

INPLASY202540039

doi: 10.37766/inplasy2025.4.0039

Received: 12 April 2025

Published: 12 April 2025

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ADMINISTRATIVE INFORMATION**Support** - No funds.**Review Stage at time of this submission** - Data extraction.**Conflicts of interest** - None declared.**INPLASY registration number:** INPLASY202540039

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 12 April 2025 and was last updated on 12 April 2025.

INTRODUCTION

Review question / Objective Population(P): Heterogeneous populations (e.g., general population, individuals with diabetes, high cardiovascular-risk groups); Intervention/Exposure (I): Glomerular hyperfiltration (defined by elevated estimated glomerular filtration rate, eGFR); Comparator (C): Normal filtration (defined by standard eGFR ranges); Outcomes (O): All-cause mortality, rate of eGFR decline, incidence of albuminuria/proteinuria, incidence of cardiovascular events; Study design (S): Observational studies.

Condition being studied Glomerular hyperfiltration (GHF) is a fascinating phenomenon observed across diverse populations. While a decline in estimated glomerular filtration rate (eGFR) is traditionally associated with impaired kidney function, an abnormally elevated eGFR does not necessarily indicate better renal health. On the contrary, glomerular hyperfiltration—defined as an excessively high eGFR—may

represent a pathological state and a potential high-risk factor for adverse clinical outcomes. In recent years, GHF has garnered increasing attention in the medical and research communities. A growing body of evidence suggests that GHF may be linked to poor long-term prognosis, but its implications likely vary depending on the population studied.

METHODS

Participant or population Since our study investigates the association of GHF across diverse populations, no restrictions were applied to the study population.

Intervention Glomerular hyperfiltration (GHF) is defined as an elevated estimated glomerular filtration rate (eGFR), with no restrictions imposed on the eGFR assessment method.

Comparator Normal filtration (GHF) is also based on eGFR.

Study designs to be included Observational study.

Eligibility criteria Inclusion Criteria: Observational studies with a sample size >1,000 participants; Must compare GHF (defined by elevated eGFR) vs. normal filtration (reference group).

Exclusion Criteria: Non-English publications; Conference abstracts, letters, editorials, or unpublished data; Studies failing to report HR with 95% confidence intervals or sufficient data for calculation; Duplicate studies.

Information sources Electronic databases: Pubmed, Embased, Cochrane library.

Main outcome(s) All-cause mortality, rate of eGFR decline, incidence of albuminuria/proteinuria, incidence of cardiovascular events.

Quality assessment / Risk of bias analysis This study will apply the Newcastle-Ottawa Scale for risk of bias analysis. It is a validated tool designed to evaluate the methodological quality of non-randomized observational studies (primarily cohort and case-control studies).

Strategy of data synthesis We will extract adjusted hazard ratios with corresponding 95% confidence intervals and reported confounding factors from included studies. Data synthesis will be performed using frequentist-based meta-analysis methods, implemented through the 'netmeta' package in R Studio.

Subgroup analysis Subgroup analyses were performed based on: Geographical regions of study populations, Different eGFR calculation methods, and Variations in adjusted confounding factors.

Sensitivity analysis Sensitivity analyses via meta-regression will assess heterogeneity attributable to variations in follow-up time among studies.

Country(ies) involved China.

Keywords glomerular hyperfiltration, eGFR, cardiovascular disease, mortality.

Contributions of each author

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