Review Article

Gut–kidney axis in chronic kidney disease: Pathophysiological mechanisms and microbiome-targeted therapeutic strategies

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Abstract

Chronic kidney disease (CKD) is increasingly linked to alterations in the gut microbiome; however, current evidence remains fragmented regarding the causal contribution of dysbiosis, the mechanisms connecting intestinal disturbances with renal injury, and the clinical effectiveness and safety of microbiome-targeted interventions. This review aims to synthesize current knowledge on the gut–kidney axis in CKD and to identify emerging therapeutic and research directions. The review discusses the physiological functions of the gut microbiota in maintaining metabolic homeostasis, intestinal barrier integrity, immune regulation, and short-chain fatty acid production. It further examines CKD-associated dysbiosis, including the depletion of beneficial saccharolytic bacteria, expansion of urease- and toxin-producing microorganisms, accumulation of indoxyl sulfate and p-cresyl sulfate, impaired intestinal barrier function, endotoxemia, systemic inflammation, oxidative stress, renal fibrosis, and progressive kidney dysfunction. Variations in gut–kidney interactions across diabetic kidney disease, hypertension, aging, pediatric populations, and kidney transplantation are also considered. Therapeutic approaches discussed include probiotics, prebiotics, synbiotics, postbiotics, dietary modification, fecal microbiota transplantation, intestinal adsorbents, selective antibiotics, bacteriophages, engineered bacteria, and other emerging precision strategies. Particular attention is given to differences in the maturity of clinical evidence, potential safety concerns, and barriers to implementation. The review highlights the need for standardized microbiome assessment, prospective clinical studies, and integration of metagenomics, metabolomics, proteomics, and artificial intelligence to support patient-specific interventions. The gut–kidney axis represents a promising therapeutic target, but its translation into routine CKD management requires stronger clinical validation.

Keywords: Kidney disease, renal insufficiency, gastrointestinal microbiome, dysbiosis, uremia therapeutic

Introduction

Chronic kidney disease (CKD) is a complex condition characterized by the progressive and irreversible loss of kidney function [1]. CKD affects more than 10% of the global population, representing over 800 million people, and imposes a substantial burden on healthcare systems worldwide [2]. It is also a leading cause of premature mortality, accounting for approximately 1.5 million deaths annually—equivalent to one death every 20 seconds—particularly as the disease progresses to end-stage renal disease [3]. Established risk factors for CKD include hypertension, diabetes mellitus, proteinuria, and systemic inflammation. However, emerging evidence also highlights the potential contribution of the gut microbiome to CKD pathogenesis and progression

Received: June 10, 2026 - Accepted: July 24, 2026 - Published online: July 31, 2026

[4-6]. The intestinal environment serves as a reservoir of precursors for systemic uremic toxins, while gastrointestinal disturbances may contribute to systemic metabolic and homeostatic abnormalities [7,8]. Therefore, understanding the mechanisms through which the gut microbiome influences CKD progression is increasingly important for identifying novel therapeutic approaches [8].

The human gut microbiome comprises a complex, dynamic, and diverse community of commensal microorganisms that plays essential roles in maintaining metabolic and immunological homeostasis [9]. Gut dysbiosis may reduce the production of beneficial short-chain fatty acids (SCFAs) while increasing the translocation of inflammatory endotoxins and uremic toxins across the intestinal mucosal barrier, thereby contributing to progressive kidney dysfunction [10-12]. Reduced microbial diversity has also been associated with greater production of toxic metabolites, including p-cresyl sulfate and indoxyl sulfate, which exert nephrotoxic effects on renal tubular cells [13,14]. However, it remains unclear whether dysbiosis primarily contributes to CKD progression or develops as a consequence of declining kidney function. In addition, considerable heterogeneity in dysbiosis patterns has been reported across CKD stages and clinical populations [15,16]. Further research is therefore needed to clarify the role of gut dysbiosis in CKD pathogenesis and to determine whether targeting the gut microbiome can meaningfully slow the progression of renal dysfunction.

