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Bimodal Neuromodulation for Tinnitus in a Clinical Practice Setting: Clinically Significant Benefit for Patients With Moderate or Worse Symptoms

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ABSTRACT

Purpose: Controlled clinical trials demonstrate the safety and efficacy of new treatments, but real-world outcomes may vary due to patient diversity and treatment variations. Tinnitus, affecting 10%–15% of the population, is a major health concern. Lenire, a bimodal neuromodulation treatment combining sound and tongue stimulations, has shown safety and effectiveness in clinical trials. This study presents the first real-world evidence (RWE) from a U.S. cohort that investigates tinnitus subgroup severities, providing further assessment of Lenire's use in clinical practice.
Method: A single-site, single-arm chart review of 140 patients treated between May 1, 2023, and January 19, 2024, was conducted. Patients were prescribed Lenire for up to 60 min daily and attended follow-ups at 6 and 12 weeks.
Results: This is the first study in a U.S. cohort to show results consistent with the U.S. Food and Drug Administration (FDA) labeling of Lenire, where positive therapeutic outcomes were achieved in patients with moderate or worse tinnitus severity as measured by the Tinnitus Handicap Inventory (THI). In this bothered tinnitus group, 81.8% (95% CI [70.9%, 89.3%]) achieved a clinically significant response (THI improvement $\geq$ 7 points) to treatment, with a mean reduction of -23.8 ± 2.3 points after only 12 weeks of treatment. In contrast, when providing Lenire treatment to tinnitus patients with less bothersome tinnitus (i.e., slight and mild categories), nearly zero change in score, on average, was observed after treatment. Additionally, responder rates based on an alternative threshold of at least an 11-point reduction in THI score show a high response to treatment even with this stricter minimal clinically important difference criterion, with 71.2% (95% CI [59.4%, 80.7%]) of the participants meeting or exceeding the threshold. Similar results were observed when using an alternative threshold based on an intrasubject percent improvement, defined as a reduction of at least 15% from each participant's THI score at the initial assessment.
Conclusions: Real-world data support Lenire's clinical benefits for patients with moderate or more severe tinnitus and demonstrate consistency with clinical trial results that led to FDA approval. These findings further confirm its successful integration into standard audiology care. Ongoing RWE collection will help identify the most responsive patients and guide tailored treatments.
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A nonsurgical bimodal neuromodulation approach, combining sound therapy and mild electrical tongue stimulation using the Lenire device (Neuromod Devices Ltd.; Boedts et al., 2024), has recently gained traction among clinicians and researchers for the treatment of tinnitus in the United States. This intervention represents an emerging

strategy for the management of tinnitus, a condition defined as a perception of sound in the absence of an external acoustic source. Tinnitus affects approximately 10% of adults in the United States (Baguley et al., 2013; Biswas et al., 2022; McCormack et al., 2016), with 6%–11% experiencing symptoms sufficiently bothersome to seek clinical intervention (Biswas et al., 2022).

The development of Lenire is supported by evidence from animal studies demonstrating that bimodal neuromodulation via electrical stimulation of the body, such as the tongue, combined with broadband sound suppresses neural activity in both the inferior colliculus and the auditory cortex more effectively than sound stimulation alone (Markovitz et al., 2015). In humans, clinical trials evaluating Lenire have demonstrated promising outcomes. The Treatment Evaluation of Neuromodulation for Tinnitus–Stage 1 (TENT-A1; NCT02669069; Conlon et al., 2020) and Treatment Evaluation of Neuromodulation for Tinnitus–Stage 2 (TENT-A2; NCT03530306; Conlon et al., 2022) studies, which enrolled a total of 517 participants, reported statistically and clinically significant improvements in tinnitus severity as measured by the Tinnitus Handicap Inventory (THI; Newman et al., 1996; Zeman et al., 2011).

In March 2023, the Lenire device received De Novo marketing authorization from the U.S. Food and Drug Administration (FDA; DEN210033) for the treatment of tinnitus. This authorization was supported by results from the third large-scale pivotal clinical trial, Treatment Evaluation of Neuromodulation for Tinnitus–Stage 3 (TENT-A3; ClinicalTrials.gov identifier: NCT05227365; Boedts et al., 2024), which enrolled 112 participants with tinnitus and was designed in consultation with the FDA. The TENT-A3 (Boedts et al., 2024) findings reinforced conclusions from the earlier TENT-A2 study (Conlon et al., 2022). TENT-A3 demonstrated that, for the majority of participants with moderate or worse tinnitus (THI score $\geq$ 38 at baseline), Lenire is clinically superior to sound-only stimulation. In TENT-A3, treatment response during the corresponding stimulation stage was defined as an improvement of at least 7 points on the THI, consistent with the validated minimal clinically important difference (MCID; Zeman et al., 2011).

Tinnitus is a known heterogeneous condition, with varying clinical profiles, comorbidities, and responses to specific treatments (Schlee et al., 2024). Thus, real-world evidence (RWE) for a tinnitus treatment is essential to assess how results from well-designed clinical trials translate into clinical practice, where there is greater heterogeneity of patient characteristics and variations in how a treatment is implemented by clinicians. A recent retrospective study at the Alaska Hearing & Tinnitus Center (AHTC; McMahan & Lim, 2025) provides a valuable point of comparison to prior clinical trials of bimodal neuromodulation with Lenire (Boedts et al., 2024; Conlon et al., 2020, 2022). While study designs differ and direct comparisons should be made with caution, the real-world results from the AHTC align well with outcomes from previous clinical trials. The TENT-A2 study (Conlon et al., 2022) provides the most relevant point of comparison, as it employed the same inclusion criteria based on THI severity, specifically including only participants with moderate or greater tinnitus severity. TENT-A2 also used the same parameter setting (PS1) during the initial 6 weeks of treatment. While TENT-A2 did not report a responder rate, participants in Arm 1 of the study achieved nearly double the MCID in THI scores at the 6-week follow-up and nearly triple the MCID, with an average improvement of 19.5 points, by the 12-week follow-up. Meanwhile, TENT-A3 (Boedts et al., 2024) was designed to compare the first 6 weeks of sound stimulation to the second 6 weeks of bimodal stimulation (PS6 parameter setting). McMahan and Lim (2025) remained within the TENT-A3 indications for use but employed the PS1 parameter setting for bimodal stimulation over approximately 12 weeks. Their findings revealed a 91.5% responder rate, strongly supporting the effectiveness of Lenire in everyday clinical settings. Together, these data suggest that Lenire delivers robust and consistent clinical outcomes in both controlled trials and real-world practice.

Adding to this growing body of RWE, the current retrospective chart review study presents RWE from 140 Lenire patients at New York Hearing Doctors (NYHD), a private hearing health care clinic that specializes in diagnosing and treating hearing loss, tinnitus, and other related auditory conditions. This study is particularly important as the NYHD protocol allowed audiologists to evaluate Lenire's performance not only in patients with moderate or worse tinnitus as per FDA indication but also in those with milder symptoms, over a full 12-week period using the same PS1 bimodal stimulation setting. By including a broader range of tinnitus severity, the NYHD study provides valuable insights into the device's effectiveness in real-world clinical practice across a wider patient population. The aim of this study was to evaluate differences in outcomes using the Lenire device for patients with mild tinnitus severity compared to those with moderate or worse tinnitus severity in a clinical population.

