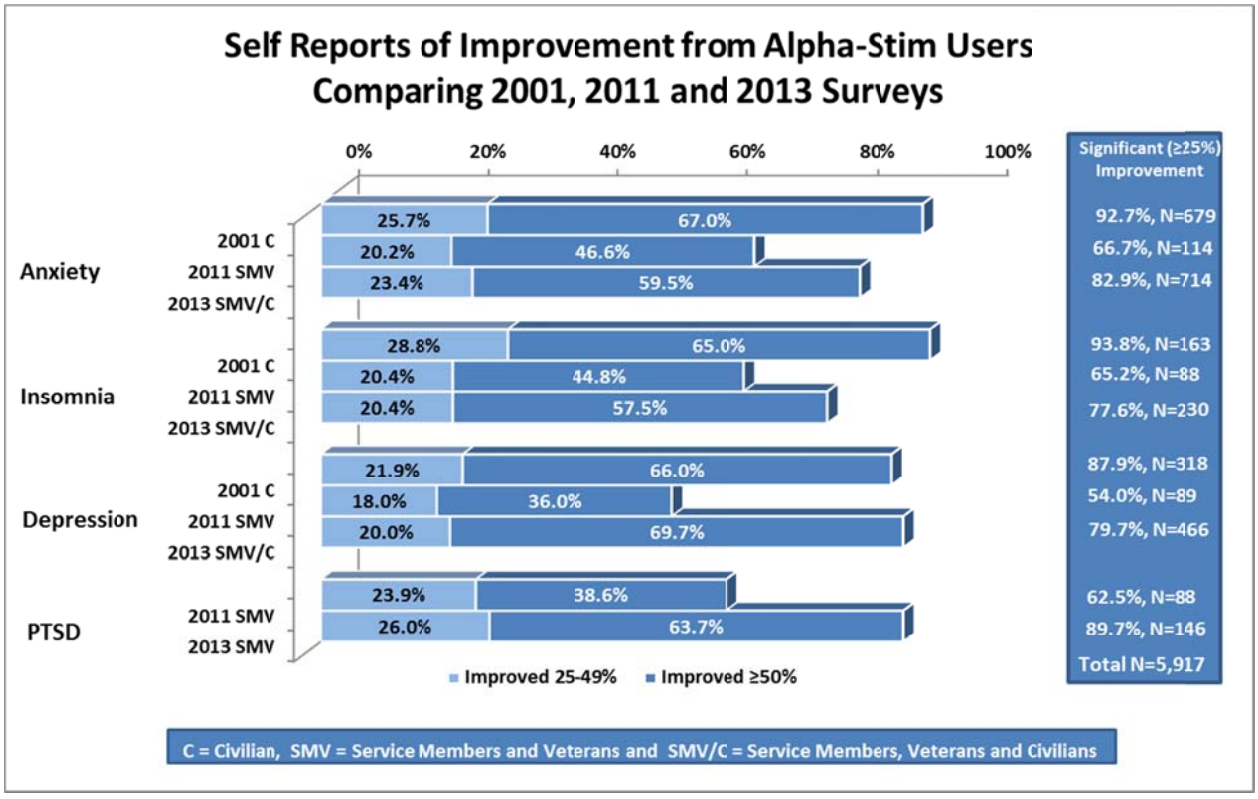
Summary of Three Post Marketing Surveys (N = 5,917)

Peer-reviewed outcomes from a post marketing survey (PMS) conducted for FDA from 2,500 patient surveys published in 2001 correlated well with 47 physicians' reports on 500 patients confirming that a significant effect of at least 25% improvement was reported by 9 out of 10 in this group of 3,000 patients.[1,2] In another post marketing survey of 152 Service Members and veterans conducted for FDA in 2011 the outcomes, while still significant, were not quite as robust as prior surveys of civilians.[3] However, results reported in the following pages representing a third post marketing survey of 2,861 Service Members, veterans and civilians conducted in 2013 for this submission were closer to the original post marketing survey of civilians. This is confirming evidence of the observation that Service Members and veterans who use Alpha-Stim CES most likely suffer from more extreme trauma and therefore experience slightly less effectiveness than a civilian-only cohort, yet the effects remain significant and can be defined as clinically important (≥ 50%) as seen below. The Table below provides a detailed summary of all three of the post marketing surveys conducted for FDA totaling nearly 6,000 Service Member, veteran and civilian self-reports.



