

Prognostic Significance of CKD-Associated Pruritus: A Systematic Review and Meta-analysis

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Abstract

Chronic kidney disease-associated pruritus (CKD-aP), historically termed uremic pruritus, is a common and burdensome symptom in patients with advanced chronic kidney disease, hemodialysis, and peritoneal dialysis. Although previous reviews have emphasized prevalence, sleep disturbance, psychological burden, treatment response, and health-related quality of life, the prognostic significance of CKD-aP for hard clinical outcomes remains uncertain.

We systematically reviewed studies published from January 1, 2000 to May 31, 2026 that evaluated CKD-aP or itch as a prognostic exposure in adults with chronic kidney disease or kidney failure. Outcomes included all-cause mortality, hospitalization, cardiovascular outcomes, infection-related outcomes, peritoneal dialysis outcomes, dialysis-related outcomes, and healthcare utilization.

Risk of bias was assessed using QUIPS, and comparable adjusted hazard ratios for all-cause mortality in hemodialysis cohorts were pooled using DerSimonian-Laird random-effects models, with REML Hartung-Knapp analyses used for robustness. Proxy exposure studies, composite endpoints, and non-comparable effect measures were excluded from the primary quantitative model.

Twenty-two reports were retained. In the primary model, severe or extreme CKD-aP was associated with higher all-cause mortality among hemodialysis patients (2 studies; pooled HR 1.33, 95% CI 1.07-1.65; I² = 39.6%). A sensitivity model including one additional cohort showed a similar association (HR 1.42, 95% CI 1.12-1.80; I² = 44.7%), although Hartung-Knapp intervals were imprecise and crossed the null. Secondary clinical outcomes were relevant but heterogeneous and were synthesized narratively. Severe CKD-aP may identify higher-risk hemodialysis patients, but certainty of evidence remains low. These findings should be interpreted cautiously in clinical practice and research due to the limitations of the available data.

Keywords: Pruritus; Chronic kidney disease; Dialysis; Mortality; Hospitalization.

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Introduction

Chronic kidney disease (CKD) is a major contributor to morbidity and mortality worldwide.^{1,2} Patients with advanced CKD and kidney failure experience substantial symptom burden.³ CKD-associated pruritus (CKD-aP), historically termed uremic pruritus, is common and associated with impaired quality of life, poor sleep, and functional limitations.⁴⁻⁹ DOPPS and related cohort evidence has linked CKD-aP with mortality, hospitalization, cardiovascular events, infection-related outcomes, and dialysis burden.^{10,11} Prior reviews have mainly

emphasized treatment and patient-reported outcomes.^{12,13} Additional prognostic reports support a broader clinical-outcomes review.¹⁴⁻¹⁸ This study evaluated CKD-aP as a prognostic factor in adults with CKD.

Materials and Methods

Study Design and Reporting

This systematic review and meta-analysis was conducted using a predefined protocol and reported according to PRISMA 2020 guidance.¹⁹ Adults with CKD, kidney failure, hemodialysis, or peritoneal dialysis were eligible when pruritus or itch was assessed as a prognostic exposure. Outcomes of interest were all-cause mortality, hospitalization, cardiovascular outcomes, infection-related outcomes, peritoneal dialysis outcomes, dialysis-related outcomes, and healthcare utilization.

Search Strategy

The search covered January 1, 2000 to May 31, 2026. PubMed was the primary bibliographic database. Europe PMC, ClinicalTrials.gov, WHO International Clinical Trials Registry Platform, and focused Google Scholar searches were used for supplementary discovery and citation linkage. English-language restriction was applied during screening. A formal Embase strategy was sent to the supervisor, who reported no additional eligible study; the full Embase export and history were not available for independent screening. Full strategies are supplied in the optional supplementary appendix.

