical analysis will be done on an intention to treat basis unless they request all data removal.

SCHEDULE

The study timescales will be finalized following ethical approvals. Recruitment will be aimed to start in August, with initial participants from the face-to-face interventions to be seen between September 2016-February 2017 for their initial and follow-up appointments. Study close out will be two months after their intervention, which is estimated to be by April 2017. A broad outline of procedures and the schedule is indicated in Tables 1 and 2 respectively.

Table 1: Procedures required during the study

PROCEDURE	DESCRIPTION	CONDUCTED BY	TIME	HOW THIS COMPARES WITH CURRENT PROTOCOLS
Information provided about the study	PIS sent together with standard hospital letter inviting patients to make appointments or given at	Letter given by PI to distribute after referral	5 minutes to do 20 minutes for patients to read	Letter sent as standard. PIS included additionally

	hospital at time of referral			
Deciding whether to participate	Patients wanting more information will be directed to the study website and the PI will answer further enquiries. Independent advice is available from members of the patient/public forum	PI and patient/public forum	15 minutes	Additional
Registering for the study	Register interest on the study website	PI	2 minutes	Additional
Online consent to partake in the research	Read the information and consent by sending back the form	PI	5 minutes	Additional
Online screening Questionnaire	Complete and online demographical questionnaire and outcome measures	PI	30 minutes	Normally done at clinics, now done online
A telephone call for those completing the online screening.	At a time that the patient has chosen as convenient, the PI will	PI	10 minutes	Additional

	telephone them. This will act as an additional filter to ensure criteria is met and to provide the opportunity for the research to be explained and additional questions to be asked.			
Randomisation	Randomization into the experimental or control group, using the centre as blocks. Email notification of group and instructions	PI. Notify clinic administrator of those participating and those requiring clinical appointments	5 minutes to read the e-mail	Additional
Experimental group: internet-based intervention (iCBT)	This group will have access to 21 Modules related to tinnitus management	PI	8 weeks	Additional
Control group: face-to-face clinical intervention	Provision of standard tinnitus management provided	CLINICAL SITES: AUDIOLOGISTS	30 min- 1-hour appointments as required, generally 2-3 appointments are	Standard practice

			required, but will be tailored to each individual	
Post-intervention outcome measures	Completing the same outcome measures as prior to starting the intervention to compare outcomes	PI	10-20 minutes	Normally done at clinics, now done online
Post-intervention phone call to	To discuss progress and provide the opportunity for participants to share experiences of the study and discuss if further help is required	PI	10 minutes	Additional
Longer term Post-intervention outcome measures	Completing the same outcome measures as before to determine the longer term effects of the treatment	PI/ collaborative research assistant	10-20 minutes	Additional

Table 2: Schedule of enrolment, interventions and assessment

STUDY PERIOD				
	Enrolment	**Allocation**	**Post-allocation**	**Close-out**
TIMEPOINT	***-T_1***	***T_0***	***T_1 (following intervention end)***	***T_x (2 months post intervention end***
ENROLMENT				
Informed consent	X			
Eligibility screen	X			
Allocation		X		
INTERVENTIONS				
Experimental group		X		
Control group		X		
ASSESSMENTS				
Tinnitus Functional Index	X		X	X
Tinnitus Handicap Inventory	X		X	X
Hearing Handicap Inventory	X		X	X
Insomnia Severity Index	X		X	X
Cognitive Failures Questionnaire	X		X	X
Hyperacusis Questionnaire	X		X	X
Patient Health Questionnaire	X		X	X
Generalised Anxiety Disorder	X		X	X
Satisfaction with Life	X		X	X

All participants will have access to face-to-face clinical care if required, as they will be registered with the local Audiology Departments and will have access to these services. They will also have continued use of the e-learning programme, despite the programme completing. In this way, they will continue to have access to materials enabling self-management.

EVALUATIONS

The format of the questionnaire delivery will remain consistent throughout the study using online questionnaires.

Those consenting will undergo an online screening questionnaire, including demographical information, tinnitus related questions and outcome measures. The outcome measures to be used will include those related to tinnitus and other life areas which may be affected, therefore looking at hearing disability, hyperacusis, insomnia, concentration, satisfaction with life, anxiety and depression, as seen in Table 3.

