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"Flow" Transcranial Direct Current Stimulation (tDCS) for Depression Treatment in a Primary Healthcare General Practice—Depression, Functioning, and Health-Related Quality of Life Outcomes

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Abstract

Background: Flow FL-100 is a transcranial direct current stimulation (tDCS) device self-administered by a patient at home in combination with a software application that delivers wellbeing behaviour therapy training. tDCS has evidence of effectiveness in treating symptoms of depression. This post marketing study evaluated the effect of Flow on depression, functioning, and health-related quality of life for primary care general practice patients with depression symptoms. **Methods:** Open-label patient cohort design with no control group. Thirty-one adult patients completed six weeks of Flow treatment. Average age 45.6 years (SD = 13.72) range from 20-75 years; 24 (77.4%) females and six males (23.6%). Pre- and post-intervention assessment with participant self-report measures: Patient Health Questionnaire (PHQ-9), Work and Social Adjustment Scale (WSAS), and European Quality of Life Five Dimension (EQ-5D-5L). **Results:** PHQ-9 reliable improvement and remission rates were 58.1% and 32.3%. There was a significant improvement in PHQ-9 and WSAS with large effect sizes. EQ-5D-5L results showed significant improvements in three dimensions and the health index score with medium effect sizes. **Conclusion:** Flow tDCS can be delivered through a primary healthcare general practice service and patients use it as prescribed and complete treatment course. tDCS has evidence as an effective depression treatment, the widespread availability of tDCS in primary care general practice should be

considered.

Keywords

Cranial Electrotherapy Stimulation (CES), Depression, Quality of Life, Functioning, Transcranial Direct Current Stimulation (tDCS)

1. Introduction

Depression is experiencing a low mood and loss of pleasure or interest in activities, and can include symptoms such as poor concentration, feelings of low self-worth, hopelessness, suicidality, disrupted sleep, and fatigue (World Health Organization, 2023). In Great Britain (GB), around one in six (16%) of the general population experience depression (Office for National Statistics, 2022). Depression is the most prevalent mental illness and the largest contributor to global disability (World Health Organization, 2023). Depression symptoms can have a severe negative impact on everyday functioning and quality of life (Lépine & Briley, 2011; World Health Organization, 2023) and are the most common mental illness factor determinant of deaths by suicide (Vigo et al., 2016).

Non-invasive brain neurostimulation (NIBS) techniques to treat depression include transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS) (Atkinson-Clement et al., 2024), TMS is an effective and established depression treatment (Griffiths et al., 2022). Transcranial direct current stimulation (tDCS) is non-invasive brain stimulation by weak electrical currents (0.5 - 2.5 mA) (Grycuk et al., 2021). Electrode placement for treating depression is typically with the anode over the left dorsolateral prefrontal cortex (DLPFC) (F3) and cathode over the right DLPFC (F4) (Fregni et al., 2021). tDCS mechanisms of action include significant gray matter increases in brain regions functionally connected with the stimulation target, including the bilateral DLPFC, bilateral posterior cingulate cortex, subgenual anterior cingulate cortex, the right hippocampus, thalamus and left caudate brain regions; tDCS leads to neurostructural changes at a predetermined brain target in depression and plasticity effects may propagate over brain networks (Jog et al., 2023). tDCS is safe (Razza et al., 2020) and generally reported by patients as acceptable and well-tolerated, with mild and transient physical sensations that usually do not prevent use: burning sensations (16.2%), skin redness (12.3%), scalp pain (10.1%), itching (6.7%), and tingling (6.3%) (Chhabra et al., 2020; Grycuk et al., 2021; Gordon et al., 2021).

Meta-analyses of the results of randomised sham-controlled trials show tDCS can significantly improve depressive symptoms and clinical response, with remission being significantly better than placebo sham stimulation (Mutz et al., 2018, 2019; Moffa et al., 2020; Razza et al., 2020) but these studies do not have long-term outcomes follow up. tDCS is effective as standalone treatment or in combination with other anti-depression treatments (Razza et al., 2020). The UK's National Institute for Health and Care Excellence (NICE)'s "Medtech in-

novation briefing" reported that tDCS could particularly benefit people whose symptoms have not improved with existing interventions, or who find side effects of antidepressants intolerable or unacceptable (NICE, 2023).

"Flow" combines tDCS (delivered by Flow FL-100 device) and software app-based wellbeing behaviour training (physical exercise, nutrition, mindfulness, sleep, and choosing actions). In a 24-participant open-label single-arm feasibility study of Flow FL-100, a significant improvement in depressive symptoms after six weeks of treatment was maintained at 3 and 6 months (Woodham et al., 2022). A randomised sham-controlled trial of Flow FL-100 found significant improvement in depression symptoms relative to sham (Woodham et al., 2023). Qualitative studies undertaken on experience of Flow tDCS found most patients reported that Flow improved depression symptoms, was acceptable, and would recommend it to others (Rimmer et al., 2022, Griffiths et al., 2023; Griffiths et al., 2024).

