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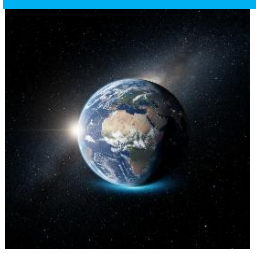

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Small Intestinal Bacterial Overgrowth in Type 2 Diabetes Mellitus: Prevalence, Pathophysiology, and Clinical Implications - A Narrative Review

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Abstract

Background. Gastrointestinal symptoms affect up to two-thirds of patients with type 2 diabetes mellitus (T2DM) and are commonly attributed to autonomic neuropathy and dysmotility. Small intestinal bacterial overgrowth (SIBO) has been proposed as a specific small bowel manifestation of diabetic dysbiosis, potentially contributing to worsened glycemic control,

impaired beta-cell function, and metabolic-associated fatty liver disease (MAFLD), however, its true prevalence in T2DM and clinical significance remain uncertain.

Aim. To synthesize current evidence on the prevalence of SIBO in adults with T2DM, to examine the methodological and clinical factors that influence prevalence estimates, to evaluate proposed pathophysiological mechanisms, and to discuss clinical implications including the distinction between hydrogen-predominant SIBO and intestinal methanogen overgrowth (IMO).

Material and methods. A narrative review was conducted based on a selective literature search in PubMed, Embase, and Web of Science up to March 2026, using combinations of the following terms: type 2 diabetes mellitus, SIBO, breath test, jejunal aspirate, gut microbiota, and intestinal permeability. Observational studies, systematic reviews, meta-analyses, and mechanistic articles reporting SIBO prevalence or associated outcomes in adults with T2DM were included. No formal risk-of-bias assessment or quantitative synthesis was performed.

Results. In a meta-analysis pooling mixed diabetic cohorts, SIBO prevalence was approximately 29%, with a probable but non-significant association with diabetes compared with controls (OR 2.91, 95% CI 0.82–10.32; $p = 0.10$). In a T2DM-specific meta-analysis, pooled SIBO prevalence was approximately 24% (range 7–54%; $I^2 = 97\%$), indicating extreme methodological heterogeneity driven by diagnostic substrate, positivity thresholds, and patient selection. SIBO in T2DM was consistently associated with poorer glycemic control, reduced beta-cell function, autonomic neuropathy, MAFLD, and use of GLP-1 receptor agonists. The distinction between hydrogen-predominant SIBO and IMO, caused by methanogenic archaea and associated with constipation-predominant enteropathy, was found to be clinically relevant in T2DM but remained largely underexplored in this population. Most available evidence was cross-sectional, derived from tertiary-care settings, and relied on breath tests whose diagnostic accuracy had been critically appraised by recent European and North American gastroenterological societies.

Conclusions. SIBO affects approximately one in four patients with T2DM when actively investigated, but prevalence estimates vary widely and causal relationships with metabolic outcomes remain unproven. Universal screening is not currently justified; targeted evaluation should be considered in patients with refractory gastrointestinal symptoms, autonomic neuropathy, unexplained deterioration of glycemic control, or MAFLD. Well-designed randomized controlled trials assessing the metabolic effects of SIBO eradication in T2DM are needed before SIBO can be positioned as a therapeutic target in this population.

Key words: type 2 diabetes mellitus; small intestinal bacterial overgrowth; gut microbiota; gastrointestinal complications

1. Introduction

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disease associated with a broad range of micro- and macrovascular complications, including neuropathy, nephropathy, cardiovascular disease, and metabolic-associated fatty liver disease (MAFLD) (Ahmed et al., 2023). Gastrointestinal (GI) symptoms such as bloating, abdominal pain, diarrhea, constipation, and dyspepsia are highly prevalent in diabetes, affecting up to two-thirds of patients in some series, and are often attributed to autonomic neuropathy and disordered gastrointestinal motility (Młynarska et al., 2024).

Small intestinal bacterial overgrowth (SIBO) is defined as an excessive number and/or abnormal composition of bacteria in the small intestine, classically quantified as $\geq 10^5$ colony-forming units per milliliter (CFU/mL) of jejunal aspirate, although more recent expert consensus has proposed a lower threshold of $\geq 10^3$ CFU/mL to improve sensitivity (Pimentel et al., 2020). Because culture of jejunal aspirate is invasive and rarely performed outside specialist centers, SIBO is increasingly defined operationally in epidemiological studies by a positive hydrogen or hydrogen-methane breath test (see Table 2), which introduces additional heterogeneity in prevalence estimates. SIBO can lead to nutrient malabsorption, bile acid deconjugation, vitamin deficiencies, mucosal inflammation, and further motility impairment (Quigley et al., 2020).

The gut microbiota has emerged as a key contributor to the pathogenesis of obesity, insulin resistance, and T2DM through mechanisms including altered short-chain fatty acid production, modulation of bile acid pools, low-grade inflammation, and disruption of intestinal barrier integrity (Chong et al., 2025; Fliegerová et al., 2025). Within this broader context, SIBO may represent a specific small-bowel manifestation of dysbiosis in T2DM, driven by autonomic neuropathy, dysmotility, anatomical changes, and exposure to medications such as proton-pump inhibitors or glucagon-like peptide-1 (GLP-1) receptor agonists (Rao & Bhagatwala, 2019).

Despite increasing interest, the reported prevalence of SIBO in T2DM varies widely between studies, and its clinical relevance remains debated.

