Specialised treatment based on cognitive behaviour therapy versus usual care for tinnitus: a randomised controlled trial

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Summary

Background **Up to 21% of adults will develop tinnitus, which is one of the most distressing and debilitating audiological problems. The absence of medical cures and standardised practice can lead to costly and prolonged treatment. We aimed to assess effectiveness of a stepped-care approach, based on cognitive behaviour therapy, compared with usual care in patients with varying tinnitus severity.**

Methods **In this randomised controlled trial, undertaken at the Adelante Department of Audiology and Communication (Hoensbroek, Netherlands), we enrolled previously untreated Dutch speakers (aged >18 years) who had a primary complaint of tinnitus but no health issues precluding participation. An independent research assistant randomly allocated patients by use of a computer-generated allocation sequence in a 1:1 ratio, stratified by tinnitus severity and hearing ability, in block sizes of four to receive specialised care of cognitive behaviour therapy with sound-focused tinnitus retraining therapy or usual care. Patients and assessors were masked to treatment assignment. Primary outcomes were health-related quality of life (assessed by the health utilities index score), tinnitus severity (tinnitus questionnaire score), and tinnitus impairment (tinnitus handicap inventory score), which were assessed before treatment and at 3 months, 8 months, and 12 months after randomisation. We used multilevel mixed regression analyses to assess outcomes in the intention-to-treat population. This study is registered with ClinicalTrials.gov, number NCT00733044.**

Findings **Between September, 2007 and January, 2011, we enrolled and treated 492 (66%) of 741 screened patients. Compared with 247 patients assigned to usual care, 245 patients assigned to specialised care improved in health-related quality of life during a period of 12 months (between-group difference 0·059, 95% CI 0·025 to 0·094; effect size of Cohen's *d*=0·24; p=0·0009), and had decreased tinnitus severity (–8·062, –10·829 to –5·295; *d*=0·43; p<0·0001) and tinnitus impairment (–7·506, –10·661 to –4·352; *d*=0·45; p<0·0001). Treatment seemed effective irrespective of initial tinnitus severity, and we noted no adverse events in this trial.**

Interpretation **Specialised treatment of tinnitus based on cognitive behaviour therapy could be suitable for widespread implementation for patients with tinnitus of varying severity.**

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Introduction

16–21% of adults develop tinnitus at some point in their lifetime, manifesting as the perception of a noxious disabling internal sound without an external source.[1] Although often not recognised by the general public, tinnitus is one of the most distressing and debilitating audiological disorders and affects almost all aspects of daily life.[2,3] Cognitive impairments and negative emotions associated with tinnitus are especially bothersome for patients and their families.[4,5]

Because tinnitus is not objectified easily, and medical efforts at cure have been unsuccessful, the effective management of tinnitus complaints is often a lengthy and troublesome treatment process involving numerous disciplines.[6] Evidence for a uniformly successful treatment of tinnitus is lacking, and present usual-care practices for tinnitus consist primarily of fragmented interventions, which often result in communication to patients that nothing can be done about the disorder and that they should learn to live with it.[6] The absence of standardised practice presents difficulties in assessment, treatment, and identification of subsets of patients with differential clinical demands, and in comparisons of clinical and research outcomes.[7]

Two main treatment approaches for tinnitus exist. First, sound-based therapies, such as tinnitus retraining therapy, which involve masking of tinnitus at the sound perception level in combination with structured counselling sessions.[8,9] This approach, which is often based on Jastreboff's neurophysiological model,[10] aims to ameliorate tinnitus distress through education and exposure to a neutral external sound. Through habituation to this neutral sound, which is expected to generalise to the threatening tinnitus sound, patients are expected to have diminished annoyance from tinnitus. Supporting evidence for the tinnitus retraining therapy approach is scarce, and most published reports derive from retrospective and uncontrolled trials.[8,11,12] The second main approach is cognitive behaviour therapy.[13–15] Such treatment is a comprehensive form of psychotherapy aimed at

modification of dysfunctional beliefs and behaviours. Typically, cognitive behaviour therapy includes psychoeducation, relaxation, exposure techniques, and behavioural reactivation, often in combination with mindfulness-based training. Although treatment of tinnitus with such therapy can reduce distress and improve quality of life, large scale and well controlled trials are needed.[5,13,15,16] The premise that the intensity of cognitive behaviour therapy could vary dependent on severity of tinnitus complaints has not been tested to our knowledge.

We developed a new multidisciplinary protocol for treatment of tinnitus, including a stepped-care cognitive behaviour therapy approach with elements from tinnitus retraining therapy. Stepped care allows a framework for organisation of health services on the basis of individual needs of patients, with a gradual increase in the intensity of care at each level.[17] In this randomised controlled study, we aimed to assess effectiveness of this specialised treatment protocol compared with care as usual.[6]

See Online for appendix

***Panel 1:* Usual care treatment protocol**

Step 1

Audiological diagnostics (105 min)

