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Review Article

Evaluation of Long-Term Efficacy and Quality of Life of Tinnitus Retraining Therapy in Patients with Chronic Tinnitus: A Meta-Analysis

Mi Wang [1], Nianci Xiao [1], Qingxiu Yao [1], Mengmeng Chen [2], *Weiliu Zhu [1]

1. *Otolaryngology Department, The First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou 310003, Zhejiang Province, China*
2. *Otolaryngology Department, Shulan (Hangzhou) Hospital, Hangzhou 310000, Zhejiang Province, China*

***Corresponding Author:** Email: Z_lovemm@126.com

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Abstract

Background: Chronic tinnitus significantly impacts patients' quality of life, with no consensus on the long-term efficacy of different interventions. This study aimed to evaluate the long-term effects of tinnitus retraining therapy (TRT) through a systematic review and meta-analysis.

Methods: Following PRISMA guidelines, literature was searched across eight databases up to November 2024. Ten randomized controlled trials were selected. A random-effects model was used to calculate weighted mean differences (MD) and 95% confidence intervals (CI) for Tinnitus Handicap Inventory (THI) and Visual Analog Scale (VAS) scores.

Results: Compared to control groups, TRT significantly improved THI scores (MD = -8.72, 95% CI: -16.65 to -0.79, *P*=0.03) and showed a trend toward improving VAS scores (MD = -2.78, 95% CI: -5.57 to 0.02, *P*=0.05). Heterogeneity was high (I^2=90-96%), but sensitivity analysis confirmed stable results.

Conclusion: TRT has a significant long-term therapeutic effect on chronic tinnitus. Future studies should increase sample sizes, standardize interventions, and optimize review processes to reduce heterogeneity and define optimal TRT strategies.

Keywords: Chronictinnitus; Tinnitus retraining therapy (TRT); Long-term effects; QoL; Meta-analysis

Introduction

Chronic tinnitus refers to the persistent or intermittent perception of sounds in or around the ear without corresponding external acoustic stimulation (1). It is not only a symptom but also a common health issue, with approximately 10% to 15% of the global population experiencing tinnitus, and a subset of these individuals suffer from persistent symptoms for years, severely affecting their quality of life (QoL) and mental health (2,3). The pathogenesis of chronic tinnitus is complex and may be closely related to inner ear damage, neurological changes, psychological factors, and

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other health issues (such as hearing loss, anxiety, depression) (4,5). However, despite tinnitus becoming a common global health issue, current treatment methods for tinnitus are still insufficient, especially in improving patients' long-term QoL (6).

Treatment for tinnitus typically includes pharmacotherapy, sound therapy, cognitive-behavioral therapy, and other methods, but for many patients, these approaches often have limited effects or fail to achieve long-term symptom relief (7). In recent years, tinnitus retraining therapy (TRT) has garnered widespread attention as a new treatment method. TRT combines tinnitus treatment with sound therapy, helping patients adjust their perception and emotional response to tinnitus through various means, with the goal of reducing the interference of tinnitus and improving QoL (8,9). The core concept of TRT is to change patients' negative emotional and cognitive responses to tinnitus through long-term auditory stimulation and psychological counseling, allowing them to gradually adapt to the presence of tinnitus, thereby reducing the discomfort and anxiety, depression, and other negative emotions caused by tinnitus (10,11). Since its introduction in the early 1990s, TRT has been widely applied in clinical settings. This treatment method has not only achieved certain effects in reducing the intensity of tinnitus but has also played a visible role in helping patients improve mental health and QoL (12,13). The treatment process of TRT is usually lengthy, and the manifestation of therapeutic outcomes often requires several months or even longer. According to different studies, the specific effects and applicable populations of TRT may vary, and the distinctions in patient groups, intervention schemes, treatment duration, and other aspects across studies lead to inconsistent research results and conclusions (14,15).

TRT can markedly reduce the intensity and frequency of tinnitus in patients and improve their emotional state, especially providing good relief for anxiety and depression associated with tinnitus symptoms. TRT can also effectively enhance patients' QoL, help them resume normal daily activities, and reduce the impact of tinnitus on work (16,17). However, these studies mainly focus on the initial and midterm assessments of therapeutic outcomes, and there is a lack of systematic comprehensive analysis on the long-term effects of TRT and its effectiveness under different intervention schemes. Particularly, the distinctions in intervention duration, treatment methods, sample selection, and scoring criteria in different studies result in visible distinctions in the evaluation of TRT's efficacy in treating chronic tinnitus.