[1] Smith RB. Is microcurrent stimulation effective in pain management? An additional perspective. *American Journal of Pain Management*, 11(2):62-66, 2001.
[2] Kirsch DL. The Science Behind Cranial Electrotherapy Stimulation, 2nd Ed. Medical Scope Publishing Corporation, Edmonton, Alberta, Canada, 2002.
[3] Kirsch DL, Price LR, Nichols F, Marksberry JA and Platoni KT. Efficacy of Cranial Electrotherapy Stimulation for Anxiety, PTSD, Insomnia and Depression: US Military Service Members and Veterans Self Reports. *The Army Medical Department Journal*, In Process, 2014.

2013 Alpha-Stim® User Effectiveness Survey Abstract

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Self-report data on the perceived effectiveness of Alpha-Stim was acquired from 2,861 respondents through a mail survey. Data collection occurred between July 2011 and July 2013. The primary focus of the survey was to acquire information regarding the effectiveness of using Alpha-Stim for the treatment of anxiety, insomnia, depression and PTSD. Eighteen percent (513) of the respondents exhibited nonresponse on at least one of the questions on diagnosis or improvement and were not included in the analyses. The final sample size used in the descriptive analyses after screening the data for overt errors in coding, aberrant or out of range values and item nonresponse was N=2,348, providing a useable response rate of 82% for the diagnosis and improvement question. One reason for the excellent response rate was that the user survey was included on the warranty card in the Alpha-Stim device kit with instructions to complete the survey and return the warranty card after using the Alpha-Stim device for at least 30 days.

Characteristics of Sample. The mean age for the analytic sample was 50 years (standard deviation of 14.5 years). The sample consisted of 69% females and 30% males with 1% not reporting sex. The average number of months respondents reported using Alpha-Stim on a continuous basis according to prescribed protocol was 106 days. However, the median (*i.e.,* exact center of the distribution) of the numbers of days of use was 1 month or 30 days. The mean days of use were higher than the median statistics due to extremely long continued use by a small number of consumers (*e.g.,* 23 respondents reported using Alpha-Stim 3 years or longer and 85 reporting 1 year or longer) who found Alpha-Stim technology effective for their condition.

Safety of CES. Over 99.9% of respondents reported that they considered Alpha-Stim to be effective (*e.g.,* either yes or no) for treating their identified medical problem. Out of 1,498 respondents to the question, “Do you consider Alpha-Stim to be safe?” only 1 person marked “no” but gave no reason for this response.

Effectiveness of Alpha-Stim® CES. This survey included civilians, Service Members and Veterans for the analysis of the perceived effectiveness of anxiety, insomnia and depression. Except the PTSD data included Service Members and Veterans only. The 2011 Alpha-Stim Service Members and Veterans Survey revealed that Service Members and Veterans rated their perceived effectiveness of Alpha-Stim lower than civilians in a previous survey. This is most likely due to Service Members and Veterans having more complex, serious injuries and medical conditions than civilians as a group. In this 2013 survey, Service Members and Veterans effectiveness ratings for PTSD were high with 63.7% reporting clinical improvement of ≥ 50% and 26% of respondents

reporting improvement between 25-49%. This is a total effectiveness response for PTSD of 89.7%.

Outcome criteria by Dworkin and colleagues (2008) for determining the importance of clinical improvement was used in this survey where ≥ 50% is considered improvement of *substantial clinical importance*. Improvement of *moderate clinical importance* was defined in this survey as 25-49% as this category was used in the validated Likert Scale that was used for the survey.

Respondents were asked to respond regarding their perceived improvement since beginning treatment using a Likert rating scale. Improvement was measured according to (a) a negative change (*i.e.,* condition worsened), (b) no change, (c) slight improvement (1-24%), (d) fair improvement (25-49%), (e) moderate improvement (50-74%), (f) marked improvement (75-99%), or (g) complete recovery (100%). Participants evaluated the effectiveness of CES for the following categories of diagnoses; anxiety, insomnia, depression and PTSD (see Figure 1).