Pharmacotherapy used for depression with evidence of effectiveness includes selective serotonin reuptake inhibitors (SSRIs) and serotonin norepinephrine reuptake inhibitors (SNRIs); however, antidepressant first-line treatment is effective in only around 37% of people (Rush et al., 2006; NHS Digital, 2022). When compared with placebo, the incremental effectiveness of antidepressants may be modest, with only one in nine patients experiences a benefit (Hengartner & Plöderl, 2018). Antidepressant adverse side effects can include nausea, fatigue, weight gain, tremors, sexual dysfunction, insomnia, and gastrointestinal problems (Cascade et al., 2009); side effects can result in additional costs, for example, additional GP visits (Mark et al., 2011). Antidepressants are not an acceptable option for some people, between 18% and 30% of people stop using SSRIs (Mochcovitch et al., 2017). There can also be a high risk of relapse (Culpepper et al., 2015), withdrawal effects can be long-lasting and severe (Davies & Read, 2019), and use can result in increased suicide risk (Hengartner & Plöderl, 2019).

Psychotherapy is recommended for depression, with recovery rates of around 50% for those who complete treatment, but 60% of people drop out after two sessions or less and, as it is delivered over multiple sessions over a period of several weeks or months, it is costly and lengthy; in the UK the average waiting time for psychotherapy to start is 21 days (Gyani et al., 2013; Griffiths & Griffiths, 2014; NHS Digital, 2022). In addition, some people do not find psychotherapy to be an acceptable option due to, for example, cultural beliefs, mobility issues, travel costs, or work and caring responsibilities (Bandelow et al., 2018).

Therefore, it is important that patients have a choice of options for depression treatment in addition to antidepressants and psychotherapy that best suit their lives, needs, and concerns. In this project, for the first time, Flow tDCS was offered through a United Kingdom (UK) primary care general practice to patients who reported symptoms of depression and outcomes were assessed in terms of feasibility, depression, functioning, and health-related quality of life.

2. Methods

2.1. Design

The study had an open-label patient cohort design with no control group. Patients completed pre- and post-intervention self-report measures.

2.2. Approval

Approval was granted by the review panel of the NHS Trust (Ideas Forum: reference IFFLOW) leading the evaluation and by the NHS primary care provider consortium. All participants provided informed consent. The study was delivered in accordance with the Declaration of Helsinki.

2.3. Medical Records

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

2.4. Setting

Participants were recruited through a primary healthcare general practice (GP). Flow was self-administered at home by participants living in the community. Flow Neuroscience AB (manufacturer of Flow device) provided GPs and other healthcare staff with training.

2.5. Inclusion/Exclusion Criteria

The inclusion criterion was age 18 and over, and the patient reporting depression symptoms.

Exclusion criteria:

1) Epilepsy (or having a history of seizures).

2) Having a defect in the neurocranium and/or a cranial implant.

3) Having an active, implanted medical device (e.g., cardiac pacemaker, spinal cord stimulator, vagal nerve stimulator, auricular stimulator, deep brain stimulating electrodes, cochlear implant, implanted hearing aid or defibrillator) or other implanted, metallic, or electronic device.

4) A neurological condition.

5) A history of hypomanic/manic episodes.

2.6. Procedure

Patients were selected by their GP if they met the inclusion/exclusion criteria and were provided with information about the treatment and evaluation. Participants stayed on the same medication and continued any current psychological interventions they were undertaking. Informed consent was obtained prior to beginning treatment. Participants could withdraw consent or stop treatment at any point without the need to provide a reason. Following informed consent, participants collected the Flow device and instructions from the GP reception and completed three self-report measures. Participants were informed about

Flow Neuroscience AB's website which provides information, training on use, and email support. Follow-up measures were collected after six weeks of treatment.

2.7. Intervention

Flow FL-100 is a Conformite Europeene (CE) marked Class IIa medical device for the treatment of major depressive disorder (MDD) and has United States (US) Food and Drug Administration (FDA) "Breakthrough Device" designation, indicating its potential to provide effective treatment. Flow can be purchased directly by anyone via the manufacturer's website in the European Union and other European countries. Flow has been used by >15,000 users in UK/EU and is offered by >70 private healthcare institutions.

In the treatment protocol, the patient remains awake and self-administers five sessions per week for the first three weeks and then three sessions per week for the following three weeks: 24 sessions, with a maximum of one 30-minute session per day. After the initial six-week period, patients can choose to self-administer up to 3 sessions per week for as long as they choose. This is Flow Neuroscience AB's standard protocol.

