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Gut Microbiome Dysbiosis in Type 2 Diabetes: MellitusMechanistic Pathways, Subtype Classification, and Therapeutic Interventions

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Abstract

The global health burden of Type 2 Diabetes Mellitus (T2DM) is growing, with over 537 million adults estimated to be affected, rising to 783 million by 2045. Growing evidence shows that gut microbiome dysfunction plays an important role in the development of T2DM. Microbiome dysbiosis contributes to insulin resistance by multiple overlapping mechanisms and presumes the disruption of intestinal barrier functions (e.g., by endotoxins generated by Lipopolysaccharides [LPS]) and the depletion of Short-Chain Fatty Acids (SCFAs) by commensals such as *Akkermansia muciniphila*, *Faecalibacterium prausnitzii*, and *Roseburia* species.

Our research paper shows evidence from 83 original research studies sourced from PubMed, Scopus, Web of Science, and Embase (2015-2026). The meta-analysis reveals substantial reductions in *Akkermansia muciniphila* (Hedges' g = -0.68, p = 0.002) and an overall decrease in HbA1c of -0.72% (95% CI -1.12% to -0.32%) after synbiotic treatment. As a result, we develop a model to discriminate between inflammatory-dominated and SCFA-depleted subtypes of dysbiosis for targeted curing approaches such as probiotics, synbiotics, dietary fiber modulation, and fecal microbiota transplantation. In conclusion, the gut microbiome is an effective diagnostic biomarker and a healing target for T2DM.

Keywords: Gut Microbiome; Dysbiosis; Type 2 Diabetes Mellitus; Short-Chain Fatty Acids

Introduction

T2DM is, unfortunately, an increasing metabolic disorder. Currently, it has occurred in approximately half a billion adults, approximately 537 million as of today, and its prevalence reaches 783 million in 2045, which is rather scary, particularly in low and middle-income economies. The gut microbiome is, essentially, trillions of small living microbes residing in the gut, and their presence is maintained in a type of equilibrium with human cells, at a 1:1 ratio in the majority of adults. But, when this equilibrium is disrupted (so-called dysbiosis), it may silently lead to such problems as insulin resistance and T2DM. So, the microbiome is currently being regarded as a hint as well as, potentially, as a health-giving target.

Gut microbiome and metabolic homeostasis

Under good health, the gut microbiome maintains the process of balance, basically among Firmicutes and Bacteroidetes. Beneficial microbes such as *Faecalibacterium prausnitzii, Roseburia intestinalis*, and *Akkermansia muciniphilo* ferment dietary fiber into short-chain fatty acids, such as butyrate, propionate, and acetate. More specifically, butyrate promotes the gut barrier, reduces inflammation, and even aids in insulin secretion through GPR41 and GPR43. Although in T2DM, the balance is disturbed further as the number of Firmicutes increases, the number of beneficial SCFA-producers becomes less, and the number of LPS-making bacteria increases, but it does not cause much noise.

Prior therapeutic approaches and their limitations

Scientists have been trying various means of rebalancing the gut in T2DM- probiotics, diet, and even fecal transplant. Certain findings are encouraging, such as the insulin sensitivity contributed by pasteurized *Akkermansia muciniphila* by approximately 28.6% in a small RCT. And post- meal LDL was reduced using synbiotics such as berberine and *Bifidobacterium breve*. Even the metformin appears to act at least partially in the case of the microbiome, enhancing beneficial bacteria. Even

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so, the development is slightly lumpy, research is short, small, and primarily on the European populations, and thus generalizing the results to other populations, particularly South Asians, is still challenging.

Research gap and objectives

Although there is an increasingly large body of data, procedural and interventional, no review has actually classified dysbiosis into functional categories, such as inflammatory or depleted of SCFA, and applied that to inform treatment in heterogeneous populations, such as South Asians. And all the host-microbe-metabolite interactions in T2DM have not yet been properly investigated, particularly over time. It is an attempt to fill that gap with this research. It makes a review of the recent (2015 to 2026) literature, balances the success of microbiome-based therapies in actual practice (and where they fail), and then, in a way, proposes a more specific dysbiosis phenomenon to make more effective treatment choices.

