FLOW
NEUROSCIENCE

The Flow Data Pack

Welcome to the Flow Data Pack!

The Flow tDCS device – medically approved for MDD

Using electric currents to treat ailments is not exactly modern technology. For example, Scribonius Largus describes how ancient Romans used electric discharges from the torpedo fish to treat nerve pain.

However, the packaging and procedure has been improved quite a lot since then.

The specific technique used in Flow Neuroscience's brain stimulation device is called transcranial Direct Current Stimulation (tDCS). There is class A evidence (definite effect) for the ability of tDCS to improve depressive symptoms.

The research behind tDCS technology indicates a link between depression and hypoactivity in the left dorsolateral prefrontal cortex of the brain (the DLPFC). The Flow tDCS device uses the neurons' favourite tool of communication – electricity – to restore brain function in the area.

The device delivers a gentle electric current to the left DLPFC, which significantly increases the neurons' ability to reach action potential.

In contrast to Transcranial Magnetic Stimulation (TMS) or Electroconvulsive Therapy (ECT), the tDCS technique offers sub-threshold stimulation. The extremely mild current of 2 mA does not force neurons to fire, but rather *encourages* them to do so.

Over time, neurons in the targeted brain area are more likely to fire together and increase activity, thereby relieving depressive symptoms.

The gentleness of this treatment ensures that it's completely non-invasive and that side effects remain unusually rare and mild in comparison to other treatments. It also means that patients may need to wait 1-4 weeks to notice an improvement in their depression.

For a majority of patients, it's well worth the wait.

A 2024 RCT (the Empower study published in Nature Medicine) showed that the Flow tDCS device offered full remission for 57.5% of the 174 depressed participants at 10 weeks. 63.0% of the patients reported a 50% or more reduction of symptoms.

Read more about the effectiveness of the Flow treatment below.

Quality control of the Flow tDCS device

In the past, tDCS treatment was only available in-clinic under the direct supervision of a trained professional. Consequently, the treatment required time and resources.

To help clinicians meet the demands of a constantly growing depressed population, Flow Neuroscience has made tDCS available for patients to use at home.

Today, clinics can monitor more patients in less time thanks to the thorough review processes which ensure that the Flow tDCS device is completely safe and effective for at-home use.

The Flow tDCS device is currently approved as a medical device for at-home depression treatment in:

- **The EU, the UK and Switzerland (since 2019)**
- **Brazil (since 2020)**

An FDA approval for at-home use in the USA is in progress.

The British Standards Institution (BSI) evaluates the safety and efficacy of the Flow tDCS device. The BSI review is supported by several large-scale RCTs demonstrating the effectiveness and impact of tDCS. See the clinical trials below.

The Flow tDCS device is CE-marked as a Class IIa medical device. In contrast to Class I devices, the BSI has thoroughly reviewed clinical studies and published safety reports in order to conclude that the Flow tDCS device treats depression effectively and safely.

Thanks to a unique safety system, the Flow tDCS device has proven safe to use. It has been tested according to IEC 60601 for electrical medical device safety.

The Flow tDCS device received **FDA Breakthrough Device Designation** for at-home depression treatment in 2022. It's the first and only tDCS device to do so.

After-market data. Since receiving the CE-marking, the Flow tDCS device has been used by over 30 000 people in Europe. As part of the certification, Flow collects extensive data from these patients and reports it to the BSI annually. The procedure ensures that the real-world effects of using the Flow tDCS device align with the effects reported in the literature.

Pending approvals

Flow Neuroscience is targeting FDA approval in the USA.

The scientific board

The Flow tDCS treatment is supported by a scientific board of experts in psychiatry and neuromodulation:

Andrew Nierenberg

Professor of Psychiatry, Harvard University

Published > 500 papers, ranked top 1% of researchers for most cited papers in psychiatry worldwide.
Listed in Best Doctors in America in every edition since 1994.
Three-time listed in World's Most Influential Scientific Minds.

Allan Young

Professor of Psychiatry, King's College

Chair of Mood Disorders & Director of Centre for Affective Disorders (Psychiatry).
Listed as World's Most Influential Scientific Minds.

Joan A. Camprodon

Associate Professor of Psychiatry, Harvard University

Leads Lab for Neuropsychiatry & Neuromodulation at Harvard University.
Founding director of TMS service at Massachusetts General Hospital.

Corey Keller

Assistant Professor of Psychiatry, Stanford University

Leads the Stanford Laboratory for Personalized Neurotherapeutics.
Former CMO of Alto Neuroscience.

Andre Brunoni

Associate Professor, USP School of Medicine

Leading researcher in Neuromodulation.
Recognized as one of the most cited, influential researchers globally 2019-21.

NHS programmes

Flow Neuroscience is working with the NHS to offer Flow in several programmes across primary and secondary care, including Community Mental Health, Primary Care via GPs, Practitioner Health, Crisis Services and Postnatal Services. Flow is currently working with:

- Northamptonshire Health Foundations Trust
- Leicestershire Partnerships Trust
- Rotherham Doncaster and South Humber Trust
- West London
- NHS Practitioner Health

Below, you will find published findings from clinical trials using the Flow tDCS treatment within the NHS.

Effectiveness of tDCS and the Flow treatment

– Clinical trials and real-world results

There are over 10 000 peer-reviewed publications on tDCS, including numerous large-scale studies and meta-analyses. And the number increases each year.

tDCS's popularity surge is probably due to four main factors:

1. **Efficacy**
2. **Tolerability**
3. **Affordability**
4. **Ease of use**

Since 2020, there has been class A evidence (definite effect) for the ability of tDCS to improve depression.

Though it would be nearly impossible to mention all significant publications, below are a few important ones:

2013 – Brunoni et al: Clinical trial with 120 patients demonstrated that tDCS was significantly superior to placebo and even more effective when combined with an SSRI (Sertraline).

2016 – Bikson et al: An ambitious study found tDCS to be absolutely safe to use across a variety of populations and over 33 000 tDCS sessions. The team concluded:

"The use of conventional tDCS protocols in human trials (≤40 min, ≤4 milliamperes, ≤7.2 Coulombs) has not produced any reports of a Serious Adverse Effect or irreversible injury across over 33,200 sessions and 1000 subjects with repeated sessions. This includes a wide variety of subjects, including persons from potentially vulnerable populations."

2019 – Mutz et al: Systematic review, including a combined group of 6,750 patients, demonstrated that tDCS is comparable to TMS in efficacy. The authors concluded:

"Given that tDCS tends to be a less expensive treatment than transcranial magnetic stimulation, ECT, or psychotherapy, this finding is particularly relevant for policy makers who might consider tDCS as a clinical therapy outside the research setting."
Indeed, TMS devices are typically priced at a significantly higher cost than the Flow tDCS device.

2020 – Razza et al: Meta-analysis of 1,092 patients demonstrated that tDCS is superior to placebo.

2020 – Fregni et al: tDCS was classified as definitely effective for depression (Level A evidence).

2024 – Zheng et al: A systematic review and meta-analysis evaluated 56 randomised controlled trials regarding the therapeutic efficacy of tDCS. The analysis demonstrated that tDCS over the left DLPFC at 2 mA was effective in reducing depressive symptoms and showed promising effects in alleviating anxiety symptoms among individuals with diverse diagnoses.

