

# INPLASY

## Preserved Benefit, Shifting Endpoint: A Systematic Review of SGLT2i in CKD After 65

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**ADMINISTRATIVE INFORMATION****Support** - NA.**Review Stage at time of this submission** - Preliminary searches.**Conflicts of interest** - None declared.**INPLASY registration number:** INPLASY202690030**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 7 September 2026 and was last updated on 7 September 2026.**INTRODUCTION**

**Review question / Objective** Sodium-glucose cotransporter 2 inhibitors slow kidney disease progression and reduce cardiovascular events in chronic kidney disease. The trials that established this enrolled populations roughly a decade younger than patients seen in routine nephrology practice, leaving the effect in adults aged 65 years and older, and particularly beyond 75 years, unsettled.

**Condition being studied** Sodium-glucose cotransporter 2 inhibitors slow kidney disease progression and reduce cardiovascular events in chronic kidney disease. The trials that established this enrolled populations roughly a decade younger than patients seen in routine nephrology practice, leaving the effect in adults aged 65 years and older, and particularly beyond 75 years, unsettled.

**METHODS**

**Participant or population** Participants will be adults with CKD of any stage, cause or albuminuria status. The prespecified age criterion will be 65 years and older; we will retain studies with mixed-age populations when they enrolled older adults or reported estimates applicable to older subgroups.

**Intervention** Interventions will be any SGLT2i, including dapagliflozin, empagliflozin, canagliflozin, ertugliflozin and sotagliflozin.

**Comparator** Comparators will be placebo, usual care, non-use, or an active alternative including dipeptidyl peptidase 4 inhibitors, glucagon-like peptide 1 receptor agonists and non-steroidal mineralocorticoid receptor antagonists.

**Study designs to be included** Evidence syntheses of randomized trials, Observational cohorts, Economic evaluation, Narrative reviews.

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**Eligibility criteria** PubMed/MEDLINE, ClinicalTrials.gov, Semantic Scholar, OpenAlex, and arXiv will be searched without date or language restrictions. Four query families combined CKD terminology with SGLT2i class terms, individual drug names, kidney function and progression terms, and albuminuria or proteinuria terms.

**Information sources** PubMed/MEDLINE, ClinicalTrials.gov, Semantic Scholar, OpenAlex and arXiv.

**Main outcome(s)** Evaluate the benefits of SGLT2i in patients aged 65 years and older.

**Quality assessment / Risk of bias analysis** Risk of bias in comparative studies will be assessed across selection, comparability and outcome or exposure ascertainment. Certainty will be rated using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach for CKD progression, KRT, albuminuria reduction, major adverse kidney events (MAKE) and serious adverse events, with explicit consideration of indirectness arising from mixed-age populations.

**Strategy of data synthesis** The synthesis is a structured narrative organized by outcome rather than by study, with evidence from defined age strata deliberately separated from evidence derived from mixed-age populations.

**Subgroup analysis** The review conducts none of its own. Pre-specified strata of 65 to 69, 70 to 74, 75 to 79, and 80 and older could not be populated.

**Sensitivity analysis** None of its own.

**Country(ies) involved** United States, Dominican Republic.

**Keywords** chronic kidney disease; sodium-glucose transporter 2 inhibitors; aged, 80 and over; systematic review.

#### **Contributions of each author**

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