This review aims to synthesize current evidence on the compositional and functional alterations of the gut microbiome across different stages of CKD and to examine their relationships with the progression of kidney dysfunction. It also discusses the potential utility of specific microbial signatures and dysbiosis patterns as biomarkers for disease monitoring and as targets for therapeutic intervention. By highlighting current evidence, knowledge gaps, and emerging microbiome-based strategies, this review seeks to inform the development of precision approaches that may help slow CKD progression and delay the transition to end-stage renal disease.

Uremic toxins as products of dysbiosis and their role in CKD progression

Uremic toxins comprise a broad range of organic and inorganic compounds derived from host metabolism and microbial activity that accumulate as the glomerular filtration rate declines [17]. Based on their molecular size and dialytic clearance characteristics, these compounds are commonly classified into three groups: small water-soluble compounds, middle molecules, and protein-bound uremic toxins [18]. Protein-bound uremic toxins are particularly relevant to CKD progression, with indoxyl sulfate and p-cresyl sulfate among the most extensively studied [19]. Because of their strong binding affinity for serum proteins, these toxins are poorly removed by conventional hemodialysis and may consequently persist in the systemic circulation [18].

Within the kidney, uremic toxins promote oxidative stress and sustained inflammatory responses in renal tubular cells, potentially contributing to tubulointerstitial fibrosis and progressive nephron loss [20]. Their effects are not limited to the kidney; systemic accumulation has also been associated with endothelial dysfunction, cardiovascular complications, immune dysregulation, and anemia [21,22]. Higher circulating concentrations of these toxins have been linked to greater cardiovascular risk, impaired immune function, and faster progression to end-stage renal disease [23]. A clearer understanding of their sources, biological effects, and clearance mechanisms is therefore needed, as uremic toxins may function not merely as metabolic waste products but also as active mediators of CKD progression and its systemic complications.

Systemic inflammation and immune dysregulation in the gut–kidney axis

Inflammation within the gut–kidney axis is largely driven by disruption of the intestinal barrier, which facilitates bacterial translocation and systemic endotoxemia [24]. Translocation of lipopolysaccharide (LPS) into the circulation activates Toll-like receptor 4 (TLR4) and subsequently triggers the nuclear factor kappa B (NF-κB) signaling pathway [25]. Activation of this pathway promotes the production of pro-inflammatory cytokines, including interleukin-6

(IL-6), tumor necrosis factor alpha (TNF-α), and interleukin-1 beta (IL-1β) [26,27]. The resulting immune dysregulation occurs at both mucosal and systemic levels, creating a state of persistent low-grade inflammation that may link gut dysbiosis with renal parenchymal injury [28]. Sustained inflammation may further induce oxidative stress, renal fibrosis, and tubular cell damage, thereby contributing to progressive kidney dysfunction [29]. Clinically, reduced glomerular filtration rate has been associated with greater systemic inflammation among patients with CKD [28].

Targeted therapeutics: Strategies for modulating the gut–kidney axis

Probiotic therapy aims to restore microbial balance by administering beneficial microorganisms that favorably modulate the colonic microbiome (**Figure 1**) [30]. In CKD, particular attention has been given to *Lactobacillus* and *Bifidobacterium* species, which may compete with pathogenic bacteria for nutrients and intestinal adhesion sites [31]. These microorganisms may also reduce the luminal pH through lactic acid production, thereby suppressing the growth of urease-producing and proteolytic bacteria [32]. Emerging evidence suggests that probiotic supplementation may reduce circulating concentrations of the gut-derived uremic toxins p-cresyl sulfate and indoxyl sulfate, potentially by improving intestinal barrier integrity and modifying microbial metabolism [33]. However, the clinical effectiveness of probiotics remains variable. Important challenges include limited survival and colonization of probiotic strains within the altered uremic intestinal environment, fluctuations in luminal pH, differences among probiotic formulations, and substantial interindividual variation in treatment response [34].