Eligibility and Study Selection

Eligible reports evaluated CKD-aP as an exposure and reported prognostic clinical outcomes. Treatment trials, studies without CKD-aP-specific prognostic information, and reports using medication exposure alone without interpretable pruritus status were excluded from synthesis. Composite outcomes were not pooled with pure mortality outcomes. Overlapping DOPPS, JDOPPS, PDOPPS, CKDopps, and Taiwan National Health Insurance Research Database cohorts were linked and handled conservatively to avoid double counting.

Data Extraction

Extracted variables included study design, population, sample size, pruritus definition, exposure contrast, comparator, outcome, effect measure, adjusted estimate, 95% confidence interval, covariates, follow-up, and pooling decision. When multiple adjusted models were available, the preferred estimate was the most fully adjusted model that did not include likely mediators where possible. Sleep-adjusted estimates were handled cautiously because sleep disturbance may lie on the causal pathway between pruritus and mortality.

Risk of Bias and Certainty

Risk of bias was assessed using the Quality in Prognosis Studies (QUIPS) tool.²⁰ Domains were study participation, attrition, prognostic-factor measurement, outcome measurement, confounding, and statistical analysis or reporting. Certainty was assessed using a GRADE-informed approach.

Statistical Analysis

Adjusted hazard ratios (HRs) for comparable all-cause mortality outcomes in hemodialysis cohorts were log transformed and pooled using generic inverse-variance DerSimonian-Laird random-effects models in R with the metafor package.^{21,22} Heterogeneity was summarized using Cochran Q, tau², and I². Because the primary model included only two studies, restricted maximum-likelihood models with Hartung-Knapp adjustment were calculated as robustness analyses. Outcomes with incompatible populations, exposure definitions, effect measures, or endpoint construction were synthesized narratively.

Results

Study Selection and Characteristics

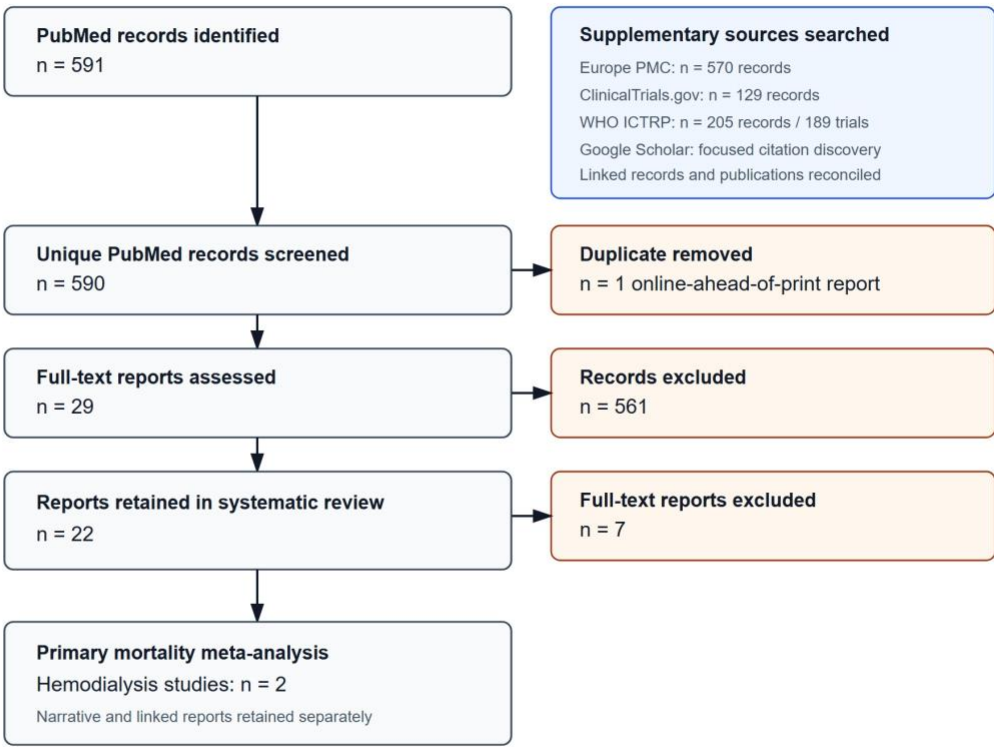
The expanded PubMed pathway identified 591 records. One duplicate online-ahead-of-print record was removed, 590 records underwent screening, 29 full-text reports were assessed, seven were excluded, and 22 reports were retained, Figure 1. Supplementary searches identified additional linked reports but did not alter the primary mortality meta-analysis. Included reports spanned hemodialysis, peritoneal dialysis, mixed dialysis, and nondialysis CKD cohorts (Table 1). Additional retained, linked, or audit-trail reports informed full-text eligibility, cohort overlap handling, and narrative synthesis.²³⁻³⁸ An additive patient total was not calculated because several reports used overlapping datasets.