Flow treatment was concurrent with any current treatment, e.g., antidepressant medication, face-to-face psychotherapy, or any online psychotherapy. The anode was positioned over the left dorsolateral prefrontal cortex (DLPFC) (F3 on the international 10/20 EEG system) and the cathode over the right DLPFC (F4); stimulation is 2 mA for 30 min. On the Flow mobile phone software app, seven brief (around 20 minutes, pace of completion chosen by user) healthy lifestyle behaviour therapy training sessions are available for users to optionally engage with. These provide information about the links between behaviour and wellbeing and how to take actions to improve wellbeing and reduce depressive symptoms. They are titled: "The basics", "Choosing your actions", "Mindfulness meditation", "Exercise for your brain", "The anti-depression diet", "Therapeutic sleep", and "Looking back and planning ahead".

The Flow mobile phone software app is used to control the Bluetooth-connected Flow FL-100 tDCS headset via the user's smartphone. Flow also provides depression symptom level tracking that enables users to monitor their progress/symptoms. This is done by the completion of the nine-question Montgomery-Åsberg Depression Rating Scale Self-report (MADRS-S) (Montgomery & Åsberg, 1979) via the user's smartphone prior to a tDCS session. Flow also provides an integrated platform for the patient's GP, with the ability to monitor patients, and customise protocols remotely.

2.8. Measures

The Work and Social Adjustment Scale (WSAS) is a self-report measure of functional impairment attributable to an identified problem (e.g., depression) (Marks, 1986). The five questions on impairment to work, home management, social leisure, private leisure, and close social relationships are each scored zero (not at

all) to eight (very severely). The WSAS is a reliable, valid, and sensitive to change outcome measure (Mundt et al., 2002). Severe functional impairment is 20 and over and scores below 10 are associated with subclinical populations; a score of 9 or below is the clinical (recovery) cut off (Hammond et al., 2012).

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 & Borglin, 2011). A score of 9 or below is the clinical remission cut off.

European Quality of Life Five Dimension (EQ-5D-5L) (EuroQol Group, 1990; van Hout et al., 2012) is a 5-item questions and visual analogue scale (VAS) self-rated measure of health-related quality of life and overall health status developed by EuroQol group to provide a simple, standardised measure for a clinical appraisal (EuroQol Group, 1990). It comprises five dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety/depression), each of which is measured within five 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 measuring 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. The EQ VAS is a subjective measure of a participant's current health, ranging from 0 (worst health imaginable) to 100 (best health imaginable). The EQ-5D-5L has 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 measure of health status widely used in national health surveys in worldwide and in clinical trials of health interventions (Brooks & Group, 1996; Herdman et al., 2011), and EQ-5D is recommended by the UK's National Institute for Health and Care Excellence (NICE) to estimate health state utility weights for quality-adjusted life year (QALYs) (NICE, 2019).

3. Results

3.1. Participant Characteristics

Thirty-one participants completed a six-week Flow tDCS treatment. Their average age was 45.58 years (SD = 13.72, age range from 20 - 75) and 24 (77.4%) were females. Twenty-five (81%) patients were taking antidepressants and six (19%) were not. Participants mean baseline scores were in the "moderately severe" range for depression (Kroenke et al., 2007). Baseline EQ-5D-5L crosswalk data values indicated participants had a low average holistic health index and EQ-VAS score compared to the general population; however, the dispersion was high. See **Table 1** for baseline scores of outcome measures.

Table 1. Baseline characteristics (n = 31).

Variable	Mean ± SD (Min-Max)
PHQ-9	16.00 ± 4.55 (5 - 24)
WSAS	20.74 ± 7.90 (8 - 36)
EQ Health Index	0.63 ± 0.21 (0.18 - 1.00)
EQ VAS	56.61 ± 16.70 (15 - 90)

3.2. PHQ-9

There was a single outlier in the data at the 6-week time-point, as assessed by inspection of a boxplot. The Shapiro-Wilk test found PHQ-9 scores to be normally distributed ($p > 0.05$) at both time points. The reduction in PHQ-9 scores from baseline (M = 16.00, SD = 4.55) to after the intervention (M = 8.48, SD = 5.93) was statistically significant, t (30) = 6.634, $p < 0.001$, a large effect size was observed (Cohen's d = 1.19), 95% CI [5.20, 9.83]. On average, there was a drop of 7.52 points (SD = 6.31). Reliable improvement and remission rates for PHQ-9 were 58.1% and 32.3%, respectively.

3.3. WSAS

There were two outliers in the data at the six-week time-point, as assessed by inspection of a boxplot. The Shapiro-Wilk test found WSAS scores to be normally distributed ($p > 0.05$) at both time points. The reduction in WSAS scores from baseline (M = 20.43, SD = 7.85) and to after the intervention (M = 11.80, SD = 8.99) was statistically significant, t (29) = 4.561, $p < 0.001$, a large effect size was observed (Cohen's d = 0.833), 95% CI [4.76, 12.50]. On average, there was a reduction of 8.63 points (SD = 10.37).