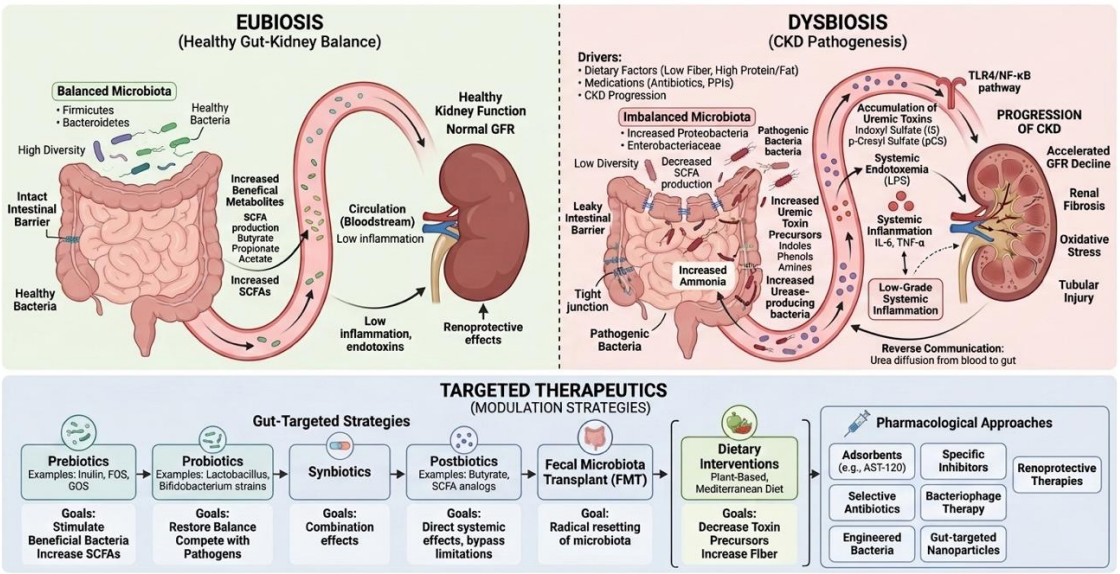

Figure 1. Overview of the gut–kidney axis in chronic kidney disease (CKD). Gut eubiosis supports intestinal barrier integrity, short-chain fatty acid (SCFA) production, and kidney health, whereas dysbiosis promotes uremic toxin generation, systemic inflammation, and CKD progression. The lower panel summarizes microbiota-targeted therapeutic strategies aimed at restoring gut–kidney homeostasis and slowing renal function decline.

Prebiotic strategies involve the administration of nondigestible carbohydrate substrates, including inulin, fructooligosaccharides, and galactooligosaccharides, which selectively promote the growth of beneficial saccharolytic bacteria [35]. Fermentation of these substrates by the gut microbiota increases the production of SCFAs, which support intestinal epithelial integrity and modulate immune responses [36]. Synbiotics combine probiotics with prebiotics, thereby providing beneficial microorganisms together with substrates that may support their survival, colonization, and metabolic activity within the intestine [37]. Evidence from clinical studies suggests that synbiotic interventions may reduce systemic inflammation and the accumulation of

gut-derived uremic toxins; however, their effectiveness may vary according to the formulation, treatment duration, CKD stage, and patient characteristics [38].

Postbiotic therapy entails the exogenous administration of bioactive compounds released by the microbiome in its healthy state, such as butyrate, propionate, and acetate [39]. Postbiotic therapy circumvents the limitations of gut dysbiosis by directly delivering bioactive compounds that exert immediate renoprotective effects through activation of G-protein-coupled receptors (GPR41/43) and modulation of the Nrf2/AMPK/sirtuin pathways [40]. It does not depend on the stable presence of bacteria within an altered gastrointestinal tract for the release of these bioactive compounds [41].

Fecal microbiota transplantation (FMT) is an emerging strategy for restoring microbial balance by transferring a diverse and functional microbial community from a healthy donor to a recipient with CKD (**Figure 1**) [42]. Evidence supporting FMT in CKD is derived predominantly from preclinical studies, in which reductions in uremic toxin concentrations and improvements in renal function-related parameters have been reported [43]. However, human evidence remains limited to small pilot studies and case series with short follow-up periods. Large-scale randomized controlled trials evaluating the safety, optimal administration protocol, dosing frequency, durability of microbiome changes, and long-term clinical efficacy of FMT in CKD are still lacking. Moreover, concerns regarding donor selection, pathogen transmission, adverse immune responses, and treatment standardization remain important barriers to clinical implementation. Consequently, FMT should currently be regarded as an experimental intervention rather than an established standard of care in nephrology [44].

