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Review

Effectiveness of Probiotics in Controlling Hypertension in Patients with Kidney Disease: MetaUmbrella

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ABSTRACT

Hypertension is highly prevalent in chronic kidney disease (CKD), and gut dysbiosis has been linked to vascular dysfunction, inflammation, and retention of microbial metabolites. This focused meta-umbrella review evaluated whether probiotics improve blood-pressure control in kidney disease using evidence published from 2015 through 31 August 2025. Searches were structured in PubMed/MEDLINE, the Cochrane Library, Europe PMC, and citation-indexed sources and synthesized as two complementary streams: CKD/dialysis reviews and blood-pressure-focused probiotic reviews. Seventeen review-level syntheses met the framework (11 renal and 6 BP-focused). None of the CKD meta-analyses provided a pooled systolic or diastolic BP estimate. In broader populations, the 2023 umbrella meta-analysis of 14 meta-analyses (15,494 participants) reported modest reductions in systolic BP (WMD −1.96 mmHg, 95% CI −2.78 to −1.14) and diastolic BP (WMD −1.28 mmHg, 95% CI −1.76 to −0.79); a long-term RCT meta-analysis found similar office reductions (−2.18/−1.07 mmHg). The 2025 overweight/obesity update found no significant systolic effect and only a small diastolic effect. CKD reviews more consistently reported changes in selected uremic toxins, BUN, inflammation, or oxidative stress than cardiovascular outcomes. Probiotics therefore show a small antihypertensive signal in general cardiometabolic populations, but effectiveness for CKD-associated hypertension remains unproven and indirect. They should not replace established antihypertensive or kidney-protective therapy.

1. Introduction

Chronic kidney disease (CKD) and hypertension are tightly interdependent: elevated blood pressure accelerates nephron loss and cardiovascular injury, while declining kidney function promotes sodium retention, neurohormonal activation, arterial stiffness, endothelial dysfunction, and treatment-resistant hypertension. In advanced CKD and dialysis, inflammation, oxidative stress, and retention of uremic solutes further amplify cardiovascular risk [1–4]. The intestinal microbiome may contribute to this kidney–vascular interaction. CKD alters transit, diet, luminal pH, medication exposure, and microbial composition; impaired barrier function and proteolytic fermentation increase exposure to metabolites such as indoxyl sulfate and p-cresyl sulfate, whereas short-chain fatty acids participate in vascular, immune, sympathetic, and renal signaling [1–5]. Probiotics could modify these pathways by favoring saccharolytic metabolism, improving barrier function, altering short-chain-fatty-acid production, and attenuating inflammatory signaling. Meta-analyses in general and cardiometabolic populations report small blood-pressure reductions, but extrapolation to CKD is uncertain because volume status, dialysis, sodium balance, polypharmacy, and the uremic microbiome may modify response [6,16,17,25,26]. Moreover, CKD reviews have mainly pooled uremic toxins, kidney-function markers, inflammation, oxidative stress, and gastrointestinal or metabolic outcomes rather than standardized systolic and diastolic blood pressure [9–11,13,14,19,21,22,27–29]. This focused meta-umbrella review therefore integrates direct CKD/dialysis evidence with broader probiotic blood-pressure evidence, without re-pooling overlapping or non-equivalent syntheses, to determine the strength and directness of evidence for probiotic-mediated hypertension control in kidney disease from 2015 through 31 August 2025.

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2. Materials and Methods

2.1 Design and reporting framework

This work was conducted as a focused meta-umbrella review of review-level evidence. Reporting was structured according to PRISMA 2020 and the PRIOR statement for overviews of reviews, while methodological confidence was judged using AMSTAR 2 domains [8,18,24]. The unit of inclusion was the systematic review or meta-analysis. Primary randomized trials were consulted only to clarify whether blood pressure had actually been measured in CKD populations or to interpret discrepancies between review-level conclusions.

2.2 Eligibility criteria

Eligible publications were systematic reviews, meta-analyses, network meta-analyses, or umbrella reviews published in English, Portuguese, or Spanish from 1 January 2015 through 31 August 2025. Two complementary streams were prespecified. The direct renal stream included adults with nondialysis CKD, kidney failure, hemodialysis, or peritoneal dialysis exposed to probiotics alone or to a biotic intervention for which the probiotic component was clinically interpretable. The blood-pressure stream included probiotic reviews in general, hypertensive, diabetic, overweight, or other cardiometabolic populations when systolic blood pressure (SBP) and/or diastolic blood pressure (DBP) were pooled. Narrative reviews were retained only for mechanistic context and were not counted in the quantitative evidence set. Reviews focused exclusively on animal studies, fermented foods without defined live microorganisms, or fecal microbiota transplantation were excluded.

2.3 Search strategy and study selection

Structured searches were performed in PubMed/MEDLINE, the Cochrane Library, and Europe PMC, supplemented by publisher/DOI indexing and backward and forward citation searching. The initial search was completed on 31 March 2025, immediately before manuscript submission, and an update was performed on 31 August 2025 before final revision. Search concepts combined probiotic, Lactobacillus/Lacticaseibacillus, Bifidobacterium, synbiotic, chronic kidney disease, renal dialysis, hypertension, blood pressure, systematic review, and meta-analysis terms. Reference lists of eligible syntheses were also screened. The 2025 update allowed incorporation of evidence published after initial submission while remaining chronologically compatible with the 2025 editorial timeline.