Risk of Bias

Twenty-one study units underwent QUIPS assessment after linked reports were reconciled. Three were rated low-to-moderate risk, seven moderate risk, two moderate-to-high risk, and nine high risk. Higher risk commonly reflected residual confounding, proxy exposure definitions, cross-sectional designs, or incomplete reporting.

PRISMA Flow Diagram: Expanded Search Update

CKD-associated pruritus prognostic systematic review | Search updated May 31, 2026



Note: Supplementary-source records were used for linkage and citation discovery and were not added to the PubMed record count.

Figure 1. PRISMA flow diagram for the expanded search and study-selection pathway.
Table 1. Characteristics of retained articles searched and finalized for the metaanalysis.

Author, year	PMID	Population	Sample size	CKD-aP exposure	Main outcome or use
Narita 2006	16672924	HD	1773	Severe uremic pruritus, VAS >=7.0	Main mortality pool candidate

CKD & Pruritis

Author, year	PMID	Population	Sample size	CKD-aP exposure	Main outcome or use
Pisoni 2006	16968725	HD	18801	Moderate to extreme pruritus	Sensitivity/narrative only
Chen 2010	20350963	HD	321	Moderate/severe uremic pruritus, VAS 4-10	Sensitivity only
Ramakrishnan 2014	24379689	HD / dialysis organization	38315 detailed HD analysis; larger preliminary dialysis sample in article	KDQOL itchiness score 1 to 5	Narrative HCRU/dialysis-utilization only
Kimata 2014	24766224	HD	6480	Moderate to extreme pruritus	Narrative/sensitivity only
Weng 2018	29913453	HD	866	Dermatologist-diagnosed uremic pruritus; VAS recorded but VAS severity itself was not a significant predictor.	Cardiovascular mortality secondary analysis
Wu 2018	30183756	PD	85	Uremic pruritus VAS intensity, continuous	PD composite narrative/separate analysis
Grochulska 2019	30673111	HD	860 baseline; 724 follow-up	Chronic itch, itch intensity, secondary scratch lesions	Narrative mortality only
Ting 2020	33104746	Mixed dialysis	14760 UP; 29520 non-UP after matching	UP proxy: long-term antihistamine prescription without other indications	Secondary/exploratory morbidity only
Sukul 2021	33604539	HD	23264	Extremely bothered by itchy skin in past 4 weeks	Core HD mortality; secondary hospitalization/dialysis outcomes
Titapiccolo 2023	37269433	HD	6221	CKD-aP severity from KDQOL-36 and 5-D Itch	Narrative HCRU only
Sukul 2023 longitudinal DOPPS	37777951	HD	7976	Persistent moderate-or-more CKD-aP at two assessments about 12 months apart	Longitudinal DOPPS sensitivity/separate analysis
Scherer 2024	38225976	ND-CKD	4401	Extremely bothered by itchy skin	ND-CKD subgroup
Tennankore 2024	39652652	PD	5535	Moderate-to-extreme CKD-associated pruritus, KDQOL-36 single itch item score ≥ 3	PD composite outcome; PD death subcomponent separate/narrative
Faucon 2025	39067660	Mixed dialysis	3281	Clinically recognized pruritus	Sensitivity/proxy mortality; infection hospitalization secondary
Fotheringham 2025	41299292	HD	747 patients; 2631 surveys	Very much/extremely bothered by itchy skin	Narrative/exploratory HCRU
Malhotra 2025	41503178	HD	81210 analysis sample; 47477 moderate+ pruritus plus 33833 low/no sampled comparator	KDQOL-36 pruritus severity	Narrative dialysis-adherence only
Green 2012	23635451	ND-CKD	184	Presence of itch at baseline consultation; symptoms not recorded were presumed absent	Narrative ND-CKD dialysis-initiation outcome
Ting 2020 JAAD letter	31940463	Mixed dialysis	25048 UP; 50096 non-UP after matching	UP proxy: more than 42 daily doses of antihistamine or ultraviolet B phototherapy within 1 year after dialysis initiation	Linked proxy-exposure mortality report; narrative / sensitivity only
Calabria 2024	38234332	HD	1239 total; 218 potentially affected by CKD-aP and 1021 without CKD-aP	Potential CKD-aP inferred from CKD-aP-related treatment supplies	Narrative healthcare-utilization and cost evidence
Thompson 2024	39822582	HD	354	Self-reported CKD-aP using validated patient-reported outcome instruments	Narrative shortened and missed HD-session evidence
Lee 2026	41877507	PD	626 PDOPPS participants; separate microbiome substudy n=76	Self-reported pruritus severity; high-grade score 4-5	Narrative PD catheter-related infection outcomes