Dietary modification is an important strategy for modulating the gut–kidney axis. Plant-based and Mediterranean dietary patterns may increase the intake of prebiotic fibers while reducing exposure to precursors of gut-derived uremic toxins, which are commonly generated from the microbial metabolism of animal-derived proteins [45]. However, dietary management in CKD requires careful balance because many fiber-rich foods also contain substantial amounts of potassium and phosphorus, which may need to be restricted in patients with advanced disease [46]. Low-protein diets supplemented with keto-analogues may further reduce renal metabolic burden and intestinal production of nitrogenous waste products, potentially creating a more favorable environment for beneficial gut bacteria [47]. These interventions should nevertheless be individualized according to CKD stage, nutritional status, electrolyte balance, and the risk of protein–energy wasting.

Pharmacological strategies targeting the gut–kidney axis aim to selectively modify microbial metabolism while minimizing disruption of the overall microbial ecosystem. AST-120, an orally administered spherical carbon adsorbent, binds uremic toxin precursors within the intestine and limits their absorption into the systemic circulation [48]. Other emerging approaches include inhibition of microbial enzymes involved in indole production and blockade of the aryl hydrocarbon receptor, which mediates some of the toxic effects of gut-derived uremic metabolites [49]. Selective antibiotics are also being investigated as a means of suppressing specific toxin-producing or otherwise harmful bacterial populations [50]. However, these strategies remain under investigation, and further clinical evidence is needed to establish their efficacy, safety, and optimal role in CKD management.

Several emerging approaches remain at the preclinical stage and have not yet been validated in randomized clinical trials involving patients with CKD. Bacteriophage therapy uses viruses to selectively target and lyse pathogenic bacteria while potentially preserving commensal microbial populations; however, evidence in CKD is currently limited to in vitro and animal studies. Engineered bacteria-based biopharmaceuticals, designed to produce toxin-neutralizing enzymes or renoprotective proteins, also remain largely confined to proof-of-concept investigations, with no established evidence regarding their safety or efficacy in humans [51]. Other experimental strategies include nanoparticle-based delivery of therapeutic agents to the intestinal mucosa and epigenetic modulation through microbiome-derived metabolites, such as butyrate-mediated histone deacetylase inhibition to regulate renoprotective gene expression. These approaches remain theoretical or preclinical and require substantial optimization before clinical application. Their translation into routine nephrology practice will depend on well-designed prospective studies evaluating safety, dosing, treatment durability, and long-term renal outcomes [52].

Although microbiome-targeted therapies represent a promising area in CKD management, interventions supported by clinical evidence should be distinguished from those evaluated primarily in preclinical studies [53]. Dietary interventions and intestinal adsorbents, such as AST-120, have been assessed in clinical settings, although their reported benefits remain modest and inconsistent [54]. Probiotics, prebiotics, and synbiotics have also been evaluated in small-to-moderate randomized controlled trials, with variable findings across populations, formulations, and outcomes [55,56]. In contrast, FMT, bacteriophage therapy, engineered bacteria, and artificial intelligence-guided precision approaches currently lack robust clinical validation in CKD. Translation of these emerging strategies into routine care will require rigorously designed trials that account for patient heterogeneity and evaluate long-term safety, sustained efficacy, and clinically meaningful renal outcomes [57,58].

Safety and implementation challenges should also be carefully considered. Probiotics may pose a risk of infection in immunocompromised patients, whereas some prebiotic formulations may worsen electrolyte disturbances in advanced CKD [59]. FMT carries a potential risk of pathogen transmission, while bacteriophages and engineered bacteria remain subject to substantial regulatory uncertainty and limited long-term safety data [60]. Dietary interventions also require close monitoring to prevent protein–energy wasting and mineral imbalances [2]. Therefore, although microbiome-targeted therapies are promising, their clinical use must be guided by the strength of available evidence, individual patient characteristics, and careful assessment of potential risks.

Gut–kidney axis in specific clinical conditions

Gut–kidney interactions may vary substantially according to the underlying clinical condition and patient characteristics [24]. In diabetic kidney disease, chronic hyperglycemia may promote gut dysbiosis and increase intestinal permeability, potentially aggravating insulin resistance and glomerular injury [61]. In hypertension, dysbiosis-associated reductions in SCFA production may impair vascular tone regulation and contribute to increased glomerular pressure [62]. Age may also modify these interactions. In older adults, age-related alterations in the gut microbiome may increase susceptibility to the adverse effects of uremic toxins, whereas in pediatric populations, dysbiosis may interfere with nutrient absorption and growth [63]. Kidney transplantation is likewise associated with substantial changes in gut microbial composition, partly because immunosuppressive therapies affect metabolic and immune pathways [64]. Therefore, interventions targeting the gut–kidney axis should be tailored to the underlying disease, age group, treatment exposure, and other population-specific characteristics [65].