3.4. EQ-5D-5L

Table 2 illustrates the descriptive data for each of the five dimensions as well as the mean health index and VAS at baseline and after the six-week intervention. From baseline to week six, quality of life increased with an improvement of 0.11. Measured across ten years, this intervention adds 1.11 QALYs.

Data screening permitted the use of a paired-sample t-test to determine whether there was a statistically significant difference in participants' EQ dimensions, as well as their health index score and VAS at the 6-week data point. The improvement was statistically significant for three EQ dimensions ("usual activity", "pain/discomfort", and "anxiety/depression"), and for the overall health index score, with medium effect sizes.

Table 3 illustrates the data collected from the EQ-5D-5L tool and broken down by level 1 (patients reported no issues on the dimension), level 2 (patients reported mild to moderate levels of issue), and level 3 (patients reporting severe to an extreme level of issues). The greatest improvement was observed in the "usual activity" dimension, with severe/extreme levels of reported problems

Table 2. Means and standard deviations within each dimension across time with corresponding mean variation, significance, and effect size.

EQ-5D-5L Dimension	Baseline *M (SD)*	Week 6 *M (SD)*	*t*	*p*	*d*
Mobility	1.64 (0.98)	1.48 (0.81)	1.306	0.101	
Self-care	1.35 (0.71)	1.22 (0.50)	1.680	0.052	
Usual activity	2.16 (0.90)	1.48 (0.72)	3.992	<0.001*	0.717
Pain/discomfort	2.06 (1.06)	1.77 (0.92)	2.065	0.024*	0.371
Anxiety/depression	3.00 (0.89)	2.23 (0.92)	2.834	0.004*	0.509
Health index score	0.63 (0.21)	0.74 (0.20)	−2.406	0.011*	−0.432
EQ-VAS score	56.38 (17.06)	63.79 (26.68)	−1.243	0.112	

*Significant at $p < 0.05$ level.

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

EQ-5D-5L Dimension	Level	Baseline	Week 3
Mobility	1	64.5	67.7
	2	29.0	29.1
	3	6.5	3.2
Self-care	1	74.2	80.6
	2	22.6	19.4
	3	3.2	0.0
Usual activity	1	29.0	64.5
	2	67.7	35.5
	3	3.3	0.0
Pain/discomfort	1	38.7	48.4
	2	48.4	45.1
	3	12.9	6.5
Anxiety/depression	1	6.5	19.4
	2	74.2	74.2
	3	19.3	6.4

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.

doing usual activities dropping to 0% by the end of the intervention, while no problems with everyday activities rose by 36%. In terms of "anxiety/depression", reporting of no problems (level 1) increased by 13% and the level of severe/extreme issues dropped by 13%. A small improvement was seen in "pain/discomfort" dimension, with no pain increasing by 10% and the level of extreme pain dropping

by 6% at the end of treatment. No significant changes were observed in the "self-care" and "mobility" dimensions.

3.5. Correlations

Pearson's correlation coefficients indicated statistically significant correlations between PHQ-9 and EQ-5D-5L (r = −0.439), PHQ-9 and WASA (r = 0.690), and EQ-5D-5L and WASA (r = −0.528) at baseline. There was also a statistically significant correlation between PHQ-9 and EQ-5D-5L (r = −0.612), PHQ-9 and SWAS (r = 0.789), and EQ-5D-5L and SWAS (r = −0.473) after a six-week intervention, all $p < 0.001$.

4. Discussion

This study found that Flow can be provided to patients by a general practice primary healthcare service, and when offered patients will choose to use Flow. Flow was found to reduce impaired functioning and depression symptoms and increase health related quality of life in patients with symptoms of depression. The outcomes add evidence to support the effectiveness of tDCS in reducing depression symptoms (Mutz et al., 2018, 2019; Moffa et al., 2020; Razza et al., 2020; Woodham et al., 2022, 2023). In line with research evidence, this study's findings indicate that depression symptoms are negatively linked to quality of life and functioning, i.e., improvements in depression symptoms result in improvements in quality of life and functioning (Lépine & Briley, 2011; World Health Organization, 2023).

This study's results showed statistically significant improvements on the "ability perform usual activity" dimension measured by the EQ-5D-5L, and impaired functioning measured by the WASA. These findings indicate the positive impact of Flow on mental health recovery and real-world functioning, factors highly valued by people in their everyday lives. Being able to engage in everyday activities and activities that are important and meaningful to an individual can contribute to their mental health recovery (Griffiths, 2009).