All-Cause Mortality in Hemodialysis

The primary quantitative synthesis included Sukul et al. and Narita et al.^{11,14} Severe or extreme CKD-aP was associated with increased all-cause mortality in the DerSimonian-Laird model (pooled HR 1.328, 95% CI 1.066-

1.653; I2 = 39.6%; tau2 = 0.012553) (Figure 2 and Table 2). The primary model included only two studies and should be interpreted cautiously.

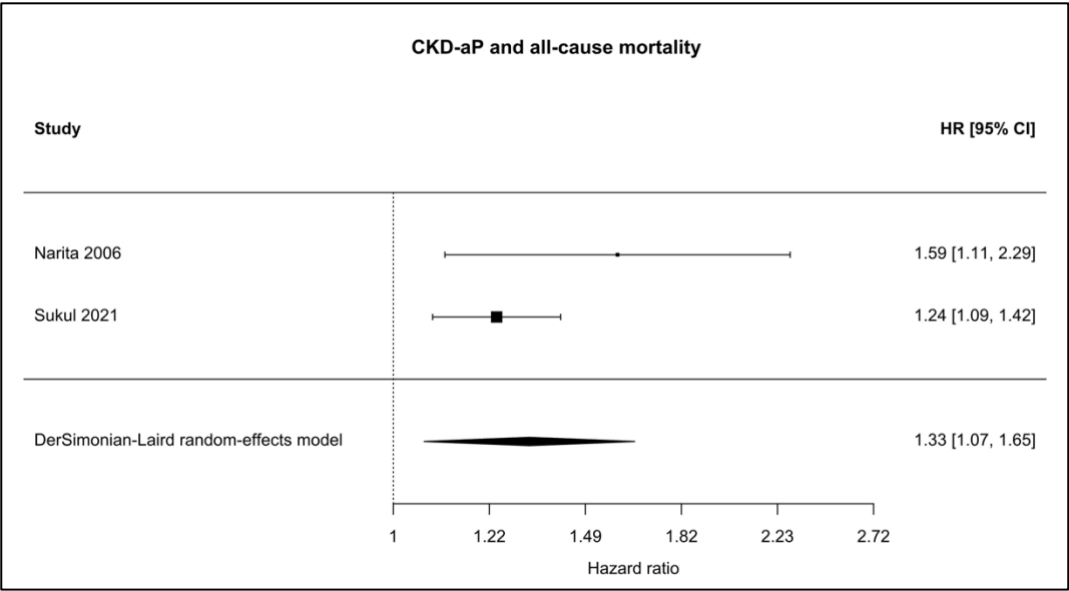


Figure 2. Primary DerSimonian-Laird random-effects meta-analysis of adjusted all-cause mortality hazard ratios among hemodialysis patients with severe or extreme CKD-aP.