Titles, abstracts, and full texts were assessed against the predefined eligibility framework. When several reviews addressed the same question, all informative syntheses could be retained for evidence mapping, but the most comprehensive or most recent high-quality estimate was prioritized for interpretation. Particular attention was given to overlap of primary randomized trials, because treating overlapping meta-analyses as independent observations can artificially narrow confidence intervals.

2.4 Data extraction and appraisal

Extracted data included publication year, population, intervention type, number of trials and participants, pooled SBP and DBP when available, renal or inflammatory outcomes, heterogeneity, treatment duration, and authors' conclusions. For CKD-focused reviews, we recorded explicitly whether blood pressure was a prespecified or pooled outcome. AMSTAR 2 appraisal emphasized protocol registration, search completeness, duplicate selection and extraction, risk-of-bias assessment, appropriateness of meta-analytic methods, discussion of heterogeneity and publication bias, incorporation of primary-study bias into conclusions, and conflict-of-interest reporting.

A retracted blood-pressure meta-analysis was not used as evidence. This exclusion was applied regardless of whether the numerical result appeared consistent with other reviews, because a retracted synthesis cannot be treated as a reliable unit in an umbrella review.

2.5 Synthesis and handling of overlap

The principal synthesis was deliberately hierarchical. First, direct CKD evidence was summarized to establish whether review-level BP effects had actually been demonstrated in kidney disease. Second, BP-focused reviews were used to estimate the magnitude and consistency of the broader probiotic antihypertensive signal. Because these reviews share many primary trials, no new grand pooled estimate across meta-analyses was calculated. Effect estimates are therefore displayed side by side in their original metric. Weighted mean differences in mmHg are interpreted directly; standardized mean differences are presented separately and not converted to mmHg without individual-study standard deviations.

2.6 Certainty and clinical interpretation

Clinical interpretation considered effect magnitude, consistency, methodological confidence, directness to CKD, and whether the outcome was a surrogate or a patient-important cardiovascular endpoint. A statistically significant BP reduction of approximately 1–2 mmHg was considered potentially relevant at a population level but insufficient, by itself, to justify replacement of evidence-based antihypertensive treatment in an individual with CKD. Directness was downgraded whenever estimates were derived predominantly from participants without kidney disease.

3. Results

3.1 Evidence selection and architecture

Seventeen review-level syntheses met the prespecified evidence framework. Eleven evaluated probiotics or broader biotic strategies in CKD or dialysis populations, whereas six evaluated blood-pressure effects of probiotics in general or cardiometabolic populations. The renal evidence spanned systematic reviews from 2018 through 2024 and included both conventional and network meta-analyses. The BP evidence spanned 2017 through 2025. No eligible 2015–2016 review-level synthesis with pooled probiotic BP data in CKD was identified, although mechanistic publications from those years informed the biological rationale.

Figure 1 summarizes the two-stream evidence architecture used to avoid conflating direct renal evidence with indirect antihypertensive efficacy. The updated search extended through 31 August 2025.

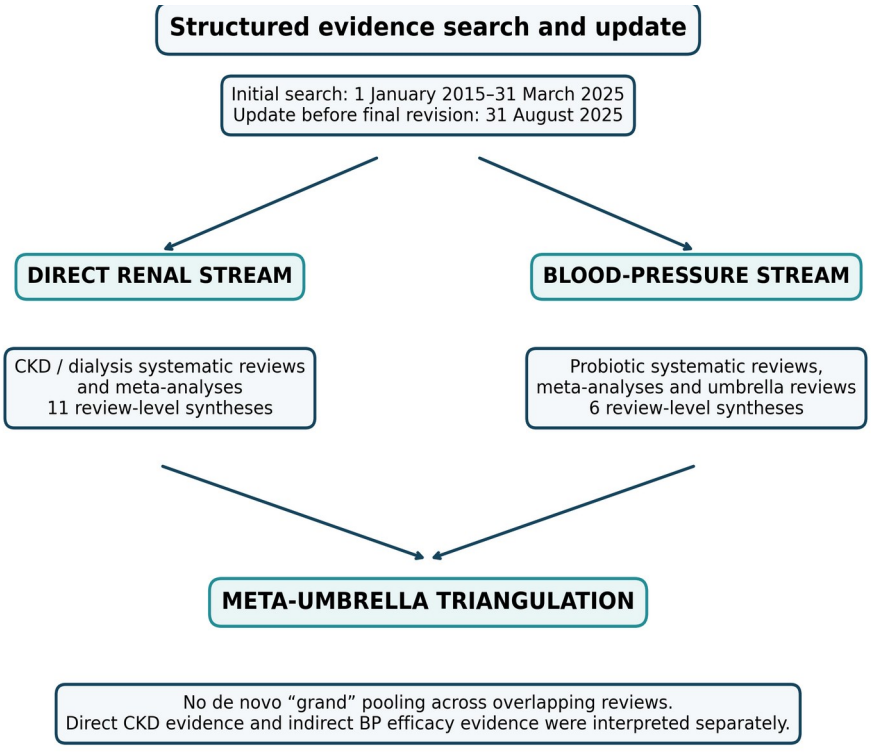

Fig. 1. Evidence architecture of the focused meta-umbrella review. Direct CKD/dialysis evidence and broader blood-pressure evidence were synthesized in parallel; overlapping review estimates were not re-pooled.

