

Alpha-Stim AID cranial electrotherapy stimulation (CES) anxiety treatment: anxiety, depression, and health-related quality-of-life outcomes in primary healthcare social prescribing services

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3 Title: Alpha-Stim AID cranial electrotherapy stimulation (CES) anxiety treatment: anxiety,
4 depression, and health-related quality-of-life outcomes in primary healthcare social
5 prescribing services
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7

8 **Abstract**

9 **Purpose**

10
11 To evaluate the effect of Alpha-Stim AID cranial electrotherapy stimulation (CES) on
12 anxiety, depression, and health-related quality of life for primary care social prescribing
13 service patients with anxiety symptoms.
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16 **Design/methodology/approach**

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18 Open-label patient cohort design with no control group. Thirty-three adult patients (average
19 age 42 years) completed 6 weeks of Alpha-Stim AID use. Pre- and post-intervention
20 assessment with participant self-report measures: Patient Health Questionnaire (PHQ-9),
21 Generalised Anxiety Disorder (GAD-7), and European Quality of Life Five Dimension (EQ-
22 5D-5L).
23
24

25 **Findings**

26
27 Reliable improvement and remission rates respectively were 53.39% and 33.3% for GAD-7;
28 46.7% and 29.5% for PHQ-9. There was a significant improvement in GAD-7 and PHQ-9
29 with large effect sizes. EQ-5D-5L results showed significant improvements in health-related
30 quality of life. Perceived quality of life increased by 0.17 on the health index score; with the
31 intervention adding 1.68 quality-adjusted life years (QALYs).
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34 **Originality**

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36 This is the first study to respond to the United Kingdom's (UK's) National Institute for
37 Health and Care (NICE) request for the collection of real-world data to understand better
38 Alpha-Stim AID in relation to people's treatment uptake, response rates, and treatment
39 completion rates (NICE, 2021).
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41

42 **Practical implications**

43
44 Alpha-Stim AID can be delivered through a primary healthcare social prescribing service and
45 most patients will use as prescribed and complete treatment course. Alpha-Stim AID CES
46 may be an effective anxiety and depression treatment for people with anxiety symptoms. The
47 widespread roll-out of Alpha-Stim AID in healthcare systems should be considered.
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54 **Keywords**

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56 Alpha-Stim, Primary Care, Social Prescribing, Cranial Electrotherapy Stimulation, Service
57 Delivery, Anxiety, Depression, Quality of Life, Co-Morbidity
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Introduction

Anxiety disorders (generalised anxiety disorder [GAD], phobias, panic disorders) are common and have a 13.6% to 28.8% lifetime prevalence (Michael *et al.*, 2007). GAD is the most common anxiety disorder and is defined as excessive and difficult-to-control anxiety or worry about issues in peoples' lives, everyday activities, or life events (APA, 2013). This anxiety and its effects can impair functioning and reduce well-being and quality of life (Locke *et al.*, 2015; Kessler *et al.*, 2012; Wittchen *et al.*, 2011).

Pharmacotherapy used for anxiety disorders with evidence of effectiveness includes selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), benzodiazepines, buspirone, and tricyclic antidepressants (TCAs) (Bespalov *et al.*, 2010; Muntingh *et al.*, 2016). Meta-analysis shows that SSRIs and SNRIs are effective in treating anxiety disorders (Jakubovski *et al.*, 2019). However, adverse side effects, which can include nausea, fatigue, weight gain, tremors, sexual dysfunction, insomnia, and gastrointestinal problems, mean the medication is not an acceptable option for some people (Bandelow *et al.*, 2017); for example, between 18% to 30% of people stop using SSRIs (Mochcovitch *et al.*, 2017). In addition, there can be a high risk of relapse (Culpepper, 2009), withdrawal effects can be long-lasting and severe (Davies and Read, 2019), and benzodiazepines are only recommended for severe anxiety symptoms and for less than four weeks of use, due to risk of dependence and withdrawal issues (NICE, 2019a).

Psychotherapy is recommended for anxiety disorders and can be effective, but as it is delivered over multiple sessions over a period of several weeks or months, it is costly and lengthy, with non-response rates of 60-66% (Gyani *et al.*, 2013; Griffiths and Griffiths, 2014; NICE, 2019b). In addition, some people do not find psychotherapy to be an acceptable option due to cultural beliefs, mobility issues, travel costs, or work or caring responsibilities (Bandelow *et al.*, 2017). Therefore, it is important that patients have a choice of treatment options for anxiety that best suit their lives, needs and concerns.

Cranial electrotherapy stimulation (CES) treatment can be offered in addition to pharmacological and psychotherapy/psychological treatment or as a standalone alternative treatment for various psychological disorders (Kirsch *et al.*, 2019). CES is a non-invasive method of applying a pulsed low-intensity electrical current through the head to cause an effect in the brain (Nardone *et al.*, 2014). CES has few side effects for users and was initially introduced to induce sleep and relaxation (Guleyupoglu *et al.*, 2013). It has subsequently been used for treating anxiety, depression, insomnia, post-traumatic stress disorder (PTSD), and pain (Kirsch *et al.*, 2019); however, there is a lack of compelling evidence from well-designed studies for beneficial effects (Brunyé *et al.*, 2021). A systematic review and meta-analysis examined the efficacy of CES for patients who reported anxiety symptoms and found CES significantly reduced anxiety symptoms with moderate effect sizes, and patients tolerated CES well (Ching *et al.*, 2022).

