Pragmatic Uncontrolled Study of Specialized Cognitive Behavioral Therapy for Adults With Chronic Tinnitus

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Objectives: Tinnitus is the perception of sound without an external source, affecting quality of life that can cause severe distress in approximately 1 to 3% of the population of people with tinnitus. Randomized controlled trials of cognitive behavioral therapy for tinnitus have demonstrated its effectiveness in improving quality of life, but the effects of their implementation on a large scale in routine practice remains unknown. Therefore, the main purpose of this study was to examine the effects of stepped-care cognitive behavioral therapy for tinnitus delivered in a tertiary audiological center of a regional hospital. Second, we wished to examine predictors of favorable outcome.

Design: Four hundred three adults with chronic tinnitus were enrolled in this prospective observational study (at 3 months, N=334, 8 months, N=261; 12 months, N=214). The primary outcome was health-related quality of life as measured by the Health Utilities Index III (HUI-III) at 12 months. Secondary outcomes were self-reported levels of tinnitus-related distress, disability, affective distress and tinnitus-related negative beliefs and fear. Measures were completed pre-intervention at 3 months, 8 months, and 12 months. Multilevel modeling was used to examine effects and their predictors.

Results: Younger participants with lower levels of tinnitus distress were more likely to dropout while those with higher tinnitus distress at baseline and quality of life were more likely to receive step 2 of treatment. MLM analyses revealed, with one exception, no relation between any baseline variable and outcome change over time. Most participants' improvement exceeded minimally clinical important difference criteria for quality of life, tinnitus-related handicap, and tinnitus distress.

Conclusions: Results from this large pragmatic study complements those from randomized controlled trials of cognitive behavioral therapy for chronic tinnitus distress and supports its implementation under "real-world" conditions.

Key words: Cognitive behavioral therapy, Chronic tinnitus, Effectiveness, Implementation, Quality of Life.

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INTRODUCTION

Developing and testing the effects of psychological interventions striving to be included in routine clinical practice and healthcare policy is a complex and challenging endeavor. Interventions typically need to demonstrate that they can work under ideal conditions (i.e., through *efficacy* or *explanatory* trials), are cost-effective and capable of being implemented under "real-world" conditions (i.e., through *effectiveness or pragmatic* trials) before they can be considered by policy makers, regulatory bodies, and insurance companies (Thorpe et al. 2009) After all, implementing efficacious interventions poorly or recommending interventions without a credible evidence base risks scarce financial resources and harm to patients (Grimshaw et al. 2012). While some policymakers consider efficacy and pragmatic studies to be independent, they are better conceived as being on a continuum on which trade-offs between internal and external validity are made depending on the purpose of the trial (Gartlehner et al. 2006; Sox & Lewis 2016).

The challenges of developing and subsequently implementing a new intervention for tinnitus are significant since assessment and intervention pathways are usually fragmented (Hoare & Hall 2011) and clinical guidelines are rare (Fuller et al. 2017). Tinnitus itself is a very common audiological symptom frequently correlated with older age and hearing loss, although only between 1 and 3% of the population of people with tinnitus suffers from it severely (Davis & El Refaie 2000; Kim et al. 2015). Although there are a large variety of intervention options; psychological, sound, electrical and electromagnetic stimulation, tinnitus has no reliable cure (Folmer et al. 2014). Accumulating evidence from randomized controlled trials (RCTs) and meta-analyses suggests that cognitive behavioral therapy (CBT) is an efficacious intervention in alleviating tinnitus-related distress (Fuller et al. 2020; Landry et al. 2020).

Cognitive behavioral therapy is the best thought of as a collection of cognitive and behavioral interventions, originally derived from psychological models explaining disorders of thought, emotion and behavior and has been traditionally provided by psychologists. CBT for tinnitus aims to reduce the distress and interference in daily activities associated with tinnitus, rather than directly aiming to cure or reduce any psychoacoustic properties of the tinnitus. Due to the scarcity of psychologists providing CBT for tinnitus (Cima et al. 2020), models of service delivery where CBT is provided in standardized formats via the internet with audiologist support [e.g., Beukes et al. (2018b)] or by entirely by audiologists are being evaluated (Aazh & Moore 2018; Taylor et al. 2020). This line of inquiry is in its infancy but to date, two retrospective service evaluations of CBT provided by audiologists have documented large-effect sizes in improvement pre/post on Tinnitus Handicap Inventory scores (Aazh et al. 2019; Aazh & Moore 2018). An RCT of an internet-based CBT program compared outcomes from two groups, one without (the control group) and with weekly email support from an audiologist (the experimental group) (Beukes et al. 2018b). This study demonstrated clinically relevant improvements for both groups but a greater reduction in tinnitus distress for the group with support from an audiologist; the improvements were maintained up to 1-year follow-up (Beukes et al. 2018a). Complementing this, studies have reported tinnitus patients to consider audiologists providing CBT is acceptable (Aazh et al. 2019).

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These studies also reveal that there is variation in the content and duration of training provided to audiologists providing psychological interventions (Aazh & Moore 2018; Taylor et al. 2020), and that there is some concern from audiologists about the skills required to provide CBT (Taylor et al. 2020).

To date, no study has yet examined the implementation of specialized CBT for tinnitus delivered in an interdisciplinary, two stepped-care model intervention (Cima et al. 2012) (hereafter referred to as CBT for tinnitus and described below). Audiologists in this intervention play an important role in the first stage of care. This two-step intervention, when compared with 'treatment as usual' in the context of a pragmatic RCT achieved small to medium effect sizes on the outcome measures (e.g., TQ, THI, HUI-III; Cima et al. 2012). The results challenged a widespread belief among audiologists, doctors, and psychologists that nothing could be done for tinnitus sufferers (Langguth 2012).

The aim of this study was to investigate whether changes in quality of life (QoL) and tinnitus-related outcome measures occurred over a 12-month period in participants who completed stepped-care CBT for tinnitus in routine clinical practice. Given the aim of the study, we used an observational study design with data collected at four time points. It was hypothesized that adult participants with tinnitus receiving stepped care CBT for tinnitus have improved QoL and decreased levels of tinnitus-related distress, negative beliefs, and fear after completing CBT for tinnitus.

MATERIALS AND METHODS

Study Design and Ethics

This observational study included 403 participants between January 2014 and November 2016. Outcome data were collected at baseline (T0), at the end of step 1 (3 months after baseline; T1); at 8 months after baseline (for some, after completion of step 2; T2); and, at 12 months after baseline (T3). Figure 1 illustrates the flow of participants throughout the study. The study was conducted in accordance with the principles of the Declaration of Helsinki, approved by the Ethical Review Committee Faculty of Psychology and Neuroscience, Maastricht University (approval number: ECP-152 05_12_2014) and registered at www.clinicaltrials.gov (NCT04310605). Participants did not report any harms or adverse events during the study.

Participants

Participants were recruited from five audiological centers located in the province of Brabant, the Netherlands. People were eligible to participate if they were 17 years or older, primarily seeking help for tinnitus related distress or its interference in daily activities, and who were able to communicate in Dutch. All prospective participants received detailed written information about the study and the associated requirements of participating. Participation in the study did not require any time commitment beyond that of the intervention. (Note: completing questionnaires was considered part of the intervention protocol, a requirement for funding from health insurers, and used as a quality control mechanism in the course of the study.)

Measures

In order to enable to facilitate comparison and inform tinnitus healthcare policy in the Netherlands, the same primary and secondary outcomes measures were used as those in the RCT by Cima et al. (2012).

