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# Safety and Efficacy of Sodium-Glucose Transport Protein 2 Inhibitors and Glucagon-like Peptide-1 Receptor Agonists in Kidney Transplant Recipients: Synthesis of Evidence

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**We use this protocol and it's working**

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## Abstract

A systematic review and meta-analysis will be conducted aiming to investigate the efficacy and safety of Sodium-Glucose Transport Protein 2 inhibitor (SGLT2-i) and Glucagon-like Peptide-1 Receptor Agonist (GLP1-RA) treatment in kidney transplant recipients, with and without diabetes mellitus. A systematic literature search will be performed and the quality of the included studies will be critically assessed using validated tools. Statistical meta-analysis will be performed using random-effects models and exploring potential sources of heterogeneity. The certainty of the existing evidence will be critically evaluated following the GRADE approach.

1 Objective To determine the efficacy and safety of Sodium-Glucose Transport Protein 2 inhibitor (SGLT2-i) and Glucagon-like Peptide-1 Receptor Agonist (GLP1-RA) treatment in kidney transplant recipients.

2 Eligibility criteria The population of the study will consist of kidney transplant recipients. The intervention of interest will be SGLT2-i or GLP1-RA administration. The intervention will be compared to placebo or standard care. The efficacy outcomes of interest will include the effects of SGLT2-i or GLP1-RA therapy on HbA1c, body weight, estimated glomerular filtration rate, proteinuria and systolic blood pressure. The safety endpoints will include any serious adverse effects, the incidence of urinary tract infections and the rate of drug discontinuation. Randomized controlled trials and observational (cohort and case-control) studies will be held eligible. Cross-sectional and descriptive studies, review articles and in vitro studies will be excluded.

3 Literature search Literature search will be performed by systematically searching from inception PubMed, Scopus, Web of Science, CENTRAL (Cochrane Central Register of Controlled Trials) and Clinicaltrials.gov. In addition, Google Scholar will be screened to provide grey literature coverage, while the full reference lists of the included studies will be examined to recognize potential missing articles. No date/language restrictions will be applied.

4 Data extraction The following data will be extracted: year of publication, country, eligibility criteria, sample size, study design, investigated drug, percentage of male sex and diabetes mellitus, median age, median body weight, median body mass index, median estimated glomerular filtration rate and follow-up period, as well as all the necessary information regarding the outcomes of interest.

5 Quality assessment The quality of randomized controlled trials will be assessed with the RoB-2 tool, which takes into account the following domains: randomization, deviations from intended interventions, missing outcome data, measurement of the outcome and selection of the reported results. The risk of bias of the included cohort studies will be evaluated with the ROBINS-I tool, which takes into account the following domains: confounding, selection of participants, classification of interventions, departures from intended interventions, missing data, measurement of outcomes and selection of the reported results.

6 Data analysis Confidence intervals will be set at 95%. Random-effects models will be fitted using the maximum likelihood method for between-study variance estimation. Pool estimates of hazard and risk ratios will be calculated. The inter-study heterogeneity will be quantified by the inconsistency index (I2), while the 95% predictive intervals will be calculated to assess the effects to be expected by future studies. Meta-regression analysis is planned based on the following parameters: study design, location, follow-up and risk of bias. Funnel plots will be constructed and the Egger's test will be performed to assess their asymmetry, if appropriate (>10 studies). The trim-fill method will be applied to account for potentially missing studies.

7 Quality of evidence The quality of the existing evidence will be appraised following the GRADE approach. Specifically, evidence will be classified as very low, low, moderate or high by judging the following domains: study limitations, consistency, directness, imprecision and publication bias.