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The effectiveness of Metformin for reducing weight gain experienced by people with severe mental health problems in South Asia

Submission date
13/03/2025

Recruitment status
Not yet recruiting

Registration date
12/05/2025

Overall study status
Ongoing

Last Edited
10/07/2025

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
People with severe mental illness (SMI), such as schizophrenia or bipolar disorder, often need to take antipsychotic medications to manage their symptoms. While these medications are essential for their mental health, they can cause significant weight gain, which increases the risk of other health problems like heart disease and diabetes. This weight gain can make it harder for individuals to stick to their treatment plan, impacting their overall well-being.

The META-SMI study aims to test whether taking metformin, a common diabetes medication, can help reduce this weight gain in people with SMI who have recently started antipsychotic treatment. We also want to identify if using Metformin is a cost-effective approach to managing the weight gain seen in this group of people.

Who can participate?
Adults (18 years or older) with a diagnosis of a severe mental illness who have recently started, or about to start, an antipsychotic medication.

What does the study involve?
The study involves comparing a group of people who take this medication to a group who do not. Half of the participants will take Metformin every day and the other half will take a placebo (dummy) drug. The results between the two groups will then be compared to see if one is better than the other.

The study will follow participants for six months, measuring changes in weight and other health indicators to see if metformin can significantly reduce weight gain compared to the placebo. Researchers will also track side effects, medication adherence, quality of life and other mental health symptoms using questionnaires. There will also be an economic analysis to see if Metformin is cost-effective when used in the real world.

What are the possible benefits and risks of participating?
Benefits:

Participants may gain further knowledge about their weight and how to manage potential weight gain better in the future. The knowledge provided from this study could be used to help improve the health of people with severe mental illness in Pakistan in the future.

Risks:
Participants may experience emotional distress from discussing their mental health symptoms and history.
Participants taking Metformin may experience side effects associated with this medication such as nausea or vomiting, or possibly rarer but more serious side effects such as lactic acidosis (when the blood becomes too acidic).
Participants will require blood tests to be taken, and so this may lead to a small risk of bruising.

Where is the study run from?
The study will take place at the Institute of Psychiatry which will be managed by Rawalpindi Medical University. Another site at Khyber Medical University may be used if more participants are required.

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

Who is funding the study?
National Institute of Health Research (NIHR) UK
Institute of Psychiatry, Pakistan

Who is the main contact?
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Contact information

Type(s)
Scientific, Principal Investigator

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
HSRGC/2025

Study information

Scientific Title
Metformin for Antipsychotic-Induced Weight Gain in People with Severe Mental Illness

Acronym
META-SMI

Study objectives
Participants receiving Metformin will have less weight gain after 6 months of commencing antipsychotic medication compared to participants receiving a placebo.

Ethics approval required
Ethics approval required

Ethics approval(s)
1. Approved 19/05/2025, University of York Research Governance Committee (Department of Health Sciences, Seebohm Rowntree Building University of York, Heslington, York, YO10 5DD, United Kingdom; +44 1904 321321; sandi.newby@york.ac.uk), ref: HSRGC/2025/677/A: META-SMI

2. Not yet submitted, National Bioethics Committee, Pakistan (NBC-R Secretariat HRI Shahrah-e-Jamhuriat, G-5/2, Islamabad, -, Pakistan; +92-51-9224325,9216793; nbcpakistan@nih.org.pk), ref: -

3. Approved 20/05/2025, Ethical Review Committee, Rawalpindi Medical University (Rawalpindi Medical University, Tipu Road, Chamanzar Colony, Rawalpindi, -, Pakistan; +92 51- 933005 0-4; info@rmur.edu.pk), ref: 182/IREF\RMU\2025

4. Not yet submitted, Drug Regulatory Authority of Pakistan (DRAP) (Prime Minister's National Health Complex Park Road, Chak Shahzad, Islamabad, -, Pakistan; 0800-03727; not@provided)

Study design
Two-armed parallel individually randomized triple-blind control trial

Primary study design
Interventional

Secondary study design
Randomised parallel trial

Study setting(s)
Community, Other therapist office

Study type(s)
Treatment, Safety, Efficacy

Participant information sheet
To follow

Health condition(s) or problem(s) studied
Attenuation of antipsychotic induced weight gain in people with severe mental illness.

Interventions
Intervention: Film coated tablets of metformin XR, starting at 500 mg daily and titrating up to 2000 mg daily over a 6-week period, orally for a total of 26 weeks.

Control: Placebo - identical-looking tablets titrated in the same way as the intervention over a period of three weeks and then continued for 26 weeks duration.

Eligible participants will be randomised to metformin or placebo in a 1:1 ratio using a computer-generated randomisation table provided by an independent, non-blinded statistician.
The randomisation table will be provided to an independent pharmacy team at each site. This pharmacy team, as well as the non-blinded statistician, will be the only services with the ability to unblind patients. Participants will be provided with a 24hours contact number in case there is an emergent situation where it is crucial that medical staff know whether they are receiving metformin or placebo.

Intervention Type
Drug

Pharmaceutical study type(s)
Pharmacoeconomic

Phase
Phase III/IV

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

Primary outcome measure
Change in body weight, measured in kg at 6 months post randomisation.

