

Evaluating antidepressants for emotionalism after stroke

Submission date 05/04/2024	Recruitment status Recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 02/08/2024	Overall study status Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
Last Edited 08/05/2025	Condition category Mental and Behavioural Disorders	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> Record updated in last year

Plain English summary of protocol

Background and study aims

One in five people with stroke will have some degree of emotionalism by 6 months. Having emotionalism means you cry or laugh without warning, often inappropriately and uncontrollably. Post-stroke emotionalism (PSE) negatively affects people's daily life, and finding treatment is a priority for them. This study aims to see if PSE symptoms can be reduced by taking sertraline (an antidepressant drug) daily for 6 months. Based on the results, the researchers will be able to recommend whether, or not, PSE patients should take sertraline.

Who can participate?

Adults with stroke in the previous year and PSE symptoms

What does the study involve?

Half of the participants will be given sertraline and the other half 'placebo' (a pill that looks like the real medicine but contains no active ingredient). Participants will be allocated to the groups at random, so that neither they or their clinical team will know which group they are in. They will be asked to complete some questionnaires at the start of the trial and again at their follow up visits at 3, 6 and 12 months. People's answers to the questions will assess any changes the medication has made to symptoms of PSE and their quality of life.

What are the possible benefits and risks of participating?

It cannot be guaranteed that the trial will help the participants, but the information from this trial may improve our ability to treat people with post-stroke emotionalism in the future. Questionnaires will take approximately 45-50 minutes to complete at each visit. The researchers will be asking for some sensitive information, in so far as they will include questions which ask participants to consider symptoms of emotionalism/depression/anxiety. Participants have the choice of completing questionnaires remotely, by email or online (direct link to the study database) or on paper by post. For participants who request assistance, or choose, the researchers will facilitate telephone/video calls to collect responses to questionnaires. Participants will be asked to take two 25 mg tablets of trial medication for 6 months with a reduced dose of one 25 mg for a further month to reduce the risk of withdrawal symptoms and to protect the blinding of the trial. Tablets can be swallowed, chewed, or crushed. In the unlikely event that a participant is unable to continue taking the tablets, due to side effects, they are

requested to discuss this with their doctor. Adverse events of special interest will be collected at each visit for safety reporting.

Where is the study run from?

Norfolk and Norwich University Hospitals NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?

June 2023 to November 2027

Who is funding the study?

National Institute for Health and Care Research (NIHR) (UK)

Who is the main contact?

Veronica Bion, easetrial@uea.ac.uk

Study website

<https://norwichctu.uea.ac.uk/ease/>

Contact information

Type(s)

Public

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Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
1008638

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
IRAS 1008638, CPMS 59291

Study information

Scientific Title
EASE: Evaluating Antidepressants for emotionalism after stroke: a multi-centre, randomised, double-blind, placebo-controlled trial to establish the effect(s) of administration of sertraline (50 mg once daily for 6 months) in people with a recent stroke and post-stroke emotionalism

Acronym
EASE

Study objectives

One in every five people with stroke will have some degree of emotionalism by 6 months. The main objective of the study is to see if a daily 50 mg dose of sertraline reduced the symptoms in people with post-stroke emotionalism. Change in emotionalism will be measured using the Center for Neurologic Studies-Lability Scale (CNS-LS) at baseline and 6 months after randomisation.

The following measures will be captured at baseline, 3, 6 and 12 months post randomisation, unless noted to the contrary;

1. CNS-LS (only 3 and 12 months after randomisation)
2. PSE Symptoms (TEARS-Q)
3. Symptoms of Depression (PHQ-9)
4. General Anxiety Disorder 2-item (GAD-2)
5. Cognitive functioning and Social functioning (WHODAS 2.0)
6. Health Related Quality of Life (EQ-5D-5L)
7. Health Related Quality of Life (ICECAP-O) (only 6 and 12 months after randomisation)
8. Acceptability of Intervention (at 6 months)
9. Cost-effectiveness (at the end of the study)
10. Serious Adverse Reaction
11. Adherence (only 3, 6 and 7 months)

Ethics approval required

Ethics approval required

Ethics approval(s)

Approved 02/08/2024, North East – Tyne & Wear South Research Ethics Committee (NHSBT Newcastle Blood Donor Centre, Holland Drive, Newcastle upon Tyne , NE2 4NQ, United Kingdom; +44 (0)2071048120, +44 (0)207 104 8286, +44 (0)2071048108; tyneandwearsouth.rec@hra.nhs.uk), ref: 24/NE/0074

Study design

Randomized double-blind placebo-controlled parallel-group trial

Primary study design

Interventional

Secondary study design

Randomised controlled trial

Study setting(s)

Hospital

Study type(s)

Efficacy

Participant information sheet

Not available in web format, please use the contact details to request a participant information sheet

Health condition(s) or problem(s) studied

Post Stroke Emotionalism (PSE)

Interventions

Participants will be asked to take 2 x 25 mg oral sertraline tablets or 2 x matched placebo, once daily with or without food for 6 months.

