Advances in Obesity, Endocrinology, and Diabetes

Volume 3 Issue 2 (July-Dec 2026) | **ISSN**: 3049-0715

Gut Microbiota in Type 2 Diabetes: Dysbiosis Signatures, Metabolic Signalling, and Microbiome-Targeted Therapeutics

Om Kolthoum SALLEM[1,2], Dorra BENSALEM[2], Yosra HASNI[3,4,5]

[1]Department of Nutrition, EPS Fattouma Bourguiba, Monastir, Tunisia
[2]Faculty of Medicine of Monastir, University of Monastir, Monastir, Tunisia
[3]Department of Endocrinology, Farhat Hached University Hospital, Sousse, Tunisia
[4] University of Sousse, Faculty of Medicine of Sousse, Sousse, Tunisia
[5]Laboratory of Clinical and Molecular Biology, Faculty of Pharmacy of Monastir, University of Monastir, Monastir, Tunisia, LR24ES15

Abstract

Introduction: Type 2 diabetes is a complex endocrine-metabolic disorder in which insulin resistance, beta-cell dysfunction, chronic low-grade inflammation and environmental exposures interact. The gut microbiota has emerged as a biologically plausible determinant of this process because it regulates nutrient fermentation, microbial metabolite production, gut barrier integrity, immune tone and endocrine-metabolic signalling.

Methods:

A structured review of the literature was conducted using PubMed/MEDLINE, ScienceDirect and Google Scholar. English and French publications were screened using terms related to gut microbiota, type 2 diabetes, dysbiosis, insulin resistance, inflammation, probiotics, prebiotics, microbiota-targeted therapy and fecal microbiota transplantation. Forty-two records were identified, and 32 references were retained for qualitative synthesis after screening and full-text eligibility assessment.

Results:

The evidence consistently indicates that type 2 diabetes is associated with dysbiosis, reduced microbial diversity, depletion of butyrate-producing or metabolically favorable taxa and enrichment of opportunistic or pro-inflammatory communities. Recurrent mechanisms include intestinal barrier dysfunction, lipopolysaccharide-mediated metabolic endotoxemia, impaired short-chain fatty acid signalling, bile acid dysregulation, excessive imidazole propionate, branched-chain amino acid metabolism, altered incretin responses and immune-metabolic activation. Microbiota-targeted interventions, including fermented foods, probiotics, prebiotics, synbiotics, resistant starch and fecal microbiota transplantation, show promise but remain clinically heterogeneous.

Conclusion:

The gut microbiota is best understood as a dynamic metabolic interface rather than a passive marker of type 2 diabetes. Microbiome-informed strategies may enrich future precision endocrinology, but standardised human trials integrating taxonomic, functional and clinical endpoints are required before routine implementation.

Keywords: gut microbiota; type 2 diabetes; dysbiosis; insulin resistance; short-chain fatty acids; lipopolysaccharides; probiotics; prebiotics; fecal microbiota transplantation

Introduction

Type 2 diabetes (T2D) is a chronic endocrine-metabolic disease characterized by persistent hyperglycemia resulting from insulin resistance, progressive beta-cell dysfunction and complex interactions among genetic, nutritional, inflammatory and environmental determinants [1,2,3]. Although classic risk factors explain a substantial proportion of disease burden, they do not fully capture interindividual differences in susceptibility, glycemic trajectory or response to treatment. This has led to growing interest in biological interfaces that connect lifestyle exposure to host metabolism.

The gut microbiota represents one such interface. It includes a dense microbial ecosystem with major functions in fiber fermentation, vitamin production, bile acid transformation, epithelial barrier maintenance and immune education [3,4]. In metabolic disease, disruption of this ecosystem, often described as dysbiosis, may alter microbial diversity, functional capacity and metabolite production. These changes can influence insulin sensitivity, inflammatory activation, adipose tissue function and glucose homeostasis [5,6,7].

In T2D, several observational and metagenomic studies have reported reduced abundance of beneficial butyrate-producing organisms, enrichment of opportunistic or Gram-negative taxa, altered Firmicutes/Bacteroidetes-related profiles and strain-specific microbial signatures [8,9,10,11]. However, the field remains complex because microbiota composition is also influenced by diet, geography, ethnicity, age, medication exposure and disease duration. Medication exposure is particularly important, since oral anti-diabetic treatment can modify microbiota composition over time [12]. Therefore, the microbiota-T2D association should be interpreted as a bidirectional and context-dependent axis rather than a simple causal chain.

This review synthesizes current evidence on the gut microbiota-T2D axis, with three objectives: to summarize dysbiosis patterns reported in T2D, to describe mechanistic pathways linking microbial changes to insulin resistance and hyperglycemia, and to appraise microbiota-targeted interventions as potential adjuncts to diabetes prevention and management.

