INPLASY

INPLASY202670113

doi: 10.37766/inplasy2026.7.0113

Received: 29 July 2026

Published: 29 July 2026

Corresponding author:
Shao-En Weng

z2670@tpech.com.tw

Author Affiliation:
National Science and Technology Council, Taiwan. National Yang Ming Chiao Tung University, Taiwan. Taipei city hospital, Taiwan.

Repurposing psychotropic agents (mirtazapine and olanzapine) for cancer-associated anorexia–cachexia syndrome: a systematic review and meta-analysis of randomized controlled trials

Chiang, PY; Chen, JH; Weng, SE; Huang, ST.

ADMINISTRATIVE INFORMATION

Support - National Science and Technology Council, Taiwan. National Yang Ming Chiao Tung University, Taiwan. Taipei city hospital, Taiwan.

Review Stage at time of this submission - Data analysis.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202670113

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 29 July 2026 and was last updated on 29 July 2026.

INTRODUCTION

Review question / Objective Among adults with cancer-associated anorexia–cachexia syndrome (CACS), do mirtazapine or olanzapine improve appetite, body weight, nutritional status, physical function, quality of life, and safety compared with placebo or active comparators?

Rationale Cancer-associated anorexia–cachexia syndrome (CACS) is a multifactorial syndrome characterized by progressive weight loss, skeletal muscle wasting, anorexia, and functional decline. It affects approximately one-third of patients with cancer and is associated with reduced treatment tolerance, poorer quality of life, and shorter survival. Current pharmacological options remain limited and no universally accepted standard treatment exists.

Mirtazapine and olanzapine are psychotropic agents with appetite-stimulating properties that have attracted increasing attention as drug repurposing candidates for CACS. Although several randomized controlled trials have evaluated these agents, their findings remain inconsistent and no comprehensive quantitative synthesis has evaluated both drugs simultaneously. Therefore, this systematic review and meta-analysis aims to synthesize current evidence regarding the efficacy and safety of mirtazapine or olanzapine for patients with cancer-associated anorexia–cachexia syndrome.

Condition being studied Cancer-associated anorexia–cachexia syndrome (CACS) in adult patients with malignant disease.

METHODS

Search strategy A comprehensive literature search will be conducted in PubMed, Embase, the Cochrane Central Register of Controlled Trials (CENTRAL), and ClinicalTrials.gov. The search strategy will combine controlled vocabulary terms (e.g., MeSH and Emtree) and free-text keywords related to cancer-associated anorexia, cachexia, mirtazapine, and olanzapine. Search strategies will

be adapted to the indexing system and syntax of each database.
No publication date restrictions will be applied. The complete electronic search strategies for all databases will be provided in an appendix to the final review.

Participant or population Eligible participants will be adults (≥18 years) diagnosed with cancer and cancer-associated anorexia–cachexia syndrome according to the diagnostic criteria defined in each included randomized controlled trial. No restrictions regarding cancer type, cancer stage, sex, or ethnicity will be applied.

Intervention The intervention of interest is treatment with either:
Mirtazapine
Olanzapine
at any dosage, treatment duration, administration schedule, or route of administration.
Studies evaluating these drugs alone or in combination with standard supportive care will be eligible.

Comparator Eligible comparators include:
Placebo
Megestrol acetate
Other active pharmacological comparators
Head-to-head comparison between mirtazapine and olanzapine
Trials without a comparator arm will be excluded.

Study designs to be included Randomized controlled trials.

Eligibility criteria Only full-text publications were considered eligible. Conference abstracts, trial registry records without an associated full report, study protocols, review articles, editorials, letters, case reports, and retracted publications were excluded. No restrictions were placed on publication year or language. When multiple reports originated from the same study population, the most complete or latest publication was included.

Information sources The following databases and trial registries will be searched:
PubMed
Embase
Cochrane Central Register of Controlled Trials (CENTRAL)
ClinicalTrials.gov
In addition, reference lists of included studies and relevant review articles will be screened manually to identify potentially eligible studies not captured by the electronic search.

