


STUDY PROTOCOL

Open Access



Cost-effectiveness of a smartphone Application for Tinnitus Treatment (the CATT trial): a study protocol of a randomised controlled trial

Sara Demoen^{1,2,3*} , Laure Jacquemin^{2,3}, Annick Timmermans¹, Vincent Van Rompaey^{2,3}, Olivier Vanderveken^{2,3}, Hanne Vermeersch², Iris Joossen², Julie Van Eetvelde^{1,2}, Winfried Schlee⁴, Wim Marneffe⁵, Janis Luyten⁵, Annick Gilles^{2,3,6†} and Sarah Michiels^{1,2†}

Abstract

Background: Tinnitus is a highly prevalent symptom, affecting 10–15% of the adult population. Tinnitus influenced by alterations in somatosensory afference from the neck or jaw is referred to as somatic tinnitus (ST). ST is known to respond positively to physiotherapy treatment; however, it is challenging to motivate patients to systematically perform home exercises correctly, and the necessary tinnitus counselling is often lacking.

The aim of this study is twofold, namely to investigate both the effectiveness and cost-effectiveness of a blended physiotherapy program for ST, including a smartphone application designed to increase exercise therapy compliance and provide tinnitus counselling.

Methods: This study is designed as a single-blind two-arm 1:1 randomised controlled trial (RCT). Adult patients diagnosed with ST, without psychiatric comorbidities and with experience in using a smartphone, will be recruited at the Ear Nose Throat (ENT) department of the Antwerp University Hospital (UZA). Patients will be randomised into two groups. The experimental group will receive the blended physiotherapy program comprising six in-clinic physiotherapy sessions over a period of 12 weeks (1x/2 weeks) and an exercise and counselling program provided by the smartphone application. The control group will receive the standard care program comprising twelve weekly in-clinic physiotherapy sessions. Each physiotherapy session has a duration of 30 min. The primary outcome measure is the change in Tinnitus Functional Index (TFI) score. Additionally, a cost-effectiveness analysis will be performed from a societal perspective considering both direct and indirect costs. There will be follow-up assessments at one and 3 months after the final treatment session.

Discussion: Our study is the first to combine both tinnitus counselling and neck/jaw treatment provided by a digital application in a blended physiotherapy program. This, in order to empower ST patients to improve and better manage their own health and, possibly, reduce economic costs by alleviating the tinnitus burden that ST patients

[†]Annick Gilles and Sarah Michiels contributed equally to this work.

*Correspondence: sara.demoen@uhasselt.be

³ Department of Translational Neurosciences, Faculty of Medicine and Health Sciences, University Antwerp, 2000 Antwerp, Belgium
Full list of author information is available at the end of the article



experience. The strengths of the planned RCT are the high-quality methodological design, the large sample size and the expertise of the involved multidisciplinary research team.

Trial registration: Clinicaltrials.gov [NCT05245318](https://clinicaltrials.gov/ct2/show/study/NCT05245318). Registered on 26 January 2022.

Keywords: Somatic tinnitus, Smartphone application, Blended physiotherapy, Telerehabilitation, Randomised controlled trial

Background

Tinnitus or ringing in the ears is a very common symptom with a variety of possible underlying diseases and/or malfunctions which may be otological, neurological, metabolic, psychogenic and/or somatic in origin [1–3]. It affects 10 to 15% of the adult population and has a widely varying clinical presentation due to the heterogeneity of underlying causes, associated symptoms and comorbidities [4–6]. In 5–10% of tinnitus patients, the symptom is associated with mood changes, anxiety, depression, sleep disorders, concentration problems and other psychological/emotional issues that lead to severe disruptions of daily functioning and health-related quality of life (HRQOL) [7] (Demoen S, Cardon E, Jacquemin L, Timmermans A, Van Rompaey V, Vanderveken O, Vermeersch H, Joossen I, Van Eetvelde J, Schlee W, Marneffe W, Luyten J, Van De Heyning P, Michiels S, Gilles A. Health-related quality of life in subjective, chronic tinnitus patients: a systematic review. Under review). Alleviation of tinnitus can improve the quality of life of many patients and, as a consequence, can reduce the economic burden of tinnitus on society. The general societal cost of tinnitus is extremely high [8, 9]. Three types of costs can be distinguished. Firstly, the direct health care costs that are related to consultations or treatment sessions by healthcare professionals and medication on prescription. Secondly, patient and family costs are additional out-of-pocket costs for the patient or his/her family, such as travel expenses or costs of over-the-counter medication. Lastly, indirect costs are considered the societal costs due to, for example, productivity loss and absence at work [8, 9]. Based upon studies from both USA and Europe, the mean annual costs per patient are estimated between 1544 euro and 3429 euro for healthcare costs, between 69 euro and 115 euro for patient and family costs and between 2565 euro and 3702 euro for indirect costs [8]. To frame, approximately 65 million adults in the European Union suffer from tinnitus, out of which 26 million patients experience bothersome tinnitus and 4 million patients severe tinnitus [10]. Especially patients with bothersome and severe tinnitus seek help, the total costs for this group of 30 million patients is estimated to be between 125 to 217 billion euros on a European level [10].

Among the many potential influencing factors of tinnitus, one group exists where the tinnitus is influenced by alterations in somatosensory afference from the cervical spine or temporomandibular area, caused by, for instance, increased muscle tension or movement restrictions. This type of tinnitus is called somatic or somatosensory tinnitus (ST) and is estimated to be present in approximately 25% of tinnitus patients [11–13]. Previous studies showed that a multimodal physiotherapy treatment directed to cervical spine and temporomandibular joint (TMJ) dysfunctions can provide tinnitus relief in ST patients [14–22]. The multimodal physiotherapy treatment comprises a combination of (home) exercises, manual mobilizations and techniques to decrease muscle tension tailored to the patient's specific cervical spine and/or TMJ dysfunction [14–17].

While the effectiveness of this multimodal physiotherapy program has been proven, there are still opportunities for improvement. Firstly, the efficacy of the home exercises could be increased, as two thirds of patients are not compliant in performing daily home exercises, and others experience difficulties to perform the exercises correctly without the guidance of a physiotherapist [23]. Secondly, the associated symptoms and comorbidities of tinnitus often demand a more multidisciplinary approach [4–7]. Apart from the physiotherapy program, patients would also benefit from additional psychological counselling and advice to account for the mental burden that comes with tinnitus [12]. Due to a lack of knowledge about tinnitus, physiotherapists often do not provide the additional tinnitus counselling, or patients receive inaccurate advice that may counteract the positive effects of the multimodal treatment. This results in suboptimal care for ST patients and often recurrent complaints that require regular treatment series in the long term. As such, ST patients would benefit from additional support to increase exercise compliance on the one hand and from the addition of psychological counselling on the other hand [4–7, 12, 23].

One way to provide these extra elements is through a smartphone application. In the last decade, computer and smartphone applications increasingly found their way into medicine and physiotherapy treatment. Recently, the COVID-19 pandemic has shown that low-contact treatment provided from a distance through applications

and videoconferencing can be used as a substitution of or addition to face-to-face clinical care for several conditions [24–26]. Telerehabilitation and internet-based psychological counselling have already proven to be as effective as standard practice in relieving pain and disability in a variety of musculoskeletal conditions [27, 28] and in reducing distress in case of tinnitus [29]. The use of a smartphone application might provide additional support to motivate the patient to perform daily exercises in order to increase exercise compliance. Furthermore, it can be used to provide psychological tinnitus counselling.

Therefore, the aim of this single-blind non-inferiority two-arm parallel group 1:1 randomised controlled trial is to investigate the effectiveness and cost-effectiveness of a blended physiotherapy program for ST, including a smartphone application designed to increase therapy compliance and provide tinnitus counselling. It is hypothesised that the blended physiotherapy program will at least be as effective as the standard physiotherapy care and that this new intervention will reduce both direct and indirect costs related to ST.

Methodology

This protocol is reported according to the Standard Protocol Items Recommendations for Interventional Trials (SPIRIT) guidelines 2013: Explanation and Elaboration: guidance for protocols of clinical trials [30].