Primary Outcome Measure • The Health Utilities Index-III (HUI; Feeny et al. 2002; Horsman et al. 2003) is a 17-item measure designed to assess health related QoL. It has eight subscales/dimensions (vision, hearing, speech, ambulation, dexterity, emotion, cognition, and pain complaints) that have five or six rating options ranked, for example, from "highly impaired" to "normal". Utility scores on the HUI-III range from −0.36 to 1.00. The HUI-III has a strong theoretical basis, is widely used in clinical research, and considered a reliable and valid measure (Horsman et al. 2003). The HUI-III has been shown to

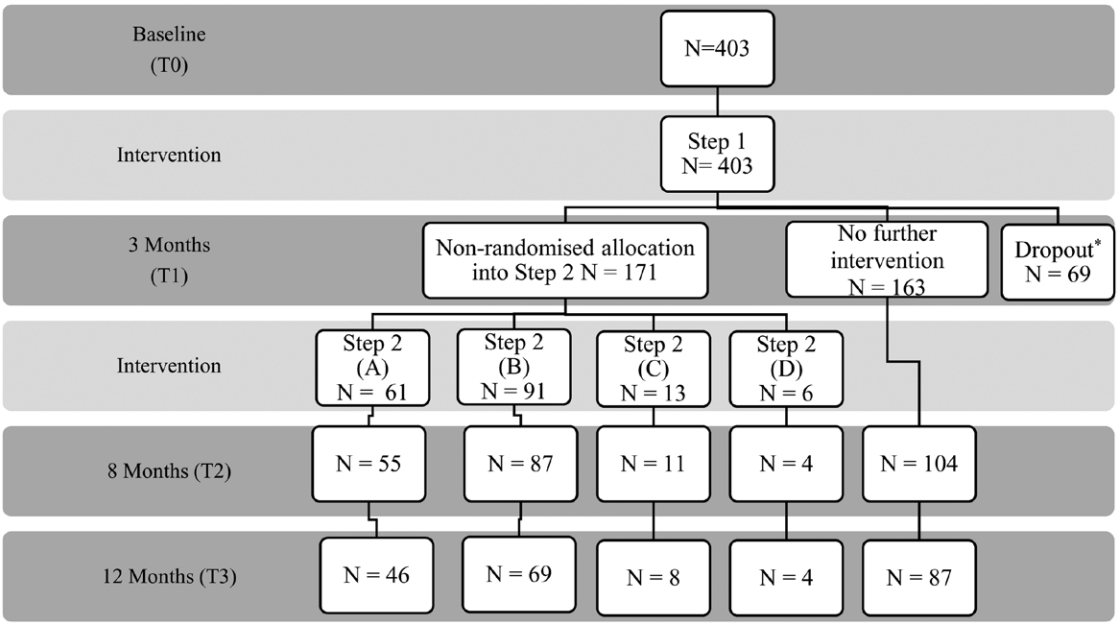

Fig. 1. Participant flow diagram. *Participants who completed baseline measures but not T1, T2 or T3.

have adequate responsiveness when used with tinnitus patients (Maes et al. 2011). The internal reliability of the HUI-III in this was study was excellent [$\alpha = 0.88$, 95% CI (0.87–0.90)].

Secondary Outcome Measures

Tinnitus Handicap Inventory

Tinnitus Handicap Inventory (THI; Newman et al. 1996; Newman et al. 1998) is a 25-item measure of the impact of tinnitus on daily life that includes three subscales (mental, social/occupational and physical functioning; emotional impact; catastrophic responses to tinnitus). The total score of the THI ranges from 0 to 100 with higher scores indicating greater levels of impact on daily life. The internal reliability of the THI in this was study was excellent [$\alpha = 0.96$, 95% CI (0.95–0.96)].

The Tinnitus Questionnaire (TQ; Hallam et al. 1988) is a self-report questionnaire designed to asses distress and interference in daily activities associated with tinnitus. It has 52 items and uses a three-point scale to indicate levels of distress on six subscales. The total score on the TQ ranges from 0 to 84. The TQ has high internal consistency, convergent and discriminant validity, and is sensitive to change (Baguley et al. 2000; Zeman et al. 2012). The internal reliability of the TQ in this was study was excellent [$\alpha = 0.96$, 95% CI (0.95–0.96)].

The Tinnitus Disability Index (TDI; Cima et al. 2011b) is a 7-item self-report questionnaire that assesses the level of interferences in daily activities attributed to tinnitus. Respondents use an 11-point scale to indicate the level of interference ranging from 0 *no disability*, to 10 *total disability*. The total score ranges from 0 to 70 with higher scores indicating higher levels of interference. The TDI has been shown to be reliable over time, and higher scores on the measure have been shown to be correlated with higher ratings of tinnitus intensity and distress, and lower levels of QoL. In the present study the internal reliability of the TDI was excellent ($\alpha = 0.90$, 95% CI [0.89 – 9.92]).

Tinnitus Catastrophizing Scale

Tinnitus Catastrophizing Scale (TCS; Cima et al. 2011a) was used to assess the degree to which people thought or expected the worst about tinnitus. The TCS is a 13-item measure based on the Pain Catastrophizing Scale (Sullivan et al. 1995), and respondents use a five-point scale to indicate the degree to which statements applies to them (e.g., *It's terrible and I think it's never going to get any better*). The total score on the TCS ranges from 0 to 65. The internal reliability of the TCS in this study was excellent [$\alpha = 0.95$, 95% CI (0.94–0.95)].

Fear of Tinnitus Questionnaire

The Fear of Tinnitus Questionnaire (FTQ) is a 17-item self-report measure intended and designed to assess respondents' level of fear regarding their tinnitus. Items in the questionnaire are presented as a series of statements (e.g., *"I am afraid that my tinnitus will become worse"*) from which respondents are asked to indicate if it is applicable to their current situation. Each statement receives a score of 1 when applicable (total score range 0 to 17). The FTQ has been shown to be sensitive to change following intervention (Cima et al. 2012) and have good psychometric properties (Fuller et al. 2019). The internal reliability of the FTQ in this was study was excellent ($\alpha = 0.91$, 95% CI [0.90–0.92]).

Hospital Anxiety and Depression Scale

Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith 1983) is a widely used measure of psychological distress in people experiencing a concurrent physical health condition. It has 14 items and respondents use a Likert-type scale to indicate how often they have had a particular feeling in the previous week (e.g., "I feel tense or wound up"). Each item is scored from 0 to 3 with lower scores indicating better psychological functioning. A large number of studies have investigated the factor structure of the HADS with some confirming a two-factor structure while others have found one, three, or four factors (Bjelland et al. 2002) leading to some debate about its utility (Coyne & van Sonderen 2012a, 2012b). For this study, the HADS total score (range 0 to 42) was used as a unidimensional measure of emotional distress. The internal reliability of the HADS in this was study was excellent [$\alpha = 0.94$, 95% CI (0.93–0.94)].

Procedure

Therapist Training • Prior to implementing the intervention, psychologists, clinical physicists in audiology, audiometricians, movement therapists, physical therapists, and social workers at the audiology rehabilitation center who expressed interest in participating in the study underwent training in specialized CBT for tinnitus. Two audiologists, four audiometric technicians, one social worker, and three psychologists participated in a 1-week (36 hours) intensive step-1-treatment training course. This consisted of observing, practicing, and providing the step-1 treatment elements per discipline, participation in multidisciplinary case-triage and instructions on the organizational and logistic aspects of the intervention. The step-2 trainees followed a 6-month training course at Adelante Audiology and Communication, Hoensbroek, the Netherlands. In sum, training was extensive and consisted of observation of therapeutic methods, practicing under supervision, and performing the intervention independently. Members of the trainee team were also provided with protocols describing in detail the aims, instructions and primary therapeutic processes for each session for the respective intervention pathway. (Details of the training are provided in Supplemental Digital Content 1, http://links.lww.com/EANDH/B15, note that therapists only deliver treatment sessions within their scope of practice; that is, for example, audiologists were not given training or required to deliver the cognitive or behavioral treatment components.)

Implementation of CBT for Tinnitus • Specialized CBT for tinnitus is a 1- or 2-step intervention *package* (i.e., it comprises multiple intervention components) delivered in person to people suffering from tinnitus. Step 1 of the intervention comprised individual audiometric diagnostics and counseling about hearing and tinnitus with an audiologist (1 hour); an educational group session with a maximum of 10 participants and their partners (2 hours); and psychological assessment regarding tinnitus and its impact on daily life (1 hour). Each participants' progress was discussed in a multidisciplinary case-discussion (10 min) after step 1 was concluded.

Indications for eligibility to receive step 2 were typically determined by participants' TQ scores at baseline (i.e., ≥47) and observed progress (or lack thereof) in step 1. Some exceptions were made though if the clinician and participant thought that there was benefit to be gained by participating in step 2. (Note: clinicians were blind to the participants' scores on outcome measures at T1.) Participants with severe hearing loss (Fletcher Index: >60dB) in addition to moderate tinnitus distress participated in groups of up to four. An individual course

was also offered if a participant scored above 47 on the TQ and was unable to participate in group-wise treatment because of physical or mental health issues. (Additional details of the indications for step 2 are provided in SDC 1.) In principle, those participants with greater need were allocated to a treatment trajectory ("A", "B", "C", or "D") that provided a greater number of sessions and vice versa.