Research directions and future prospects

Future research on the gut–kidney axis should increasingly incorporate multi-omics approaches integrating metagenomics, metabolomics, and proteomics to provide a more comprehensive understanding of microbiome–kidney interactions [66]. Artificial intelligence and machine learning may facilitate the integration of these complex datasets and support biomarker discovery in CKD. However, current applications remain largely exploratory and are predominantly based on retrospective analyses and proof-of-concept algorithms. Prospective clinical validation, standardized protocols for microbiome sampling and analysis, and reproducible predictive models are therefore required before artificial intelligence-guided microbiome interventions can be incorporated into routine clinical practice [67,68]. Validated microbial and metabolic biomarkers may support earlier detection, disease monitoring, and the development of interventions tailored to patient-specific microbiome profiles rather than relying exclusively on generalized therapeutic approaches [69]. As clinical evidence accumulates, assessment of the gut–kidney axis may ultimately inform future guidelines and complement established approaches to CKD management [53].

Conclusion

This review highlights the gut–kidney axis as an important bidirectional pathway linking gut dysbiosis with CKD progression. Dysbiosis may increase the production of gut-derived uremic

toxins, impair intestinal barrier integrity, and promote lipopolysaccharide-mediated activation of inflammatory pathways, including TLR4/NF-κB signaling. These processes may contribute to systemic inflammation, oxidative stress, renal fibrosis, and progressive decline in glomerular filtration rate. However, patterns of dysbiosis vary across CKD stages and patient populations, including those with diabetes mellitus, hypertension, different age profiles, and kidney transplantation. Accordingly, microbiome-targeted interventions may need to account for individual clinical and microbial characteristics. Integration of multi-omics approaches with artificial intelligence may support biomarker discovery and the development of precision strategies. Nevertheless, emerging interventions, including postbiotics, bacteriophages, fecal microbiota transplantation, engineered bacteria, and precision dietary approaches, require validation in well-designed prospective clinical trials before they can be incorporated into routine CKD management.

Ethics approval

Not required.

Acknowledgments

None.

Competing interests

The authors declare that there are no conflicts of interest.

Funding

This study received no external funding.

Underlying data

Derived data supporting the findings of this study are available from the corresponding author on request.

Declaration of artificial intelligence use

Artificial intelligence (AI) tool, ChatGPT, was used for language refinement. Authors confirm that all AI-assisted processes were critically reviewed by the authors to ensure the integrity and reliability of the results. The final decisions and interpretations presented in this article were made solely by the authors.

How to cite

Tamara F, Dzhyvak V. Gut–kidney axis in chronic kidney disease: Pathophysiological mechanisms and microbiome-targeted therapeutic strategies. Narra Intern Med 2026; 1 (2): e15 - http://doi.org/10.52225/narraim.v1i2.15.

References

1. Chen TK, Knicely DH, Grams ME. Chronic kidney disease diagnosis and management: A review. JAMA 2019;322(13):1294-1304.
2. Kovesdy CP. Epidemiology of chronic kidney disease: An update 2022. Kidney Int Suppl (2011) 2022;12(1):7-11.
3. Ortiz A, Lees JS, Torra R, *et al.* The updated global burden of chronic kidney disease: One death every 20 seconds. Nephrol Dial Transplant 2026;gfag040.
4. Mallamaci F, Tripepi G. Risk factors of chronic kidney disease progression: Between old and new concepts. J Clin Med 2024;13(3):678.
5. Liu C, Wang J, Lei L, *et al.* Gut microbiota therapy for chronic kidney disease. Front Immunol 2025;16:1660226.
6. Setiawan IR, Salsabila S, Prasetyawan B, *et al.* Diabetes mellitus and hypertension as risk factors of acute kidney injury induced by COVID-19: A systematic review and meta-analysis. Pneumon 2022;35(4):29.