The precise mechanisms of action of CES remain unclear. It has been suggested that the effects could be related to modulation of the central and peripheral nervous system, which alters resting state and limbic system activation, which then increases cortical alpha-based

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3 activity and the release of neurotransmitters and hormones (Bunyé *et al.*, 2021, Ching *et al.*,
4 2022). In addition, CES is associated with changes detected by electroencephalography
5 (EEG) from delta (0.1-3.5 Hz) and beta (12.5-30 Hz) frequencies to more relaxing alpha
6 frequencies (8-12 Hz) (Kennerly, 2004), and increased theta activity in the left frontal region
7 (Kim *et al.*, 2021).
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11 The Alpha-Stim AID (Anxiety, Insomnia, and Depression) CES is a mobile phone sized
12 device that is connected via soft pad clips to both earlobes and used for up to an hour a day. It
13 has been found to reduce anxiety by 32% (Barclay and Barclay, 2014). A systematic review
14 found that Alpha-Stim AID reduces symptoms of anxiety and depression and is safe without
15 serious side effects (Shekelle *et al.*, 2018). Open-label with no control group design studies in
16 primary care, nurse-led services for university students, and in an Improving Access to
17 Psychology Treatment (IAPT) service, reported significant improvements in anxiety,
18 depression, and quality of life for patients experiencing anxiety symptoms (Griffiths *et al.*
19 2021; Morriss *et al.* 2019; Royal *et al.*, 2022). These studies found Alpha-Stim AID to have
20 few minor side effects, that it was safe, well-tolerated, and acceptable, and that users will use
21 it in line with the required treatment instructions.
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26 In March 2021, the National Institute for Health and Care Excellence (NICE) published
27 guidance on Alpha-Stim AID (MTG56) (NICE, 2021). This study responds to the request in
28 this guidance for collecting real-world data to understand better Alpha-Stim AID in relation
29 to people's treatment uptake, response rates, and treatment completion rates (NICE, 2021). In
30 this project, Alpha-Stim AID was offered through a United Kingdom (UK) primary care
31 social prescribing service to patients who reported symptoms of anxiety and assessed
32 outcomes in terms of usage of the device and impact on anxiety, depression, and health-
33 related quality of life.
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40 **Methods**

41 *Design*

42 The study had an open-label patient cohort design with no control group. Pre- and post-
43 intervention assessments with participant self-report measures were collected.
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47 *Ethics approval*

48 Ethical approval was granted by the review panel of the NHS Trust leading the study and by
49 the NHS primary care provider consortium. All participants provided informed written
50 consent.
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54 *Medical Records*

55 Following informed consent, demographic information (gender, date of birth) was extracted
56 from clinical records containing routinely collected data.
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Setting

Participants were recruited through a social prescribing service. A general practice (GP) patient is referred to a primary care-based social prescribing link worker (SPLW), who assesses their needs and goals (what matters to them) and provides practical and emotional support. SPLW makes appropriate links and referrals to healthcare and community-based resources and services to facilitate behaviour change to healthier lifestyles (NHS England, 2021).

Alpha-Stim AID intervention

Alpha-Stim AID is a mobile phone sized device worn via a neck lanyard delivering small electric currents via soft pads conducting through metal clips to the earlobes. Light activities can be performed whilst it is in use, but the person is advised not to drive a vehicle. Once the participants provided informed consent to try the Alpha-Stim AID (Conformite Europeenne [CE] marked as a class IIa medical device), the devices were sent by tracked postal service or given to participants by their SPLW with instructions on how to use them. They were advised to use it once a day for an hour for six weeks at level 1 (2 bars on screen) (0.5 Hz, 100 - 500 μ A, 50% duty cycle, biphasic asymmetrical rectangular waves).

The SPLW showed the patient how to use the Alpha-Stim AID CES device, outlined how to obtain support while using it, and how to return it. In addition, SPLWs could be contacted to ask questions about the device and its effects. Patients remained on any prescribed medication and continued other medical or psychological interventions. Following six week's use, they were required to return the Alpha-Stim AID.

Inclusion/exclusion

Informed consent to the study and agreement to return Alpha-Stim AID equipment at the end of the study was required. The inclusion criterion was the patient reporting anxiety symptoms. The exclusion criteria were implantation with a pacemaker or an implantable cardioverter device (ICD), or pregnancy.

Procedure

Patients were referred to a SPLW by their GP, and the SPLW then identified if the patient had anxiety symptoms. Patients were selected if they met inclusion/exclusion criteria and they were then provided with information about the treatment and evaluation. Informed consent was sought and required in order to begin treatment. Patients could withdraw consent or stop treatment at any point without the need to provide a reason. Following informed consent, participants were required to fill in the three self-report questionnaires. This was completed a three time points: baseline (pre Alpha-Stim AID use), week 3 (during Alpha-Stim AID use), and week 6 (post Alpha-Stim AID use). In total 33 data sets from 84 individuals approached were suitable for use in the research, see Figure 1, the participant flow diagram.

Insert Figure I. Participant flow diagram

Measures

The Generalised Anxiety Disorder-7 (GAD-7) is a seven-item self-report measure of generalised anxiety disorder (GAD) (Spitzer *et al.*, 2006). A score of 0-4 represents no or minimal anxiety, 5-9 mild anxiety, 10-14 moderate anxiety, and 15-21 severe anxiety. Remission is defined as a score of 7 or less, and reliable improvement is defined as a reduction of 5 points (Kroenke *et al.*, 2007; Spitzer *et al.*, 2006). The GAD-7 has good sensitivity and specificity for GAD and is moderately good at screening three other anxiety disorders: panic disorder, social anxiety disorder, and post-traumatic stress disorder (PTSD) (Kroenke *et al.*, 2007). It has good internal consistency, shown by Cronbach's Alpha value of $\alpha = 0.92$ (Kroenke *et al.*, 2007).