Patients

Adult patients (+18 years old) can be included in the study in case they are diagnosed with ST, according to the diagnostic criteria for ST, listed in Table 1 [31]. The diagnosis will be made by an experienced multidisciplinary team of Ear Nose Throat (ENT) specialists, audiologists, physiotherapists and psychiatrists at the University Hospital of Antwerp (UZA) (Belgium), in order to identify and take into account all potential influencing factors of a patient's tinnitus. Patients will only be diagnosed with ST in case the somatosensory influence on the tinnitus is one of the major influencing factors. Tinnitus patients who present themselves with one or more of the 'Accompanying symptoms' described in Table 1 are considered suffering from ST in case their tinnitus appeared or aggravates simultaneously with the neck or jaw symptoms. Additionally, in case the occurrence of the tinnitus is closely related to a neck or head trauma, patients are considered to suffer from ST [32].

Patients should be fluent in Dutch, in order to complete all questionnaires and perform all tests (including speech-in-noise tests). Additionally, all included patients should own a smartphone and should be able to use the most common applications without support. Patients with other types of tinnitus, active middle ear pathology or diagnosed psychiatric disorders will be excluded from the study.

Table 1 Diagnostic criteria for somatic tinnitus (ST) listed by a group of ST experts [31]

Tinnitus modulation

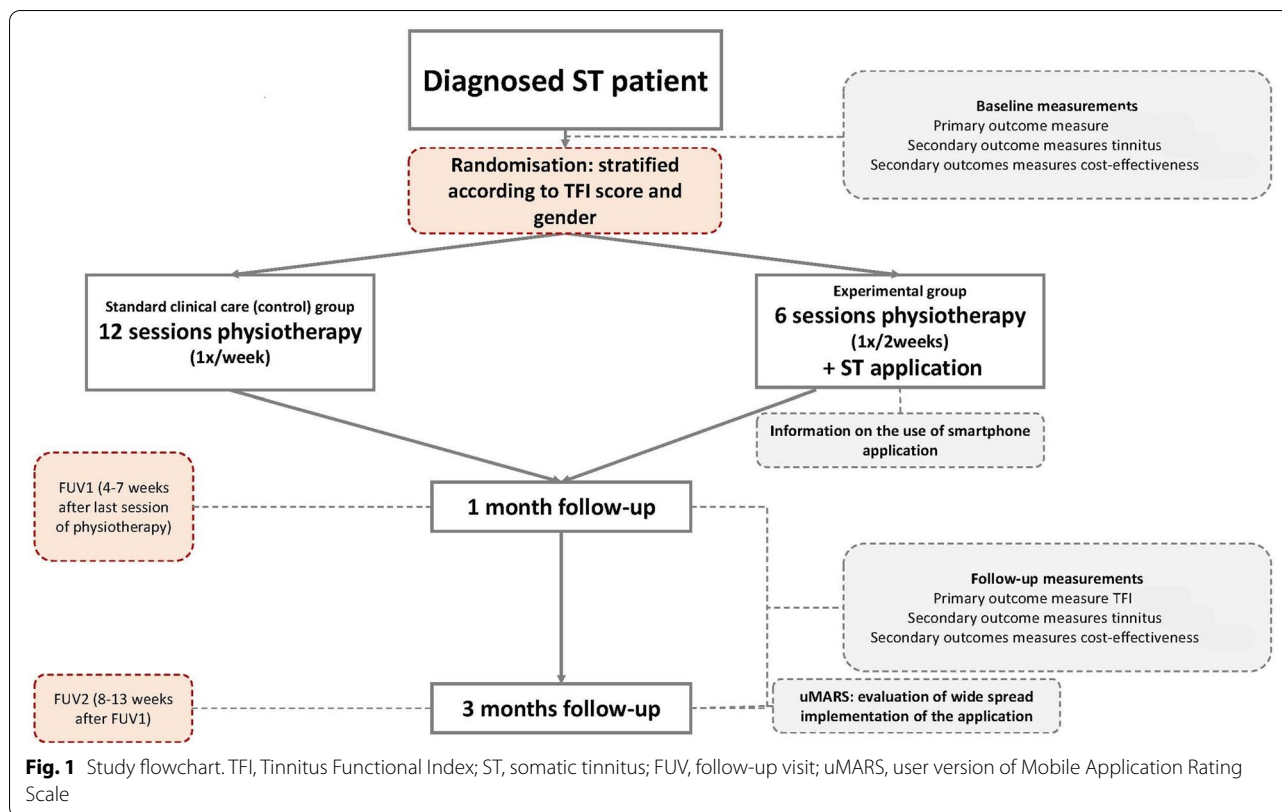
- By voluntary movements of head, neck, jaw or eyes
- By somatic manoeuvres
- By pressure on myofascial trigger points

Tinnitus characteristics

- Simultaneous appearance of tinnitus and neck or jaw pain
- Simultaneous aggravation of tinnitus and neck or jaw pain
- Preceded neck or head trauma
- Increase in tinnitus during certain postures
- Varying tinnitus pitch, loudness and/or location
- For unilateral tinnitus, the audiogram does not account for unilateral tinnitus

Accompanying symptoms

- Frequent pain in the cervical spine, head or shoulder girdle
- Presence of pressure tender myofascial trigger points
- Increased muscle tension in the suboccipital muscles
- Increased muscle tension in the extensor muscles of the cervical spine
- Temporomandibular disorders
- Teeth clenching or bruxism
- Dental disease



Study design and randomisation procedure

The study is designed as a single-blind two-arm 1:1 randomised controlled trial. After baseline measurements, patients will be randomised into either the experimental group or the control group. A stratified randomisation according to the grade of tinnitus severity obtained by use of the Tinnitus Functional Index (TFI) and gender will be used. The TFI categorises patients from grade 1 (no tinnitus distress) to grade 5 (very severe tinnitus distress) [33–35]. Only grades 2–5 are considered for this study: light distress (7 to 28), moderate distress (29 to 47), severe tinnitus distress (48 to 65) and very severe tinnitus distress (66 to 100) [35]. The stratified randomisation assures an even distribution of patients of each tinnitus grade and of men and women in both treatment arms. A minimisation procedure will be used to perform the stratified randomisation using the web-based online randomisation tool Qminim [36]. Patients will be informed that the study investigates the effectiveness of two different physiotherapy approaches for ST but will not receive in-detail information about the content of the treatment before randomisation. Hence, patients are blinded towards the group they are randomised to. The therapist cannot be blinded. To limit the risk of bias related to lack of blinding of the therapist, all evaluation measurements will be performed by a blinded assessor and data analysts

will be blinded as well. An overview of the study design and randomisation procedure is presented in Fig. 1.

Outcome measures

The following outcome measures will be collected at baseline and during the two follow-up visits. The first follow-up visit is planned 1 month (range: 4 to 7 weeks) after the last treatment session. The second follow-up visit will take place 3 months (range: 8 to 13 weeks) after the last treatment session. In between the first and second follow-up moment should be a minimum period of 4 weeks. For certain outcome measures additional measuring moments are planned, these are specified individually below. See Fig. 2 for an in-detail schedule of enrolment, interventions and assessments in accordance with the SPIRIT 2013 guidelines [30].

Primary outcome measure

The primary outcome is the change in Tinnitus Functional Index (TFI) score from baseline to 1 month after the treatment. This time point was chosen since previous research indicated that the largest treatment effect on TFI is to be expected 1 month after the last treatment session [37–40]. For the cost-effectiveness analysis, an additional time point, immediately after the last treatment session, is added to be able to link the amount of decrease on

TIMEPOINT**	STUDY PERIOD																
	Enrolment	Allocation	Post-allocation										Follow-up				
	-t ₁	0	t ₁	t ₂	t ₃	t ₄	t ₅	t ₆	t ₇	t ₈	t ₉	t ₁₀	t ₁₁	t ₁₂	1 month	2 months	3 months
ENROLMENT:																	
Eligibility screen	X																
Informed consent	X																
Allocation		X															
INTERVENTIONS:																	
Standard care			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Blended physiotherapy program			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
ASSESSMENTS:																	
Tinnitus Functional Index (TFI)	X													X	X		X
Joint Repositioning Accuracy (JRA)		X													X		X
Cervical Range of motion (ROM)		X													X		X
Strength and coordination neck- and shoulder muscles		X													X		X
Temporomandibular ROM		X													X		X
Myofascial triggerpoints		X													X		X
Pure tone hearing thresholds		X													X		X
Speech-in-quiet		X													X		X
Speech-in-noise		X													X		X
Tinnitus Pitch matching		X													X		X
Tinnitus Loudness Matching		X													X		X
Visual Analogue Scale (VAS) for tinnitus Loudness		X													X		X
Neck Bournemouth Questionnaire (NBQ)		X													X		X
Temporomandibular disorder (TMD) pain screener		X													X		X
Hospital Anxiety and Depression Scale (HADS)		X													X		X
Hyperacusis Questionnaire (HQ)		X													X		X
Euroqol (EQ)-5D		X											X	X		X	
Productivity Costs Questionnaire (PCQ)		X			X			X				X	X	X	X	X	
Diary of medical costs																	X