Please note: *The careful process behind the CE marking of the Flow tDCS device ensures that the effects of using Flow align with the effects seen in the literature.*

The Empower Study

October 2024 – Woodham and colleagues presented one of the largest randomised, double-blind, placebo-controlled tDCS trials ever conducted for depression. The results were published in Nature Medicine in October 2024.

The study showed that active stimulation with the Flow tDCS device was superior to sham stimulation for the treatment of Major Depressive Disorder (MDD).

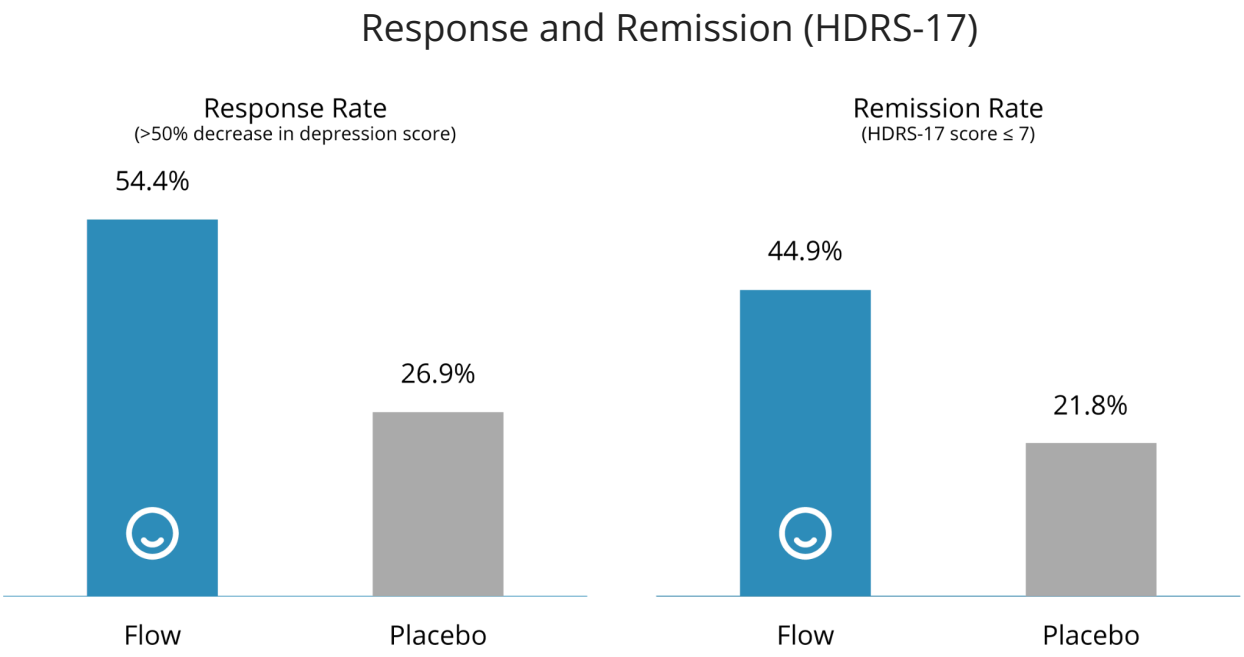
The study involved two research centres – the University of East London (UK) and the University of Texas (US).

174 participants with moderate to severe depression used the Flow tDCS device at home. The treatment protocol included 10 weeks of treatment with 3-5 stimulation sessions a week. Each session was 30 minutes long.

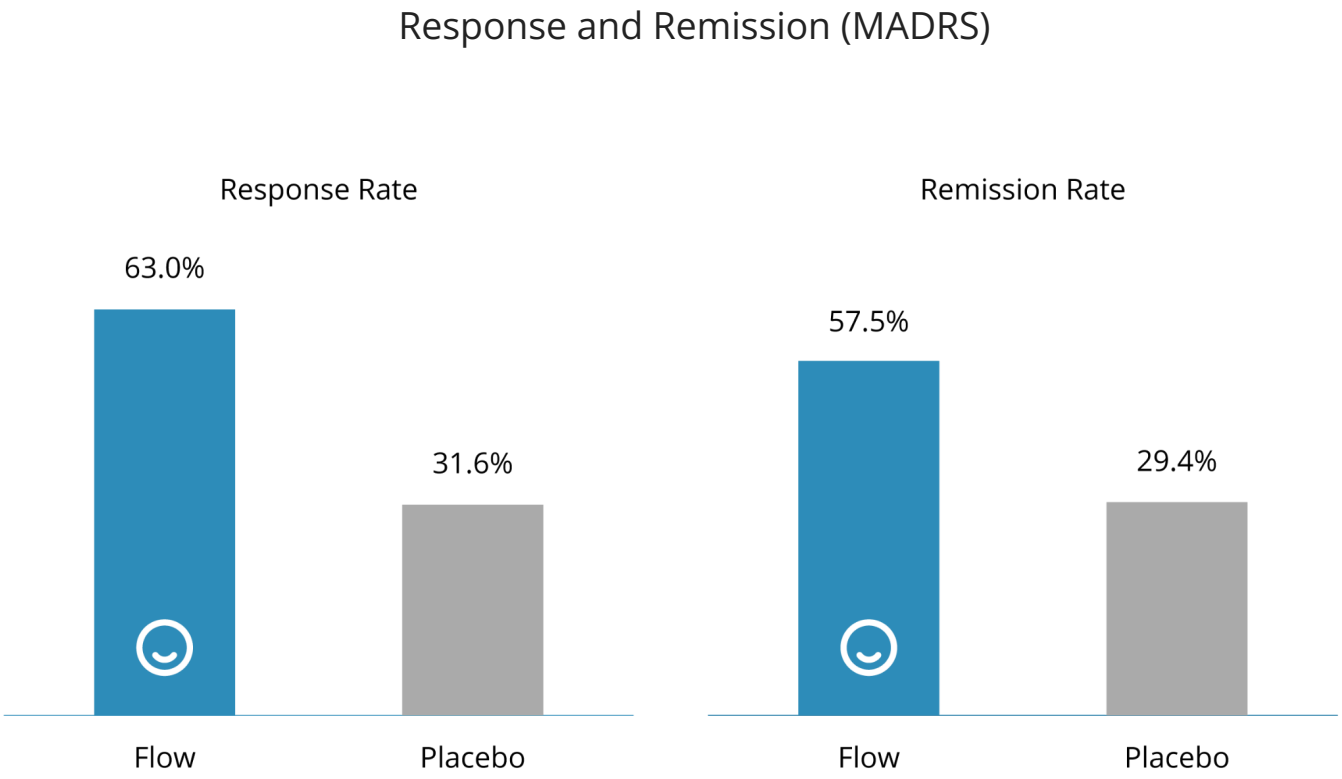
Outcomes were measured using the HDRS-17 and MADRS depression surveys.