Research Objective

The objective of this narrative review is to synthesize current evidence on the prevalence of SIBO in adults with T2DM, to discuss factors that influence prevalence estimates (including diagnostic methods and patient characteristics), and to critically evaluate the pathophysiological

mechanisms and clinical implications, including therapeutic strategies for SIBO management in T2DM.

Research Problems

- What is the prevalence of SIBO in patients with T2DM, and which pathophysiological mechanisms drive elevated risk?
- Is SIBO associated with poorer glycemic control, beta-cell dysfunction, and more advanced liver disease in T2DM?
- Which patients with T2DM should be considered for SIBO screening?
- Does the distinction between hydrogen-predominant SIBO and intestinal methanogen overgrowth (IMO) influence therapeutic strategy?

2. Research materials and methods

This work was designed as a narrative review, focusing on a broad and critical appraisal of the existing literature rather than exhaustive systematic coverage.

2.1. Participants

Inclusion criteria for primary observational studies were: (1) adult participants with T2DM or mixed diabetic cohorts in which data for T2DM could be separately identified; (2) explicit assessment of SIBO using standard diagnostic methods (hydrogen or hydrogen–methane breath testing with glucose or lactulose substrate, or jejunal aspirate culture); and (3) reporting of SIBO prevalence or sufficient data to calculate it. Studies focused exclusively on type 1 diabetes, case reports, conference abstracts without full data, and articles lacking clear diagnostic definitions were excluded unless they provided unique data unavailable from other sources. In addition, major systematic reviews and meta-analyses on SIBO in diabetes, narrative or systematic reviews on the gut microbiota in T2DM, and mechanistic or clinical studies addressing autonomic neuropathy, MAFLD, intestinal permeability, or GLP-1 receptor agonist therapy in relation to SIBO were included to provide broader contextual evidence.

2.2. Procedure

A selective literature search was conducted in PubMed, Embase, and Web of Science covering publications up to March 2026, using combinations of the following keywords: "type 2 diabetes mellitus", "T2DM", "diabetes mellitus", "small intestinal bacterial overgrowth", "SIBO", "breath test", "jejunal aspirate", "gut microbiota", and "intestinal permeability". No language restrictions were applied. Retrieved records were screened by title and abstract, followed by full-text review of potentially eligible sources.

2.3. Data collection and analysis

2.3.1. Statistical Software

Given the narrative design of this review, no quantitative synthesis was performed and no statistical software was used for data analysis.

2.3.2. Thematic framework and data presentation

Given the narrative design, no formal risk-of-bias assessment or quantitative synthesis was performed. Instead, findings were organized thematically into the following domains:

- SIBO prevalence in mixed diabetic cohorts;
- SIBO prevalence specifically in T2DM;
- associated risk factors and clinical phenotypes;
- pathophysiological mechanisms;
- clinical implications and research gaps.

3. Research results

3.1. Prevalence of SIBO in diabetes (overall)

A recent comprehensive systematic review and meta-analysis provided the best available estimates of SIBO prevalence across all types of diabetes (Feng & Li, 2022). In the larger analysis, which pooled data from 14 observational studies including 1,417 individuals with diabetes (type 1 and type 2) and 649 non-diabetic controls, the overall prevalence of SIBO among patients with diabetes was approximately 29% (95% CI: 20–39%). When diabetes was treated as a single group, the odds of having SIBO were approximately 2.9-fold higher in patients with diabetes than in non-diabetic participants, suggesting a probable but non-significant association between the diabetic state and small intestinal bacterial overgrowth (OR 2.91, 95% CI 0.82–10.32; $p = 0.10$). Importantly, subgroup analyses did not reveal a statistically significant difference in pooled prevalence between type 1 and type 2 diabetes, although the number of type-specific datasets was modest and confidence intervals remained wide. This meta-analysis also highlighted the profound heterogeneity underlying prevalence estimates. Statistical heterogeneity was very high ($I^2 = 92\%$ for the pooled prevalence estimate; $I^2 = 89\%$ for the odds ratio analysis), reflecting variation in diagnostic methods, study settings, and geographical regions. Studies using jejunal aspirate culture (often considered a reference standard) reported higher pooled prevalence (~39%) than those employing hydrogen or hydrogen-methane breath tests with glucose or lactulose substrates (~29–31%), although aspirate-based studies were small and typically conducted in highly selected, symptomatic

patients. Geographical differences were also evident, with higher pooled prevalence in Western populations compared with Eastern cohorts, suggesting that diet, healthcare access, and background microbiota may modify risk. Together, these findings suggested that diabetes constitutes a major risk state for SIBO, while simultaneously illustrating the need for more standardized methodologies and better characterization of patient populations - issues that become even more salient when focusing specifically on T2DM.

3.2. Prevalence of SIBO specifically in type 2 diabetes mellitus

A dedicated systematic review and meta-analysis concentrating exclusively on adults with T2DM synthesized data from six observational studies comprising 1,072 participants (Tarigan et al., 2021). Across these cohorts, the pooled prevalence of SIBO was approximately 24%, with individual study estimates ranging from about 7% to over 50% and a 95% confidence interval for the pooled estimate spanning approximately 10–39%. Statistical heterogeneity was extreme (I^2 = 97%), indicating that true prevalence varied substantially between clinical contexts and that methodological factors played a crucial role. Despite this variability, several consistent patterns emerged. Patients with SIBO tended to have higher HbA1c values and lower fasting insulin levels than SIBO-negative individuals, suggesting that SIBO in T2DM was associated with poorer glycemic control and impaired beta-cell function rather than being a benign incidental finding.