Method

Study Design

The study was a single-site, single-arm chart review for patients who underwent treatment with the Lenire device (see Figure 1a) at NYHD. Between May 1, 2023,

Figure 1. (a) Lenire bimodal neuromodulation device by Neuromod Devices Ltd. intended to reduce the symptoms of tinnitus in patients with moderate or worse tinnitus (Tinnitus Handicap Inventory score ≥ 38). The device consists of a Tonguetip, an intraoral device designed to sit comfortably in the mouth and deliver gentle electrical stimulation on the tongue's surface; Bluetooth headphones to play personalized sounds to the ear; and a handheld controller that enables patients to adjust the duration and intensity of the treatment. (b) Lenire standard-of-care procedure at New York Hearing Doctors. *When prescribed, Lenire is typically fitted within 2 weeks of consultation or on the same day, if possible. **Telehealth appointments are available upon request.

and January 19, 2024, 140 patients were seen at NYHD for tinnitus symptoms and were prescribed the Lenire device for up to 60 min per day.

Patients first attended an initial assessment conducted by an audiologist at NYHD, which included evaluations to identify hearing loss, obtain medical history, and assess overall auditory health (see Supplemental Material S1). Structured tinnitus education and counseling were also delivered during this visit (see Supplemental Material S1). Patients received personalized information about the nature and causes of tinnitus, as well as strategies for management and coping, tailored to their specific needs to help build self-awareness and promote a more positive outlook of their condition (see Supplemental Material S1).

If the patient was prescribed Lenire, a device-fitting visit was scheduled within 2 weeks of the initial assessment. In rare cases such as when patients had traveled from a distance, the fitting took place on the same day as the initial assessment. At the fitting visit, patients were provided with the Lenire device, trained in its use, and given the Lenire user manual (see Supplemental Material S1).

As part of the treatment plan, patients were recommended to return approximately 6 weeks after device fitting (FU1) to assess progress and report any issues (see Supplemental Material S1). A second follow-up was also recommended approximately 12 weeks after the initial fitting (FU2; see Figure 1b).

Patients could contact the audiologist at any time between appointments if they encountered any issues or concerns. All patients consented to the Lenire standard-of-care procedure, including the assessment of their THI score during clinic visits.

The Lenire neuromodulation system is a take-home device, and treatment sessions are self-administered by the patients. The description of the device in the following sections is similar to the published TENT trials (Boedts et al., 2024; Conlon et al., 2020, 2022), with specific details on certain procedures applied in this retrospective chart review. The Lenire device delivered sound through wireless Bluetooth headphones, whereas electrical stimulation was delivered via a wired 32-site electrode array to the surface of the tongue. Pure-tone audiometry (PTA)

thresholds ranging from 250 Hz to 8 kHz were recorded during the patients' initial assessments. These thresholds were used to customize the sound stimulus intensity so that it was comfortably audible above each patient's hearing threshold at each frequency. These PTA results spanning 250 Hz–8 kHz were included in this study. During treatment, patients had the option to adjust the default audio stimulus volume within a range of −12 to +12 dB using the controller's volume buttons. To ensure safety, the maximum sound level was restricted based on each patient's level of hearing loss. The intensity of electrical tongue stimulation was individually set by increasing the stimulus from a level just below the perception threshold to a clearly perceptible yet comfortable level across different electrodes. This calibrated setting served as the default, and patients were permitted to adjust the intensity up or down by up to six steps, with each step corresponding to an 8% change in pulse width. The calibration process is designed to deliver the lowest amount of electrical stimulation needed to achieve a perceptible stimulus for each individual participant. The treatment device reverts to the default intensities at the start of each new session, and all changes to stimulation settings are recorded on the device log. All patients used the PS1 stimulus setting throughout the treatment period. PS1 consists of tongue stimulation that is temporally and spatially synchronized with different pure tones (500–8000 Hz) with background noise.

Patients

All patients in this study paid for the device and services as per the NYHD price plan. Patients fitted with Lenire are at least 18 years of age and have subjective tinnitus. The device is contraindicated for those who are under the age of 18 years; have objective tinnitus; have oral piercings that cannot be removed (the device must not be used in the presence of oral piercing); have a pacemaker, a defibrillator, or any other active implantable device (unless directed by a physician); are pregnant; have epilepsy or other conditions that may cause loss of consciousness; have conditions that cause impaired sensitivity in the tongue; have lesions, sores, or inflammation of the oral cavity; have any intermittent or chronic neuralgia in the head and neck area; and/or have Ménière's disease.

The Lenire treatment is indicated for tinnitus patients with moderate or greater tinnitus severity (THI ≥ 38). However, based on the comprehensive tinnitus evaluation conducted during initial assessments, audiologists at NYHD who are experienced in tinnitus assessment and management determined that some patients with lower THI scores still reported to be significantly bothered by their tinnitus and may benefit from Lenire. In line with the accepted medical practice, off-label use of FDA-approved devices is permitted when deemed clinically appropriate. These patients were informed that their THI scores did not meet the approved indication and were made aware that their likelihood of responding to treatment might be lower. The patient's decision to proceed with treatment was based on a clear understanding of the potential benefits and limitations in consultation with an experienced audiologist. There were no additional clinical criteria used to determine whether patients in the slight or mild category would be eligible for Lenire.

All patients included in this retrospective chart review signed a Health Insurance Portability and Accountability Act Privacy Policy agreement prior to initiating treatment at NYHD, which allowed for data to be used for research purposes once reviewed by an ethics committee. This study protocol was reviewed by an independent registered institutional review board (IRB), Advarra (Columbia, MD; IRB No. 00000971; Study Protocol No. Pro00075168). The study received a waiver for IRB approval and was determined to be exempt from IRB oversight based on the Department of Health and Human Services *Code of Federal Regulations* (C.F.R.) found at 45 C.F.R. 46.104(d)(4), which includes a waiver for the need to obtain informed consent. The study procedures, including the analysis of patient subgroups by THI severity, were included in the protocol reviewed by the IRB. All methods were carried out in accordance with relevant guidelines and regulations.

Clinical End Points

Consistent with previously published Lenire clinical trial results (Boedts et al., 2024; Conlon et al., 2020, 2022), the THI was used to assess tinnitus symptom severity pre- and posttreatment. The THI is a validated psychometric questionnaire used to determine the severity of tinnitus symptoms and is one of the most widely established instruments for assessing tinnitus symptom severity. The validity and reliability of the THI have previously been demonstrated (Newman et al., 1996).

The THI comprised 25 questions, which can be answered with "no," "yes," or "sometimes," to which a numerical score of 0, 4, or 2 is assigned, respectively. The total THI score is the sum of all item scores and can range from 0 (*no handicap*) to 100 (*catastrophic handicap*). The THI scores can also be categorized into five standard severity levels of tinnitus handicap: none/slight (0–16), mild (18–36), moderate (38–56), severe (58–76), and catastrophic (78–100; Newman et al., 1996). The MCID reported for the THI is 7 points and represents a clinically meaningful change in tinnitus symptoms (Zeman et al., 2011). A more recent study suggests that the MCID may be higher, reporting an 11-point change after 12 weeks of treatment (Engelke et al., 2025). Additionally, there have been recommendations for reporting intrasubject percent

improvements (i.e., 15% reduction from the THI score at the initial assessment) instead of an absolute point change (Langguth & De Ridder, 2023).