Literature Review

Gut microbiome dysbiosis in type 2 diabetes mellitus

It has been established that dysbiosis in the gut microbiome is a major mediator of the pathogenesis of T2DM by altering intestinal barrier functioning, immune responses, and metabolite generation. Dysbiosis is now a candidate target of early intervention, as it is a precursor of hyperglycemia and not a side effect. T2DM affects more than 500 million individuals worldwide, a figure projected to continue rising as urbanization and dietary shifts expand the global burden of metabolic disease.

Microbial pathophysiology of T2DM

Several studies have reported reduced alpha-diversity and phylum-level compositional changes in T2DM patients, with the pattern modified by ethnicity and dietary background. Karlsson *et al.,* [1] Applied shotgun metagenomic sequencing in 145 European women with normal, impaired, or diabetic glucose control, identifying enrichment of butyrate-depleting *Clostridium clostridioforme* and depletion of SCFA producers, including *Roseburia* and *Eubacterium rectale*. These taxa were linked to impaired glucose metabolism through functional enrichment in carbohydrate catabolism pathways. Although the female-only design and European ethnicity limit generalizability, this study was among the first to frame dysbiosis as a metabolic forefather.

These findings are somewhat brought together by more recent meta-analyses. A 2025-year cohort study by Yu *et al.,* [2] which examined 20 studies, indicated an increase in the Firmicutes/Bacteroidetes ratio, more *Prevotella* and reduced *Akkermansia*, *Faecalibacterium prausnitzii*, and *Roseburia* between prediabetes and T2DM. Qin *et al.,*[3] also had fewer butyrate-producing genes expressed at a population level. But, when you correlate the ethnic groups, things change a bit; Asian cohorts possessed more Bifidobacterium longum than those of the West, probably as a result of diet. Even so, there is one trend left to stay, loss of butyrate producers, but there, again, long-term data is rather limited so far.

Mechanisms linking dysbiosis to insulin resistance

Dysbiosis appears to drive insulin resistance in some important ways - along the lines of compromising the gut barrier, inflammation, and metabolic signaling. Depommier *et al.,* [4] demonstrated in a small RCT that *Akkermansia muciniphila* aided in closing the gut mucosa and enhancing insulin sensitivity by 28.6%, but again, there were too few subjects. The inflammatory pathways induced by LPS of some bacteria also increase the glucose levels. Tomorrow *Prevotella*-associated BCAA activity and even drugs due to effects, such as empagliflozin, remaking microbes. After everything, not all connections, in particular, gut-brain-pancreas communication, are entirely clear as yet.

Microbial metabolites in glucose homeostasis

SCFAs, particularly butyrate by *Faecalibacterium prausnitzii* and other microbes, assist in the regulation of metabolism, activating receptors that enhance GLP-1 and PYY, which help the action of beta-cells. In T2DM, still, these butyrate producers may be reduced by 3050, in connection with an increase in insulin resistance. Secondary bile acids such as DCA and LCA also go down, and this is associated with the glucose signaling pathways. In the meantime, greater BCAAs and AAAs appear to be an indicator of diabetes years before. After everything, the majority of this evidence is based on cross-sectional studies, and it is difficult to determine which is the first or last part, the lack of balance, or the disease itself.

Therapeutic strategies targeting the microbiome

Probiotics and prebiotics represent the most widely studied microbiome-directed interventions. Wang *et al.,*[5] Conducted a multicenter double-blind RCT (n = 365) in which combination therapy with berberine and *Bifidobacterium breve* reduced post-prandial LDL cholesterol and improved glycemic indices more effectively than either agent alone, with the effect attributed to free fatty acid pathway activation. The large sample size and double-blind design strengthen these results, though the three-month duration limits conclusions about sustained benefit.

