ISRCTN78782742 https://doi.org/10.1186/ISRCTN78782742

# Gut feeling: testing probiotics to help sertraline work better for depression

**Submission date**
29/04/2025

**Recruitment status**
Not yet recruiting

**Registration date**
26/06/2025

**Overall study status**
Ongoing

**Last Edited**
26/06/2025

**Condition category**
Mental and Behavioural Disorders

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

## Plain English summary of protocol

Background and study aims
Depression is a common condition that affects millions of people worldwide. Research suggests that the balance of bacteria in the gut may influence mental health. Probiotics, which are beneficial bacteria, have shown potential in improving gut health and possibly supporting mental well-being. However, their effectiveness in treating depression, especially when used alongside antidepressants like sertraline, remains unclear.
This study aims to explore whether taking probiotics alongside sertraline leads to better outcomes for people with moderate depression, compared to taking sertraline with a placebo (a substance with no active ingredients).

Who can participate?
People aged 18 to 60 years with moderate depression

What does the study involve?
Participants will be randomly assigned to receive either sertraline with the probiotic liquid drink, Symprove (containing predominantly Lactobacillus strains), or sertraline with a placebo, identical in appearance but lacking active ingredients, for 12 weeks. Neither the participants nor researchers know who is receiving the real treatment (probiotics) and who is receiving the placebo (a dummy treatment with no active ingredients). This makes the study as fair and reasonable as possible.
Informed consent will be obtained through face-to-face discussions, highlighting potential side effects and ensuring the right to withdraw at any time without compromising clinical care. The participant's GP will be informed of their involvement in the study, in case it affects their care. Confidentiality will be maintained through anonymisation, with physical documentation stored securely and digital data encrypted.
The overall burden of participation will be 5 visits over 14 weeks. Changes in depression symptoms will be assessed using two widely used mental health questionnaires, the Hamilton Depression scale and the Patient Health Questionnaire. Blood markers related to inflammation (hs C-reactive protein) and metabolism (lipid or fat levels) will also be examined, along with the validated gastrointestinal symptom rating scale (GSRS) to monitor bowel symptoms. Depression and heart health can have an influence on the level of these markers and bowel symptoms.
Visit 1: Check eligibility and consent. £20 participation voucher will be offered at completion.

Visit 2: Randomisation, confirm consent, answer questionnaires with a psychologist and have bloods, BP and BMI taken. Participants will be issued a code to collect the liquid drink.
Visit 3: See health care to assess progress, concordance with liquid drink, discuss any adverse effects, review consent with freedom to withdraw. Access to medical advice if needed. Further code for liquid drink.
Visit 4: Same as visit 3.
Visit 5: As visit 3 but without the code for the liquid drink. There will be repeat questionnaires with a psychologist, bloods, BMI and issue of voucher. Participants will be informed of the results of the study 3 months after completion, in a manner of their choosing, either by post, email or accessing the practice website.

What are the possible benefits and risks of participating?
Participants will benefit from regular check-ups on their mental and physical health throughout the study. Some may experience mild side effects from the probiotic, such as bloating or more frequent bowel movements, but previous research has found these to be minor. While we cannot guarantee that taking part will improve mood or heart health, there is a possibility of these benefits.
The main purpose of the study is to help advance research, which could lead to better treatment options in the future. It may provide the first clinically meaningful evaluation of probiotics as an addition to sertraline in the treatment of moderate depression in real-life primary care, offering valuable insights for future research and clinical practice.

Where is the study run from?
Denmark Street Surgery (UK)

When is the study starting and how long is it expected to run for?
December 2024 to July 2026

Who is funding the study?
Symprove (UK)

Who is the main contact?
Dr ACMC Young, micaelayoung@nhs.net

# Contact information

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Principal Investigator

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## Additional identifiers

### EudraCT/CTIS number
Nil known

### IRAS number
354842

### ClinicalTrials.gov number
Nil known

### Secondary identifying numbers
Nil known

## Study information

## Scientific Title
Effect of probiotic supplementation on depression severity in primary care patients treated with sertraline: a randomized placebo-controlled trial

## Acronym
PROSPECT

## Study objectives
The proposed study will investigate the effectiveness of an add-on probiotic with sertraline in moderate to major depression in primary care. The hypothesis is that the combination of probiotic and sertraline will reduce validated depression questionnaire scores as the primary outcome and reduce inflammatory and metabolic markers as secondary outcomes.