Methods

This manuscript was prepared as a review article informed by a structured literature search. PubMed/MEDLINE, ScienceDirect and Google Scholar were searched for publications in English and French. The search strategy combined terms such as “gut microbiota”, “intestinal microbiota”, “type 2 diabetes”, “dysbiosis”, “insulin resistance”, “inflammation”, “short-chain fatty acids”, “lipopolysaccharides”, “bile acids”, “probiotics”, “prebiotics”, “synbiotics”, “resistant starch”, “fecal microbiota transplantation” and “microbiota-targeted therapy”.

Eligible publications included observational human studies, case-control studies, metagenomic studies, randomized or non-randomized intervention studies, meta-analyses, systematic reviews and mechanistic studies that addressed microbiota composition, microbial metabolites, gut barrier dysfunction, inflammation, insulin resistance or microbiota-targeted interventions in the context of T2D or closely related metabolic disorders. Non-empirical articles, editorials, inaccessible full texts and studies without clear relevance to the review question were excluded.

Initially, 42 records were identified. After screening titles, abstracts and full texts, 32 references were retained for qualitative synthesis. The selection process is summarized in Figure 1 and Table 1. Data

Volume 3 Issue 2 (July-Dec 2026) | **ISSN**: 3049-0715

extraction used a structured grid covering authors, year, study design, population or sample, key findings and relevance to the review question. The retained evidence base is summarized in Table 2, and microbiota-targeted intervention studies are presented in Table 3. Because this work used only previously published literature, ethical approval was not required.

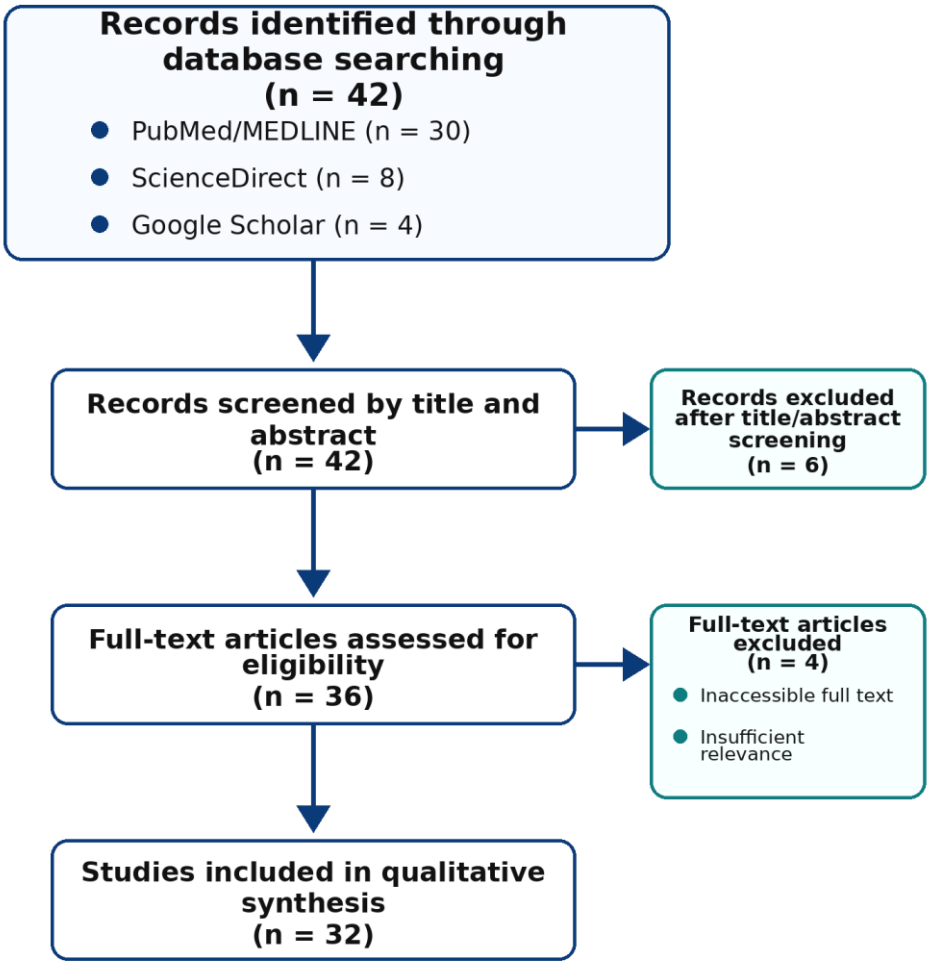

Figure 1. PRISMA-style flow diagram summarizing the identification, screening, eligibility assessment and inclusion of studies in the qualitative synthesis.

Table 1. Identification and selection of studies by database source.

Source	Records identified	Reports retained	Role in evidence synthesis
PubMed/MEDLINE	30	23	Core biomedical and endocrine-metabolic evidence
ScienceDirect	8	7	Mechanistic, microbiology and clinical review evidence
Google Scholar	4	2	Complementary identification of full-text studies
Total	42	32	Final qualitative synthesis after screening

Volume 3 Issue 2 (July-Dec 2026) | **ISSN**: 3049-0715

Source	Records identified	Reports retained	Role in evidence synthesis
			and eligibility assessment

Volume 3 Issue 2 (July-Dec 2026) | **ISSN**: 3049-0715

Table 2. Summary of the main retained publications, study design, population, key findings and relevance to the review.