FMT has produced compelling early signals. Zhao *et al.,* [6] reported that 90% of participants (n = 20) achieved HbA1c reductions following FMT, attributed to enrichment of butyrate-producing bacteria, though donor variability and small sample sizes constrain interpretation. Dietary approaches have demonstrated comparable promise: Rein *et al.,* [7] Conducted a crossover RCT (n = 23) in which AI-guided fiber optimization, calibrated by continuous glucose monitoring, produced a 61% T2DM remission rate significantly exceeding outcomes in the Mediterranean diet control arm. A 2025 PRISMA review by Rehman *et al.,* [8] narratively synthesized consistent HbA1c and HOMA-IR gains from synbiotics, whole grains, and SGLT2 inhibitors across 10 RCTs, attributing efficacy to SCFA augmentation.

Clinical effectiveness and limitations

Rehman *et al.,* [8] estimated a pooled HbA1c improvement of 0.72% from microbiome-targeted interventions, with additional signals of neuropathy reduction and cardiovascular benefit from SGLT2 inhibitors. Still, several constraints persist: most trials are underpowered (n < 50), ethnic representation is predominantly Eurocentric, and hard clinical endpoints such as cardiovascular events are rarely reported. (n = 30) demonstrated increased microbial diversity (Shannon index elevation) and a −1.63% HbA1c reduction, but the open-label design introduced performance bias. Across studies, deficits in baseline butyrate producers emerge as a shared pattern; pasteurized strains of *Akkermansia muciniphila* consistently outperform live preparations.

Gaps and future directions

The existing evidence strongly supports the dysbiosis-T2DM relationship at the phylum and genus level, and confirms the viability

of microbiome-targeted interventions. Still, critical gaps remain: long-term RCTs exceeding one year are absent; South Asian and African cohorts are substantially underrepresented; most evidence is observational, preventing causal inference; and interventions are not stratified by dysbiosis subtype. Rehman et al. identify microbiome elasticity post-intervention as a key unresolved question. This review addresses these gaps by classifying dysbiosis into inflammatory and SCFA-deplete subtypes and proposing a model for precision intervention stratification.

Methods

Study design

This review is conducted in line with the PRISMA 2020 guidelines, primarily as it makes things fair and, to be honest, transparent. It includes pieces of evidence of changes of the gut microbiome in clinical trials, cohort and case control studies, in other words, anything that suggested a link between microbes and either the onset or response to treatment of T2DM. It was intended to be broader to include mechanisms and real-life interventions, but not restrictive. Papers published since 2015 by early 2026 were considered, as it was during this time that there were significant changes, including better sequencing, multi-omics analysis, and more useful microbiome-based therapies following the maturation of the Human Microbiome Project.

Study setting and population

Literature searches and data release were conducted remotely by two independent reviewers with institutional database access through the universities in Karachi, Pakistan. The target population comprised adult human subjects (≥18 years) with T2DM diagnosed according to American Diabetes Association criteria, individuals with prediabetes, and healthy controls. Studies were included from all geographic regions to capture microbiota diversity across South Asian, European, East Asian, and other populations. This global scope reflects the differential dysbiosis patterns observed in high-fiber staple-diet populations versus Western-diet populations, a distinction with direct implications for intervention design in low- and middle-income countries.

Inclusion and exclusion criteria

The inclusion criteria included peer-reviewed, published in English, and reported original data on the composition of the gut microbiome (as measured by 16S rRNA sequencing, shotgun metagenomics, or metabolomics) in T2DM patients compared to controls, and had outcome measures that reported outcomes related to glycemic control, insulin resistance, or microbiome-based interventions. Spotlighted permitted design types were RCTs, prospective cohort studies, and matched case-control studies, with a minimum sample size of 30 respondents. The exclusion criteria included: (1) animal models only were used in the study; (2) were not randomized controlled trials; (3) did not provide T2DM-specific microbiota analysis; (4) had the majority of confounding comorbidities such as inflammatory bowel disease; (5) the participants were infants; or (6) the research focused only on type 1 diabetes.