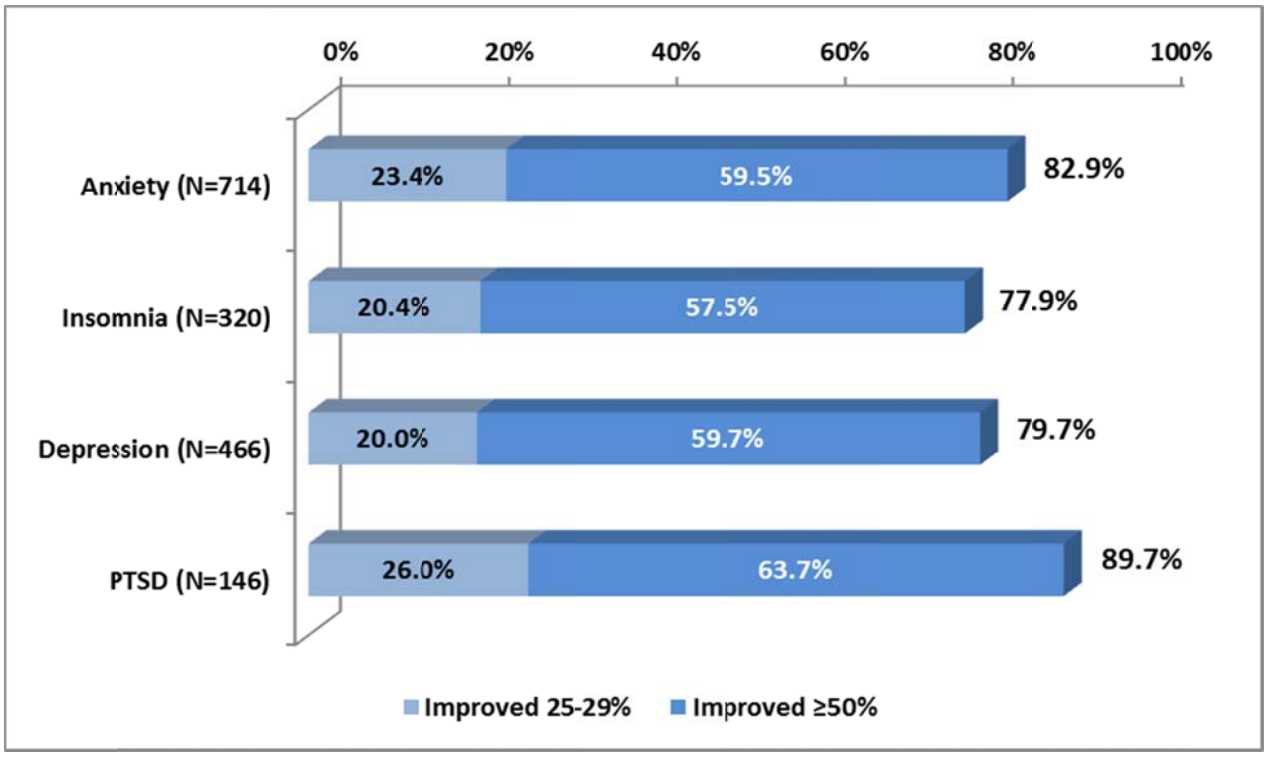

Figure 1. *Perceived effectiveness of Alpha-Stim for anxiety, insomnia, depression, pain and PTSD (N of respondents = 2,348).* ***PTSD data includes Service Members and Veterans only.*** *Anxiety, insomnia and depression categories include civilians, Service Members and Veterans. The dark blue indicates improvement of substantial clinical importance (≥50%). The light blue indicates improvement of moderate clinical importance (25-49%). The total percent of respondents for improvement categories of both substantial and moderate clinical importance is shown at the end of each bar. The N of cases for each category of diagnosis is under each diagnosis. If a respondent had multiple diagnoses, they rated improvement for each diagnosis separately.*

Combining the diagnostic categories of anxiety, insomnia, depression and PTSD, 60% of respondents reported having either moderate, marked or complete improvement (≥50%) from baseline or starting treatment, while 23% percent reported fair improvement (25-49%). Sixteen percent (16%) of respondents reported slight

improvement (1-24%). Approximately 2% reported no change in improvement while 3 individuals out of 2,348 respondents reported that their condition became worse.

The final question asked whether Alpha-Stim was more effective than anything else they had used for their respective medical condition. Thirty-six percent (36%) of the respondents reported that Alpha-Stim was more effective than anything else they had used for anxiety, 17% for depression and 11% for insomnia.

Note:

The criteria developed by Dworkin and colleagues (2008) to evaluate the importance of clinical improvements were used for the following reason. In addition to the ≥ 50% improvement that was termed improvement of substantial clinical importance, it includes a category of improvement called improvement of moderate clinical importance (30-49%). The reporting of the moderate clinical importance category is recommended because it provides a more complete picture of the response to treatment. These criteria were developed as outcome guidelines for use in clinical trials investigating pain. However, the criteria are also useful for determining meaningful response to treatment for other conditions.

Reference:

Dworkin RH, Turk DC, Wyrwich KW, Beaton D, Cleeland CS, Farrar JT, et al. Interpreting the clinical importance of treatment outcomes in chronic pain clinical trials: IMMPACT recommendations. *Journal of Pain*, 2008; 9:105-12.