After 6 months, or on discontinuation of treatment, participants should take one sertraline 25 mg or one matched placebo for 1 month to reduce the risk of withdrawal symptoms and protect the blinding of the trial.

All participants will be followed up at 2 weeks, 3, 6, 7 and 12 months. Follow-up will include safety checks, medication review, and completion of measures for primary and secondary outcomes.

Randomisation will be online, permuted block, participant level randomisation across three strata: recruitment centre, time since stroke, and current use of permitted anti-depressants.

Intervention Type

Drug

Pharmaceutical study type(s)

Pharmacoeconomic

Phase

Phase III

Drug/device/biological/vaccine name(s)

Sertraline hydrochloride

Primary outcome measure

Difference between sertraline and placebo groups in the change of symptoms of Post Stroke Emotionalism (PSE), measured by CNS-LS between baseline and 6 months

Secondary outcome measures

1. Symptoms of post-stroke emotionalism (PSE) measured using the Center for Neurologic Study-Ability Scale (CNS-LS) at 3 and 12 months post-randomisation (baseline and 6 months as primary outcome)
2. Symptoms of post-stroke emotionalism (PSE) measured using the Testing for Emotionalism After Recent Stroke-Questionnaire Crying-Questionnaire Crying (TEARS-Q) at baseline, 3, 6 and 12 months post-randomisation
3. Depression is measured using Patient Health Questionnaire – 9 (PHQ-9) at baseline, 3, 6 and 12 months post-randomisation
4. Anxiety is measured using the General Anxiety Disorder Scale (2 questions) (GAD-2) at baseline, 3, 6 and 12 months post-randomisation
5. Cognitive functioning, activities of daily living, social functioning and impact on relationships is measured using the World Health Organization Disability Assessment Schedule 2.0 (WHODAS 2.0) at baseline, 3, 6 and 12 months post-randomisation
6. Health-related quality of life is measured using the EuroQol Group EQ-5D-5L at baseline, 3, 6 and 12 months post-randomisation
7. Wellbeing is measured using the ICEpop CAPability measure for Older people (ICECAP-O) at baseline, 6 and 12 months post-randomisation
8. Acceptability of intervention is measured using an acceptability of intervention questionnaire at 6 months post-randomisation

9. Cost-effectiveness will be determined over 12 months from the perspective of the NHS and social care, with resource use data being collected via a modified Client Service Receipt Inventory (CSRI) at baseline, 6 and 12 months post-randomisation
10. Safety (serious adverse reactions) measured throughout, specifically at 2 weeks, 3, 6, 7 and 12 months post-randomisation
11. IMP adherence will be measured by a tablet count at 2 weeks and then at the end of each treatment period at 3, 6 and 7 months post-randomisation

Overall study start date

01/06/2023

Completion date

30/11/2027

Eligibility

Key inclusion criteria

1. Age ≥ 18 years
2. Clinical diagnosis of first or repeat acute stroke (all types) in past one year with imaging compatible with ischaemic or haemorrhagic stroke (including those with normal CT if clinical history strongly suggestive of stroke).
3. Any PSE sub-type (crying, laughter, combined) defined by CNS-LS score ≥ 13
4. Capacity, as assessed by the patient's attending physician, to consent and complete trial assessments

Participant type(s)

Patient

Age group

Adult

Lower age limit

18 Years

Sex

Both

Target number of participants

310

Key exclusion criteria

Current exclusion criteria as of 05/08/2024:

1. Significant medical condition that in the opinion of the patient's attending physician would affect subject safety or influence the study outcomes
2. Allergy to sertraline
3. Contraindication to sertraline - known hepatic impairment, known long QT syndrome, close angle glaucoma, history of chronic kidney disease (CKD) or chronic obstruction pulmonary disease (COPD), using a medication that could interact seriously with sertraline e.g. pimozide, monoamine oxidase inhibitors and other serotonergic drugs (amphetamines, triptans and fentanyl)