Fig. 2 Schedule of enrolment, interventions and assessments in accordance with the SPIRIT 2013 guidelines

TFI to the EuroQoL (EQ)-5D-5L that assesses HRQOL. The TFI is a self-report questionnaire comprising 25 questions, each scored on an eleven-point Likert scale, objectifying the impact and severity of tinnitus. Eight subscores are differentiated, namely intrusiveness, sense of control, cognitive complaints, sleep disturbance, auditory difficulties, relaxation, quality of life (QOL) and emotional distress. The total score and subscores will be noted on a scale of 0 to 100 with higher scores indicating higher levels of tinnitus-related distress [33, 34]. A change of 13 points out of 100 is considered a clinically relevant change [33]. TFI has a high sensitivity to change, a good test-retest reliability (r : 0.78), discriminant validity with the Beck Depression Inventory-Primary Care

(r : 0.56) and convergent validity with both the Tinnitus Handicap Inventory (THI) (r : 0.86) and the visual analogue scale (VAS) for tinnitus loudness (r : 0.75) [33, 41, 42].

Secondary outcome measures

Clinical cervical and temporomandibular outcome measures The following tests will be used to assess the dysfunction of the cervical spine and temporomandibular area. Firstly, cervical spine mobility and joint repositioning accuracy (JRA) will be measured using the NeckCare Unit (<https://www.neckcare.com/>). This

device, using accelerometer and gyroscope data, is specifically designed for investigating the cervical range of motion and JRA. Additionally, the strength and coordination of the deep neck flexor and extensor muscles and the shoulder stabilising muscles will be assessed according to the standardised protocol proposed by Segarra et al. [43].

The mobility of the temporomandibular joint will be measured using a ruler. Mouth opening, protrusion and laterotrusion will be objectified in this manner. Finally, active myofascial trigger points will be looked for in the masseter and temporalis muscle and in the sternocleidomastoid, splenius capitis, upper trapezius and levator scapulae muscles [44, 45].

Audiological outcome measures

- Pure tone hearing thresholds

Pure tone audiometry, to objectify the presence of hearing loss, will be performed according to current clinical standards (ISO 8253-1, 1989) using a two-channel Interacoustics AC-40 audiometer in a silent room. Air conduction thresholds are measured by the use of headphones at 125 Hz, 250 Hz, 500 Hz, 1 kHz, 2 kHz, 3 kHz, 4 kHz, 6 kHz and 8 kHz. In cases where air conduction thresholds exceed the normality level of 20 dB HL at one or more frequencies between 250 Hz and 4 kHz, bone conduction thresholds will be measured at 250 Hz, 500 Hz, 1 kHz, 2 kHz, 3 kHz and 4 kHz.

- Speech-in-quiet (SPIQ) and speech-in-noise (SPIN) understanding

Speech reception in quiet (SPIQ) will be measured using the Dutch open-set NVA lists developed by the Nederlandse Vereniging voor Audiologie (NVA) (Dutch Society for Audiology) [46]. Each list consists of twelve monosyllabic words (consonant-vowel-consonant), of which one is a training item. The speech recognition score is the percentage of correctly identified phonemes. The lists will be presented through headphones. The speech reception in noise (SPIN) will be assessed by means of the Leuven Intelligibility Sentences Test (LIST) using an adaptive procedure [47]. The frequency spectrum of the noise signal is equal to the long-term average speech spectrum of the sentences. The level of the noise is fixed at 65 dB SPL, while the level of the speech signal is altered depending on the response of the patient. If the participant repeats

the keywords of the sentence correctly, the level of the next sentence is decreased by 2 dB SPL. If the participant fails to repeat the keywords correctly, the level is increased by 2 dB SPL. Each list consists of ten sentences, and the speech reception threshold (SRT) is calculated as the mean level of the last five sentences together with the level of the imaginary 11th sentence of the list. This speech in noise test is performed using headphones.

- Psychoacoustic tinnitus measures

Tinnitus pitch matching

The pitch is the psychoacoustic equivalent of the physical parameter frequency. The tinnitus pitch is obtained by use of a pitch matching technique which is the quantitative and qualitative description of the spectral characteristics of the tinnitus. For this technique, a two-alternative forced-choice procedure will be used using the contralateral ear as the reference ear. In cases where tinnitus is perceived bilaterally, the choice of the ear is the side where the tinnitus is perceived the loudest. By this technique, an attempt is made to identify the centre pitch of the tinnitus. When multiple tinnitus sounds are perceived, it is suggested to concentrate on the most troublesome tinnitus sound. Each time, a pair of pure tones (or noises in case of noise-like tinnitus), differing by one or more octaves, are presented to the subject, who has to indicate which of the tones resembles the tinnitus the most. This procedure is repeated, and finer adjustments are made to obtain a match of tinnitus pitch as exact as possible.

Tinnitus loudness matching

Loudness is the perceptual correlate of the sound intensity. The tone (or noise) defined as the pitch match is presented to the ipsilateral ear (when appropriate), and a loudness match is made by the use of an alternating forced-choice procedure with an accuracy of 1 dB.

Questionnaires related to the effectiveness analysis

- VAS for tinnitus loudness

Patients are asked to score the mean and maximum loudness of their tinnitus in the previous week on a 100-mm horizontal line ranging from left: 0 (absence of tinnitus) to right: 100 (as loud as possible, cannot be any louder) [48].

- Neck Bournemouth Questionnaire (NBQ) score

The presence and severity of neck complaints will be evaluated using the NBQ. The NBQ [49] consists of seven questions on the severity of the neck complaints and its interference with the patient's wellbeing and professional and daily activities. Each item is scored on an eleven-point Likert scale. A higher score out of the maximum of 70 represents higher levels of neck pain and disability [49]. Scores from 13 points upwards are considered to represent a clinically important neck dysfunction [49]. The test-retest reliability of the NBQ is moderate (ICC: 0.65). The construct validity is acceptable with both the Neck Disability Index (r : 0.50) and the Copenhagen Neck Functional Index (r : 0.44). The effect size was high (Cohen's d : 1.67), which indicates that the NBQ is highly responsive to changes in cervical spine complaints [49–51]. The clinically relevant change of the NBQ is a 12 points decrease [49, 50].

- Temporomandibular disorder (TMD) pain screener score

The presence and severity of temporomandibular disorders (TMD) will be evaluated using the TMD pain screener. The TMD pain screener is a 6-item questionnaire regarding pain complaints from the orofacial region and their dependency on functions, like opening wide or chewing. One item has three answer options, scored zero, one or two. The five remaining items are answered dichotomously with yes or no, respectively scored as one or zero. The minimal score is zero and the maximal score is seven. In case a patient scores at least a three out of seven on the TMD pain screener, the patient is suspected to suffer from a painful TMD (sensitivity 0.99 and specificity 0.95–0.98, respectively) [52]. Internal consistency of the questionnaire is excellent, with a coefficient α value of 0.93, reliability is good (ICC: 0.79), and excellent sensitivity and specificity for diagnosing TMD (0.99 and 0.95–0.98, respectively) [51, 53].

- Hospital Anxiety and Depression Scale (HADS)

The Hospital Anxiety and Depression Scale (HADS) is used to detect signs of depression and anxiety symptoms [54]. It is a self-assessment scale and was developed to identify the possibility and probability of the presence of anxiety and depression among patients in non-psychiatric clinics [54]. It exists of two subscales, an anxiety subscale (HADS-A) and a depression subscale (HADS-D), both containing seven intermingled items. Each subscale is scored out of a total of 21; a score greater than eight

indicates the presence of anxiety or depression symptoms, respectively [54]. A high internal consistency was stated for a both the depression and anxiety scale, with respectively a mean coefficient α value of 0.83 and 0.82 [55]. In addition, both scales also demonstrated a good sensitivity and specificity of approximately 0.80 [55]. The HADS is found to be an instrument of moderate reliability (ICC: 0.56) for screening states of depression and anxiety in the setting of a hospital medical outpatient clinic [51, 54, 55].