## Ethics approval required
Ethics approval required

## Ethics approval(s)
Not yet submitted (Address not provided, City not provided, Zip/postal code not provided, United Kingdom; Telephone number not provided; a@a), ref: Reference number not provided

## Study design
Single-centre interventional double-blinded randomized controlled trial pilot

## Primary study design
Interventional

## Secondary study design
Randomised controlled trial

## Study setting(s)
GP practice

## Study type(s)
Efficacy

## Participant information sheet
See study outputs table

## Health condition(s) or problem(s) studied
Depression

## Interventions
The pilot will be conducted over 14 weeks. 106 participants will be randomly allocated, using a computer generator (Sealed Envelope) to ensure double-blindedness, into two groups. Group 1 will be composed of participants diagnosed with depression and prescribed sertraline with Symprove probiotic supplement. Group 2 will be composed of participants diagnosed with depression prescribed sertraline with a placebo. The daily 70 ml dose of the investigational liquid product will initially be administered by the practice health researcher, to be continued by the participant.

### Intervention Type
Supplement

### Primary outcome measure
Depression symptoms will be assessed using the Hamilton Depression Scale (HAM-D17) and Patient Health Questionnaire (PHQ-9) at the commencement and conclusion of the pilot at week 1 and week 14

### Secondary outcome measures
1. Lipid profile, cholesterol, high density lipoprotein (HDL), low density lipoprotein (LDL) and triglycerides measured with point of care Cardiochek at week 2 and week 14
2. High sensitivity C-reactive protein (hs-CRP) measured with point of care Eurolyser at week 2 and week 14

### Overall study start date
01/12/2024

### Completion date
01/07/2026

## Eligibility

### Key inclusion criteria
1. Depressive disorder diagnosed by the International Classification of Diseases (ICD)-11
2. Age 18 to 60 years
3. HAM-D17 score of 17 and PHQ-9 score of 10
4. Therapeutic antidepressant dose unchanged in the prior 3 weeks

### Participant type(s)
Patient

### Age group
Adult

### Lower age limit
18 Years

### Upper age limit
60 Years

### Sex
Both

### Target number of participants
106

### Key exclusion criteria
1. Pregnancy
2. An infection/vaccination and/or antibiotics
3. Supplementation with pro- or prebiotics

4. Autoimmune disease, inflammatory bowel disease, coeliac disease
5. BMI >35
6. Cancer,
7. Atherosclerotic cardiovascular disease (ASCVD), ischaemic heart disease (IHD), transient ischaemic attack (TIA ), peripheral arterial disease (PAD)
8. Kidney failure with estimated glomerular filtration rate (eGFR) <30 ml/min1.72m2
9. Unstable thyroid function (thyroid stimulating hormone [TSH] <0.27 or >4.2 µIU/ml)
10. Psychiatric comorbidities of psychosis, emotionally unstable personality disorder (EUPD), eating disorder, obsessive compulsive disorder (OCD) and neurodevelopmental disorders
11. Formal psychological interventions
12. Concomitant medication of benzodiazepines, z drugs and quetiapine
13. Regular treatment (more than 3 days a week) with proton pump inhibitors, metformin, laxatives, systemic steroids, or non-steroidal anti-inflammatories
14. Significant change in dietary, smoking pattern or daily physical activity in the previous 4 weeks
15. High suicide risk, assessed by Columbia Suicide Severity Rating Scale (C-SSRS)
16. Substance or alcohol misuse
17. Participation in, or recently participated in, another study involving interventions which might affect the study outcomes
18. Any other condition which would affect the compliance or safety of the individual

### Date of first enrolment
01/09/2025

### Date of final enrolment
01/03/2026

## Locations

### Countries of recruitment
England

United Kingdom

### Study participating centre
### Denmark Street Surgery
Denmark Street
Darlington
United Kingdom
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## Sponsor information

### Organisation
Symprove UK

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### Sponsor type
Industry

### Website
https://symprove.com

## Funder(s)

### Funder type
Industry

### Funder Name
Symprove UK

## Results and Publications

### Publication and dissemination plan
Planned publication in a peer review journal

### Intention to publish date
01/06/2027

### Individual participant data (IPD) sharing plan
The data set generated during and /or analysed during the current study will be available on request from Dr ACMC Young (micaelayoung@nhs.net). Anonymised data will be made available, with participant consent at the conclusion of the study for 6 months on request from validated researchers for clinical analyses.

### IPD sharing plan summary
Available on request

### Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| Participant information sheet | | | 01/05/2025 | No | Yes |