Step 2 group sessions were 2 hours long and held weekly over a 12-week period. Trajectory "A" was provided once per week, for up to 12 participants per group. In addition to the group sessions, four additional evening sessions of 2 hours each, with significant others, were held. Trajectory "B" consisted of twice weekly sessions for a maximum of eight participants. In addition, six evening sessions of 2 hours each, with significant others invited to attend, were held. Trajectory "C" was for up to four participants at a time and comprised weekly sessions. In addition to these sessions, four evening sessions of two hours each, with significant others invited to attend, were held. An individual intervention trajectory ("D") was also provided, following the respective intervention plan (A, B, or C) for patients whose participation in groups was contraindicated. (See Fig. 1 for the number of participants who were allocated to the respective treatment trajectories.)

Two therapists (a psychologist and a movement- or physiotherapist) were present at any one time for step 2 sessions. Over the course of these sessions, therapists would change leadership role after 1 hour, when, for example, there was also a clear change in activity (e.g., from playing badminton to a relaxation exercise).

Step 2 included psycho-education; exposure therapy to reduce fear and avoidance of stimuli that predict the occurrence or the increase of tinnitus complaints, and extinction of associated safety-seeking behaviors; movement therapy and attention-focused/mindfulness exercises to facilitate the exposure to tinnitus-related stimuli; cognitive restructuring of negative thoughts about the meaning of tinnitus and the consequences of living with tinnitus; attention-redirecting techniques; stress reduction; and relaxation techniques (e.g., progressive muscle relaxation). The content of Trajectory B was equivalent to that in the other less intense trajectories (i.e., A, C, D), but over the twice weekly sessions allowed for greater repetition and variation in the activities and exercises. If required, a social worker would assist with employment and social matters such as describing the burden of tinnitus to participants' employers and providing advice on policies regarding sick leave due to tinnitus.

Two-hour group sessions where partners, family members, carers, or friends of participants were also provided. These sessions were usually conducted in the evenings and reinforced or discussed the audiological, health-related, and psychosocial content covered in the participant only groups.

During the implementation phase, monthly supervisory visits and weekly online meetings between expert and novice therapists were conducted to address clinical issues. Project team meetings were also held monthly to enable the project coordinators, management of the rehabilitation center and the researchers to monitor the progress of the enrollment, allocation, and intervention fidelity.

Statistical Analyses

Predicting Dropout by 3 Months and Predicting Receipt of Step 2 • We conducted two logistic regression analyses prior to examining changes in outcome measures over time. The first was conducted to inform our understanding of participants' characteristics of those who did (or did not) complete outcome measures beyond baseline measurement; and the second was a manipulation check of the (main) criteria for participants to receive step 2. The first regression included the total sample (N=403) to examine what factors predicted dropout by Time 1; and, the second included the total sample, minus dropouts at T1. We expected that baseline TQ score would be a predictor of step 2 inclusion if the study protocol/criteria were followed. However, we did not know if other variables measured at baseline would also predict the likelihood of undertaking step 2.

For the purposes of the first logistic regression (predictors of dropout), participants who did not complete any outcome measures after baseline were considered to have "dropped out" (see Fig. 1). The regression model included as predictors of dropout: demographic and clinical variables (i.e., age, tinnitus duration, hearing loss, education, sex, employment status, season in which participants commenced intervention), and baseline scores on outcome measures (i.e., HUI-III, THI, HADS, TCS, FTQ, TQ, TDI). In the second logistic regression (predictors of step 2 involvement), the scores on the outcome measures at three months after baseline (i.e., T1) were also included as predictors in addition to those used in the first logistic regression examining dropout. Participants who had dropped out were not included in this analysis.

For both logistic regressions, a decision rule for reducing/simplifying the model was applied whereby predictors with p values >0.05 were removed in a stepwise fashion. Using an iterative process and following the removal of the variable with the highest p value, the model was re-run and p values examined until the model only included variables with p values less than $\alpha = 0.05$ (two-tailed). A Bonferroni correction was applied for drawing conclusions to statistically correct for the problem of making multiple comparisons; that is, alpha was divided by the number of *predictors* in the initial full model (14), giving: $0.05/14 = 0.0036$. However, since the Bonferroni correction is considered an overcorrection, we rounded it up slightly to set the alpha at 0.005 in order to minimize the chance of type 2 errors (i.e., false negative).

Examining Changes Over Time • The results from the RCT of specialized CBT compared with usual care for tinnitus indicated that participants in the specialized care condition improved more than those receiving usual care, and that the improvement in each treatment group was maintained over the follow-up period (Cima et al. 2012). In addition, tinnitus-related fear appeared to mediate part of the intervention effect on other outcomes (Cima et al. 2017). While we might expect that participants will improve over the course of the intervention, without a control group, we could not specifically assess treatment effects (or mediators thereof) per se. Given that, no specific hypotheses regarding these effects were made.

Mixed (multilevel) regression was used to examine if changes in outcomes occurred over the intervention and follow-up period, and if so, which variables predicted the change. Mixed regression is able to account for nesting of data (i.e., repeated measures within participants) and is robust against missing outcome data. This means that all patients with at least one measurement can be included into the analysis and that the results are valid even if outcome missingness depends on any measurement prior to dropout (Verbeke & Molenberghs 2000). We conducted three sets of analyses on the primary (HUI-III)

and each of the secondary outcomes (THI, HADS, TCS FTQ, TQ, and TDI). The first set examined participants who only completed step 1 of CBT for tinnitus, that is, baseline (T0) to 3 months (T1). This was done to assess whether there was any interaction between the predictor variables included in the model and time, or equivalently, to assess predictors of change from baseline to T1. The second set included the same participants but now the outcome measures at all time points. The third set of analyses focused on participants who undertook both step 1 and 2 at each time point.

Before conducting the mixed regressions, we checked for collinearity between predictor variables. All predictor variables had a variance inflation factor below 10 indicating absence of collinearity (variance inflation factor's range, 1.04–6.44) and hence were included into the regression analyses. For each set of analyses, we initially conducted maximum likelihood (ML) estimation, assuming an unstructured covariance matrix of the repeated measures (which is the most flexible and thus safe choice). A Bonferroni correction was applied to compensate for multiple testing (testing 14 predictor*time interactions on each of the seven outcomes), giving an alpha of 0.05/98, which was rounded upward to 0.001 as Bonferroni gives an overcorrection.

Model selection for step 1 only participants, and step 1 and 2 participants, respectively, proceeded through a stepwise process. Models initially included the set of predictor variables, time (with baseline as reference category and a dummy indicator for each other time point), and the interaction of each predictor with *time*. We ran a model and subsequently deleted the *predictor* by *time interaction* with the highest *p*-value and checked its accuracy by a likelihood ratio test. This process continued until all predictor by time interactions either were below the 0.001 criterion or were deleted from the model. As an additional check for statistically significant interaction effects, we also re-introduced each predictor by time interaction separately into the final model to examine if any reached the level of significance (i.e., we started with a backward stepwise regression from the full model, followed by a forward regression from the final model). We used restricted maximum likelihood (REML) regression to produce a final estimate of effects of the predictor variables and their standard errors, as REML is the best method for estimating standard errors, but ML was needed for likelihood ratio comparisons between models (Verbeke & Molenberghs 2000). Histograms were used to check for normality of the residual distribution and outliers in the residuals per time point. If outliers were identified, the effect of removing the respective participants from the analysis was checked by re-running the particular model. In all analyses with outliers, removing participants from the analysis did not affect the predictor selection or effects. Therefore, we report the results using the data set including all participants.

Participants were post hoc classified as having improved or not using observed data points, and on available minimal clinically important difference (MCID) criteria for HUI-III, THI, TQ, and HADS. Specifically, participants were classified as '*improved*' if there was at least an increase of 0.03 for HUI-III (Horsman et al. 2003; Marra et al. 2005); a decrease of 7 points on the THI (Zeman et al. 2011); and a decrease of 12 points on the TQ (Hall et al. 2018). In the absence of an MCID derived from tinnitus patient data, participants were also classified as 'improved' on HADS if their total score decreased by 1.7 points (reference group cardiovascular patients; Lemay et al. 2019) and 1.5 points (reference group chronic obstructive pulmonary disease patients; Puhan et al. 2008). For each outcome, the percentage of participants who improved was calculated between baseline and 3 months, baseline and 8 months, and baseline and 12 months.