- Hyperacusis Questionnaire (HQ)

Hyperacusis, a symptom that often co-occurs with tinnitus, is quantified and characterised using the Dutch version of the Hyperacusis Questionnaire (HQ) [47, 56]. This questionnaire consists of 14 questions that are answered on a 4-point scale, ranging from 'No' (0 points), 'Yes, a little' (1 point), 'Yes, quite a lot' (2 points) to 'Yes, a lot' (3 points). Scores on the HQ consequently range from 0 to 42, and the traditional cut-off value for hyperacusis is 28 points [47]. Moderate correlations between the HQ, uncomfortable loudness levels and other health questionnaires and a high internal consistency of the HQ have been demonstrated [57].

Questionnaires related to the cost-effectiveness analysis

- EuroQoL (EQ)-5D [58]

The EuroQoL EQ-5D questionnaire is the most commonly used method to collect health-related Quality of Life (HRQOL) data and is recommended by worldwide economic evaluation guidelines such as the NICE recommendations [59, 60]. This questionnaire measures HRQOL using 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression [58]. The response pattern produces a code which represents a health state of the participant. Each health state is associated with a health utility value between 0 and 1 in which 0 represents death and 1 corresponds to perfect health [60]. To calculate utility values, the recently published utility value sets for Belgium will be used [61]. HRQOL is necessary to calculate quality-adjusted life years (QALYs), the most important outcome from the health economics point of view [60]. The five level (5L)-version is preferred over the three level (3L)-version as it is more nuanced and thus more sensitive to gains (or losses) in general health [62]. The EQ-5D-5L will be assessed at baseline and both follow-up moments and will additionally be collected after the final treatment session.

- Productivity Cost Questionnaire (*i*PCQ) [63]

The *i*MTA Productivity Cost Questionnaire (*i*PCQ) includes three modules measuring productivity losses of paid work due to (1) absenteeism and (2) presenteeism (productivity loss due to paid work) and productivity losses related to (3) unpaid work. The *i*PCQ delivers the necessary input to calculate productivity loss. *i*PCQ will be collected monthly, meaning every 3 to 5 weeks. To organise this systematically, patients of the intervention group will be asked to complete this questionnaire at treatment session two, four and six and patients of the control group at treatment session four, eight and twelve. Both groups will additionally receive the *i*PCQ at 1 month follow-up and 3 months follow-up, as defined above. An additional two-month follow-up moment is planned for the *i*PCQ (range: 3 to 5 weeks after 1 month follow-up assessment).

Diary of medical costs As patients are allowed to seek medical help outside the participating hospital between the 1 month and 3 months follow-up visits, healthcare/medication use cannot be monitored using the hospital's financial records. Therefore, patients will be handed a diary in which they should collect all information regarding tinnitus related medical help, such as physician consultations (including general practitioners), psychological consultations, medication use and treatments in the context of their tinnitus complaints.

Ethics

Every patient will impart written consent for participation. The study protocol and the use of the developed smartphone application received a consolidated positive advice by the Belgian Federal Agency for Medicine and Health Products (FAMHP) and an independent Ethical Committee (Ref. CIV-BE-21-09-037760). The study protocol was registered at Clinicaltrials.gov (ref. NCT05245318).

Intervention

Standard clinical care (control treatment)

The standard care treatment comprises 12 face-to-face individual physiotherapy sessions at a ratio of 1 session of 30 min a week [14, 37]. Every patient in the control group will be treated in a tailored manner according to their results on the baseline measurements and will thus receive a personalised 12-week treatment program. The multimodal treatment program will consist of exercises to increase strength, endurance and coordination of the cervical spine (deep neck flexors and extensor muscles)

and shoulder stabilising muscles, exercises to increase mobility and improve posture [14, 15]. In case of jaw complaints, stretching exercises of the masticatory muscles to increase jaw mobility are added to the program [15, 19]. In addition, manual mobilisations can be performed if limitations in the mobility of the neck or temporomandibular joints are observed. In the same manner, manual techniques to decrease muscle tension in neck and jaw muscles can be added to the exercise program [14, 15, 19]. Additionally, patients receive counselling to learn about their neck/jaw complaints and to guide them to good posture and movement habits, such as emphasising the importance to change posture when sedentary and specific advice concerning mouth habits and sleep hygiene in patients with jaw complaints [15]. Patients will be motivated to perform the exercise program at home on a daily basis but will not receive additional support on the home exercises between sessions. The patient's performance on the exercises will be evaluated during the weekly session in the clinic. Patients in the control group will not receive any tinnitus counselling.

Blended physiotherapy program (experimental treatment)

The experimental group will receive a blended physiotherapy program consisting of only six instead of twelve physiotherapy treatments over a period of 12 weeks, meaning one treatment session of 30 min every 2 weeks. In addition, a smartphone application will offer the patients a daily exercise program, based upon the standard physiotherapy treatment for ST [14–22], and psychological tinnitus counselling. This tinnitus counselling program consists of two sessions a week and is developed by psychologists of the University of Regensburg [64, 65]. Before the start of the program, the exercises will be tailored to the area, type and degree of the patient's dysfunctions. During the six physiotherapy treatment sessions, patients will, if needed, receive manual mobilisations to increase mobility of the neck and/or temporomandibular joints or manual techniques to decrease muscle tension in neck and jaw muscles [14–22]. Additional counselling on knowledge about neck and jaw pain and advice about posture and movement habits will also be provided by the physiotherapist during these six treatment sessions.

Post-trial care

Patients of both intervention groups will be followed up by the multidisciplinary team of the University Hospital of Antwerp after the study trajectory and if requested by the patient post-trial care will be provided when necessary.

Sample size and power

The study is designed as a non-inferiority trial of a continuous response variable comparing independent control and experimental subjects. The primary outcome is the change in TFI from baseline to 1-month follow-up. We hypothesise that there is no significant difference between the control and experimental group for this outcome. A non-inferiority margin is chosen at 6.5 points, being half of the minimally clinically important difference [66]. Assuming a standard deviation of 20 points (SD found in international literature [67] as well as in previously performed own studies [14, 18]) and a significance level (α) of 0.025, an achieved sample size of 150 patients per group is required to have 80% power to show non-inferiority using a one-sided, independent samples *t*-test. Considering a possible 10% drop-out, based on previous studies in ST [14, 37], 167 patients will be recruited into each group. Hence, a total of 334 patients will be recruited for the study.

Data analysis and statistics

Effectiveness analysis

Primary analysis Our primary hypothesis is that the change in TFI-score from baseline to 1-month follow-up will be non-inferior in the experimental group compared to the control group. After calculating a TFI-change score from baseline to 1-month follow-up, a two-sided 95% confidence interval for the mean difference in this change score between experimental and control group will be compared to the non-inferiority margin of 6.5.

Secondary analysis The continuous secondary outcomes and baseline characteristics, measured at the different time points, will be used in a linear mixed model allowing correction for repeated measurements from the same patient to compare their profiles over time and identify at which time points the groups differ. Other variables such as age, gender and tinnitus grade can also be included in these models.

Considering this is a non-inferiority trial, primary and secondary endpoints are analysed in first instance in the per-protocol population. The per-protocol population are all eligible patients who adhered to the complete protocol. The intention-to-treat population will be taken into consideration in a sensitivity analysis afterwards.

Cost-effectiveness analysis (CEA)

The outcome of the CEA is the incremental cost-effectiveness ratio (ICER) of the blended physiotherapy program compared to the usual care program. The ICER is

calculated as incremental costs divided by incremental effects. The analysis thus consists of two components: (1) incremental costs and (2) the incremental health outcomes (effects).

Costs In accordance with the European Network for Health Technology Assessment (EUnetHTA) guidelines, the CEA will comprise two parts: a base case analysis, which only takes into account direct medical costs, and an extended analysis, which additionally considers relevant indirect costs such as work absenteeism and productivity loss [68]. As all relevant direct medical costs (i.e. consultation fees, scans, medication, etc.) stem from inpatient care provision, the costs for the base case analysis will be collected using the financial records of the Antwerp University Hospital. Relevant medication use is registered as a standard practice in the RCT described above. To assign costs to medication use, we will use the official unit prices of the Rijksinstituut voor Ziekten en Invaliditeitsverzekering (RIZIV)/ l'Assurance soins de santé et indemnités (INAMI). As discussed above, patients are allowed to seek medical help outside the hospital between the two follow-up moments. As a consequence, healthcare and medication use cannot be monitored using hospital's financial records in this period of time. Therefore, patients will keep a diary specifically designed for this study in which they should report all information regarding tinnitus related medical help and medication use. The content of this diary is discussed elaborately above.