The most important selection finding was not a numerical treatment effect but an evidence gap: none of the included CKD-focused meta-analyses reported a pooled SBP or DBP effect attributable specifically to probiotics. Blood pressure was either absent from the outcome set, reported too sparsely for pooling, or embedded in broader cardiometabolic reporting. This distinction materially limits the certainty of any claim about “hypertension control” in kidney disease.

3.2 Characteristics of included review-level evidence

The CKD syntheses ranged from small early reviews of probiotic RCTs to the 2023 Cochrane review of synbiotics, prebiotics, and probiotics in CKD. They consistently documented substantial heterogeneity in strain composition, dose, dialysis status, diet, treatment duration, and measured outcomes [9–11,13,14,19,21,22,27–29]. The broader BP literature included meta-analyses of diabetes, defined Lactobacillus plantarum-containing products, long-term probiotic exposure, and umbrella-level comparisons [6,16,17,25,26,32].

Table 1 displays the 17 included syntheses and highlights a central contrast: the strongest quantitative BP estimates come from populations not restricted to CKD, while the most direct renal syntheses generally focus on non-BP surrogates.

Review	Population	Evidence base	Intervention	Principal result	BP directness	AMSTAR 2	Interpretation
He et al. 2017	T2DM	10 RCTs; 591	Probiotics	BP reported; larger early estimate, reporting imprecision	Indirect	Low	Suggestive; interpret cautiously
Fagundes et al. 2018	CKD	8 RCTs	Probiotics	Mostly renal/uremic outcomes; no pooled BP	Direct CKD	Low	No renal BP estimate
Jia et al. 2018	CKD 3–5 ± dialysis	8 studies; 261	Probiotics	PCS SMD −0.57; renal markers mostly NS	Direct CKD	Moderate	Biological signal, not BP efficacy
Pisano et al. 2018	Renal patients	17 studies; 701	Pre/pro/synbiotics	eGFR, creatinine, CRP, urea largely NS	Direct CKD	Moderate	Clinical outcomes sparse
McFarlane et al. 2019	CKD	16 studies; 645	Pre/pro/synbiotics	Urea and toxins largely unchanged overall	Direct CKD	Moderate	Limited evidence
Tao et al. 2019	CKD	10 RCTs	Probiotics	Urea lower in nondialysis; eGFR/Cr/CRP NS	Direct CKD	Moderate	No pooled BP
Ejtahed et al. 2020	Mixed / HTN / T2DM	5 meta-analyses; 2,703	Probiotic foods/supplements	Review-level BP reductions ~3.1–5.0 SBP	Indirect	Moderate	Supports modest class signal
Lewis-Mikhael et al. 2020	Mixed adults	7 studies; 653	L. plantarum-containing	SBP −1.58 (−3.05, 0.11); DBP −0.92 (−1.49, −0.35)	Indirect	Moderate	Small strain-focused effect
Bakhtiary et al. 2021	CKD	14 articles	Pre/pro/synbiotics	Improved glucose, hsCRP, oxidative markers	Direct CKD	Moderate	No pooled BP effect

Review	Population	Evidence base	Intervention	Principal result	BP directness	AMSTAR 2	Interpretation
Liu et al. 2022	CKD 3–5 / ESRD	23 studies; 842	Biotics	Uremic toxins/oxidative markers improved selectively	Direct CKD	Moderate	No pooled BP
Yu et al. 2022	Dialysis ESRD	25 studies; 1,106	Pre/pro/synbiotics	Inflammatory/uremic outcomes improved variably	Direct CKD	Moderate	No BP endpoint
Zarezadeh et al. 2023	Mixed	14 meta-analyses; 15,494	Probiotics	SBP −1.96; DBP −1.28 mmHg	Indirect	Moderate	Best umbrella BP anchor
Zhao et al. 2023	Mixed; ≥8 wk	26 RCTs; 1,624	Probiotics	Office SBP −2.18; DBP −1.07 mmHg	Indirect	Moderate–high	Consistent modest effect
Chen et al. 2023	Dialysis	18 RCTs	Pre/pro/synbiotics	CRP, IL-6, IS lower; HDL higher	Direct CKD	Moderate	No pooled BP
Cooper et al. 2023	CKD 1–5 ± dialysis	45 studies; 2,266	Pre/pro/synbiotics	Clinical evidence low/very low certainty	Direct CKD	High	No support/refutation for routine use
Liu et al. 2024	CKD	21 studies; 869	Pro/synbiotics	BUN SMD −0.23; CRP −0.34	Direct CKD	Low	No pooled BP; analytic caution
Sefidgari-Abrasi et al. 2025	Overweight/obesity	26 RCTs; 1,755	Probiotics	SBP SMD −0.09 NS; DBP −0.27	Indirect	Moderate	2025 update tempers effect size

Table 1. Review-level evidence included in the meta-umbrella synthesis. BP, blood pressure; CKD, chronic kidney disease; DBP, diastolic BP; SBP, systolic BP; WMD, weighted mean difference; SMD, standardized mean difference.