RESULTS

Participant Flow and Sample Characteristics

All participants completed step 1 of the intervention, with 42.4% subsequently entering into step 2, and 40.4% not requiring further intervention after step1 (see Fig. 1). Although the main criterion for entering step 2 was a baseline TQ score greater than or equal to 47, actually 25 of the 171 participants in step 2 (14.6%) had a baseline TQ score below this level. Participants who were bothered by tinnitus for an average of 54 months were more likely to be male, employed, perceive tinnitus in both ears, and did not use a hearing aid. Nearly 30% (28.9%) of the participants who were employed received sickness benefits (Tables 1 and 2 in Supplemental Digital Content 2, http://links.lww.com/EANDH/B15). Sixty-nine of the 403 participants (17.1%) did not complete any outcome measures at 3-, 8-, or 12 months after baseline. Although they did not complete outcome measures, most completed some or all treatment elements of step 1. Specifically, 68 (98.5%) participants attended an appointment with the audiologist, 67 (97.1%) attended the tinnitus information session, and 41 (59.4%) participants attended the appointment with the psychologist.

Predicting dropout at 3 Months

The final logistic regression model for dropout at 3 months explained 14.3% of the dropout (Nagelkerke R^2) and classified 84.4% of the cases correctly in terms of being a dropout or not (note, however, that a model with no predictors at all classified 83% of dropouts correctly by using the data that 17% dropped out). When using alpha = 0.005 for drawing conclusions in view of multiple testing, the final model revealed that a younger age and lower THI baseline score were associated with an increased likelihood of dropping out (Table 3 in Supplemental Digital Content 2, http://links.lww.com/EANDH/B15).

Predicting Who Would Receive Step 2 of Specialized CBT for Tinnitus

We used logistic regression to examine the variables predicting participants who received step 2. The chi-square test of the final model was statistically significant χ^2 (4) = 95.722, $p < 0.001$ and explained 33.2% (Nagelkerke R^2) of the variance in the prediction of entering step 2 of the CBT intervention. The final model correctly predicted 72.5% of cases (to compare, the model without predictors correctly predicted 51.2% of cases). Higher scores on QoL (HUI-III) and tinnitus handicap (THI) at baseline, and on tinnitus distress (TQ) scores at T1 were associated with increased likelihood of participating in step 2 of the intervention (Table 4 in in Supplemental Digital Content 2, http://links.lww.com/EANDH/B15).

Changes Over Time on Outcome Measures

The primary aim of this research was to investigate participants' change over time and predictors of change. Observed mean and standard deviations on the respective outcome measures of interest by time and intervention trajectory are shown in Table 1. In sum, the observed scores across all outcomes reveal

TABLE 1. Mean observed score and standard deviations on outcome measures by time point and intervention group

		Baseline (T0)			3 Months (T1)			8 Months (T2)			12 Months (T3)		
Intervention group	Outcome	Mean	SD	N	Mean	SD	N	Mean	SD	N	Mean	SD	N
Step 1 only	HUI-III	0.53	0.31	231	0.62	0.29	162	0.65	0.28	104	0.64	0.29	87
	THI	42.95	22.49	231	32.06	22.79	163	27.38	22.41	104	25.24	22.05	87
	HADS	6.82	4.05	231	5.65	3.92	163	5.1	3.88	104	4.68	3.8	87
	TCS	21.62	11.78	231	15.77	11.91	162	13.03	11.39	104	11.15	10.16	87
	FTQ	7.69	3.83	231	5.37	3.82	163	4.3	3.59	104	3.89	3.62	87
	TQ	51.2	19.11	230	39.51	20.3	163	34.71	19.95	104	32.16	18.13	87
	TDI	21.9	16.0	231	16.3	15.4	161	14.5	16.8	104	14.3	15.9	87
Step 1 and 2	HUI-III	0.53	0.3	172	0.54	0.28	169	0.57	0.3	157	0.62	0.25	126
	THI	57.33	18.33	172	52.96	19.67	169	45.26	20.62	157	39.86	20.3	127
	HADS	8.9	3.7	172	8.28	3.78	170	7.57	3.77	157	6.71	3.61	127
	TCS	26.92	9.61	172	24.08	10.55	169	19.18	10.96	155	16.97	11.3	127
	FTQ	9.11	3.37	172	8.04	3.62	170	6.43	3.8	157	5.42	3.78	127
	TQ	62.47	14.98	172	57.11	15.62	171	47.94	18.7	154	43.44	18.63	126
	TDI	29.6	15.3	172	26.1	14.4	168	24.0	16.3	153	20.0	14.3	125
Total sample	HUI-III	0.53	0.3	403	0.58	0.29	331	0.6	0.3	261	0.63	0.27	213
	THI	49.09	21.98	403	42.7	23.67	332	38.14	23.04	261	33.92	22.18	214
	HADS	7.71	4.03	403	6.99	4.06	333	6.59	4	261	5.89	3.81	214
	TCS	23.88	11.21	403	20.01	11.97	331	16.71	11.51	259	14.6	11.2	214
	FTQ	8.3	3.7	403	6.73	3.94	333	5.58	3.86	261	4.79	3.78	214
	TQ	56.02	18.31	402	48.52	20.07	334	42.61	20.25	258	38.84	19.21	213
	TDI	25.2	16.2	403	21.3	15.7	329	20.1	17.1	257	17.7	15.2	212

Note: T0 = baseline; T1 = 3 mos after baseline; T2 = 8 mos after baseline; T3 = 12 mos after baseline.
FTQ, Fear of Tinnitus Questionnaire; HADS, Hospital Anxiety and Depression Scale; HUI, Health Utilities Index-III; TCS, Tinnitus Catastrophizing Scale; TDI, Tinnitus Disability Index; THI, Tinnitus Handicap Inventory; TQ: Tinnitus Questionnaire.

that, at a group level, participants improve over time. Note, however, that the time courses might be biased due to the dropout (17.1% after baseline measures) as each mean (and SD) is based on the observed cases at that time point. Therefore, plots of predicted values based on mixed regression including dropouts were generated to correct for this bias as much as possible.

Mixed (multilevel) regression analyses were used to examine what variables might predict change in the outcome over the 12-month follow-up. These analyses generate a large amount of output. For the sake of transparency and completeness, this is presented in Supplemental Digital Content files 3 to 5, http://links.lww.com/EANDH/B15; http://links.lww.com/EANDH/B16. Tables 1 to 3 in Supplemental Digital Content 3 (http://links.lww.com/EANDH/B15) present a summary of the statistically significant predictors of change (predictor by time effect) and of average outcome (predictor main effect) per participant subgroup (step 1 only/ step 1 and 2), per outcome. Briefly, no significant predictor by time interactions were found, except for an interaction of baseline TCS score with time with respect to the outcome HADS in the group of participants who completed both step 1 and 2. This suggests that the effect of time on HADS score is dependent on the baseline TCS score. The results also reveal that no single predictor was consistently associated with all outcomes in both participant groups. The absence of a consistent pattern also applied to near-significant predictors. Log ratio tests of initial full model (all interactions in) versus final model (no interactions), using ML estimation, were also conducted for each outcome as another check for interactions. These tests confirmed the absence of predictor by time interactions, except for a possible season by time effect on TQ for participants who undertook step 1 only (Supplemental Digital Content 4, http://links.lww.com/EANDH/B16).

Figures 2 and 3 show the comparison of observed and predicted (based on the final REML models) mean values for quality of life. The figures reveal a divergence between observed and predicted HUI-III, which suggests selective dropout. To see this more clearly, Figures 4 and 5 show the HUI time course per subgroup based on the measures completed by participants at the respective time points. In both samples (step 1 only and step 1 and 2), the complete cases have a higher HUI-III at baseline (T0) and 3 months (T1) than the incomplete cases. As a result, in Figures 2 and 3, observed means at 8 months (T2) and 12 months (T3) are artificially higher due to missingness of those participants who had a lower HUI at T0 and T1 (and who are included into the computation of the observed means at T0 and T1). The predicted values adjust for this bias by using the correlation between the repeated measures to estimate what the missing values would have been, had they not been missing. The predicted means rather than the observed means are therefore the basis for our further discussion. On average, step 1 participants improved between 0 and 3 months and remained stable thereafter, whereas step 1 and 2 participants showed improvement between 3 and 12 months, that is, after step 2 onset. Furthermore, across all outcomes, the figures (see also Figures 1 to 12 in Supplemental Digital Content 3, http://links.lww.com/EANDH/B15) show that the observed scores indicate a greater degree of improvement than the predicted scores.