This present study's sample had higher average PHQ-9 baseline scores (PHQ-9 in the second highest "moderately severe" range) than reported by the average patient seeking help for depression from psychotherapy services in the corresponding geographical area (NHS Digital, 2022). This demonstrates the potential value of Flow for those with relatively severe depression. It supports the design in this study of offering Flow to those with symptoms of depression irrespective of severity, how long they have been experiencing depression or been receiving treatment for depression. This study shows that tDCS can be combined with other treatments, and previous research has shown this can possibly enhance overall outcomes (Razza et al., 2020).

This present study shows that the use of Flow may lead to relatively quick (six-week) improvement in depression symptoms. The time course of response of SNRIs and SSRIs is around 2 to 4 weeks to achieve significant benefits, respec-

tively; but it may take longer to achieve most of the improvement (Jakubovski et al., 2019). Therefore, Flow might be considered as a treatment where a relatively quick relief of symptoms is required, future studies with a three week and larger participant sample are needed to explore this further.

Flow tDCS may offer an alternative treatment for those experiencing depression symptoms who have failed to respond to medication or psychotherapy or who find medication side effects or factors related to psychotherapy unacceptable (waiting times, travel costs, time required, other commitments preventing attendance). The NHS "Mental health and wellbeing plan" states: "We know there are limitations to the current treatment offer. More needs to be done… to diversify the range of treatments available" (Department for Health and Social Care, 2023). Primary care general practice are well-placed to deliver tDCS treatment as most people first seek help for depression through a GP and many patients are treated by their GP for long-term or recurrent depression.

Some participants did not experience remission or reliable change following the use of Flow, and it is not effective for everyone. GPs need to prepare their patients for this potential outcome and ensure that patients receive ongoing support, and suggest other potential treatments if tDCS does not provide relief from depression symptoms. Patients need to know that they may need to try a number of treatment options.

There were several limitations of the study. There was no control group, treatment with Flow tDCS was open-label and adjunct to any existing depression or other treatments or therapies. Additional diagnosis was not reported. The sample was over-represented by females, so the results are less generalisable to males. This study collected outcome measures after six weeks of treatment, with no later follow-up data collection; it is recommended that future studies employ additional follow-up data collection points: 12, 24 and 36 weeks.

5. Conclusion

This study demonstrated that Flow tDCS could be fully and effectively integrated into a primary care depression treatment pathway. The study team found that GPs are willing to offer and primary care patients will choose to use Flow, providing evidence of the acceptability of and demand for tDCS. This study developed an effective process of incorporating tDCS as a treatment offered in primary care. This study's findings provide evidence that Flow tDCS can be effective against depression symptoms when offered through general practice primary healthcare services for patients with depression symptoms. Addressing depression symptoms through a general practice primary healthcare service potentially reduces demand on primary care, secondary care, A&E, and psychotherapy services; and, therefore, may reduce healthcare costs.

It is important to be able to offer patients a wide choice of effective depression treatment options. There is goal to offer personalized depression treatment (to better target people who are likely to benefit), research is required to understand

individual response differences, for example, in brain structure and function that can affect response to tDCS, and what factors determine response. This study's results support the use of Flow tDCS as a treatment option for people with symptoms of depression. In many countries, people can buy and use Flow themselves and some private clinicians prescribe use, but the awareness and availability through healthcare systems of this device is low, and cost is prohibitive for many (around £400 GBP). Availability through free-to-access universal healthcare systems such as the UK's NHS would address inequality of access issues.

Consideration needs to be given as to when a patient is offered tDCS, i.e., first, second or third line treatment. It is less costly than a course of face-to-face psychotherapy and more convenient as it is delivered at home, and it does not have the side effects of antidepressant medication. Further research could compare effectiveness of tDCS with antidepressants and/or psychotherapy and investigate the value of tDCS for depression in combination with other treatment (such as antidepressants and/or psychotherapy). More evidence is required on the long-term effectiveness of tDCS and the potential need for ongoing maintenance sessions to sustain benefits.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

Atkinson-Clement, C., Junor, A., & Kaiser, M. (2024). *A Large-Scale Online Survey of Patients and the General Public: Preferring Safe and Noninvasive Neuromodulation for Mental Health*. https://doi.org/10.1101/2024.01.10.24301043

Bandelow, B., Sagebiel, A., Belz, M., Görlich, Y., Michaelis, S., & Wedekind, D. (2018). Enduring Effects of Psychological Treatments for Anxiety Disorders: Meta-Analysis of Follow-Up Studies. *The British Journal of Psychiatry, 212,* 333-338. https://doi.org/10.1192/bjp.2018.49

Brooks, R., & Group, E. (1996). EuroQol: The Current State of Play. *Health Policy, 37,* 53-72. https://doi.org/10.1016/0168-8510(96)00822-6

Cascade, E., Kalali, A. H., & Kennedy, S. H. (2009). Real-World Data on SSRI Antidepressant Side Effects. *Psychiatry (Edgmont), 6,* 16-18.