Across the renal reviews, modest favorable signals were reported for selected uremic toxins, blood urea nitrogen, oxidative stress, or inflammatory markers, but kidney function and clinical cardiovascular outcomes were inconsistent. The 2023 Cochrane review concluded that available evidence was of low or very low certainty for many outcomes and was insufficient to support or refute routine biotic therapy in CKD [28]. The 2024 meta-analysis reported small reductions in BUN and C-reactive protein but did not establish a BP effect [29].

3.3 Blood-pressure effect in the broader probiotic literature

The most comprehensive BP estimate was provided by Zarezadeh et al. in 2023. Their umbrella meta-analysis incorporated 14 meta-analyses encompassing 15,494 participants and found a modest reduction in SBP (WMD −1.96 mmHg, 95% CI −2.78 to −1.14) and DBP (WMD −1.28 mmHg, 95% CI −1.76 to −0.79) [25]. Subgroup findings suggested that baseline cardiometabolic risk, dose, age, and intervention characteristics could modify the observed effect, but the magnitude remained small [25].

Zhao et al. examined long-term probiotic use (at least 8 weeks) across 26 randomized trials and 1,624 participants. Office SBP decreased by 2.18 mmHg (95% CI −3.41 to −0.94) and DBP by 1.07 mmHg (95% CI −1.72 to −0.41); ambulatory estimates from three trials were similar in direction [26]. Lewis-Mikhael et al. reported a smaller strain-focused effect for Lactobacillus plantarum-containing products: SBP WMD −1.58 mmHg (95% CI −3.05 to 0.11) and DBP WMD −0.92 mmHg (95% CI −1.49 to −0.35) [17]. The SBP confidence interval crossed the null, emphasizing uncertainty for strain-specific systolic effects.

3.4 Evidence updated through 2025

The 2025 meta-analysis by Sefidgari-Abrasi et al. extended the evidence in overweight and obese adults. The pooled systolic effect was not statistically significant (SMD −0.09, 95% CI −0.45 to 0.26), whereas DBP showed a small reduction (SMD −0.27, 95% CI −0.53 to −0.02) [32]. These results temper the assumption that increasing the number of probiotic trials necessarily produces a larger or more clinically important antihypertensive effect. A 2025 comprehensive CKD review continued to describe a plausible microbiota-targeted therapeutic rationale but did not supply a kidney-specific pooled BP estimate [31].

3.5 Direct kidney-disease evidence for blood pressure

Direct randomized evidence is limited. In a double-blind hemodialysis trial of 42 participants, synbiotic supplementation for two months had no significant effect on blood pressure compared with placebo [33]. In the 12-month SYNERGY II feasibility trial in stage 3–4 CKD, between-group blood-pressure differences were not demonstrated despite substantial baseline hypertension and antihypertensive medication use [20]. By contrast, the ProLowCKD trial reported improved blood-pressure levels and permitted reductions in antihypertensive and loop-diuretic medication doses in the probiotic arm, but this was an exploratory treatment-management observation rather than a prespecified pooled BP endpoint [23].

3.6 Renal, inflammatory, and uremic-toxin outcomes

Earlier CKD meta-analyses suggested that probiotics or broader biotic interventions can affect selected biological pathways relevant to vascular health without proving antihypertensive efficacy. Jia et al. reported lower p-cresyl sulfate (SMD −0.57, 95% CI −0.99 to −0.14), whereas Tao et al. found reduced urea in nondialysis CKD but no significant effect on creatinine, eGFR, uric acid, or C-reactive protein [10,14]. Liu et al. reported improvement in total antioxidant capacity, malondialdehyde, interleukin-6, and selected uremic toxins, while Yu et al. found differential effects of prebiotics, probiotics, and synbiotics on inflammatory and uremic outcomes in dialysis [21,22]. These changes are mechanistically relevant but cannot be used as substitutes for measured BP reduction.

3.7 Safety and methodological confidence

Adverse events in the included renal and BP reviews were generally mild and predominantly gastrointestinal, but reporting was inconsistent and trials were often too small to detect rare events. Methodological confidence was highest for the Cochrane review and generally moderate for more recent prospectively registered meta-analyses. Common limitations included primary-study overlap, small sample sizes, mixed probiotic and synbiotic interventions, inconsistent strain-level reporting, short follow-up, selective availability of BP outcomes, and variable handling of risk of bias. A published 2024 commentary raised additional concerns about aggregation and analytic choices in one CKD meta-analysis, reinforcing the need for conservative interpretation [30].

