SUMMARY OF CLINICAL EFFICACY DATA
Summary of Clinical Efficacy Data

The initial demonstration of Neuromonics clinical efficacy is documented in four published papers in peer reviewed medical journals demonstrating the results achieved with the Neuromonics treatment.


This paper describes the results of a randomized, controlled study where the Neuromonics treatment was randomized against two control groups. We typically refer to this as the “second clinical trial” because it followed a small feasibility trial that has not been published. After 6 months of treatment, 86% of the Neuromonics patients met the minimum criterion for clinical success, defined as an alleviation of tinnitus disturbance of at least 40% (as determined by the Tinnitus Reaction Questionnaire score). By contrast, only 47 and 23% of the patients in the two control groups reported a successful result according to this criterion. Mean improvements in tinnitus disturbance scores in the Neuromonics treatment group was 66% as compared to 22% and 15% in the control groups. The differences between the Neuromonics group and the control groups were statistically significant and significant differences were observed in other clinical outcomes as well.

We propose that this study is a well-designed and well-conducted investigation showing measurable improvement in the disease condition compared to other available treatments. In addition, not only are the risk for harmful effects extremely low, patient reports of user acceptability were more consistently positive in the Neuromonics group, showing the treatment is not only more efficacious but more tolerable as well.


This paper, referring to the “third clinical trial”, presents the results of a clinical trial comparing an abbreviated version of the Neuromonics treatment protocol to determine if it is superior to the standard protocol that was studied in the second clinical trial above. The trial concluded that the abbreviated treatment protocol was not statistically superior and, in fact, the results suggest it was inferior to the standard protocol. However, there were a number of extremely important outcomes from the study, particularly the consistency of the benefit compared to the previously described trial. At six months, 91% of all patients showed a clinically significant benefit (defined as an alleviation of tinnitus disturbance of at least 40%) which is very consistent with the 86% in the previous trial. In addition, the patients were followed to 12 months and the benefit persisted, with 86% showing a clinically significant benefit at that time point. The mean improvement in TRQ at 6 months was 65% as compared to 66% in the previous trial, showing a remarkably consistent benefit.


The previous two trials documented the clinical efficacy of the treatment under controlled clinical studies for the most suitable patients. This paper documents the results in real-world clinics across a very diverse patient population with a very large patient base (n=470). The most suitable patients, described as Tier 1 patients (n=237), demonstrated a clinical success rate of 92% with a mean improvement of 72%, value which are extremely consistent with prior studies. Even less suitable Tier 2 patients (n=223) demonstrated a clinical success rate of 60% with a mean improvement of 49%.


This paper describes the essential underlying scientific principles behind the Neuromonics Tinnitus Treatment as supported by the medical literature. It also summarizes evidence for clinical efficacy from the previous controlled clinical studies and the private practice clinical setting, where it has been shown to provide consistently positive outcomes, particularly among those patients meeting specific criteria. This supports the rationale for the consistent and significant clinical benefit of the treatment.
In summary, three clinical trials involving 555 patients demonstrated a remarkably consistent clinical benefit that persisted to 12 months in suitable patients.

A recent independent study of Neuromonics clinical efficacy is documented in the following paper in a peer reviewed medical journal demonstrating the results achieved with the Neuromonics treatment.


This paper documents the results of a major independent study of the Neuromonics Tinnitus Treatment on 45 patients over 9 separate clinical sites, including some of the best-regarded tinnitus clinics in the US. The patient population had experienced chronic unremitting tinnitus from 6 months to more than 20 years with poor or no response to previous treatments. Mean results found close to a halving of tinnitus distress over the first two months, followed by more gradual improvements resulting in a 75.7% improvement in TRQ score from baseline at the 24 month time point *. The final success rate was 83.3% patients with clinically significant important changes in TRQ scores (≥ 40% reduction from baseline) at 24 months *. The authors conclude the results of this study confirm the reported findings of earlier NTT studies and that the Neuromonics treatment may be offered to patients with chronic unremitting tinnitus with a significant chance of relief.