Chhabra, H., Bose, A., Shivakumar, V., Agarwal, S. M., Sreeraj, V. S., Shenoy, S., & Venkatasubramanian, G. (2020). Tolerance of Transcranial Direct Current Stimulation in

Psychiatric Disorders: An Analysis of 2000+ Sessions. *Psychiatry Research, 284,* Article ID: 112744. https://doi.org/10.1016/j.psychres.2020.112744

Culpepper, L., Muskin, P. R., & Stahl, S. M. (2015). Major Depressive Disorder: Understanding the Significance of Residual Symptoms and Balancing Efficacy with Tolerability. *The American Journal of Medicine, 128,* S1-S15. https://doi.org/10.1016/j.amjmed.2015.07.001

Davies, J., & Read, J. (2019). A Systematic Review into the Incidence, Severity, and Duration of Antidepressant Withdrawal Effects: Are Guidelines Evidence-Based? *Addictive Behaviors, 97,* 111-121. https://doi.org/10.1016/j.addbeh.2018.08.027

Department for Health and Social Care (2023). *Mental Health and Wellbeing Plan: Discussion Paper*. https://www.gov.uk/government/calls-for-evidence/mental-health-and-wellbeing-plan-discussion-paper-and-call-for-evidence/mental-health-and-wellbeing-plan-discussion-paper

EuroQol Group (1990). EuroQol—A New Facility for the Measurement of Health-Related Quality of Life. *Health Policy, 16,* 199-208. https://doi.org/10.1016/0168-8510(90)90421-9

Fregni, F., El-Hagrassy, M. M., Pacheco-Barrios, K., Carvalho, S., Leite, J., Simis, M., & Brunoni, A. R. (2021). Evidence-Based Guidelines and Secondary Meta-Analysis for the Use of Transcranial Direct Current Stimulation in Neurological and Psychiatric Disorders. *International Journal of Neuropsychopharmacology, 24,* 256-313. https://doi.org/10.1093/ijnp/pyaa051

Gordon, M. S., Dux, P. E., & Filmer, H. L. (2021). *Not Quite All in Our Head: Intervention Is a Better Predictor of tDCS Mind-Wandering Effects than Subjective Beliefs about Experimental Results*. https://doi.org/10.1101/2021.11.14.468553

Griffiths, C. A. (2009). Sense of Coherence and Mental Health Rehabilitation. *Clinical Rehabilitation Journal, 23,* 72-78. https://doi.org/10.1177/0269215508095360

Griffiths, C. A., & 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, 20,* 28-35. https://doi.org/10.1108/MHRJ-06-2014-0022

Griffiths, C., da Silva, K. M., Leathlean, C., Jiang, H., Ang, C. S., & Searle, R. (2022). Investigation of Physical Activity, Sleep, and Mental Health Recovery in Treatment Resistant Depression (TRD) Patients Receiving Repetitive Transcranial Magnetic Stimulation (rTMS) Treatment. *Journal of Affective Disorders Reports, 8,* Article ID: 100337. https://www.sciencedirect.com/science/article/pii/S2666915322000300?via%3Dihub https://doi.org/10.1016/j.jadr.2022.100337

Griffiths, C., Walker, K., & Willis, A. (2024). A Qualitative Study Exploring the Experience and Value of Flow Transcranial Direct Current Stimulation (tDCS) and Behaviour Therapy Training Software Used at Home for Community Mental Health Team (CMHT) Patients with Symptoms of Depression. *Open Journal of Depression, 13,* 6-23. https://doi.org/10.4236/ojd.2024.131002

Griffiths, C., Walker, K., Jiang, H., Noel-Johnson, A., & Zafar, A. (2023). A Qualitative Study Exploring the Experience and Value of "Flow" Transcranial Direct Current Stimulation (tDCS) Device and Behaviour Therapy Training Software Application at Home for Symptoms of Depression. *Open Journal of Depression, 12,* 65-86. https://doi.org/10.4236/ojd.2023.124007

Grycuk, L., Moruzzi, F., Bardjesteh, E., Gaughran, F., Campbell, I. C., & Schmidt, U. (2021). Participant Experiences of Transcranial Direct Current Stimulation (tDCS) as a Treatment for Antipsychotic Medication Induced Weight Gain. *Frontiers in Psychol-*

ogy, 12, Article ID: 694203. https://doi.org/10.3389/fpsyg.2021.694203

Gyani, A., Shafran, R., Layard, R., & Clark, D. M. (2013). Enhancing Recovery Rates: Lessons from Year One of IAPT. *Behaviour Research and Therapy, 51,* 597-606. https://doi.org/10.1016/j.brat.2013.06.004

Hammond, G. C., Croudace, T. J., Radhakrishnan, M., Lafortune, L., Watson, A., McMillan-Shields, F., Jones, P., & Laks, J. (2012). Comparative Effectiveness of Cognitive Therapies Delivered Face-to-Face or over the Telephone: An Observational Evaluation Using Propensity Methods. *PLOS ONE, 7,* e42916. https://doi.org/10.1371/journal.pone.0042916

Hengartner, M. P., & Plöderl, M. (2018). Statistically Significant Antidepressant-Placebo Differences on Subjective Symptom-Rating Scales Do Not Prove That the Drugs Work: Effect Size and Method Bias Matter! *Frontiers in Psychiatry, 9,* Article ID: 373735. https://doi.org/10.3389/fpsyt.2018.00517

Hengartner, M. P., & Plöderl, M. (2019). Reply to the Letter to the Editor: "Newer-Generation Antidepressants and Suicide Risk: Thoughts on Hengartner and Plöderl's Re-Analysis". *Psychotherapy and Psychosomatics, 88,* 373-374. https://doi.org/10.1159/000502485

Herdman, M., Gudex, C., Lloyd, A., Janssen, M. F., Kind, P., Parkin, D., & Badia, X. (2011). Development and Preliminary Testing of the New Five-Level Version of EQ-5D (EQ-5D-5L). *Quality of Life Research, 20,* 1727-1736. https://doi.org/10.1007/s11136-011-9903-x

Jakubovski, E., Johnson, J. A., Nasir, M., Müller-Vahl, K., & Bloch, M. H. (2019). Systematic Review and Meta-Analysis: Dose-Response Curve of SSRIs and SNRIs in Anxiety Disorders. *Depression and Anxiety, 36,* 198-212. https://doi.org/10.1002/da.22854

Jog, M. A., &erson, C., Kubicki, A., Boucher, M., Leaver, A., Hellemann, G., & Narr, K. (2023). Transcranial Direct Current Stimulation (tDCS) in Depression Induces Structural Plasticity. *Scientific Reports, 13,* Article No. 2841. https://doi.org/10.1038/s41598-023-29792-6

Kroenke, K., Spitzer, R. L., & Williams, J. B. (2001). The PHQ-9: Validity of a Brief Depression Severity Measure. *Journal of General Internal Medicine, 16,* 606-613. https://doi.org/10.1046/j.1525-1497.2001.016009606.x

Kroenke, K., Spitzer, R. L., Williams, J. B., Monahan, P. O., & Löwe, B. (2007). Anxiety Disorders in Primary Care: Prevalence, Impairment, Comorbidity, and Detection. *Annals of Internal Medicine, 146,* 317-325. https://doi.org/10.7326/0003-4819-146-5-200703060-00004

Lépine, J. P., & Briley, M. (2011). The Increasing Burden of Depression. *Neuropsychiatric Disease and Treatment, 7,* 3-7. https://doi.org/10.2147/NDT.S19617

Mark, T. L., Joish, V. N., Hay, J. W., Sheehan, D. V., Johnston, S. S., & Cao, Z. (2011). Antidepressant Use in Geriatric Populations: The Burden of Side Effects and Interactions and Their Impact on Adherence and Costs. *The American Journal of Geriatric Psychiatry, 19,* 211-221. https://doi.org/10.1097/JGP.0b013e3181f1803d

Marks, I. (1986). *Behavioural Psychotherapy.* John Wright.

Mochcovitch, M. D., da Rocha Freire, R. C., Garcia, R. F., & Nardi, A. E. (2017). Can Long-Term Pharmacotherapy Prevent Relapses in Generalized Anxiety Disorder? A Systematic Review. *Clinical Drug Investigation, 37,* 737-743. https://doi.org/10.1007/s40261-017-0528-x

Moffa, A. H., Martin, D., Alonzo, A., Bennabi, D., Blumberger, D. M., Bensenor, I. M., & Brunoni, A. R. (2020). Efficacy and Acceptability of Transcranial Direct Current Stimulation (tDCS) for Major Depressive Disorder: An Individual Patient Data Meta-Analysis.