7. Gryp T, De Paepe K, Vanholder R, *et al.* Gut microbiota generation of protein-bound uremic toxins and related metabolites is not altered at different stages of chronic kidney disease. Kidney Int 2020;97(6):1230-1242.
8. Oncel S, Basson MD. Gut homeostasis, injury, and healing: New therapeutic targets. World J Gastroenterol 2022;28(17):1725-1750.
9. Thursby E, Juge N. Introduction to the human gut microbiota. Biochem J 2017;474(11):1823-1836.
10. Magliocca G, Mone P, Di Iorio BR, *et al.* Short-chain fatty acids in chronic kidney disease: Focus on inflammation and oxidative stress regulation. Int J Mol Sci 2022;23(10):5354.
11. Vaziri ND. CKD impairs barrier function and alters microbial flora of the intestine: A major link to inflammation and uremic toxicity. Curr Opin Nephrol Hypertens 2012;21(6):587-592.
12. Laiola M, Koppe L, Larabi A, *et al.* Toxic microbiome and progression of chronic kidney disease: Insights from a longitudinal CKD-Microbiome Study. Gut 2025;74(10):1624-1637.
13. Ramezani A, Raj DS. The gut microbiome, kidney disease, and targeted interventions. J Am Soc Nephrol 2014;25(4):657-670.
14. Rysz J, Franczyk B, Ławiński J, *et al.* The impact of CKD on uremic toxins and gut microbiota. Toxins (Basel) 2021;13(4):252.
15. Suliman IL, Panculescu FG, Fasie D, *et al.* Gut microbiome in patients with chronic kidney disease stages 4 and 5: A systematic literature review. Int J Mol Sci 2025;26(21):10706.
16. Shen Y, Fan N, Ma SX, *et al.* Gut microbiota dysbiosis: Pathogenesis, diseases, prevention, and therapy. MedComm (2020) 2025;6(5):e70168.
17. Xu Y, Bi WD, Shi YX, *et al.* Derivation and elimination of uremic toxins from kidney-gut axis. Front Physiol 2023;14:1123182.
18. Magnani S, Atti M. Uremic toxins and blood purification: A review of current evidence and future perspectives. Toxins (Basel) 2021;13(4):246.
19. Altamura S, Pietropaoli D, Lombardi F, *et al.* An overview of chronic kidney disease pathophysiology: The impact of gut dysbiosis and oral disease. Biomedicines 2023;11(11):3033.
20. Rapa SF, Di Iorio BR, Campiglia P, *et al.* Inflammation and oxidative stress in chronic kidney disease—Potential therapeutic role of minerals, vitamins and plant-derived metabolites. Int J Mol Sci 2020;21(1):263.
21. Cunha RSD, Santos AF, Barreto FC, Stinghen AEM. How do uremic toxins affect the endothelium? Toxins (Basel) 2020;12(6):412.
22. Fajar JK, Mahendra AI, Tamara F, *et al.* The association between complete blood count and the risk of coronary heart disease. Turkiye Klinikleri J Med Sci 2019;39(1):56-64.
23. Stopic B, Medic-Brkic B, Savic-Vujovic K, *et al.* Biomarkers and predictors of adverse cardiovascular events in different stages of chronic kidney disease. Dose Response 2022;20(3):15593258221127568.
24. Rusu M, Ichim C, Anderco P, *et al.* Gut-kidney axis: Unraveling the role of the microbiome in chronic kidney disease. Biomedicines 2026;14(1):109.
25. Guijarro-Muñoz I, Compte M, Álvarez-Cienfuegos A, *et al.* Lipopolysaccharide activates Toll-like receptor 4 (TLR4)-mediated NF-κB signaling pathway and proinflammatory response in human pericytes. J Biol Chem 2014;289(4):2457-2468.
26. Tanaka T, Narazaki M, Kishimoto T. IL-6 in inflammation, immunity, and disease. Cold Spring Harb Perspect Biol 2014;6(10):a016295.
27. Fajar JK, Azharuddin A. The association between interleukin 6 -174 G/C gene polymorphism and the risk of osteoporosis: A meta-analysis. J Taibah Univ Med Sci 2017;12(3):212-220.
28. Mihai S, Codrici E, Popescu ID, *et al.* Inflammation-related mechanisms in chronic kidney disease prediction, progression, and outcome. J Immunol Res 2018;2018:2180373.
29. Nediani C, Ruzzolini J, Dinu M. Oxidative stress and inflammation as targets for novel preventive and therapeutic approaches in non-communicable diseases III. Antioxidants (Basel) 2024;13(11):1404.
30. Kennedy MS, Chang EB. From gut dysbiosis to eubiosis: Understanding microbiome recovery as an ecological process. Gut Microbes 2026;18(1):2649448.
31. Wang Q, Zhou Z, Pang L, *et al.* Gut microbiota in chronic kidney disease-mineral and bone disorder: Shared mechanisms, disease-specific signatures, and therapeutic prospects. Front Endocrinol (Lausanne) 2026;17:1802845.
32. Pessione E. Lactic acid bacteria contribution to gut microbiota complexity: Lights and shadows. Front Cell Infect Microbiol 2012;2:86.

