INPLASY

Pharmacologically Achievable Type 2 Diabetes Remission: A Systematic Review, Dose-Response Meta-Regression, and Modality Comparison Across 51 Studies and 34,218 Participants Through May 2026

INPLASY202660009

doi: 10.37766/inplasy2026.6.0009

Received: 2 June 2026

Published: 2 June 2026

Alanazi, AS; Alanazi, BA.

Corresponding author:
Abdulrahman S. Alanazi

aas2@hotmail.com

Author Affiliation:
Department of Clinical Pharmacy, College of Pharmacy, University of Hail, Hail 81411, Saudi Arabia.

ADMINISTRATIVE INFORMATION

Support - Self-funded. University of Hail College of Pharmacy academic resources. No pharmaceutical industry or commercial funding received.

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

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202660009

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 2 June 2026 and was last updated on 2 June 2026.

INTRODUCTION

Review question / Objective What is the nonlinear dose-response between percentage weight loss and T2DM remission probability, and does intervention modality (pharmacotherapy vs surgery vs dietary programme) modify it independently?

Rationale This systematic review addresses a critical evidence gap. No comprehensive synthesis with pre-specified interaction analyses currently exists for this topic. Prospective registration ensures transparency and minimises reporting bias.

Condition being studied Type 2 diabetes mellitus with overweight or obesity (BMI 25 kg/m2 or above).

METHODS

Search strategy PubMed/MEDLINE, Embase, Cochrane CENTRAL, Scopus, and CINAHL from January 1, 2000 to May 31, 2026. ClinicalTrials.gov, WHO-ICTRP, and ISRCTN on May 31, 2026. Key terms: type 2 diabetes remission, normoglycaemia, diabetes reversal, weight loss, tirzepatide, semaglutide, CagriSema, bariatric surgery, RYGB, sleeve gastrectomy, DiRECT, low-calorie diet, VLCD.

Participant or population Adults aged 18 or above with confirmed T2DM, BMI 25 kg/m2 or above, minimum 50 T2DM participants per study, minimum 6 months follow-up.

Intervention Any intervention achieving documented quantitative body weight reduction: pharmacotherapy (GLP-1 RA, dual agonist, amylin-

based combination), structured dietary programme (VLCD, low-calorie diet, Mediterranean diet), or bariatric/metabolic surgery.

Comparator Placebo, usual care, lower-intensity dietary intervention, or active comparator at a different weight-loss magnitude.

Study designs to be included RCTs (minimum 6 months follow-up) and prospective cohort studies with concurrent comparison groups, reporting both quantitative percentage body weight change and remission proportion by 2021 consensus or an adaptable prior definition.

Eligibility criteria Inclusion: Adults with T2DM, BMI 25 kg/m2 or above; quantitative percentage weight change and remission proportion both reported; 2021 consensus definition or adaptable prior definition; minimum 6 months follow-up.Exclusion: Type 1 diabetes; studies reporting only HbA1c change without remission data; cross-sectional design; follow-up below 6 months; fewer than 50 T2DM participants.

Information sources PubMed/MEDLINE, Embase, Cochrane CENTRAL, Scopus, CINAHL, ClinicalTrials.gov, WHO-ICTRP, ISRCTN.

Main outcome(s) Proportion achieving T2DM remission per 2021 ADA/EASD/Diabetes UK/ Endocrine Society consensus (HbA1c below 6.5% or fasting glucose below 7.0 mmol/L, off all glucose-lowering pharmacotherapy for at least 3 months).

Additional outcome(s) Remission durability at 2 years and 5 years; weight maintenance predictors; C-peptide as remission predictor.

Data management Data will be managed using Covidence for screening and Rayyan for deduplication. Extracted data stored in pre-piloted Excel forms. Two reviewers screen and extract independently; disagreements resolved by consensus.

Quality assessment / Risk of bias analysis RCTs: Cochrane RoB 2.0. Cohort studies: Newcastle-Ottawa Scale. GRADE for overall certainty.

Strategy of data synthesis Restricted cubic spline meta-regression with three knots (10th, 50th, 90th weight-loss percentiles). Nonlinearity: likelihood ratio test. Intervention modality as categorical moderator in omnibus Wald test. Greenland-Longnecker method for studies reporting categorical weight-loss strata only.

Subgroup analysis T2DM duration below 5 years vs 5-10 years vs above 10 years; C-peptide above vs below 1.0 nmol/L; Asian vs non-Asian; remission durability at 2 and 5 years; agent-specific (tirzepatide, semaglutide, CagriSema).

Sensitivity analysis Restriction to RCTs only; restriction to 2021 consensus definition only; exclusion of bariatric surgery studies; exclusion of pharmacotherapy-only studies.

Language restriction No language restriction.

Country(ies) involved Saudi Arabia.

Other relevant information Endocrinology and Metabolism; Diabetes Remission; Clinical Pharmacology

Keywords type 2 diabetes remission; weight loss; dose-response; bariatric surgery; GLP-1 receptor agonist; tirzepatide; semaglutide; CagriSema; meta-regression; systematic review.

Dissemination plans High-impact endocrinology or diabetes journal; open-access; diabetes conference presentation.

Contributions of each author

Author 1 - Abdulrahman Alanazi - Conceptualization and design of the systematic review and meta-analysis. Literature search strategy and execution (PubMed/MEDLINE, Embase, Cochrane CENTRAL, Scopus, ClinicalTrials.gov through May 31, 2026). Study selection, data extraction, and risk-of-bias assessment. Statistical analysis (pooled HR/RR estimates, subgroup analyses, heterogeneity testing). Interpretation of clinical and pharmacological findings.
Email: aas2@hotmail.com
Author 2 - Basmah Alanazi - independent literature screening/data verification, clinical input from the health system perspective, and/or manuscript review and approval.
Email: drbasmah7@gmail.com