Article Title	Authors & Year	Study Design	Sample Size & Population	Key Findings	Relevance to Our Study
A Metabolite Perspective on the Involvement of the Gut Microbiota in Type 2 Diabetes	Fu et al., 2023	Narrative/mechanistic review	Published experimental and clinical literature	Microbial metabolites, including SCFAs, bile acids, imidazole propionate and lipopolysaccharides, are linked to insulin resistance and glycemic regulation.	Frames T2D as a metabolite-mediated host-microbiota disorder.
Association between gut microbiota, inflammation, and type 2 diabetes	Liu et al., 2024	Observational/mechanistic study	Patients with T2D and non-diabetic comparators	Microbiota alterations correlated with inflammatory profiles and metabolic status.	Links dysbiosis to low-grade inflammation.
Role of gut microbiota in type 2 diabetes pathophysiology	Gurung et al., 2020	Mechanistic review	Experimental and human evidence	Dysbiosis contributes to insulin resistance through inflammation, bile acid metabolism and microbial metabolites.	Supports biological plausibility of causality.
Gut microbial metabolites as multi-kingdom intermediates	Krautkramer et al., 2021	Mechanistic review	Preclinical and human metabolomics literature	Microbial metabolites mediate signaling between host and microbiota.	Supports metabolite-focused mechanism section.
A metagenome-wide association study of gut microbiota in type 2 diabetes	Qin et al., 2012	Metagenome-wide association study	T2D patients and non-diabetic controls	T2D was associated with functional dysbiosis, fewer butyrate-producing bacteria and more opportunistic pathogens.	Landmark evidence for functional dysbiosis in T2D.
Microbially Produced Imidazole Propionate Impairs Insulin Signaling through mTORC1	Koh et al., 2018	Mechanistic translational study	Human metabolomics and experimental models	Imidazole propionate impaired insulin signaling through mTORC1 activation.	Strong mechanistic link between microbial metabolites and insulin resistance.

Volume 3 Issue 2 (July-Dec 2026) | **ISSN**: 3049-0715

Article Title	Authors & Year	Study Design	Sample Size & Population	Key Findings	Relevance to Our Study
Human gut microbes impact host serum metabolome and insulin sensitivity	Pedersen et al., 2016	Multi-omics human study	Adults characterized by gut microbiome, metabolome and insulin sensitivity	Specific microbial communities affected serum metabolites and insulin sensitivity.	Connects gut microbiome to host metabolic phenotype.
Gut Microbiota in Human Adults with Type 2 Diabetes Differs from Non-Diabetic Adults	Larsen et al., 2010	Case-control sequencing study	Adults with T2D and non-diabetic adults	Adults with T2D displayed a distinct microbial profile compared with non-diabetic controls.	Provides foundational evidence that T2D is associated with altered microbiota.
Characteristics of gut microbiota in adult patients with type 1 and type 2 diabetes based on 16S rRNA sequencing	Salamon et al., 2020	Sequencing-based observational study	Adults with type 1 diabetes, T2D and controls	Diabetes subtypes were associated with distinctive taxonomic profiles, including altered Firmicutes/Bacteroidetes patterns.	Illustrates disease-specific microbiota variation.
Strain-specific gut microbial signatures in type 2 diabetes identified in a cross-cohort analysis of 8,117 metagenomes	Mei et al., 2024	Cross-cohort metagenomic analysis	8,117 metagenomes from multiple international cohorts	T2D-related signatures were strain-specific; different strains of the same species may carry different metabolic-risk functions.	Modernizes the review with strain-level precision.
Gut metagenome in European women with normal, impaired and diabetic glucose control	Karlsson et al., 2013	Metagenomic case-control study	European women across glycemic states	Metagenomic profiles differed by glucose tolerance status and medication exposure.	Shows gradient of dysbiosis across glycemic control.
Intestinal microbiota composition in patients with type 2 diabetes and effects of 12 weeks of oral antidiabetic treatment	Yorulmaz et al., 2022	Case-control interventional study	24 adults with T2D and 10 healthy controls	Diversity indices were lower in T2D; Gemmiger and Collinsella predominated in diabetes, whereas Faecalibacterium, Bacteroides and Alistipes predominated in controls.	Supports dysbiosis and medication-related microbiota modification.