- Audiology assistant
  - Pure tone and speech audiometry, tympanometry (stapedial reflexes)
  - Tinnitus analyses: pitch mask frequency and minimum masking level
  - Uncomfortable loudness level measurement
  - Hearing aid check and optimisation (if present)
  - Questions about duration and location of the tinnitus
- Individual consult by clinical physicist in audiology
  - Audiological anamnesis
  - Assessment of audiometry and explanation
  - Information about tinnitus and hearing loss
  - Assessment of severity of complaints
  - Prescription hearing aid (when indicated by hearing loss)
  - Prescription tinnitus masker* (when indicated by patient)

Audiological rehabilitation (30 min)

- Audiology assistant
  - Check-up after 8 weeks of hearing aid use
  - Hearing aid check and optimisation

Audiological follow-up (40 min)

- Audiology assistant
  - Pure tone and speech audiometry, tympanometry (stapedial reflexes)
  - Uncomfortable loudness level measurement
  - Hearing aid check and optimisation (if present)
  - Tinnitus analyses: pitch mask frequency and minimum masking level
- Clinical physicist in audiology
  - Individual consult
  - Referral to social work (when indicated)

Step 2

Intake social work (60 min)

- Social worker
  - General inventory of complaints and use of hearing aids or maskers
  - Social work trajectory of maximum nine follow-up contacts (when indicated)

Follow-up social work (60 min)

- Social worker
  - Maximum nine contacts including counselling sessions, telephone contacts, extraneous appointments with third parties, house calls

*Sound-generators were prescribed when specifically asked for by the patient, and were adjusted to produce a small band noise around the pitch match frequency and slightly below the tinnitus masking level.

Methods

Study design and participants

We undertook a two group, two step, randomised controlled trial at Adelante Department of Audiology and Communication (Hoensbroek, Netherlands), in adult patients with tinnitus, with follow-up assessments at 3, 8, and 12 months after randomisation (appendix). Patients with tinnitus who were referred to our centre were invited to an off-centre baseline assessment, after which they were randomly allocated to either usual care or specialised care. We postulated that specialised care would be more effective than usual care in terms of improvement of generic health-related quality of life and reduction of tinnitus severity, impairment, general negative affect, catastrophic misinterpretation, and tinnitus-related fear.

Adult patients referred to our centre with a primary complaint of subjective tinnitus were eligible for inclusion. We excluded patients who were unable to read and write in Dutch, had health issues that impaired attendance or prevented participation (eg, terminal illness or physical disability), or had undergone treatment at our centre within 5 years before trial enrolment. Patients were assessed by an otolaryngologist to rule out pathological changes that needed immediate medical care. We obtained written informed consent before assessment and trial entry.

The medical ethical board of the Rehabilitation Foundation Limburg reviewed and approved the study protocol (METC-SRL 11/09/2006).

Randomisation and masking

An independent research assistant, who was based outside of Adelante, Department of Audiology and Communication, randomly allocated patients by use of a computer-generated allocation sequence to usual care or specialised care in a 1:1 ratio after receipt of informed consent and baseline assessments. Randomisation was stratified by tinnitus severity (<47 *vs* ≥47 points on the tinnitus questionnaire [TQ]) and hearing impairment (pure tone average of <60 dB *vs* ≥60 dB hearing level in worst ear). Within each of the four strata, patients were randomised in blocks of four patients.

Patients and investigators were masked to treatment group allocation. Before trial enrolment, patients were informed that they would be allocated to one of two different treatments aimed at tinnitus management, with a client-centred, stepped-care approach. Patients were also aware that by giving their consent they would not be informed to which treatment they were allocated. Early in

the intervention procedure detailed information about the treatment received was unveiled, while the participants remained masked to the content of the alternative treatment.

Procedures

Usual care and specialised care were provided with a stepped approach (appendix). Step 1 and step 2 in usual care and specialised care were completed by 8 months and followed by a no-contact period of 4 months before the last follow-up assessment at 12 months. Treatment in step 2 lasted for up to 12 weeks in both treatment approaches. Patients started step 2 within 4–6 weeks after 3 month assessment, depending on group-treatment schedule. We used case record forms for every patient to

Panel 2: **Specialised care treatment protocol**

Step 1

Audiological diagnostics (105 min)

- Audiology assistant
  - Pure tone and speech audiometry, tympanometry (stapedial reflexes)
  - Tinnitus analyses: pitch mask frequency and minimum masking level
  - Uncomfortable loudness level measurement
  - Hearing aid check and optimisation (if present)
  - Tinnitus anamnesis using structured interview
- Individual consult by clinical physicist in audiology (trained in tinnitus retraining counselling)*
  - Audiological anamnesis, assessment of audiometry and explanation
  - Information about tinnitus and hearing loss
  - Introduction to the neurophysiological model[10]
  - Reading materials and treatment rationale are provided
  - Explanation of treatment protocol in the first step and explanation of stepped-care approach
  - Prescription hearing aid (when indicated by hearing loss)
  - Prescription sound generator† (when indicated by patient)

Audiological rehabilitation (30 min)

- Audiology assistant
  - Check-up after 8 weeks of hearing aid or masking device use
  - Hearing aid check or masking device optimisation

Tinnitus educational session provided within the cognitive behaviour therapy framework (120 min; maximum ten patients with partners)

- Psychology assistant
  - Tinnitus retraining therapy counselling elements
  - Extensive explanation of neurophysiological model
  - Fear avoidance discussion
  - General information about step 2 care is provided
  - Group discussion and remaining questions answered