Apart from the direct medical costs, the CEA will also incorporate relevant indirect costs in a separate, extended analysis. The abovementioned *i*PCQ will be used to collect the necessary input to calculate the costs associated to absenteeism and productivity loss due to tinnitus complaints following the Human Capital Approach (HCA) [68]. The HCA values the time during the whole period of work inability due to sick leave by multiplying the total number of days of work absenteeism by the national average labour cost per day. To calculate the productivity loss at work, the number of days with productivity loss will be multiplied by efficiency loss and the daily average of hours worked. Next, to value the productivity loss, this result will be multiplied by the national average labour cost per hour. All cost data will be collected over the entire study period starting at baseline.

Health outcomes To evaluate the potential health gains of ST patients due to the blended physiotherapy program, this study will employ quality-adjusted life years (QALYs). QALYs combine both length of life (LoL) and health-related quality of life (HRQOL) in one composite

measure. One QALY gained because of the blended physiotherapy program can thus be interpreted as living one additional year in perfect health due to the proposed treatment.

HRQOL will be determined using the EuroQoL EQ-5D-5L questionnaire, which is discussed elaborately above. While we expect HRQOL to be equal across groups at visit 1, data collection at baseline is necessary to be able to adjust for possible, but unlikely, baseline differences between the control group and intervention group. The resulting health states will be converted into health utilities (ranging from 0 to 1 with 0 equal to death and 1 to perfect health) using the recently published utility value sets for Belgium and will at its turn be used to calculate QALYs [61]. Next, incremental health gains will be calculated by comparing the QALYs of the intervention group to the control group.

Cost-effectiveness

Finally, the ICER will be calculated by dividing incremental costs by incremental health gains and is by consequence expressed as €/QALY gained. This outcome can thus be interpreted as the additional amount of costs needed for the blended physiotherapy program to gain one additional QALY compared to the usual care program. The robustness of the results will be assessed by bootstrapping (>1000 samples) and be presented on a cost-effectiveness plane. The results will consist of a base case analysis taking into account only the direct medical costs and an extended analysis taking into account both direct and indirect costs.

Discussion

The aim of this study is twofold, namely investigating the effectiveness and cost-effectiveness of a blended physiotherapy program for ST, including a smartphone application designed to increase therapy compliance and provide tinnitus counselling.

The study population in scope are adult ST patients. Patients will be diagnosed with ST by a multidisciplinary team of specialists in their field. This team will exist of ENT doctors, audiologists, physiotherapists and psychiatrists. The ENT doctors and audiologists will examine the presence of possible hearing loss, underlying disorders and tinnitus. The physiotherapists will assess the presence of neck and jaw dysfunctions and the link between these dysfunctions and the tinnitus using the diagnostic criteria for somatic tinnitus [31]. Any active psychiatric disorders, such as anxiety or depression disorders, will be excluded by the psychiatrist. This extensive diagnostic

process by a multidisciplinary team is a major strength of our study.

The main scientific risks associated with the present study protocol are insufficient enrolment and patient drop-out. However, every year 2500 patients suffering from tinnitus seek help at the ENT department at UZA. As a quarter of these patients are diagnosed with ST, a maximum of 625 patients will be available for inclusion in our study on an annual basis. Therefore, we expect sufficient enrolment during the inclusion period of 2.5 years. In addition, the willingness of participants to complete the full treatment program and all follow-up tests is crucial for the power of the study results. The risk for drop-out is especially high in patients who do not experience the expected treatment results. To maximise treatment adherence and minimise drop-out, patients will be encouraged to complete the treatment and follow-up phase by the therapist, the study nurse and the researcher. Nonetheless, a drop-out of 10% was considered in the sample size calculation.

This study will use a high-quality methodological design to perform a single blind two-arm randomised controlled trial. A total of 334 patients will be randomised into two groups and the current standard care will be compared to the use of a blended physiotherapy program. In studies investigating physiotherapy treatment, blinding of subjects and therapists is typically difficult. In our study, patients will be blinded towards the group they will be randomised to, but the therapist cannot be blinded, as she knows whether a patient receives the treatment every week or every 2 weeks. To limit the risk of bias related to lack of blinding of the therapist, all evaluation measurements will be performed by a blinded assessor. All physiotherapy sessions will be provided in the clinic by the same therapist. This approach was chosen to ensure all patients will receive the same treatment and to limit therapist-dependent differences in outcome in our study. This approach might decrease the transferability of our study results to a clinical situation but was deemed necessary to avoid bias.

The proposed approach of the blended physiotherapy program using a smartphone application offering both an exercise program and tinnitus counselling has never been used before in ST treatment. Similar app-based programs, however, have proven to be effective and feasible for the treatment of neck pain [69, 70]. There is also an increasing interest in the use of smartphone applications for tinnitus patients [71, 72]. This study combines both tinnitus counselling and neck/jaw treatment providing a digital application to empower ST patients to improve and better manage their own health. Earlier research has already proven that the content of the application, both the exercise program and the

counselling, is effective when used in a clinical face-to-face setting [14–22, 73, 74]. However, it was never examined in the context of a smartphone application as part of a blended physiotherapy treatment. The use of our developed smartphone application is expected to help overcome common hurdles related to the in-clinic treatment of patients with ST.

In standard care, patients with somatic tinnitus receive weekly face-to-face therapeutic sessions of 30 min to reduce their neck and jaw complaints in order to also alleviate the tinnitus. On average, 9 to 12 weeks are needed to achieve the desired effect [13, 34]. In addition, patients are always recommended to perform exercises at home. This has proven to be effective in decreasing neck pain and avoiding recurrence of the complaints, but only if patients adhere [75, 76]. Compliance to home exercises is often impeding reducing positive long-term effects of the treatment [75–80]. This is not only the case for the treatment of patients with neck complaints, but a general hurdle in musculoskeletal treatment. Reasons for low compliance to home exercises are mostly investigated in studies on low back pain but are expected to be similar for other musculoskeletal dysfunctions [77, 79]. The most important defined barrier was ‘lack of support’, as patients indicated they did not receive sufficient instructions and follow-up to perform the exercises correctly and consistently [75, 77]. Other contributing factors are patient attitudes and beliefs, self-efficacy, locus of control, stage of change and psychosocial issues [79]. The proposed blended physiotherapy program might give answer to some of the barriers experienced by standard care. The smartphone application will change patients locus of control and promote self-efficacy by providing sufficient support and clear instructions on how to perform the exercises correctly and regularly. The psychological counselling provided by the app will increase the knowledge of patients about tinnitus improving patient attitudes and beliefs about the treatment.

The current standard physiotherapy treatment is, although effective, costly and time consuming, especially in case of recurrent complaints where patients often need several follow-up consultations and additional treatment. The longevity of the need of treatment due to recurrent complaints leads to high direct health care costs [8, 9]. Furthermore, also indirect costs, such as work absenteeism and productivity losses are high in these patients [8, 9]. Our investigated blended physiotherapy program aims to decrease the patient’s need for in-clinic treatment, without reducing the effectiveness of the treatment. The alleviation of tinnitus improves the quality of life and, as a

consequence, is expected to increase productivity and reduce absenteeism. In addition, the blended physiotherapy program will reduce the need for face-to-face clinical care and is expected to improve the patient’s self-management skills, rather than depending on the therapist’s care in case of recurrent symptoms. All these factors are expected to contribute to a significant decrease in both direct and indirect costs due to somatic tinnitus. The proposed blended physiotherapy program has the potential to be a valuable alternative for the current standard care, with a better cost-effectiveness without decreasing the effectiveness of the treatment.

Trial status

This is the first version of the protocol registered on 26 January 2022 at Clinicaltrials.gov: NCT05245318. The trial is currently (February 2022) in the starting phase of recruitment and is anticipated to be completed in December 2025. In case of a substantial amendment to the protocol, this will be altered through clinicaltrials.gov.

