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Management of Pulmonary Hypertension in Patients with End-Stage Renal Disease: Protocol for a Systematic Review

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ADMINISTRATIVE INFORMATION**Support** - NA.**Review Stage at time of this submission** - Completed but not published.**Conflicts of interest** - None declared.**INPLASY registration number:** INPLASY2026100016

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 3 October 2026 and was last updated on 3 October 2026.

INTRODUCTION

Review question / Objective Review question: In adults with end-stage renal disease (ESRD) receiving maintenance hemodialysis or peritoneal dialysis, and in kidney transplant candidates or recipients, which management interventions lower pulmonary artery pressure or improve pulmonary hypertension (PH)-related outcomes?

PICOS: Population – adults with ESRD on maintenance dialysis, kidney transplant candidates and recipients, with PH defined by echocardiography or right heart catheterization, or ESRD populations not selected for PH that report a PH-specific outcome before and after an intervention. Intervention – any management strategy applied for at least several weeks or as a definitive procedure (volume removal or dry-weight reduction, dialysis modality or prescription changes, arteriovenous access flow reduction or ligation, kidney transplantation, PH-targeted or other pharmacotherapy, exercise,

parathyroidectomy). Comparator – baseline values, usual care, an alternative treatment, or remaining on dialysis or the transplant wait-list. Outcomes – change in pulmonary artery pressure or PH prevalence (primary); wedge pressure, pulmonary vascular resistance, right ventricular function, functional capacity, transplant candidacy, mortality, graft outcomes and adverse events (secondary). Study designs – randomized trials, non-randomized controlled studies, cohort studies, before-after studies and case series with at least five patients.

Objective: To identify, appraise and synthesize primary studies of interventions intended to lower pulmonary pressure or improve PH-related outcomes in adults with ESRD.

Rationale PH affects roughly 4 in 10 patients receiving maintenance hemodialysis and about doubles mortality in dialysis patients and kidney transplant recipients. The hemodynamic phenotype in ESRD is predominantly post-capillary or combined pre- and post-capillary, and the 2022

ESC/ERS guidelines classify PH associated with chronic kidney failure in group 5. Volume overload, left heart disease, high-output arteriovenous access, uremic toxins and pulmonary vascular remodeling all contribute. Management is largely extrapolated from other forms of PH, and clinicians face unresolved questions about dry-weight probing, access flow reduction or ligation, the role of PH in transplant candidacy, and the use of pulmonary vasodilators. Previous meta-analyses addressed prevalence and prognosis rather than treatment, and the primary intervention literature has not been systematically collected and appraised.

Condition being studied Pulmonary hypertension (PH) in patients with end-stage renal disease (ESRD), defined hemodynamically by right heart catheterization or estimated by Doppler echocardiography (systolic pulmonary artery pressure or right ventricular systolic pressure above study-specific thresholds), in patients receiving maintenance hemodialysis or peritoneal dialysis and in kidney transplant candidates and recipients. PH in this setting is common, is classified by the 2022 ESC/ERS guidelines in group 5 (unclear or multifactorial mechanisms), is usually post-capillary or combined pre- and post-capillary, and is associated with higher mortality and worse post-transplant outcomes.

METHODS

Search strategy Databases: MEDLINE via PubMed (NCBI E-utilities), Ovid MEDLINE ALL, Web of Science Core Collection (all editions) and ClinicalTrials.gov, from inception to October 2, 2026, without date limits. Supplementary targeted PubMed searches (PH-targeted drugs; access ligation or banding; parathyroidectomy and calcimimetics; intensive or home hemodialysis; bioimpedance or lung ultrasound-guided fluid management) and backward citation chasing.

PubMed strategy: ("Hypertension, Pulmonary"[Mesh] OR "pulmonary hypertension"[tiab] OR "pulmonary arterial hypertension"[tiab] OR "pulmonary artery pressure"[tiab] OR "pulmonary arterial pressure"[tiab] OR "pulmonary artery systolic pressure"[tiab] OR "right ventricular systolic pressure"[tiab] OR "pulmonary vascular resistance"[tiab]) AND ("Kidney Failure, Chronic"[Mesh] OR "Renal Dialysis"[Mesh] OR "Peritoneal Dialysis"[Mesh] OR "Kidney Transplantation"[Mesh] OR "end-stage renal"[tiab] OR "end stage renal"[tiab] OR "end-stage kidney"[tiab] OR "end stage kidney"[tiab] OR

"kidney failure"[tiab] OR hemodialysis[tiab] OR haemodialysis[tiab] OR "peritoneal dialysis"[tiab] OR "kidney transplant"[tiab] OR "renal transplant"[tiab] OR "arteriovenous fistula"[tiab] OR "arteriovenous access"[tiab]) NOT (animals[Mesh] NOT humans[Mesh]).

The strategy was translated to Ovid syntax (exp Hypertension, Pulmonary/ and .ti,ab. free text, with animal exclusion) and to Web of Science topic-field syntax (TS=). Records were deduplicated by PubMed unique identifier and by title.

Participant or population Adults (18 years or older) with end-stage renal disease receiving maintenance hemodialysis or peritoneal dialysis, kidney transplant candidates, and kidney transplant recipients, with pulmonary hypertension defined by echocardiography or right heart catheterization; or ESRD populations not selected for PH that report a PH-specific outcome before and after an intervention. Pediatric populations are excluded.