Results:

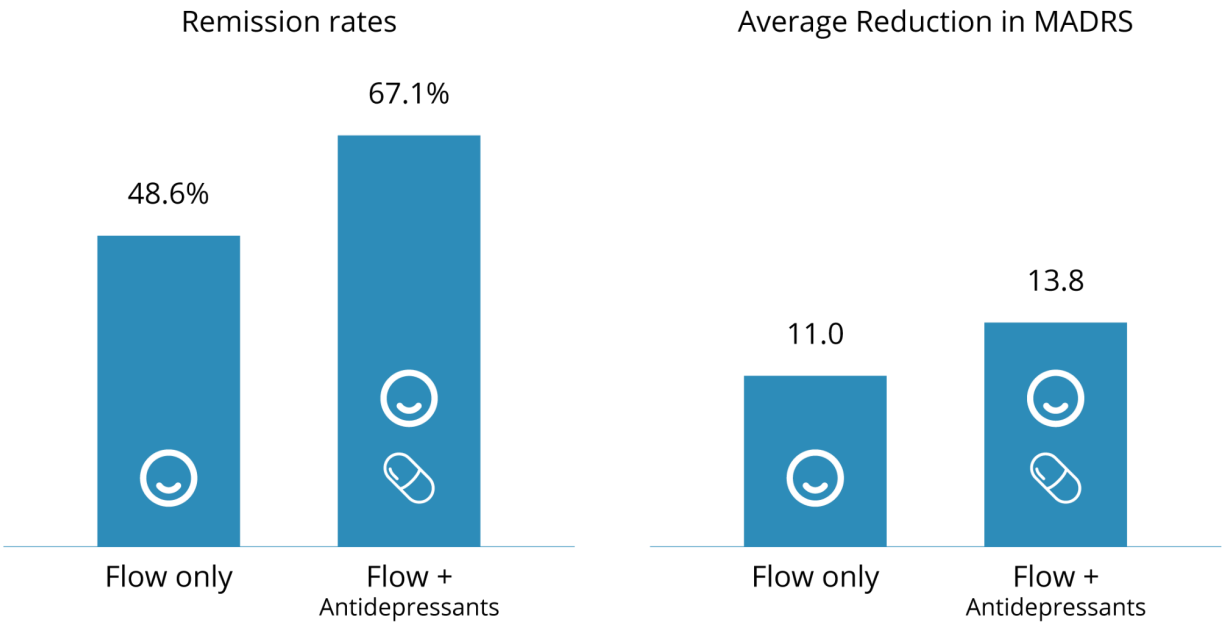
- **Results based on HDRS-17:** 44.9% remission (vs 21.8% placebo) and 54.4% response rate (vs 26.9% placebo) at week 10.



- **Results based on MADRS:** 57.5% remission (vs 29.4% placebo) and 63.0% response rate (vs 31.6% placebo) at week 10.



Participants who were on a stable dose of antidepressant medication showed greater improvements than those who didn't take antidepressants:



- No serious adverse events were reported.
- The only statistically significant adverse event was skin irritation (difference 6.9% (1.9% to 14.5%) $p = 0.03$).
- There were no differences in discontinuation rates between the treatment group and the control group.
- More information on the trial can be found here.

Studies conducted within the NHS

July 2024 – NHS Primary Healthcare General Practice: In this open-label cohort study, Griffiths and colleagues evaluated the effect of the Flow tDCS treatment on depression for primary care patients within the United Kingdom's National Health Service (NHS).

Adult participants used the Flow tDCS treatment at home, administering five 30-minute sessions for the first three weeks, and three sessions per week following this.

Outcomes were measured using the Montgomery-Åsberg Depression Rating Scale (MADRS-s).

Results:

There was a significant improvement in MADRS-s scores with large effect sizes at all time points.

At 3 weeks remission rates were between 29 and 30%.

At 6 weeks remission rates were between 33 and 34%.

At 10 weeks remission rates were 50%.

The study concluded that the Flow tDCS treatment is suitable to be delivered through a primary care general practice service and that patients will choose to use this treatment. They found the treatment effective for depression, both as an addition to and as an alternative to antidepressants and psychotherapy.

In addition, the research team noted:

“This present study shows that the use of Flow may lead to relatively quick (three-week) improvement in depression symptoms for some participants. The time course of response of SNRIs and SSRIs is around 2 to 4 weeks to achieve significant benefits; but it may take longer to achieve most of the improvement. Therefore, Flow might be considered as a treatment where a relatively quick relief of symptoms is required, future studies with a larger participant sample are needed to explore this further.”

(Griffiths et al., 2024)

Find more information about the study here.

May 2024 – NHS Primary Healthcare: In this open-label trial, Griffiths and colleagues (2024) evaluated the effect of the Flow tDCS treatment on depression,

functioning, and health-related quality of life in primary care patients with depressive symptoms.

Participants were offered the Flow treatment through a primary healthcare general practice (GP) within the United Kingdom's National Health Service (NHS).

These were the only exclusion criteria:

1) Epilepsy.
2) Having a defect in the neurocranium or a cranial implant.
3) Having an active implanted medical device.
4) A neurological condition.
5) A history of hypomanic/manic episodes.

31 adult patients with depressive symptoms completed 6 weeks of the Flow treatment at home. The study did not include a control group.

Results:

PHQ–9. Reliable improvement in depression, as measured by the Patient Health Questionnaire (PHQ-9), was 58.1% and the remission rate was 32.3% with a large effect size.

WSAS. There was a significant improvement in the Work and Social Adjustment Scale (WSAS) with a large effect size.

EQ-5D. In addition, the European Quality of Life Five Dimension (EQ-5D-5L) was administered. The scale comprises five dimensions – mobility, self-care, usual activity, pain/discomfort, and anxiety/depression.

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.

The greatest improvement was observed in the "usual activity" dimension.

Severe/extreme levels of problems doing usual activities dropped to 0% by the end of the intervention. No reported problems with everyday activities rose by 36%.

The researchers concluded:

“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.”

In addition, the research team noted that the study sample had higher average baseline depression scores (in the moderately severe range of the PHQ-9) than reported by the average patient seeking depression treatment in the area.

“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.”

Find more information about the study here.

August 2024 – NHS Maternal Mental Health: Baukaite and colleagues conducted an interpretative phenomenological study to investigate the value of the Flow treatment for depressed patients within the NHS Specialist Perinatal Mental Health Service and Maternal Loss Psychology Service.

The study included thirteen participants with depression. Five experienced maternal loss and eight reported postpartum depression.

Semi-structured interviews were conducted with the participants after six weeks with the Flow treatment.

Results:

Overall, the participants appreciated a non-medication treatment for depression. They reported improvements in:

- Depressive symptoms (including mood)

- Sleep quality
- General well-being

An analysis of the interview data revealed ten important themes:

1. Effortless collection, setup & navigation
2. Acknowledging the value of non-medication treatment options
3. Manageable discomfort, physical sensations, and side effects
4. Practical challenges in Flow device usage
5. Convenience and challenges of new routine
6. Divided engagement with training app
7. Comparatively short timeframes to notice improvements
8. Improvements in depressive symptoms, mood, and sleep quality
9. Motivated to implement positive behaviour
10. Overall positive addition to their lives

Participants reported additional benefits of Flow beyond symptom reduction:

“Participants reported a positive impact on broader aspects of life, including increased motivation, social interaction, and achievement of life goals. These findings underscore the holistic impact of Flow on participants’ overall well-being, highlighting its potential to promote resilience and improve quality of life beyond symptom reduction.