Most prevalence data in T2DM derived from hydrogen or hydrogen–methane breath tests using glucose or lactulose as substrates. One of the best-characterized series compared 84 patients with T2DM to 45 non-diabetic controls using the glucose hydrogen breath test. SIBO was diagnosed in 15.5% of patients with T2DM versus 2.2% of controls; in the same cohort, orocecal transit time measured by a separate lactulose hydrogen breath test was significantly prolonged in patients with T2DM compared with controls ($p < 0.001$), and was further delayed in those with SIBO compared with those without ($p < 0.001$) (Rana et al., 2011) - findings that supported a mechanistic link between diabetic dysmotility and increased risk of SIBO. In contrast, a study of 200 hospitalized adults with diabetes (including 109 with T2DM) and 20 ostensibly healthy volunteers, evaluated using lactulose hydrogen breath testing, reported SIBO in 41% of patients with diabetes but unexpectedly in 75% of controls (Adamska et al., 2015) (Table 1). Logistic regression even suggested that being in the control group was independently associated with SIBO, a counter-intuitive result likely reflecting marked selection bias: many controls were recruited from a gastroenterology ward and may have harbored unrecognized motility disorders or structural lesions predisposing to SIBO, while inpatients with diabetes were more intensively investigated and possibly treated before testing. Collectively, studies

confirmed that breath-test-defined SIBO was common in T2DM, but also highlighted how strongly estimates depended on who was tested (outpatients vs. inpatients; symptomatic vs. asymptomatic) and how the tests were interpreted (Feng & Li, 2022).

Table 1. Selected primary studies of SIBO in diabetes mellitus.

Study (Author, Year)	Population & characteristics	SIBO diagnostic method	SIBO prevalence	Key finding
(Adamska et al., 2015)	200 hospitalized T1/T2DM patients vs 20 healthy controls, single center in Poznań, Poland.	Lactulose H_2 breath test (20 g in 200 ml water), positive if baseline ≥20 ppm or rise ≥12 ppm in first 60 min.	41% (82/200) in diabetes T1+T2; 75% (15/20) in controls.	Diabetes associated with ~5-fold lower odds of SIBO vs controls (OR 0.18, 95% CI 0.06–0.56).
(Cherniavskyi & Didyk, 2024)	51 patients with MAFLD + T2DM (27 with SIBO, 24 without) vs 20 healthy controls, single center in Kyiv, Ukraine.	Lactulose hydrogen breath test using Micro H2 Meter.	53% (27/51) in MAFLD + T2DM.	SIBO linked to higher serum I-FABP and dysbiotic microbiota (↑Bacteroidetes, ↓Firmicutes, low F/B ratio).
(Rana et al., 2011)	84 T2DM patients with chronic diarrhea vs 45 healthy controls, tertiary center in North India.	Glucose hydrogen breath test (80 g glucose; rise >12 ppm H_2/CH_4 in two samples = SIBO); OCTT by lactulose HBT.	15.5% (13/84) in T2DM; 2.2% (1/45) in controls.	SIBO observed only in diabetics with markedly delayed orocecal transit (>90 min) and OCTT was the main independent determinant of SIBO.
(Radionova et al., 2020)	92 patients with chronic active gastritis + T2DM vs 80 with gastritis without diabetes, multicenter in Ukraine.	Glucose hydrogen breath test, positive if rise >12 ppm above baseline.	75% (69/92) in T2DM; 41.3% (33/80) in non-diabetic gastritis.	In T2DM, SIBO strongly associated with bloating (OR 8.82), nausea (OR 5.15) and belching (OR 2.53).
(Sun et al., 2025)	216,173 GLP-1/dual GIP initiators vs 216,173 other second-line T2DM agents in the TriNetX global EHR database	Database-identified SIBO diagnoses supported by documented hydrogen breath tests in routine care.	12-month incidence 0.177 vs 0.083 per 1000 person-years (GLP-1/dual GIP vs comparators).	GLP-1–based therapy associated with about two-fold higher 12-month SIBO risk (HR 2.14, GLP-1–95% CI 1.13–4.07) vs other agents.
(Yan et al., 2020)	104 clinic T2DM patients, tertiary center in Tianjin, China.	H_2/CH_4 breath test with lactulose load (20 g); combined H_2/CH_4 criteria with early rise and ≥20 ppm/≥12 ppm cut-offs.	53.85% (56/104).	SIBO independently associated with reduced early- and total-phase insulin secretion indices (lower HOMA-β, InsAUC/GluAUC).

3.2.1. Geographical and population differences

Geographical variation also appeared to influence reported SIBO prevalence in T2DM. Studies from East Asia, particularly China and Korea, tended to report prevalences toward the lower end of the spectrum (often 10–25%), whereas European and North American cohorts more frequently yielded estimates in the 20–40% range (Feng & Li, 2022; Tarigan et al., 2021), although direct head-to-head comparisons were scarce. Differences in dietary patterns, background microbiota, diagnostic availability, and healthcare-seeking behavior may all have contributed (Barlow & Mathur, 2022).

Study setting was another important determinant. Many T2DM cohorts with higher reported prevalence were assembled from tertiary endocrinology or gastroenterology clinics, where patients typically had longer disease duration, higher rates of autonomic neuropathy, MAFLD, and complex medication regimens (Feng & Li, 2022; Rao & Bhagatwala, 2019). In contrast, community-based or primary-care cohorts, although rare, tended to show lower prevalence, suggesting that SIBO might cluster in a subset of patients with more advanced or complicated T2DM rather than being ubiquitous across the entire T2DM population (Rao & Bhagatwala, 2019; Tarigan et al., 2021). The predominance of single-center series from referral hospitals in the current literature therefore limited the generalizability of pooled estimates to the broader T2DM population.