Volume 3 Issue 2 (July-Dec 2026) | **ISSN**: 3049-0715

Article Title	Authors & Year	Study Design	Sample Size & Population	Key Findings	Relevance to Our Study
Gut Microbiome Profiles Are Associated With Type 2 Diabetes in Urban Africans	Doumatey et al., 2020	Cross-sectional metagenomic study	Urban African adults with and without T2D	Specific microbial signatures were associated with T2D in an African population.	Highlights population-specific microbiome patterns.
Particularities of the intestinal microbiome composition in Romanian patients with metabolic syndrome and type 2 diabetes	Corb Aron et al., 2021	Cross-sectional comparative study	150 patients/controls	Microbiota composition differed between healthy controls and patients with T2D/metabolic syndrome.	Adds European population data.
Intestinal Microbiota Composition in Iranian Diabetic, Pre-diabetic and Healthy Individuals	Ghaemi et al., 2020	Case-control study	Iranian diabetic, pre-diabetic and healthy adults	Microbiota composition differed across glycemic categories.	Suggests microbiota shifts may emerge before overt diabetes.
Analyzing Type 2 Diabetes Associations with the Gut Microbiome in Individuals from Two Ethnic Backgrounds Living in the Same Geographic Area	Balvers et al., 2021	Cross-sectional multiethnic study	Individuals from two ethnic backgrounds	Microbiome-T2D associations differed by ethnic background despite shared geography.	Emphasizes confounding by ethnicity and lifestyle.
Gut Bacterial Characteristics of Patients With Type 2 Diabetes Mellitus and the Application Potential	Que et al., 2021	Clinical microbiome study	Patients with T2D and controls	Distinct gut bacterial features were identified as potential diagnostic or therapeutic targets.	Supports translational biomarker potential.
Gut microbiota dysbiosis associated with glucose metabolism disorders and metabolic syndrome in older adults	Lippert et al., 2017	Cross-sectional cohort study	Older adults with metabolic syndrome/glucose disorders	Dysbiosis was associated with impaired glucose metabolism and metabolic syndrome.	Connects microbiota with metabolic risk before and during T2D.

Article Title	Authors & Year	Study Design	Sample Size & Population	Key Findings	Relevance to Our Study
Characteristics of gut microbiota and its response to a Chinese herbal formula in elder patients with metabolic syndrome	Ni et al., 2018	Interventional clinical study	Elderly patients with metabolic syndrome	Microbial patterns changed after herbal intervention, suggesting modifiability of metabolic dysbiosis.	Shows therapeutic modulation of microbiota in metabolic disease.
Comparison of gut microbiota in adult patients with type 2 diabetes and healthy individuals	Sedighi et al., 2017	Case-control study	Adults with T2D and healthy controls	Reduced beneficial bacteria and increased potentially pathogenic taxa were observed in T2D.	Supports recurrent dysbiotic profile in T2D.
A purified membrane protein from Akkermansia muciniphila or the pasteurized bacterium improves metabolism in obese and diabetic mice	Plovier et al., 2017	Experimental preclinical study	Obese and diabetic mouse models	Pasteurized Akkermansia muciniphila or its membrane protein improved metabolic parameters in experimental obesity and diabetes.	Supports the biological plausibility of Akkermansia-related metabolic benefits.
Akkermansia muciniphila: a promising probiotic against inflammation and metabolic disorders	Zhao et al., 2024	Narrative/mechanistic review	Published experimental and clinical literature	Summarizes evidence linking Akkermansia muciniphila to inflammation, barrier function and metabolic regulation.	Supports the discussion of Akkermansia as a metabolically favorable taxon.
Potential of gut microbiota for lipopolysaccharide biosynthesis in European women with type 2 diabetes based on metagenome	Dong et al., 2022	Metagenomic analysis	European women with T2D	T2D was associated with increased microbial potential for LPS biosynthesis.	Supports metabolic endotoxemia hypothesis.

Article Title	Authors & Year	Study Design	Sample Size & Population	Key Findings	Relevance to Our Study
Dysbiosis of Gram-negative gut microbiota and serum lipopolysaccharide in diabetic kidney disease	Salguero et al., 2019	Clinical observational study	T2D patients with chronic kidney disease	Gram-negative dysbiosis and serum LPS were associated with inflammation.	Links microbiota, LPS and diabetic complications.
A metabolic pathway for bile acid dehydroxylation by the gut microbiome	Funabashi et al., 2020	Experimental mechanistic study	Microbial biochemical pathway analysis	Identified microbiota-mediated bile acid transformation pathways.	Supports bile acid mechanism in insulin sensitivity.
Gut symbionts alleviate MASH through a secondary bile acid biosynthetic pathway	Nie et al., 2024	Experimental mechanistic study	Preclinical models	Gut symbionts modified secondary bile acid biosynthesis and metabolic inflammation.	Connects microbial bile acid metabolism to metabolic disease.
Increased intestinal permeability as a risk factor for type 2 diabetes	Cox et al., 2017	Clinical observational study	Adults assessed for permeability and metabolic status	Increased intestinal permeability was associated with T2D risk.	Supports gut barrier dysfunction mechanism.
Effect of probiotic fermented milk supplementation on glucose and lipid metabolism in T2D	Zhong et al., 2024	Meta-analysis of randomized trials	Patients with T2D	Probiotic fermented milk reduced fasting glucose and HbA1c in pooled analyses.	Supports probiotic/fermented dairy intervention.
Effects of 12 weeks of fermented milk on glucose metabolism and cardiovascular risk in T2D	Hove et al., 2015	Randomized double-blind placebo-controlled trial	41 patients with T2D	Fermented milk reduced fasting glucose but did not significantly affect HbA1c.	Illustrates modest and endpoint-dependent probiotic effects.
Efficacy of increased resistant starch consumption in human type 2 diabetes	Bodinham et al., 2014	Dietary intervention study	17 adults with T2D	Resistant starch improved postprandial glucose and GLP-1-related responses.	Supports prebiotic fiber/resistant starch pathway.
Effects of synbiotic supplementation on metabolic factors and	Velayati et al., 2020	Randomized double-blind placebo-controlled trial	50 patients with T2D	Synbiotic supplementation reduced	Supports combined prebiotic-probiotic strategy.