Abbreviations

CATT: Cost-effectiveness of a smartphone Application for Tinnitus Treatment; ST: Somatic or Somatosensory Tinnitus; RCT: Randomised controlled trial; ENT: Ear Nose Throat; UZA: University Hospital Antwerp; TFI: Tinnitus Functional Index; HRQOL: Health-related quality of life; TMJ: Temporomandibular joint; SPIRIT: Standard Protocol Items Recommendations for Interventional Trials; FUV: Follow-up visit; EQ-5D: EuroQoL-5 dimensions; VAS: Visual analogue scale; NVA: Nederlandse Vereniging Audiologie; SPIQ: Speech in quiet; SPIN: Speech in noise; LIST: Leuven Intelligibility Sentences Test; SRT: Speech reception threshold; NBQ: Neck Bournemouth Questionnaire; TMD: Temporomandibular disorder; HADS: Hospital Anxiety and Depression Scale; HQ: Hyperacusis Questionnaire; iPCQ: Productivity Cost Questionnaire; FAHMP: Federal Agency for Medicine and Health Products; CEA: Cost-effectiveness analysis; ICER: Incremental cost-effectiveness ratio; EUnetHTA: European Network for Health Technology Assessment; RIZIV: Rijksinstituut voor Ziekte- en Invaliditeitsverzekering; INAMI: l’Assurance soins de santé et indemnités; QALYs: Quality-adjusted life years; LoL: Length of life.

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s13063-022-06378-7>.

Additional file 1. A completed SPIRIT checklist 2013: Recommended Items to address in a clinical trial protocol and related documents (Ethical approval document and funding documentation (copy of original and English translation)) [30].

Acknowledgements

All authors thank FWO for funding this research.

Conduct in case of adverse events (AEs) or serious adverse events (SAEs)

The investigated device is a smartphone application that will be installed on the participant’s own smartphone. The use of the smartphone application is expected to cause very little adverse events. The only adverse event that might be present, as for any treatment for tinnitus, our smartphone application program, as well as the physiotherapy sessions, can, for a short while, increase the patient’s tinnitus loudness. This effect is caused by increased focus on the tinnitus and disappears automatically after completion of the

session. From previous studies in the same population, we know that this temporary effect appears in 0–5%. The risk will be minimised, by informing the patient and explaining why the temporary increase in tinnitus loudness might appear, so the patient can prevent the risk by actively avoiding to focus on the tinnitus.

No adverse device effects, device deficiencies, serious adverse device effects or serious adverse events are expected in our clinical investigation. All adverse events, adverse device effects... will be collected in the dossier for the Clinical Trials Centre monitoring. The responsible researcher will inform the sponsor within 48 h after an adverse event, adverse device effect... is reported. In case of a serious adverse event, the sponsor will notify the FAMHP at ct.rd@fagg.be by using the European form.

Auditing trial conduct

The project management group, consisting of SM, AG, VVR and WS, will meet once a year. The advisory board will have a yearly meeting as well. In addition, the independent data monitoring team will visit at least twice a year.

Authors' contributions

SM, AG and WS conceived of the study. SM, AG, WS, AT, VVR, OV, WM, LJ and JL participated in the design of the study. SD drafted the manuscript. SM and AG coordinated the design of the study and helped to the draft and revise the manuscript. All authors reviewed the manuscript and read and approved the final version.

Funding

This project is funded by an applied biomedical research with a primary social finality research (TBM) grant from the Research foundation Flanders (FWO) (Fonds voor Wetenschappelijk Onderzoek Vlaanderen (Egmontstraat 5, 1000 Brussel, Belgium) (T002221N). Research foundation Flanders (FWO) is an independent funding body and was not involved in the research idea, the design of the study protocol and the writing of this manuscript. The funding agency will neither be involved in the completion of the study and in collection, management, analysis and interpretation of data throughout the study trajectory. This TBM grant was dedicated to the Hasselt University (Sponsor) (Martelarenlaan 42, 3500 Hasselt, Belgium), University Hospital of Antwerp, University of Antwerp and the University of Regensburg. FWO assigned the role of sponsor to Hasselt University. FWO, as a funder, finances the study and Hasselt University, as a sponsor, leads the project. Hasselt University will be involved in the entire study process.

Availability of data and materials

As stated by the SPIRIT guidelines, the authors assure that breaking of the blind will occur at the end of the study and that data that break the blind will not be presented before release of mainline results. Data collected within the study will be disseminated to the public through scientific publications (according to the CONSORT guidelines), conferences and lectures. Results will be reported regardless of the outcome of the study. The raw data will be stored in RedCap, a secure web platform for building and managing online databases and surveys used at UZA. After publication of the results, an anonymous version of the raw data will be made available via an online repository server upon motivated request. The data management team consist of WS, SM, AG and VVR. The project will also be monitored by an independent study monitoring agency. In addition, there will be an e board of General practitioners, physiotherapists, audiologists, psychologists and patients.

Declarations

Ethics approval and consent to participate

Ethics approval by the Belgian Federal Agency for Medicine and Health Products (FAMHP) and an independent Ethical Committee (Ref. CIV-BE-21-09-037760). Original ethical approval (in English) is submitted as an [additional file](#). Written informed consent to participate will be obtained from all participants.

On the consent form, participants will be asked if they agree to use of their data should they choose to withdraw from the trial. Participants will also be asked for permission for the research team to share relevant data with people from the universities taking part in the research or from regulatory authorities,

where relevant. This trial does not involve collecting biological specimens for storage.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Author details

¹Rehabilitation Research Center, REVAL, faculty of Rehabilitation Sciences, Hasselt University, 3500 Hasselt, Belgium. ²Department of Otorhinolaryngology and Head and Neck Surgery, Antwerp University Hospital, 2650 Edegem, Belgium. ³Department of Translational Neurosciences, Faculty of Medicine and Health Sciences, University Antwerp, 2000 Antwerp, Belgium. ⁴Department of Psychiatry and Psychotherapy, University of Regensburg, 93053 Regensburg, Germany. ⁵Faculty of Business Economics, Hasselt University, 3500 Hasselt, Belgium. ⁶Department of Human and Social Welfare, University College Ghent, 9000 Ghent, Belgium.

Received: 18 February 2022 Accepted: 4 May 2022

Published online: 23 May 2022

References

1. Baguley D, McFerran D, Hall D. Tinnitus. *Lancet*. 2013;382(9904):1600–7.
2. Crummer RW, Hassan GA. Diagnostic approach to tinnitus. *Am Fam Physician*. 2004;69(1):120–6.
3. Folmer R, Martin W, Shi Y. Tinnitus: questions to reveal the cause, answers to provide relief. *J Fam Pract*. 2004;53:532–40.
4. Cima RF, Andersson G, Schmidt CJ, Henry JA. Cognitive-behavioral treatments for tinnitus: a review of the literature. *J Am Acad Audiol*. 2014;25(1):29–61.
5. Jastreboff PJ. Tinnitus retraining therapy. *Prog Brain Res*. 2007;166:415–23.
6. Aazh H, Moore BCJ, Glasberg BR. Simplified form of tinnitus retraining therapy in adults: a retrospective study. *BMC Ear Nose Throat Disord*. 2008;8(1):7.
7. Henry JA, Dennis KC, Schechter MA. General review of tinnitus: prevalence, mechanisms, effects, and management. *J Speech Lang Hear Res*. 2005;48(5):1204–35.
8. Trochidis I, Lugo A, Borroni E, Cederroth CR, Cima R, Kikidis D, et al. Systematic review on healthcare and societal costs of tinnitus. *Int J Environ Res Public Health*. 2021;18(13):6881.
9. Maes IH, Cima RF, Vlaeyen JW, Anteunis LJ, Joore MA. Tinnitus: a cost study. *Ear Hear*. 2013;34(4):508–14.
10. Biswas R, Lugo A, Akeroyd MA, Schlee W, Gallus S, Hall DA. Tinnitus prevalence in Europe: a multi-country cross-sectional population study. *Lancet Reg Eur*. 2022;12:100250.
11. Michiels S, De Hertogh W, Truijien S, Van de Heyning P. Cervical spine dysfunctions in patients with chronic subjective tinnitus. *Otol Neurotol*. 2015;36(4):741–5.
12. Ostermann K, Thill M, Vincent Y, Debaty M, Cotton P, Lurquin P. Incidence of somatic tinnitus in current ENT practice; 2014.
13. Ward JD, Sutton PC, Werner AD, Costanza R, Mohr SH, Simmons CT. Is decoupling GDP growth from environmental impact possible? *PLoS One*. 2016;11(10):e0164733.
14. Michiels S, Van de Heyning P, Truijien S, Hallemans A, De Hertogh W. Does multi-modal cervical physical therapy improve tinnitus in patients with cervicogenic somatic tinnitus? *Man Ther*. 2016;26:125–31.
15. Michiels S, Naessens S, Van de Heyning P, Braem M, Visscher C, Gilles A, et al. The effect of physical therapy treatment in patients with subjective tinnitus: a systematic review. *Front Neurosci*. 2016;10:545.
16. Oostendorp RA, Bakker I, Elvers H, Mikolajewska E, Michiels S, De Hertogh W, et al. Cervicogenic somatosensory tinnitus: an indication for manual therapy? Part 1: theoretical concept. *Man Ther*. 2016;23:120–3.
17. Oostendorp RAB, Bakker I, Elvers H, Mikolajewska E, Michiels S, De Hertogh W, et al. Cervicogenic somatosensory tinnitus: an indication for manual therapy plus education? Part 2: a pilot study. *Man Ther*. 2016;23:106–13.