Table 2. Quantitative mortality synthesis

Analysis	Studies	k	Pooled estimate	Heterogeneity	Role
Primary DL mortality model	Narita 2006; Sukul 2021	2	HR 1.328 (95% CI 1.066-1.653)	I2 39.6%; tau2 0.012553	Primary hemodialysis analysis
Sensitivity DL mortality model	Narita 2006; Sukul 2021; Chen 2010	3	HR 1.419 (95% CI 1.115-1.804)	I2 44.7%; tau2 0.021684	Sensitivity analysis only
Primary REML Hartung-Knapp robustness	Narita 2006; Sukul 2021	2	HR 1.328 (95% CI 0.320-5.503)	Imprecise	Crossed the null
Sensitivity REML Hartung-Knapp robustness	Narita 2006; Sukul 2021; Chen 2010	3	HR 1.423 (95% CI 0.859-2.357)	Imprecise	Crossed the null

A sensitivity analysis included Chen et al. using the preferred non-interaction adjusted model.²³ The pooled association remained positive (HR 1.419, 95% CI 1.115-1.804; I2 = 44.7%; tau2 = 0.021684) (Figure 3 and Table 2). Protocol-aligned REML Hartung-Knapp analyses were less precise and crossed the null: HR 1.328 (95% CI 0.320-5.503) for the primary model and HR 1.423 (95% CI 0.859-2.357) for the sensitivity model.

Pisoni et al. and Kimata et al. reported mortality signals but were not pooled because exact confidence intervals were unavailable and cohort overlap required caution.^{10,25} Pisoni et al. also reported attenuation after sleep-

quality adjustment. Faucon et al. found no detectable association between clinically recognized pruritus and all-cause mortality in a contemporary dialysis cohort; its exposure definition was proxy based.³¹

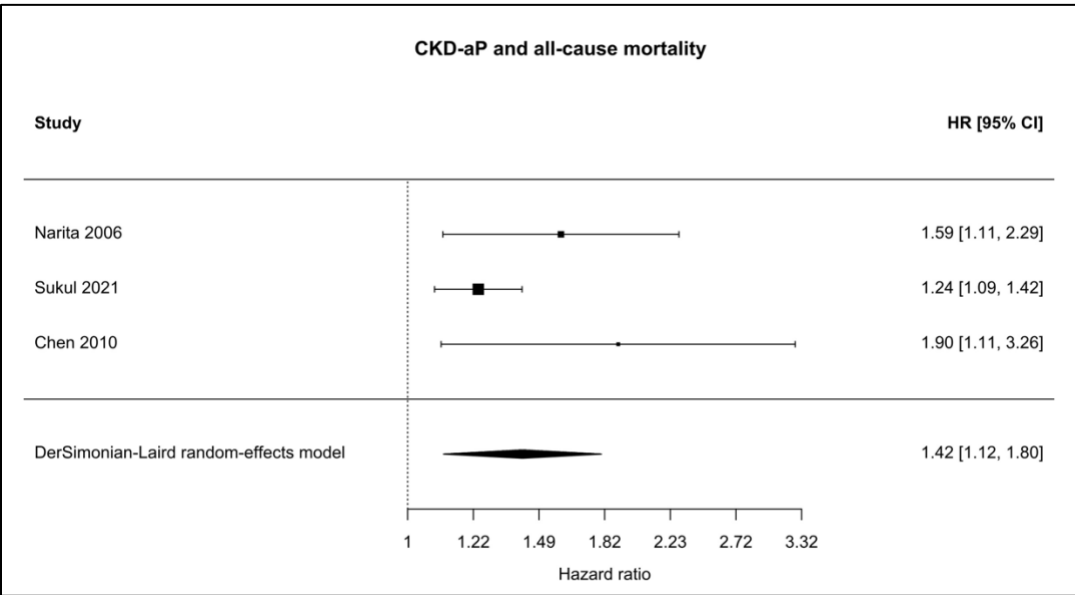


Figure 3. Sensitivity DerSimonian-Laird random-effects meta-analysis of adjusted all-cause mortality hazard ratios among hemodialysis patients, including Chen 2010²³.

