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Gut feeling: probiotics with sertraline in primary care depression

Submission date	Recruitment status	[X] Prospectively registered
29/04/2025	Recruiting	[ ] Protocol
Registration date	Overall study status	[ ] Statistical analysis plan
26/06/2025	Ongoing	[ ] Results
Last Edited	Condition category	[ ] Individual participant data
22/08/2025	Mental and Behavioural Disorders	[X] Record updated in last year

Plain English summary of protocol

Background and study aims

Depression is a common mental health condition affecting millions of people worldwide. Despite existing treatments, many people continue to experience symptoms that reduce their quality of life. Research suggests that the balance of bacteria in the gut may influence mood, and that probiotics (beneficial bacteria that support gut health) might help improve mental well-being. This pilot study will explore whether it is practical and acceptable for people with moderate depression to take a probiotic alongside the antidepressant sertraline. We will also look for early signs that this combination may affect quality of life, depressive symptoms, and gastrointestinal health compared with sertraline plus a placebo (a dummy treatment 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 the 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. Preliminary changes in quality of life will be assessed using two validated questionnaires: WHOQOL-BREF and the QLDS at baseline week 2 and at endpoint week 14. Blood markers related to inflammation (hs C-reactive protein) and metabolism (lipid or fat levels) will also be examined, along with the validated mental health questionnaires, the Hamilton Depression scale, the Patient Health Questionnaire and the Gastrointestinal Symptom Rating Scale (GSRS). Depression and heart health can affect

quality of life, mood, and bowel symptoms, as well as influence levels of certain blood markers.
Visit 1: Check eligibility and consent. A £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. This pilot study will test whether it is practical and acceptable to add a probiotic supplement to usual sertraline treatment for adults with depression and explore possible early improvements in quality of life and related health measures. The results will help design a larger, definitive trial in the future.

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 September 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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Public

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
362598

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
Nil known

Study information

Scientific Title
Pilot proof-of-concept study of probiotics adjunctive to sertraline in primary care depression, exploring quality of life outcomes

Acronym
PROSPECT

Study objectives
Current study objectives as of 20/08/2025:
This proof-of-concept pilot study hypothesises that adjunctive probiotic supplementation alongside sertraline is feasible and acceptable in primary care and may provide preliminary signals of benefit for quality of life, biological markers, and depressive and gut symptoms compared with sertraline alone.

Previous 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)
notYetSubmitted (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

Study type(s)
Other

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(s)
Current primary outcome measure as of 20/08/2025:
Quality of life examined over 12 weeks using validated questionnaires World Health Organization Quality-of-Life Scale (WHOQOL-BREF) and the Quality of Life in Depression Scale (QLDS) at baseline week 2 and endpoint week 14

Previous 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

Key secondary outcome(s))
Current secondary outcome measures as of 20/08/2025:
1. Lipid profile, cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL) and triglycerides measured with the point-of-care Cardiochek at baseline week 2 and endpoint week 14
2. High sensitivity C-reactive protein (hs-CRP) measured with point of care Eurolyser at baseline week 2 and endpoint week 14

Tertiary outcome measures:
Preliminary changes in depressive and gastrointestinal symptoms assessed using the validated questionnaires Hamilton Depression Scale 17 items (HAM-D17), Patient Health Questionnaire (PHQ-9) and Gastrointestinal Symptoms Rating Scale (GSRS). at baseline (week 2) and endpoint (week 14)

Feasibility outcomes:
1. Recruitment: Ability to recruit ≥20 participants per month across participating sites until the target sample of 106 participants is achieved. Timeline from initiation of study to 6 months.
2. Retention: Retention of ≥50 % of enrolled participants with dropout limited to ≤15% from baseline (week 2) to endpoint (week 14).
3. Adherence: Adherence defined as participants taking ≥80% of the allocated probiotic doses between baseline (week 2) and endpoint (week 14).
4. Acceptability and data completeness: Acceptability of study procedures assessed by the completeness of outcome data, defined as ≥80% of planned questionnaires and biological samples collected between baseline (week 2) and endpoint (week 14).

Previous 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

Completion date
01/09/2026

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

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
60 years

Sex
All

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 kg/m²
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
12/01/2026

Date of final enrolment
12/07/2026

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Denmark Street Surgery
Denmark Street
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Sponsor information

Organisation
Symprove UK

Funder(s)

Funder type
Industry

Funder Name
Symprove UK

Results and Publications

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	version 1.3		22/08/2025	No	Yes