18. Van der Wal A, Michiels S, Van de Heyning P, Braem M, Visscher C, Topsakal V, et al. Treatment of somatosensory tinnitus: a randomized controlled trial studying the effect of orofacial treatment as part of a multidisciplinary program. *J Clin Med*. 2020;9(3):705.
19. Michiels S, Nieste E, Van de Heyning P, Braem M, Visscher C, Topsakal V, et al. Does conservative temporomandibular therapy affect tinnitus complaints? A systematic review. *J Oral Facial Pain Headache*. 2019;33(3):308–17.
20. Gil-Martínez A, Paris-Alemány A, López-de-Uralde-Villanueva I, La Touche R. Management of pain in patients with temporomandibular disorder (TMD): challenges and solutions. *J Pain Res*. 2018;11:571–87.
21. Michiels S, De Hertogh W, Truijens S, Van De Heyning P. The effect of cervical physical therapy in patients with cervicogenic somatic tinnitus. *Man Ther*. 2016;25:e102.
22. Michiels S, van der Wal AC, Nieste E, Van de Heyning P, Braem M, Visscher C, et al. Conservative therapy for the treatment of patients with somatic tinnitus attributed to temporomandibular dysfunction: study protocol of a randomised controlled trial. *Trials*. 2018;19(1):554.
23. Sluijs EM, Kok GJ, van der Zee J. Correlates of exercise compliance in physical therapy. *Phys Ther*. 1993;73(11):771–82 discussion 83–6.
24. Prvu Bettger J, Resnik LJ. Telerehabilitation in the age of COVID-19: an opportunity for learning health system research. *Phys Ther*. 2020;100(11):1913–6.
25. Turolla A, Rossetini G, Viceconti A, Palese A, Geri T. Musculoskeletal physical therapy during the COVID-19 pandemic: is telerehabilitation the answer? *Phys Ther*. 2020;100(8):1260–4.
26. Seron P, Oliveros M-J, Gutierrez-Arias R, Fuentes-Aspe R, Torres-Castro RC, Merino-Osorio C, et al. Effectiveness of telerehabilitation in physical therapy: a rapid overview. *Phys Ther*. 2021;101(6):pzab053.
27. Cottrell MA, Galea OA, O'Leary SP, Hill AJ, Russell TG. Real-time telerehabilitation for the treatment of musculoskeletal conditions is effective and comparable to standard practice: a systematic review and meta-analysis. *Clin Rehabil*. 2017;31(5):625–38.
28. Cottrell MA, Russell TG. Telehealth for musculoskeletal physiotherapy. *Musculoskelet Sci Pract*. 2020;48:102193.
29. Nagaraj MK, Prabhu P. Internet/smartphone-based applications for the treatment of tinnitus: a systematic review. *Eur Arch Otorhinolaryngol*. 2020;277(3):649–57.
30. Chan A-W, Tetzlaff JM, Gøtzsche PC, Altman DG, Mann H, Berlin J, et al. SPIRIT 2013 explanation and elaboration: guidance for protocols of clinical trials. *BMJ*. 2013;346:e7586.
31. Michiels S, Ganz Sanchez T, Oron Y, Gilles A, Haider HF, Erlandsson S, et al. Diagnostic criteria for somatosensory tinnitus: a Delphi process and face-to-face meeting to establish consensus. *Trends Hear*. 2018;22:2331216518796403.
32. Michiels S, Cardon E, Gilles A, Goedhart H, Vesala M, Van Rompaey V, Van de Heyning P, Schlee W. The Rapid Screening for Somatosensory Tinnitus Tool: a Data-Driven Decision Tree Based on Specific Diagnostic Criteria. *Ear Hear*. 2022. <https://doi.org/10.1097/AUD.0000000000001224>. Epub ahead of print.
33. Meikle MB, Henry JA, Griest SE, Stewart BJ, Abrams HB, McArdle R, et al. The tinnitus functional index: development of a new clinical measure for chronic, intrusive tinnitus. *Ear Hear*. 2012;33(2):153–76.
34. Rabau S, Wouters K, Van de Heyning P. Validation and translation of the Dutch tinnitus functional index. *B-ent*. 2014;10(4):251–8.
35. Fackrell K, Hall DA, Barry JG, Hoare DJ. Performance of the Tinnitus Functional Index as a diagnostic instrument in a UK clinical population. *Hear Res*. 2018;358:74–85.
36. Saghaei MS, Saghaei S. Implementation of an open-source customizable minimization program for allocation of patients to parallel groups in clinical trials. *J Biomed Sci Eng*. 2011;4:734–9.
37. van der Wal A, Van de Heyning P, Gilles A, Jacquemin L, Topsakal V, Van Rompaey V, et al. Prognostic indicators for positive treatment outcome after multidisciplinary orofacial treatment in patients with somatosensory tinnitus. *Front Neurosci*. 2020;14:561038.
38. Cardon E, Van Rompaey V, Jacquemin L, Mertens G, Vermeersch H, Joosen I, et al. Sequential dual-site High-Definition transcranial Direct Current Stimulation (HD-tDCS) treatment in chronic subjective tinnitus: study protocol of a double-blind, randomized, placebo-controlled trial. *Trials*. 2019;20(1):471.
39. Luyten TR, Jacquemin L, Van Looveren N, Declau F, Fransen E, Cardon E, et al. Bimodal therapy for chronic subjective tinnitus: a randomized controlled trial of EMDR and TRT versus CBT and TRT. *Front Psychol*. 2020;11:2048.
40. Jacquemin L, Shekhawat GS, Van de Heyning P, Mertens G, Fransen E, Van Rompaey V, et al. Effects of electrical stimulation in tinnitus patients: conventional versus high-definition tDCS. *Neurorehabil Neural Repair*. 2018;32(8):714–23.
41. Newman CW, Jacobson GP, Spitzer JB. Development of the tinnitus handicap inventory. *Arch Otolaryngol Head Neck Surg*. 1996;122(2):143–8.
42. Jacquemin L, Mertens G, Van de Heyning P, Vanderveken OM, Topsakal V, De Hertogh W, et al. Sensitivity to change and convergent validity of the Tinnitus Functional Index (TFI) and the Tinnitus Questionnaire (TQ): clinical and research perspectives. *Hear Res*. 2019;382:107796.
43. Segarra V, Dueñas L, Torres R, Falla D, Jull G, Lluch E. Inter-and intra-tester reliability of a battery of cervical movement control dysfunction tests. *Man Ther*. 2015;20(4):570–9.
44. Rocha CB, Sanchez TG. Efficacy of myofascial trigger point deactivation for tinnitus control. *Braz J Otorhinolaryngol*. 2012;78(6):21–6.
45. Teachey WS, Wijnmans EH, Cardarelli F, Levine RA. Tinnitus of myofascial origin. *Int Tinnitus J*. 2012;17(1):70–3.
46. Bosman AJ, Smoorenburg GF. Intelligibility of Dutch CVC syllables and sentences for listeners with normal hearing and with three types of hearing impairment. *Audiology*. 1995;34(5):260–84.
47. Khalfa S, Dubal S, Veuillet E, Perez-Diaz F, Jouvent R, Collet L. Psychometric normalization of a hyperacusis questionnaire. *ORL J Otorhinolaryngol Relat Spec*. 2002;64(6):436–42.
48. Heller GZ, Manuguerra M, Chow R. How to analyze the visual analogue scale: myths, truths and clinical relevance. *Scand J Pain*. 2016;13:67–75.
49. Bolton JE, Humphreys BK. The Bournemouth Questionnaire: a short-form comprehensive outcome measure. II. Psychometric properties in neck pain patients. *J Manipulative Physiol Ther*. 2002;25(3):141–8.
50. Gay RE, Madson TJ, Cieslak KR. Comparison of the Neck Disability Index and the Neck Bournemouth Questionnaire in a sample of patients with chronic uncomplicated neck pain. *J Manipulative Physiol Ther*. 2007;30(4):259–62.
51. Koo TK, Li MY. A guideline of selecting and reporting intraclass correlation coefficients for reliability research. *J Chiropr Med*. 2016;15(2):155–63.
52. Schiffman E, Ohrbach R, Truelove E, Look J, Anderson G, Goulet JP, et al. Diagnostic Criteria for Temporomandibular Disorders (DC/TMD) for Clinical and Research Applications: recommendations of the International RDC/TMD Consortium Network* and Orofacial Pain Special Interest Groupdagdag. *J Oral Facial Pain Headache*. 2014;28(1):6–27.
53. Gonzalez YM, Schiffman E, Gordon SM, Seago B, Truelove EL, Slade G, et al. Development of a brief and effective temporomandibular disorder pain screening questionnaire: reliability and validity. *J Am Dent Assoc*. 2011;142(10):1183–91.
54. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand*. 1983;67(6):361–70.
55. Bjelland I, Dahl AA, Haug TT, Neckelmann D. The validity of the Hospital Anxiety and Depression Scale. An updated literature review. *J Psychosom Res*. 2002;52(2):69–77.
56. Meeus OM, Spaepen M, Ridder DD, Heyning PH. Correlation between hyperacusis measurements in daily ENT practice. *Int J Audiol*. 2010;49(1):7–13.
57. Fackrell K, Fearnley C, Hoare DJ, Sereda M. Hyperacusis questionnaire as a tool for measuring hypersensitivity to sound in a tinnitus research population. *Biomed Res Int*. 2015;2015:290425.
58. Herdman M, Gudex C, Lloyd A, Janssen M, Kind P, Parkin D, et al. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Qual Life Res*. 2011;20(10):1727–36.
59. National Institute for Health and Care Excellence (NICE). *NICE process and methods guides. Guide to the methods of technology appraisal 2013*. London: National Institute for Health and Care Excellence (NICE) Copyright © 2013 National Institute for Health and Clinical Excellence, unless otherwise stated. All rights reserved; 2013.
60. Whitehead SJ, Ali S. Health outcomes in economic evaluation: the QALY and utilities. *Br Med Bull*. 2010;96:5–21.
61. Bouckaert N, Gerkens S, Devriese S, Cleemput I. An EQ-5D-5L value set for Belgium – how to value health-related quality of life? In: *Health Services*