Secondary Outcomes

Hospitalization outcomes were clinically relevant but not sufficiently comparable for pooling. DOPPS and nondialysis CKD reports assessed all-cause hospitalization, while other reports assessed emergency visits, infection-related encounters, or healthcare utilization.^{11,17,28,29,32} Cardiovascular outcomes included cardiovascular mortality, cardiovascular events, major adverse cardiac and cerebrovascular events, and heart failure; these endpoints were synthesized separately because they were not interchangeable.^{15,26,28,29}

Peritoneal dialysis evidence included death or technique-related outcomes. Wu et al. evaluated technique failure or death, while Tennankore et al. reported death or permanent transfer to hemodialysis (HR 1.12, 95% CI 1.02-1.23).^{16,30} Death alone in Tennankore et al. was HR 1.14 (95% CI 0.99-1.30) and was not pooled with hemodialysis mortality.

Infection-related evidence also remained narrative. Ting et al. and Faucon et al. reported infection-related outcomes using proxy or clinically recognized exposure definitions.^{15,31} Lee et al. reported that high-grade pruritus was associated with catheter-related infection in a Korean PDOPPS cohort (adjusted HR 2.57, 95% CI 1.27-5.22) and with Staphylococcus aureus catheter-related infection (adjusted HR 5.93, 95% CI 2.18-16.15).³⁸ Dialysis-related outcomes included missed or shortened treatments, withdrawal, recovery time, and healthcare utilization (Table 3).^{11,17,24,32,33,36,37}

Certainty of Evidence

Certainty for the primary mortality outcome was low because the evidence was observational, the primary quantitative model contained two studies, residual confounding remained possible, and robustness analyses were imprecise. Other outcome families were rated low or very low-to-low because of heterogeneity (Table 4).

Table 3. Narrative synthesis by outcome family

Outcome family	Contributing reports	Approach	Reason for narrative synthesis
Hospitalization	Sukul 2021; Sukul 2023; Scherer 2024; Fotheringham 2025; Titapiccolo 2023	Narrative	Definitions included all-cause hospitalization, emergency visits, and utilization endpoints.
Cardiovascular outcomes	Weng 2018; Ting 2020; Sukul 2021; Sukul 2023; Scherer 2024	Narrative	Cardiovascular mortality, events, MACCE, and heart failure were not interchangeable.
Infection-related outcomes	Ting 2020; Faucon 2025; Fotheringham 2025; Lee 2026	Narrative	Populations, exposure definitions, and infection endpoints differed.
Peritoneal dialysis outcomes	Wu 2018; Tennankore 2024	Narrative	Composite technique-failure or modality-transfer outcomes were kept separate from mortality.
Dialysis burden and utilization	Sukul 2021; Ramakrishnan 2014; Titapiccolo 2023; Fotheringham 2025; Malhotra 2025; Calabria 2024; Thompson 2024	Narrative	Missed or shortened treatments, withdrawal, recovery time, and healthcare use varied.
Nondialysis CKD	Scherer 2024; Green 2012	Narrative subgroup	Mortality, hospitalization, cardiovascular events, and dialysis initiation were retained separately.