*At the time of publication, 12 patients had completed the 24-month questionnaire. All remaining data for 24 and 36 months will be reported in a follow up article.

**Poster and Podium Presentations**

In addition to the papers presented above that are available on Medline, there have been additional studies presented at recent medical meetings and, while they are not as accessible, they do provide additional evidence of clinical efficacy. The results are summarized below and additional data can be provided if needed.

1) **Podium Presentation:** March 2009, Joint Defense/Veterans Audiology Conference, Phoenix, AZ  
**Presenter:** Emily White, Miami Veterans Administration Outpatient Clinic, Hollywood, FL  
**Title:** Prevalence and Management of Tinnitus  
**Link:** www.afasl.org/AVAA%20conferences/White2009_Prev_and_mgmnt_tinnitus.pdf  
**Summary:** Interim presentation of data from an independent efficacy study of the Neuromonics Tinnitus Treatment program. At the time of the presentation, 35 patients were enrolled, 12 completed treatment and 23 were ongoing. **Results:** For the group of patients who have been in treatment at least 4 months, 22 of 23 (or 96%) have 40% or more improvement in at least 1 of 3 criteria (TRQ, % Awareness, or % Disturbed). For the 12 patients who have completed the treatment, mean improvement in TRQ is 72% (see chart below).
2) **Poster Presentation:** April 2009, American Academy of Audiology Annual Meeting, Dallas, TX  
**Presenter:** Sharon Sandridge PhD and Craig Newman PhD of the Cleveland Clinic  
**Title:** *Long-Term Benefits of Neuromonics Treatment: Preliminary Findings*  
**Summary:** The purposes of this study (CALM trial) are to demonstrate changes in perceived tinnitus distress and activity limitation/participation over selected time intervals up to 3 years following the initiation of NTT for up to 50 patients. The current data set represents preliminary findings at 6 months of the longitudinal study.  
**Results:** This study used both the TRQ and the THI (Tinnitus Handicap Questionnaire) and interim results showed significant benefit at 6 months as illustrated in the figure below (from the poster).

![Figure 3. Total score for the THI and TRQ over a 6-month period](image)

3) **Poster Presentation:** June 2009, 9th European Federation of Audiology Societies (EFAS), Tenerife, Canary Islands, Spain  
**Presenter:** Dayse Tavora-Vieira, Medical Audiology Services, WA, Australia  
**Title:** *Long-Term Clinical Outcomes of Tinnitus Treatment Based On Acoustic Stimulation*  
**Summary:** This preliminary study intended to determine the long-term tinnitus relief achieved by patients treated with the Neuromonics Tinnitus Treatment, ensuring that the benefits experienced during the first six months are still sustained in the longer term, with the measurement of outcomes to twelve months.  
**Results:** A total of 15 patients were studied and mean reduction in TRQ was 52% at six months and 44% at twelve months (see chart below for absolute TRQ results).

![Change in TRQ over time](image)
4) **Poster Presentation:** June 2009, 3rd Tinnitus Research Initiative Meeting (TRI), Stresa, Italy  
**Presenter:** Dayse Tavora,  
**Title:** Acoustic Stimulation in Tinnitus Treatment for Patients with Significant Levels of Hearing Loss  
**Summary:** To assess the efficacy of a variation of the standard Neuromonics treatment protocol for patients with high levels of hearing loss. Twenty-five patients with high hearing loss randomized to the standard (Group 1) vs. non-standard (experimental) treatment protocol. The non-standard treatment protocol maintained patients in the “Phase 1” of the treatment for 4 months instead of the typically 2 months.  
**Results:** The non-standard protocol demonstrated an improved benefit at 4 months (mean improvement of 46% vs. 29% for the standard protocol) but at 6 months the results were similar with a mean improvement in TRQ of 60% in the non-standard protocol vs. 52% in the standard protocol. This study showed that it may be possible to alter the treatment protocol for patients who fall outside the standard parameters and still achieve a significant clinical benefit.

![Graph showing improvement in TRQ over time for experimental group vs. Group 1.](image)

5) **Podium Presentation:** February 2010, DOD Acoustic Trauma Meeting in San Diego, CA  
**Presenter:** Melinda Hill, Au.D., U.S. Army Aeromedical Research Laboratory, Fort Rucker, AL  
**Title:** Evaluation of a New Treatment for Tinnitus  
**Summary:** The researcher presented interim results of an ongoing independent clinical trial with the stated goal to “Provide a treatment recommendation to the Surgeon General of the Army for debilitating tinnitus adversely affecting Soldier retention, deployability and operational performance”. A total of 40 soldiers are being recruited for the study and preliminary results from the Neuromonics cohort were presented.  
**Results:** The results show that after just 8 weeks, the group showed a mean reduction in TRQ of >40%.
6) **Podium Presentation: February 2010, Joint VA/DOD Audiology Meeting in Orlando, FL**  
**Presenter:** Margaret Peak and Kathy Duncan, VA Gulf Coast Veterans Health Care System  
**Title:** Impact of Setting Up a Tinnitus Clinic  
**Summary:** The researcher presented results from a review of 2,093 tinnitus patients in FY '09. Of those, a total of 75 (3.6%) proceeded to individualized treatment with Neuromonics and 52 completed treatment through to phase 2.  
**Results:**  
The results show a reduction in the TRQ score of ~60% which is consistent with previous trials. The awareness and disturbance of tinnitus also decreased significantly.

7) **Poster Presentation: April 2010, American Academy of Audiology Meeting in San Diego, CA**  
**Presenter:** Steven L. Benton, Au.D., Atlanta VA Medical Center  
**Title:** Clinical Experience with Progressive Tinnitus Management (PTM)  
**Summary:** The researcher reviewed the records of 2,543 subjects referred to the Atlanta VA Audiology Clinic over a 14 month period. The stated goals were:
1. To compare various characteristics of subjects who are referred for tinnitus services with those who are referred for hearing problems; and
2. to identify and describe any differences in the characteristics between subjects referred for tinnitus services who do or do not progress from one PTM level to the next.

Results:
The results showed that only a small percentage (1.4%) progressed to individualized management (PTM Level 5).

The Atlanta VA uses the Neuromonics Tinnitus Treatment for patients who require individualized management and the author presented the results from a total of 61 patients treated with Neuromonics. The mean reduction in the TRQ score was 69%, slightly better than previous trials.
8) **Poster Presentation:** April 2010, American Academy of Audiology Meeting in San Diego, CA  
*Presenter:* Dayse Tavora-Vieara, Medical Audiology Services, WA Australia  
**Title:** Long Term Clinical Outcomes of Tinnitus Management Applying Customized Acoustic Stimulation – an Independent Private Practice Study  
**Summary:** This study aimed to review the long term tinnitus relief achieved by patients treated with the Neuromonics Tinnitus Treatment. The researcher reviewed the records of 70 patients from the US and Australia who had completed Neuromonics treatment at least six months prior.  
**Results:** At the mean long-term follow up point of 94 weeks, the clinical benefit persisted at a level almost identical to the benefit achieved at the final appointment with a mean reduction in TRQ of 60%. This is very consistent with previous trials and shows the longer term benefit of the treatment.

9) **Podium Presentation:** May 2010, American Otological Society Meeting in Las Vegas, NV  
*Presenter:* Jack Wazen MD, Silverstein Institute, Sarasota, FL  
**Title:** Interim Results from a Long Term Tinnitus Treatment Study  
**Summary:** Dr. Wazen is the medical PI for a longer term clinical study of the Neuromonics treatment called the CALM trial. The trial is an independent assessment of clinical efficacy to 36 months and has recruited a total of 50 patients. Interim results were presented on patients out to 24 months.  
**Results:** The results showed both a clinically and statistically significant benefit at all time points when measured using either the TRQ or THI questionnaires. The mean reduction in the TRQ at 12 months was 68% and the benefit actually increased at the 24 month time point. The boxplots below indicate the distribution of continuous data by means of percentiles. The top and bottom edges of the box represent the 25th and 75th percentiles of the data. The 5th and 95th percentiles are represented by the whiskers extending from the top and bottom of the box. The bold line in the middle of the box represents the median of the data.
10) **Podium Presentation: July 2012, Audiology Australia 2012 National Conference Adelaide, Australia**