33. Chen L, Shi J, Ma X, *et al.* Effects of microbiota-driven therapy on circulating indoxyl sulfate and p-cresyl sulfate in patients with chronic kidney disease: A systematic review and meta-analysis of randomized controlled trials. Adv Nutr 2022;13(4):1267-1278.
34. Sun C, Zhang Z, Sun Y, *et al.* Enteric delivery of probiotics: Challenges, techniques, and activity assays. Foods 2025;14(13):2318.
35. Monteiro CRAV, Bogea EG, Campos CDL, *et al.* Prebiotics and gut health: Mechanisms, clinical evidence, and future directions. Nutrients 2026;18(3):372.
36. Fusco W, Lorenzo MB, Cintoni M, *et al.* Short-chain fatty-acid-producing bacteria: Key components of the human gut microbiota. Nutrients 2023;15(9):2211.
37. Markowiak P, Śliżewska K. Effects of probiotics, prebiotics, and synbiotics on human health. Nutrients 2017;9(9):1021.
38. Kędzierska-Kapuza K, Grudniewska A, Durma A, *et al.* Dietary and nutritional strategies to prevent uremic toxin formation and slow the progression of diabetic kidney disease. J Clin Med 2025;14(13):4701.
39. Asefa Z, Belay A, Welelaw E, Haile M. Postbiotics and their biotherapeutic potential for chronic disease and their feature perspective: A review. Front Microbiomes 2025;4:1489339.
40. Favero C, Giordano L, Mihaila SM, *et al.* Postbiotics and kidney disease. Toxins (Basel) 2022;14(9):623.
41. Benameur T, Porro C, Twfieg ME, *et al.* Emerging paradigms in inflammatory disease management: Exploring bioactive compounds and the gut microbiota. Brain Sci 2023;13(8):1226.
42. Zheng L, Ji YY, Wen XL, *et al.* Fecal microbiota transplantation in the metabolic diseases: Current status and perspectives. World J Gastroenterol 2022;28(23):2546-2560.
43. Bian J, Liebert A, Bicknell B, *et al.* Faecal microbiota transplantation and chronic kidney disease. Nutrients 2022;14(12):2528.
44. Falconi CA, Junho C, Fogaça-Ruiz F, *et al.* Uremic toxins: An alarming danger concerning the cardiovascular system. Front Physiol 2021;12:686249.
45. Wakino S, Hasegawa K, Tamaki M, *et al.* Kidney-gut axis in chronic kidney disease: Therapeutic perspectives from microbiota modulation and nutrition. Nutrients 2025;17(12):1961.
46. Cigarrán Guldris S, Latorre Catalá JA, Sanjurjo Amado A, *et al.* Fibre intake in chronic kidney disease: What fibre should we recommend? Nutrients 2022;14(20):4419.
47. Ariyanopparut S, Metta K, Avihingsanon Y, *et al.* The role of a low protein diet supplemented with ketoanalogues on kidney progression in pre-dialysis chronic kidney disease patients. Sci Rep 2023;13(1):15459.
48. Schulman G, Vanholder R, Niwa T. AST-120 for the management of progression of chronic kidney disease. Int J Nephrol Renovasc Dis 2014;7:49-56.
49. Vanholder R, Nigam SK, Burtey S, *et al.* What if not all metabolites from the uremic toxin generating pathways are toxic? A hypothesis. Toxins (Basel) 2022;14(3):221.
50. Dalhoff A. Selective toxicity of antibacterial agents—still a valid concept or do we miss chances and ignore risks? Infection 2021;49(1):29-56.
51. Xiang X, Zhou Z, Rao X, Jiang XR. Recent advances of engineered bacteria for therapeutic applications. Mol Ther 2026;34(2):714-733.
52. Reva K, Laranjinha J, Rocha BS. Epigenetic modifications induced by the gut microbiota may result from what we eat: Should we talk about precision diet in health and disease? Metabolites 2023;13(3):375.
53. Alobaidi S. The gut-kidney axis in chronic kidney disease: Mechanisms, microbial metabolites, and microbiome-targeted therapeutics. Front Med (Lausanne) 2025;12:1675458.
54. Su PY, Lee YH, Kuo LN, *et al.* Efficacy of AST-120 for patients with chronic kidney disease: A network meta-analysis of randomized controlled trials. Front Pharmacol 2021;12:676345.
55. Zhuang K, Luo H, Zeng M, *et al.* Effects of probiotics, prebiotics, and synbiotics on gut microbiota in older adults: A systematic review and meta-analysis of randomized controlled trials. Nutr J 2025;24(1):147.
56. Martinez Guevara D, Vidal Cañas S, Palacios I, *et al.* Effectiveness of probiotics, prebiotics, and synbiotics in managing insulin resistance and hormonal imbalance in women with polycystic ovary syndrome (PCOS): A systematic review of randomized clinical trials. Nutrients 2024;16(22):3916.
57. Bautista J, Echeverría CE, Maldonado-Noboa I, *et al.* The human microbiome in clinical translation: From bench to bedside. Front Microbiol 2025;16:1632435.
58. Zhou Z, Fu H, Li M, *et al.* Bacteriophage therapy: Current strategies and future perspectives. MedComm (2020) 2026;7(3):e70645.