Table 4. GRADE-informed certainty assessment

Outcome	Estimate or synthesis	Certainty	Reasons for rating
All-cause mortality in hemodialysis	Primary DL: HR 1.328 (95% CI 1.066-1.653); REML Hartung-Knapp robustness: HR 1.328 (95% CI 0.320-5.503)	Low	Downgraded for observational design, small number of primary pooled studies, moderate heterogeneity, residual confounding risk, exposure-definition differences, and substantial imprecision in robustness analysis.
All-cause hospitalization	Narrative synthesis only	Low	Downgraded for heterogeneity in population, hospitalization definitions, exposure measurement, and effect measures.
Infection-related outcomes	Narrative/exploratory synthesis only	Low	Downgraded for mixed dialysis populations, proxy or clinically recognized exposure definitions in some studies, mixed effect measures, and outcome heterogeneity.
Cardiovascular outcomes	Narrative synthesis only	Low	Downgraded for mixed outcomes including CV mortality, CV events, MACCE, and heart failure; populations and effect measures differ.
Peritoneal dialysis composite outcomes	Tennankore composite HR 1.12 (95% CI 1.02-1.23); Wu composite narrative	Low	Downgraded for composite endpoints, small number of studies, population specificity, and inability to pool pure mortality with technique failure or HD transfer.
Dialysis-related outcomes and healthcare utilization	Narrative synthesis only	Very low to Low	Downgraded for descriptive or cross-sectional designs, varying outcome windows, heterogeneous effect measures, proxy exposure definitions in some studies, and risk of residual confounding.

Discussion

This review found that severe or extreme CKD-aP was associated with approximately 33% higher all-cause mortality among hemodialysis patients in the primary DerSimonian-Laird model. The direction of effect remained similar after inclusion of Chen et al. in sensitivity analysis.²³ However, the primary synthesis contained only two studies and Hartung-Knapp robustness intervals crossed the null. The association should therefore be interpreted as a clinically relevant prognostic signal rather than proof of causality.

Several pathways may connect CKD-aP with adverse outcomes. Persistent itching may impair sleep, mood, physical recovery, and dialysis tolerance. In Pisoni et al., adjustment for sleep-quality variables attenuated the mortality association, suggesting that sleep disturbance may be a mediator rather than only a confounder.¹⁰ CKD-aP may also reflect inflammatory or higher-risk biological phenotypes. Chen et al. reported an association

between moderate or severe pruritus, elevated C-reactive protein, and mortality.²³ Repeated scratching and skin-barrier impairment may plausibly contribute to infection susceptibility, although the available infection studies varied substantially.^{15,31,38}

The review extends previous work that emphasized prevalence, quality of life, and patient-reported burden.^{5,7,13} Its central contribution is a conservative prognostic synthesis. We avoided combining standard HRs with subdistribution HRs or odds ratios, proxy exposure studies with validated symptom-scale studies in the primary pool, and composite endpoints with pure mortality outcomes. We also avoided simultaneous inclusion of overlapping DOPPS-derived cohorts.

The findings support routine recognition of CKD-aP in nephrology practice. Severe symptoms may identify patients who warrant closer assessment for sleep disturbance, inflammation, nutrition, cardiovascular risk, infection risk, dialysis tolerance, and adherence. Evidence does not establish that treatment of CKD-aP reduces mortality. Prospective studies should evaluate whether systematic symptom identification and effective treatment improve hospitalization, dialysis attendance, recovery time, and survival.

This review has limitations. Evidence was observational, exposure definitions varied, residual confounding was likely, and only two studies were eligible for the primary mortality model. Publication bias could not be meaningfully assessed. Subscription-database access was incomplete: an Embase strategy was supplied to the supervisor, but the result export and search history were unavailable for independent audit. Several clinically important secondary outcomes could not be pooled because their definitions differed. These limitations support cautious interpretation and the need for standardized contemporary prognostic cohorts.

Conclusion

Severe or extreme CKD-aP may identify hemodialysis patients at possible increased risk of all-cause mortality. The broader literature suggests clinically relevant associations with hospitalization, cardiovascular, infection-related, and dialysis-related outcomes, but heterogeneity limits quantitative synthesis. Standardized CKD-aP definitions and complete reporting of adjusted estimates are needed.

Conflict of Interest: None declared

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