Classifying participants as '*improved*' (or not) from baseline to 12-months using MCID criteria and observed data, revealed that over half of participants improved on QoL (i.e., HUI-III $\Delta \geq 0.03$, n = 115/213, 54.0%; Horsman et al. 2003; Marra et al. 2005), tinnitus impact on daily life (i.e. THI $\Delta \geq 7$, n = 145/214, 67.8%; Zeman et al. 2011), and tinnitus distress (i.e., TQ $\Delta \geq 12$, n = 133/213, 62.45%; Hall et al. 2018). Just under and slightly over half, respectively, also '*improved*' on levels of psychological distress when using cardiovascular patients' (i.e., HADS $\Delta \geq 1.7$, n = 100/214, 46.7%; Lemay et al. 2019) and when using COPD patients' (i.e., HADS $\Delta \geq 1.5$, n = 115/214, 53.7%; Puhan et al. 2008) MCID as a reference. On these

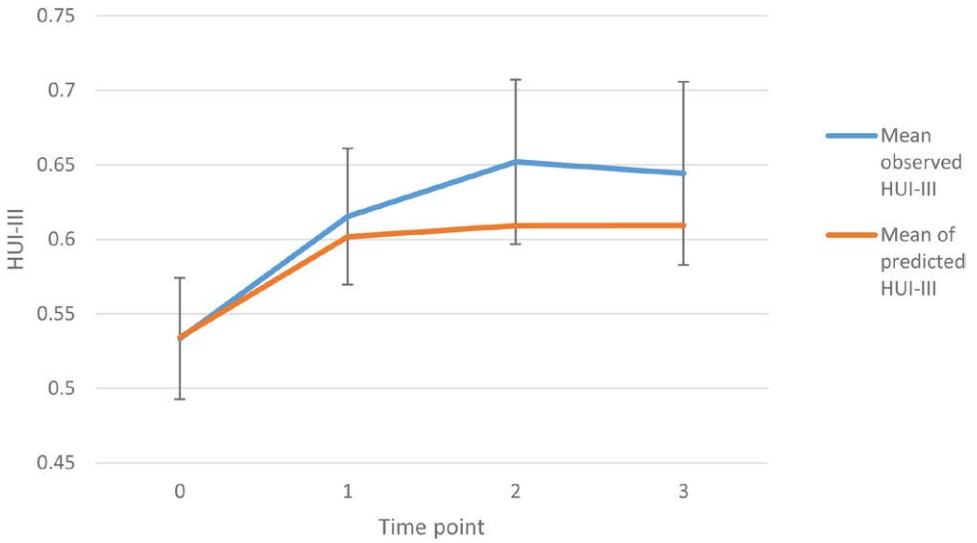

Fig. 2. Step 1 only participants quality of life: observed and predicted HUI-III scores by time (error bars: 2*SE mean observed score).

four outcomes, the percentage of participants who improved increased over time (Table 8 in Supplemental Digital Content 5, http://links.lww.com/EANDH/B15).

DISCUSSION

This pragmatic uncontrolled study collected data at four time points over a 12-month period, from 403 participants undertaking a stepped-care specialized CBT intervention for tinnitus-related distress. Participants had been bothered by tinnitus for over 4.5 years on average and were all assigned to step 1 of the intervention; subsequently, 171 of these participants also received step 2 over the course of 12 weeks. Results from multilevel modeling indicated that, on average, both groups of participants' scores on all patient reported outcomes showed improvement over a 12-month period. Given that few inclusion and exclusion criteria were applied, the results from this study could be generalized to other contexts or at least similarly resourced healthcare settings and countries.

Analyses revealed that participants younger in age and with lower THI scores at baseline were more likely to drop out from the study—defined as not completing outcome measures beyond baseline—than other participants. In other words, those who were older and with higher THI scores were more likely to complete outcome measures at the follow-up time points. Given that many of these participants who did not complete the outcome measures after baseline did complete the audiological assessment and tinnitus information session of step 1, they could be better thought of as being less likely to complete outcome measures rather than actually 'dropping out' from the intervention. Fewer participants subsequently attended the session with the psychologist, which could further indicate that they did not consider their tinnitus a psychological problem

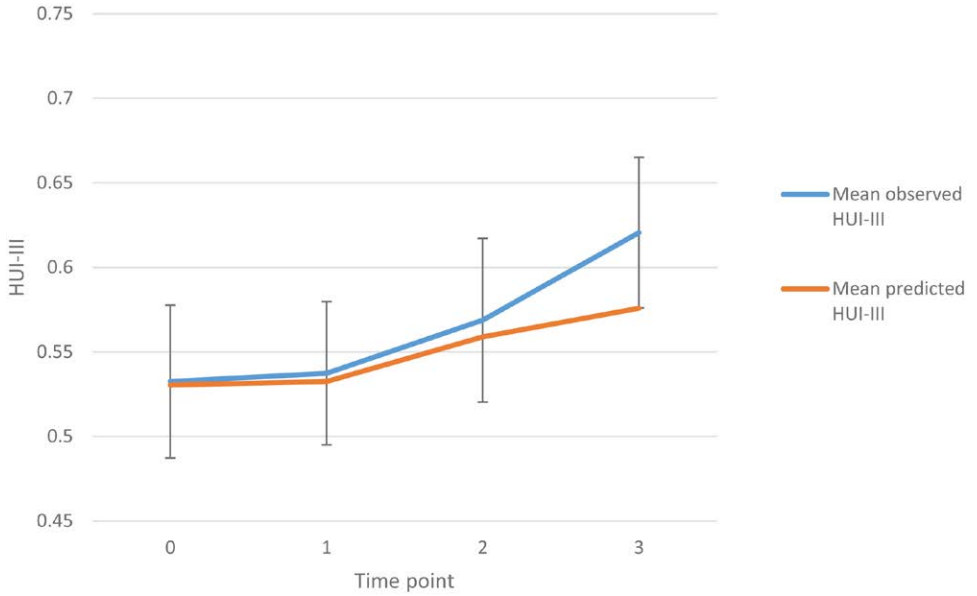

Fig. 3. Step 1& 2 participants quality of life: observed and predicted HUI-III scores by time (error bars: 2*SE mean observed score).

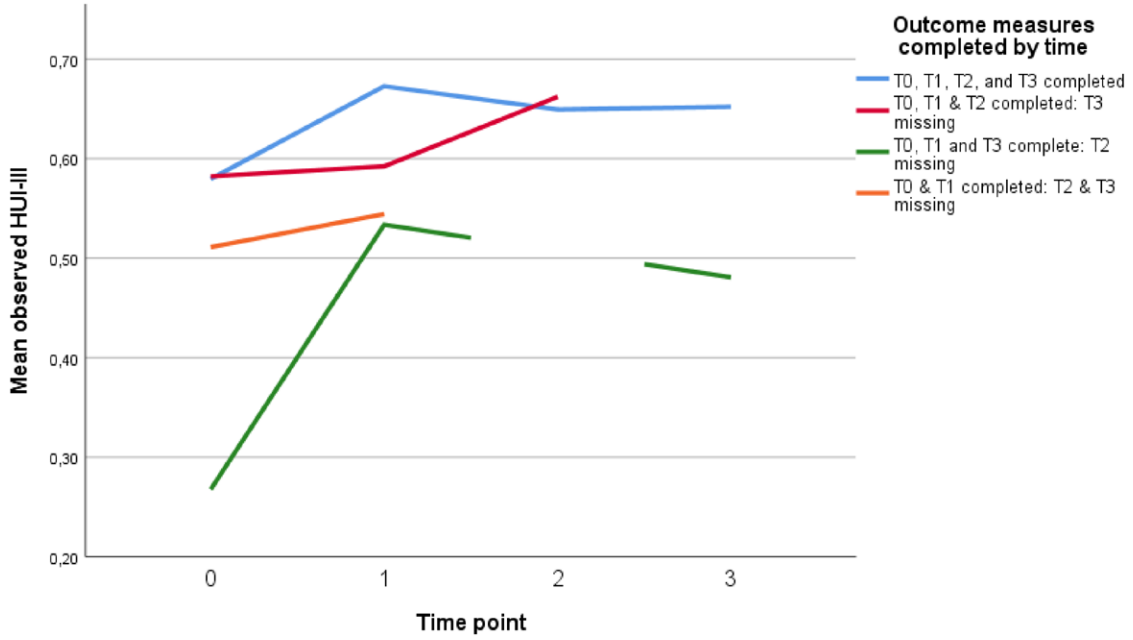

Fig. 4. Step 1 only participants quality of life (observed HUI-III scores) by time point, per missingness pattern.

or felt some stigma at the prospect of seeing a psychologist. Together, this suggests that audiologists have a valuable opportunity in their assessment to also ask participants about beliefs they might have about the causes of distress and disability associated with their tinnitus and beliefs about efficacy of treatment. This in turn can be used to further inform triage or referral to step 2 care. The rate at which participants did not complete outcome measures is comparable to other studies of tinnitus treatment effectiveness (e.g., Aazh & Moore 2018).