Patient Health Questionnaire-9 (PHQ-9) is a self-report measure of depression; it has good sensitivity and specificity for major depression as well as good internal consistency (Kroenke *et al.*, 2001); scores for depression severity are: 0-4 none, 5-9 mild, 10-14 moderate, 15-19 moderately severe, and 20-27 severe (Kroenke *et al.*, 2007). Remission is defined as a score of 9 or less, and reliable improvement is a drop of 6 points (Richards and Borglin, 2011).

European Quality of Life Five Dimension (EQ-5D-5L) (EuroQol Group, 1990; van Hout *et al.*, 2012) is a 5-item and visual analogue scale (VAS) self-rated measure of health-related quality of life and overall health status. It is a standardised measure of health developed by EuroQol group to provide a simple, standardised measure for a clinical appraisal (EuroQol Group, 1990). The descriptive system comprises of five dimensions (mobility, self-care, usual activities, pain/ discomfort, anxiety/ depression), each of which is measured within 5 levels (no problems, slight problems, moderate problems, severe problems, and extreme problems). The digits from the five dimensions are combined to create a five-digit number describing a participant's holistic health state. Each health state can be assigned an index score based on societal preference weights for the health state. Health state index scores 1 = the value of full health, with higher scores indicating higher health utility. Additionally, EQ VAS is a subjective measure of a participant's current health, ranging from 0 (meaning the worst health imaginable) to 100 (best health imaginable). The EQ-5D-5L demonstrates good construct validity and is sensitive to change in patients with depression and anxiety (Peasgood *et al.*, 2012). The EQ-5D-5L is a validated, generic, preference-based measure of health status, widely used in national health surveys in the UK and worldwide and in clinical trials of health interventions (Brooks and Group, 1996; Herdman *et al.*, 2011), and EQ-5D is recommended by NICE to estimate health state utility weights for quality-adjusted life year (QALYs) (NICE, 2019c).

Statistical Analysis

Data were analysed using the statistics software package SPSS® Statistics v28. Data screening confirmed the dataset met all the requirements of the general linear model. Following descriptive analysis, one-way repeated measures ANOVAs were conducted to determine whether there were statistically significant improvements for the mental health assessments between baseline, week three, and week six. Frequencies and percentages were

used to determine reliable improvement and remission rates. The average EQ-5D-5L digit calculated within each dimension was combined at baseline and post-intervention to create comparative five-digit health states. These digits were converted into the corresponding holistic health index scores to calculate QALYs. A one-way repeated measure ANOVA was conducted on each participant's converted health index score at the three time points to assess significant improvement. Pearson's correlations were used to determine the relationship between the three scales and EQ subscales. ANCOVA was utilised to test whether Alpha-Stim AID usage acted as a significant covariate of any improvement observed.

Results

Participant Characteristics

Of the 77 participants who agreed to participate, 33 (42.9%) completed six weeks of treatment, baseline, 3 and 6-week assessments. Their average age was 41.97 years ($SD = 10.58$), 61.3% were females, 35.5% males and one participant identified as 'other'. As illustrated by Table 1, participant mean baseline scores were in the 'severe' range for GAD and the 'moderately severe' range for depression (Spitzer *et al.*, 2006; Kroenke *et al.*, 2001). Baseline EQ-5D-5L crosswalk data values indicated participants had a low average holistic health index and EQ VAS score; however, the dispersion was high.

Table I insert here

GAD-7 and PHQ-9

There were no outliers in the data, as assessed by inspection of a boxplot. The Shapiro-Wilk test found both the GAD-7 and PHQ-9 measures to be normally distributed ($p > 0.05$) at baseline, week 3 and 6. Mauchly's test of sphericity indicated that the assumption of sphericity had not been violated, $\chi^2(2) = 0.98, p = .694$.

The reduction in GAD-7 scores were statistically significant, $F(2, 64) = 24.60, p < 0.001$, a large effect size was observed: partial $\mu^2 = 0.435$. Thus, 44% of the improvement in GAD-7 score was attributed to the intervention. Post-hoc analysis with a Bonferroni adjustment revealed that there was a decrease in GAD-7 scores from baseline ($M = 15.52, SD = 3.84$) to week 3 ($M = 10.73, SD = 5.72$), a statistically significant mean decrease of 4.79, 95% CI [2.75, 6.83], $p < 0.001$; and from baseline to week 6 ($M = 10.15, SD = 5.05$). Reliable improvement and remission rates for GAD-7 at the end of the study were 53.39% and 33.3%, respectively.

The PHQ-9 Mauchly's test of sphericity indicated that the assumption of sphericity had not been violated, $\chi^2(2) = 0.95, p = .429$. The reduction in PHQ-9 scores were statistically significant at all time points during the intervention, $F(2, 32) = 32.56, p < 0.001$, with a large effect size, partial $\mu^2 = 0.503$. The large effect size confers that the intervention accounted for 50% of the improvement in PHQ-9. Post-hoc analysis with Bonferroni adjustment revealed

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3 that there was a decrease in PHQ-9 scores from baseline ($M = 16.85$, $SD = 4.66$) to week
4 three ($M = 11.67$, $SD = 6.37$), a statistically significant mean decrease of 5.18, 95% CI [3.05,
5 7.32], $p < 0.001$; and from baseline to week 6 ($M = 11.00$, $SD = 5.97$), a statistically
6 significant decrease of 5.71, 95% CI [3.25, 8.45], $p < 0.001$. Reliable improvement and
7 remission rates for PHQ-9 at the end of the study were 46.7% and 29.5%, respectively.
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10 Pearson's correlation coefficients indicated statistically significant correlations between
11 PHQ-9 and GAD-7 at baseline ($r = .834$), after 3 weeks ($r = .824$) and after 6 weeks ($r =$
12 $.741$), all $p < 0.001$.
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15 *EQ-5D-5L*