Volume 3 Issue 2 (July-Dec 2026) | **ISSN**: 3049-0715

Article Title	Authors & Year	Study Design	Sample Size & Population	Key Findings	Relevance to Our Study
systemic inflammation in T2D				fasting glucose, insulin and HOMA-IR.	
Clinical response to fecal microbiota transplant therapy in type 2 diabetes patients	Ding et al., 2022	Open-label FMT intervention	17 patients with T2D and 20 healthy controls	FMT improved glycemic parameters in some patients; baseline microbiota influenced response.	Introduces microbiota transfer and responder profiling.

Volume 3 Issue 2 (July-Dec 2026) | **ISSN**: 3049-0715

Results

The retained studies included human observational studies, case-control microbiome analyses, metagenomic association studies, mechanistic translational studies, randomized or non-randomized intervention studies, meta-analyses and narrative reviews. Overall, the evidence supports a recurrent association between T2D and gut microbiota dysbiosis. This association was observed across different populations, including European, African, Iranian, Romanian and multiethnic cohorts, although the exact microbial signatures differed by geography, ethnicity, diet and medication exposure [13,14,15,16,17]. Similar dysbiosis patterns have also been described in older adults with glucose-metabolism disorders or metabolic syndrome and in intervention contexts using microbiota-modulating herbal formulas [18,19].

At the taxonomic level, T2D has frequently been associated with lower microbial richness or diversity and a reduction in beneficial bacteria involved in butyrate production or mucosal homeostasis, including Faecalibacterium, Akkermansia and selected Clostridial taxa [5,9,20]. Akkermansia muciniphila is of particular interest because experimental and review data suggest beneficial effects on metabolic inflammation and glucose-related pathways [21,22]. Conversely, several studies reported enrichment of opportunistic species or Gram-negative bacterial communities that may increase inflammatory tone through lipopolysaccharide biosynthesis [5,23,24]. Evidence from a large cross-cohort metagenomic analysis also suggests that species-level associations may be insufficient; strain-level differences may determine whether a microbial organism is metabolically harmful, neutral or potentially beneficial [10].

Microbial metabolite data provide mechanistic support for these observations. Reduced production of short-chain fatty acids (SCFAs), particularly butyrate, can weaken epithelial barrier function, reduce anti-inflammatory signalling and impair metabolic homeostasis [4,5]. In contrast, increased imidazole propionate may interfere with insulin signalling through mTORC1 activation [6]. Altered bile acid metabolism may affect FXR and TGR5 pathways, with consequences for glucose metabolism, hepatic lipid handling and incretin physiology [25,26].

Gut barrier dysfunction is another central pathway. Dysbiosis can increase intestinal permeability and facilitate translocation of lipopolysaccharides into the circulation, promoting metabolic endotoxemia, low-grade inflammation and impaired insulin signalling [23,24,27]. These mechanisms are biologically coherent with the inflammatory phenotype of T2D and may contribute to disease progression as well as diabetic complications. The main mechanistic links between dysbiosis and

T2D are summarized in Figure 2.

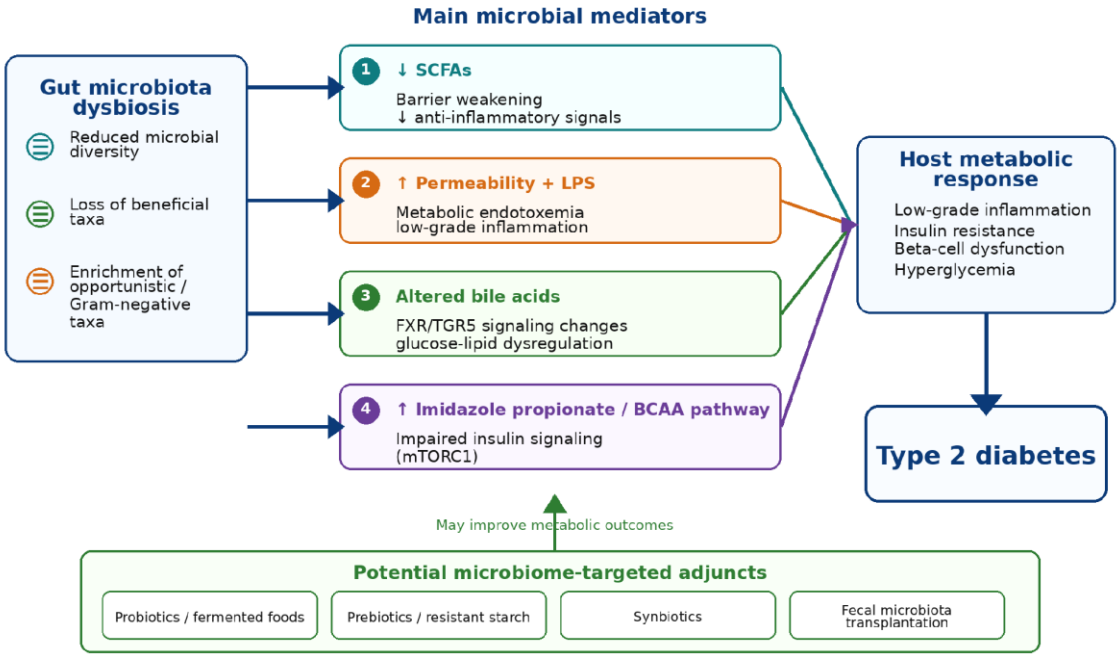

Figure 2. Conceptual mechanistic pathways linking gut microbiota dysbiosis to insulin resistance, metabolic inflammation and type 2 diabetes, with potential microbiome-targeted therapeutic approaches.

Therapeutic evidence remains promising but heterogeneous. Fermented milk and probiotic interventions have shown reductions in fasting glucose and, in pooled analyses, possible improvements in HbA1c [28,29]. Resistant starch may improve postprandial glycemia and incretin-related responses [30]. Synbiotic supplementation may reduce fasting glucose, insulin and HOMA-IR in selected patients [31]. Fecal microbiota transplantation has shown glycemic improvement in some individuals with T2D, but response appears dependent on baseline microbial characteristics and remains experimental [32].

Table 3. Microbiota-targeted interventions reported in human type 2 diabetes or related metabolic studies.

Intervention	Representative Evidence	Metabolic Signal	Clinical Interpretation
Probiotic fermented milk	Zhong et al., 2024; Hove et al., 2015	Lower fasting glucose; possible HbA1c reduction depending on trial/pooling	Promising adjunct, but strain, dose and duration remain important.
Resistant starch/prebiotic substrates	Bodinham et al., 2014	Improved postprandial glycemia and increased GLP-1 response	Supports fiber-fermentation-SCFA/incretin axis.
Synbiotic supplementation	Velayati et al., 2020	Lower fasting glucose, insulin and HOMA-IR	Combined substrate and bacterial supplementation may improve insulin resistance.

Volume 3 Issue 2 (July-Dec 2026) | **ISSN**: 3049-0715

Intervention	Representative Evidence	Metabolic Signal	Clinical Interpretation
Fecal microbiota transplantation	Ding et al., 2022	Improved glycemic markers in selected patients	Experimental; requires donor selection, safety monitoring and responder prediction.

Discussion

This review supports the concept that the gut microbiota is a clinically relevant component of the metabolic network underlying T2D. Rather than identifying a single microbial cause of diabetes, the available literature points to a multidimensional dysbiosis phenotype involving microbial diversity, functional capacity, metabolite production, barrier integrity and inflammatory regulation. This interpretation is consistent with the complexity of T2D, a disease in which host genetics, diet, adiposity, medication and environment shape the same biological pathways that the microbiota can modulate.

A key implication is that microbiota signatures should be interpreted functionally. The same taxonomic group may have different effects depending on strain-level gene carriage, substrate availability and host context. The recent strain-level evidence from more than 8,000 metagenomes is particularly important because it suggests that future clinical translation will require more than broad phylum-level markers [10]. Functional metagenomics, metabolomics and host metabolic phenotyping are likely to be more informative than taxonomy alone.

The metabolite-centered model also provides a plausible bridge between microbiology and endocrinology. SCFAs can support epithelial integrity, regulate immune responses and influence incretin secretion. Bile acid derivatives can signal through receptors involved in glucose and lipid metabolism. Conversely, imidazole propionate, excess branched-chain amino acid-related metabolism and lipopolysaccharides can promote insulin resistance or inflammatory activation [4,6,23,25,26]. These pathways explain why dysbiosis may be associated not only with the presence of T2D but also with variable treatment response.

From a therapeutic perspective, microbiota-targeted strategies are attractive but not yet ready for uniform clinical adoption. Probiotics, prebiotics and synbiotics are generally accessible interventions, but clinical results vary according to strain selection, dose, duration, baseline diet, antidiabetic medication and initial microbiota profile. Fecal microbiota transplantation is even more complex because donor selection, durability, safety, route of administration and metabolic responder identification remain unresolved. These strategies should therefore be viewed as research-informed adjuncts rather than replacements for evidence-based diabetes care.