3.8 Clinical evidence translation

Table 2 integrates directness, magnitude, and confidence for the clinical question of CKD-associated hypertension. The evidence supports a small antihypertensive signal for probiotics in broader populations but not a kidney-specific treatment effect of comparable certainty.

Evidence domain	Review-level finding	Directness to CKD hypertension	Clinical interpretation
General probiotic BP effect	SBP ≈ −2 mmHg; DBP ≈ −1 mmHg in major 2023 syntheses	Indirect	Small adjunctive signal; not a substitute for therapy
CKD-specific pooled BP effect	No CKD review produced a pooled SBP/DBP estimate	Direct but absent	Effectiveness in CKD remains unproven
Direct CKD trials reporting BP	Mostly neutral; ProLowCKD exploratory medication reduction	Direct	Insufficient for recommendation
Uremic toxins / BUN	Selected favorable effects; inconsistent across syntheses	Direct	Mechanistic support, not BP evidence
Inflammation / oxidative stress	Small improvements in some analyses	Direct	Potential vascular relevance; surrogate outcomes
Safety	Mostly mild GI events; rare harms poorly quantified	Partly direct	Use quality-controlled products; caution in vulnerable patients
Overall clinical role	Evidence gap persists through Aug 2025	Directness limited	Investigational/adjunctive only for CKD hypertension

Table 2. Clinical translation of the review-level evidence for probiotic use in CKD-associated hypertension.

The practical implication is a separation between biological plausibility and proven efficacy. A patient with CKD may have gut dysbiosis and may experience changes in microbial metabolites after probiotic or synbiotic therapy, but the current review-level literature does not demonstrate that these changes reliably translate into clinically meaningful BP control.

Figure 2 compares the principal review-level BP estimates expressed in mmHg. These estimates are displayed without a new pooled diamond because the underlying randomized trials overlap substantially across reviews.

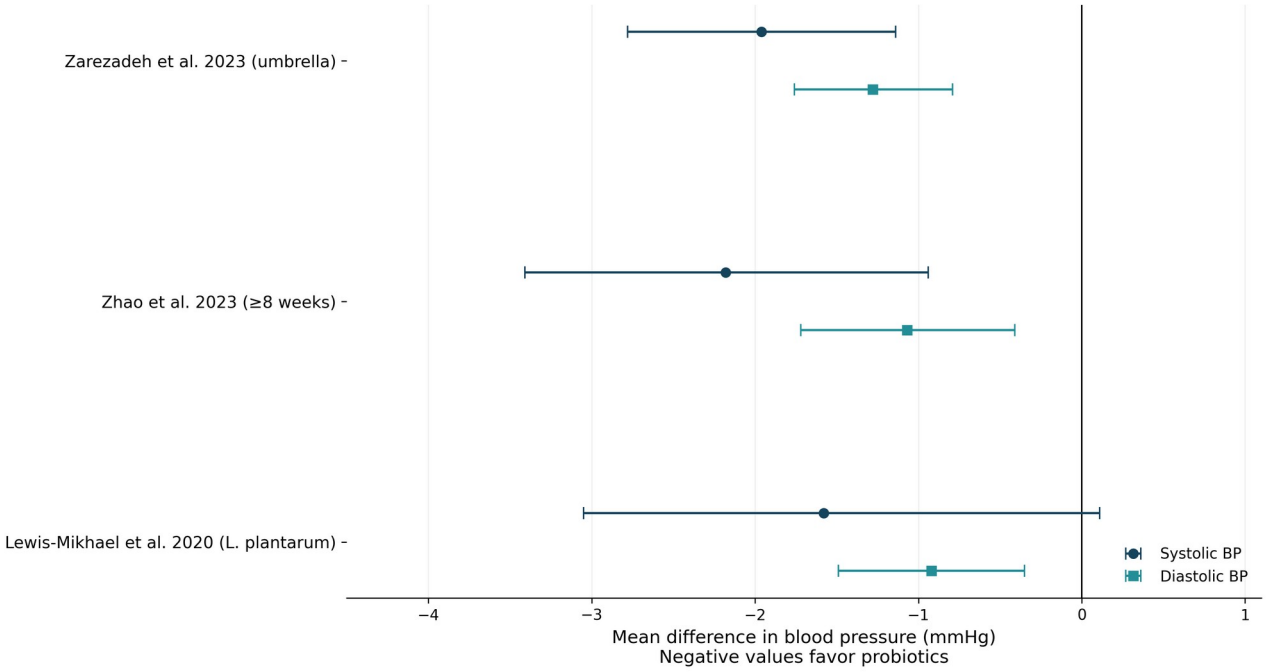

Fig. 2. Review-level systolic and diastolic blood-pressure estimates from selected meta-analyses. Negative values favor probiotics. No grand pooled estimate is shown because of overlap between underlying randomized trials.

The concordant direction of effect across the 2023 umbrella review and long-term meta-analysis supports a modest average reduction, approximately 1–2 mmHg. However, the magnitude is smaller than typical treatment effects expected from established pharmacological BP therapies, and direct renal evidence remains insufficient to establish equivalence in CKD.