3.3. Impact of diagnostic methods and positivity criteria

Methodological differences in SIBO diagnosis (summarized in Table 2) were perhaps the most important drivers of heterogeneity in prevalence estimates. As noted earlier, jejunal aspirate culture, while often treated as a reference standard, was invasive and rarely used in large epidemiological studies; when it was employed, it generally detected SIBO in a high proportion of carefully selected, highly symptomatic patients. Most T2DM studies instead relied on breath tests, where multiple variables could influence results: choice of substrate (glucose vs. lactulose), dose and concentration, sampling intervals, duration of the test, and the criteria chosen to define a positive hydrogen or methane response (Feng & Li, 2022; Rao & Bhagatwala, 2019; Silva et al., 2025).

Glucose breath tests had higher specificity because glucose was absorbed in the proximal small intestine; a rise in breath hydrogen therefore typically reflected fermentation by bacteria located in the jejunum or proximal ileum, but late peaks might be missed in patients with delayed transit (Pimentel et al., 2020). Lactulose tests, in contrast, could detect overgrowth in more distal segments of the small intestine (a potential advantage over glucose) but were substantially more prone to false positives, as the substrate invariably reached the colon where fermentation generated hydrogen peaks that could be misinterpreted as SIBO if sampling and cut-off thresholds were not carefully calibrated (Silva et al., 2025). In patients with T2DM, where orocecal transit was often prolonged due to autonomic neuropathy, standard interpretation windows derived from healthy volunteers might not apply, increasing the risk of both under- and overdiagnosis (Rana et al., 2011).

Thresholds for defining a positive test varied considerably between studies - some used an absolute rise in hydrogen of ≥20 ppm within 90 minutes, others applied different magnitude or time cut-offs, and only a minority considered combined hydrogen–methane patterns or

incorporated symptom reproduction during testing (Pimentel et al., 2020; Rao & Bhagatwala, 2019; Rezaie et al., 2017; Silva et al., 2025). This methodological diversity meant that two studies of otherwise similar T2DM populations could report markedly different SIBO prevalences purely as a result of how the test was interpreted.

Table 2. Diagnostic methods for SIBO: mechanisms, advantages, and limitations specific to T2DM.

Diagnostic method	Mechanism / positivity criteria	Advantages	Specific limitations in T2DM
Jejunal aspirate culture	Endoscopic aspiration of proximal jejunal fluid; quantitative culture, usually $\geq 10^3 - 10^5$ CFU/mL as cut-off (Pimentel et al., 2020).	Direct bacterial count and speciation; unaffected by colonic fermentation; treated as reference standard in guidelines.	Invasive and costly; used mainly in highly symptomatic referral patients → selection bias and inflated prevalence; small samples, contamination and sampling-site error; impractical for routine use or large T2DM cohorts.
Glucose hydrogen/ methane breath test	Oral glucose; serial breath H2/CH4 (e.g. every 10–15 min); positivity usually defined as ≥ 20 ppm rise within 90 min (Feng & Li, 2022; Pimentel et al., 2020; Silva et al., 2025)	Non-invasive, cheap, widely available; higher specificity for proximal SIBO because glucose is absorbed before reaching the colon (Feng & Li, 2022)	Prolonged orocecal transit in T2DM can shift peaks beyond standard 90-min windows → false negatives; heterogeneous doses, sampling intervals and cut-offs across studies; glucose load may be problematic in brittle diabetes (Rana et al., 2011).
Lactulose hydrogen/ methane breath test	Non-absorbable lactulose; 2–3 h breath test; early H2/CH4 rise or double peak interpreted as SIBO, with widely differing criteria (Silva et al., 2025).	Can detect more distal overgrowth; simultaneously provides orocecal transit time; safe in hyperglycemia since lactulose is not absorbed.	High false-positive risk from colonic fermentation, especially with delayed transit; large variation in dose, duration and positivity rules → major contribution to between-study heterogeneity in T2DM SIBO prevalence.
Combined hydrogen–methane testing	Standard glucose or lactulose test with simultaneous H2, CH4 ± H2S measurement to classify hydrogen SIBO, IMO, or H2S SIBO (Pimentel et al., 2020; Villanueva-Millan et al., 2022).	Links gas phenotype with symptoms (e.g. methane–constipation, H2S–diarrhea); may reduce false-negatives when one gas scavenges another.	Limited availability and higher cost; interpretation algorithms derived mainly from IBS cohorts; virtually no validation in T2DM with autonomic neuropathy and markedly altered transit, adding further methodological heterogeneity.

3.4. Intestinal methanogen overgrowth (IMO) in the context of T2DM

In recent years, the terminology and understanding of small intestinal dysbiosis had evolved, leading to the distinction between classic SIBO (driven by hydrogen-producing bacteria) and intestinal methanogen overgrowth (IMO) (Pimentel et al., 2020). IMO was primarily caused by methanogenic archaea, such as Methanobrevibacter smithii, which consumed hydrogen to produce methane and could colonize both the small and large intestines. Clinically, IMO was strongly associated with constipation rather than diarrhea, as methane gas appeared to actively slow intestinal transit. This distinction was highly relevant for patients with T2DM, many of

whom suffered from severe diabetic autonomic neuropathy manifesting as chronic constipation or alternating bowel habits. However, most existing prevalence studies in T2DM had relied either exclusively on hydrogen breath testing or on combined tests without reporting hydrogen and methane positivity separately. Consequently, the specific prevalence and clinical impact of IMO in the population with diabetes remained largely unexplored (Pimentel et al., 2020; Rezaie et al., 2017).

