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# A proof-of-concept study of an accessible lithium supplement

**Submission date**
25/07/2024

**Recruitment status**
No longer recruiting

**Registration date**
01/08/2024

**Overall study status**
Ongoing

**Last Edited**
29/06/2026

**Condition category**
Mental and Behavioural Disorders

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

**Plain English summary of protocol**
Background and study aims:
Lithium is the gold-standard medication for bipolar depression and mania, and is also effective in unipolar depression, but is under-used because it requires frequent blood tests to ensure safety for patients. Non-medication forms of lithium are available at a low dose (20mg) over-the-counter as a 'nutraceutical' ("LiOr") and could be accessible for many people to take, if found to be effective. My previous research shows that low-dose lithium is safe, and that – anecdotally – people find it helpful for low/fluctuating mood, cognition, anxiety and agitation, all particularly relevant for depression. However, LiOr's potential has not been explored in any reasonable-quality human studies.
This project will provide a 'proof of concept' to see whether LiOr could be assessed as a potential therapy at a large scale. We will recruit 40 people with depression who are under stable ongoing treatment for depression, and measure 1) whether they agree to take 20mg LiOr daily, and how long they take it over a period of up to 6 months, 2) their levels of lithium in the blood, 3) any positive changes (e.g., to mood) over the 6-month study, 3) any negative effects or difficulties participants experience, 4) whether the measures and visits participants are asked to complete are acceptable for people. The results will give us enough information to plan a clinical trial, where LiOr can be robustly compared with a placebo to help determine whether LiOr could have benefits for people with depression.

Who can participate?
We are looking for people aged 18 - 65 years, who are fluent in English, who do not have a diagnosis of bipolar disorder or are currently very suicidal but are having treatment for depression. People also have to be suitable and willing to try supplementary lithium and visit our research centre for measures 5 times over 6 months (as below).

What does the study involve?
Participants will be asked to visit our research centre 5 times over 6 months for a blood test and some questionnaires. Between visits they will be asked to take LiOr each day, so long as they are willing to do so during this time. After the first visit, we ask that the following visits are 2 weeks, 2 months, 4 months and 6 months after the first visit.

What are the possible benefits and risks of participating?
We do not expect any significant risks or negative effects from taking part in the study. It is possible that people may feel some distress during blood tests or some of the questionnaires in visits. It is possible that people may not get on well with the lithium supplement, in which case they can lower the dose or stop taking it. On the other hand, we hope people will find benefits to mood and/or thinking skills and possibly other areas of life from the lithium supplement. Some people find the questionnaire visits interesting. Whether people experience benefits or not, findings from this study may help people in the future, as supplementary lithium is being tested to see if it is helpful for people experiencing a range of mood and brain conditions.

Where is the study run from?
South London and Maudsley NHS Foundation Trust (UK)

When is the study starting and how long is it expecting to run for?
July 2024 to January 2027

Who is funding the study?
Psychiatry Research Trust (UK)

Who is the main contact?
The study team's email address is lithium@kcl.ac.uk.
The lead researcher is Dr Rebecca Strawbridge, becci.strawbridge@kcl.ac.uk

# Contact information

### Type(s)
Public, Scientific, Principal investigator


### Contact name
Dr Rebecca Strawbridge

### ORCID ID
https://orcid.org/0000-0002-2984-1124

### Contact details
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# Additional identifiers

### Integrated Research Application System (IRAS)
329291

# Study information

## Scientific Title
Lithium orotate: a potential accessible supplement for people experiencing depression

## Acronym
MixLi

## Study objectives
To establish initial feasibility of studying a commercially available supplement (lithium orotate; LiOr) for its potential mood effects in people with depression including mixed features (DMF).

## Ethics approval required
Ethics approval required

## Ethics approval(s)
Approved 08/10/2024, Westminster Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 207 1048146; westminster.rec@hra.nhs.uk), ref: 24/LO/0620

## Primary study design
Interventional

## Study design
Open label single arm proof of concept study

## Study type(s)
Other

## Health condition(s) or problem(s) studied
People experiencing an episode of depression

## Interventions
A lithium supplement which is currently available to purchase worldwide over the counter.
Formulation: Lithium orotate
Dose: up to 20 mg per day
Duration: Up to 6 months

## Intervention Type
Supplement

## Primary outcome(s)
Current primary outcome(s) as of 21/04/2026:

1. LiOr bioavailability is measured via lithium levels in serum (as per standard assay) at 2, 8, 16 and 26 weeks from baseline
2. LiOR acceptability is measured via self-report adherence (using the Tablet Routine Questionnaire) at baseline, 2, 8, 16 and 26 weeks – and via discontinuation rates at the same time points
3. LiOr subjective experiences is measured using participant-reported positive (using non-validated questions) and negative experiences (using the LiSERS scale) baseline, 2, 8, 16 and 26

weeks
4. Protocol feasibility - rates of recruitment, attrition and missing data (in putative primary outcome; below) at 2, 8, 16 and 26 weeks from baseline