Presenters: Tom Garwood, Julie Quarterman, Joyce Dalgleish, & Nina Quinn, The Neurosensory Unit, Australia

**Title: Do tinnitus sufferers receiving treatment as part of a compensation process face extra difficulty in overcoming their condition?**

**Summary:** In this retrospective and descriptive study, researchers reviewed the records of 39 patients from a private tinnitus clinic with the aim of describing and comparing the outcomes for two groups of patients who completed the Neuromonics Tinnitus Treatment (NTT) over the previous 5 years. Group 1 included 20 patients who had self-funded the NTT program and Group 2 included 19 patients who had the program fully funded by a 3rd party as part of a compensation process. The mean success rate for all the study patients combined was 92% based upon their responses to the Tinnitus Reaction Questionnaire (TRQ). Results for the two groups were separated and group outcomes were compared to observe if tinnitus suffers receiving compensation related to, for instance, a workplace accident or long-term occupational noise exposure may face extra difficulties in overcoming their tinnitus disturbance.

**Results:** Mean improvements in tinnitus disturbance scores were significant for both groups as indicated by a reduced score on the TRQ and other self-reported measures, and these outcomes are noted to be highly consistent with prior clinical trial data and independent studies. However those patients who self-funded the treatment achieved a significantly greater level of improvement on average. The success rate was also slightly higher for the self-funded group. These results can provide clinicians with guidance as to outcomes that might be expected for NTT patients who participate in the compensation process, namely clinical success with the treatment, but at a somewhat lower level than that of self-funded patients.

![Graph](image)

11) **Podium Presentation: July 2012, Audiology Australia 2012 National Conference Adelaide, Australia**

Presenters: Tom Garwood, Cara Hailes, & Julie Quarterman, The Neurosensory Unit, Australia

**Title: Different strokes: long-term outcomes for tinnitus suffers using either Neuromonics Tinnitus Treatment or Counselling and sound Enrichment**

**Summary:** In this independent study, researchers reviewed the records of patients from a private tinnitus clinic to compare the long-term outcomes of two approaches to tinnitus rehabilitation; Neuromonics Tinnitus Treatment (NTT) and Counselling/Sound Enrichment. All patients included in this review were referred to the tinnitus clinic between January 2009 and December 2010 and were identified as suitable candidates for NTT, based primarily upon their responses to the Tinnitus Reaction Questionnaire (TRQ). 18 patients elected to receive Neuromonics Tinnitus Treatment and 22 patients elected to receive Counselling/Sound Enrichment. The initial TRQ score of the NTT Group was 57 ± 25 ±SD and for the Counseling/Sound Enrichment Group it was 44 ± 22. At a period of at least 12 months, and including up to 18 months, the TRQ was mailed to both groups for a long-term outcome measurement *.
Results: Mean improvements in tinnitus disturbance scores were significant for both groups, however non-parametric statistical analysis revealed that the Neuromonics Group had significantly greater improvement on this outcome measure than did the Counselling/Sound Enrichment Group. In addition, for the Counselling/Sound Enrichment group a high level of variability was evident in the median change in TRQ score.

In conclusion, the Neuromonics group achieved a significantly greater average improvement in TRQ score and this outcome is highly consistent with prior clinical trial data and independent studies. The authors conclude this study suggests the NTT protocol may achieve better long-term outcomes with severe tinnitus suffers than standard counseling and sound enrichment methods.

*n = 10 for the NTT Group at > 12 month