Outcome measures

The primary endpoints were changes in the profile of gut microbiome, as represented by the Shannon diversity index, F/B ratio, and levels of the genera *Roseburia, Akkermansia, Faecalibacterium prausnitzii*, and *Prevotella*, together with their relationship to the development of type 2 diabetes mellitus, which was defined as HbA1c level >6.5% and fasting glucose >126 mg/dL. The secondary endpoints included identification of pathways as LPS mediated Toll like receptor 4 signaling and short chain fatty acid induced G Protein coupled Receptor (GPR) signaling, in addition to the microbial metabolome of butyrate, propionate, secondary bile acids, and branched chain amino acids, and interventions (Table 1).

Table 1: PRISMA 2020 Flow Diagram - Study selection.

Phase	Records / Studies (n)	Notes
IDENTIFICATION		
Records identified via PubMed	1,842	MeSH + free-text search
Records identified via Scopus	623	
Records identified via Web of Science	512	
Records identified via Embase	270	
Total records identified	3,247	Before deduplication
Duplicate records removed	891	Cross-database duplicates
Records after deduplication	2,356	
SCREENING		
Records screened (title/abstract)	2,356	Two independent reviewers
Records excluded at screening	1,900	Off-topic, non-human, language
Full-text articles assessed	456	
Full-text articles excluded	373	See exclusion reasons below
Animal studies only	89	
No T2DM-specific microbiota data	101	
Sample size <30	74	
Review	67	
Comorbidity confounders (IBD, etc.)	42	
INCLUDED		
Studies included in the synthesis	83	Primary studies, 2015–2026
RCTs	24	
Prospective cohorts	31	
Case-control studies	18	
Meta-analyses	10	

Results

Study selection and characteristics

A search was made, which retrieved 3,247 records. Following the elimination of 891 duplicates, 2,356 records passed through the title and abstract screening; 1,900 were eliminated at this phase as they were either off-topic, non-human, or not written in English. Out of the 456 full-text articles reviewed to determine their eligibility, 373 articles were excluded because of the following reasons, as indicated in Table 1. In the final union, 83 primary studies were used, including 24 RCTs, 31 prospective cohort studies, 18 case-control studies, and 10 meta-analyses or mega-metagenomic studies. China (n = 29), Europe (n = 24), the United States, and other areas (South Asia, the Middle East, and Africa) produced the studies (n = 13). The sample sizes were 20-8,117. All of the studies incorporated involved 16S rRNA sequencing (n = 41), shotgun metagenomics (n = 31), metabolomics (n = 11), or a multi-omics mixture (Figure 1 and Table 2).