In response to these issues, this article aims to comprehensively assess the long-term effects of TRT on chronic tinnitus and its impact on patients' QoL through systematic review and meta-analysis of existing literature. Meta-analysis, as a powerful statistical method, can effectively reduce biases that may exist in individual studies and provide more reliable conclusions. Through the comprehensive analysis of existing literature, it is hoped to provide a more systematic and comprehensive understanding for clinicians treating tinnitus, patients, and related researchers, promoting the further application of TRT in the treatment of chronic tinnitus, and ultimately improving patients' tinnitus symptoms and QoL.

Materials and Methods

Article searching

This study strictly adhered to the methods of systematic review and meta-analysis. The study was conducted in accordance with the *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA) guidelines. First, literature published up to Nov 2024 was searched in the following databases: PubMed, Embase, Web of Science, Cochrane Library, MEDLINE, China National Knowledge Infrastructure (CNKI), WanFang Data, and the Chinese Science Citation Database (VIP). The search strategy utilized core terms such as "Tinnitus Retraining Therapy" (TRT), "Chronic Tinnitus," "Long-term Effects," "Quality of Life," "Tinnitus Handicap Inventory"

(THI), "Visual Analogue Scale" (VAS), and "Randomized Controlled Trial," combined using Boolean operators "AND" and "OR." For example:

("Tinnitus Retraining Therapy" OR "TRT")
AND ("Chronic Tinnitus")
AND ("Long-term Effects" OR "Quality of Life")
AND ("Tinnitus Handicap Inventory" OR "Visual Analogue Scale")
AND ("randomized controlled trial").

Additionally, manual searches of key journals and their reference lists were conducted to track citations of the included studies, ensuring the comprehensiveness of the search.

Article selection

Selection

Regarding study design, the studies included in this review were randomized controlled trials (RCTs), cohort studies, or case-control studies.

Regarding study population, the participants were adult patients with chronic tinnitus (tinnitus lasting ≥3 months), diagnosed according to internationally recognized criteria.

Regarding interventions, the intervention group (IG) clearly adopted TRT, while the control group (CG) received either no intervention, a placebo, or another form of control treatment.

Regarding outcome measures, the studies reported baseline and post-intervention data on tinnitus assessment scales, such as the THI or the visual analogue scale (VAS).

Regarding language and publication date, the studies were published in English or Chinese, with publication dates up to Nov 2024.

Removal

Review articles, meta-analyses, conference abstracts, case reports, and other studies with non-original data.

Studies where the intervention was unclear or did not involve TRT.

Studies with complex intervention factors that prevent independent assessment of the TRT effect.

Studies that did not provide sufficient THI or VAS data.

Studies with a high risk of bias (RoB) based on methodological quality assessment.

Literature screening process

Two researchers independently conducted the literature screening and data extraction:

Initial screening (Title and Abstract): researchers excluded studies unrelated to the research topic.

Full-text screening: researchers evaluated the study design and data completeness according to the inclusion/exclusion criteria.

Data extraction: researchers used a pre-designed *Excel* spreadsheet to extract basic study information, patient characteristics, intervention details, and THI and VAS scores.

Discrepancy resolution: in case of disagreement, consensus was reached through discussion or arbitration by a third-party expert.

Systematic review methodology

This study followed the systematic review process:

Study protocol development: the research question, population, intervention, comparator, outcomes, study design (PICOS) elements were clearly defined, and the protocol was registered.

Literature search and screening: a standardized search strategy was employed, with a joint search across multiple databases, and the search log was recorded.

Quality assessment: the Cochrane RoB tool was applied to evaluate randomization, blinding, outcome reporting, and other factors, categorizing each study as "low RoB," "high RoB," or "unclear RoB."

Data synthesis: homogeneous studies were aggregated, and the effect size of TRT on THI and VAS was quantified in the meta-analysis.

Sensitivity analysis and publication bias detection: sensitivity analysis was performed by sequentially excluding studies, and funnel plots were used to assess the robustness of the results and detect publication bias.

Statistical methods

Meta-analysis was performed using *Review Manager 5.3*.

