# INPLASY PROTOCOL

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# Prevalence and prognosis of pulmonary hypertension in patients with chronic kidney disease

Lin, CL1.

Review question / Objective: Pulmonary hypertension (PH) is common in patients with chronic kidney disease (CKD) and may have serious prognostic and therapeutic implications. However, the PH prevalence varies greatly depending on CKD status. Moreover, it remains controversial whether the magnitude of PH prognosis differs based on patient characteristics or not. This study is a systematic review and meta-analysis aiming to estimate the prevalence and prognostic value of PH in CKD patients.

Condition being studied: Pulmonary hypertension (PH) is defined as the presence of mean pulmonary artery pressure ≥ 25 mmHg at resting using right heart catheterization. Approximately 10% of people older than 65 years are affected by PH, which is a common occurrence in chronic kidney disease (CKD) owing to a higher risk of heart failure, volume overload, and vascular calcification. Moreover, PH in patients was associated with an elevated risk of all-cause and cardiovascular-related mortality. Although several systematic reviews and meta-analyses have addressed the PH prevalence in patients at various stages of CKD, it is still controversial whether the PH prevalence and prognosis differ or not according to individual characteristics. Therefore, this systematic review aimed to assess the prevalence and prognostic value of PH in patients with CKD.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 13 February 2023 and was last updated on 13 February 2023 (registration number INPLASY202320051).

## **INTRODUCTION**

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with chronic kidney disease (CKD) and may have serious prognostic and therapeutic implications. However, the PH prevalence varies greatly depending on CKD status. Moreover, it remains controversial whether the magnitude of PH prognosis differs based on patient characteristics or not. This study is a systematic review and meta-analysis aiming to estimate the prevalence and prognostic value of PH in CKD patients.

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# **METHODS**

Search strategy: ("chronic kidney disease" OR "CKD" OR "chronic renal failure" OR "chronic renal insufficiency" OR "CRF" OR "end-stage kidney disease" OR "ESKD" OR "end-stage renal disease" OR "ESRD" OR "dialysis") AND ("pulmonary" AND ("hypertension" OR "pressure")).

Participant or population: All patients diagnosed with CKD, irrespective of disease status.

Intervention: The PH prevalence should be reported.

**Comparator: CKD patients without PH.** 

Study designs to be included: Observational studies, including cross-sectional, retrospective, and prospective.

Eligibility criteria: The inclusion criteria were as follows: (1) patients: all patients diagnosed with CKD, irrespective of disease status; (2) exposure: the PH prevalence should be reported; (3) control: CKD patients without PH; (4) outcome: PH prevalence or prognosis in CKD patients should report at least one all-cause mortality, major cardiovascular events (MACEs), and cardiac death, and (5) study design: observational studies, including cross-sectional, retrospective, and prospective.

Information sources: PubMed, Embase, Cochrane Library, and the reference lists of relevant reviews and original articles.

Main outcome(s): PH prevalence or prognosis in CKD patients should report at least one all-cause mortality, major cardiovascular events, and cardiac death.

Data management: The information extracted from the selected studies included the first authors' surname, publication year, study design, country, sample size, mean age, male sex, cardiovascular disease (CVD), diabetes mellitus (DM), hypertension, ejection fraction (EF), CKD stage, PH definition, PH diagnostic methods, PH prevalence, and the association between PH and the risk of all-cause mortality, major cardiovascular events (MACEs), and cardiac death in CKD patients.

### Quality assessment / Risk of bias analysis:

Methodological quality was assessed using the Newcastle-Ottawa scale (NOS), which is a comprehensive and validated method for assessing the quality of observational studies in meta-analysis. The NOS included eight items in three subscales (selection: four items; comparability: one item, and outcome: three items), whereas the "star system" for individual studies ranged from 0-9.

Strategy of data synthesis: PH prevalence was calculated based on PH events and sample size, whereas the pooled incidence and 95% confidence intervals (CI) were calculated using a random-effects model.

Moreover, the prognostic role of PH in the risk of all-cause mortality, MACEs, and cardiac death in patients were assigned as relative risk (RR) with 95%CI, whereas the pooled analyses were performed using the random-effects model, which could consider the underlying variations across the included studies.

Subgroup analysis: The prevalence of PH in patients with CKD was assessed according to CKD status, and subgroup analyses were performed based on study design and country. Moreover, subgroup analyses for the prognostic role of PH with the risk of all-cause mortality, MACEs, and cardiac death in CKD patients were conducted based on study design, country, mean age, male sex, CVD, DM, hypertension, disease status, and PH definition.

Sensitivity analysis: Sensitivity analyses were performed to assess the role of PH in patients to assess the robustness of the pooled conclusions by sequentially removing a single study.

Language restriction: No restriction were placed on published language.

Country(ies) involved: China.

Keywords: pulmonary hypertension; prevalence; prognosis; chronic kidney disease; systematic review; meta-analysis.

**Contributions of each author:** 

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