3.5. Hydrogen sulfide SIBO (SIBO-H_2S) in the context of T2DM

A third phenotype, hydrogen sulfide SIBO (SIBO-H_2S), had been described following advances in breath testing technology that allowed quantification of exhaled H_2S. This variant was associated with diarrhea-predominant symptoms and was linked to the expansion of sulfate-reducing bacteria such as Desulfovibrio spp., Bilophila wadsworthia, and Desulfobacter spp. In patients with T2DM, where diarrhea was a common manifestation of autonomic enteropathy, SIBO-H_2S might have been clinically relevant; however, dedicated breath testing for H_2S was not widely available, and no prevalence data in T2DM populations had been published to date (Pimentel et al., 2020; Villanueva-Millan et al., 2022).

3.6. Pathophysiology: mechanisms linking T2DM and SIBO

The interplay between T2DM and SIBO was complex and likely bidirectional. While T2DM created an environment conducive to bacterial proliferation in the small bowel, the presence of SIBO might, in turn, have exacerbated the metabolic and inflammatory disturbances underlying diabetes and its complications. The key pathophysiological mechanisms could be broadly categorized into dysmotility, altered intestinal barrier function, and disruptions in systemic metabolic signaling.

3.6.1. Dysmotility, neuropathy, and intestinal stasis

The most established mechanistic link between T2DM and SIBO was gastrointestinal dysmotility driven by diabetic autonomic neuropathy. Under physiological conditions, the migrating motor complex (MMC) - a cyclic pattern of gastrointestinal motility occurring during fasting, acted as an intestinal "housekeeper", sweeping residual undigested food and bacteria from the small intestine into the colon (Barlow & Mathur, 2022; Quigley et al., 2020). In patients with long-standing or poorly controlled T2DM, autonomic neuropathy frequently damaged the enteric nervous system, particularly the vagus nerve networks that regulate gastric emptying and intestinal peristalsis. This neurological impairment dampened the amplitude and frequency of the phase III contractions of the MMC, leading to prolonged orocecal transit times and localized stasis of chyme. This stagnation disrupted the normal anterograde propulsion of intestinal contents, promoting retrograde colonization of the small bowel by colonic-type

bacteria (Quigley et al., 2020). Furthermore, chronic hyperglycemia itself directly inhibited gastrointestinal smooth muscle contractility via oxidative stress and the accumulation of advanced glycation end products (AGEs), creating a vicious cycle of dysmotility and bacterial proliferation even in the absence of severe irreversible neuropathy.

3.6.2. Dysbiosis, increased permeability, and metabolic endotoxemia

While dysmotility explained the numerical overgrowth of bacteria, the qualitative shift in microbial composition (dysbiosis) was equally critical. The gut microbiota in T2DM was generally characterized by a relative expansion of potentially pro-inflammatory Gram-negative taxa, notably certain Enterobacteriaceae, alongside shifts in the Bacteroides-to-Firmicutes balance, with a decrease in beneficial butyrate-producing species such as Faecalibacterium prausnitzii (Alqahtani, 2025; Barlow & Mathur, 2022). When these dysbiotic shifts occurred in the small intestine, an area heavily populated by immune cells, the consequences for host metabolism were profound. A key consequence of this dysbiosis was the impairment of intestinal barrier function, commonly referred to as "leaky gut". Overgrown bacteria and their metabolites, such as lipopolysaccharides (LPS), could damage the mucosal lining and disrupt tight junctions between enterocytes. This phenomenon had been well-documented in patients presenting with the triad of T2DM, SIBO, and MAFLD (Bielka et al., 2022). The resulting breach in the intestinal barrier allowed LPS and other pathogen-associated molecular patterns (PAMPs) to translocate into the portal and systemic circulation, triggering a state of metabolic endotoxemia. This systemic influx of bacterial products activated Toll-like receptor 4 (TLR-4) pathways in macrophages, adipocytes, and hepatocytes, releasing pro-inflammatory cytokines (e.g., TNF-α, IL-6) (Barlow & Mathur, 2022). This low-grade, chronic systemic inflammation directly interfered with insulin signaling pathways, thereby exacerbating peripheral insulin resistance (Alqahtani, 2025; Cherniavskyi & Didyk, 2024; Sadagopan et al., 2023).

3.6.3. Implications for incretin secretion, bile acids, and beta-cell function

Beyond inflammation, SIBO likely influenced host metabolism by interfering with specific signaling molecules, particularly incretins and bile acids, ultimately impacting pancreatic beta-cell function.

Bile acids were synthesized in the liver, secreted into the small intestine to aid lipid absorption, and were extensively modified by the gut microbiota. In the presence of SIBO, excessive bacterial deconjugation of primary bile acids in the proximal small bowel prevented their normal reabsorption in the terminal ileum (Quigley et al., 2020). This premature deconjugation disrupted the activation of the farnesoid X receptor (FXR) and Takeda G-protein receptor 5 (TGR5) in the gut and liver. Because FXR and TGR5 signaling regulated hepatic

gluconeogenesis, lipid metabolism, and the secretion of glucagon-like peptide-1 (GLP-1) from enteroendocrine L-cells, SIBO-induced bile acid dysmetabolism might directly have contributed to the hyperglycemia and dyslipidemia observed in T2DM (Byndloss et al., 2024). Furthermore, the physical presence of excessive bacteria in the small intestine could lead to competitive uptake of dietary nutrients, altering the nutrient signals that reached the distal L-cells and K-cells, thereby blunting the physiological secretion of endogenous GLP-1 and glucose-dependent insulinotropic polypeptide (GIP) (Gutierrez-Aguilar & Woods, 2011).

