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A study looking at whether metformin (a diabetes drug) can prevent weight gain caused by antipsychotics in people experiencing their first episode of psychosis

Submission date
06/10/2025

Recruitment status
Recruiting

Registration date
27/01/2026

Overall study status
Ongoing

Last Edited
30/10/2026

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
Many people in the UK with psychosis are started on antipsychotic medication to help with their symptoms. However, these drugs can cause a lot of weight gain, which can cause other problems in the future, such as heart disease or diabetes. It also has an impact on how people feel about themselves. Importantly, it may make people want to stop taking their antipsychotic treatment. Metformin is a drug that has been used for over 60 years in the treatment of diabetes. Small studies suggest that it might help stop some of the weight gain caused by antipsychotics and prevent diabetes. This study will look at whether metformin can stop, or reduce, weight gain for people taking antipsychotics in their first episode of psychosis.

Who can participate?
The study will involve 340 people who are experiencing psychosis for the first time and have started their antipsychotic medication no longer than a month ago. The study will take place in approximately 15 UK mental health services.

What does the study involve?
Patients will be randomly split into two groups. One group will be asked to take metformin for a year. The other group will be asked to take a placebo. A placebo - also known as a “dummy” or “sham” drug - doesn’t contain any active treatment. METRIC is a blinded trial, meaning that participants and their doctors will not know which drug they are given, until all participants have finished the trial. This is important so we can measure the true effect of metformin by comparing the weight of those taking metformin with those taking placebo.
Participants will be seen by their mental health team every 3 months while taking the drug and for up to 6 months afterwards. We will measure weight, mental health symptoms and how people feel in general about their health. We will also ask if they have been to other services about their psychosis or weight.

What are the possible benefits and risks of participating?
The risks of metformin are low but we will take some blood tests to make sure that taking the drug is not causing any side effects to patients. The study treatment, metformin, may not directly benefit participants as we do not know if the drug will be effective. This is why we are doing this trial. However, participation will help healthcare professionals in the future to manage weight gain for others with first episode psychosis.

Where is the study run from?
Pennine Care NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
June 2025 to May 2029

Who is funding the study?
National Institute for Health and Care Research (NIHR) (UK).

Who is the main contact?
METRIC_RCT@sheffield.ac.uk

Contact information

Type(s)
Public, Scientific

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Additional identifiers

Integrated Research Application System (IRAS)
1010474

Central Portfolio Management System (CPMS)
63386

National Institute for Health and Care Research (NIHR)
167171

Study information

Scientific Title
Metformin in psychosis for weight gain prevention

Acronym
METRIC

Study objectives
Primary objective:
To determine if metformin plus usual care reduces weight gain by at least 4 kg (equivalent to 5% of the expected baseline body weight) at 1 year compared to placebo plus usual care.

Secondary objectives:
1. To conduct an economic evaluation alongside the clinical trial and long-term cost effectiveness modelling from NHS and societal perspectives.
2. To undertake a process evaluation to understand acceptability of adding metformin to usual care alongside considerations for future implementation.
3. To assess the effect of withdrawing metformin and matching placebo on weight, up to 6 months post withdrawal.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 11/03/2026, Brighton and Sussex Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0) 2071048202; brightonandsussex.rec@hra.nhs.uk), ref: 26/LO/0126

Primary study design
Interventional

Allocation
Randomized controlled trial

Masking
Blinded (masking used)

Control
Placebo

Assignment
Parallel

Purpose
Treatment, Safety

Study type(s)

Health condition(s) or problem(s) studied
Antipsychotic induced weight gain in first episode psychosis

Interventions
Intervention: Modified release (MR) metformin tablets and usual care. Dose titrated to reduce side effects. Tablets will be commenced at 500mg daily orally with food, increasing by 500mg daily every 10-15 days to the maximum of 2g daily, in accordance with BNF and product licence. Participants not tolerating the increased dose will be asked to remain on the highest tolerated dose. Taken orally at home (or if an inpatient, within hospital). Participants will be randomised within 4 weeks of AP initiation, following which treatment will commence. Treatment will be continued for 1 year, after which there will be a 3-6month washout period during which we will observe the effects of treatment cessation.

Control: Blinded, matched placebo tablets, and usual care. Placebo tablets will be prescribed in line with the intervention group.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Metformin

Primary outcome(s)
Weight (kg) measured using calibrated scales at baseline and 1 year post randomisation.