Effect size calculation: for continuous variables, the mean difference (MD) and its 95% confidence interval (CI) were used to represent the effect size.

Heterogeneity assessment: Cochran's Q test and the I^2 statistic were employed to assess between-study heterogeneity. A fixed-effect model was applied when $P > 0.10$ and $I^2 \leq 50\%$; a random-effects model was used when $P \leq 0.10$ or $I^2 > 50\%$, with further exploration of potential sources of heterogeneity.

Sensitivity analysis: the stability of the results was validated by excluding individual studies or changing the analysis model.

Publication bias: funnel plots were constructed to evaluate the possibility of small-study effects and publication bias.

Significance testing: a *P*-value of less than 0.05 was considered indicative of statistical significance.

Results

Searching results

This article employed a comprehensive multi-database search strategy and, after combining various keywords and their expanded terms, 212 relevant articles were retrieved. Finally, 10 articles were included in the meta-analysis (Fig. 1).

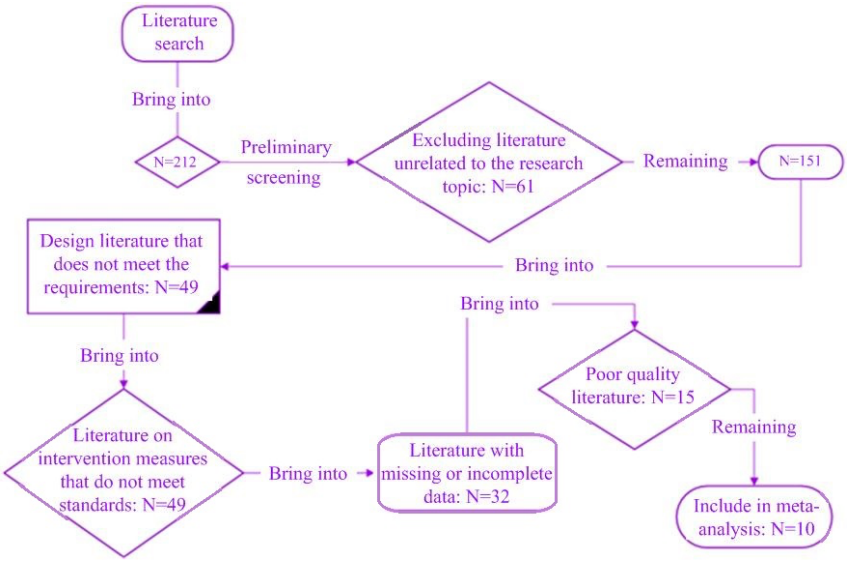

Fig. 1: Flowchart of articles searching

Basic information

Ten studies involving different clinical trials of TRT for chronic tinnitus were included, with the age range of subjects varying from 38.8 to 62.4 yr. All studies' IG received TRT, and most adopted a comprehensive intervention plan combining sound therapy, counseling therapy, or other auxiliary measures. The CG' remedy plans included standard remedy, tinnitus masking therapy, hearing aid application, etc., and some studies also had a no-IG. The duration of intervention in different studies ranged from 6 months to 36 months, with most studies having an intervention duration of 18 months or 3 months, and a few studies set a shorter intervention period of 4 wk to 12 wk. Specifically, some studies adopted TRT in combination with other therapies, such as transcranial direct current stimulation (TDCS), tinnitus control instrument (TCI), and other studies combined innovative forms like educational counseling, personalized sound therapy, and smart applications. The sample size of the studies

also varied, with the number of cases ranging from 11 to 247, with most studies having a sample size between 40 and 90. In addition, all studies focused on THI as the primary outcome measure, verifying the efficacy of TRT by assessing changes in the severity of tinnitus before and after remedy (Table 1).