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17 Table II illustrates the descriptive data for each of the five dimensions as well as the mean
18 health index and VAS at baseline, week 3 and week 6. From baseline to week 6, quality of
19 life increases with an improvement of 0.17. Measured across ten years, this intervention adds
20 1.68 QALYs.
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23 Table II. here

24
25 Data screening permitted the use of a one-way repeated measure ANOVA to determine
26 whether there was a statistically significant difference in participants' EQ dimensions, as well
27 as their health index score and VAS at the 6-week data point. The improvement was
28 statistically significant for two EQ dimensions ('usual activity' and 'anxiety/depression'), for
29 the health index score and the VAS score. A large effect size was observed for
30 'anxiety/depression' and medium effect sizes for 'usual activity', health index score, and EQ-
31 VAS scores. Post-hoc analysis with a Bonferroni adjustment revealed an improvement from
32 baseline to weeks 3 and/or 6 but not between weeks 3 and 6.
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36 Table III illustrates the data collected from the EQ-5D-5L tool and broken down by level 1
37 (patients reported no issues on the dimension), level 2 (patients reported mild to moderate
38 levels of issue), and level 3 (patients reporting severe to an extreme level of issues). The
39 greatest improvement was observed in the 'anxiety/depression' dimension, with
40 severe/extreme levels of reported anxiety and depression dropping by 29.1% by the end of
41 the intervention. In terms of 'usual activity', reporting of no problems (level 1) did not
42 change over time; however, the level of severe/extreme issues dropped by 18.9%. No
43 statistically significant changes were observed in the 'pain/discomfort', 'self-care', and
44 'mobility' dimensions, although the trends showed improvement over time.
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53 A participant usage survey indicated that the majority of participants were mostly compliant
54 with usage instructions (6 participants using the device every day and 5 virtually every day
55 [79%]). Descriptives of usage are presented in Table IV.
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57 The frequency of use categories was analysed as a covariate between PHQ-9 and GAD-7
58 improvement. The ANCOVA results were non-significant for PHQ-9 and GAD-7, indicating
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3 that failure to adhere to daily treatment did not have a significant detrimental impact on
4 improvement.
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6 Insert table IV here
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10 Costs

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12 The EQ-5D-5L health index conversion scores indicated that the improved quality of life is
13 equivalent to 1.7 QALYs (life year gains) across a span of 10 years. The cost per QALY
14 threshold stipulated by NICE for England and Wales ranges between £20,000 and £30,000
15 (GOV.UK, 2020). Cost modelling has estimated a per-person treatment cost of £70 (GBP) for
16 a course of Alpha-Stim; inclusive of all staff and ad hoc costs (NICE, 2021). This present
17 study concluded an estimate of staff time costs and postage costs of (£62 [GBP]) and device
18 cost of £100 (GBP) per single patient cycle. The cost of device is estimated as £600 [GBP]
19 (with six uses of six weeks consumables), and each device was estimated to have a six use
20 life (due to damage, lack of ability to clean to an acceptable level for re-use, and non-return).
21 This indicated an estimate of £162 per patient. Thus, the intervention is highly cost-effective,
22 as the price per QALY is well below the stipulated thresholds.
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30 Discussion

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32 This study showed that Alpha-Stim AID can be provided to patients through a primary
33 healthcare social prescribing service. When offered, the majority of patients will choose
34 Alpha-Stim AID as an alternative form of treatment and use it as per instructions. Alpha-Stim
35 AID can be effective in reducing anxiety and depression, and increasing health related quality
36 of life and health status in patients with symptoms of anxiety. The outcomes add evidence to
37 support the effectiveness of Alpha-Stim AID in reducing anxiety and depression reported by
38 published RCTs and health service based studies (Barclay and Barclay, 2014; Shekelle *et al.*,
39 2018; Morriss *et al.*, 2019; Griffiths *et al.*, 2021; Royal *et al.*, 2022).
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44 The results from the current study for the depression and anxiety remission and reliable
45 improvement rates add to evidence from three other NHS service based Alpha-Stim studies
46 suggesting that community based patients' depression and anxiety symptoms can be treated
47 with Alpha-Stim AID through the NHS (Griffiths *et al.*, 2021; Morriss *et al.*, 2019; Royal *et al.*,
48 2022). However, compared to the GAD-7 anxiety assessment, a lower percentage of
49 participants achieved PHQ-9 depression symptom reliable improvement and remission. This
50 perhaps indicates that Alpha-Stim is less beneficial in terms of treating symptoms of
51 depression than symptoms of anxiety.
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55 This present study shows that the use of the device may lead to relatively quick improvement,
56 aligning with other findings (Morriss *et al.*, 2019). Most of the improvements in anxiety and
57 depression with Alpha-Stim AID was seen in the first 3 weeks. The time course of response
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of SNRIs and SSRIs is around 2 to 4 weeks to significant benefits, respectively; but it may take longer than 3 weeks to achieve most of the improvement (Jakubovski *et al.*, 2019).

The results indicated statistically significant improvements on two of the five dimensions measured by the EQ-5D-5L: 'ability perform usual activity' and 'anxiety/depression'. Levels of severe/extreme issues in the ability to perform usual activities dropped by 18.9%, and the severe/extreme levels of reported depression and anxiety dropped by 29.1%. These findings indicate the positive impact of Alpha-Stim AID on mental health, wellbeing, recovery, and real-world functioning, factors highly valued by people in their everyday lives.

This present study's sample had higher GAD-7 and PHQ-9 baseline scores (GAD-7 average was in the highest 'severe anxiety' range and PHQ-9 in the second highest 'moderately severe' range) than reported by patients seeking help for anxiety and depression from IAPT services in the corresponding geographical area (NHS Digital, 2022). This indicates the potential high level of need for anxiety and depression identification and treatment in patients seen by social prescribing services.

This study found that a primary healthcare social prescribing service can set up and deliver the Alpha-Stim AID treatment and collect patient assessment measures. Primary care social prescribing services are well-placed to deliver this treatment as social prescribing is a universal service across the UK and seeks to get an in-depth understanding of patients' holistic needs, issues, and goals (NHS England, 2021). In addition, primary care services have extensive experience with other medical devices - such as the transcutaneous electrical nerve stimulation (TENS) unit used to manage pain, as well as blood pressure monitoring devices - which are given to and retrieved from patients; they can apply processes and experience of these devices to the supply of Alpha-Stim AID. Alpha-Stim AID devices have the potential to be distributed by post direct to a patient's home, therefore preventing the stigma and barriers of attending an IAPT clinic or psychiatric service. Offering via home, online or phone based services can make the treatment more accessible for some people, such as those with transport, mobility or disabilities issues.

Alpha-Stim AID treatment was acceptable to most patients; most used the device as instructed and returned it following use, aligning with other findings (Griffiths *et al.*, 2021; Morriss *et al.*, 2019; Royal *et al.*, 2022). This intervention may offer an alternative solution to those experiencing anxiety symptoms who have failed to respond to medication or psychotherapy or find medication side effects or factors related to psychotherapy unacceptable.

Individual and system level cost-benefit analysis is required to understand the potential savings that could be derived by the wider implementation of Alpha-Stim for people with symptoms of anxiety. To better target people who are likely to benefit, further research is required to investigate why some people respond, and others do not: what factors determine response. Mechanisms of action studies are required, and there is a need for an appropriately powered RCT on effectiveness for anxiety: a RCT comparing Alpha-Stim AID with individual cognitive behavioural therapy (CBT), medication, or both (NICE, 2021).

Limitations

There was no control group or randomisation to another treatment. Only 33 out of 57 participants who began treatment (58%) completed treatment and every assessment, indicating a high participant drop-out. The reasons for this high drop-out needs to be further investigated. Treatment with Alpha-Stim AID was open-label and adjunct to any existing anxiety or other treatments or therapies. The sample was over-represented by females (61%), and so results are less generalisable to males; however, this reflects the higher proportion of females who present with anxiety symptoms. This study collected outcome measures at 3 weeks and at the end of the treatment point, with no later follow-up data collection; it is recommended that future studies employ a 12 and 24-week follow-up data collection point.

Conclusion

This study's findings provide further evidence that Alpha-Stim AID may be clinically effective against anxiety and depression symptoms when offered through healthcare services for patients with anxiety symptoms. This study developed an effective SP service based pathway and delivery by SPLWs. Addressing anxiety and depression symptoms through a social prescribing service potentially reduces demand on primary care, secondary care, and IAPT services; and, therefore, may reduce healthcare costs.

Consideration needs to be given as to when a patient is offered Alpha-Stim AID, it is less costly than a course of face-to-face psychotherapy and more convenient as it is delivered at home, and it has fewer side effects than anti-anxiety medication. However, it may require more staff time to support its use than to provide medication, and there are more convenient forms of psychotherapy than face-to-face, such as online psychotherapy. The current availability of Alpha-Stim AID in universal healthcare systems is very limited. The results support the wider availability of Alpha-Stim AID through primary care as a treatment option for people with anxiety symptoms. Many people cannot afford the cost of the device for themselves, and making it freely available through a universal healthcare provider (possibly through personal health budgeting), would address this issue.

References

- APA (2013), "Diagnostic and statistical manual of mental disorders", *American Psychiatric Association*, Vol. 21 No. 21, pp. 591-643.
- Bandelow, B., Michaelis, S., and Wedekind, D. (2017), "Treatment of anxiety disorders", *Dialogues in Clinical Neuroscience*, Vol 19, pp. 93-107.
- Barclay, T. H., and Barclay, R. D. (2014), "A clinical trial of cranial electrotherapy stimulation for anxiety and comorbid depression", *Journal of Affective Disorders*, Vol 164, pp. 171-177.
- Bespalov, A. Y., vanGaalén, M. M., and Gross, G. (2010), "Antidepressant treatment in anxiety disorders", Stein, M.B., and Steckler, T. (Eds.), *Behavioral neurobiology of anxiety and its treatments*, Springer, New York, pp. 361-390
- Brooks, R., and Group, E. (1996), "EuroQol: the current state of play" *Health policy*, Vol 37, No. 1, pp. 53-72.
- Brunyé, T. T., Patterson, J. E., Wooten, T., and Hussey, E. K. (2021), "A critical review of cranial Electrotherapy Stimulation for neuromodulation in clinical and non-clinical samples", *Frontiers in Human Neuroscience*, Vol. 15, No. 625321, pp. 1-15
- Ching, P. Y., Hsu, T., Chen, G., Pan, C. C., Chu, C. S., and Chou, P. H. (2022), "Efficacy and tolerability of cranial electrotherapy stimulation in the treatment of anxiety: A systemic review and meta-analysis", *Frontiers in Psychiatry*, Vol. 13 No. 899040, pp. 1-13
- Culpepper, L. (2009), "Generalized anxiety disorder and medical illness", *Journal of Clinical Psychiatry*, Vol. 70 No. 2, pp. 20-24.
- Davies, J., and Read, J. (2019), "A systematic review into the incidence, severity, and duration of antidepressant withdrawal effects: are guidelines evidence-based?", *Addictive Behaviors*, Vol. 97, pp. 111-121.
- EuroQol Group (1990), "EuroQol-a new facility for the measurement of health-related quality of life", *Health policy*, Vol. 16 No.3, pp. 199-208.
- GOV.UK. (2020), "Cost utility analysis: health economic studies", available at <https://www.gov.uk/guidance/cost-utility-analysis-health-economic-studies> (accessed 16 October 2022)
- Guleyupoglu, B., Schestatsky, P., Edwards, D., Fregni, F., & Bikson, M. (2013), "Classification of methods in transcranial electrical stimulation (tES) and evolving strategy from historical approaches to contemporary innovations". *Journal of Neuroscience Methods*, Vol 219 No. 2, pp. 297-311.
- Griffiths, C. A. and Griffiths, L. J. (2014), "Recovery and reliable change rates for patients scoring severe on depression, anxiety or impaired functioning in a psychological therapies service: IAPT", *Mental Health Review Journal*, Vol. 20 No.1, pp. 28-35.
- Griffiths, C., Leathlean, C., Smart, D., Zafar, A., Hall, C-L, and Deeks, S. (2021), "Alpha-Stim cranial electrotherapy stimulation (CES) for anxiety treatment: outcomes in a United

- 1
2
3 Kingdom (UK) primary care practice”. *Open Journal of Psychiatry*, Vol. 11No. 3, pp. 186-
4 201.
5
6 Gyani, A., Shafran, R., Layard, R., and Clark, D. M. (2013), “Enhancing recovery rates:
7 lessons from year one of IAPT”, *Behaviour Research and Therapy*, Vol. 51 No. 9, pp. 597-
8 606.
9
10 Herdman, M., Gudex, C., Lloyd, A., Janssen, M. F., Kind, P., Parkin, D., ... and Badia, X.
11 (2011), “Development and preliminary testing of the new five-level version of EQ-5D (EQ-
12 5D-5L)”, *Quality of Life Research*, Vol. 20 No. 10, pp. 1727-1736.
13
14 Jakubovski, E., Johnson, J. A., Nasir, M., Müller-Vahl, K., and Bloch, M. H. (2019),
15 “Systematic review and meta-analysis: Dose–response curve of SSRIs and SNRIs in anxiety
16 disorders”, *Depression and Anxiety*, Vol. 36 No.3, pp. 198-212.
17
18 Kennerly, R. (2004), “QEEG analysis of cranial electrotherapy: A pilot study”, *Journal of*
19 *Neurotherapy*, Vol. 8, pp. 112-113.
20
21 Kessler, R. C., Petukhova, M., Sampson, N. A., Zaslavsky, A. M., & Wittchen, H. U. (2012),
22 “Twelve-month and lifetime prevalence and lifetime morbid risk of anxiety and mood
23 disorders in the United States”, *International Journal of Methods in Psychiatric Research*,
24 Vol. 21 No. 3, pp. 169-184.
25 Kim, J., Kim, H., Kim, D. H., Lee, S. K., Roh, J. Y., Kim, C. H.,
26 ... and Roh, D. (2021), “Effects of cranial electrotherapy stimulation with novel in-ear
27 electrodes on anxiety and resting-state brain activity: A randomized double-blind placebo-
28 controlled trial” *Journal of Affective Disorders*, Vol. 295, pp. 856-864.
29
30 Kirsch, T. B., Kuhn, J., Price, L. R., Marksberry, J., and Haltiwanger, S. G. (2019), “A Novel
31 Medical Device that Relieves Anxiety, Depression and Pain While Improving Sleep in a
32 Population of Teachers”, *Journal of Depression and Anxiety*, Vol. 8 No. 2, pp. 334.
33
34 Kroenke, K., Spitzer, R. L., and Williams, J. B. (2001), “The PHQ-9: validity of a brief
35 depression severity measure”, *Journal of General Internal Medicine*, Vol. 16 No.9, pp. 606-
36 613.
37
38 Kroenke, K., Spitzer, R. L., Williams, J. B., Monahan, P. O., and Löwe, B. (2007), “Anxiety
39 disorders in primary care: prevalence, impairment, comorbidity, and detection”, *Annals of*
40 *Internal Medicine*, Vol. 146 No. 5, pp. 317-325.
41
42 Locke, A. B., Kirst, N., and Shultz, C. G. (2015), “Diagnosis and management of generalized
43 anxiety disorder and panic disorder in adults”. *American Family Physician*, Vol. 91 No. 9, pp.
44 617-624.
45
46 Michael, T., Zetsche, U., and Margraf, J. (2007). “Epidemiology of anxiety
47 disorders”, *Psychiatry*, Vol. 6 No 4, pp. 136-142.
48
49 Mochcovitch, M. D., da Rocha Freire, R. C., Garcia, R. F., and Nardi, A. E. (2017), “Can
50 long-term pharmacotherapy prevent relapses in generalized anxiety disorder? A systematic
51 review”, *Clinical Drug Investigation*, Vol. 37 No. 8, pp. 737-743.
52
53 Morriss, R., Xydopoulos, G., Craven, M., Price, L., and Fordham, R. (2019), “Clinical
54 effectiveness and cost minimisation model of Alpha-Stim cranial electrotherapy stimulation
55
56
57
58
59
60

1
2
3 in treatment seeking patients with moderate to severe generalised anxiety disorder”, *Journal*
4 *of Affective Disorders*, Vol. 253, pp. 426-437.

6
7 Muntingh, A. D., van der Feltz-Cornelis, C. M., van Marwijk, H. W., Spinhoven, P., and van
8 Balkom, A. J. (2016), “Collaborative care for anxiety disorders in primary care: a systematic
9 review and meta-analysis”, *BMC Family Practice*, Vol. 17 No. 1, pp. 1-15.

11
12 Nardone, R., Höller, Y., Leis, S., Höller, P., Thomschewski, A., Golaszewski, S., Brigo, F.,
13 and Trinka, E. (2014), “Invasive and non- invasive brain stimulation for treatment of
14 neuropathic pain in patients with spinal cord injury: A review”, *Journal of Spinal Cord*
15 *Medicine*, Vol. 37 No.1), pp. 19-31.

16
17 NHS Digital (2022), “Psychological Therapies, Annual report on the use of IAPT services -
18 England, 2021-22”, available at [https://digital.nhs.uk/data-and-](https://digital.nhs.uk/data-and-information/publications/statistical/psychological-therapies-annual-reports-on-the-use-of-iapt-services/annual-report-2021-22)
19 [information/publications/statistical/psychological-therapies-annual-reports-on-the-use-of-](https://digital.nhs.uk/data-and-information/publications/statistical/psychological-therapies-annual-reports-on-the-use-of-iapt-services/annual-report-2021-22)
20 [iapt-services/annual-report-2021-22](https://digital.nhs.uk/data-and-information/publications/statistical/psychological-therapies-annual-reports-on-the-use-of-iapt-services/annual-report-2021-22) (accessed 10 October 2022)

22
23 NICE (2021). Alpha-Stim AID for anxiety disorders. Medical technologies guidance.
24 Published: 8 March 2021 www.nice.org.uk/guidance/mtg56 (accessed 10 October 2022)

25
26 NICE (2019a), “Benzodiazepine and z-drug withdrawal”, available at
27 <https://cks.nice.org.uk/topics/benzodiazepine-z-drug-withdrawal/> (accessed 10 October 2022)

28
29 NICE (2019b), “Generalised anxiety disorder and panic disorder in adults: management.
30 Clinical guideline [CG113]”, available at <https://www.nice.org.uk/guidance/cg113> (accessed
31 16 October 2022)

33
34 NICE (2019c) Position statement on use of the EQ-5D-5L value set for England (updated
35 October 2019) [https://www.nice.org.uk/about/what-we-do/our-programmes/nice-](https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/technology-appraisal-guidance/eq-5d-5l)
36 [guidance/technology-appraisal-guidance/eq-5d-5l](https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/technology-appraisal-guidance/eq-5d-5l) (accessed 16 October 2022)

37
38 NHS England (2021). Social prescribing (2021). NHS England.
39 <https://www.england.nhs.uk/personalisedcare/social-prescribing/> (accessed 16 October 2022)

41
42 Peasgood, T., Brazier, J. and Papaioannou, D. (2012), “A systematic review of the validity
43 and responsiveness of EQ-5D and SF-6D for depression and anxiety”, *HEDS Discussion*
44 *Paper*, 12-15.

45
46 Richards, D. A., and Borglin, G. (2011), “Implementation of psychological therapies for
47 anxiety and depression in routine practice: two year prospective cohort study”, *Journal of*
48 *affective disorders*, Vol. 133 No. 1-2, pp. 51-60.

49
50 Royal, S., Keeling, S., Kelsall, N., Price, L., Fordham, R., Xydopoulos, G., Dawson, G. R.,
51 Kingslake, J., and Morriss, R. (2022), “Feasibility, acceptability and costs of nurse-led alpha-
52 stim cranial electrostimulation to treat anxiety and depression in university students”, *BMC*
53 *Primary Care*, Vol. 23 No.97, pp. 1-14.

55
56 Shekelle, P. G., Cook, I. A., Miake-Lye, I. M., Booth, M. S., Beroes, J. M., and Mak, S.
57 (2018), “Benefits and harms of cranial electrical stimulation for chronic painful conditions,
58 depression, anxiety, and insomnia”, *Annals of Internal Medicine*, Vol. 168, pp. 414-421.
59
60

1
2
3 Spitzer, R. L., Kroenke, K., Williams, J. B., and Löwe, B. (2006), "A brief measure for
4 assessing generalized anxiety disorder: the GAD-7", *Archives of Internal Medicine*, Vol. 166
5 No.10, pp. 1092-1097.
6

7
8 Van Hout, B., Janssen, M. F., Feng, Y. S., Kohlmann, T., Buschbach, J., Golicki, D., ... and
9 Pickard, A. S. (2012), "Interim scoring for the EQ-5D-5L: mapping the EQ-5D-5L to EQ-
10 5D-3L value sets", *Value in Health*, Vol. 15 No.5, pp. 708-715.
11

12 Wittchen, H. U., Jacobi, F., Rehm, J., Gustavsson, A., Svensson, M., Jönsson, B., ... and
13 Steinhausen, H. C. (2011), "The size and burden of mental disorders and other disorders of
14 the brain in Europe 2010", *European Neuropsychopharmacology*, Vol. 21 No.9, pp. 655-679.
15
16
17
18
19
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21
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Figure I. Participant flow diagram