Intake psychology (extensive tinnitus specific and general psychological diagnostic anamnesis; 60 min)

- Clinical psychologist
  - When indicated by scores on tinnitus questionnaire and tinnitus handicap inventory, and by anamnesis, treatment goals for step 2 are formulated in concordance with patient and planned in multidisciplinary team meeting

Audiological follow-up (40 min)

- Audiology assistant
  - Pure tone and speech audiometry, tympanometry (stapedial reflexes)
  - Tinnitus analyses: pitch mask frequency and minimum masking level
  - Uncomfortable loudness level measurement
  - Hearing aid check and optimisation (if present)
- Clinical physicist in audiology (trained in tinnitus retraining counselling)
  - Individual consult*

Multidisciplinary team meeting (10 min per patient)

- All professionals involved in specialised care
  - All tinnitus patients are discussed and, when indicated by scores on tinnitus questionnaire/tinnitus handicap inventory and clinical view of psychologist, multidisciplinary treatment goals for step 2 are integrated in a plan of treatment

Step 2

Group treatments (treatment intensity and group size varies according to severity; 120 min per session over 12 weeks)

- Clinical psychologist, movement therapist, physical therapist, clinical physicist in audiology, social worker, speech therapist
  - Group sessions (of 10–12 patients, 6–8 patients, or 3–4 patients, dependent on tinnitus severity level and hearing level): cognitive behaviour therapy, psychoeducation, cognitive restructuring, exposure techniques, mindfulness-based elements, stress relief, and attention redirecting techniques by means of movement therapy, and applied relaxation
  - Themed group counselling sessions (including partners)

Individual trajectory if group treatment is contraindicated (60 min per discipline per patient for up to 12 weeks)

- Clinical psychologist, movement therapist
  - Combination of cognitive behaviour therapy, psychoeducation, cognitive restructuring, exposure techniques, mindfulness-based elements, stress relief, attention redirecting techniques by means of movement therapy, and applied relaxation applied on individual basis (with optional addition of a combination of professionals involved in group treatments)

*Specifically, the counselling elements of tinnitus retraining therapy were part of intervention, which aimed to educate patients about tinnitus and the neurophysiological model. †Sound-generators were prescribed when specifically asked for by the patient and were adjusted to produce a small band noise around the pitch match frequency and slightly above hearing threshold, as measured with the small band noise of the sound generator.

	Overall (n=492)	Usual care (n=247)	Specialised care (n=245)
Age, years	54·19 (11·54)	54·63 (12·02)	53·74 (11·05)
Sex, male	308 (63%)	150 (61%)	158 (65%)
Education (%)			
Low	225 (46%)	117 (47%)	108 (44%)
Middle	136 (28%)	61 (25%)	76 (31%)
High	131 (27%)	70 (28%)	61 (25%)
Employed	263 (53%)	124 (50%)	139 (57%)
Duration of tinnitus			
<1 year	147 (30%)	81 (33%)	67 (27%)
1–5 years	191 (39%)	94 (38%)	98 (40%)
>5 years	153 (31%)	73 (30%)	81 (33%)
Mild complaints (tinnitus questionnaire score <47)	224 (46%)	112 (45%)	112 (46%)
Tinnitus sound (pure tone)	71 (14%)	24 (10%)	44 (18%)
Tinnitus in left ear or head	123 (25%)	61 (25%)	62 (25%)
Tinnitus in right ear or head	98 (20%)	48 (19%)	49 (20%)
Continuous tinnitus	413 (84%)	206 (83%)	207 (85%)
Interval tinnitus	34 (7%)	7 (3%)	26 (11%)
Hearing aid	91 (19%)	45 (18%)	46 (19%)
Sound generator	93 (19%)	46 (19%)	47 (19%)
PTA right ear	29·74 (19·40)	30·30 (20·58)	29·18 (18·15)
PTA left ear	31·05 (20·64)	30·96 (20·25)	31·14 (21·06)
PTA bilateral	30·57 (17·60)	30·77 (17·85)	30·37 (17·38)
Health utilities index score	0·635 (0·289)	0·641 (0·295)	0·629 (0·283)
Tinnitus questionnaire score	49·05 (18·85)	48·78 (19·23)	49·32 (18·49)
Tinnitus handicap inventory score	38·96 (22·88)	38·65 (23·19)	39·27 (22·60)
Hospital anxiety and depression scale	12·20 (8·04)	11·79 (8·03)	12·60 (8·05)
Tinnitus catastrophising scale score	21·11 (12·19)	21·36 (12·57)	20·86 (11·81)
Fear of tinnitus questionnaire score	7·25 (3·59)	7·31 (3·65)	7·19 (3·54)

Data are mean (SD) or n (%). PTA=pure tone average for 1 kHz, 2 kHz, and 4 kHz.

Table 1: **Demographic and baseline characteristics**

standardise treatments and for collection of trial data in place of medical charts. All case record forms included detailed protocols for every separate professional, including supporting staff, and for multidisciplinary patient-related activities.