Table 1: Basic data of the included articles

Reference No.	Age (yr)		Remedy options		Duration of intervention	
	CG	IG	CG	IG	CG	IG
(18)	50.6±11.3	50.6±11.3	Standard of Care (SoC)	TRT (TC and ST combined with conventional sound generators	18 months	18 months
(19)	57.9±11.1	57.9±11.1	Simplified group consultation by a single clinician (1-4 patients per group)	An interactive smart tablet app was adopted for instruction-based consultations on ear anatomy, neurophysiological models of tinnitus, habituation concepts, and sound therapy	The first session lasted about 45-60 min, and the second and third sessions lasted about 10-20 min	At least 45 min for the first session (if all questions are answered quickly and correctly), at least 25 min for the second and third sessions, and possibly more than 1 h for some patients
(20)	55.37±7.26	56.23±9.81	TDCS: current intensity of 2 mA and stimulation duration of 20 min	TDCS combined with TRT	5 sessions per week for 4 wk	4 wk
(21)	42.8±12.91	42.8±12.91	Participants can choose their favorite music from the software's built-in music library and listen to the processed gap-filtered music in a quiet environment. The software automatically generated gap-filtered music based on the characteristics of the participant's tinnitus	Instruction counseling and sound therapy were included. Mentoring educational counseling organizes an initial TRT session for the group at the beginning of therapy that covers: ear anatomy, auditory physiology, neurophysiological mechanisms of tinnitus and causes of tinnitus, guiding the correct remedy goals, and tinnitus habituation advice. TRT-related counseling was continued during follow-up. Sound therapy requires participants to listen to broadband nature sounds (e.g., wind, rain, and waves) for 2 h per day	3 months	3 months
(22)	62.4±9.8	60.1±10.1	Tinnitus masking therapy, using a combination of ear sound generator, hearing aids or equipment	TRT therapy, combining sound therapy and structured educational counseling	18 months	18 months

Table 1: Continued …

(23)	38.8±1.9	38.8±1.9	No intervention	Two methods: Using hearing Aids and a sound generator. Method 1: Wearing a Viennatone broadband sound generator in both ears. The sound generator produces sustained broadband sound with adjustable volume. The frequency spectrum is adjusted for tinnitus tone. Method 2: Wearing ResoundAir open digital hearing Aids in both ears, the hearing aids were programmed according to standard fitting procedures	/	At least 8 h a day for 12 months
(24)	60.3±11.7	60.3±11.7	No intervention	TRT combined with TCI	/	6 months
(25)	60.1±8.7	59.4±10.8	Telephone survey on the efficacy of TRT, directive counseling and sound therapy based on the Jastreboff neurophysiological model, with no subsequent therapy after the initial consultation	Telephone surveys about the efficacy of TRT, mentoring counseling, and sound therapy based on the Jastreboff neurophysiological model, with 15-min ongoing counseling every 1-2 months	5.3±2.2 months	4.7±1.6 months
(26)	54±14	54±14	No intervention	TRT, including consulting and sound therapy, broadband noise generator (bilateral application, for the unilateral tinnitus patients without hearing loss); Hearing aids (for those with hearing loss, with integrated sound generators)	At the end of remedy (18 months) and 18 months after the end of remedy (36 months)	At the end of remedy (18 months) and 18 months after the end of remedy (36 months)
(27)	54.63±12.02	53.74±11.05	Standard audiological interventions (step 1); Patients with severe tinnitus proceed to step 2 (social work intervention, up to nine follow-up visits)	Multidisciplinary diagnosis and specific TRT counseling (step 1, within the cognitive behavioral framework); Patients with severe tinnitus proceed to step 2 (12-week group therapy, intensity varies according to tinnitus severity and hearing loss)	Step 1: 8 months (followed by a 4-month contact-free period). Step 2: Up to 12 wk	Step 1: 8 months (followed by a 4-month contact-free period). Step 2: Up to 12 wk

Assessment of included articles

The 10 articles were assessed using the Cochrane Reviewer's Handbook, and a comprehensive graph of the RoB assessment was plotted using Review Manager 5.3 software, with all articles having "low risk" for selective reporting (Figs. 2 and 3).