Intervention Any management strategy applied for at least several weeks or as a definitive procedure: volume removal or dry-weight reduction (including intensified ultrafiltration and bioimpedance-guided fluid management), changes in dialysis modality or prescription (home, intensive or nocturnal hemodialysis, peritoneal dialysis, dialysate sodium), arteriovenous access flow reduction (banding, proximal artery restriction or ligation) or ligation, kidney transplantation, pharmacotherapy (PH-targeted drugs such as endothelin receptor antagonists, phosphodiesterase-5 inhibitors, prostacyclin pathway agents, riociguat or sotatercept, and other drugs such as sacubitril-valsartan), exercise training, and parathyroidectomy or calcimimetics.

Comparator Baseline (pre-intervention) values, usual care, an alternative active treatment, or remaining on dialysis or on the kidney transplant wait-list.

Study designs to be included Randomized controlled trials, non-randomized controlled studies, prospective or retrospective cohort studies, before-after studies, and case series with at least five patients. Case reports, reviews, editorials and conference abstracts are excluded.

Eligibility criteria Exclusions: studies of transient manoeuvres lasting less than one day (single dialysis sessions, temporary fistula compression, acute vasoreactivity testing); studies in which arteriovenous access creation is the exposure;

prognostic studies without an intervention; pediatric studies; non-English reports. When only an abstract is available, the study is retained if the abstract reports the direction of effect for an eligible outcome. Overlapping reports from the same centre are identified from author lists, institutions and enrollment periods.

Information sources MEDLINE (PubMed and Ovid MEDLINE ALL), Web of Science Core Collection, and ClinicalTrials.gov (registered and unpublished trials), supplemented by targeted PubMed searches for specific interventions and backward citation chasing of included studies and relevant reviews.

Main outcome(s) Change in pulmonary artery pressure (echocardiographic systolic pulmonary artery pressure or right ventricular systolic pressure, or catheter-measured mean pulmonary artery pressure) or change in the prevalence or resolution of PH after the intervention, compared with baseline or with the comparator. Effect measures are extracted as reported (mean or median change, proportions, hazard ratios with 95% CI).

Additional outcome(s) Pulmonary artery wedge pressure; pulmonary vascular resistance; cardiac output; right ventricular function (e.g., TAPSE, TAPSE/PASP ratio); functional capacity (6-minute walk distance, NYHA or WHO functional class); transplant candidacy; mortality; graft outcomes (delayed graft function, graft failure); high-output heart failure; and adverse events (e.g., intradialytic hypotension, hyperkalemia).

Data management Search results are exported and deduplicated by PubMed unique identifier and by title. Titles and abstracts are screened against the eligibility criteria, followed by full-text assessment with reasons for exclusion recorded. Data are extracted into a standardized form: first author, year, country, design, sample size, population, PH definition and method of confirmation, timing of echocardiography relative to dialysis, intervention, comparator, follow-up, pulmonary pressure outcomes, secondary outcomes, funding, and whether data came from the full text or abstract only. Effect estimates are transcribed as reported.

Quality assessment / Risk of bias analysis Randomized trials: revised Cochrane risk-of-bias tool (RoB 2). Comparative non-randomized studies: ROBINS-I. Uncontrolled before-after studies and case series: JBI critical appraisal checklist for case series. Certainty of evidence for

the primary outcome in each intervention category is rated with GRADE (risk of bias, inconsistency, indirectness, imprecision, publication bias).

Strategy of data synthesis Studies are grouped by intervention category: volume removal and dialysis prescription; exercise; arteriovenous access; kidney transplantation; pharmacotherapy. Meta-analysis is planned only if at least two studies with comparable populations, PH definitions, interventions and outcome measures report poolable effects; otherwise a structured narrative synthesis following the Synthesis Without Meta-analysis (SWiM) guideline is used, tabulating direction and magnitude of effect, giving greater weight to catheter-confirmed populations, controlled designs and lower risk of bias, and using vote counting based on direction of effect. Reporting follows PRISMA 2020.

Subgroup analysis If data permit: dialysis modality (hemodialysis vs peritoneal dialysis vs transplant), method of PH confirmation (right heart catheterization vs echocardiography), and PH phenotype (post-capillary vs pre-capillary). Otherwise these factors are explored narratively.

Sensitivity analysis If meta-analysis is performed: exclusion of studies at high or critical risk of bias, of abstract-only studies, and of reports with probable patient overlap. In a narrative synthesis, the influence of these studies on the direction of findings is described.

Language restriction English only.

Country(ies) involved United States.

Other relevant information This protocol is registered retrospectively: at the time of registration, searches, screening, data extraction, risk-of-bias assessment and synthesis had been completed, and the review had not been published. The methods described here are those applied in the review. The searches were run on October 2, 2026.

Keywords pulmonary hypertension; end-stage renal disease; renal dialysis; kidney transplantation; arteriovenous fistula; ultrafiltration.

Dissemination plans Publication in a peer-reviewed journal (Canadian Journal of Kidney Health and Disease) and presentation at scientific meetings.

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