Usual care was provided on the basis of a standardised protocol modelled on the care typically provided by secondary-care audiological centres across the Netherlands. We surveyed all 26 audiological centres operative in the Netherlands by telephone as a qualitative study. We averaged the number of professionals involved and counselling hours provided, and two independent assessors categorised discipline type and health-care activities. Panel 1 shows the usual care treatment protocol.

Step 1 of usual care was a standard audiological intervention. For patients with mild complaints, treatment ended after the first step but these patients remained in the trial for follow-up. When tinnitus was more severe (as measured at baseline and after audiological counselling), patients entered step 2 of treatment.

Panel 2 shows the specialised care treatment protocol. Step 1 of specialised care consisted of multidisciplinary diagnostics and specific tinnitus retraining counselling, which were undertaken in a cognitive behaviour framework (including audiological rehabilitation when necessary). For patients with mild complaints this basic intervention was expected to be sufficient, and they were measured for follow-up only. When tinnitus was more severe (as measured at baseline and after psychological screening), patients entered step 2 of treatment, which consisted of three different 12-week group treatment options with levels of care dependent on tinnitus severity and hearing loss (panel 2).

We assessed treatment fidelity in a post-hoc investigation of case record forms, attendance lists, and electronic databases, for a random sample of 40 patients per treatment group (usual care and specialised care), to verify whether both treatments were provided according to treatment protocols (adherence) and not influenced overly (contamination) by contrasting elements from the other treatment.[18] The appendix shows specifics of the data collection.

Outcomes

Before randomisation, we assessed hearing impairment with pure tone audiometry and tinnitus severity with the TQ to provide data for stratification.[19] Pure tone audiometry was done bilaterally at 1 kHz, 2 kHz, and 4 kHz with a mobile audiometer (Interacoustics AS208, Assens, Denmark) with audiometry headphones (Telephonics TDH-39, Peltorcapped, New York, NY, USA) and we calculated the pure-tone average for each frequency.

The primary outcome measures were health-related quality of life (by the health utilities index [HUI] mark 3), tinnitus severity, and tinnitus impairment, which were assessed at baseline and at 3 months, 8 months, and 12 months after randomisation.

HUI mark 3 is a 17-item questionnaire designed to assess health-related quality of life or generic health on eight dimensions: vision, hearing, speech, ambulation, dexterity, emotion, cognition, and pain or complaints. Every question has five or six levels, and 972 000 possible health states can be computed. Possible utility scores range from –0·36 to 1·00 for the HUI mark 3.[20] This index has shown adequate responsiveness in the tinnitus population.[21] We assessed tinnitus severity with the TQ,[22] which consists of 52 items rated on a 3-point scale and assesses psychological distress associated with tinnitus. Psychometric properties of the questionnaire have proved excellent in different languages.[23] The tinnitus handicap inventory is a 25-item instrument scored on a 3-label category scale, and assesses tinnitus-related impairment on three domains: functional, emotional, and catastrophic.[24–26] Both overall and subscale internal consistency were satisfactory in our population.

For secondary outcomes, we measured negative affect with the hospital anxiety and depression scale (HADS),