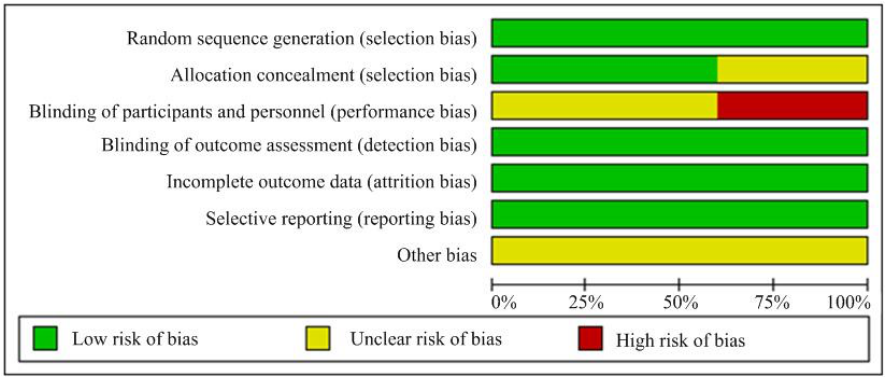

Fig. 2: Bar chart of RoB assessment of included articles

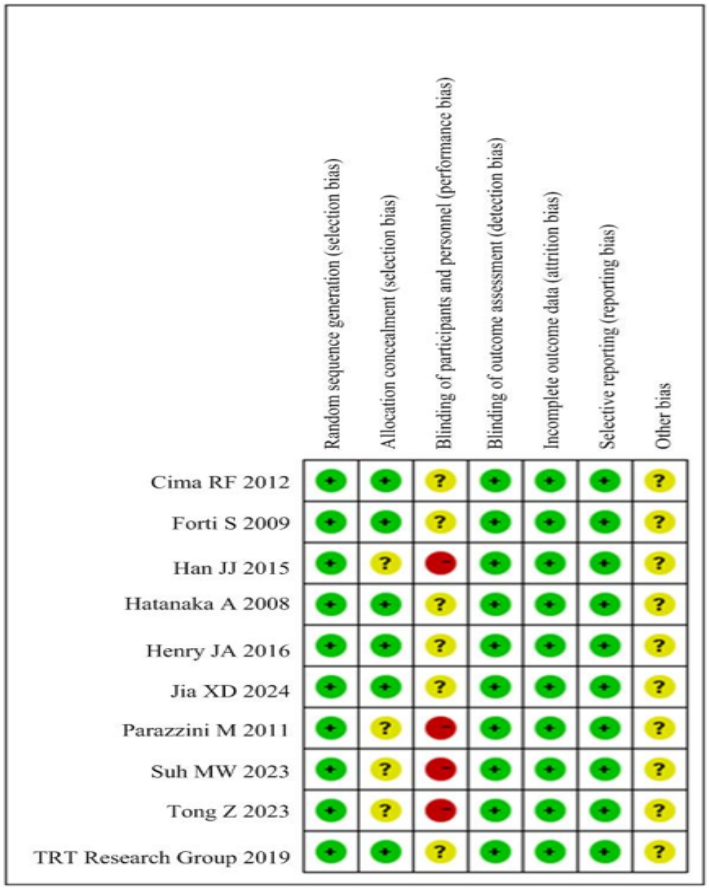

Fig. 3: Summary chart of RoB assessment of included articles

Sensitivity analysis of THI score

Due to the significant heterogeneity observed in the meta-analysis of the THI scores, a sensitivity analysis was conducted by sequentially excluding individual studies to investigate the sources of heterogeneity and verify the robustness of the results. After excluding different studies, although the heterogeneity indicators fluctuated, they remained at a relatively high level. The estimates of treatment effects showed minimal variation, and the CIs remained largely consistent (Table 2).

Table 2: Sensitivity analysis of THI scores

Articles removal	MD	95%CI	I^2
No removal	-8.72	-16.65 - -0.79	90%
Only Cima RF 2012 was removed	-8.82	-20.37 - 2.73	92%
Only Forti S 2009 was removed	-5.33	-12.53 - 1.87	87%
Only Han JJ 2015 was removed	-10.46	-18.71 - -2.20	91%
Only Hatanaka A 2008 was removed	-6.26	-14.41 - 1.89	89%
Only Henry JA 2016 was removed	-8.72	-16.65 - -0.79	90%
Only Jia XD 2024 was removed	-9.10	-20.67 - 2.47	92%
Only Parazzini M 2011 was removed	-8.72	-16.65 - -0.79	90%
Only Suh MW 2023 is removed	-8.72	-16.65 - -0.79	90%
Only Tong Z 2023 is removed	-12.07	-19.97 - -4.17	88%
Only TRT Research Group 2019 was removed	-8.72	-16.65 - -0.79	90%

Long-term effects of TRT in patients with chronic tinnitus

Ten studies evaluated the therapeutic effects of TRT intervention compared to a CG in patients with chronic tinnitus, including 1368 participants, with 675 in the IG and 693 in the CG. Given the variations between studies, a random-effects model was applied in this meta-analysis. The combined results indicated that, compared to the CG, TRT intervention significantly improved the therapeutic outcomes in patients with chronic tinnitus (Fig. 4).