This review has limitations. The available studies were heterogeneous in design, sequencing platform, bioinformatic pipeline, population characteristics and endpoints. Some studies were observational and cannot prove causality. In addition, medication exposure, especially metformin, can itself remodel the gut microbiota and may confound microbiome-disease associations. Future trials should integrate standardized microbiome profiling, metabolomic endpoints, dietary assessment, medication stratification and clinically meaningful outcomes such as HbA1c, insulin sensitivity, weight trajectory and complication risk.

Volume 3 Issue 2 (July-Dec 2026) | **ISSN**: 3049-0715

Conclusion

The gut microbiota is a dynamic metabolic interface that may contribute to the development, progression and therapeutic variability of type 2 diabetes. Dysbiosis in T2D is characterized by altered diversity, loss of beneficial metabolite-producing bacteria, enrichment of opportunistic or inflammatory taxa, impaired barrier function and disruption of microbial metabolites involved in insulin signalling and glucose homeostasis. Microbiome-targeted interventions, including dietary fibers, probiotics, synbiotics, fermented foods and fecal microbiota transplantation, are promising but require stronger clinical validation. The next phase of research should move from descriptive dysbiosis toward precision microbiome-endocrinology trials combining taxonomic, functional and metabolic endpoints.

Statements

Ethical Statement: Because this review is based exclusively on previously published literature, ethical approval was not required.

Artificial Intelligence (AI) Disclosure Statement: During the preparation of this manuscript, the authors used OpenAI ChatGPT for English-language editing, manuscript organization and formatting support. After using this AI tool, the authors revised and edited the content and take full responsibility for the publication.

Data Sharing Statement: All evidence tables are included in the published article. No original patient-level data were generated.

Acknowledgement: None.

Funding: No funding was received for the preparation of this review.

Conflict of Interest Statement: The authors declare no conflict of interest.

Author Contributions: Om Kolthoum SALLEM contributed to conceptualization, literature synthesis, manuscript drafting and critical revision. Dorra BENSALEM and Yosra HASNI contributed to literature screening, data extraction and critical revision. All authors approved the final version of the manuscript.

References

1. Fu Y, Li S, Xiao Y, Liu G, Fang J. A metabolite perspective on the involvement of the gut microbiota in type 2 diabetes. Int J Mol Sci. 2023;24:14991.

2. Liu N, Yan X, Lv B, Wu Y, Hu X, Zheng C, et al. A study on the association between gut microbiota, inflammation, and type 2 diabetes. Appl Microbiol Biotechnol. 2024;108:213.

3. Gurung M, Li Z, You H, Rodrigues R, Jump DB, Morgun A, et al. Role of gut microbiota in type 2 diabetes pathophysiology. EBioMedicine. 2020;51:102590.

4. Krautkramer KA, Fan J, Backhed F. Gut microbial metabolites as multi-kingdom intermediates. Nat Rev Microbiol. 2021;19:77-94.

5. Qin J, Li Y, Cai Z, Li S, Zhu J, Zhang F, et al. A metagenome-wide association study of gut microbiota in type 2 diabetes. Nature. 2012;490:55-60.

6. Koh A, Molinaro A, Stahlman M, Khan MT, Schmidt C, Manneras-Holm L, et al. Microbially produced imidazole propionate impairs insulin signaling through mTORC1. Cell. 2018;175:947-961.e17.

7. Pedersen HK, Gudmundsdottir V, Nielsen HB, Hyotylainen T, Nielsen T, Jensen BAH, et al. Human gut microbes impact host serum metabolome and insulin sensitivity. Nature. 2016;535:376-381.

8. Larsen N, Vogensen FK, van den Berg FWJ, Nielsen DS, Andreasen AS, Pedersen BK, et al. Gut microbiota in human adults with type 2 diabetes differs from non-diabetic adults. PLoS One. 2010;5:e9085.

9. Salamon D. Characteristics of gut microbiota in adult patients with type 1 and type 2 diabetes based on next-generation sequencing of the 16S rRNA gene fragment. Pol Arch Intern Med. 2020.

10. Mei Z, Wang F, Bhosle A, Dong D, Mehta R, Ghazi A, et al. Strain-specific gut microbial signatures in type 2 diabetes identified in a cross-cohort analysis of 8,117 metagenomes. Nat Med. 2024;30:2265-2276. doi:10.1038/s41591-024-03067-7.

11. Karlsson FH, Tremaroli V, Nookaew I, Bergstrom G, Behre CJ, Fagerberg B, et al. Gut metagenome in European women with normal, impaired and diabetic glucose control. Nature. 2013;498:99-103.

12. Yorulmaz G, Kalkan AT, Akalin A, Varis A, Kaya M, Dinleyici EC. Intestinal microbiota composition in patients with type 2 diabetes and effects of 12 weeks of oral anti-diabetic treatment. J Endocr Soc. 2022;6(Suppl 1):A427. doi:10.1210/jendso/bvac150.888.

13. Doumatey AP, Adeyemo A, Zhou J, Lei L, Adebamowo SN, Adebamowo C, et al. Gut microbiome profiles are associated with type 2 diabetes in urban Africans. Front Cell Infect Microbiol. 2020;10:63.

14. Corb Aron RA, Tit DM, Moleriu R, Bungau S, Toma MM, et al. Particularities of the intestinal microbiome composition in Romanian patients with metabolic syndrome and type 2 diabetes. Arch Balk Med Union. 2021;56:413-421.

15. Ghaemi F, Fateh A, Sepahy AA, Zangeneh M, Ghanei M, Siadat SD. Intestinal microbiota composition in Iranian diabetic, pre-diabetic and healthy individuals. J Diabetes Metab Disord. 2020;19:1199-1203.

16. Balvers M, Deschasaux M, van den Born BJ, Zwinderman K, Nieuwdorp M, Levin E. Analyzing type 2 diabetes associations with the gut microbiome in individuals from two ethnic backgrounds living in the same geographic area. Nutrients. 2021;13:3289.

17. Que Y, Cao M, He J, Zhang Q, Chen Q, Yan C, et al. Gut bacterial characteristics of patients with type 2 diabetes mellitus and the application potential. Front Immunol. 2021;12:722206.

18. Lippert K, Kedenko L, Antonielli L, Kedenko I, Gemeier C, Leitner M, et al. Gut microbiota dysbiosis associated with glucose metabolism disorders and the metabolic syndrome in older adults. Benef Microbes. 2017;8:545-556.

19. Ni Y, Mu C, He X, Zheng K, Guo H, Zhu W. Characteristics of gut microbiota and its response to a Chinese herbal formula in elder patients with metabolic syndrome. Drug Discov Ther. 2018;12:161-169.

20. Sedighi M, Razavi S, Navab-Moghadam F, Khamseh ME, Alaei-Shahmiri F, Mehrtash A, et al. Comparison of gut microbiota in adult patients with type 2 diabetes and healthy individuals. Microb Pathog. 2017;111:362-369.

21. Plovier H, Everard A, Druart C, Depommier C, Van Hul M, Geurts L, et al. A purified membrane protein from Akkermansia muciniphila or the pasteurized bacterium improves metabolism in obese and diabetic mice. Nat Med. 2017;23:107-113.

22. Zhao Y, Yang H, Wu P, Yang S, Xue W, Xu B, et al. Akkermansia muciniphila: a promising probiotic against inflammation and metabolic disorders. Virulence. 2024;15:2375555.

23. Dong Y, Wang P, Yang X, Chen M, Li J. Potential of gut microbiota for lipopolysaccharide biosynthesis in European women with type 2 diabetes based on metagenome. Front Cell Dev Biol. 2022;10:1027413.

24. Salguero M, Al-Obaide M, Singh R, Siepmann T, Vasylyeva T. Dysbiosis of Gram-negative gut microbiota and the associated serum lipopolysaccharide exacerbates inflammation in type 2 diabetic patients with chronic kidney disease. Exp Ther Med. 2019;18:3461-3469.

25. Funabashi M, Grove TL, Wang M, Varma Y, McFadden ME, Brown LC, et al. A metabolic pathway for bile acid dehydroxylation by the gut microbiome. Nature. 2020;582:566-570.

26. Nie Q, Luo X, Wang K, Ding Y, Jia S, Zhao Q, et al. Gut symbionts alleviate MASH through a secondary bile acid biosynthetic pathway. Cell. 2024;187:2717-2734.e33.

27. Cox AJ, Zhang P, Bowden DW, Devereaux B, Davoren PM, Cripps AW, et al. Increased intestinal permeability as a risk factor for type 2 diabetes. Diabetes Metab. 2017;43:163-166.

28. Zhong H, Wang L, Jia F, Yan Y, Xiong F, Hidayat K, et al. Effect of probiotic fermented milk supplementation on glucose and lipid metabolism parameters and inflammatory markers in patients with type 2 diabetes mellitus: a meta-analysis of randomized controlled trials. Biology. 2024;13:641.

29. Hove KD, Brons C, Faerch K, Lund SS, Rossing P, Vaag A. Effects of 12 weeks of treatment with fermented milk on blood pressure, glucose metabolism and markers of cardiovascular risk in patients with type 2 diabetes: a randomised double-blind placebo-controlled study. Eur J Endocrinol. 2015;172:11-20.

30. Bodinham CL, Smith L, Thomas EL, Bell JD, Swann JR, Costabile A, et al. Efficacy of increased resistant starch consumption in human type 2 diabetes. Endocr Connect. 2014;3:75-84.

31. Velayati A, Kareem I, Sedaghat M, Sohrab G, Nikpayam O, Hedayati M, et al. The effects of synbiotic supplementation on metabolic factors and systemic inflammation in patients with type 2 diabetes: a randomized, double-blind, placebo-controlled study. 2020.

32. Ding D, Yong H, You N, Lu W, Yang X, Ye X, et al. Prospective study reveals host microbial determinants of clinical response to fecal microbiota transplant therapy in type 2 diabetes patients. Front Cell Infect Microbiol. 2022;12:820367.