This combination of altered incretin signaling, altered bile acid pools, and systemic inflammation provided a compelling mechanistic explanation for the clinical observations linking SIBO to impaired beta-cell function. As demonstrated in clinical cohorts, patients with T2DM and SIBO exhibited lower early- and total-phase insulin secretion indices compared with those without SIBO, independent of BMI and fasting glucose (Yan et al., 2020). SIBO might thus have acted as a chronic stressor on the pancreas, accelerating beta-cell exhaustion in T2DM through a combination of incretin deficiency and cytokine-mediated lipotoxicity (Barlow & Mathur, 2022).

4. Discussion

4.1. Interpretation of prevalence estimates

Across systematic and narrative reviews, SIBO affects approximately one quarter to one third of individuals with diabetes, with similar pooled prevalence in type 1 and type 2 diabetes when examined together (Feng & Li, 2022). When attention is restricted to T2DM, the best available meta-analysis suggests a prevalence of around 24%, but with a wide range (7%–54%) and very high heterogeneity across primary studies (I^2 = 97%) (Tarigan et al., 2021). Given this heterogeneity, any single pooled estimate should be interpreted with caution. Multiple factors likely account for this variability.

First, diagnostic methods differ markedly: jejunal aspirate culture may detect more cases but tends to be reserved for highly selected patients with severe symptoms, potentially inflating prevalence estimates (Feng & Li, 2022). Breath tests are less invasive and more widely used but are influenced by substrate choice, transit time, and interpretation rules (Pimentel et al., 2020). In patients with diabetes and autonomic neuropathy or delayed gastric or small-bowel transit, conventional time windows for hydrogen peaks may misclassify results and either over- or underestimate SIBO (Rana et al., 2011).

Second, most studies are based in tertiary or specialized clinics and include patients with longstanding, complicated diabetes, which may not reflect the broader community population of individuals with T2DM (Tarigan et al., 2021). Third, sample sizes are often modest, and

control groups may be small or non-representative, as illustrated by the Polish study in which SIBO prevalence was unexpectedly higher in controls than in patients with diabetes (Adamska et al., 2015).

Taken together, most, but not all, studies report higher SIBO prevalence in cohorts with diabetes than in controls, suggesting a probable association between T2DM and small intestinal bacterial overgrowth. However, this association remains statistically uncertain: the pooled odds ratio of 2.91 (95% CI 0.82–10.32) reported by Feng and Li (2022) did not reach statistical significance ($p = 0.10$), and became significant (OR 4.18, 95% CI 1.34–13.05; $p = 0.01$) only after exclusion of the Adamska et al. (2015) dataset, underscoring the sensitivity of pooled estimates to individual outlier studies (Adamska et al., 2015; Feng & Li, 2022). These statistical limitations are compounded by a more fundamental diagnostic uncertainty: a 2024 clinical practice update endorsed by ESNM and ANMS (Kashyap et al., 2024) concluded that breath tests, on which most prevalence estimates in this field depend, do not reliably distinguish true small intestinal bacterial overgrowth from normal variation or accelerated colonic transit. While this critique was directed primarily at functional gastrointestinal disorders rather than T2DM with structural dysmotility, it reinforces the need to interpret pooled SIBO prevalence data with a degree of skepticism commensurate with the quality of the underlying diagnostic methods.

4.2. Risk factors and clinical phenotypes in T2DM with SIBO

4.2.1. Autonomic neuropathy and dysmotility

A consistent theme across the literature is the central role of diabetic autonomic neuropathy and gastrointestinal dysmotility in predisposing to SIBO in T2DM. Early work in T2DM cohorts demonstrated that patients with autonomic neuropathy had markedly higher rates of small-bowel bacterial overgrowth than those without neuropathy (Rana et al., 2011), supporting a mechanistic link between autonomic damage and stasis of intestinal contents. Subsequent studies have confirmed that measures of autonomic dysfunction correlate with abnormal hydrogen breath tests compatible with SIBO, although sample sizes have generally been small and not always restricted to T2DM (Barlow & Mathur, 2022; Quast et al., 2023).

Transit-time data provide complementary evidence. In a study using glucose hydrogen breath testing, patients with T2DM had significantly prolonged orocecal transit time compared with controls without diabetes, and SIBO was diagnosed more frequently in the T2DM group (15.5% vs. 2.2%) (Rana et al., 2011). This pattern is consistent with the dysmotility mechanism described in Section 3.6.1, in which autonomic impairment of MMC phase III contractions creates conditions for bacterial stasis and retrograde colonization of the small bowel. Not all data are straightforward, however. The study that reported a higher SIBO prevalence in

hospitalized controls without diabetes than in patients with diabetes (Adamska et al., 2015) underscores how selection bias and differences in symptom profiles or medications can obscure true associations.

Taken together, the available evidence indicates that autonomic neuropathy and resulting dysmotility are key risk factors for SIBO in T2DM, but their impact is modulated by other factors such as comorbid gastrointestinal disease, prior surgery, and medication use. Future studies with objective quantification of autonomic function, motility, and anatomical abnormalities will be required to disentangle these contributions more rigorously.