- Research (HSR). Brussels: Belgian Health Care Knowledge Centre (KCE). KCE reports 342; 2021.
62. Thompson AJ, Turner AJ. A comparison of the EQ-5D-3L and EQ-5D-5L. *Pharmacoeconomics*. 2020;38(6):575–91.
 63. Bouwmans C, Krol M, Severens H, Koopmanschap M, Brouwer W, Hakkaart-van Roijen L. The iMTA productivity cost questionnaire: a standard instrument for measuring and valuing health-related productivity losses. *Value Health*. 2015;18(6):753–8.
 64. Schlee W, Schoisswohl S, Staudinger S, Schiller A, Lehner A, Langguth B, et al. Chapter 21 - Towards a unification of treatments and interventions for tinnitus patients: the EU research and innovation action UNITI. In: Schlee W, Langguth B, Kleinjung T, Vanneste S, De Ridder D, editors. *Progress in brain research*, vol. 260: Elsevier; 2021. p. 441–51.
 65. Schlee W, Neff P, Simoes J, Langguth B, Schoisswohl S, Steinberger H, et al. Smartphone-guided educational counseling and self-help for chronic tinnitus. Preprints. 2022:2022010469. <https://doi.org/10.20944/preprints202201.0469.v1>.
 66. Julious SA. Sample sizes for clinical trials with normal data. *Stat Med*. 2004;23(12):1921–86.
 67. Fackrell K, Hall DA, Barry JG, Hoare DJ. Psychometric properties of the Tinnitus Functional Index (TFI): assessment in a UK research volunteer population. *Hear Res*. 2016;335:220–35.
 68. Neyt M, Cleemput I, Sande SV, Thiry N. Belgian guidelines for budget impact analyses. *Acta Clin Belg*. 2015;70(3):175–80.
 69. Lee J, Lee M, Lim T, Kim T, Kim S, Suh D, et al. Effectiveness of an application-based neck exercise as a pain management tool for office workers with chronic neck pain and functional disability: a pilot randomized trial. *Eur J Integr Med*. 2017;12:87–92.
 70. Lee M, Lee SH, Kim T, Yoo HJ, Kim SH, Suh DW, et al. Feasibility of a smartphone-based exercise program for office workers with neck pain: an individualized approach using a self-classification algorithm. *Arch Phys Med Rehabil*. 2017;98(1):80–7.
 71. Mehdi M, Dode A, Pryss R, Schlee W, Reichert M, Hauck FJ. Contemporary review of smartphone apps for tinnitus management and treatment. *Brain Sci*. 2020;10(11):867.
 72. Mehdi M, Stach M, Riha C, Neff P, Dode A, Pryss R, et al. Smartphone and mobile health apps for tinnitus: systematic identification, analysis, and assessment. *JMIR Mhealth Uhealth*. 2020;8(8):e21767.
 73. Cima RF, Maes IH, Joore MA, Scheyen DJ, El Refaie A, Baguley DM, et al. Specialised treatment based on cognitive behaviour therapy versus usual care for tinnitus: a randomised controlled trial. *Lancet*. 2012;379(9830):1951–9.
 74. Cima RFF, Mazurek B, Haider H, Kikidis D, Lapira A, Noreña A, et al. A multi-disciplinary European guideline for tinnitus: diagnostics, assessment, and treatment. *Hno*. 2019;67(Suppl 1):10–42.
 75. Gialanella B, Comini L, Olivares A, Gelmini E, Ubertini E, Grioni G. Pain, disability and adherence to home exercises in patients with chronic neck pain: long term effects of phone surveillance. A randomized controlled study. *Eur J Phys Rehabil Med*. 2020;56(1):104–11.
 76. Ylinen J, Häkkinen A, Nykänen M, Kautiainen H, Takala EP. Neck muscle training in the treatment of chronic neck pain: a three-year follow-up study. *Eura Medicophys*. 2007;43(2):161–9.
 77. Palazzo C, Klinger E, Dorner V, Kadri A, Thierry O, Boumenir Y, et al. Barriers to home-based exercise program adherence with chronic low back pain: patient expectations regarding new technologies. *Ann Phys Rehabil Med*. 2016;59(2):107–13.
 78. Pedersen MT, Andersen CH, Zebis MK, Sjøgaard G, Andersen LL. Implementation of specific strength training among industrial laboratory technicians: long-term effects on back, neck and upper extremity pain. *BMC Musculoskelet Disord*. 2013;14:287.
 79. Middleton A. Chronic low back pain: patient compliance with physiotherapy advice and exercise, perceived barriers and motivation. *Phys Ther Rev*. 2004;9(3):153–60.
 80. Zebis MK, Andersen CH, Sundstrup E, Pedersen MT, Sjøgaard G, Andersen LL. Time-wise change in neck pain in response to rehabilitation with specific resistance training: implications for exercise prescription. *PLoS One*. 2014;9(4):e93867.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Ready to submit your research? Choose BMC and benefit from:

- fast, convenient online submission
- thorough peer review by experienced researchers in your field
- rapid publication on acceptance
- support for research data, including large and complex data types
- gold Open Access which fosters wider collaboration and increased citations
- maximum visibility for your research: over 100M website views per year

At BMC, research is always in progress.

Learn more biomedcentral.com/submissions