Except for the HUI-III score at baseline, step 1-only participants reported higher QoL at all time points than participants completing step 1 and 2. This suggests that there is further room for improvement for those participants who received both interventions (i.e., Step 1 and Step 2). The predictors of step 2 involvement—higher baseline THI, TQ at 3 months, and higher QoL – appear to partially reflect the selection criteria for step 2 as scores between THI and TQ have been found to be highly correlated (Zeman et al. 2012). It is possible that despite relatively

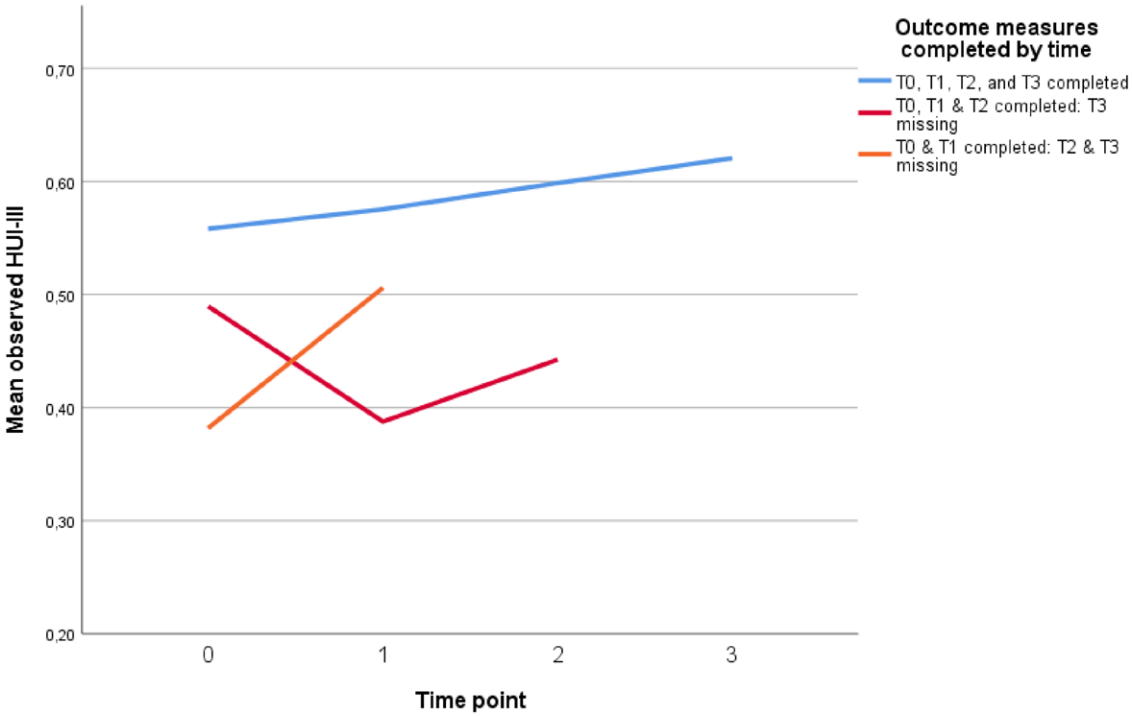

Fig. 5. Step 1& 2 participants quality of life(observed HUI-III scores) by time point, per missingness pattern.

high tinnitus distress, participants in step 2 with higher QoL score might have greater personal resources (i.e., e.g., stronger social/family support, secure employment with sick leave benefits) to be able to '*afford'* the time required for step 2 of the intervention.

Improvement, up to or at differing time points, occurred regardless of whether participants received step 1 or step 1 & 2 (see Figures 2, 3 and Figures 1 to 12 in Supplemental Digital Content 3, http://links.lww.com/EANDH/B15). For step 1, only participants improvement stops after T1, whereas for step 1 and 2 participants, improvement continues up to T3. We cannot say though to what extent this is due to the intervention because of the non-randomized assignment of participants to step 2 care. Nevertheless, the change from baseline to 12 months was greater than established minimal clinically important difference (MCID) criteria for four outcome measures (HUI-III, THI, TQ, HADS) for most of participants (the exception being when a higher cut off was applied for MCID on HADS). Currently, MCID reference data does not exist for the TCS, FTQ, and TDI, making it impossible to ascertain whether the observed changes on these measures are meaningful from a clinical perspective.

From a theoretical perspective, it is surprising that there were no baseline variables that consistently predicted outcome change over time. Two influential models of tinnitus—the cognitive-behavioral (McKenna et al. 2014) and the fear avoidance models of tinnitus (Cima et al. 2011b; Kleinstäuber et al. 2013)—both propose that tinnitus-related fear and negative beliefs respectively contribute to distress experienced by people suffering from tinnitus. Several studies support the inclusion of these variables in the models (e.g., Cima et al. 2011a; Cima et al. 2017; Weise et al. 2013), and it might be predicted that high baseline levels of tinnitus-related fear might be associated with decreases in tinnitus distress; yet, the analyses reported here did not reveal such an association.

Overall, the results complement those of the RCT of specialized CBT for tinnitus reported by Cima et al. (2012). The samples in the respective studies shared similarities in demographic characteristics (e.g., average age of participants 54 years, and percentage of female participants 37% and 39%, respectively) but differed on most patient-reported outcome measures at baseline. Specifically, the sample in the current study reported poorer QoL (HUI-III, 0.53 vs 0.64), higher mean levels of tinnitus-related interference in daily life (THI, 49 vs 39), tinnitus-related distress (TQ, 56 vs 49), tinnitus-related negative beliefs (TCS, 24 vs 21), and tinnitus-related fear (FTQ, 8.3 vs 7.3) at baseline. The sample in Cima et al. (2012), however, reported higher levels of psychological distress as measured by the HADS (7.7 vs 12.2). Overall this suggests that the beneficial effects of undertaking specialized stepped care CBT for tinnitus can be achieved in other audiological rehabilitation centers beyond the one in which the original trial was conducted. In other words, the results provide additional "real world" evidence to support the claim that specialized CBT for tinnitus can be an effective intervention package for reducing tinnitus distress and improving quality of life. The decrease that occurred in THI scores was also comparable to that reported in an effectiveness trial of audiologist-delivered CBT for tinnitus (Aazh & Moore 2018). Note though, that there is a lack of evidence regarding question of whether it matters, which healthcare professional provides CBT for tinnitus.

Limitations and Strengths of the Study

Four limitations should be considered in the interpretation and weight given to the results. First, as with any uncontrolled observational study, it is not possible to draw conclusions relating to the efficacy of the intervention itself. In other words, it is not possible to rule out that the changes between participants' baseline and 12-month scores on the outcome measures were caused by spontaneous recovery, non-specific factors, response shift effects, or other unknown factors. Similarly, without randomized allocation to a control intervention for step 2 after 3 months, it is not possible to comment specifically on the added benefit of step 2 for participants (Van Breukelen 2006).

A further general limitation related to the design of this study is that it treats and analyses participants at the group level. That is, the results only give an indication of the change that occurred in participants from baseline to 12 months, *on average* and consequently do not generalize to the participating individuals. An alternative that could be used in future to examine implementation under real-world conditions but with higher internal validity is the Single Case Experimental Design (Schork 2015). These designs typically consist of replications of studies including a single participant, require few resources, and can relatively easily be incorporated into routine clinical practice (Onghena et al. 2018; Vlaeyen et al. 2020).