As outlined by McCombe et al. (2001), patients in the moderate or worse THI severity categories may have tinnitus that interferes with their ability to carry out normal daily activities and frequently experience sleep disturbances. Tinnitus at this severity level is also commonly associated with emotional distress, mood disorders, somatic pain, stress responsivity, and reduced quality of life. In comparison, patients in the none/slight and mild THI severity groups experience but are often not troubled by their tinnitus. The tinnitus is often easily masked by environmental sounds and easily forgotten with activities. The tinnitus may occasionally interfere with sleep but not daily activities (McCombe et al., 2001). Based on these severity categories, it is anticipated that patients within the moderate or worse group (THI score of 38–100) are more bothered by their tinnitus and would be more likely to seek treatment at clinics. In this study, two broader categories were included: THI score greater than or equal to 38 (at least moderately bothered) and THI score less than 38 (none/slight and mild). This classification reflects the cutoff used in the TENT-A3 study, which compared bimodal stimulation and sound therapy. It also aligns with the screening criteria in TENT-A2, where patients were selected based on tinnitus severity that was sufficiently bothersome to allow for measurable improvement with an intervention.

Field Safety Reporting

Health care professionals prescribing the Lenire device may submit information in relation to medical or technical issues, as well as general feedback, directly to the manufacturer (Neuromod Devices Ltd.). All feedback is assessed to determine whether medical, technical, or other assistance is required. When an issue or feedback is received, the manufacturer first determines whether a Field Product Experience Report (FPER) is necessary. Issues are then assessed for causality and seriousness to determine whether a report to the FDA is required as per 21 C.F.R. Part 803. Under the Medical Device Reporting regulation, it is mandatory for manufacturers, importers, and device user facilities to report certain device-related adverse events and device issues to the FDA. The regulations also stipulate the process and timelines to be adhered to for the reporting of an event to the FDA. Issues could relate to alleged device malfunction, undesired device performance, or treatment side effects (e.g., undesirable medical symptoms). In the event that a problem was reported, certain actions may need to have been taken to prevent further reports from the field such as correction, removal, market withdrawal, or product recall. There were no medical FPERs submitted to the manufacturer from the NYHD clinic, and all technical queries were resolvable with no reporting actions required.

Statistical Analyses

No patients were excluded from the analysis as stipulated in the protocol. Consistent with TENT-A3, responder rates were calculated as the percentage of participants who achieved a reduction of at least 7 points in THI score (corresponding to the established MCID) from the initial assessment to FU1 or from the initial assessment to FU2. Responder rates were reported along with their corresponding 95% confidence intervals (CIs). Additionally, responder rates based on the more recent MCID threshold of an 11-point reduction in THI score were also calculated. Separately, we assessed percent improvement, defined as the proportion of patients achieving a reduction of 15% or more from the THI score relative to their initial score (i.e., [follow-up score − initial score]/initial score × 100). To compare responder rates between the slight or mild (THI $<$ 38) group and the moderate or worse (THI $\geq$ 38) group from the initial assessment to FU1 and from the initial assessment to FU2, two-sided z tests of proportions were performed.

Additionally, mean changes in tinnitus symptoms on the THI scale from the initial assessment to FU1 and from the initial assessment to FU2, along with their corresponding standard errors of the mean, were presented for both the THI $<$ 38 and THI $\geq$ 38 groups. To assess differences in performance between these two THI severity groups from the initial assessment to FU1 and from the initial assessment to FU2, independent t tests were performed on mean changes.

Furthermore, a repeated-measures analysis of variance (ANOVA) was conducted, with time (initial assessment, FU1, and FU2) as the within-subject factor and group (THI $<$ 38 vs. THI $\geq$ 38) as the between-subjects factor, to evaluate changes in tinnitus symptoms over time and between severity groups. The main effects of time and group, as well as the interaction between time and group, were examined. Effect sizes were reported using partial eta squared. Post hoc analyses comparing time effects within groups were conducted.

A multiple linear regression was performed to explore the extent to which demographic and tinnitus characteristics at the initial assessment predicted THI scores at FU2. The independent variables included age, tinnitus duration, gender, hearing thresholds, and severity group at the initial assessment. Model significance was assessed using the F test, and the proportion of variance

explained was evaluated by the adjusted R^2. Individual regression coefficients were examined to identify the significant predictors of THI scores at FU2. PTAs were collected only at the initial assessment and calculated separately for the right and left ears by averaging hearing thresholds at 0.25, 0.5, 1, 2, 3, 4, 6, and 8 kHz.

All data analyses were performed using Stata 15.1. p values less than .05 were considered statistically significant.

RWE Quality Assurance

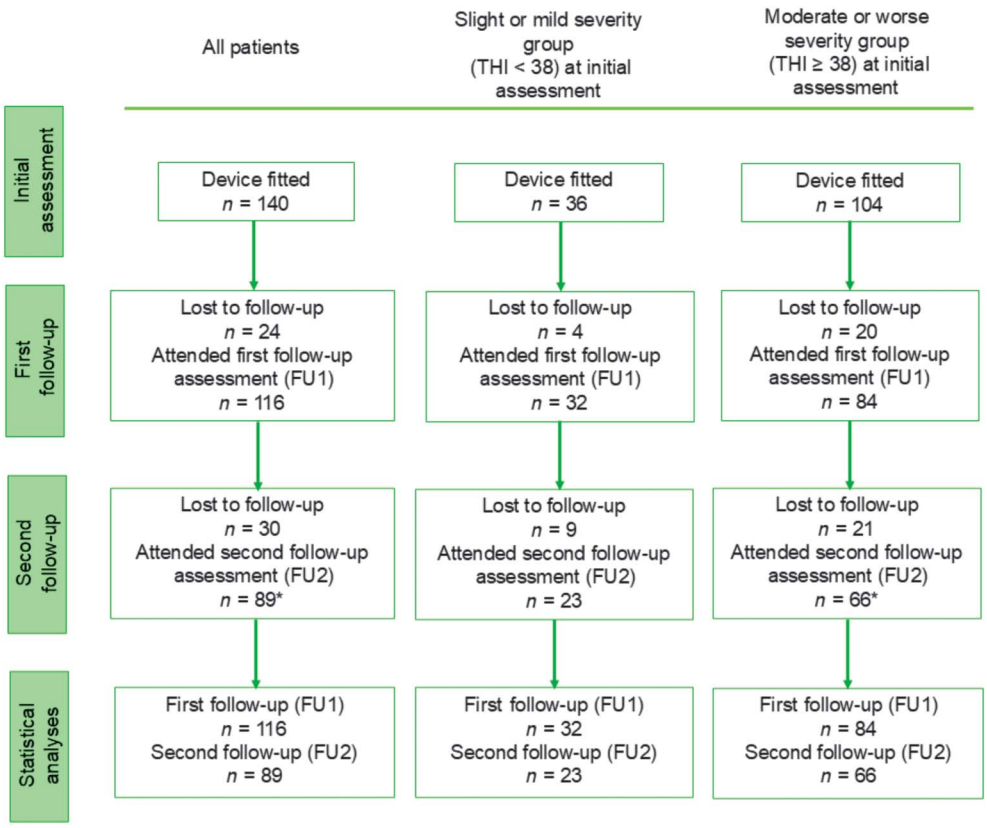
The primary analysis database consisting of THI, age, and PTA was verified against the source data (i.e., Sycle Pro or Lenire fitting software [LFS]) by means of an onsite monitoring visit. Source data verification was performed on these variables for 100% of the data of all patients included in the study database for this retrospective chart review. This approach was deemed appropriate as the data set results from a transcription of the source data, which are manually entered by health care professionals, and hence, discrepancies could occur in single data entries; therefore, a strict approach of completing 100% verification was followed. For any discrepancies found, the study database was updated onsite for the THI questionnaire, and an offline comparison of the data (age and PTA) exported from the LFS to the study database was completed directly after the monitoring visit. The analysis was completed on the final clean and validated data set. Monitoring was performed by appropriately qualified and trained personnel. The study monitor was briefed on the investigation prior to completing any monitoring-related tasks and site visit. The selected monitor was independent from the investigation site. The data were monitored on April 10, 2024.