Main outcome(s) The primary outcomes will include:
Change in body weight (kg).
Proportion of patients achieving ≥5% body weight gain.
Appetite and anorexia-related outcomes measured using validated assessment tools, including the Functional Assessment of Anorexia/Cachexia Therapy (FAACT) score.

Additional outcome(s) Secondary outcomes will include:
Body mass index (BMI)
Lean body mass
Handgrip strength
Appetite measured using visual analogue scale (VAS)
FAACT anorexia/cachexia subscale
Quality of life outcomes
Incidence of adverse events.

Data management All records retrieved from the searches will be imported into reference-management software and duplicate citations will be removed.
Two reviewers will independently screen titles and abstracts for eligibility. Potentially relevant studies will undergo full-text review. Disagreements will be resolved through discussion, and if consensus cannot be reached, a third reviewer will adjudicate.
The study selection process will be documented using a PRISMA 2020 flow diagram. Study screening will be conducted using Rayyan.

Quality assessment / Risk of bias analysis Risk of bias will be assessed independently by two reviewers using the Cochrane Risk of Bias 2 (RoB 2) tool.
The following domains will be evaluated:Bias arising from the randomization process, Bias due to deviations from intended interventions, Bias due to missing outcome data, Bias in measurement of outcomes, Bias in selection of reported results
Each domain will be rated as: Low risk, Some concerns, High risk
Disagreements will be resolved through consensus.

Strategy of data synthesis Meta-analysis will be performed when at least two clinically comparable studies report the same outcome.
For continuous outcomes, pooled effects will be calculated as mean differences (MDs) with 95% confidence intervals (CIs).
For dichotomous outcomes, pooled effects will be calculated as risk ratios (RRs) with 95% confidence intervals.

Statistical heterogeneity will be assessed using: Cochran's Q test, Tau² statistic, I² statistic.
An I² value greater than 50% will be considered indicative of substantial heterogeneity.
Random-effects models will be used as the primary analytical approach when clinical or statistical heterogeneity is anticipated. Fixed-effect models may be used when heterogeneity is minimal and methodological characteristics are sufficiently similar.
Meta-analyses will be conducted using Review Manager (RevMan) version 5.4.1.

Subgroup analysis Where sufficient data are available, subgroup analyses will be performed according to:
Drug type: Olanzapine, Mirtazapine
Treatment duration: ≤ 1 month, 1 month
Analysis population: Intention-to-treat (ITT), Per-protocol (PP)
Subgroup analyses will primarily focus on body-weight outcomes.

Sensitivity analysis Sensitivity analyses will be conducted to assess the robustness of pooled estimates.
For studies requiring imputation of change-score standard deviations, different baseline-to-follow-up correlation coefficients will be applied: R = 0.2, R = 0.5, R = 0.8
The influence of these assumptions on pooled estimates will be evaluated.

Language restriction We will input no language restrictions.

Country(ies) involved Taiwan.

Keywords Cancer cachexia, Cancer-associated anorexia, Mirtazapine, Olanzapine, Drug repurposing, Randomized controlled trial, Systematic review, Meta-analysis.

Dissemination plans The findings of this systematic review and meta-analysis will be disseminated through publication in a peer-reviewed journal and presentation at scientific conferences to inform evidence-based management of cancer-associated anorexia–cachexia syndrome.

Contributions of each author
Author 1 - Poyen Chiang - Study conception and design, literature search, study selection, data extraction, risk of bias assessment, statistical analysis, and manuscript drafting.
Email: a1665230@gmail.com
Author 2 - Jo-Hsi Chen- Literature screening, data extraction, risk of bias assessment.
Author 3 - Shao-En Weng- Methodological and statistical support, resolution of screening discrepancies, and manuscript revision.
Author 4 - Shih-Tsung Huang- Study supervision, methodological oversight, interpretation of findings, manuscript revision, and final approval of the manuscript.