Methodological (Podsakoff et al. 2003) and personal biases (Dunning et al. 2004) are known to affect measures of health-related outcomes and could also have also had an impact in this study. In particular, the reliance on self-report questionnaires could be problematic. That is, if participants were optimistic about the benefits of participating in the study, it is possible that this biased the way they responded to the outcome measures. For example, they might have overestimated the benefits of the intervention to align with considerable investment they made in participating in the intervention. Alternatively, if they had high expectations for the intervention that were not met, they might have systematically underestimated the changes/benefits that occurred. All outcome measures were however completed online which might have, at least, minimized the social desirability of participants' responses. The use of independent assessors of outcome (e.g. a psychologist separate from the audiological rehabilitation center involved in the study) at, for example, 12 months could have generated data that provided an indication of the magnitude and direction of any response bias. Although this limitation applies here, it should be noted that it is also common a limitation of many RCTs of CBT for tinnitus (Fuller et al. 2020).

Last, the fidelity to the protocol with which the intervention was delivered was not taken into consideration in the analysis. This might be important as, for example, the fidelity of audiologists implementing a manualized psychological intervention has been reported to be low in a recent study (Taylor et al. 2020). Intervention sessions were recorded, but limited resources prevented an unbiased assessment of protocol adherence being undertaken in time to be considered within this study. The absence of protocol fidelity data limits also prevents any assessment of the degree to which sessions might be "contaminated" by intervention components that were not intended to be included in the sessions. Furthermore, data on the acceptability of the intervention from study participants and therapists perspectives', as well as data on other facilitators and barriers

to the implementation of the intervention are currently missing. Such data would be valuable for future implementation.

Despite these limitations, it should be noted that this study was intended to examine participants' changes over time in a "real world" context. The sample size included here is the largest to date for an implementation study of any CBT protocol for tinnitus and along with the analytical procedures followed, engenders confidence that the results are applicable to a treatment seeking population of people with tinnitus in the Netherlands if not beyond. Furthermore, the steps followed for the analysis mean that we can be confident that we have not overlooked any consistent interactions between the predictors (e.g. baseline TQ score) and time or any consistent main effects. MLM analyses can include all observed data including of participants with missing outcome data. In our analyses, we also considered the question of whether to include intervention related variables for participants who completed step 2 (e.g., number of sessions in step 2 completed) but ultimately did not do so. This decision was taken on the grounds that any results obtained from such analysis would be difficult to interpret because the number of sessions taken and any other process measure that might have been affected by the outcome as measured at T0 and T1, which in turn correlate strongly with outcome at T2 and T3. This might have produced spurious correlations between process measures and outcome at T2 and T3 if the process measure has no effect on the outcome. For the same reason, an analysis of the full sample, with participation in step 2 (or not) as extra predictor is questionable, as the decision to give a patient step 2 is partly based on that participants' TQ score at baseline and perceptions of progress/need after completing step 1.

CONCLUSIONS

In sum, data collected at 3-, 8-, and 12 months after baseline showed that of those who completed follow-up measures, on average, improved by clinically meaningful amounts on outcome measures where MCID criteria exist (i.e., HUI-III, THI, TQ, and HADS) regardless of whether they received step 1 only or both steps 1 and 2 of the intervention. Participants who were younger and with lower levels of tinnitus distress were less likely to complete follow-up outcome measures. The observational study design prevents attributions of causality to the intervention itself from being made but results suggest that specialized CBT for tinnitus as described by Cima et al. (2012) can be effectively implemented at other audiological rehabilitation centers providing that appropriate resources are available. Stepped care CBT for tinnitus is an intervention intended for those bothered by tinnitus, and step 2 in particular for those more severely affected by it. In addition to the results from the earlier RCT (Cima et al. 2012), the findings of the current study can be used to inform patients, policy makers, health authorities, and insurance companies in deciding whether to use, fund, or promote this promising intervention for reducing tinnitus-related distress and improving health-related quality of life.

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The authors have no conflicts of interest to disclose.

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REFERENCES

Aazh, H., Bryant, C., Moore, B. C. J. (2019). Patients' perspectives about the acceptability and effectiveness of audiologist-delivered cognitive behavioral therapy for tinnitus and/or hyperacusis rehabilitation. *Am J Audiol, 28*, 973–985.

Aazh, H., & Moore, B. C. J. (2018). Effectiveness of audiologist-delivered cognitive behavioral therapy for tinnitus and hyperacusis rehabilitation: Outcomes for patients treated in routine practice. *Am J Audiol, 27*, 547–558.

Baguley, D. M., Humphriss, R. L., Hodgson, C. A. (2000). Convergent validity of the tinnitus handicap inventory and the tinnitus questionnaire. *J Laryngol Otol, 114*, 840–843.

Beukes, E. W., Allen, P. M., Baguley, D. M., Manchaiah, V., Andersson, G. (2018a). Long-term efficacy of audiologist-guided internet-based cognitive behavior therapy for tinnitus. *Am J Audiol, 27*(3S), 431–447.

Beukes, E. W., Baguley, D. M., Allen, P. M., Manchaiah, V., Andersson, G. (2018b). Audiologist-guided internet-based cognitive behavior therapy for adults with tinnitus in the United Kingdom: A randomized controlled trial. *Ear Hear, 39*, 423–433.

Bjelland, I., Dahl, A. A., Haug, T. T., Neckelmann, D. (2002). The validity of the Hospital anxiety and depression Scale. An updated literature review. *J Psychosom Res, 52*, 69–77.

Cima, R. F., Crombez, G., Vlaeyen, J. W. (2011a). Catastrophizing and fear of tinnitus predict quality of life in patients with chronic tinnitus. *Ear Hear, 32*, 634–641.

Cima, R. F. F., Kikidis, D., Mazurek, B., Haider, H., Cederroth, C. R., Norena, A., Lapira, A., Bibas, A., Hoare, D. J. (2020). Tinnitus healthcare: A survey revealing extensive variation in opinion and practices across Europe. *BMJ Open, 10*, e029346.

Cima, R. F., Maes, I. H., Joore, M. A., Scheyen, D. J., El Refaie, A., Baguley, D. M., Anteunis, L. J., van Breukelen, G. J., Vlaeyen, J. W. (2012). Specialised treatment based on cognitive behaviour therapy versus usual care for tinnitus: A randomised controlled trial. *Lancet, 379*, 1951–1959.

Cima, R. F. F., van Breukelen, G., Vlaeyen, J. W. S. (2018). Tinnitus-related fear: Mediating the effects of a cognitive behavioural specialised tinnitus treatment. *Hear Res, 358*, 86–97.

Cima, R. F., Vlaeyen, J. W., Maes, I. H., Joore, M. A., Anteunis, L. J. (2011b). Tinnitus interferes with daily life activities: A psychometric examination of the Tinnitus Disability Index. *Ear Hear, 32*, 623–633.

Coyne, J. C., & van Sonderen, E. (2012a). The hospital anxiety and depression scale (HADS) is dead, but like Elvis, there will still be citings. *J Psychosom Res*, *73*, 77–78.

Coyne, J. C., & van Sonderen, E. (2012). No further research needed: Abandoning the Hospital and Anxiety Depression Scale (HADS). *J Psychosom Res, 72*, 173–174.

Davis, A., & El Refaie, A. (2000). Epidemiology of Tinnitus. In R. S. Tyler (Ed.), *Handbook of Tinnitus* (pp. 1–24). Singular thompson Learning.

Dunning, D., Heath, C., Suls, J. M. (2004). Flawed self-assessment: Implications for health, education, and the workplace. *Psychol Sci Public Interest, 5*, 69–106.

Feeny, D., Furlong, W., Torrance, G. W., Goldsmith, C. H., Zhu, Z., DePauw, S., Denton, M., Boyle, M. (2002). Multiattribute and single-attribute utility functions for the health utilities index mark 3 system. *Med Care, 40*, 113–128.

Folmer, R. L., Theodoroff, S. M., Martin, W. H., Shi, Y. (2014). Experimental, controversial, and futuristic treatments for chronic tinnitus. *J Am Acad Audiol, 25*, 106–125.

Fuller, T. E., Cima, R. F. F., Langguth, B., Mazurek, B., Vlaeyen, J. W., Hoare, D. J. (2020). Cognitive behavioural therapy for tinnitus. *Cochrane Database Syst Rev*, *1*, Cd012614.