Results

Patient Disposition and Characteristics of Study Patients

A total of 140 patients were fitted with the Lenire device from May 1, 2023, to January 19, 2024 (see Figure 2). Of the 140 patients, 25.7% (n = 36) had a THI score of less than 38, and 74.3% (n = 104) had a THI score of greater than or equal to 38. In these analyses,

Figure 2. Patient disposition per visit. *Three patients attended FU2 but not FU1. THI = Tinnitus Handicap Inventory.



only patients who completed their initial assessment and at least one follow-up could be included. While it is recommended for patients to be reassessed at the NYHD clinic, it is not mandatory for patients to return for assessment. Additional analyses (see Supplemental Material S2) comparing response rates and mean changes in THI scores at FU1 for patients who did not return at FU2 suggest that some patients with initially moderate or worse symptom severity may not have returned for a second follow-up because their tinnitus symptoms had sufficiently improved and did not feel a need to return to see an audiologist. Patients can schedule additional follow-up appointments if needed. Note that the Lenire treatment proved to be safe and well tolerated with no treatment-related serious adverse events that varied from normal day-to-day issues experienced at the NYHD clinic prior to prescribing Lenire. There were no field safety reports from the NYHD clinic that required reporting to the FDA, as well as no correction, removal, market withdrawal, or product recall.

Results presented in Figure 3 show that the distribution of patients based on tinnitus severity groupings (i.e., below vs. above the THI score of 38) is relatively similar for the patients included in the THI analyses at each follow-up visit and those whose data were not available for analyses. Among the 116 patients with initial-assessment and FU1 THI scores, 72.4% had a THI score of at least 38 points, whereas 27.6% had a THI score of less than 38 points at the initial assessment prior to starting bimodal treatment (see Figure 3a). For the 24 patients who did not have THI scores at FU1, 83.3% had a THI score of at least 38 points, and 16.7% had a THI score of less than 38 points at the initial assessment (see Figure 3b). Also, of the 89 patients with initial-assessment and FU2 scores, 74.2% had a THI score of at least 38 points, whereas 25.8% had a THI score of less than 38 points at the initial assessment (see Figure 3c). Among the 51 patients who did not have a THI assessment at FU2, 74.5% had a THI score of at least 38 points, and 25.5% had a THI score of less than 38 points at the initial assessment (see Figure 3d).

Of the 140 patients who completed an initial assessment with THI scores, the mean age was 57.0 ± 12.0 years (see Table 1). Of the 140 available responses, 73.6% were male and 26.4% were female. There were 131 patients who provided information regarding tinnitus duration,

Figure 3. Percentage of patients with Tinnitus Handicap Inventory (THI) scores above or below the cutoff of 38 at the initial assessment. (a) Patients who had THI scores available for both the initial assessment and the first follow-up (FU1). (b) Patients who did not have THI scores available for FU1. (c) Patients who had THI scores available for both the initial assessment and the second follow-up (FU2). (d) Patients who did not have THI scores available for FU2.

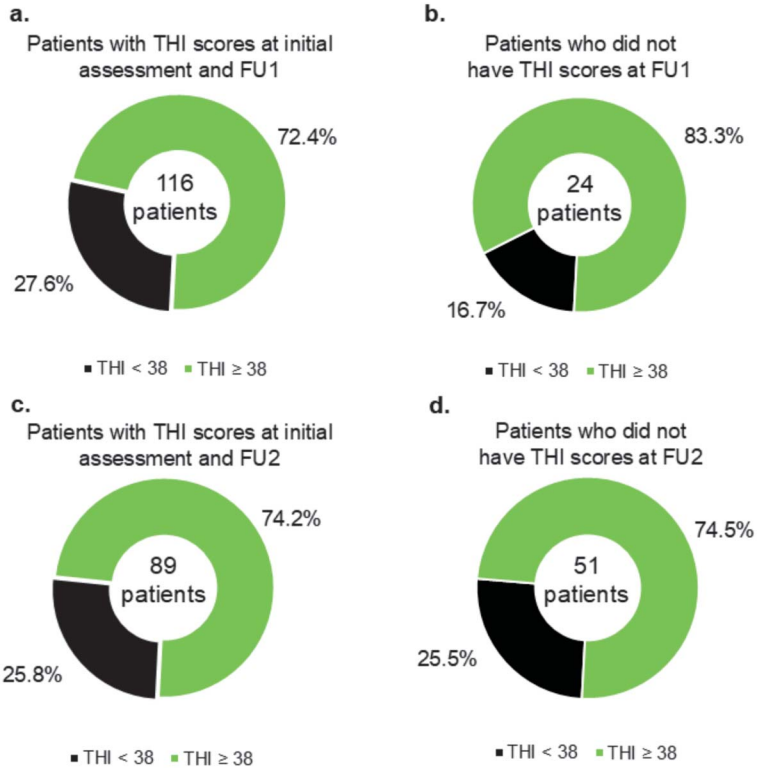


Table 1. Demographic characteristics of patients who completed the initial assessment with Tinnitus Handicap Inventory (THI) scores.

Demographic characteristics	
Age (years)	
M ± *SD* (*n*)	57.0 ± 12.0 (140)
Gender, % (*n*/*N*)	
Male	73.6 (103/140)
Female	26.4 (37/140)
Tinnitus duration (years), % (*n*/*N*)	
< 1 year	10.7 (14/131)
1 to < 5 years	55.0 (72/131)
5 to < 10 years	7.6 (10/131)
10 to < 20 years	14.5 (19/131)
20 years and more	12.2 (16/131)
PTA[a] (250 Hz–8 kHz; dB HL), *M* ± *SD* (*n*)	
Right ear	28.8 ± 15.4 (128)
Left ear	22.6 ± 13.8 (140)
THI at the initial assessment	
M ± *SD* (*n*)	55.8 ± 23.1 (140)

[a]Pure-tone audiometry (PTA) averages were calculated separately for the right and left ears by averaging hearing thresholds at 0.25, 0.5, 1, 2, 3, 4, 6, and 8 kHz. For the right ear, there were missing data at specific frequencies for eight patients at 0.25, 0.5, 3, and 4 kHz: One patient was missing data at 0.25 and 4 kHz; one patient, at 3 and 4 kHz; one patient, at 4 kHz only; and one patient, at 0.25, 0.5, and 4 kHz.

with 34.3% reporting a tinnitus duration of 5 years or more. There were 128 patients with PTA assessment available for the right ear, with a mean hearing loss of 28.8 ± 15.4 dB HL (average of 250 Hz–8 kHz), and 140 patients for the left ear, with a mean hearing loss of 22.6 ± 13.8 dB HL (average of 250 Hz–8 kHz). The mean THI score at the initial assessment was 55.8 ± 23.1 points. Supplemental Material S3 provides the same demographic characteristics as those in Table 1 in this article, but for the 116 patients who returned for FU1 and the 89 patients who returned for FU2; consistent patient characteristics are observed for both scenarios.

High Responder Rate in the Moderate or Worse Tinnitus Severity Group With Further Improvements Over Time

At the first follow-up (FU1; approximately 6 weeks posttreatment), a high responder rate to Lenire treatment was observed among participants with moderate-to-severe tinnitus (THI ≥ 38). Using the 7-point MCID threshold, 72.6% (95% CI [62.2%, 81.0%]) of this group demonstrated clinically meaningful improvement, compared to 21.9% (95% CI [11.0%, 38.8%]) of participants with THI scores less than 38 (see Figure 4a; two-sided z test for proportions, $p < .001$). When applying an alternative 11-point MCID threshold, 59.5% (95% CI [46.6%, 71.4%]) in the THI ≥ 38 group were classified as responders, compared to 15.6% (95% CI [6.9%, 31.7%]) in the THI < 38 group (see Figure 4b; $p < .001$). Similarly, using an intrasubject percent improvement criterion, defined as a reduction of at least 15% from each participant's initial-assessment THI score, 63.1% (95% CI [52.4%, 72.6%]) of participants with THI scores of at least 38 showed improvement, compared to 28.1% in the THI < 38 group (see Figure 4c; $p < .001$).

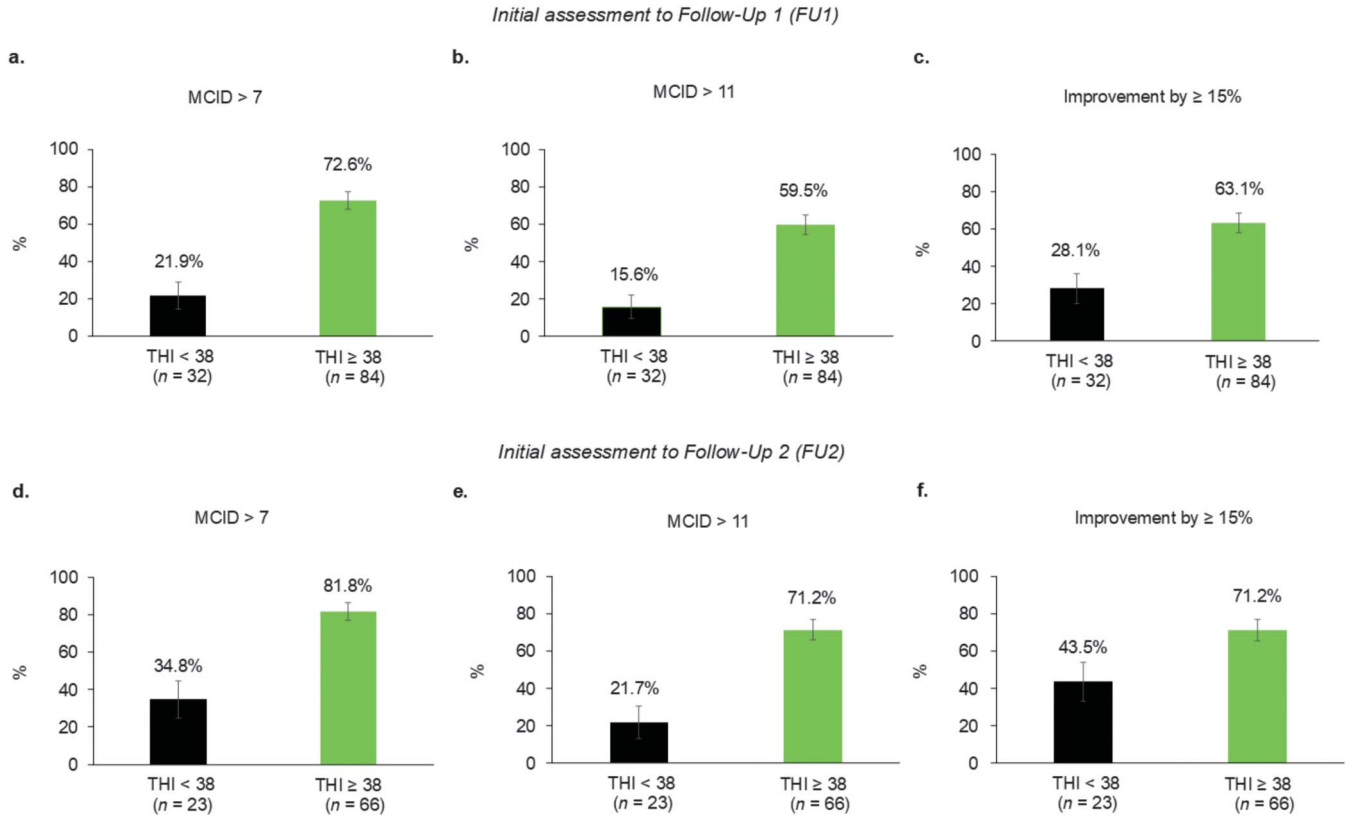
By the second follow-up (FU2; approximately 12 weeks posttreatment), further improvements were observed in the THI ≥ 38 group. At this point, 81.8% (95% CI [70.9%, 89.3%]) of participants in the THI ≥ 38 group exceeded the 7-point MCID threshold (see Figure 4-d; $p < .001$), whereas 71.2% (95% CI [59.4%, 80.7%]) met or exceeded the 11-point threshold (see Figure 4e; $p < .001$). In addition, 71.2% (95% CI [59.4%, 80.7%]) of participants in the THI ≥ 38 group achieved an intrasubject percent improvement of at least 15% in their THI scores by FU2 (see Figure 4f; $p = .020$).

Corresponding mean reductions in THI scores are presented in Figure 5. At FU1, participants with THI scores of at least 38 showed a mean reduction of 16.6 ± 1.8 points, whereas those with THI scores less than 38 experienced a worsening of 3.3 ± 3.0 points (see Figure 5a; $p < .001$). At FU2, participants with THI scores of at least 38 demonstrated a mean reduction of 23.8 ± 1.8 points, whereas the THI < 38 group showed a mean worsening of 0.5 ± 3.5 points (see Figure 5b; $p < .001$).

The individual THI scores for each patient in the moderate or worse tinnitus severity group at different time points are shown in Figures 5c and 5d for FU1 and FU2, respectively (the individual THI scores for the THI < 38 group are shown later in Figure 6). At FU1, 90.5% of patients in the moderate or worse severity group had improvements in THI scores. A high percentage was sustained in this cohort at FU2, with 90.9% of the patients reporting improvements.

Because THI scores correspond to defined severity categories, it is also informative to examine how these categories shift following treatment. Notably, the proportion of patients in the "catastrophic" category decreased from 21.2% at the initial assessment to 4.6% at FU2 (see Figure 5f). Similarly, the proportion in the "severe" category decreased from 34.8% to 19.7% at FU2 (see Figure 5-f). The "moderate" category also showed a reduction, with proportions dropping from 43.9% to 22.7% at FU2 (see Figure 5f). These shifts indicate a general trend toward lower tinnitus severity following treatment. Results are

Figure 4. Responder rates were evaluated using three clinical improvement criteria. (a) A minimal clinically important difference (MCID) of greater than 7 points in the Tinnitus Handicap Inventory (THI) score from the initial assessment to the first follow-up (FU1; two-sided *z* test for proportions for comparison between groups; $p < .001$). (b) An MCID of greater than 11 points in the THI score from the initial assessment to FU1 (two-sided *z* test for proportions for comparison between groups; $p < .001$). (c) An intrasubject percent improvement of at least 15% in the THI score from the initial assessment to FU1 (two-sided *z* test for proportions for comparison between groups; $p < .001$). (d) An MCID of greater than 7 points in the THI score from the initial assessment to the second follow-up (FU2; two-sided *z* test for proportions for comparison between groups; $p < .001$). (e) An MCID of greater than 11 points in the THI score from the initial assessment to FU2 (two-sided *z* test for proportions for comparison between groups; $p < .001$). (f) An intrasubject percent improvement of at least 15% in the THI score from the initial assessment to FU2 (two-sided *z* test for proportions for comparison between groups; $p = .020$).



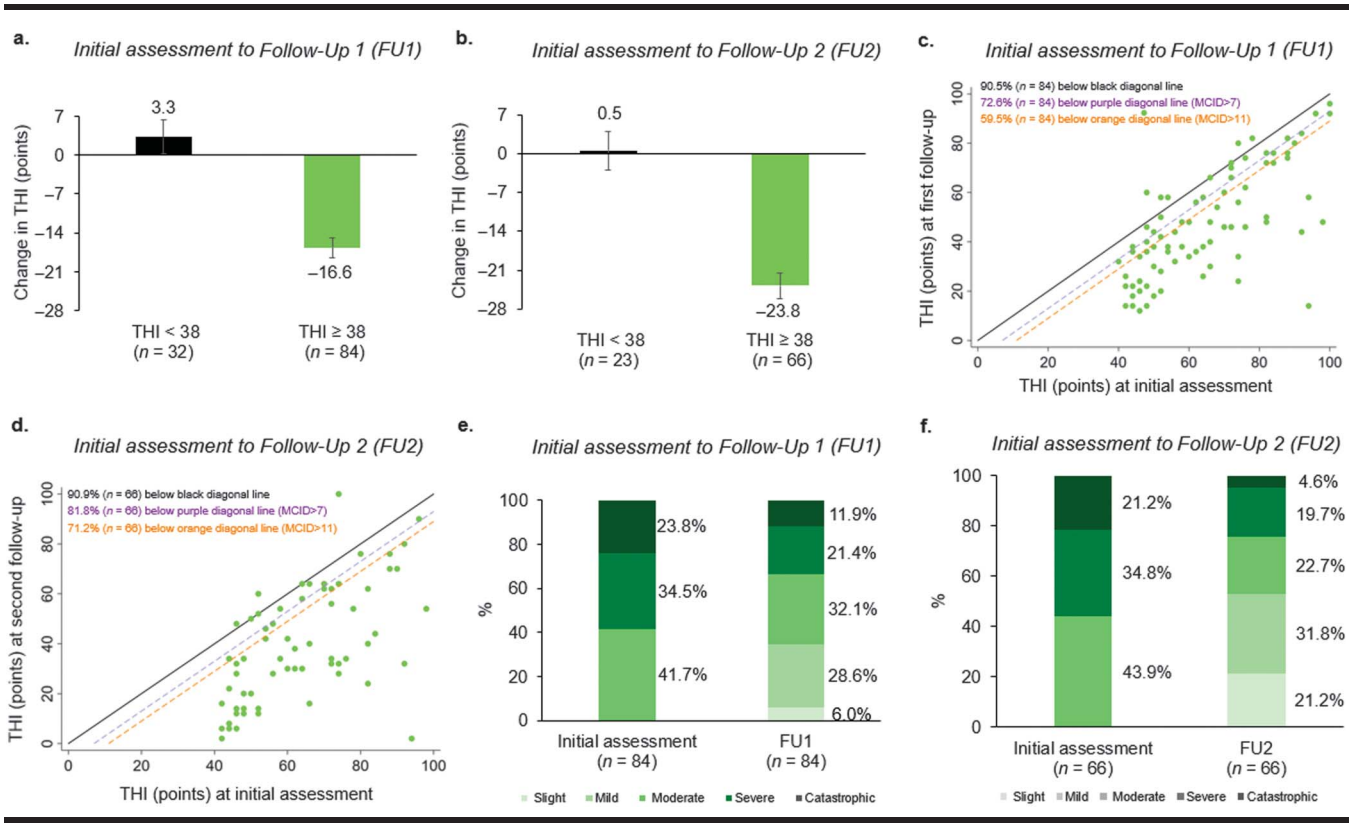
also presented for the shift in THI categories for FU1 in Figure 5e.

Better Outcomes With Lenire Treatment for More Severe Tinnitus Patients

Results of a pairwise correlation analysis revealed that patients with more severe tinnitus symptoms achieved larger improvements in THI score after bimodal neuromodulation at FU1 (see Figure 6a; $r = -.4$, $p < .001$) and FU2 (see Figure 6b; $r = -.5$, $p < .001$). These scatter plots generally show that patients with a THI score of less than 38 do not demonstrate improvement in tinnitus symptoms. Furthermore, these results support the importance of performing stratified analysis of the data based on two broader THI severity categories: slight or mild group (THI < 38) and moderate or worse group (THI ≥ 38). Interestingly, there are a few tinnitus patients with initial-assessment THI scores of less than 38 (i.e., THI ≥ 24; gray points exceeding the MCID dashed line) who have shown clinical benefit from Lenire treatment.

These results were supported by a repeated-measures ANOVA that showed a significant main effect of time, $F(2, 201) = 19.4$, $p < .001$, $\eta_p^2 = .2$, indicating that THI scores changed across follow-up periods (see Supplemental Material S4). There was also a significant main effect of group, $F(1, 138) = 52.1$, $p < .001$, $\eta_p^2 = .3$, with higher overall scores at the initial assessment in the THI ≥ 38 group (see Supplemental Material S4). Importantly, a significant interaction between time and group was observed, $F(2, 201) = 24.4$, $p < .001$, $\eta_p^2 = .2$, suggesting that the pattern of change in THI scores over time differed significantly between the THI < 38 and THI ≥ 38 groups (see Supplemental Material S4). Post hoc contrasts showed that patients in the THI ≥ 38 group had significant reductions in THI scores from the initial assessment to both follow-ups (both $p < .001$; see Supplemental Material S5).

Figure 5. (a) Mean change (*SE*) in Tinnitus Handicap Inventory (THI) scores from the initial assessment to the first follow-up (FU1) for two clinically relevant THI severity groups (independent *t* test for comparison between groups; $p < .001$). (b) Mean change (*SE*) in THI scores from the initial assessment to the second follow-up (FU2) for two clinically relevant THI severity groups (independent *t* test for comparison between groups; $p < .001$). (c) Scatter plot of individual THI scores at FU1 versus the initial assessment for patients with bothersome tinnitus (THI ≥ 38) at the initial assessment: Points below the black diagonal line indicate an improvement (reduction) in tinnitus symptoms, points below the purple diagonal line indicate an improvement of greater than 7 points, and points below the orange diagonal line indicate an improvement of greater than 11 points. (d) Scatter plot of individual THI scores at FU2 versus the **Follow-Up 2** (FU2) for patients with bothersome tinnitus (THI ≥ 38) at the initial assessment: Points below the black diagonal line indicate an improvement (reduction) in tinnitus symptoms, points below the purple diagonal line indicate an improvement of greater than 7 points, and points below the orange diagonal line indicate an improvement of greater than 11 points. (e) Percentage of patients in the various THI severity categories at the initial assessment and FU1 for patients with bothersome tinnitus (THI ≥ 38) at the initial assessment. (f) Percentage of patients in the various THI severity categories at the **Follow-up 2** (FU2) and FU2 for patients with bothersome tinnitus (THI ≥ 38) at the initial assessment. MCID = minimal clinically important difference.



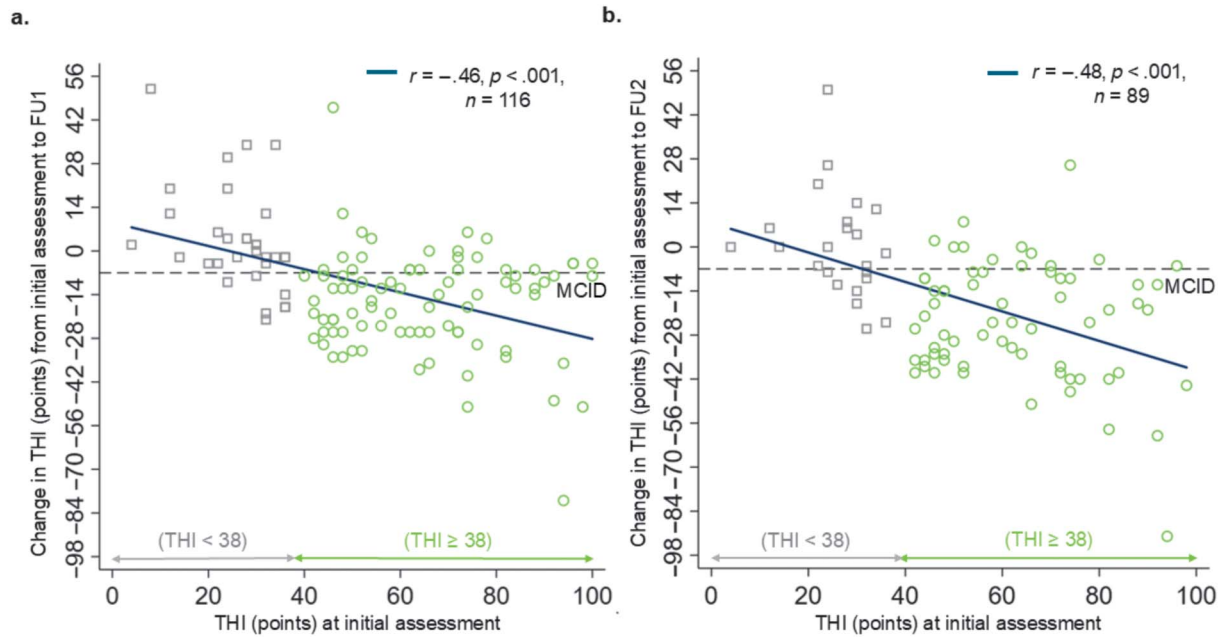
In contrast, patients with THI scores less than 38 showed no significant change over time ($p > .25$; see Supplemental Material S5). These results indicate that improvement occurred mainly in the higher severity group (THI ≥ 38 group).

In addition, an exploratory multiple linear regression was used to predict THI scores at FU2 using age, tinnitus duration, gender, hearing thresholds, and baseline severity group as independent variables. The model was significant, $F(9, 69) = 3.9$, $p = .0004$, explaining 34% of the variance (adjusted $R^2 = .3$). Of the available demographic and tinnitus characteristics, only the severity group at the initial assessment significantly predicted THI at follow-up. Participants with THI scores of at least 38 had significantly lower THI scores at FU2 (*B* [coefficient] = −23.8, $p < .001$), indicating greater improvement than in patients with THI scores of less than 38.

Discussion

The efficacy of bimodal neuromodulation through combined sound therapy and electrical tongue stimulation for the treatment of tinnitus has been demonstrated in several large-scale clinical trials, including a controlled pivotal clinical trial that recently led to the FDA granting De Novo approval for the Lenire device in the United States (Boedts et al., 2024; Conlon et al., 2020, 2022). Previous published RWE in Europe and more recently in the United States (Boedts et al., 2024; Buechner et al., 2022;

Figure 6. (a) Scatter plot showing the change in Tinnitus Handicap Inventory (THI) scores at the first follow-up (FU1) versus the initial assessment separated by two THI severity groups at the initial assessment. Pairwise correlations indicate a significant ($p < .001$) inverse relationship between the change in THI scores from the initial assessment to FU1 and THI scores at the initial assessment. (b) Scatter plot showing the change in THI scores at the second follow-up (FU2) versus the initial assessment separated by two THI severity groups at the initial assessment. Pairwise correlations indicate a significant ($p < .001$) inverse relationship between the change in THI scores from the initial assessment to FU2 and THI scores at the initial assessment. The minimal clinically important difference (MCID) line represents 7 points.



McMahan & Lim, 2025) also support the in-clinic effectiveness of the Lenire treatment in improving tinnitus symptoms. The current RWE from NYHD complements earlier findings showcasing the effectiveness, repeatability, and generalizability of the Lenire bimodal treatment. Collectively, these results strongly indicate that greater clinical benefit is achievable with the Lenire treatment in patients who are sufficiently bothered by their tinnitus (THI ≥ 38), compared to those with less or not bothersome tinnitus. Performing the main analysis on the cohort of patients spanning the moderate, severe, and catastrophic THI groups represents a more informative analysis (McCombe et al., 2001). In this study, patients with bothersome tinnitus had a high response to treatment, with 72.6% of patients achieving an MCID of 7 points after just 6 weeks of treatment, and a higher response to treatment attainable after continued use, with 81.8% responding after at least 12 weeks of treatment. The robustness of the findings was further supported using a recently published responder criterion. When applying a more stringent MCID threshold of 11 points, as recently proposed by Engelke et al. (2025), the responder rate remained high at 71.2% at FU2. Additionally, to account for individual baseline severity and the 3-point resolution of the THI, we also examined intrasubject percent improvement using a threshold of at least 15% reduction from the initial assessment, as suggested by Langguth and De Ridder (2023). This approach also yielded a comparable responder rate of 71.2%, reinforcing the consistency of treatment effects.

The clinical relevance of these findings is strengthened by the observed improvement in tinnitus severity categories. Notably, over 50% of participants who were classified as having moderate or greater tinnitus severity at the initial assessment transitioned to the mild or slight category following approximately 12 weeks of treatment. This categorical improvement is particularly meaningful, as tinnitus in the mild or slight severity range is typically associated with minimal to no interference in daily functioning. In contrast, higher severity levels are frequently linked to substantial impairments in sleep, quality of life, and mental health (McCombe et al., 2001). These results suggest that the observed improvements may translate into meaningful enhancements in patients' overall well-being.

While this study primarily focused on changes in tinnitus symptom severity as measured by the THI, future research could benefit from incorporating additional patient-centered outcomes related to coping and functional impact. Understanding how patients adapt to and manage their tinnitus in daily life may offer deeper

insight into the real-world effectiveness of bimodal neuromodulation. Validated tools such as the Tinnitus Coping Style Questionnaire could provide complementary information beyond symptom severity alone (Budd & Pugh, 1996). Including these measures in future RWE studies would allow for a more comprehensive evaluation of Lenire's clinical utility, particularly in terms of emotional well-being, coping strategies, and quality-of-life improvements. Also, future studies should compare the results of this severity analysis using alternative validated outcome measures, such as the Tinnitus Functional Index, which uses a 10-point Likert scale compared to the THI's 3-point response options ("yes," "no," and "sometimes"). This could help determine whether the THI's lower response resolution contributed to the results observed in the group with milder symptoms.

The positive net impact of bimodal stimulation in this study is reinforced by the safety and acceptability of the treatment. Previous clinical trials have demonstrated that Lenire is inherently safe with zero procedure- or device-related serious adverse events (Boedts et al., 2024; Conlon et al., 2020, 2022). Moreover, the recent FDA clinical trial showed that any nonserious adverse events were generally resolved, further supporting the nonconsequential or reversible nature of these adverse events and the very low risk profile of bimodal stimulation (Boedts et al., 2024; Conlon et al., 2020, 2022). The current RWE study for tinnitus patients treated at NYHD also had no field safety reports that required reporting to the FDA, and neither has any correction, removal, market withdrawal, or product recall been required.

There was a high percentage of patients who readily used the device on a regular basis; however, given the real-world nature of the current study, it was encouraged, but not mandated, that patients return for follow-up assessments. In order to assess any potential for analysis bias related to missing data, the response rate for the 21 patients with bothersome tinnitus who returned for FU1 but not FU2 was assessed. Based on this additional analysis, 57.1% improved by an MCID of 7 points at FU1, highlighting that not attending the FU2 appointment does not necessarily indicate a negative treatment outcome by FU1. Instead, it could be due to early benefit from the treatment and a decreased need for additional clinical support. Considering that continued use of the device may drive further therapeutic benefit as shown in Figure 5, a higher responder rate may have been observed at FU2 if more patients had returned. There was no difference in demographic variables (i.e., age, gender, tinnitus duration, and PTA) and baseline THI scores between patients who completed only the initial assessment, those who returned for only FU1, and those who returned for only FU2, indicating minimal analysis bias from other attributing factors to missing data (see Table 1 in this article and Supplemental Material S3).

RWE studies are critical to understanding how a device performs and is utilized in routine clinical practice setting. However, this type of study also has inherent design limitations. Most notably, when data are collected as part of a chart review, the analysis is restricted to the information already recorded in patient records. This contrasts with structured clinical trials, where data collection is predefined and comprehensive. Depending on the data set, this may limit the patient characteristics available for analysis, including previous treatments patients may have completed prior to attending the NYHD clinic. Additionally, retrospective RWE may preclude the possibility of a control group depending on data availability for alternative treatment options. The aforementioned limitations may retract from the ability to fully assess treatment response in comparison to standard of care to determine the optimal treatment segmentation needed to achieve the best outcomes.

It should be noted that all participants received education and counseling prior to initiating treatment, and any positive effects from this support cannot be fully separated from the effects of bimodal neuromodulation. Previous research, including the Unification of Treatments and Interventions for Tinnitus patients trial (Schoisswohl et al., 2025), has shown that structured counseling can enhance outcomes when combined with other treatments. However, counseling alone appears to have limited clinical impact. For example, Scherer and Formby (2019) reported only a 2.3-point THI improvement after 12 weeks of using a counseling protocol comparable to that provided in this study. Similarly, a meta-analysis by Xiang et al. (2020), which reviewed nine randomized controlled trials on educational counseling alone, found minimal benefit. Among the included studies, Cima et al. (2012) reported a 1.35-point THI improvement at 12 weeks, and Henry et al. (2016) found that only 21.8% of participants achieved a clinically meaningful THI score reduction after 6 months, twice the duration of the current study. These findings suggest that the substantial improvements observed here are largely unrelated to the effects of educational counseling.

Although controlled clinical trials are the gold research standard for assessing the effectiveness of a treatment, they do not always or directly translate to the treatment's effectiveness in a real-world clinical setting. RWE is critical in confirming whether a treatment is relevant to patients and health care professionals at the point of care. The RWE collected as part of this study further demonstrates how a novel treatment can successfully fit into the standard-of-care setting within audiology practices and achieve significant treatment benefits for tinnitus patients, particularly in a specific patient population that has moderate or worse tinnitus symptoms. The collection of additional

RWE will further help identify and predict which tinnitus patients can achieve optimal outcomes with the Lenire device, which could successfully guide clinicians how best to treat each individual patient.

Author Contributions

Craig A. Kasper: Conceptualization, Methodology, Investigation, Data validation, Formal analysis, Writing – original draft, Writing – review & editing. **Juliana M. May:** Conceptualization, Methodology, Investigation, Data validation, Formal analysis, Writing – original draft, Writing – review & editing. **Natalie E. Crossland:** Investigation, Writing – original draft, Writing – review & editing. **Hubert H. Lim:** Conceptualization, Methodology, Data validation, Formal analysis, Writing – original draft.

Data Availability Statement

All relevant data associated with the published study are present in the article or in the supplemental materials. Source data related to the images presented in the article are included with this article. Access to the raw individual-level data may be obtained, contingent upon appropriate ethics approval and data-sharing agreements, by contacting Craig A. Kasper via clinicaldataqueries@neuromoddevices.com for the purpose of confirming the analysis in the article. Responses to valid requests will be reasonably attempted and initiated within 10 working days of receipt beginning 3 months and ending 5 years after the publication of this article.

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