The main outcome measure will be the Tinnitus Functional Index (Meikle MB, Henry JA, Griest SE, et al. The Tinnitus Functional Index: development of a new clinical measure for chronic, intrusive tinnitus. Ear Hear 2012; 33:153–76). Secondary outcome measures are shown in Table 2.

TABLE 3: OUTCOME MEASURES USED DURING THE STUDY

Measure and validation reference	Items	Scale used	Internal consistency (Cronbach's alpha)
Tinnitus Functional Index	25	1-10	0.97
Tinnitus Handicap Inventory	20	1-3	0.87
Hearing Handicap Inventory: Screening	10	1-3	0.93
Insomnia Severity Index	7	0-4	0.74
Cognitive Failures Questionnaire	25	0-4	0.89
Hyperacusis Questionnaire	14	0-4	0.66-0.68
Patient Health Questionnaire	9	0-3	0.83
Generalised Anxiety Disorder	7	0-3	0.89
Satisfaction with Life Scales	5	1-7	0.87

INTERVENTIONS

Both groups will have access to the following within the hospitals Audiology departments and this will be seen essential hearing aid care and will not form part of the study:

- Any hearing aid required work will be done outside the remits of this study by the Audiology clinics
- Any additional tinnitus equipment required and given as standard will be provided by the Audiology Departments regardless of group allocation.

The interventions provided for this study are those based on counselling and not on equipment or amplification.

Experimental Group:

The intervention to be followed has been built on an internet-based CBT self-help programme (iCBT) developed by Gerhard Andersson in Sweden. It incorporates a combination of a cognitive rational, and a learning theory approach. The PI has designed this material in an interactive e-learning version. This will ensure the

intervention is visually stimulating, engaging and responsive to participant's progress.

The intervention is tailored, consisting of suggested modules and optional modules, covered over a period of eight weeks, as shown in Table 4. The modules contain a mixture of information, videos, quizzes, diagrams, suggested techniques to apply to daily life, worksheets to keep track of progress, solutions for common problems and downloadable information.

The iCBT intervention will be delivered on a secure web platform, for which participants will receive password protected login information.

Table 4: The components of the iCBT intervention

Week	Module	Explanation	Application
1	About this treatment	Introduction to the modules	Reading
	Tinnitus overview	In depth information	Quizzes
2	Relaxation: step 1	Deep relaxation	10-15 min, twice/day
	Identifying negative thoughts	The link between thoughts and feelings	Writing down thoughts
	*Sound enrichment	Using background sounds	Applying external sounds
3	Relaxation: step 2	Diaphragmatic breathing	5-7 min, twice/day
	Cognitive restructuring	Analysing thoughts	Writing down situation, thoughts, feelings
	*Sleep guidelines	Various Techniques	Choose and apply techniques
4	Relaxation: step 3	Entire body relaxation	2-3 min, twice/day

	Positive imagery	Use to enhance relaxation	Twice/day after relaxation
	*Concentration tips	Techniques discussed	Engage in mentally engaging activities
5	Relaxation: step 4	Rapid relaxation	20-60 sec, 5-10 times/day
	Focus exercises	Mindful awareness	Twice/day after relaxation
	*Sensitivity to sound	Gradual exposure	Listen to non-damaging, non-annoying sounds
6	Relaxation: step 5	Rapid relaxation in more difficult situations	30-60 sec, 10-15 times/day
	Reinterpretation of tinnitus	Change negative tinnitus associations	Writing about tinnitus thoughts
	* Hearing tactics	Communication advice	Follow advice
7	Relaxation: step 6	Making relaxation part of daily routines and habits	Rapid relaxation 10-20 times/day
	Exposure to tinnitus	Decrease negative emotions and avoidance of tinnitus	Actively listen to tinnitus for 5-10 min, once/day, after relaxation
8	Key points summary	Highlighting key concepts	Online quiz
	Future planning	Maintenance and relapse prevention	Making a plan to use tools in daily life

Optional modules are marked with an *

Control group:

This group will receive standard face-to-face clinical care and local protocols will be followed. Care will be individualized and 1-3 appointments may be required, which may last between 30-60 minutes each. Table 5 shows what these appointments may include:

Table 5: Control group (standard clinical care interventions)