4.2.2. Glycemic control and beta-cell function

Several studies have examined the relationship between SIBO and glycemic control in T2DM, suggesting that SIBO is more common in patients with poorer metabolic status. In the meta-analysis restricted to T2DM, SIBO-positive patients had significantly higher HbA1c levels and lower fasting insulin concentrations compared with SIBO-negative individuals (Tarigan et al., 2021), even though body mass index and duration of diabetes were broadly similar between groups. This pattern raises the possibility that SIBO is linked not only to insulin resistance but also to impaired insulin secretion.

A detailed cross-sectional study of 104 adults with T2DM provides further insight. Participants were stratified according to SIBO status based on glucose hydrogen breath testing and underwent oral glucose tolerance testing with calculation of indices of insulin sensitivity and beta-cell function. Those with SIBO exhibited higher two-hour post-load glucose and HbA1c, higher insulin-sensitivity indices, but significantly lower HOMA-β and reduced early- and total-phase insulin secretion (InsAUC30/GluAUC30 and InsAUC120/GluAUC120) (Yan et al., 2020). In multivariable regression models, SIBO remained independently associated with diminished insulin secretory capacity after adjustment for fasting glucose and BMI, suggesting that SIBO is not merely a surrogate for obesity or hyperglycemia.

The direction of causality remains uncertain. It is plausible that chronic exposure to luminal and systemic bacterial products, altered bile-acid pools, and low-grade inflammation in SIBO may impair beta-cell function and incretin signaling, thereby worsening glycemic control. Conversely, long-standing poorly controlled T2DM may predispose to SIBO through neuropathy and dysmotility, with SIBO then acting as a marker of advanced disease. Longitudinal studies are lacking, and current evidence cannot distinguish clearly between these possibilities. Nonetheless, the consistent association of SIBO with higher HbA1c and reduced beta-cell function suggests that SIBO should be considered when evaluating unexplained

deterioration of glycemic control in T2DM (Barlow & Mathur, 2022; Bielka et al., 2022; Młynarska et al., 2024; Sadagopan et al., 2023).

4.2.3. MAFLD and liver disease

The interplay between SIBO, T2DM, and metabolic-associated fatty liver disease forms an increasingly recognized clinical phenotype. In cohorts of patients with MAFLD and T2DM, the presence of SIBO has been associated with more advanced hepatic steatosis, higher liver stiffness values, and more adverse metabolic and inflammatory profiles (Gudan et al., 2022), including elevated levels of interleukin-6, leptin, and markers of insulin resistance. These associations fit within the broader concept of a gut–liver axis in which small-intestinal dysbiosis and increased intestinal permeability promote translocation of bacterial products to the portal circulation, fueling hepatic inflammation and fibrogenesis (Barlow & Mathur, 2022; Młynarska et al., 2024; Sadagopan et al., 2023).

Biomarker studies support this mechanistic framework. In patients with MAFLD and T2DM, those with SIBO have been found to exhibit higher circulating concentrations of a commercially available protein marker referred to as zonulin (used as a putative indirect marker of tight-junction disruption and increased intestinal permeability) alongside elevated levels of intestinal and liver fatty acid-binding proteins (I-FABP and L-FABP), which provide more direct evidence of enterocyte and hepatocyte injury (Bielka et al., 2022; Gudan et al., 2022). It should be noted, however, that the specificity of available ELISA-based zonulin assays has been questioned, as they may primarily detect complement proteins rather than the actual tight-junction modulator pre-haptoglobin-2 (Ajamian et al., 2019; Scheffler et al., 2018); results relying on this marker should therefore be interpreted with caution. Analyses of gut microbiota composition in these patients have also reported shifts in the Firmicutes/Bacteroidetes ratio, with some cohorts showing a relative reduction consistent with broader patterns of dysbiosis in T2DM, although the direction and magnitude of this change vary considerably between studies and populations (Cherniavskyi & Didyk, 2024; Gudan et al., 2022; Quigley et al., 2020).

It is important to note that not all patients with MAFLD and T2DM develop SIBO, and the determinants of this divergence remain poorly understood. Genetic factors, dietary patterns, prior antibiotic exposure, and medication profiles may all modulate individual susceptibility (Młynarska et al., 2024; Sadagopan et al., 2023). Moreover, the available studies are cross-sectional and cannot ascertain whether SIBO precedes and accelerates MAFLD or emerges as a consequence of established liver disease and portal hypertension. Nevertheless, the clustering of SIBO, MAFLD, and T2DM in a subset of patients suggests a distinct phenotype with potentially greater risk of progressive liver disease, which may warrant more aggressive

surveillance and targeted interventions. These observations fit with broader evidence that obesity-related dysbiosis, altered short-chain fatty acid (SCFA) profiles, and bile acid signaling contribute both to MAFLD and to systemic insulin resistance (Łysynkiewicz et al., 2026).

4.3. Medications, especially GLP-1 and GLP-1/GIP receptor agonists

Modern pharmacotherapy for T2DM includes several drug classes that affect gastrointestinal motility, luminal pH, and microbial ecology, making medication exposure a plausible risk factor for SIBO. Among these, GLP-1 receptor agonists and dual GLP-1/GIP receptor agonists are of particular interest because of their well-known effects on slowing gastric emptying and modifying small-bowel transit.