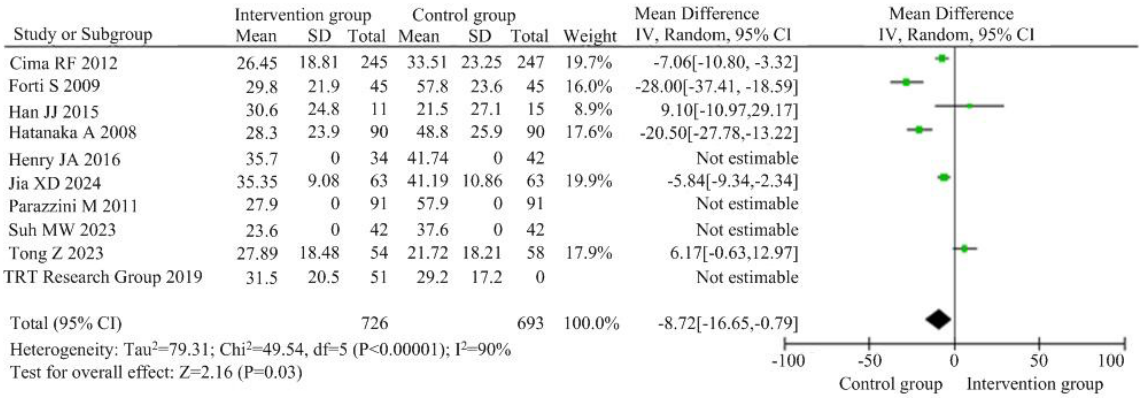

Fig. 4: Forest plot (FOP) of THI scores for subjects

The research points were primarily concentrated on both sides of the funnel, with a distribution that exhibited a certain degree of symmetry. Although there were a few research points that were more deviated from the center, overall, the graph suggested a relatively balanced distribution trend (Fig. 5).

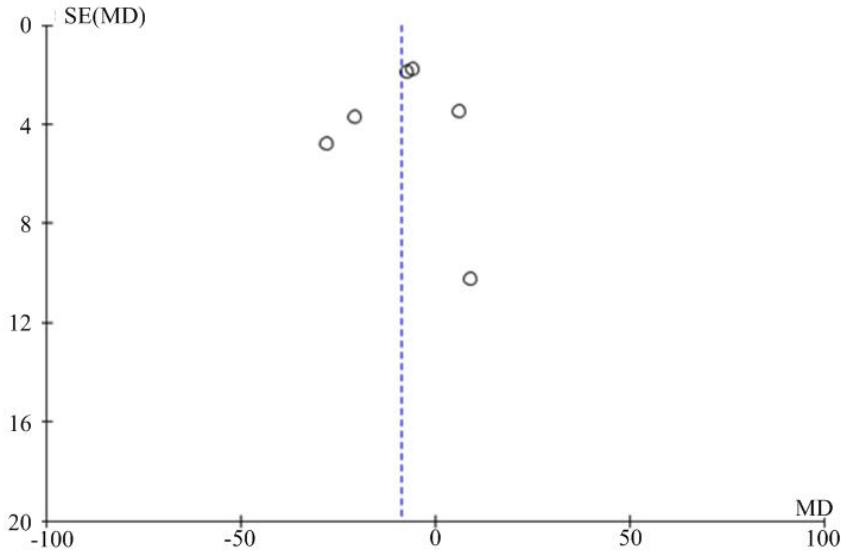

Fig. 5: FUP of subjects' THI scores

Sensitivity analysis of VAS scores

Table 3 lists the impact of excluding individual studies on the effect size and CIs for the VAS scores. Although the effect sizes and inter-study differences fluctuated after the removal of certain studies, the overall heterogeneity remained high. Compared to the CG, TRT intervention still demonstrates a significant therapeutic effect in improving the VAS scores in patients with chronic tinnitus.