Figure 3 summarizes the evidence profile across effect magnitude, consistency, directness, and methodological confidence. Directness is intentionally rated differently for general BP efficacy and CKD-specific hypertension.

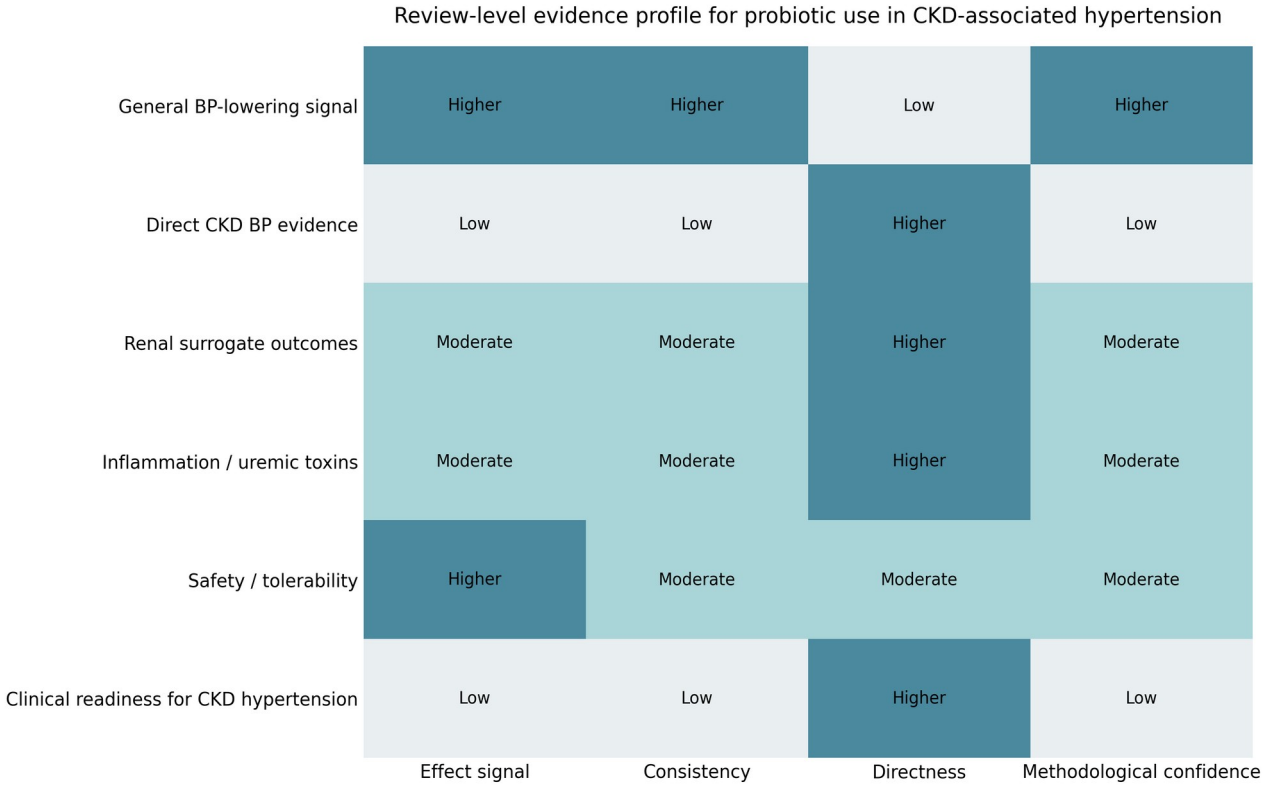

Fig. 3. Evidence profile for probiotic use in CKD-associated hypertension. Higher ratings indicate stronger review-level support within each dimension, not a clinical recommendation grade.

The profile demonstrates why the overall conclusion is cautious: the general BP signal is reasonably consistent, but kidney-specific direct evidence and clinical readiness remain low. By contrast, evidence for some renal surrogate pathways is more substantial, although still heterogeneous.

4. Discussion

This meta-umbrella synthesis finds a consistent but modest antihypertensive effect of probiotics in the broader randomized-trial literature and, simultaneously, a striking lack of direct pooled blood-pressure evidence in CKD. The most defensible interpretation is therefore not that probiotics are ineffective, but that effectiveness for CKD-associated hypertension has not yet been demonstrated with the methodological specificity required for clinical recommendation.

The distinction between statistical significance and clinical significance is important. A mean SBP reduction near 2 mmHg can be meaningful at a population level if it is safe, sustained, and widely applied, but it is modest for an individual with CKD who may require multiple antihypertensive agents, sodium restriction, diuretic optimization, renin–angiotensin system blockade, and other kidney-protective strategies. The current evidence does not support reducing standard therapy on the expectation that a probiotic will deliver a comparable antihypertensive effect.

Biological plausibility nevertheless remains strong. CKD-associated dysbiosis can favor proteolytic fermentation and accumulation of gut-derived uremic toxins, while reduced production or altered signaling of short-chain fatty acids may affect endothelial function, immune activation, sympathetic tone, and renal sodium handling [1–5]. Probiotic effects on barrier integrity, microbial competition, metabolite production, and inflammation could therefore influence vascular physiology. The challenge is that mechanistic improvement does not guarantee a measurable BP response, particularly when extracellular volume and kidney-mediated sodium balance dominate the phenotype.