Fuller, T. E., Cima, R. F. F., Van den Bussche, E., Vlaeyen, J. W. S. (2019). The fear of tinnitus questionnaire: Toward a reliable and valid means of assessing fear in adults with tinnitus. *Ear Hear, 40*, 1467–1477.

Fuller, T. E., Haider, H. F., Kikidis, D., Lapira, A., Mazurek, B., Norena, A., Rabau, S., Lardinois, R., Cederroth, C. R., Edvall, N. K., Brueggemann, P. G., Rosing, S. N., Kapandais, A., Lungaard, D., Hoare, D. J., Cima, R. F. (2017). Different teams, same conclusions? A systematic review of existing clinical guidelines for the assessment and treatment of tinnitus in adults. *Front Psychol, 8*, 206.

Gartlehner, G., Hansen, R. A., Nissman, D., Lohr, K. N., Carey, T. S. (2006). A simple and valid tool distinguished efficacy from effectiveness studies. *J Clin Epidemiol, 59*, 1040–1048.

Grimshaw, J. M., Eccles, M. P., Lavis, J. N., Hill, S. J., Squires, J. E. (2012). Knowledge translation of research findings. *Implementation Sci*, *7*, 50.

Hall, D. A., Mehta, R. L., Argstatter, H. (2018). Interpreting the Tinnitus Questionnaire (German version): What individual differences are clinically important? *Int J Audiol, 57*, 553–557.

Hallam, R. S., Jakes, S. C., Hinchcliffe, R. (1988). Cognitive variables in tinnitus annoyance. *Br J Clin Psychol, 27*, 213–222.

Hoare, D. J., & Hall, D. A. (2011). Clinical guidelines and practice: A commentary on the complexity of tinnitus management. *Eval Health Prof, 34*, 413–420.

Horsman, J., Furlong, W., Feeny, D., Torrance, G. (2003). The Health Utilities Index (HUI): Concepts, measurement properties and applications. *Health Qual Life Outcomes, 1*, 54.

Kim, H. J., Lee, H. J., An, S. Y., Sim, S., Park, B., Kim, S. W., Lee, J. S., Hong, S. K., Choi, H. G. (2015). Analysis of the prevalence and associated risk factors of tinnitus in adults. *PLoS One, 10*, e0127578.

Kleinstäuber, M., Jasper, K., Schweda, I., Hiller, W., Andersson, G., Weise, C. (2013). The role of fear-avoidance cognitions and behaviors in patients with chronic tinnitus. *Cogn Behav Ther, 42*, 84–99.

Landry, E. C., Sandoval, X. C. R., Simeone, C. N., Tidball, G., Lea, J., Westerberg, B. D. (2020). Systematic Review and Network Meta-analysis of Cognitive and/or Behavioral Therapies (CBT) for Tinnitus. *Otol Neurotol, 41*, 153–166.

Langguth, B. (2012). Tinnitus: The end of therapeutic nihilism. *Lancet, 379*, 1926–1928.

Lemay, K. R., Tulloch, H. E., Pipe, A. L., Reed, J. L. (2019). Establishing the minimal clinically important difference for the Hospital anxiety and depression scale in patients with cardiovascular disease. *J Cardiopulm Rehabil Prev, 39*, E6–E11.

Maes, I. H., Joore, M. A., Cima, R. F., Vlaeyen, J. W., Anteunis, L. J. (2011). Assessment of health state in patients with tinnitus: A comparison of the EQ-5D and HUI mark III. *Ear Hear, 32*, 428–435.

Marra, C. A., Woolcott, J. C., Kopec, J. A., Shojania, K., Offer, R., Brazier, J. E., Esdaile, J. M., Anis, A. H. (2005). A comparison of generic, indirect utility measures (the HUI2, HUI3, SF-6D, and the EQ-5D) and disease-specific instruments (the RAQoL and the HAQ) in rheumatoid arthritis. *Soc Sci Med, 60*, 1571–1582.

McKenna, L., Handscomb, L., Hoare, D. J., Hall, D. A. (2014). A scientific cognitive-behavioral model of tinnitus: Novel conceptualizations of tinnitus distress. *Front Neurol, 5*, 196.

Newman, C. W., Jacobson, G. P., Spitzer, J. B. (1996). Development of the Tinnitus Handicap Inventory. *Arch Otolaryngol Head Neck Surg, 122*, 143–148.

Newman, C. W., Sandridge, S. A., Jacobson, G. P. (1998). Psychometric adequacy of the Tinnitus Handicap Inventory (THI) for evaluating treatment outcome. *J Am Acad Audiol, 9*, 153–160.

Onghena, P., Michiels, B., Jamshidi, L., Moeyaert, M., Van den Noortgate, W. (2018). One by One: Accumulating evidence by using meta-analytical procedures for single-case experiments. *Brain Impairment*, *19*, 33–58.

Podsakoff, P. M., MacKenzie, S. B., Lee, J.-Y., Podsakoff, N. P. (2003). Common method biases in behavioral research: A critical review of the literature and recommended remedies. *J Appl Psychol*, *88*, 879–903.

Puhan, M. A., Frey, M., Büchi, S., Schünemann, H. J. (2008). The minimal important difference of the hospital anxiety and depression scale in patients with chronic obstructive pulmonary disease. *Health Qual Life Outcomes, 6*, 46.

Schork, N. J. (2015). Personalized medicine: Time for one-person trials. *Nature, 520*, 609–611.

Sox, H. C., & Lewis, R. J. (2016). Pragmatic trials: Practical answers to "Real World" questions. *JAMA, 316*, 1205–1206.

Sullivan, M. J. L., Bishop, S. R., Pivik, J. (1995). The pain catastrophizing scale: Development and validation. *Psychological Assessment*, *7*, 524–532.

Taylor, J. A., Thompson, D. M., Hall, D. A., Walker, D. M., McMurran, M., Casey, A., Featherstone, D., MacDonald, C., Stockdale, D., Hoare, D. J. (2020). The TinMan study: Feasibility trial of a psychologically informed, audiologist-delivered, manualised intervention for tinnitus. *Int J Audiol, 59*, 905–914.

Thorpe, K. E., Zwarenstein, M., Oxman, A. D., Treweek, S., Furberg, C. D., Altman, D. G., Tunis, S., Bergel, E., Harvey, I., Magid, D. J., Chalkidou, K. (2009). A pragmatic-explanatory continuum indicator summary (PRECIS): A tool to help trial designers. *J Clin Epidemiol, 62*, 464–475.

Van Breukelen, G. J. (2006). ANCOVA versus change from baseline: More power in randomized studies, more bias in nonrandomized studies [corrected]. *J Clin Epidemiol, 59*, 920–925.

Verbeke, G., & Molenberghs, G. (2000). Linear Mixed Models for Longitudinal Data. Springer-Verlag.

Vlaeyen, J. W. S., Wicksell, R. K., Simons, L. E., Gentili, C., De, T. K., Tate, R. L., Vohra, S., Punja, S., Linton, S. J., Sniehotta, F. F., Onghena, P. (2020). From boulder to stockholm in 70 years: Single case experimental designs in clinical research. *Psychological Record*, *70*, 659–670.

Weise, C., Hesser, H., Andersson, G., Nyenhuis, N., Zastrutzki, S., Kröner-Herwig, B., Jäger, B. (2013). The role of catastrophizing in recent onset tinnitus: Its nature and association with tinnitus distress and medical utilization. *Int J Audiol, 52*, 177–188.

Zeman, F., Koller, M., Figueiredo, R., Aazevedo, A., Rates, M., Coelho, C., Kleinjung, T., de Ridder, D., Langguth, B., Landgrebe, M. (2011). Tinnitus handicap inventory for evaluating treatment effects: Which changes are clinically relevant? *Otolaryngol Head Neck Surg, 145*, 282–287.

Zeman, F., Koller, M., Schecklmann, M., Langguth, B., Landgrebe, M.; TRI database study group. (2012). Tinnitus assessment by means of standardized self-report questionnaires: Psychometric properties of the Tinnitus Questionnaire (TQ), the Tinnitus Handicap Inventory (THI), and their short versions in an international and multi-lingual sample. *Health Qual Life Outcomes, 10*, 128.

Zigmond, A. S., & Snaith, R. P. (1983). The hospital anxiety and depression scale. *Acta Psychiatr Scand, 67*, 361–370.