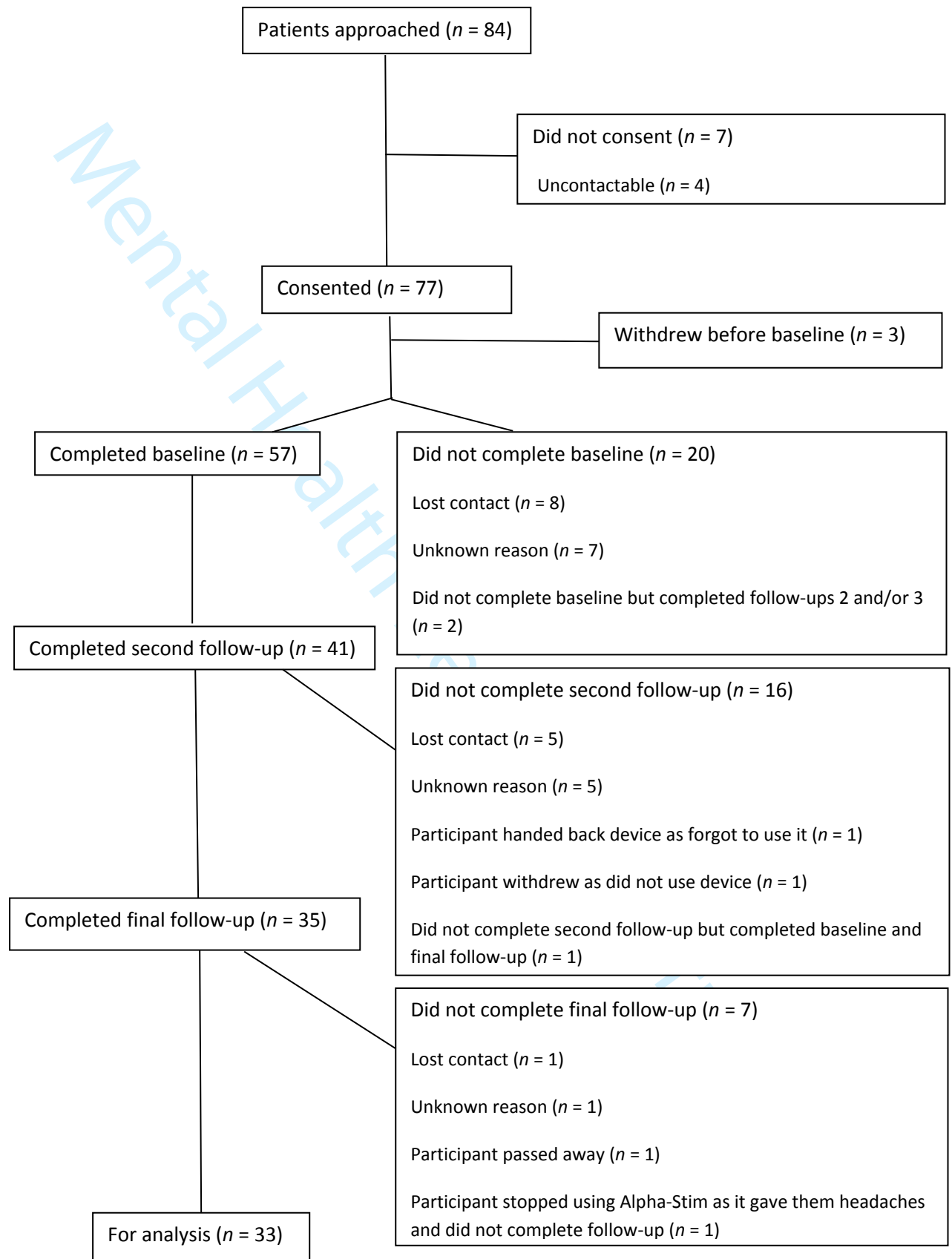


Table I. Baseline characteristics ($n = 57$).

Variable	Mean \pm SD (Min-Max)
GAD-7	16.05 \pm 4.43 (4-21)
PHQ-9	17.54 \pm 5.42 (7-27)
EQ Health Index	.41 \pm .35 (-.35-.88)
EQ VAS	46.82 \pm 25.45 (0-95)

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Table II. Means and standard deviations within each dimension across time with corresponding mean variation, significance, and effect size

EQ-5D-5L Dimension	Baseline	Week 3	Week 6	<i>F</i>	<i>p</i>	μ^2
	<i>M (SD)</i>	<i>M (SD)</i>	<i>M (SD)</i>			
Mobility	1.81 (1.06)	1.63 (1.04)	1.66 (.90)	1.00	.374	
Self-care	1.94 (1.22)	1.88 (1.07)	1.56 (.80)	2.179	.132	
Usual activity	2.88 (1.45)	2.34 (1.36)	2.19 (1.03)	4.223	.019*	.120
Pain/discomfort	2.44 (1.29)	2.53 (1.34)	2.16 (1.08)	2.45	.110	
Anxiety/depression	3.25 (1.11)	2.53 (1.16)	2.69 (.93)	8.99	< 0.001*	.225
Health index score	.46 (.36)	.55 (.37)	.63 (.26)	6.150	< 0.001*	.166
EQ-VAS score	51.69 (22.19)	58.78 (20.77)	62.56 (20.60)	3.956	.024*	.113

*Significant at $p < 0.05$ level

Table III. Percentage of participants reporting levels 1 to 3 on EQ-5D-5L by dimension and time

EQ-5D-5L Dimension		Baseline	Week 3	Week 6
Mobility	Level 1	49.1	60.5	54.3
	Level 2	40.3	25.6	40.0
	Level 3	10.6	13.9	5.7
Self-care	Level 1	43.9	41.9	57.1
	Level 2	45.6	50.1	42.9
	Level 3	10.5	7.0	-
Usual activity	Level 1	21.2	27.9	25.7
	Level 2	45.6	46.5	60.0
	Level 3	33.2	25.6	14.3
Pain/discomfort	Level 1	31.6	34.9	31.4
	Level 2	54.4	46.5	54.3
	Level 3	14.0	18.6	14.3
Anxiety/depression	Level 1	1.8	16.3	5.7
	Level 2	49.1	60.4	74.3
	Level 3	49.1	23.3	20.0

Level 1 consists of responses where no problems are reported. Level 2 indicated responses reporting a mild to moderate level of issues on a given dimension, and level 3 refers to severe to extreme issues reported.

Table IV. Descriptives from the usage survey

Usage	<i>n</i> (%)
Frequency of use:	
Every day	6(43)
Virtually every day	5(36)
Most days	1(7)
Half the time	1(7)
A couple of times	1(7)
Routinely used at set time	
Yes	12(86)
No	2(14)
Anxiety reduced	
Yes	8(57)
No	2(14)
Don't know	1(7)
No answer	3(21)
Was it useful	
Yes	9(64)
No	3(21)
Don't know	2(14)
Use it again	
Yes	8(57)
No	1(7)
No answer	5(35)