Secondary outcome measures
1. Abdominal circumference measured using Seca 201 Ergonomic circumference measuring tape at baseline, 3 months, and 6 months.
2. Height measured using portable stadiometer at baseline, 3 months, and 6 months (this will be used to calculate BMI).
3. Blood pressure measured using OMRON blood pressure monitor at baseline, 3 months, and 6 months.
4. HbA1c measured using laboratory analysis at baseline and 6 months.
5. Lipid profile measured using laboratory analysis at baseline and 6 months.
6. Liver function tests (LFTs) using laboratory analysis at baseline and 3 months.
7. Renal function using laboratory analysis at baseline:
7.1. Complete blood count using laboratory analysis at baseline.
7.2. Serum B12 using laboratory analysis at baseline and if abnormal, will be repeated at 6 months.
7.3. Thyroid function using laboratory analysis at baseline.
7.4. Liver function using laboratory analysis at baseline and if abnormal, will be repeated at 6 months.
8. Health-related quality of life measured using EQ-5D-5L at baseline, 3 months, and 6 months.
9. Depressive symptoms measured using PHQ-9 at baseline, 3 months, and 6 months.
10. Anxiety symptoms using GAD-7 at baseline, 3 months, and 6 months.
11. Psychotic symptoms using BPRS at baseline, 3 months, and 6 months.
11.1. Mental health admissions - self reported at baseline, 3 months and 6 months.
11.2. Hospital admissions - self reported at baseline, 3 months and 6 months.
11.3. Physical activity - measured using IPAQ tool at baseline, 3 months and 6 months.
11.4. Diet - measured using questions from WHO STEPwise survey at baseline, 3 months and 6 months.
11.5. Tobacco use - measured using questions adapted from the tobacco section of the WHO STEPwise survey at baseline, 3 months and 6 months.
11.6. Drug use - measured using questions adapted from the tobacco section of the WHO STEPwise survey at baseline, 3 months and 6 months.
11.7. Sleep Quality - measured using the PSQI tool at baseline, 3 months and 6 months.
11.8. Appetite - measure using the SNAQ tool at baseline, 3 months and 6 months.
12. Healthcare resource using client service receipt inventory at baseline and 6 months.
13. Adverse events using standard reporting procedure at 3 months and 6 months.
14. Metformin side effects using standard reporting procedure at 3 months and 6 months.
15. Process evaluation using mixed methods at 3 months and 6 months.
16. Concomitant medications - self-reported at baseline, 3 months, and 6 months.

Overall study start date
01/07/2024

Completion date
01/01/2027

Eligibility

Key inclusion criteria

1. Clinical diagnosis of SMI (i.e. schizophrenia, schizoaffective disorder, bipolar affective disorder, psychosis, severe depression with psychosis)
2. Antipsychotic naive
3. Able to, and willing to provide informed consent
4. >18 years of age
5. BMI > 18.5 kg/m²
6. Taking antipsychotic medication for < 28 days

Participant type(s)
Patient, Service user

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
270

Key exclusion criteria
1. BMI < 18.5 kg/m²
2. Known allergies or contra-indications to metformin or any part of the formulation of the placebo or investigational product
3. Diagnosis of type 1 or type 2 diabetes, or already taking metformin
4. Found to have HbA1c within diabetes range from blood tests
5. Prior diagnosis of a condition which is directly associated with obesity (self-reported)
6. Obesity induced by other endocrine disorder
7. Chronic kidney disease (eGFR < 30 mL/min)
8. Concomitant disease or condition (neurodegenerative disease, cognitive impairment) that investigators consider makes the patient unsuitable for trial participation
9. Taking weight-lowering therapy including: pramlintide, sibutramine, orlistat, zonisamide, topiramate or phentermine (or part of a clinical trial of such treatments)
10. Previous surgical treatment of obesity
11. Women who are pregnant or breast-feeding, or of childbearing age and not using contraceptives
12. Unable to provide informed consent, or lacking capacity

Date of first enrolment
01/09/2025

Date of final enrolment
01/09/2026

Locations

Countries of recruitment

Pakistan

Study participating centre
Rawalpindi Medical University
Tipu Rd, Chamanzar Colony
Rawalpindi
Pakistan
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Sponsor type
Hospital/treatment centre

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ROR
https://ror.org/04m01e293

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
The study will be published in a peer-reviewed journal, and the findings will be disseminated at relevant national and international conferences.

Intention to publish date
30/09/2027

Individual participant data (IPD) sharing plan
The following data sharing plan is stipulated in the Centre for Impact data management plan.

The datasets generated during and/or analysed during the current study will be stored in a non-publicly available repository-the University of York, Department of Health Sciences Filestore Area. The datasets included will be from the primary statistical analysis as well as the sensitivity analyses that will be carried out - this will be quantitative data.
It will be available upon official request to the corresponding author.

In accordance with the University of York Research Data Management Policy, all anonymised Centre for IMPACT research data, which underpin published results or have a long-term value will be retained for 10 years after the completion of Centre for IMPACT activities.

The datasets will be anonymised therefore no identifiable information will be associated with this. All identifiable information will be stored separately and kept in strict confidence, only to be accessed by authorised personnel.

The trial will use secure electronic systems to manage data integrity and confidentiality.

Informed consent to use participant data in the trial will be gained from all eligible participants before they take part in the trial. The participant information sheet also outlines how participant data will be used in the trial, and that results will be made publicly available upon publication.

Ethics authority approval will also be obtained from Rawalpindi Medical University and the Drug Regulatory Authority of Pakistan

IPD sharing plan summary
Stored in non-publicly available repository, Available on request