A large retrospective multicenter cohort study using the TriNetX global database evaluated incident SIBO diagnoses in adults with T2DM initiated on GLP-1 or GLP-1/GIP receptor agonists compared with those started on other second-line antihyperglycemic agents (Sun et al., 2025). Over short-term follow-up, the incidence of clinically coded SIBO was approximately doubled in the GLP-1/GLP-1+GIP group relative to comparators (0.177 vs. 0.083 per 1,000 patient-years), corresponding to a hazard ratio of 2.14. The association attenuated over longer follow-up, and absolute event rates remained low, but these findings nonetheless suggest that GLP-1-mediated motility changes may increase SIBO risk in susceptible individuals.

SGLT2 inhibitors, now widely prescribed in T2DM for cardiorenal protection, have not been systematically investigated in relation to SIBO risk; their induction of glycosuria and potential osmotic effects on intestinal fluid and microbiota composition represent an underexplored variable that prospective studies should address (Barlow & Mathur, 2022; Gozhenko et al., 2026).

Other commonly used medications may also contribute. Proton-pump inhibitors reduce gastric acid secretion and can promote bacterial colonization of the upper gastrointestinal tract; opioids impair motility; and metformin has complex effects on the gut microbiota and bile-acid metabolism. However, few studies have systematically examined their independent associations with SIBO in T2DM, and available analyses are often confounded by indication and disease severity (Barlow & Mathur, 2022; Bielka et al., 2022; Młynarska et al., 2024). For instance, patients with more severe neuropathy or MAFLD may be more likely to receive certain drugs while simultaneously being more prone to SIBO, making causal inference difficult.

Overall, current evidence indicates that medication profiles, particularly use of GLP-1/GLP-1+GIP receptor agonists and possibly acid-suppressive or opioid therapy, should be considered when evaluating SIBO risk in T2DM. At the same time, the substantial cardiometabolic benefits of these agents mean that concerns about SIBO must be weighed against their proven efficacy,

and further prospective studies are needed to define which patients, if any, require targeted screening or prophylactic strategies.

4.3.1. Metformin

Metformin, the first-line pharmacotherapy for T2DM, is increasingly recognized as a gut microbiome modulator beyond its classical hepatic mechanism. A randomized, double-blind trial (Wu et al., 2017), demonstrated that metformin significantly reshaped the gut microbiota of treatment-naive patients with T2DM compared with placebo, notably enriching short-chain fatty acid (SCFA)-producing bacteria and improving glycemic control. Fecal transplants from metformin-treated donors to germ-free mice partially transferred the hypoglycemic effect, implying a causal role of the microbiome in the drug's action. A landmark metagenomic study (MetaHIT consortium et al., 2015), analyzing 784 gut metagenomes, revealed that many previously described "type 2 diabetes microbiome signatures" were, in fact, attributable to metformin exposure rather than the disease itself. Metformin treatment was associated with enrichment of Escherichia spp. and Akkermansia muciniphila, alongside depletion of butyrate producers. These metformin-driven microbiome alterations are clinically relevant in the context of SIBO. SIBO prevalence in T2DM reaches approximately 25–30%, driven by autonomic neuropathy and impaired gut motility (Pavlo Petakh et al., 2023). The gastrointestinal side effects of metformin (bloating, flatulence, and diarrhea) overlap substantially with SIBO symptomatology, complicating differential diagnosis (Wu et al., 2017). Metformin-associated dysbiosis (E. coli enrichment, altered bile acid metabolism, and increased intestinal permeability) may further modulate SIBO risk and clinical presentation, although a direct causal link requires prospective validation.

4.4. Clinical consequences and the role of treatment

4.4.1. Gastrointestinal symptom burden and overlapping conditions

Clinically, SIBO in T2DM most commonly manifests through non-specific gastrointestinal symptoms, including bloating, postprandial fullness, abdominal pain or discomfort, excessive flatulence, and chronic or alternating diarrhea. These symptoms frequently overlap with other established complications of diabetes, such as diabetic gastroparesis, autonomic enteropathy, or concurrent upper gastrointestinal diseases, making it difficult to distinguish SIBO from the broader spectrum of "diabetic enteropathy" based on clinical presentation alone. Studies in T2DM populations confirm that patients with confirmed SIBO experience a significantly higher burden of upper gastrointestinal symptoms. For instance, in a cohort of patients with T2DM and chronic active gastritis, the presence of SIBO was strongly associated with bloating, nausea, and belching. In contrast, concurrent Helicobacter pylori infection was more closely correlated

with epigastric pain. Interestingly, this study also noted that patients with diabetes and active gastritis reported classical pain less frequently than controls without diabetes despite similar histological inflammation - a finding consistent with altered visceral pain perception due to autonomic neuropathy (Feng & Li, 2022; Radionova et al., 2020). In clinical practice, this implies that the absence of classical abdominal pain does not exclude significant gastrointestinal pathology, and symptoms such as bloating, early satiety, or unexplained diarrhea in a patient with T2DM should prompt consideration of SIBO.

4.4.2. Metabolic complications, MAFLD, and quality of life

The clinical consequences of SIBO in T2DM extend beyond the gastrointestinal tract, significantly impacting metabolic health. In patients presenting with both T2DM and MAFLD, the presence of SIBO is associated with elevated liver enzymes, more advanced non-invasive markers of hepatic steatosis, and a highly adverse inflammatory profile, including higher levels of interleukin-6, leptin, and greater insulin resistance (Cherniavskyi & Didyk, 2024). These clinical findings extend the gut–liver axis framework outlined in Sections 3.6.2 and 4.2.3, providing direct patient-level evidence that the endotoxemia pathway operates in patients with concurrent T2DM and MAFLD. