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LITERATURE REVIEW

Measuring disease-specific health-related quality of life to evaluate treatment outcomes in tinnitus patients: A systematic review

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ABSTRACT

OBJECTIVE: To identify all disease-specific health-related quality-of-life (HR-QoL) instruments used to assess tinnitus in clinical trials and detail their psychometric properties.

DATA SOURCES: A literature search was performed in the bibliographical databases of PubMed and Embase to identify all articles using specific HR-QoL instruments in tinnitus trials.

REVIEW METHODS: The HR-QoL instruments used in these articles were investigated in more detail, focusing on characteristics and psychometric values by two independent reviewers.

RESULTS: Seventeen studies were identified by the systematic search. The most used HR-QoL questionnaire was the Tinnitus Questionnaire, followed by the Tinnitus Handicap Inventory, the Tinnitus Reaction Questionnaire, and the Tinnitus Handicap Questionnaire. Internal consistency (Cronbach's $\alpha > 0.9$) and reproducibility (> 0.8) were high for all questionnaires, and there was heterogeneity in responses between patients, endorsing the use of these questionnaires for discriminative purposes. However, the responsiveness, i.e., the usefulness of these questionnaires in evaluating treatment effects, is not known yet.

CONCLUSION: The HR-QoL instruments used in tinnitus trials appear not to be validated to measure effectiveness of interventions. Using tests or instruments that are valid and reliable is a crucial component of research quality, and both should therefore be studied before final conclusions can be drawn from the questionnaires in upcoming clinical trials.

Tinnitus is a phantom auditory perception in the absence of an external acoustic stimulus; a chronic and disabling disease. It can have a large impact on the quality of life experienced by the patient.[1-4] Tinnitus is difficult to assess because it is a subjective symptom. Currently there are no accurate objective measurement options available. The subjective perceived quality of life by tinnitus patients is often evaluated using health-related quality-of-life (HR-QoL) questionnaires. Over time, many different disease-specific HR-QoL instruments have been developed to measure the tinnitus burden, e.g., the Tinnitus Questionnaire, Tinnitus Handicap Questionnaire, and Tinnitus Handicap Inventory.[5-7]

These questionnaires are commonly used in clinical practice, particularly to discriminate between patients, and validated as such. Further, these instruments are increasingly used as an outcome measure in clinical trials; however, no consensus has been reached regarding which HR-QoL questionnaire is most powerful for this purpose. To be useful in clinical trials, validation regarding the responsiveness, i.e., the ability of the instrument to detect clinically important changes in HR-QoL over time, is also very important. An instrument should be able to detect at least that amount of change that patients experience as important. This responsiveness is essential for outcome measures.[8]

This systematic review presents the different HR-QoL instruments currently used in clinical trials measuring effects of tinnitus therapy. For each of the instruments identified, its characteristics and validation details are reported.

Material and Methods

Search Strategy

The bibliographical databases PubMed (1966-March 2009) and Embase (1988-March 2009) were searched using the terms *tinnitus*, *therapy* (clinical query), *quality of life questionnaire*, and their synonyms to identify all randomized-controlled clinical trials on tinnitus treatment measuring HR-QoL (Table 1). In addition, a reference and related article search was performed.

Study Selection

Two reviewers independently screened identified titles and abstracts without blinding to authorship or journal. Poten-

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Table 1
PubMed and Embase Search Strategy

Search term	PubMed	Embase (only)
Tinnitus	Tinnitus	Tinnitus/exp
AND		
Therapy	Clinical query, broad	Therapy/exp
AND		
Questionnaire	(Questionnaire OR Questionnaires OR Score OR Scale OR Index OR Inventory OR THI OR TQ OR THQ OR TSI OR TRQ)	Questionnaire/exp
OR	OR	OR
Quality of life	Quality of Life OR Health Status OR Functional Health Status	Quality of life/exp

Search in PubMed entering words as free text words or corresponding MeSH terms.
Limits: English language.

tially relevant studies were obtained and the full text examined. Discrepancies between reviewers were resolved by discussion. Criteria for inclusion were: tinnitus patients and evaluation of treatment with HR-QoL questionnaire. Studies were excluded if the study population consisted of specific patient groups (e.g., Ménière's disease), patients with co-morbidity (e.g., hypertension), or patients with tinnitus as a symptom of another disease (e.g., acoustic neurinoma). Studies were also excluded if HR-QoL outcomes (means and standard deviations) were not reported for both the patient and control groups.

For each identified HR-QoL questionnaire, we subsequently searched for the published details regarding its test characteristics.

Data Extraction

Information was gathered for each study on design, study population, number of included patients, type of intervention, duration of this intervention, and HR-QoL questionnaire used.

From the papers on the test characteristics, we extracted the following psychometric information: number of items, scaling, range of scale, number of domains, construct validity, internal consistency, reproducibility, and responsiveness.

Results

Initially, 439 articles were identified with PubMed, whereas Embase revealed 205 studies that were not found with PubMed. Of these 644 studies, only 17 articles met the inclusion criteria.

The 17 unique studies[9-25] are listed in Table 2, with respect to the therapies evaluated and the questionnaire used. The number of patients studied varied between 10 and 269. Furthermore, different control groups were used, i.e., other forms of psychological counseling or cognitive behavior, patients on the waiting list, and placebo controls. In general, large variations in means and standard deviations were found between studies, and most placebo-controlled trials reported large placebo effects.[9,10]

Six different HR-QoL questionnaires were used in the 17 included studies: the Tinnitus Handicap Inventory (THI) (n = 7 studies),[9-15] Tinnitus Questionnaire (TQ) (n = 5),[16-20] Tinnitus Reaction Questionnaire (TRQ) (n = 3),[12,21,22] Tinnitus Severity Index (TSI) (n = 2),[19,23] Tinnitus Handicap Questionnaire (THQ) (n = 1),[24] and the Tinnitus Severity Questionnaire (TSQ) (n = 1).[25] Two studies used two different questionnaires simultaneously, i.e., THI/TRQ and TQ/TSI HR-QoL.[12,19]

The test characteristics of the six HR-QoL questionnaires[3,5-7,26,27] are presented in Table 3. All instruments measure disease-specific HR-QoL, i.e., tinnitus burden. The shortest instruments are the TSI and TSQ, with 12 and 10 items, respectively, whereas the TQ has 52 items covering six domains. All questionnaires, with the exception of the THQ, use ordinal scales for each item. In the THQ, the patients score the percentage they agree with the item (0-100%).

The psychometric characteristics (construct validity, internal consistency, reproducibility, and responsiveness) of each of the six HR-QoL questionnaires are given in Table 4.[3,5-7,26,27] The construct validity, which examines the extent to which the concepts of interest are comprehensively represented by the items in the questionnaire,[28-31] is good for four of the six questionnaires. For the TSI and TSQ, the construct validity has not been assessed.

The internal consistency, which measures the correlation between the different items in the instrument,[28-31] for which Cronbach's α is mostly used, was higher than 0.9 for five HR-QoL instruments, but the subscales of the THQ and THI lack internal consistency. The internal consistency of the TSQ is unknown. The reproducibility, which is the ability to reproduce the same results when nothing has changed, was high (> 0.8) for all instruments.[28-31] Responsiveness, which measures the ability to detect a clinically important change over time, was not reported for any of the six instruments.

Table 2
Overview of studies measuring HR-QoL to evaluate treatment outcome in tinnitus patients

Authors	Therapy	Instrument
Mirz et al[9]	Low-power laser through external acoustic meatus	THI
Piccirillo et al[10]	Gabapentine	THI
Ghossaini et al[11]	Electromagnetic therapy	THI
Kaldo et al[12]	Cognitive behavioral treatment	THI, TRQ
Rejali et al[13]	Ginkgo biloba	THI
Rosenberg et al[14]	Melatonin	THI
Westerberg et al[15]	Baclofen	THI
Kroner-Herwig et al[16]	Tinnitus coping training	TQ
Langguth et al[17]	Active rTMS	TQ
Rief et al[18]	Psychophysiologic intervention	TQ
Bakhshaee et al[19]	Gabapentin	TQ, TSI
Mazurek et al[20]	Vardenafil	TQ
Andersson et al[21]	Internet-based cognitive behavioral treatment	TRQ
Andersson et al[22]	Cognitive behavioral treatment	TRQ
Henry et al[23]	Educational group counseling	TSI
Robinson et al[24]	Paroxetine	THQ
Zoger et al[25]	Sertraline	TSQ

THI, Tinnitus Handicap Inventory; *TRQ*, Tinnitus Reaction Questionnaire; *TQ*, Tinnitus Questionnaire; *rTMS*, repetitive transcranial magnetic stimulation; *TSI*, Tinnitus Severity Index; *THQ*, Tinnitus Handicap Questionnaire; *TSQ*, Tinnitus Severity Questionnaire.

Discussion

This review identified six different HR-QoL instruments that are currently used to measure treatment outcomes in tinnitus trials. All instruments were validated only for discriminative use. None of them were validated for evaluative purposes, which is necessary to be useful in clinical trials. To our knowledge, we are the first to present an overview of the HR-QoL questionnaires currently used to measure outcome in clinical trials and list their psychometric properties. On the other hand, publication bias cannot be precluded, i.e., articles presenting (negative) data on responsiveness might not have been published. Several experts in the field,

Table 3
Characteristics of HR-QoL instruments used to evaluate outcome

Instrument	Items	Score	Range	Domains
THI by Newman et al[6]	25 items	0-2-4 (0) never, (2) sometimes, (4) yes	0-100	Three domains: functional, emotional, catastrophic responses
TQ by Hallam[7]	52 items	True, partly true, not true	0-84	Six domains: emotional distress, cognitive distress, intrusiveness, auditory perceptual difficulties, sleep disturbance, somatic complaints
TRQ by Wilson et al[26]	26 items	0-4 (0) not at all-(4) almost all of the time	0-104	Four domains: general distress, interference, severity, avoidance
TSI by Meikle et al[27]	12 items	0-4 (0) never-(4) always	0-48	No domains
THQ by Kuk et al[5]	27 items	0-100 (0) strongly disagree, (100) strongly agree	0-2700	Three domains: physical health/emotional status/social consequences, hearing and communication, personal viewpoint
TSQ by Coles et al[3]	10 items	0-4 0 (not affected)-4 (always affected)	0-40	No domains

THI, Tinnitus Handicap Inventory; *TQ*, Tinnitus Questionnaire; *TRQ*, Tinnitus Reaction Questionnaire; *TSI*, Tinnitus Severity Index; *THQ*, Tinnitus Handicap Questionnaire; *TSQ*, Tinnitus Severity Questionnaire.

Table 4
Psychometrics of identified HR-QoL instruments

Instrument	Construct validity	Internal consistency (Cronbach's α)	Reproducibility (test re-test)	Responsiveness
THI[6]	+	0.93 subscales: 0.56-0.87	0.92	–
TQ[7]	+	0.95	0.94 subscales 0.86-0.93	–
TRQ[26]	+	0.96	0.88	–
TSI[27]	–	0.92	0.88	–
THQ[5]	+	0.94 subscales: 0.47-0.95	0.88	–
TSQ[3]	–	–	–	–

THI, Tinnitus Handicap Inventory; +, validated, positive; *TQ*, Tinnitus Questionnaire; *TRQ*, Tinnitus Reaction Questionnaire; *TSI*, Tinnitus Severity Index; –, not validated; *THQ*, Tinnitus Handicap Questionnaire; *TSQ*, Tinnitus Severity Questionnaire.

however, were asked their opinion on this issue, and their general response was that the responsiveness factor has indeed not been studied yet.

Validation of test responsiveness is necessary to optimize the usefulness of these HR-QoL instruments in tinnitus trials. Responsiveness is the ability of a measure to detect change over time in the construct of interest. For outcome measures intended to evaluate the effects of medical or educational interventions, responsiveness to changes that result from the intervention is required. Reliability is a crucial component of responsiveness. The "noise" that is due to measurement error can mask changes that may, in fact, be attributable to the intervention. A new disease-specific quality-of-life instrument that has not demonstrated stability over time when there is no change in health status (which may be an indication of measurement error) may not be able to detect health status changes. Furthermore, measures that have ceiling effects have a limited ability to assess positive changes that may result from the intervention because there is limited room for subjects to improve their scores. Responsiveness to change can legitimately differ from one population to another, which is why the measure must be appropriate to the subjects being studied.[8] Only when the responsiveness of a questionnaire is validated can an HR-QoL instrument be used to study the effectiveness of different interventions.

The Tinnitus Research Consortium is currently validating a new questionnaire, the Tinnitus Functional Index, which was developed specifically to measure treatment outcome.[32] The psychometric quantities of this new questionnaire should be compared with those of the questionnaires that are already available. Recommendation should be made as to which questionnaire can best be used to optimize treatment evaluations. Future clinical studies on tinnitus will benefit from such recommendations since it will enable better comparisons between such trials and subsequently increase the possibilities of meta-analyses in this field.

In conclusion, the disease-specific HR-QoL instruments used in clinical tinnitus trials appear not to be validated to measure the effectiveness of intervention therapies and, therefore, should not be used as such.

The validity, reliability, and responsiveness of each tinnitus-specific HR-QoL should be studied before final conclusions can be drawn regarding the utility of these questionnaires in future clinical studies.

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Digna M. Kamalski, search strategy, screening articles, data analysis, first version of article; **Carlijn E. Hoekstra,** working same field, familiar with this literature, new input on interpretation; **Bert G. van Zanten,** final editing, critical comments, audiologist's view; **Wilko Grolman, MD,** final editing, critical comments, discussion; **Maroeska M. Rovers,** supervisor, second independent screener of the articles, data analysis, epidemiologist's view.

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References

1. Tyler RS, editor. Tinnitus Handbook. San Diego: Singular, Thomson Learning; 2000. p. 3–21.
2. El Rafaie A, Davis A, Kayan A, et al. A questionnaire study of the quality of life and quality of family life of individuals complaining of tinnitus pre- and post-attendance at a tinnitus clinic. Int J Audiol 2004;43:410–6.

3. Coles RRA, Lutman ME, Axelsson A, et al. Tinnitus severity gradings: cross-sectional studies. In: Aran JM, Dauman R, editors. Proceedings of the Fourth International Tinnitus Seminar. New York/Amsterdam/Bordeaux: Kugler; 1992. p. 453–5.
4. Coles RR. Epidemiology of tinnitus: (1) prevalence. J Laryngol Otol Suppl 1984;9:7–15.
5. Kuk FK, Tyler RS, Russell D, et al. The psychometric properties of a tinnitus handicap questionnaire. Ear Hear 1990;11:434–45.
6. Newman CW, Jacobson GP, Spitzer JB. Development of the Tinnitus Handicap Inventory. Arch Otolaryngol Head Neck Surg 1996;122:143–8.
7. Hallam RS. Manual of the Tinnitus Questionnaire (TQ). London: Psychological Corporation; 1996.
8. Kimberlin CL, Winterstein AG. Validity and reliability of measurement instruments used in research. Am J Health Syst Pharm 2008;65:2276–84.
9. Mirz F, Zachariae R, Andersen SE, et al. The low-power laser in the treatment of tinnitus. Clin Otolaryngol Allied Sci 1999;24:346–54.
10. Piccirillo JF, Finnell J, Vlahiotis A, et al. Relief of idiopathic subjective tinnitus: is gabapentin effective? Arch Otolaryngol Head Neck Surg 2007;133:390–7.
11. Ghossaini SN, Spitzer JB, Mackins CC, et al. High-frequency pulsed electromagnetic energy in tinnitus treatment. Laryngoscope 2004;114:495–500.
12. Kaldo V, Cars S, Rahnert M, et al. Use of a self-help book with weekly therapist contact to reduce tinnitus distress: a randomized controlled trial. J Psychosom Res 2007;63:195–202.
13. Rejali D, Sivakumar A, Balaji N. Ginkgo biloba does not benefit patients with tinnitus: a randomized placebo-controlled double-blind trial and meta-analysis of randomized trials. Clin Otolaryngol Allied Sci 2004;29:226–31.
14. Rosenberg SI, Silverstein H, Rowan PT, et al. Effect of melatonin on tinnitus. Laryngoscope 1998;108:305–10.
15. Westerberg BD, Roberson JB Jr., Stach BA. A double-blind placebo-controlled trial of baclofen in the treatment of tinnitus. Am J Otol 1996;17:896–903.
16. Kroner-Herwig B, Frenzel A, Fritsche G, et al. The management of chronic tinnitus: comparison of an outpatient cognitive-behavioral group training to minimal-contact interventions. J Psychosom Res 2003;54:381–9.
17. Langguth B, Kleinjung T, Marienhagen J, et al. Transcranial magnetic stimulation for the treatment of tinnitus: effects on cortical excitability. BMC Neurosci 2007;8:45.
18. Rief W, Weise C, Kley N, et al. Psychophysiologic treatment of chronic tinnitus: a randomized clinical trial. Psychosom Med 2005;67:833–8.
19. Bakhshaee M, Ghasemi M, Azarpazhooh M, et al. Gabapentin effectiveness on the sensation of subjective idiopathic tinnitus: a pilot study. Eur Arch Otorhinolaryngol 2008;265:525–30.
20. Mazurek B, Haupt H, Szczepek AJ, et al. Evaluation of vardenafil for the treatment of subjective tinnitus: a controlled pilot study. J Negat Results Biomed 2009;8:3.
21. Andersson G, Stromgren T, Strom L, et al. Randomized controlled trial of internet-based cognitive behavior therapy for distress associated with tinnitus. Psychosom Med 2002;64:810–6.
22. Andersson G, Porsaeus D, Wiklund M, et al. Treatment of tinnitus in the elderly: a controlled trial of cognitive behavior therapy. Int J Audiol 2005;44:671–5.
23. Henry JA, Loovis C, Montero M, et al. Randomized clinical trial: group counseling based on tinnitus retraining therapy. J Rehabil Res Dev 2007;44:21–32.
24. Robinson SK, Viirre ES, Bailey KA, et al. Randomized placebo-controlled trial of a selective serotonin reuptake inhibitor in the treatment of nondepressed tinnitus subjects. Psychosom Med 2005;67:981–8.
25. Zoger S, Svedlund J, Holgers KM. The effects of sertraline on severe tinnitus suffering—a randomized, double-blind, placebo-controlled study. J Clin Psychopharmacol 2006;26:32–9.
26. Wilson PH, Henry J, Bowen M, et al. Tinnitus reaction questionnaire: psychometric properties of a measure of distress associated with tinnitus. J Speech Hear Res 1991;34:197–201.
27. Meikle MB, Griest SE, Stewart BJ. Measuring the negative impact of tinnitus: a brief severity index. Abstr Assoc Res Otolaryngol 1995;167.
28. Terwee CB, Bot SD, de Boer MR, et al. Quality criteria were proposed for measurement properties of health status questionnaires. J Clin Epidemiol 2007;60:34–42.
29. Kirshner B, Guyatt G. A methodological framework for assessing health indices. J Chronic Dis 1985;38:27–36.
30. Guyatt GH, Naylor CD, Juniper E, et al. Users' guides to the medical literature. XII. How to use articles about health-related quality of life. Evidence-Based Medicine Working Group. JAMA 1997;277:1232–7.
31. Testa MA, Nackley JF. Methods for quality-of-life studies. Annu Rev Public Health 1994;15:535–59.
32. Snow JB Jr. Strategies of the Tinnitus Research Consortium. Acta Otolaryngol Suppl 2006;556:89–92.