Appointment	Content	Explanation	Application
1	Providing explanations about hearing loss	Go through individual's hearing loss and implications	Look at audiograms
	Provide information about tinnitus	Explain the tinnitus model	Counselling, use of diagrams
	Develop and individual management plan	Consider patient history and outcomes to discuss together	Clinician/ patient discussion
	Sound enrichment	Discussing the principles of using sound therapy	Counselling/ leaflet
	Sleep management	Provide guidelines to assist sleep management	Counselling/ leaflet
	Relaxation advice	Providing guidelines on the use of relaxation	Counselling/ leaflets
	Negative though management	Managing unhelpful thought patterns	Counselling/ leaflets
	Other	Tailored to the individual	

2	Discuss progress of the individual management plan	Review progress and in which areas attention is still required	Clinician/ patient discussion
	Cover any areas above not covered in appointment 1 or still requiring attention	Consider progress and difficulties following appointment 1	Counselling/ leaflet
3	Discuss progress of the individual management plan	Review progress and in which areas attention is still required	Clinician/ patient discussion
	Cover any areas above not covered in appointment 1 or still requiring attention	Consider progress and difficulties following appointment 2	Counselling/ leaflet

Following each session, the clinician will complete a form ticking what was done in the appointment with a study code of the patient seen, using an online questionnaire link. This will be sent to the PI to record what intervention took place.

SAFETY AND CLINICAL MONITORING

The online questionnaires will identify scores indicative of additional problems which are often co-existent with tinnitus such as anxiety and depression. If these scores are significantly high at any point, a letter will be passed onto the clinical site to send to the General Practitioner. The patient will also be informed.

All personal data will be kept confidentiality. Due to the nature of the guided treatment protocol the main researcher needs to have access to some personal data of the participants to help to contact them. This information will be kept strictly confidential and used only for the purpose of contacting participants during the course of the treatment programme. It is imperative to ensure that individual's personal data is protected. A protocol for this has been set up to

ensure the security of the data on the web-portal which will be used at Linköping University in Sweden. During data analysis, data will be anonymised as unique reference codes will be used. Linköping University has conductive similar CBT trials for a range of conditions and is recognised as a center of excellence in Disability research. They have sophisticated methods of developing web-based treatment protocol and measures to protect personal data within this protocol. Personal information will also be destroyed after 12 months of the completion of the study.

Another risk is that participants may become emotionally distressed having to face their tinnitus while undergoing the intervention. The intervention is specifically aimed to reduce the distress associated with tinnitus, so by undertaking the intervention we hope to reduce the distress associated with tinnitus. Participants will be able to contact the researcher by email at any stage should this be required. If any participants become distressed during the intervention, they will be guided by the research team. As there is a Clinical Psychologist on the research team he will be able to advise on the best course of action, depending on the level of distress shown. If there are issues outside the scope of this research, participants will be asked to make an appointment with their general practitioner and a letter explaining what has happened will be sent to the participant and the general practitioner.

The risk of participants running into difficulties during the intervention is also present. They will be able to contact the researcher who will assist in problem-solving these difficulties.

Participants in the iCBT experimental group will be monitored by the therapist evaluating their worksheets and communications via a secure online messaging system. This therapeutic alliance will allow for feedback and assistance if participants have any difficulties. Participants in the face-to-face group will be monitored by the Audiologist they see.

STATISTICAL CONSIDERATIONS

Data analysis will be in accordance with Consolidated Standards of Reporting Trials (CONSORT) guidelines for non-inferiority randomised clinical trials. SPSS V.23.0 will be used, and the data analyst will be blinded to the groups to minimise bias. Results at post-treatment will be based on a per-protocol analysis and compared with an intention-to-treat paradigm, in which incomplete data sets will be analysed using multiple imputations offered by SPSS.

DATABASE MANAGEMENT PLANS

Data will be kept on the secure web portal. Data exported for statistical analysis will be kept for 1 year following the end of the study at http://www.data-archive.ac.uk/ and then destroyed following this.

TRAINING

Undertaking good clinical practice training prior to research involvement is advisable at https://www.crn.nihr.ac.uk/learning-development/good-clinical-practice/. The principle investigator will meet regularly with clinical sites prior to the study starting to ensure the protocol is understood and the research can be undertaken.