# INPLASY PROTOCOL

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**Review Stage at time of this submission:** **The review has not yet started.**

**Conflicts of interest:**
**None.**

# The efficacy and safety of metformin for olanzapine-induced elevated triglyceride levels:a meta-analysis of randomized controlled trials

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## ABSTRACT

**Review Question:** **P:Schizophrenia; I:The experimental group was treated with olanzapine combined with metformin; C:The control group was treated with olanzapine alone or olanzapine combined with placebo; O:Triglyceride levels; S:Ramdomized controlled studies.**

**Rationale:** **Whether metformin can reduce the elevated triglyceride level caused by olanzapine has been controversial in clinical practice. Metformin is rarely used alone to reduce triglyceride level. However, metformin, as a drug that can regulate glucose metabolism, has been considered to have potential value in regulating lipid metabolism.**

**Strategy of data synthesis:** **Literature retrieved in PubMed, Cochrane Library, Web of Science, embase, PsycINFO, CNKI, Wanfang, Clinical Trials were imported into EndNoteX9.After reviewing and screening the literature separately, the two researchers conducted full-text screening and extracted the data of qualified literature, mainly including: author, years of publication, country, diagnostic system, study design, trial duration, baseline and end-stage clinical symptom indicators, and side effects description.The extracted data is summarized in an Excel spreadsheet.**

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 31 March 2020 and was last updated on 31 March 2020 (registration number INPLASY202030020.

## INTRODUCTION

**Objectives / Review question:** **P:Schizophrenia; I:The experimental group was treated with olanzapine combined with metformin; C:The control group was treated with olanzapine alone or olanzapine combined with placebo; O:Triglyceride levels; S:Ramdomized controlled studies.**

**Condition being studied:** **Second-generation antipsychotics, widely used in the treatment of schizophrenia in recent decades, are much less likely to cause**

extrapyramidal side effects than first-generation antipsychotics,but the side effects of metabolic disorder are getting more and more attention from clinicians, and this disorder is more obvious in patients taking clozapine and olanzapine.Metabolic syndrome not only affects patients' compliance with medication, but also their prognosis.A study by Jiang Guangfen et al. showed that olanzapine induced metabolic syndrome made schizophrenics significantly weaker in disease recovery, immediate memory, attention and delayed memory than patients without metabolic syndrome.In addition to reducing drug dosage, changing drug types, and non-drug therapies, metformin has become one of the currently available methods for the control of metabolic syndrome, and its efficacy and safety have been confirmed by numerous randomized controlled trials and meta-analyses, especially in the control of weight gain However, there has been controversy over whether metformin can reduce the elevated triglyceride levels caused by olanzapine.Clinically, metformin is rarely used alone to reduce triglyceride levels. However, as a drug that can regulate glucose metabolism, metformin has been considered to have potential value in regulating lipid metabolism.

**Rationale:** Whether metformin can reduce the elevated triglyceride level caused by olanzapine has been controversial in clinical practice. Metformin is rarely used alone to reduce triglyceride level. However, metformin, as a drug that can regulate glucose metabolism, has been considered to have potential value in regulating lipid metabolism.

## METHODS

**Participant or population:** Patients with schizophrenia.

**Intervention:** The experimental group was treated with olanzapine combined with metformin.

**Comparator:** The control group was treated with olanzapine alone or olanzapine combined with placebo.

**Study designs to be included:** Ramdomized controlled studies.

**Eligibility criteria:** Inclusion criteria: 1. Compliance with relevant diagnostic criteria for schizophrenia; 2. The experimental group was treated with olanzapine combined with metformin, while the control group was treated with olanzapine alone or olanzapine combined with placebo;3. The study results included the blood triglyceride level or the degree of change before and after treatment;4. The study type was randomized controlled trial;5. The study lasted no less than 12 weeks. Exclusion criteria: 1. The patient is younger than 18 years old or older than 65 years old; 2. A history of substance dependence or substance abuse;3. Using the same data.

**Information sources:** Relevant literature was retrieved from PubMed, Cochrane Library, Web of Science, embase, PsycINFO, CNKI, and wanfang databases, and gray literature was retrieved from Clinical Trials.Search keywords: "schizophrenia","olanzapine","metformin"

**Main outcome(s):** Triglyceride levels :triglyceride levels were measured at the beginning and at the end of the trial.

**Additional outcome(s):** fasting glucose, weight gain, adverse events.

**Quality assessment / Risk of bias analysis:** We will assess the methodological quality of the included studies based on the risk assessment tools in the Cochrane manual, including randomized methods, distributive concealment, blinding, data integrity, selective reporting, and other biases.The two researchers conducted the quality assessment separately, and when there was disagreement, all participants were required to discuss and reach a consensus. If the number of literatures is sufficient, we will evaluate whether the included

literatures have publication bias through funnel plot and begg test.

**Strategy of data synthesis:** Literature retrieved in PubMed, Cochrane Library, Web of Science, embase, PsycINFO, CNKI, Wanfang, Clinical Trials were imported into EndNoteX9.After reviewing and screening the literature separately, the two researchers conducted full-text screening and extracted the data of qualified literature, mainly including: author, years of publication, country, diagnostic system, study design, trial duration, baseline and end-stage clinical symptom indicators, and side effects description.The extracted data is summarized in an Excel spreadsheet.

**Search strategy:** Relevant literature was retrieved from PubMed, Cochrane Library, Web of Science, Embase, PsycINFO, CNKI, and Wanfang databases, and gray literature was retrieved from Clinical Trials.Search keywords:"schizophrenia","olanzapine","metformin".

**Subgroup analysis:** We will conduct subgroup analysis of the included studies according to the study duration, study population, and diagnostic system.

**Sensibility analysis:** We will conduct sensitivity analysis by separately excluding the impact of each study on the overall combined results.

**Language:** There's no limit to that.

**Keywords:**
metformin;schizophrenia;olanzapine.

**Contributions of each author:**
Author 1 - Retrieval of literature, screening of the literature; data extraction; the data analysis; thesis writing.
Author 2 - Retrieval of literature, screening of the literature; data extraction; data the data analysis.
Author 3 - Retrieval of literature;Screening of the literature; The data analysis.