4. Current or recent (within 1 month) treatment with any SSRI antidepressant or irreversible monoamine oxidase inhibitors (MAOIs)
5. Recent (within 1 month) change in non-SSRI antidepressants. Those on a stable dose for 1 month or more will still be eligible, including those having psychological therapies for anxiety /depression
6. Current or known history of hyponatraemia
7. Enrolment in another CTIMP interventional study or not available for full follow-up duration
8. A known history of a drug overdose, self-harm or attempted suicide in the last three months
9. Pregnant or breastfeeding
10. Women of childbearing potential (WOCBP) and not using a highly effective form of contraception (see section 6.3 for full definitions)
11. Unable or prefers not to undertake trial assessments remotely. Options to participate will include by post, telephone or video calls or completion of assessments online

Previous exclusion criteria:

1. Significant medical condition that in the opinion of the patient's attending physician would affect subject safety or influence the study outcomes
2. Allergy to sertraline
3. Contraindication to sertraline - including known hepatic impairment, known long QT syndrome, close angle glaucoma, history of Chronic Kidney Disease (CKD) or Chronic Obstruction Pulmonary disease (COPD), using a medication that could interact seriously with sertraline e.g. pimozide, monoamine oxidase inhibitors and other serotonergic drugs (amphetamines, triptans and fentanyl)
4. Current or recent (within 1 month) treatment with any SSRI antidepressant or irreversible monoamine oxidase inhibitors (MAOIs)
5. Recent (within 1 month) change in non-SSRI antidepressants. Those on a stable dose for 1 month or more will still be eligible, including those having psychological therapies for anxiety /depression
6. Enrolment in another CTIMP interventional study or not available for full follow-up duration
7. A known history of a drug overdose, self-harm or attempted suicide in the last three months
8. Pregnant, breastfeeding or of childbearing age and not using contraception
9. Unable or prefers not to undertake trial assessments remotely. Options to participate will include by post, telephone or video calls or completion of assessments online

Date of first enrolment

13/01/2025

Date of final enrolment

30/06/2026

Locations

Countries of recruitment

England

United Kingdom

Study participating centre

Norfolk and Norwich University Hospital
Colney Lane
Colney
Norwich
United Kingdom
NR4 7UY

Study participating centre
Torbay Hospital
Newton Road
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TQ2 7AA

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St Georges Hospital
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TA1 5DA

Study participating centre
New Cross Hospital
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WV10 0QP

Study participating centre
Addenbrookes
Addenbrookes Hospital
Hills Road
Cambridge

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CB2 0QQ

Study participating centre
Royal Victoria Infirmary
Queen Victoria Road
Newcastle upon Tyne
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NE1 4LP

Study participating centre
Aintree University Hospital
Longmoor Lane
Liverpool
United Kingdom
L9 7AL

Study participating centre
Fairfield General Hospital
Fairfield General Hospital
Rochdale Old Road
Bury
United Kingdom
BL9 7TD

Study participating centre
Maidstone Hospital
Hermitage Lane
Maidstone
United Kingdom
ME16 9QQ

Study participating centre
Luton and Dunstable University Hospital
Lewsey Road
Luton
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LU4 0DZ

Study participating centre
Arrowe Park Hospital
Arrowe Park Road
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United Kingdom
CH49 5PE

Sponsor information

Organisation

Norfolk and Norwich University Hospitals NHS Foundation Trust

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Sponsor type

University/education

Website

<https://www.uea.ac.uk/>

ROR

<https://ror.org/01wspv808>

Funder(s)

Funder type

Government

Funder Name

National Institute for Health and Care Research

Alternative Name(s)

National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type

Government organisation

Funding Body Subtype

National government

Location

United Kingdom

Results and Publications

Publication and dissemination plan

1. Peer-reviewed scientific journals
2. Internal report
3. Conference presentation
4. Publication on website
5. Submission to regulatory authorities

Participants will be asked to consent to sharing their anonymous data at the end of the trial, for other research. Access to the anonymous dataset will be made available after the publication of the main trial, through reasonable request made to the Chief Investigator and Sponsor. Their contact details will be made available for this purpose. Requests for access to trial data will be considered, and approved in writing where appropriate, after formal application to the TMG and TSC. Consideration for approving access is documented in the TMG/TSC Terms of Reference.

Intention to publish date

30/11/2028

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study will be available upon request from Niall Broomfield, Lead Investigator (easetrial@uea.ac.uk).

IPD sharing plan summary

Available on request