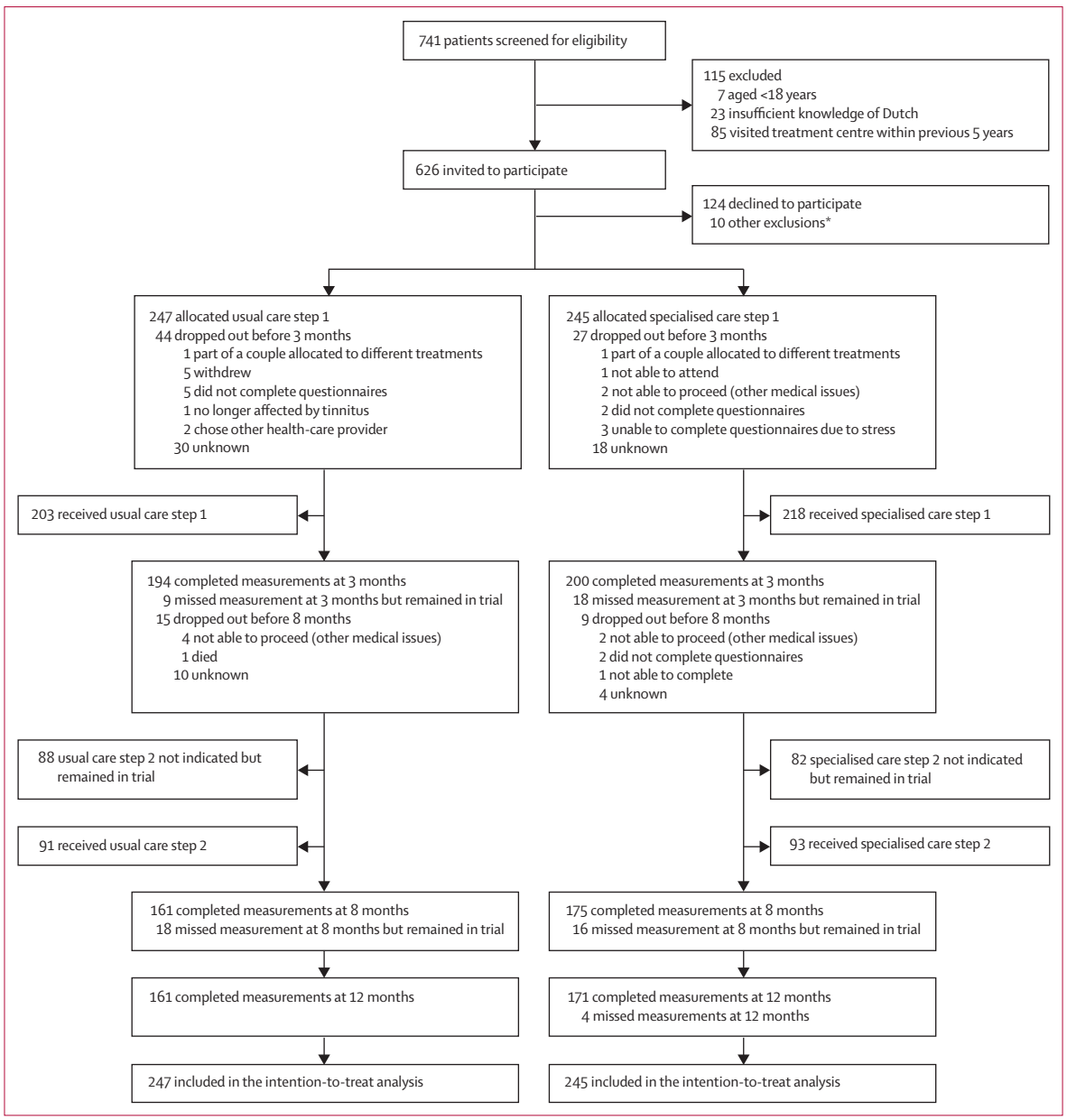

Figure: **Trial profile**
*Patients not able to enroll because of other medical issues or life events (ie, moved to another area or started another job).

which contained 14 items and has good reliability and validity.[27] The tinnitus catastrophising scale is an adapted version of the pain catastrophising scale[28] and assesses catastrophic misinterpretations of the tinnitus sound with 13 items rated on a 5-point scale (0 is not at all, 4 is always). The tinnitus catastrophising scale has been tested with patients[29] and internal consistency of the total score in our population was excellent (Cronbach's α=94). The fear of tinnitus questionnaire (FTQ) measures fear related to tinnitus. Some of the items on this questionnaire were derived from the Tampa scale for kinesiophobia and the pain anxiety symptoms scale.[30,31] This questionnaire was pretested with patients[29] and has 17 items rated on a true or false scale. Internal consistency of the total score in our population was excellent (Cronbach's α=82). Adverse events were surveyed throughout the trial and at all assessments.

We gathered demographic data with a 5-item questionnaire to establish sex, age, duration of complaints, educational achievement, and adherence area.

Statistical analysis

We identified only one study[5] about quality of life of tinnitus patients attending a specialised tinnitus centre.

	Baseline (n=247 in usual care; n=245 in specialised care)	3 months (n=194 in usual care; n=200 in specialised care)	8 months (n=161 in usual care; n=175 in specialised care)	12 months (n=161 in usual care; n=171 in specialised care)
Primary outcomes				
Health-related quality of life (HUI)				
Usual care	0·641 (0·295)	0·640 (0·294)	0·634 (0·287)	0·631 (0·279)
Specialised care	0·628 (0·284)	0·620 (0·285)	0·656 (0·254)	0·681 (0·250)
Tinnitus severity (TQ)				
Usual care	48·87 (19·22)	45·51 (19·65)	42·36 (19·62)	42·12 (19·81)
Specialised care	49·39 (18·50)	42·01 (19·81)	36·47 (17·48)	33·43 (16·89)
Tinnitus impairment (THI)				
Usual care	38·73 (23·20)	37·38 (23·74)	34·14 (24·60)	33·51 (23·25)
Specialised care	39·25 (22·65)	34·25 (23·44)	28·85 (20·51)	26·45 (18·81)
Secondary outcomes				
Negative effect (HADS)				
Usual care	11·83 (8·03)	12·08 (8·75)	11·47 (8·55)	10·83 (8·03)
Specialised care	12·61 (8·07)	11·91 (7·96)	10·52 (7·21)	10·22 (7·01)
Tinnitus catastrophising (TCS)				
Usual care	21·42 (12·56)	18·65 (11·76)	17·14 (11·54)	15·95 (11·79)
Specialised care	20·89 (11·83)	16·20 (11·65)	12·45 (10·30)	11·73 (9·91)
Tinnitus-related fear (FTQ)				
Usual care	7·32 (3·66)	6·60 (3·70)	6·19 (4·06)	6·04 (4·00)
Specialised care	7·19 (3·54)	5·60 (3·87)	4·52 (3·50)	4·20 (3·16)

Data are mean (SD) and were based on all available patients. HUI=health utilities index. TQ=tinnitus questionnaire. THI=tinnitus handicap inventory. HADS=hospital anxiety and depression inventory. TCS=tinnitus catastrophising scale. FTQ=fear of tinnitus questionnaire.

Table 2: **Primary and secondary outcomes at baseline and 3 months, 8 months, and 12 months after baseline**

We used the reported mean change over time of 0·065 (SD 0·15) in health utility score in that study as measured with the short form-36,[32] to calculate our sample size. Assuming an α level of 0·05 (two-sided), power of 80%, and 15% loss to follow-up, we calculated that we would need 99 patients per treatment group.

We did a post-calculation during the trial to detect a relevant difference within the subgroup of patients receiving treatment step 2. As our second treatment step was much the same as treatment in an earlier study,[13] the effect size of d=0·62 on the TQ in that study was used to compute power for our step 2. Assuming an α of 0·05 (two-sided) and a power of 80%, we needed 41 patients per group in the second step of care. Assuming that 21% of all patients entering step 1 would enter step 2, and accounting for 15% attrition, 232 patients were needed per group in step 1. The increment in inclusion was approved by the medical ethical board (METC-SRL 08/07/2008) and the steering committee of the funding party (ZonMW). We followed consolidated standards for reporting trials (CONSORT) guidelines[33] and used SPSS version 18.0 for all statistical analyses.

Treatment fidelity was checked first by assessing protocol adherence; dividing the number of required observed elements (essential and unique, and essential but not unique) by the maximum possible number of these elements.[18] Furthermore, treatment contamination was assessed by dividing the number of observed not allowed treatment elements by the maximum number of these elements. Finally, analysis of variance was used to assess equality of adherence and contamination between usual care and specialised care, by using scores calculated for all rated cases (80 patients; see appendix for details).

We used an intention-to-treat approach; all patients who were measured at baseline and allocated to treatment were included irrespective of their participation in subsequent treatment or follow-up measurements. We used mixed (multilevel) regression analyses for all available data per outcome, without imputation of missing data, and treatment, time, and covariates as predictors (appendix).

To assess whether specialised care and usual care treatment was different (measured with HUI and HADS) for patients who had severe tinnitus and entered step 2 and those who had mild tinnitus and step 1 care only, we tested the interaction between tinnitus severity at baseline and treatment (α=0·01 for the interaction test with respect to these outcome variables).

This study is registered with ClinicalTrials.gov, number NCT00733044.

Role of the funding source

The sponsor of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. RFFC and JWSV had full access to the data; IHM, MAJ, and LJCA had insight into data upon request; all authors approved the final report; and RFFC had final responsibility for the decision to submit for publication.

Results

Table 1 shows baseline values of the study population and the figure shows the trial profile, including numbers of patients who dropped out and non-responders, with reasons if known. Non-response was defined as missed measurements at one or more follow-up assessments; participants leaving the trial permanently and informing investigators were regarded as having dropped out.

Of 741 participants screened for eligibility, 626 were invited for participation, and 492 completed baseline measurements and were randomised to the first step of treatment (247 allocated to usual care and 245 to specialised care). Randomisation and treatment allocation took place between September, 2007, and December, 2009, and follow-up was completed in January, 2011.

Numbers of participants who did not respond or dropped out did not differ between groups at any follow-up (α=0·01, p>0·20), as measured with logistic regression with missing/not-missing as the dependent variable, and group, baseline characteristics (age, sex, education, duration of complaints, tinnitus severity at baseline, and hearing loss) and scores on the HUI, the TQ, and the THI at the previous timepoint as independent variables. We noted a positive association

between age and absence of response or dropout at 3 months (p=0·0162) and at 12 months (p=0·0070) after randomisation. All other predictors and time points did not reach significance (p>0·832).

86 (35%) of 247 patients in the usual care group and 74 (30%) of 245 patients in the specialised care group were lost to follow up by month 12. Reasons for non-response seemed unrelated to treatment content.

In the treatment fidelity check the inter-rater reliability between both independent raters for the identification of treatment (usual care *vs* specialised care) was excellent (Cohen's κ=0·96), and good for the identification of step 2 treatment (κ=0·79) and specific treatment elements (κ=0·74). Correct classifications of treatment (usual care *vs* specialised care) for each of the observed elements occurred 97% of the time, supporting sufficient differentiation between treatments. About 88% of essential treatment elements (unique and not unique) occurred during the delivery of both treatments (mean 88·4% [SD 9·02] for usual care and mean 87·5% [12·6] for specialised care), indicating satisfactory protocol adherence. About 6% of the prohibited treatment elements occurred during treatment delivery (mean 4·6% [SD 2·6] in usual care and mean 8·1% [6·1] in specialised care), suggesting absence of contamination. Analysis of variance suggested no significant differences between usual care and specialised care in terms of protocol adherence and contamination (p>0·6079).

We noted significant improvements in favour of specialised care compared with usual care for all primary outcomes during follow-up (tables 2, 3, appendix). Health-related quality of life increased with specialised care compared with usual care at 8 months and 12 months (table 3). Tinnitus severity and impairment related to tinnitus were reduced by specialised care compared with usual care at all three follow-ups (table 3). Compared with usual care, specialised care reduced negative affect at 8 months and 12 months, and tinnitus catastrophising and fear related to tinnitus at all three follow-ups (table 3).

The difference between specialised care and usual care that occurred by 8 months seemed to persist to 12 months, and was larger than that noted at 3 months. We tested this simplified treatment effect pattern against the general model with the following post-hoc analysis: the terms group×$t_{(3\ months)}$, group×$t_{(8\ months)}$, group×$t_{(12\ months)}$ were replaced with one group term (group×t) with time coded as 0,0,1,1 for the HUI and 0,1,2,2 for all other outcomes. For all six outcomes, the simplified treatment-effect pattern was supported (p>0·05 for the likelihood ratio test with 2 degrees of freedom), suggesting that the outcome difference between specialised care and usual care increased from baseline to 8 months and remained stable to 12 months.

We did not note any significant interaction effect of tinnitus severity and treatment on HUI (p=0·26) or HADS (p=0·33) at any timepoints, suggesting that the difference noted between treatment groups did not depend on tinnitus severity. Adverse events as a result of treatment or measurements did not occur.

	Group difference (95% CI)*	p value	Effect size (absolute values)
Primary outcomes			
Health-related quality of life (HUI)†			
3 months	−0·009 (0·056 to 0·039)	0·6420	0·04
8 months	0·038 (0·005 to 0·071)	0·0258	0·18
12 months	0·059 (0·025 to 0·094)	0·0009	0·24
Tinnitus severity (TQ)‡			
3 months	−3·315 (−5·612 to −1·019)	0·0048	0·20
8 months	−7·070 (−9·561 to −4·580)	<0·0001	0·41
12 months	−8·062 (−10·829 to −5·295)	<0·0001	0·43
Tinnitus impairment (THI)§			
3 months	−4·257 (−7·065 to −1·449)	0·0031	0·32
8 months	−7·626 (−10·713 to −4·539)	<0·0001	0·52
12 months	−7·506 (−10·661 to −4·352)	<0·0001	0·45
Secondary outcomes			
Negative affect (HADS)¶			
3 months	−0·857 (−2·180 to 0·465)	0·0941	0·15
8 months	−2·086 (−3·514 to −0·658)	0·0002	0·35
12 months	−1·507 (−2·867 to −0·148)	0·0043	0·24
Tinnitus catastrophising (TCS)‖			
3 months	−2·102 (−3·955 to −0·249)	0·0035	0·31
8 months	−4·683 (−6·938 to −2·428)	<0·0001	0·60
12 months	−3·830 (−6·185 to −1·475)	<0·0001	0·41
Tinnitus-related fear (FTQ)**			
3 months	−0·785 (−1·486 to −0·084)	0·0039	0·35
8 months	−1·550 (−2·353 to −0·748)	<0·0001	0·58
12 months	−1·502 (−2·317 to −0·688)	<0·0001	0·48

HUI=health utilities index. TQ=tinnitus questionnaire. THI=tinnitus handicap inventory. HADS=hospital anxiety and depression inventory. TCS=tinnitus catastrophising scale. FTQ=fear of tinnitus questionnaire. *99% CI for secondary outcomes. Because usual care was coded as 0 and specialised care was coded as 1, a negative group difference shows lower scores in usual care than specialised care at the follow-up measurements. Group difference values shown are group×time effects as shown in the appendix, in which time=0 for baseline, time=1 for 3 months, time=2 for 8 months, and time=3 for 12 months. Effect size was calculated by dividing the group difference values (ignoring their sign) by the square root of the average of residual variances at 3 months, 8 months, and 12 months giving a mixed regression version of Cohen's *d*. †Adjusted for the main effects of hearing loss and tinnitus severity at baseline, and time (by use of dummy coding with baseline as reference category). ‡Adjusted for the main effects of education, hearing loss, and time. §Adjusted for the main effects of age, duration, education, tinnitus severity at baseline, and time, and for interaction effects of time by education and by tinnitus severity at baseline. ¶Adjusted for the main effects of duration, hearing loss and tinnitus severity, time, and for interaction effects of time by duration and by tinnitus severity at baseline. ‖Adjusted for the main effects of education, tinnitus severity at baseline, time, and for the interaction effects of time by education and by tinnitus severity at baseline. **Adjusted for the main effects of tinnitus severity at baseline, time, and for the interaction effects of time by tinnitus severity at baseline.

Table 3: **Estimated group difference for primary and secondary outcomes at 3 months, 8 months, and 12 months, based on intention-to-treat analysis**

Discussion

Stepped-care tinnitus management, combining elements of tinnitus retraining therapy within a cognitive behaviour therapy framework, is more effective than is usual care for improvement of health-related quality of life and reduction of tinnitus severity and impairment. Moreover, specialised care generates greater improvements in general negative emotional states, tinnitus-related catastrophic thinking,

and tinnitus-related fear than does usual care. We showed the effectiveness of specialised care compared with usual care not only after the first 3 months of first-step treatment, but also after the more intensive second-step treatment approach ended and 4 months of no treatment. Notably, our findings were established even though patients with mild tinnitus complaints, receiving only first-step treatment, were included in all analyses.

Patients with mild or severe tinnitus seemed to benefit equally from specialised care compared with usual care. These findings support our main hypothesis that a stepped-care approach based on cognitive behaviour therapy with elements from tinnitus retraining therapy is effective in tinnitus management, both for mild forms of tinnitus and for more severe tinnitus.

Panel 3 shows a systematic review of present treatment approaches in management of tinnitus. Our combination of two main theoretical models and treatment approaches had not been studied previously.[6] Two main treatment approaches have dominated the management of patients with tinnitus complaints. Tinnitus retraining therapy, with its focus on sound habituation, and cognitive behaviour therapy, with its focus on dysfunctional beliefs about tinnitus and associated safety behaviours, have been widely applied and studied.[8,11,15,16] However, a combination of the two, although previously proposed,[29,34] has to our knowledge never before been investigated in a randomised controlled trial of this scale.

Our study has several strengths, including a comparatively large sample size, masking of investigators to treatment assignment, assessment of treatment fidelity to strengthen internal validity, and delivery of treatments according to protocols. Other strengths were that no patients dropped out from step 2 of treatment, both generic and tinnitus-specific outcome measures showed consistent findings and, moreover, the differences between treatment groups over time were likely to be clinically relevant. The percentage of patients reporting clinically relevant changes[19,35] after 12 months in health-related quality of life and in tinnitus severity was larger in the specialised care group than the usual care group.

Our study also has some limitations. Specialised care had several elements, and which of these elements contributed to the overall effectiveness is unknown. Future studies might adopt a dismantling approach, leaving out potentially redundant treatment components. Second, treatment was done in an outpatient clinic for audiological rehabilitation. Thus, whether our results can be generalised to other health-care settings or if generalisability is dependent on their similarity to the present setting is unclear. We are presently investigating implementation routes in both primary and secondary care.

In addition to the analyses reported presently, we are undertaking moderation and mediation analyses to provide additional information about underlying mechanisms of change, contributing to further refinement, tailoring, and increased effectiveness of the treatment. We also plan to report separate cost-effectiveness data for specialised care compared with usual care. Data were also collected with the tinnitus coping and cognitions list (TCCL) as specified in our trial protocol. The main reason for including this measure was to test the psychometric properties of this new measure in patients with tinnitus. The TCCL has considerable content overlap with the tinnitus catastrophising scale, and thus omission of this measure from the presented effect analyses should not affect our conclusions. We plan to report psychometric analyses separately.

Our findings provide firm evidence for an effective new treatment approach in management of tinnitus. The results are highly relevant for clinical practice because best practice for tinnitus has not been defined,[7] and current treatment strategies are fragmented and costly.[6] Delay of psychoeducation and effective treatment is expected to aggravate tinnitus complaints, thereby increasing psychological strain. Our findings could lead to consensus in policy about best practice in treatment of tinnitus, standard choices in referral trajectories, and the implementation of standardised tinnitus assessment and thereby more easily comparable outcomes.

Panel 3: Research in context

Systematic review

We searched various databases to identify relevant studies and review articles on tinnitus treatment in adults. Full details of the search are shown in the appendix. We identified 216 reports, and two reviewers (RFFC and DJWMS) independently assessed all studies for inclusion quality in this systematic review. We identified eight systematic reviews, nine randomised controlled trials, three follow-up or case-control studies, one non-randomised controlled trial, and one assessment of current practice that were relevant to our report.

Interpretation

The combination of two main theoretical models and treatment approaches that we used (cognitive behaviour therapy and tinnitus retraining therapy) was novel. Cognitive behaviour therapy for tinnitus seems the most promising approach in diminishing tinnitus-related distress and decreasing the main complaints of patients. The use of sound-generating devices, whether masking devices, wearable players, or hearing aids, even when combined with directive counselling sessions, have not been proven to be effective as a single treatment approach. Furthermore, as is the case in tinnitus retraining therapy-based approaches, effects seem modest at best. An integral treatment strategy might be best, with a standardised approach in diagnostics, treatment, and assessments because serial approaches (in random order) could lead to an unwanted increase of health-care use and costs. Moreover, a framework based on cognitive behaviour therapy in tinnitus management is advisable.

Contributors

The trial project members RFFC (principal investigator and main author), MAJ (project adviser and co-promoter), LJCA (project co-leader), and JWSV (project leader) designed the study and obtained funding. RFFC and DJWMS (project member and clinical audiology adviser) did the literature search for the systematic review and carried out the qualitative study for the development of the protocol of usual care. RFFC and DJWMS, in close collaboration with the specialised care professionals of Adelante, Department of Audiology and Communication, developed the specialised care protocol. Treatment manuals of usual care and specialised care were developed by RFFC and DJWMS, and MAJ and LJCA commented on drafts of the manuals. Further trial development and

design was carried out by the trial management group RFFC, MAJ, LJCA, JWSV, and IHM (principal investigator economic evaluation). Supporting literature searches were done by all members of the trial management group. Data collection was done by RFFC and IHM, who monitored data collection and integrity of randomisation. The statistical analysis plan was set up by RFFC, JWSV, and GJPB (adviser statistical analyses). The statistical analyses were done by RFFC with support from GJPB. Data interpretation was done by RFFC and GJPB. Trial treatments and the usual care and specialised care treatment teams were coordinated and monitored by RFFC. RFFC, JWSV, and GJBP were involved in the writing of the report, and the design of tables, figures, appendices, and panels. RFFC was responsible for writing and for the decision to submit the final paper for publication. All co-authors commented on drafts of the manuscript and approved the final report.

Conflicts of interest

We declare that we have no conflicts of interest.

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