The broader BP literature also illustrates strain and formulation specificity. Meta-analyses combine dairy foods, capsules, multi-strain mixtures, different viable counts, and heterogeneous treatment durations. The Lactobacillus plantarum-focused review showed a statistically favorable DBP estimate but an SBP confidence interval that crossed zero [17]. Thus, even a reproducible class-level effect cannot be assumed for every commercial product. In CKD, this problem is magnified by dietary restrictions, pill burden, gastrointestinal symptoms, and potential differences in colonization or metabolite handling.

The 2025 update is informative because it does not simply strengthen the efficacy signal. In overweight and obese adults, the new meta-analysis found no significant systolic effect and only a small diastolic effect [32]. This pattern is compatible with genuine heterogeneity: probiotics may have larger effects in participants with higher baseline BP or specific metabolic phenotypes, while effects in other populations are negligible. CKD trials will therefore need stratification by baseline BP, dialysis status, residual kidney function, sodium intake, diabetes, and antihypertensive regimen.

Renal surrogate outcomes should be interpreted as hypothesis-supporting rather than antihypertensive endpoints. Reductions in p-cresyl sulfate, indoxyl sulfate, BUN, oxidative stress, or inflammatory markers may be biologically desirable, but these outcomes do not establish lower cardiovascular event rates or sustained BP reduction. The Cochrane synthesis is particularly important because it highlights the low to very low certainty of many clinical outcomes despite a growing number of small trials [28].

4.1 Implications for clinical practice

Probiotics should not currently be prescribed as a replacement for evidence-based blood-pressure therapy in CKD. If a probiotic is used for another supported indication or as part of a supervised nutrition strategy, any BP effect should be considered ancillary. Clinicians should verify strain identity, viable dose, product quality, renal dietary compatibility, and the patient's clinical vulnerability. Products with poorly defined strain composition or unverified viable counts cannot be assumed equivalent to those studied in randomized trials.

For patients who choose probiotic supplementation, blood

pressure should continue to be assessed with standard methods and treatment should be titrated according to accepted CKD and hypertension targets rather than presumed microbiome effects. In dialysis, interpretation requires particular attention to interdialytic weight gain, ultrafiltration, dry-weight assessment, and timing of BP measurement. A small probiotic-related vascular effect could be clinically obscured by changes in volume status.

Safety is generally reassuring in ambulatory trial populations, but caution remains appropriate in patients with severe immunosuppression, central venous catheters, critical illness, disrupted intestinal barriers, or other settings in which translocation or product contamination could have greater consequences. The absence of frequent serious adverse events in small trials does not establish zero risk.

4.2 Priorities for future research

Future CKD trials should make BP a prespecified primary or key secondary endpoint and use standardized office measurement, home BP, or preferably 24-hour ambulatory monitoring. Reporting should include baseline BP, number and dose of antihypertensive medications, sodium intake or urinary sodium, volume-status measures, dialysis modality, residual kidney function, diabetes status, and changes in medication during follow-up.

Interventions should be described at strain level, with accession or deposit identifiers when possible, total and strain-specific CFU, formulation, viability through shelf life, storage requirements, adherence, and duration. Trials should avoid treating “probiotics” as a homogeneous pharmacological class. Head-to-head comparisons of well-characterized formulations may be more informative than repeated small placebo-controlled studies using poorly described mixtures.

Mechanistic outcomes should be integrated with clinical outcomes rather than substituted for them. Simultaneous measurement of short-chain fatty acids, indoxyl sulfate, p-cresyl sulfate, TMAO, inflammatory markers, endothelial function, and ambulatory BP could help identify responders and test whether microbiome changes mediate vascular benefit. Adequately powered multicenter studies are needed to determine whether any BP reduction persists beyond a few months and whether it affects cardiovascular events or kidney-disease progression.

4.3 Strengths and limitations

Strengths of this review include the 2015–2025 evidence window, the updated search before final revision, separation of direct CKD evidence from indirect BP evidence, avoidance of invalid re-pooling across overlapping meta-analyses, and appraisal of methodological confidence. The principal limitation is the same feature that defines the clinical evidence gap: few CKD trials report BP in a form suitable for review-level pooling. Several renal syntheses combine prebiotics, probiotics, and synbiotics, and many BP meta-analyses include participants without kidney disease. Overlap of primary trials, heterogeneity in strain composition, and short follow-up further limit certainty. Finally, this review uses published aggregate data and therefore cannot perform patient-level analyses by CKD stage, dialysis status, or antihypertensive regimen.

