# INPLASY PROTOCOL

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

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

# SGLT2 inhibitors for the prevention of renal outcomes in Patients with CKD: a systematic review and meta-analysis

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**Review question / Objective:** **1.Whether SGLT2 inhibitors can improves the renal outcomes in patients with CKD 2.Whether CKD patients grouped with different glomerular filtration rates all can benefit from SGLT2.**
**Condition being studied:** **Sodium-glucose co-transporter-2 inhibitors(SGLT2 inhibitors) have been proved a significant reduction of the kidney outcome on substantial loss of kidney function, ESKD, or death due to kidney disease in type 2 diabetes, however, for patient with Chronic kidney disease (CKD), no systematic review has demonstrated that SGLT2 inhibitors is effective in improving renal outcomes . So we decided to do a systematic review and meta analysis to evaluate the SGLT2 inhibitors on kidney outcome in patient with chronic kidney disease.**

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 12 April 2021 and was last updated on 12 April 2021 (registration number INPLASY202140067).

## INTRODUCTION

**Review question / Objective:** **1.Whether SGLT2 inhibitors can improves the renal outcomes in patients with CKD 2.Whether CKD patients grouped with different glomerular filtration rates all can benefit from SGLT2.**

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## METHODS

**Participant or population:** Inclusion criteria: Patient with Chronic kidney disease (Define as glomerular filtration rate(GFR)＜60mL/min per 1·73 m² or urinary albumin/creatinine ratio(UACR)＞300mg/g.

**Intervention:** SGLT2 inhibitors.

**Comparator:** Placebo.

**Study designs to be included:** Randomized controlled trials(RCTS) will be included.

**Eligibility criteria:** Inclusion criteria: Patient with Chronic kidney disease (Define as glomerular filtration rate(GFR)＜60mL/min per 1·73 m² or urinary albumin/creatinine ratio(UACR)＞300mg/g) Exclusion criteria: Participant with acute renal failure, type 1 diabetes or those younger than 18 years were excluded.

**Information sources:** We searched Embase, PubMed, Web of Science, Cochrane Library and other databases from database inception to December 1, 2020 to find the relevant studies about the SGLT2 inhibitors used in CKD . We also searched the clinical trial to find the study which may be ongoing or not yet published. Additionally, the references in each study and the Meta-analysis for SGLT2-inhibitors were also searched.Just in case we missed some important studies.

**Main outcome(s):** 1.The primary outcome of this study included:worsening kidney function(defined as doubling of serum creatinine or sustained 40% decline in GFR, We gave priority to sustained 40% decline in GFR for evaluation), ESRD (defined as chronic dialysis, kidney transplantation, or sustained eGFR lower than 15 mL/min per 1·73 m²)or Renal death.

**Quality assessment / Risk of bias analysis:** The Cochrane quality assessment tool which provided by RevMan will be used to evaluate the quality of each trail.Two authors (Ning Li, Dan lv) assess the risk of bias independently.The assessment including random sequence generation, allocation concealment, blinding of participants and the personnel, blinding of outcome assessment, incomplete outcome assessment, incomplete outcome data, selective reporting, and other bias

**Strategy of data synthesis:** To explore the kidney benefit of SGLT2 inhibitors, we set up different renal outcomes, for the full analysis of data, we use the random effects model, using Hazard ratio to evaluate the primary renal outcome , secondary renal composite, and Mace also use Hazard ratio to analyze, safety outcomes (amputations, fracture, acute kidney injury, consumption capacity) also use the Hazard ratio analysis, if the definition of renal outcomes are different, we will exclude the different renal outcome, and keep the same outcome for statistics .For the continuous variables (such as slope glomerular filtration rate and albuminuria change), we adopt Mean difference to analysis, We assess heterogeneity between studies using the $I^2$ statistic and p values.If $I^2$ values lower than 25%, representing a low heterogeneity, moderate if $I^2$=50%, If $I^2$ higher than 75%, representing a high heterogeneity, All statistics will performed at STATA version16.0.

**Subgroup analysis:** 1.Patient with different glomerular filtration rate (Such as 45-60 mL/min per 1·73 m²,, 30-45mL/min per 1·73 m² or ≤30 mL/min per 1·73 m²) 2.Patient with different underlying diseases (Such as Type 2 diabetes, Heart failure, Atherosclerotic cardiovascular disease or Multiple cardiovascular risks ).

**Sensitivity analysis:** For different definition of renal outcomes among the studies, We

**excluded inconsistent renal outcomes and retained identical renal outcomes for sensitivity analysis.**

**Country(ies) involved:** China.

**Keywords:** SGLT2 inhibitors; Kidney; Chronic kidney disease.

**Contributions of each author:**

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