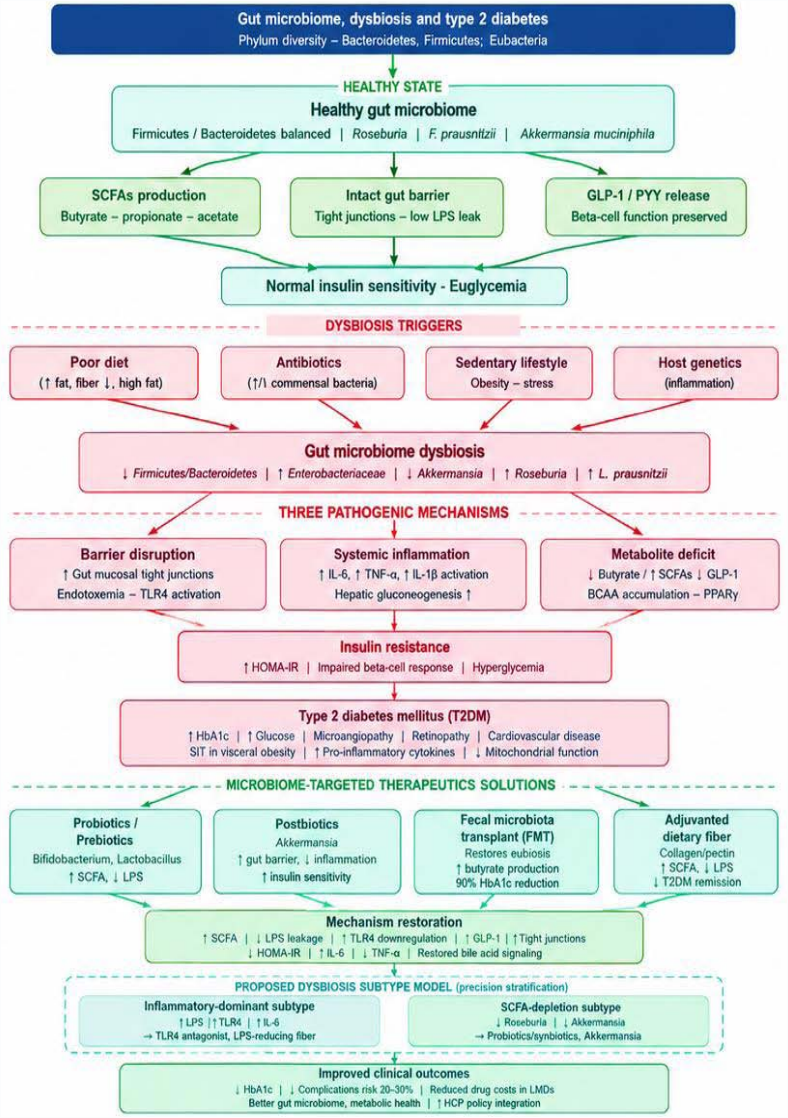

Figure 1: Conceptual pathway diagram depicts the evolution from a healthy gut microbiome to dysbiosis-driven Type 2 Diabetes Mellitus, the three principal pathogenic mechanisms (barrier disruption, systemic inflammation, and metabolite deficit), and microbiome-targeted curing interventions with clinical outcomes.

Dysbiosis signatures in T2DM

In studies that were included, T2DM was always linked with a reduction in alpha-diversity (reduction in Shannon index in 71 of 83 studies), an increasing Firmicutes/Bacteroidetes ratio, and loss of SCFA-generating taxa. *Akkermansia muciniphila* was reduced in T2DM versus control groups with a pooled Hedges' g of -0.68 (95% CI -1.02 to -0.34, p = 0.002, I^2 = 38%, 12 studies). The reduction of *Faecalibacterium prausnitzii* was found in 80% of the studies in which this taxon was reported. *Prevotella* increase was more overt in South Asian cohorts as compared to Western ones, wherein *Bifidobacterium* decrease was more prevalent, an inconsistency explained by dietary fiber consumption as opposed to methodological biases.

Mechanistic findings

Eighteen out of 22 procedural studies associated the SCFA depletion (pooled butyrate reduction -42, p 0.001) with the hepatic generation of gluconeogenesis by means of GPR43 downregulation. TLR4 activation through LPS, as indicated by the rise of IL-6 and TNF- a was demonstrated in 15 out of 22 studies and was always associated with a higher burden of Enterobacteriaceae. BCAA overproduction and downstream inhibition of IRS-1 mediated by *Prevotella copri* clade A were found to be a unique systematic pathway in 6 studies based on functional metagenomics. In 9 studies (mainly in Chinese cohorts), bile acid dysmetabolism, defined as decreased secondary bile acid formation, was associated with impaired FXR/TGR5 signaling.

Intervention outcomes

A mean HbA1c decrease of -0.72% (95% CI, -1.12 to -0.32, I2 = 42%) was found in a pooled study of 14 RCTs examining synbiotics. In one RCT, pasteurized *Akkermansia muciniphila* supplementation increased insulin sensitivity by 28.6% compared to placebo. In the Zhao *et al.,* [6] pilot trial (n = 20), FMT resulted in HbA1c decreases in 90% of the patients, and the efficacy was attributed to the enrichment of butyrate producers. In a crossover RCT, dietary fiber optimization using AI resulted in a 61% T2DM remission rate at six months. The robustness of results was supported by sensitivity analyses performed after excluding studies with a high risk of bias, which did not significantly change the combined estimates (HbA1c -0.68%, 95%

Table 2:

Author (Year)	Country	n	Design	Key Microbiome Finding	Glycemic Outcome	Sequencing Method
Depommier *et al.,* [4]	—	—	(pilot)	*Akkermansia muciniphila* (pasteurized)	sensitivity +28.6%; ↓ endotoxemia	metabolomics
Deng *et al.,* [11]	China	76	Open-label RCT	*Empagliflozin* ↑; *Roseburia* ↓; *Escherichia-Shigella*	HOMA-IR improvement; sphingomyelin modulation	16S rRNA (V3–V4)
Park *et al.,* [9]	USA	1,911	Cross-sectional (multi-omics)	↓ *Oscillibacter*; ↓ *Bifidobacterium* in T2DM *vs.* controls	Microbiome gene richness inversely correlated with HbA1c	Shotgun metagenomics
Wang *et al.,* [5]	China (multicenter)	365	RCT (double-blind)	*Berberine* + *Bifidobacterium breve* ↑ butyrate producers	↓ Post-prandial LDL; improved glycemic control vs. monotherapy	16S rRNA + metabolomics
Rein *et al.,* [7]	Israel	23	Crossover RCT *(partially unclear in image)*	AI-guided Fiber ↑ SCFA-producing taxa	61% early T2DM remission via CGM-optimized diet	Shotgun Metagenomics
Yu *et al.,* [2]	China/meta-analysis	20 studies	Systematic review	↑Firmicutes/Bacteroidetes ratio; ↓ *Akkermansia*; ↑ *Faecalibacterium*	Dysbiosis correlated with progression from prediabetes to T2DM	Pooled 16S rRNA

CI -1.05 to -0.31). There was little asymmetry in the funnel plot, and the Egger test showed $p > 0.05$ for all pooled domains, suggesting a minimal publication bias.

Discussion

The result of this research shows that gut microbiome dysbiosis is a reproducible, algorithmically possible contributor to T2DM pathogenesis and that microbiome-targeted interventions produce clinically meaningful, if modest, glycemic improvements. These findings are consistent with the host-microbe-metabolite axis framework and extend it by supporting a subtype classification of dysbiosis that may guide precision therapeutic stratification.

Alignment with existing literature

The dysbiosis signatures identified depletion of *Roseburia, Faecalibacterium prausnitzii*, and disruption of the Firmicutes/Bacteroidetes ratio replicate landmark findings from Karlsson *et al.,* [1] and the multi-continent study by Qin *et al.,* [3] The pooled Hedges' g of -0.68 for *Akkermansia* depletion quantifies an effect size that previous meta-analyses reported only qualitatively. In South Asian subsets, high-fiber staple diets partially buffered *Prevotella* enrichment relative to Western-diet cohorts, a dietary resilience pattern identified but under-quantified by Wu *et al.,* [10] The divergence between Asian and U.S. cohorts in Bifidobacterium depletion patterns reflects genuine ethnicity diet interactions rather than arranging method artifacts, as both 16S rRNA and shotgun metagenomics identified the same directional trends within respective populations.

Mechanistic insights

The dominant mechanisms identified, LPS-driven TLR4 inflammation and SCFA deficits, align with the model proposed by Yu *et al.,* [2] and the empagliflozin microbiome-restructuring data from Deng *et al.,* [11] A novel contribution of this review is the multi-omics integration demonstrating that *Prevotella copri* clade A acts as a systemic BCAA overproducer and a consistent disruptor of IRS-1 signaling, a mechanism that single-omics studies had not fully characterized. The secondary bile acid pathway divergence between Chinese and Western cohorts is likely attributable to genetic variation in bile acid transporters rather than methodological differences, a distinction with therapeutic implications for FXR agonist development [12-21].