Table 3: Sensitivity analysis of VAS scores

Articles removal	MD	95%CI	I^2
No removal	-2.78	-5.57 - 0.02	96%
Only Forti S 2009 was removed	-2.39	-5.40 - 0.61	94%
Only Han JJ 2015 was removed	-3.72	-6.99 - -0.45	97%
Only Hatanaka A 2008 was removed	-0.56	-2.77 - 1.64	94%
Only Suh MW 2023 was removed	-2.78	-5.57 - 0.02	96%
Only Tong Z 2023 was removed	-4.29	-8.15 - -0.43	95%
Only TRT Research Group 2019 was removed	-4.13	-8.11 - -0.16	97%

Effect of TRT on VAS score in patients with chronic tinnitus

Six studies were included, comprising 592 patients, with 293 in the IG and 299 in the CG. Due to the differences between studies, a random-effects model was applied in this meta-analysis. TRT intervention can improve the VAS scores in patients with chronic tinnitus (Fig. 6).

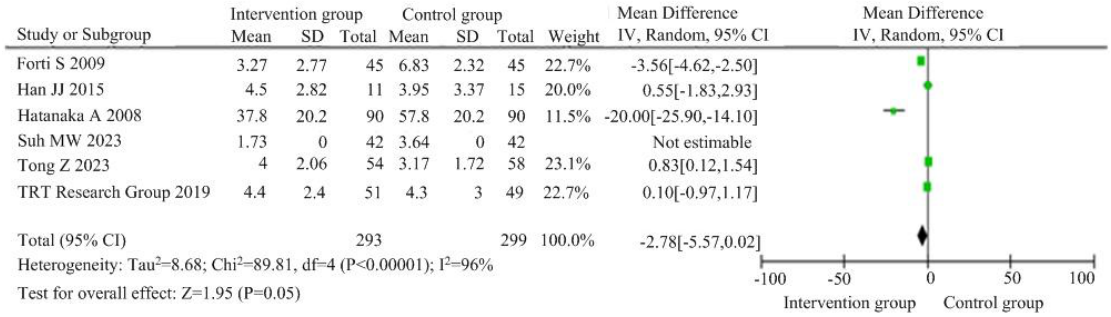

Fig. 6: FOP of subjects' VAS scores

Fig. 7 displays that although some study points deviated relatively from the centerline, the overall distribution trend was balanced. Despite a certain degree of Heterogeneity, no visible PB was indicated.

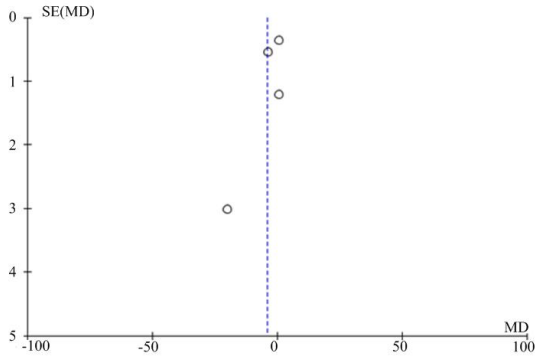

Fig. 7: FUP of VAS scores of subjects

Discussion

This article assessed the long-term efficacy of TRT in patients with chronic tinnitus through a Meta-analysis. 10 clinical trials were involved, including 1368 patients, and the distinctions between the IG and the CG were analyzed across various assessment dimensions. The analysis suggested that TRT intervention had visible clinical effects in treating chronic tinnitus, but there was also considerable heterogeneity among studies that warrants further exploration.

Firstly, regarding the THI scores, the IG showed a visible improvement in patients' tinnitus symptoms compared to the CG. The THI score is an important indicator for measuring the severity of tinnitus and its impact on patients' lives, with higher scores indicating a greater impact. Sensitivity analysis revealed that although individual studies had a certain impact on the results, such as a decrease in I^2 after excluding Forti S, the overall Heterogeneity remained high. This suggests visible distinctions in intervention effects, related to study design, patient baseline characteristics, or details of remedy implementation. Among these studies, the design of TRT intervention varied, with some combining other therapies like TDCS and TCI, and different intervention periods ranging from 3 months to 36 months, contributing to the Heterogeneity in remedy effects. However, despite these distinctions, most studies still demonstrated that TRT markedly improved tinnitus symptoms (28-30), indicating that the intervention effect of TRT was stable and visible overall.