Several participants expressed feeling more energised and willing to engage in activities they previously avoided, such as going for walks or doing household chores. Many reported increased motivation, productivity, and optimism, alongside a reduction in anxiety and depressive symptoms.

Some noted positive changes in social interactions and a newfound ability to address personal challenges and responsibilities.

Additionally, participants observed improvements in eating habits, weight management, and the establishment of healthier routines, including regular exercise."

(Baukaite et al., 2024)

More information about the study can be found here.

July 2023 – NHS Primary Healthcare: Griffiths and colleagues performed a qualitative study using the Flow tDCS treatment in primary care within the United Kingdom's National Health Service (NHS).

The aim of the study was to explore the experience and value of using the Flow tDCS treatment for depression at home.

The patients were offered six weeks of the Flow treatment by their General Practitioner (GP). In addition to 24 home-based brain stimulation sessions, patients were offered to engage in the behaviour therapy training sessions included in the Flow app.

The results of the study provided support for offering Flow as a treatment option for depression in primary care.

The research team concluded:

"Flow has been successfully integrated into a primary care service depression treatment. It is important to offer patients an evidence-based alternative to existing depression treatments (antidepressant medication and talking therapies). The results support the use of Flow as a treatment option for people with symptoms of depression."

Of the 47 patients using the Flow treatment, 18 agreed to in-depth interviews about their experience.

Results:

Following the analysis of the interview data, four main themes emerged:

1. **Feasibility**
2. **Useability**
3. **Acceptability**
4. **Value**

Feasibility
The patients described how Flow was easily and conveniently integrated and used in combination with other treatments such as medication and talking therapies.

The initial process of getting Flow was easy, convenient, and patient friendly. Patients also described setting it up as user-friendly.

Useability
The patients found that they could fit Flow into their day-to-day routine, without too many problems. Side effects such as itching and tingling could easily be managed.

“It’s dead simple to be honest, once the app is on there, which is easy to download. I mean, I’m not particularly techie. Because I think anybody, especially when you get older… so simple…” (NHS patient)

The behaviour therapy training facilitated some positive behaviour changes. A majority of patients found it helpful.

“It gives you suggestions for habits and you know it is almost like a mini therapist, I really like that element and I’m finding it most helpful.” (NHS patient)

“I did love the therapeutic sleep training. It has made a massive difference to my sleep. I’ve since had no TV on, I’ve done my meditation before bed, and then it’s been like pitch black…” (NHS patient)

Acceptability

For the majority of the patients, the fact that Flow was an alternative to medication to treat their depression was an important factor.

For those still on medication, Flow was perceived by some as a means to eventually help them come off their medication.

Flow was perceived to be something that worked. Many of the patients felt very strongly about keeping Flow.

“Because I felt it was making a huge difference. After six weeks, I stopped using it with the idea of giving it back. But after a week, I could feel that my mood was going backward again. Then I used it for the following couple of days. And I was back to being how I was. So yeah, then I was, no it’s mine you are not having it back!” (NHS patient)

Value

The Flow treatment had a significant positive impact on patients’ depression and anxiety.

Several talked about feeling like their old self. Others felt it had relieved them of their depression and anxiety completely.
In addition, patients reported improvements in mood, optimism, confidence, sleep and motivation.

“The effect it’s [Flow] had on me, and I think it’s been quite groundbreaking for me and my depression and anxiety, it’s been a life changer.” (NHS patient)

“I don’t feel sad anymore. I feel a lot more optimistic, and happier. I have just got a better outlook on things. Using the Flow changes your train of thought. My thinking is now positive rather than negative all of the time… and I feel better in my mood.” (NHS patient)

More information about the study can be found here.

February 2024 – NHS Community Mental Health Team: Another research team led by Griffiths explored participants' experiences and views on the Flow treatment for depression.

In this study, the Flow treatment was offered by a community mental health team (CMHT) within the United Kingdom's National Health Service (NHS). CMHTs deliver community-based mental health care for adults and older adults with severe mental health needs, as close to their home geographical area as possible.

All participants used the Flow treatment at home for at least 6 weeks.

The research team concluded:

"This study provides support for the acceptability, feasibility, useability, and value of Flow, evidencing that successful integration of Flow as part of CMHT patient's depression treatment can be achieved and can be beneficial. Findings suggest that patients in a CMHT (who often have an extensive history of depression and have tried various antidepressants and psychotherapies) were open, willing and want to try tDCS as an alternative treatment."

Out of 27 participants, 14 agreed to in-depth, semi-structured interviews.

Results:

From an Interpretative Phenomenological Analysis (IPA), 11 themes were developed.

1. **A user-friendly device, simple and easy to operate**
   Across all the narratives, the Flow device and its software app training was identified as easy to use. There were no issues in putting it on, starting it, functionality, or using the training.

   "But it's so easy to use. I think that's the key bit. I'm a bit of a technophobe, so am not awfully good with stuff like that, but it's very easy to use…it's almost idiot proof…now, it's just like second nature."

   (Henry)

2. **Mindset: willing and open, nothing to lose**
   Participants were willing, wanting, and needing to try an alternative treatment.

   "I haven't got any other option. There's…nothing else"
   (Robert)

3. **Active agent, taking control of own treatment**
   By using Flow, participants felt they were taking ownership and responsibility in their recovery.

   "You're empowered, to take steps in the right direction…, like have that kind of self-control and self-determination with it and being able to see and measure that impact over time."
   (Calum)

4. **Fits into my personal routine, flexible and convenient**

   "I can choose when I use it. It's certainly different to going to (mental health clinical) appointments, it is easier to use."
   (Jane)

5. **"Uncomfortable" (but not inhibitory) sensations using Flow**
   Participants experienced some physical sensations when using Flow that were perceived to be uncomfortable and unpleasant. The important factor was that it did not stop participants from using Flow regularly.

   "Tingly, sometimes stingy sensation, but nothing unbearable… I did get like dry patches on my head as well. But nothing unbearable, or that prevented me from using it." (Emma)

6. **Individual obstacles interfere with engagement**
   Some participants were at times unable to commit to using Flow, for a variety of reasons such as neurodiversity or external stresses.

   "I've been making my way through quite slowly, to be honest, I have ADHD, it very hard for me to sit down and concentrate."
   (Oliver)

7. **Offers a viable alternative to prior ineffective treatments**
   Several participants found that previous treatments have not worked for them, and Flow offers an alternative option. A non-pharmacological alternative was an attractive option.

   "I've suffered with mental health, for as long as I can remember, since childhood and looking back, I've been on so many different medications that have worked for a while, and then it's sort of back to square one again. So, anything I can have that will offer something different, a change that might be the one, is great."

   (Katherine)

8. **Gaining new or recapitulating existing knowledge to support recovery**
   The behavioural training app contributed to knowledge and behaviour changes.

   "It was a lot of stuff on the diet stuff that I didn't really know. I mean, I try to do some of it... I use a lot less processed foods... I eat a lot more nuts now. So, I have changed my behaviour."