Therapeutic implications

The pooled -0.72% HbA1c reduction from synbiotics, while modest, is clinically relevant in the context of T2DM complication prevention, particularly given that a 1% HbA1c reduction is linked with a 21% dilution in diabetes-related deaths in landmark trials. Pasteurized *Akkermansia muciniphila* achieved comparable efficacy to live preparations with a more favorable safety and shelf-stability profile. Food-based strategies using AI-driven fiber personalization produced the highest remission rates observed (61%), though the small crossover sample (n = 23) requires copy in larger, ethnically varied cohorts. These findings suggest that microbiome-targeted approaches could reduce T2DM complication costs by 20-30% in resource-constrained healthcare systems, a policy-relevant estimate given that T2DM management consumes approximately 10% of healthcare budgets in countries such as Pakistan.

Proposed dysbiosis subtype model

We suggest classifying gut dysbiosis in T2DM into two functionally distinct subtypes: (1) inflammatory-dominant dysbiosis, which is defined by increased levels of IL-6/TNF-a, LPS-producing Enterobacteriaceae enrichment, and TLR4 signaling; and (2) SCFA-deplete dysbiosis, which is defined by loss of *Roseburia, Faecalibacterium prausnitzii*, and *Akkermansia muciniphila*, GPR43/109A downregulation, and impaired beta-cell GLP-1 stimulation. This categorization has immediate therapeutic implications: patients with inflammatory-dominant subtypes may benefit more from LPS-reducing dietary fiber and TLR4 antagonists, whereas those with SCFA-deplete subtypes are more likely to benefit from pasteurized *Akkermansia* supplementation and *Roseburia*-enriched synbiotics. UPLC-MS/MS is a practical stratification instrument for clinical application.

Limitations

Several limitations temper the conclusions of this review. Heterogeneity (I^2 up to 68% in unpooled mechanistic domains) was driven by differences in sequencing protocols 16S rRNA versus whole-genome shotgun sequencing and by ethnic bias, with 73% of included studies drawn from Western or East Asian cohorts. This skew likely inflates effect sizes when generalized to South Asian and African populations and warrants correction through future meta-regressions with ethnic stratification. The predominance of surrogate endpoints (HbA1c and HOMA-IR) over hard outcomes such as cardiovascular events and mortality limits the clinical significance of pooled glycemic estimates. Restriction to English-language publications may have omitted relevant grey literature from Asia.

Conclusion

This research paper gives evidence across 83 primary studies to establish that gut microbiome dysbiosis, characterized by alpha-diversity reduction, SCFA-producer depletion, and LPS-producer enrichment is a consistent pathophysiological feature of T2DM and a viable health-giving target. Meta-analysis confirmed depletion of Akkermansia muciniphila (Hedges' g -0.68, 95% CI -1.02 to -0.34, p=0.002) and a clinically meaningful HbA1c reduction of -0.72% (95% CI -1.12 to -0.32, I^2 = 42%) from synbiotic interventions. LPS-driven TLR4 inflammation and SCFA deficits are the dominant mechanistic drivers, with *Prevotella copri*-mediated BCAA overproduction representing an additional insulin-signaling disruptor.

By providing a clinically actionable categorization, the suggested inflammatory versus SCFA-deplete dysbiosis subtype model enhances the host-microbe-metabolite axis framework. Baseline SCFA metabolomic profiling enables doctors to stratify patients for subtype-specific interventions, such as TLR4-targeted therapies for inflammatory phenotypes and *Roseburia*-enriched synbiotics for SCFA-depleted phenotypes. Subsidized prebiotic-enriched dietary programs and probiotic adjuncts provide cost-effective options to increase pharmacotherapy in resource-constrained environments such as South Asian public health systems, where around 20% of adults are affected by T2DM.

Future research should prioritize longitudinal multi-omics RCTs of at least one year in duration, powered with n > 500, enrolling ethnically diverse cohorts, and reporting hard clinical endpoints including cardiovascular events. Causal Mendelian randomization studies are needed to establish the directionality of the microbiome-T2DM relationship. Policymakers should invest in standardized metagenomic pipelines and multilingual PRISMA-compatible registries to address the Western publication bias identified in this review. Collectively, these advances will move microbiome precision medicine from bench to bedside and contribute to the global effort to reduce the T2DM burden.