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Previous primary outcome(s):

1. LiOr bioavailability is measured via lithium levels in serum (as per standard assay) at 2, 4, 8, 16 and 26 weeks from baseline
2. LiOR acceptability is measured via self-report adherence (using the Tablet Routine Questionnaire) at baseline, 2, 4, 8, 16 and 26 weeks – and via discontinuation rates at the same time points
3. LiOr subjective experiences is measured using participant-reported positive (using non-validated questions) and negative experiences (using the LiSERS scale) baseline, 2, 4, 8, 16 and 26 weeks
4. Protocol feasibility - rates of recruitment, attrition and missing data (in putative primary outcome; below) at 2, 4, 8, 16 and 26 weeks from baseline

### Key secondary outcome(s)

Current key secondary outcome(s) as of 21/04/2026:

1. Candidate biomarker changes i.e., c-reactive protein is measured (as per standard assay) at baseline, 2, 8, 16 and 26 weeks.
2. Mood (putative primary outcome measure) changes are measured at baseline, 2, 8, 16 and 26 weeks, using 1) the Maudsley visual analogue scales for depression and mania, 2) the internal states scale (ISS), 3) the generalised anxiety disorder 7-item questionnaire (GAD7), 4) the inventory of depressive symptoms (IDS) and 5) the young mania rating scale (YMRS).
3. Functioning and cognition (putative secondary measures) changes are measured at baseline, 2, 8, 16 and 26 weeks, using 1) the Functional Assessment Short Test (FAST) and 2) Perceived Deficits Questionnaire - Depression (PDQ-D), Digit Span, Digit Symbol Coding Test (DSCT)

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Previous key secondary outcome(s):

1. Candidate biomarker changes i.e., c-reactive protein is measured (as per standard assay) at baseline, 2, 4, 8, 16 and 26 weeks.
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3. Functioning and cognition (putative secondary measures) changes are measured at baseline, 2, 4, 8, 16 and 26 weeks, using 1) the Functional Assessment Short Test (FAST) and 2) the THINC-IT cognitive battery.

### Completion date

31/01/2027

## Eligibility

## Key inclusion criteria
Current key inclusion criteria as of 21/04/2026:

1. Aged between 18 - 65 years at study entry
2. Meet DSM-5 criteria for a current depressive episode (MINI)
3. Undergoing stable pharmacological treatment for depression (intervention/dose unchanged for >6 weeks)
4. Willing to try a commercially available lithium supplement
5. Willing to attend planned study visits

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Previous key inclusion criteria:

1. Aged between 18 - 65 years at study entry
2. Meet DSM-5 criteria for a current depressive episode (MINI) and exceed thresholds indicating presence of mixed features (Internal States Scale; ISS)
3. Undergoing stable pharmacological treatment for depression (intervention/dose unchanged for >6 weeks)
4. Willing to try a commercially available lithium supplement
5. Willing to attend planned study visits

## Participant type(s)
Patient

## Healthy volunteers allowed
No

## Age group
Mixed

## Lower age limit
18 Years

## Upper age limit
65 Years

## Sex
All

## Total final enrolment
0

## Key exclusion criteria
1. Clinical diagnosis of bipolar disorder.
2. Other health condition that is severely impairing
3. Known contraindication to lithium treatment. This includes currently taking lithium
4. Unable to communicate fluently in English
5. Suicide risk

## Date of first enrolment

28/10/2024

**Date of final enrolment**
24/07/2026

# Locations

**Countries of recruitment**
United Kingdom

England

**Study participating centre**
**South London and Maudsley NHS Foundation Trust**
Bethlem Royal Hospital
Monks Orchard Road
Beckenham
England
BR3 3BX

# Sponsor information

**Organisation**
Institute of Psychiatry, Psychology & Neuroscience and South London & Maudsley NHS Foundation Trust joint office

# Funder(s)

**Funder type**
Charity

**Funder Name**
Psychiatry Research Trust

**Alternative Name(s)**
The Psychiatry Research Trust, PRT

**Funding Body Type**
Private sector organisation

**Funding Body Subtype**
Trusts, charities, foundations (both public and private)

**Location**
United Kingdom

# Results and Publications

### Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Dr Rebecca Strawbridge, becci.strawbridge@kcl.ac.uk, with the type of (anonymised) data depending on the request, available from 26 weeks after data collection has been completed, subject to participants' consent.

### IPD sharing plan summary
Available on request

### Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| Participant information sheet | version 1.1 | 18/09/2024 | 09/10/2024 | No | Yes |
| Participant information sheet | version 5 | 18/03/2026 | 21/04/2026 | No | Yes |
| Protocol file | version 1.2 | 08/10/2024 | 09/10/2024 | No | No |
| Protocol file | version 7 | 16/02/2026 | 21/04/2026 | No | No |
| Study website | Study website | 11/11/2025 | 11/11/2025 | No | Yes |