59. Cooper TE, Khalid R, Chan S, *et al.* Synbiotics, prebiotics and probiotics for people with chronic kidney disease. Cochrane Database Syst Rev 2023;10(10):CD013631.
60. Merrick B, Allen L, Masirah MZN, *et al.* Regulation, risk and safety of faecal microbiota transplant. Infect Prev Pract 2020;2(3):100069.
61. Zhang Y, Qing J, Saed YA, Li Y. Gut microbiota implication in diabetic kidney disease: Mechanisms and novel therapeutic strategies. Ren Fail 2025;47(1):2517402.
62. Xu J, Moore BN, Pluznick JL. Short-chain fatty acid receptors and blood pressure regulation: Council on Hypertension Mid-Career Award for Research Excellence 2021. Hypertension 2022;79(10):2127-2137.
63. Sun L, Li Z, Hu C, *et al.* Age-dependent changes in the gut microbiota and serum metabolome correlate with renal function and human aging. Aging Cell 2023;22(12):e14028.
64. Chen Z, Chang X, Ye Q, *et al.* Kidney transplantation and gut microbiota. Clin Kidney J 2024;17(8):sfae214.
65. Cao H, Sun J, Lv Y, *et al.* Targeting the gut-kidney axis to improve kidney transplantation prognosis: From mechanisms to clinical intervention strategies. Ren Fail 2026;48(1):2642487.
66. Aya V, Pardo-Rodriguez D, Vega LC, *et al.* Integrating metagenomics and metabolomics to study the gut microbiome and host relationships in sports across different energy systems. Sci Rep 2025;15:15356.
67. Li T, Chen K, Sun Y, Zhang L. Diabetic kidney disease: Integrating multi-omics insights, artificial intelligence, and novel therapeutics for precision medicine. Front Genet 2026;17:1760654.
68. Syukri M, Bersot CD, Alemayehu A. Artificial intelligence in chronic kidney disease, dialysis and kidney transplantation: Current evidence, clinical applications, implementation challenges, and future directions. Narra Intern Med 2026;1(1):e5.
69. Mizdrak M, Kumrić M, Kurir TT, Božić J. Emerging biomarkers for early detection of chronic kidney disease. J Pers Med 2022;12(4):548.