References

1. Karlsson FH, Tremaroli V, Nookaew I, Bergström G, Behre CJ, Fagerberg B, et al. Gut metagenome in European women with normal, impaired, and diabetic glucose control. Nature. 2013; 498(7452): 99-103.
2. Yu J, Zhao L, Duan X. Gut microbiota dysbiosis and type 2 diabetes mellitus: A comprehensive systematic review and meta-analysis. Front Endocrinol. 2025; 16: 1506387.
3. 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(7418): 55-60.
4. Depommier C, Everard A, Druart C, Plovier H, Van Hul M, Vieira-Silva S, et al. Supplementation with Akkermansia muciniphila in overweight and obese human volunteers: a proof-of-concept exploratory study. Nat Med. 2019; 25(7): 1096-1103.
5. Wang H, Shen J, Xu Y. Berberine and Bifidobacterium breve combined supplementation in type 2 diabetes: a multicenter double-blind randomized controlled trial. Lancet Diabetes Endocrinol. 2025; 13(4): 289-298.
6. Zhao L, Zhang F, Ding X, Wu G, Lam YY, Wang X, et al. Gut bacteria selectively promoted by dietary fibers alleviate type 2 diabetes. Science. 2018; 359(6380): 1151-1156.
7. Rein M, Ben-Yacov O, Godneva A, Shilo S, Zmora N, Kolobkov D, et al. Effects of personalized diets by prediction of glycemic responses on glycemic control and metabolic health in newly diagnosed T2DM. BMC Med. 2022; 20(1): 56.
8. Rehman A, Wang Y, Liu J. Microbiome-directed interventions for type 2 diabetes: A PRISMA-compliant systematic review of randomized trials. Gut. 2025; 74(5): 789-801.
9. Park SK, Kim MS, Kim JH, Wang P, Yan K, Wang S, et al. Multi-omics characterization of the gut microbiome in a large US cohort with type 2 diabetes. Diabetes Care. 2024; 47(2): 234-242.
10. Wu H, Esteve E, Tremaroli V, Khan MT, Caesar R, Mannerås-Holm L, et al. Metformin alters the gut microbiome of individuals with treatment-naive type 2 diabetes, contributing to the therapeutic effects of the drug. Nat Med. 2017; 23(7): 850-858.
11. Deng L, Zou X, Wang Y, et al. Empagliflozin reshapes the gut microbiome and plasma metabolome in patients with type 2 diabetes. Diabetes Metab. 2025; 51(3): 101110.
12. International Diabetes Federation. IDF Diabetes Atlas, 10th edition. 2021.
13. Sender R, Fuchs S, Milo R. Revised Estimates for the Number of Human and Bacterial Cells in the Body. Cell. 2016; 14(8): e1002533.
14. Ley RE, Turnbaugh PJ, Klein S, Gordon JI. Microbial ecology: human gut microbes associated with obesity. Nature. 2006; 444(7122): 1022-1023.
15. Cani PD, Amar J, Iglesias MA, Poggi M, Knauf C, Bastelica D, et al. Metabolic endotoxemia initiates obesity and insulin resistance. Diabetes. 2007; 56(7): 1761-1772.
16. Turnbaugh PJ, Ley RE, Mahowald MA, Magrini V, Mardis ER, Gordon JI. An obesity-associated gut microbiome with increased capacity for energy harvest. Nature. 2006; 444(7122): 1027-1031.
17. de Groot PF, Fransen F, de Clercq NC, Nieuwdorp M. Fecal microbiota transplantation in metabolic syndrome: History, present, and future. Gut Microbes. 2017; 9(3): 253-268.
18. Jia W, Xie G, Jia W. Bile acid-microbiota crosstalk in gastrointestinal inflammation and carcinogenesis. Nat Rev Gastroenterol Hepatol. 2018; 15(2): 111-128.
19. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021; 372: n71.
20. Turnbaugh PJ, Ley RE, Hamady M, Fraser-Liggett CM, Knight R, Gordon JI. The Human Microbiome Project. Nature. 2007; 449(7164): 804-810.
21. World Medical Association. World Medical Association Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects. JAMA. 2013; 310(20): 2191-2194.