5. Conclusion

Probiotics are associated with a small reduction in blood pressure in broader randomized-trial and umbrella-review evidence, with the most comprehensive 2023 synthesis estimating average reductions of approximately 2 mmHg systolic and 1 mmHg diastolic. However, review-level evidence directly demonstrating blood-pressure control in CKD is absent, and the few renal trials that report BP are neutral, exploratory, or confounded by medication and volume-management changes. Probiotics may influence uremic toxins, inflammation, oxidative stress, and other pathways relevant to cardiovascular health, but those effects should not be equated with proven antihypertensive efficacy. At present, probiotics should be viewed as investigational or adjunctive in CKD-associated hypertension and should not replace established BP and kidney-protective treatment. Dedicated, strain-specific CKD trials with standardized ambulatory BP endpoints are needed before routine clinical use can be recommended.

Declarations

Ethics approval: Ethical approval was not required because this study analyzed published aggregate data and involved no individual participant data.

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Competing interests: The authors declare no competing interests.

Data availability: All data summarized in this meta-umbrella review are available in the cited systematic reviews, meta-analyses, and randomized trials.

Author contributions: All authors contributed to conception, evidence interpretation, critical revision, and approval of the final manuscript. Rafaela Nonato de Menezes coordinated the review synthesis and manuscript organization.

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Appendix A. Full electronic search strategies

Appendix Table A1 presents the database-specific search architecture. Searches were run as two complementary streams so that kidney-specific reviews were not missed and broader blood-pressure efficacy reviews could be used to assess indirectness. The initial search ended 31 March 2025 and was updated 31 August 2025.

Source	Search strategy
PubMed/MEDLINE	Stream A: (probiotic* OR synbiotic* OR Lactobacillus OR Lacticaseibacillus OR Bifidobacterium) AND (chronic kidney disease OR CKD OR renal dialysis OR hemodialysis) AND (systematic review OR meta-analysis). Stream B: the same probiotic terms AND (hypertension OR blood pressure OR systolic OR diastolic) AND (systematic review OR meta-analysis). Publication window 2015–2025; final update 31 Aug 2025.
Cochrane Library	Probiotic/synbiotic concepts combined separately with CKD/dialysis and hypertension/blood-pressure concepts. Cochrane review and controlled-trial records were used to verify renal review coverage and outcome reporting.
Europe PMC	Title/abstract queries combined probiotic/biotic concepts with CKD/dialysis or hypertension/blood-pressure concepts and systematic-review/meta-analysis terms; date window 2015–31 Aug 2025.
Publisher / DOI indexing	Targeted verification of title, author list, journal, issue year, DOI, publication status, corrections/retractions, and full-text metadata for potentially eligible syntheses.
Citation searching	Backward reference screening and forward-citation checks of eligible review-level syntheses.

Appendix Table A1. Database-specific search strategies used for the 2015–2025 evidence update.

Search syntax was adapted to the indexing rules of each database. Citation searching was used to identify eligible review-level publications not retrieved by title/abstract indexing.

Appendix B. Review-level appraisal criteria

AMSTAR 2 domains were applied at review level, with particular attention to protocol registration, comprehensive searching, duplicate study selection and extraction, risk-of-bias assessment, appropriate quantitative methods, interpretation in light of bias, publication-bias assessment, and conflicts of interest. Confidence categories were used comparatively within this umbrella review and should not be interpreted as a substitute for outcome-specific GRADE certainty.

Appendix C. Review-level methodological appraisal

Appendix Table A2 summarizes the domains that most influenced confidence in the 17 included syntheses. The Cochrane review provided the strongest methodological anchor; lower ratings reflect critical limitations such as incomplete protocol information, intervention aggregation, or uncertainty in handling overlapping studies.

Review	Protocol	Search	Duplicate	Excluded studies	Risk of bias	Meta-analysis	Bias in interpretation	COI/funding
He 2017	±	+	±	−	+	+	±	+
Fagundes 2018	−	+	+	±	±	N/A	±	+
Jia 2018	±	+	+	±	+	+	±	+
Pisano 2018	±	+	+	±	+	+	+	+
McFarlane 2019	+	+	+	±	+	+	+	+
Tao 2019	±	+	+	±	+	+	±	+
Ejtahed 2020	±	+	+	±	+	N/A	±	+
Lewis-Mikhael 2020	±	+	+	±	+	+	+	+
Bakhtiary 2021	+	+	+	±	+	+	+	+
Liu 2022	+	+	+	±	+	+	+	+
Yu 2022	+	+	+	±	+	+	+	+
Zarezadeh 2023	+	+	+	±	+	+	+	+
Zhao 2023	+	+	+	±	+	+	+	+

Review	Protocol	Search	Duplicate	Excluded studies	Risk of bias	Meta-analysis	Bias in interpretation	COI/funding
Chen 2023	+	+	+	±	+	+	+	+
Cooper 2023	+	+	+	+	+	+	+	+
Liu 2024	+	+	+	±	+	±	±	+
Sefidgari-Abrasi 2025	+	+	+	±	+	+	+	+

Appendix Table A2. Review-level appraisal of the main AMSTAR 2 domains. COI, conflicts of interest; +, adequate; ±, partial/unclear; −, important limitation.

Interpretive note

Methodological quality improved over time, but directness to CKD-associated hypertension did not. Even a methodologically strong renal review cannot establish a BP effect when the primary studies do not report or pool standardized blood-pressure outcomes. This is the principal reason the overall clinical conclusion remains cautious.