Regarding the VAS scores, the TRT intervention also suggested positive improvement effects. The VAS score was adopted to assess the discomfort

and QoL of patients with chronic tinnitus, reflecting the subjective feeling of patients about the annoyance caused by tinnitus, usually assessed by the patient's perception of tinnitus intensity and its impact on their QoL (31,32). Despite the Meta-analysis of VAS scores showing high Heterogeneity, indicating visible distinctions in effect sizes across studies, the MD values for VAS scores remained relatively stable after excluding certain data, also indicating that TRT had certain effects in improving the QoL of patients with chronic tinnitus and reducing the discomfort caused by tinnitus. Especially in some high-quality studies, TRT intervention could bring visible improvements in VAS scores, although some studies had larger sample sizes or intervention intensity distinctions. Although the *P*-value was 0.05, right on the edge of statistical significance, the absolute value of the MD still suggested a certain clinical significance of TRT intervention, particularly in improving the discomfort caused by tinnitus. During Sensitivity analysis, by excluding data one by one, the I^2 value fluctuated, indicating that individual studies had a visible impact on the results. After excluding Han JJ (2015) and TRT Research Group (2019), the I^2 value remained high, indicating that although removing certain studies reduced Heterogeneity, high Heterogeneity still existed. This Heterogeneity may be related to factors such as sample size, intervention plans, and follow-up time in different studies. For the Meta-analysis of VAS scores, although excluding certain data led to fluctuations in MD values, these fluctuations were not visible, and in most cases, the MD values remained within the significant range, further validating the effect of TRT intervention in improving the QoL of patients with tinnitus (33,34). The FUP analysis suggested that despite a certain degree of Heterogeneity, there was no visible PB overall, indicating that the results of this Meta-analysis had a certain degree of credibility. The symmetry of the FUP suggested that although there were larger fluctuations in some small-sample studies, there was no systematic bias affecting the estimation of remedy effects.

Overall, TRT intervention had relatively consistent supportive evidence for improving the long-term effects in patients with chronic tinnitus. Whether from the perspective of THI scores or VAS scores, TRT intervention effectively alleviated tinnitus symptoms, reduced the discomfort caused by tinnitus, and thereby improved the QoL of patients (35,36). Especially in treating the anxiety and discomfort caused by tinnitus, TRT showed its long-term efficacy, helping patients rebuild coping mechanisms and adaptation abilities for tinnitus. However, the high Heterogeneity of the results also reminded that the efficacy of TRT may be markedly affected by individual distinctions in patients. Therefore, the formulation of individualized remedy plans should pay more attention to factors such as the characteristics of patients' tinnitus, life background, and intervention methods to achieve the best results in the remedy process.

Conclusion

Through the Meta-analysis of 10 clinical trials on TRT intervention in patients with chronic tinnitus, the impact of TRT on the long-term effects in patients with chronic tinnitus was assessed. TRT intervention had relatively consistent effects in improving chronic tinnitus symptoms, especially in alleviating the emotional distress caused by tinnitus and improving patients' coping abilities. However, there was a high degree of Heterogeneity, related to distinctions in intervention plans, remedy duration, and patient populations. Although Sensitivity analysis to some extent verified the robustness of the results, Heterogeneity still can't be ignored. Secondly, the small sample size in some studies may affect the stability and generalizability of the results. Future studies should focus on addressing the following issues: first, further standardizing the intervention plan of TRT, unifying remedy duration and methods to reduce Heterogeneity; second, increasing sample size, especially in subgroup analyses of specific populations (such as patients of different age groups, duration of tinnitus), to improve the pre-

cision and applicability of the study; third, exploring the effects of TRT in combination with other remedy methods, assessing its therapeutic outcomes in different individuals, and finding the best remedy strategies. In conclusion, despite some shortcomings, this article provided evidence to support the remedy of chronic tinnitus with TRT, and future studies will further optimize remedy plans and verify their effects in different populations.

Journalism Ethics considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

Availability of Data and Materials

The data and materials used in this article are derived from public clinical trial databases and published literature. All literature included in the meta-analysis has been selected and meets the preset inclusion criteria, and the relevant data is publicly available for inquiry. If necessary, the data and materials of this article can be obtained from the authors.

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Conflicts of interest

The authors declare that they have no conflict of interest.

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