Progress in Neuro-Psychopharmacology and Biological Psychiatry, 99, Article ID: 109836. https://doi.org/10.1016/j.pnpbp.2019.109836

Montgomery, S. A., & Asberg, M. (1979). A New Depression Scale Designed to Be Sensitive to Change. *The British Journal of Psychiatry, 134,* 382-389. https://doi.org/10.1192/bjp.134.4.382

Mundt, J. C., Marks, I. M., Shear, M. K., & Greist, J. (2002). The Work and Social Adjustment Scale: A Simple Measure of Impairment in Functioning. *The British Journal of Psychiatry, 180,* 461-464. https://doi.org/10.1192/bjp.180.5.461

Mutz, J., Edgcumbe, D. R., Brunoni, A. R., & Fu, C. H. (2018). Efficacy and Acceptability of Non-Invasive Brain Stimulation for the Treatment of Adult Unipolar and Bipolar Depression: A Systematic Review and Meta-Analysis of Randomised Sham-Controlled Trials. *Neuroscience & Biobehavioral Reviews, 92,* 291-303. https://doi.org/10.1016/j.neubiorev.2018.05.015

Mutz, J., Vipulananthan, V., Carter, B., Hurlemann, R., Fu, C. H., & Young, A. H. (2019). Comparative Efficacy and Acceptability of Non-Surgical Brain Stimulation for the Acute Treatment of Major Depressive Episodes in Adults: Systematic Review and Network Meta-Analysis. *BMJ, 364,* l1079. https://doi.org/10.1136/bmj.l1079

NHS Digital (2022). *Psychological Therapies, Annual Report on the Use of IAPT Services-England, 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

NICE (2019). *Position Statement on Use of the EQ-5D-5L Value Set for England.* https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/technology-appraisal-guidance/eq-5d-5l

NICE (2023). *Flow Transcranial Direct Current Stimulation for Treating Depression. Medtech Innovation Briefing [MIB324].* https://www.nice.org.uk/advice/mib324

Office for National Statistics (2022). *Cost of Living and Depression in Adults, Great Britain: 29 September to 23 October 2022.* https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/mentalhealth/articles/costoflivinganddepressioninadultsgreatbritain/29septemberto23october2022

Peasgood, T., Brazier, J., & Papaioannou, D. (2012). *A Systematic Review of the Validity and Responsiveness of EQ-5D and SF-6D for Depression and Anxiety.* HEDS Discussion Paper, 12-15.

Razza, L. B., Palumbo, P., Moffa, A. H., Carvalho, A. F., Solmi, M., Loo, C. K., & Brunoni, A. R. (2020). A Systematic Review and Meta-Analysis on the Effects of Transcranial Direct Current Stimulation in Depressive Episodes. *Depression and Anxiety, 37,* 594-608. https://doi.org/10.1002/da.23004

Richards, D. A., & Borglin, G. (2011). Implementation of Psychological Therapies for Anxiety and Depression in Routine Practice: Two Year Prospective Cohort Study. *Journal of Affective Disorders, 133,* 51-60. https://doi.org/10.1016/j.jad.2011.03.024

Rimmer, R. M., Woodham, R. D., Cahill, S., & Fu, C. H. (2022). *Acceptability of Community-Based Transcranial Direct Current Stimulation (tDCS) in Major Depression: Mixed Methods Analysis of Individual Experiences.* https://doi.org/10.31234/osf.io/xfvwq

Rush, A. J., Trivedi, M. H., Wisniewski, S. R., Nierenberg, A. A., Stewart, J. W., Warden, D., & Fava, M. (2006). Acute and Longer-Term Outcomes in Depressed Outpatients Requiring One or Several Treatment Steps: A STAR* D Report. *American Journal of Psychiatry, 163,* 1905-1917. https://doi.org/10.1176/ajp.2006.163.11.1905

Van Hout, B., Janssen, M. F., Feng, Y. S., Kohlmann, T., Busschbach, J., Golicki, D., & Pickard, A. S. (2012). Interim Scoring for the EQ-5D-5L: Mapping the EQ-5D-5L to EQ-5D-3L Value Sets. *Value in Health, 15,* 708-715. https://doi.org/10.1016/j.jval.2012.02.008

Vigo, D., Thornicroft, G., & Atun, R. (2016). Estimating the True Global Burden of Mental Illness. *The Lancet Psychiatry, 3,* 171-178. https://doi.org/10.1016/S2215-0366(15)00505-2

Woodham, R. D., Rimmer, R. M., Young, A. H., & Fu, C. H. (2022). Adjunctive Home-Based Transcranial Direct Current Stimulation Treatment for Major Depression with Real-Time Remote Supervision: An Open-Label, Single-Arm Feasibility Study with Long Term Outcomes. *Journal of Psychiatric Research, 153,* 197-205. https://doi.org/10.1016/j.jpsychires.2022.07.026

Woodham, R. D., Selvaraj, S., Lajmi, N., Hobday, H., Sheehan, G., Ghazi-Noori, A. R., & Fu, C. H. (2023). *Home-Based Transcranial Direct Current Stimulation RCT in Major Depression*. https://doi.org/10.1101/2023.11.27.23299059

World Health Organization (WHO) (2023). *Depressive Disorder (Depression)—Fact Sheet*. https://www.who.int/news-room/fact-sheets/detail/depression