METfoRmin In psyChosis (METRIC) for Weight Gain Prevention Trial

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Introduction

Background

- Antipsychotic medications (APs), although effective for managing psychosis, are associated with weight gain and adverse metabolic changes (1).
- In people with first episode psychosis (FEP), weight gain is approximately 3-4 times greater than in chronic populations (2); ~ 6 kg gained within the first 6 months (3, 4, 5).
- Weight gain may lead to health issues (like heart disease or diabetes (6)) and can also affect adherence to the medication (7).

- Metformin is a widely used diabetes medication that improves insulin sensitivity.
- Early evidence suggests metformin can reduce weight gain in people taking APs (8).

Aims

✓ To evaluate the clinical and cost effectiveness of metformin plus usual care compared with placebo plus usual care for preventing antipsychotic-induced weight gain in FEP.

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

✓ To conduct an economic evaluation alongside the clinical trial and long-term cost effectiveness modelling from NHS and societal perspectives.

✓ To undertake a process evaluation to understand acceptability of adding metformin to usual care alongside considerations for future implementation.

✓ To assess the effect of withdrawing metformin and matching placebo on weight, up to 6 months post withdrawal.

Methods

METRIC is a UK, multicentre, double-blinded, superiority, randomised controlled trial.

- 15-20 UK NHS Mental Health Trusts
- 340 participants aged ≥ 16 years
- Randomised (1:1) to receive metformin or placebo for 12 months, in addition to usual care.

Primary outcome: absolute change in weight at 12 months.

- Analysis will follow the intention-to-treat principle, comparing mean weight change between groups with adjustment for baseline covariates.
- Embedded health economic evaluation and accompanying process evaluation.

Interventions

Intervention: Modified release (MR) metformin tablets and usual care.
Control: Blinded, matched placebo tablets, and usual care. Placebo tablets will be prescribed in line with the intervention group.

- Participants will be randomised within 4 weeks of AP initiation.
- 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.
- The dose will be titrated to reduce side effects.

- Treatment will be continued for 1 year.

Results and Discussion

Recruitment is scheduled to commence in July 2026. Results are expected to be available from May 2029.

METRIC will provide robust evidence on whether metformin can prevent antipsychotic-induced weight gain in FEP. If effective, this scalable intervention could be implemented early in treatment pathways to reduce long-term cardiometabolic risk and improve patient outcomes.

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Acknowledgments

This study is funded by the National Institute for Health Research (NIHR) Health Technology Assessment (HTA) Programme (NIHR 167171).

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