   (Giles)

9. **Improvements in symptoms of depression, a lift in mood**

   "I just feel lighter, in general... I feel a lot more confident... I don't feel like I am so bogged down by my own brain. I feel less like the future is like a black void that's never going to come about, I feel less worthless... I feel more genuinely happy about things." (Oliver)

10. **Benefitting from "knock-on effects", a positive feedback loop**

    Through Flow lifting their depression, participants experienced cumulative effects. They were able to engage in things like a better diet, they had more energy, slept better, had more motivation, and they could enjoy engaging in activities (e.g., socialising, doing physical exercise), all of which in turn positively impacts on their depression.

    "But I feel now that my motivation has got better, definitely more motivation. I am getting knock-on effects, I am more motivated and finding it easier to go

out and socialise people that then has impacted my mental health positively because I'm feeling better for doing that."

(Sally)

11. **It didn't work for me, no noticeable impact**
    For three participants, they experienced no noticeable difference using Flow.

    "I don't think Flow made me any worse. I just don't think it's made me any better."

    (Robert)

More information about the study can be found here.

Real-World Results

In addition to conducting clinical trials, Flow Neuroscience collects data from the patients on the Flow platform (via the Flow app). Up to September 2024, over 30 000 patients have used the Flow treatment.

Depression scores are collected weekly from all patients using the Montgomery and Åsberg Depression Rating Scale (MADRS-s) – a reputable and clinically-validated questionnaire for measuring depressive symptoms.

According to the MADRS-s data, around 77% of Flow patients report an improvement of at least 3 points within 3 weeks. And 90% of the overall improvements usually occur within the first 10 weeks of treatment.

An analysis of the real-world data collected between March 2019 and March 2024 indicated that 28.7% of Flow patients had reached full remission within 3 weeks. At week 10, 36.3% had reached remission. The analysis included Flow patients with a minimum of 60% adherence to the standard treatment protocol.

The results are particularly noteworthy considering that a vast majority of Flow patients report that they have already tried one or several treatments before choosing Flow. A consistent theme in patient feedback and interviews is that antidepressant medication and/or psychotherapy have had little or no effect (or have been unmanageable due to side effects or waiting times). Consequently, treatment resistance may be over-represented among Flow patients.

Please note: *The rates of improvement may vary with time because of the constantly growing number of Flow patients.*

Why are the real-world results different from the clinical trial results?

In general, real-world results are expected to underperform controlled trials for depression treatment. This is typically due to:

1. **Patient selection in trials:** Real-world results usually include patients with multiple comorbidities, which can complicate results and make it more difficult to achieve an impact on depression scores.

2. **Clinician influence:** In clinical trials, clinicians usually administer depression score questionnaires and supervise patients through the treatment protocol. When it comes to real world data, patients report symptoms themselves. Clinicians tend to report bigger improvements in depression scores than patients.

Patient groups

The Flow treatment is evidence-based and medically approved (CE-marked Class IIa) to treat Major Depressive Disorder (MDD) in people aged 18 or older.

Flow can be used to treat all forms of MDD. It's effective for all levels of severity – from mild to severe depression.

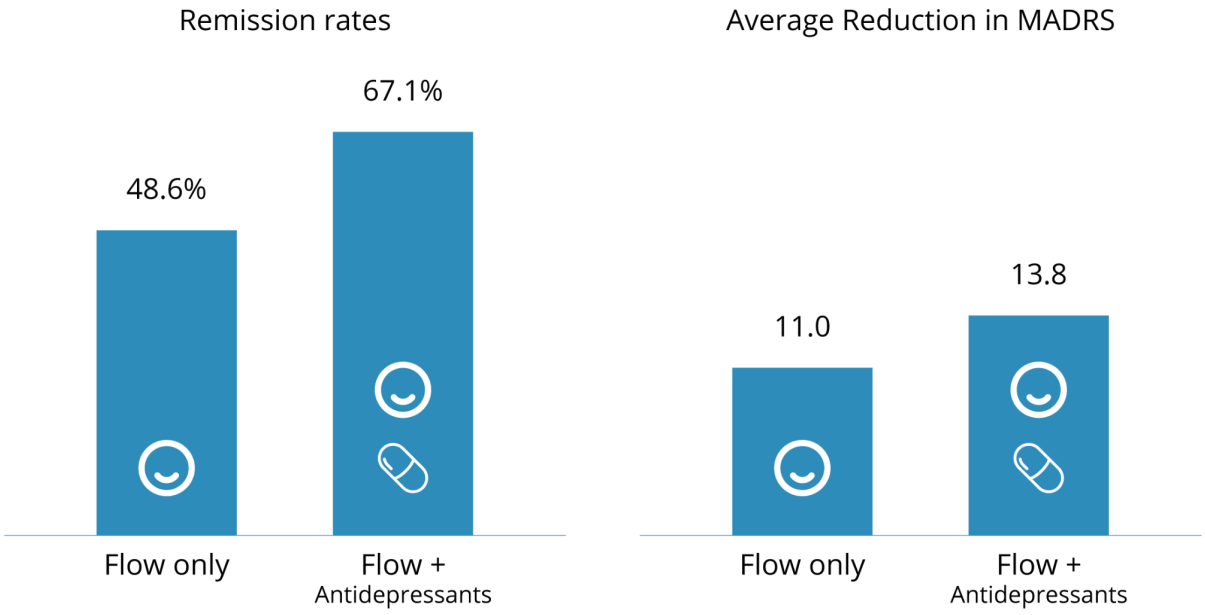
It can be used in primary care to treat a patient's first depressive episode, as well as in psychiatric care to treat a severe episode in a patient with recurrent depression, including those who have finished a course of ECT or TMS.

The Flow treatment is especially useful to offer patients who are reluctant or unable to take antidepressant medication, who do not experience full remission with antidepressants or who suffer from the side effects of antidepressants.

Note that there is no need to interrupt the patient's current treatment to begin the Flow treatment.

Flow can be offered as an add-on treatment to both antidepressant medication and psychotherapy. There is scientific evidence to suggest that combining tDCS treatment with antidepressant medication enhances the efficacy of both treatments (see for example Woodham et al., 2024, McLaren et al., 2018 and Brunoni et al., 2013).

In the Empower study (2024), 67.1% of participants who were on a stable dose of antidepressant medication reached remission with the Flow treatment within 10 weeks. Of participants who did not take antidepressants, 48.6% reached remission.



In case of long waiting lists, Flow can advantageously be offered while a patient is waiting to begin psychotherapy, rTMS or other forms of treatment.

Tapering antidepressant medications. Flow patients report that they have successfully been able to taper their antidepressant medication while using the Flow treatment. This practice is not yet studied in clinical trials and therefore Flow Neuroscience can't provide a best practice guide for tapering. We are constantly learning and improving our treatment, and we hope to soon be able to provide more detailed guidance.

Side effects

tDCS treatment is usually highly tolerable with mild or no side effects.

Real-world reports

Up to September 2024, over 30 000 people have used the Flow tDCS treatment. Less than 5% have spontaneously reported any side effects.

The most commonly reported side effects from the Flow treatment are:

- Headache (~1,5%)
- Skin irritation (~1%)
- Tinnitus (~0,6%)
- Mild skin burn (~0,3%)
- Anxiety (~0,2%)
- Skin redness (~0,1%)
- Worsening of symptoms (~0,1%)

Please note: *The percentages may vary slightly with time because of the constantly growing number of Flow patients.*

These side effects typically resolve within a few hours to no more than a few days. Flow patients tend to adapt to the treatment over time, resulting in a reduction or disappearance of side effects with continued use.