Key secondary outcome(s)
1. Weight is measured using calibrated scales at baseline, 3 months, 6 months, 9 months, and 12 months
2. Body Mass Index (BMI) is calculated from height and weight measurements using calibrated scales at baseline, 3 months, 6 months, 9 months, and 12 months
3. Proportion of participants who have gained more than 5% and 10% of their baseline body weight is assessed using weight measurements at 12 months
4. Proportion of participants with BMI ≥25 kg/m² and BMI ≥30 kg/m² is assessed using BMI calculations at 12 months
5. Change in BMI category is assessed using BMI calculations at baseline and 12 months
6. Waist circumference is measured using a tape measure at baseline, 3, 6 and 9 months
7. Lipid profile (total cholesterol, HDL, LDL, triglycerides), HbA1c, and vitamin B12 are measured using venous blood samples at baseline and 12 months (all), and at 3 and 6 months (lipid profile and HBA1c)
8. Adverse events are recorded by site staff using the METRIC Adverse Event CRF. Site staff will check for adverse events at each study visit (baseline, 3, 6, 9, 12, 15 and 18 months). Events identified outside of study visits at routine care appointments will also be recorded.
9. Mental health status is measured using the Clinical Global Impressions Scale (CGI) at 3, 6 and 12 months.
10. Medication adherence is measured using pill counts for metformin/placebo and clinician survey for antipsychotic medication at 3, 6, 9 and 12 months.
11. Quality of life is measured using the Recovering Quality of Life questionnaire (ReQoL-10) at baseline, 3, 6 and 12 months.
12. Health-related quality of life is measured using the EQ-5D-5L questionnaire at baseline, 3, 6 and 12 months.
13. Health resource use is measured using the METRIC healthcare resource use form at baseline, 3, 6 and 12 months.
14. Cost effectiveness is assessed using via an embedded health economic analysis.
15. Weight is measured using calibrated scales at 12 months and 18 months to assess the effect of withdrawing metformin or placebo
16. Acceptability and factors influencing adherence are evaluated via an embedded process evaluation, incorporating qualitative interviews with participants and site staff.

Completion date
31/05/2029

Eligibility

Key inclusion criteria
1. Adults with FEP (age ≥18 yrs <65 yrs)
2. Within 4 weeks of starting any APs
3. Intention to continue AP drugs for ≥1 year

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
16 Years

Upper age limit
65 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Body Mass Index (BMI) < 18.5 kg/m²
2. Current prescription of metformin
3. Contraindication to the use of metformin (as advised by the SmPC and British National Formulary (BNF)): chronic stable heart failure, concomitant use of drugs that can acutely impair renal function, renal dysfunction (eGFR <30mL/minute/1.73m2.), significant liver disease with increased likelihood of tissue hypoxia, hypersensitivity or previous intolerance to metformin
4. Any diabetes mellitus
5. Other condition that would independently affect body weight, e.g. Cushing's syndrome, untreated thyroid dysfunction
6. Current engagement in any systematic weight management programme (or within the past 3 months). Including the use of GLP-1 receptor agonists and GLP-1 receptor GIP dual agonists
7. Any concomitant physical or mental condition that according to the investigator's assessment makes the participant unsuitable for trial participation
8. Lack of capacity

Date of first enrolment
01/06/2026

Date of final enrolment
31/08/2027

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Hampshire and Isle of Wight Healthcare NHS Foundation Trust
Tatchbury Mount Hospital
Calmore
Southampton
England
SO40 2RZ

Study participating centre
Norfolk and Suffolk NHS Foundation Trust
County Hall
Martineau Lane
Norwich
England
NR1 2DH

Study participating centre
Oxford Health NHS Foundation Trust
Littlemore Mental Health Centre
Sandford Road
Littlemore
Oxford
England
OX4 4XN

Study participating centre
Pennine Care NHS Foundation Trust
225 Old Street
Ashton-under-lyne
England
OL6 7SR

Study participating centre
Rotherham Doncaster and South Humber NHS Foundation Trust
Woodfield House
Tickhill Road

Doncaster
England
DN4 8QN

Study participating centre
Somerset NHS Foundation Trust
Trust Management
Lydeard House
Musgrove Park Hospital
Taunton
England
TA1 5DA

Study participating centre
South West London and St George's Mental Health NHS Trust
Springfield Hospital
61 Glenburnie Road
London
England
SW17 7DJ

Study participating centre
South West Yorkshire Partnership Teaching NHS Foundation Trust
Trust Headquarters
Fieldhead Hospital
Ouchthorpe Lane
Wakefield
England
WF1 3SP

Study participating centre
Tees, Esk and Wear Valleys NHS Foundation Trust
Trust Headquarters
West Park Hospital
Edward Pease Way
Darlington
England
DL2 2TS

Sponsor information

Organisation
Pennine Care NHS Foundation Trust

ROR
https://ror.org/03t59pc95

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

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Data sharing statement to be made available at a later date