The high tolerability of tDCS is repeated across clinical trials where drop out rates usually don't differ between treatment group and sham/control group.

For more information, watch a webinar on contraindications, precautions and side effects.

Clinical evidence

Clinical studies, such as the one performed by Bikson (2016) and colleagues examining over 33 000 tDCS sessions, show that the current used in tDCS treatment protocols is not strong enough to cause any damage to the brain.

A 2020 study by Chhabra and colleagues, examining adverse effects of over 2000 tDCS sessions, found side effects to be mild, transient and well-tolerated. The most commonly reported side effects included:

- Burning sensations (16.2%)
- Skin redness (12.3%)
- Scalp pain (10.1%)
- Itching (6.7%)
- Tingling (6.3%)

The randomised, controlled Empower study (2024) included 174 participants and investigated the effects of the Flow tDCS treatment on moderate to severe depression.

The only statistically significant adverse event was skin irritation (difference 6.9% – 1.9% to 14.5%, $p = 0.03$).

Two participants in the active group reported burns at the left electrode site from using sponges which had dried out. Both burns healed, and neither developed into skin lesions.

Two people in the treatment group and in the control group respectively reported temporary tinnitus as a side effect.

There were no differences in discontinuation rates between the treatment group and the control group.

Read more about side effects and how to minimise them below.

Antidepressant medication. In comparison, a large international cohort (2018) including people from 38 different countries showed that a majority of antidepressant users experienced several adverse effects.

61% of the participants reported at least 10 adverse effects. Some of the most common ones are listed below:

- Feeling emotionally numb (reported by 71%)
- Feeling foggy or detached (70%)
- Feeling not like myself (66%)
- Sexual difficulties (66%)
- Drowsiness (63%)
- Reduction in positive feelings (60%)
- Suicidality (50%)

Withdrawal effects were reported by 59%. 40% reported an addiction to the drug.

How to minimise side effects from the Flow treatment

- Use the device pads as instructed in the app.
- Don't reuse pads.
- Don't moisten pads with water or another solution not recommended by Flow Neuroscience.
- Place the headset correctly, making sure that the electrodes are placed over the desired area as instructed in the app.
- Moisturise the skin after use.

This 1-minute video shows how to prepare and start the Flow device correctly.

For more information, watch a webinar on contraindications, precautions and side effects.

Skin reactions

Skin reactions are the most common side effects of tDCS, both in the literature and in the real-world data.

Skin reactions can happen for a number of reasons:

- **Disruption of the skin's protective barrier**: tDCS can disrupt the skin's outer layer, which acts as a protective barrier. This disruption can cause a loss of fats and make the skin more permeable, meaning things can pass through it more easily.

- **Damage to skin cells**: The electrical current used in tDCS can harm the cell walls of the main skin cells called keratinocytes. These cells are found in the top layer of our skin.

- **Release of inflammatory substances**: tDCS might make keratinocytes release substances that can cause inflammation in the skin. These substances include interleukins and tumor necrosis factor (TNF), which can lead to skin becoming inflamed.

- **Stimulation of the skin's defence**: tDCS might activate the skin's natural defence mechanisms, essentially making the skin more alert to potential threats.

In the short term, the Flow treatment might lead to mild erythema or itching at the electrode site. These effects are generally transient and resolve after the termination of stimulation.

Long-term use of tDCS can lead to more pronounced skin changes, such as hyperkeratosis. Typically the appearance is of dry, sometimes flaking skin which can be red or slightly darker tone of skin colour (hyperpigmented). If not moisturised regularly the skin can also become thicker. The risk of developing tolerance or "hardening" to these effects is not well-documented and might vary among individuals.

How to reduce the risk of skin reactions

Skin preparation:

- The skin should be dry and clean before using the Flow device. There should be no oil, make up or other products on the skin.

- When cleaning the forehead before treatment, avoid wiping too vigorously because that can lead to more unevenness in the skin which means there can be more ‘hotspots’ for reactions to occur. If a cleanser is to be used, non-alcoholic and gentle wipe only. The cleanser should not leave any oil on the skin.

- Use new pads for every session and make sure they are moist.

- Regularly moisturise the skin. If the patient is prone to dry skin they are advised to apply moisturisers several times daily.

- Cool the skin with an ice pack for a few minutes before stimulation and make sure that the skin is dry before putting on the device. A cooling gel or cream is not recommended because the skin should be dry and clean before using the device.

- Avoid re-stimulating until the skin has settled.

Monitoring: Encourage patients, especially long-term users, to monitor the skin regularly for any signs of irritation or burns.

Please report any cases of skin burns to support@flowneuroscience.com.

Headaches

Clinical trials often report similar rates of headaches in both active and sham tDCS groups. This suggests that the headache is not a direct result of the electrical current.

There's no clear neurological mechanism by which the low-level electrical current used in tDCS could directly cause headaches. The current is not high enough to induce pain or significant neural disruption that could lead to a headache.

The most common causes of headaches are:

- **Pressure from the headset or electrodes:** This is the most common cause of headaches. If these components are too tight, incorrectly positioned, or worn for an extended period, they can cause discomfort or tension headaches.

- **Psychological anticipation or anxiety:** In some cases, the anticipation of undergoing a tDCS session or anxiety about the procedure might contribute to tension-type headaches. This is psychological in nature and can occur among research participants in both active and sham groups.

- **Positional discomfort:** If the patient maintains an uncomfortable position during the tDCS session, this might contribute to the development of a headache.

- **Nocebo effect:** Similar to the placebo effect, the nocebo effect can occur when negative expectations lead to the reporting of symptoms. In sham groups, where no active stimulation is delivered, reports of headaches can be attributed to the nocebo effect.

- **Environmental and personal factors:** Other factors such as the room's lighting, noise, or personal predispositions (like a history of migraines or tension headaches) might also play a role.

Please report any cases of headaches to support@flowneuroscience.com.

Migraine

Migraines are intense headaches that can cause throbbing pain, nausea, and sensitivity to light and sound. They're different from regular headaches because they involve changes in brain blood flow and brain chemicals.

Here's how tDCS might affect migraines:

- **Neurovascular changes:** tDCS can change how blood flows in the brain. For some patients, this might trigger a migraine.
- **Neurotransmitter effects:** tDCS can affect brain chemicals like serotonin, which is involved in migraine pain. This might increase or decrease migraine occurrence.

How to reduce headache and migraine risk

Adjust the headset: Make sure the headset fits comfortably. It shouldn't be too tight or press too hard on any part of the head.

Relax before the session: Encourage patients to relax before starting the session. Deep breathing or listening to calm music might help reduce anxiety-related headaches.

Comfortable position: Encourage patients to sit or lie down comfortably during the session. Changing positions gently during the sessions can help.

Hydration: Encourage patients to drink plenty of water before and after the session. Staying hydrated can help prevent headaches.

Please report any cases of migraines to support@flowneuroscience.com.

Tinnitus

Tinnitus as a side effect of the Flow treatment is temporary, but in a small group of individuals it has persisted beyond a few weeks.

Research participants who receive active and sham tDCS report tinnitus at similar rates, suggesting it's not directly caused by the electrical current. In active tDCS treatment, tinnitus may be a consequence of the following processes:

- **Induced neural changes in auditory pathways**: In individuals without pre-existing tinnitus, tDCS over the DLPFC might inadvertently influence neural pathways connected to auditory processing. This unintended modulation may induce temporary changes in auditory perception, manifesting as tinnitus.

- **Individual variability in brain connectivity**: The brain's response to tDCS is highly individual, depending on factors like underlying brain structure and functional connectivity. In some people, DLPFC stimulation might unexpectedly affect areas involved in auditory processing due to unique neural network configurations.

- **Neurotransmitter fluctuations**: tDCS can alter neurotransmitter levels, which play a role in auditory processing. Changes in neurotransmitters like glutamate or GABA in or around auditory pathways could contribute to the perception of tinnitus in previously unaffected individuals.

How to reduce the risk of tinnitus

Correct electrode placement: Make sure the electrodes are placed as instructed in the app. Proper placement helps to ensure that the electrical current affects only the intended areas of the brain. The electrodes are placed high up on the forehead, approximately two finger-widths above the eyebrow. Sometimes the electrodes go into the hair line, which is fine.
This 1-minute video shows how to correctly prepare and start the Flow device.

Encourage patients to stay relaxed: Sometimes, stress or tension can contribute to tinnitus.

In case a patient experiences tinnitus, instruct them to:

- Pause the session.
- Write down when the tinnitus started and how long it lasted.
- Discontinue the treatment if tinnitus becomes a regular occurrence after the tDCS sessions.

Please report any cases of tinnitus to support@flowneuroscience.com.

White flashes/photopsia

Photopsia involves seeing flashes or flickers of light without an external light source. It's a harmless, visual disturbance that can result from various conditions affecting the eye or brain.

When using tDCS, photopsia may be induced by the stimulation of visual cortex areas or the modulation of neuronal activity that affects visual pathways. tDCS influences neuronal excitability and neurotransmitter systems, which may stimulate the visual cortex or visual pathways directly, leading to the perception of light flashes.

Photopsia is rare, and more commonly experienced when removing the device before shutting down or if the device powers down in the middle of a stimulation session due to low battery.

Most patients who use the Flow treatment never see these light flashes. If it does occur, the flashes disappear within a few seconds or straight after stimulation. Photopsia shouldn’t cause any other changes to the eye. However, should the patient experience blurry vision, pain or redness to the eye, they should be examined by a professional.

How to avoid photopsia:

- Make sure to power down the device via the app before removing it. Avoid removing the device before the stimulation has fully stopped.
- If the patient needs to remove the device during stimulation, instruct them to always use the pause button in the upper right corner of the app before removing the device.
- Make sure the device is charged before the session. It’s recommended to charge it once a week.
- Have a clean forehead before stimulating.
- Keep the smartphone within Bluetooth range of the device while stimulating.

- Never reuse refill pads.

Contraindications

There are no universal contraindications to using the Flow tDCS treatment.

The following conditions may require extra precautions, such as careful monitoring:

- Broken/inflamed/infected skin (for example psoriasis) at the site of the electrodes
- A cranial or intracranial implant
- The skull is not intact (eg. after a craniectomy)
- An active implanted medical, metallic or electronic device (such as a cardiac pacemaker, spinal cord stimulator, cochlear implant, implanted hearing aid or defibrillator)
- Epilepsy (or a history of seizures)
- Bipolar disorder

Please note that the Flow tDCS treatment is not licensed for use in pregnancy or for people below 18 years of age.

The treatment is safe to use while breastfeeding and with postpartum depression (PPD).

For more information, watch a webinar on contraindications, precautions and side effects.

Checklist for prescribing the Flow treatment

Download this checklist.

Use during pregnancy

Please note that the Flow treatment is not licensed for use in pregnancy.

There is no evidence in the literature to suggest that tDCS treatment could be harmful to use when pregnant. The electric current targets the brain directly without affecting the hormonal or digestive systems, making tDCS a tempting option for treating depression during the peripartum period.

However, more large-scale controlled trials are needed before any definitive conclusions can be drawn.

Today, the option to use tDCS during pregnancy should be carefully evaluated in each individual case.

Please note that the Flow treatment is safe to use while breastfeeding and with postpartum depression (PPD).

Encouraging research results for tDCS during pregnancy:

2022 – Laurin et al: A systematic review including seven studies and 33 women. No serious adverse effects for the mothers or children.

2019 – Vigod et al: A pilot randomised controlled trial showing promising results for tDCS during pregnancy. There were no serious adverse events.

2018 – Kurzeck et al: A systematic review concluding that the scientific evidence for tDCS during pregnancy is sparse but promising.

Use in children

The Flow treatment is only medically approved (CE-marked Class IIa) for adults aged 18 years or older with Major Depressive Disorder.

Further questions are referred to support@flowneuroscience.com.

Long-term use

There is promising evidence indicating that tDCS is safe to use long-term and can be effective at preventing relapse.

Daily tDCS sessions over the DLPFC have been used for 6 consecutive months without any adverse events, suggesting it is suitable for long-term use (see for example Im et al., 2019 on Alzheimer's disease).

There is no evidence to suggest that adverse events would increase beyond 6 months, but few such long-term studies exist. Randomised, controlled studies are still needed to draw firm conclusions about the long-term effects of tDCS use.

The following studies indicate the safety and efficacy of tDCS long-term treatment for depression:

2022 – Woodham et al: An open-label, single-arm feasibility study with long term outcomes investigated home-based tDCS treatment for depression.

At week 6, 22 participants (91.7%) showed a clinical response. 21 participants (87.5%) achieved remission.

At the 6-month follow up, clinical response was 21 out of 23 participants (91.3%). Remission was 17 out of 23 participants (73.9%).

The treatment was described as "very acceptable" or "quite acceptable" by all participants (n=24).

2021 – Razza et al: A systematic review and meta analysis investigated the follow-up effects of tDCS for depression. The analysis included 11 studies and showed that depressive symptoms continued to improve during the tDCS follow-up phase. It suggested that maintenance treatment might further improve the gains from acute tDCS treatment.

2019 – Aparicio et al: A 6-month follow-up clinical trial investigated the effects of tDCS for preventing depression relapse. The study included 24 patients who had responded to tDCS treatment in the acute treatment phase (15 tDCS sessions over 3 weeks). The participants were followed for up to 6 months.

The maintenance treatment included 2 weekly tDCS sessions.

tDCS was well tolerated, both during the acute phase and the follow up phase. No adverse events were reported.

The studies main findings were:

1) Patients presented approximately a 50% improvement in depression during the follow up phase.
2) The overall relapse rate was 26.5%.
3) Antidepressants treatment-resistant depression was associated with higher levels of relapse.

2013 – Valiengo et al: The SELECT-TDCS trial followed participants for 6 months and found that tDCS was effective both as a treatment in the acute phase of depression and as relapse prevention.

However, the relapse rate was higher in comparison to Aparicio's study (53% vs 26.5%). According to Aparicio (2019), the probable explanation was that the SELECT trial included significantly fewer maintenance sessions.

2 weekly maintenance sessions are likely more effective than 1.

Read more about How to Use the Flow Treatment long-term in Clinical Practice.

The treatment protocol

As a starting point, the following protocol is available for all patients:

The first 3 weeks of treatment – The Activation Phase

The patient completes 5 stimulation sessions a week at home (each session is 30 minutes long).

Week 4 and beyond – The Strengthening Phase
The patient completes 2-3 stimulation sessions a week at home for a minimum of 7 weeks.

The 10 week milestone: If the treatment has proven helpful at week 10, the Strengthening phase is continued for 6-12 months to help maintain progress and prevent relapse.

Note 1: It is common for patients to experience a transient and mild increase in depressive symptoms as the treatment protocol is reduced to 2-3 sessions a week. This tends to last a few days.

However, if it persists for more than one week and/or if it is a significant worsening of symptoms (sometimes described as “my depression has come back”) – consider the following steps:

1. Increase the number of stimulation sessions to 5 for another 3 weeks (the protocol can be adjusted via the Clinician Platform).

2. After 3 weeks have passed, try again to reduce the number of stimulation sessions to 2-3 per week and re-evaluate the results.

3. Should the same problem appear again, the stimulation schedule can be set to 5 sessions a week for the next few months.

Note 2: The standard protocol for the Strengthening phase is automatically set to 2 sessions/week. However, the Empower study (2024) used 3 sessions/week with positive results. The protocol from the Empower study can be used from the start of treatment.

For more information about long-term use of the Flow treatment and when to customise the stimulation protocol, please visit this webinar.

Long-term protocols

The recommended protocols for long-term use of the Flow treatment are rooted in the scientific literature and have been reviewed by Flow Neuroscience's scientific board, including Professor of Psychiatry at King's College London, Allan Young, and leading researcher in neuromodulation at the University of São Paulo, André Russowsky Brunoni.

The protocol is based on how the patient responds to the Flow treatment during the initial 10 weeks.

Patients with a high risk of depression relapse are recommended a slightly different protocol than patients with a low risk of relapse **– a minimum of 12 months treatment instead of 6 months.**

High risk factors include:

- Childhood maltreatment (such as physical, emotional or sexual abuse, physical or emotional neglect, family conflict or violence).
- Residual symptoms from the last depressive episode.
- A history of depressive episodes.
- Chronic physical or mental health disorders.
- An anxiety disorder.
- Rumination – experiencing repetitive negative thinking or easily dwelling on negative feelings/thoughts.

Low risk of relapse patients are exempt from these risk factors.

Below, you'll find the recommended long-term protocols for three common scenarios.

Scenario #1: The patient reaches remission by week 10

Recommendations for high risk of relapse patients: a minimum of 3 stimulation sessions a week for a minimum of 12 months to help maintain remission.

For low risk of relapse patients: 2-3 stimulation sessions a week for a minimum of 6 months to help maintain remission.

Note: if the patient has a customised stimulation schedule it can be used for the whole duration of the treatment. For more information about when to customise the treatment protocol, please visit this webinar.

Scenario #2: The patient achieves a 50% reduction of symptoms or a significant improvement (but not full remission) by week 10

What signifies a significant improvement? Ultimately, the patient will decide if the treatment is helpful or not. If they find the treatment helpful and tolerable, long-term use is recommended.

Common examples of a significant improvement:

- The patient's depression score improves from severe depression to moderate/mild, or from moderate depression to mild.

- The patient experiences that the Flow treatment is preventing their depression from worsening during challenging times or periods of intense stress.

For all such patients: Consider increasing the number of stimulation sessions to 5 per week.

For high risk of relapse patients: Continue the treatment for a minimum of 12 months to help maintain the results.

For low risk of relapse patients: Continue the treatment for a minimum of 6 months to help maintain the results.

In this scenario, a combination of evidence-based treatments can be beneficial. For example, combining tDCS treatment with antidepressant medication may enhance

the efficacy of both treatments (see Woodham et al., 2024, McLaren et al., 2018, Brunoni et al., 2013).

Scenario #3: The patient does not reach an improvement, response or remission by week 10

For all such patients: Re-evaluate the use of the Flow treatment. Usually, the largest improvements occur within the first 10 weeks. If the patient does not report any improvements at all at this point, the Flow treatment is probably not effective for them.

However, if the patient reports significant value from the Flow treatment, continued treatment is still relevant. In such cases, a combination of evidence-based treatments should be considered. For example, combining tDCS treatment with antidepressant medication may enhance the efficacy of both treatments (see Woodham et al., 2024, McLaren et al., 2018, Brunoni et al., 2013).

For more information, watch this webinar on long-term usage of the Flow treatment.

Or, visit this article on How to Use the Flow Treatment in Clinical Practice.

Customisation of patient protocols

It's recommended to customise a patient protocol under the following circumstances:

Return of symptoms. It is common for patients to experience a transient and mild increase in depressive symptoms as the treatment protocol is reduced from 5 sessions a week (from the Activation phase) to 2-3 sessions a week (to the Strengthening phase). This tends to last a few days.

However, if it persists for more than one week and/or if it is a significant worsening of symptoms (sometimes described as "my depression has come back") – consider the following steps:

1. Increase the number of stimulation sessions to 5 for another 3 weeks.

2. After 3 weeks have passed, try again to reduce the number of stimulation sessions to 2-3 per week and re-evaluate the results.

3. Should the same problem appear again, the stimulation schedule can be set to 5 sessions a week for the next few months.

As long as the patient experiences side effects as minor and tolerable, the new schedule can be used long-term. If side effects increase, consider returning to the standard protocol or discontinue the treatment.

Response but not remission. If a patient experiences a positive response to the Flow treatment but does not recover fully from depression within 10 weeks, they may benefit from a customised stimulation schedule.

If any of the below scenarios apply, consider increasing the number of stimulation sessions to 5 per week. Provided that side effects are minor and tolerable, the new schedule can be used long-term.

- The patient reports a 50% reduction of symptoms at week 10.

- The patient's depression score improves from severe depression to moderate/mild, or from moderate depression to mild within 10 weeks.

- The patient experiences that the Flow treatment is preventing their depression from worsening during challenging times or periods of intense stress.

Depression relapse. If the patient experiences a depression relapse while using the standard protocol, consider increasing the number of stimulation sessions to 5 per week. Provided that side effects are minor and tolerable, the new schedule can be used long-term.

Each new episode of depression is followed by a minimum of 6-12 months of maintenance treatment.

Protocol in case of relapse

Unfortunately, there are no depression treatments with complete protection against depression relapse.

In case a patient relapses while using the Flow tDCS treatment, consider increasing the number of stimulation sessions to 5 per week. If the patient finds side effects tolerable, the new protocol can be used long-term.

Each new episode of depression is followed by a minimum of 6-12 months of maintenance treatment.

Uses of tDCS

To date, the only tDCS treatment with Level A evidence (definite effect) is the treatment of Major Depressive Disorder (MDD).

The Flow tDCS device is solely classified as a Class IIa medical device for the treatment of depression in adults.

For further questions, please contact support@flowneuroscience.com

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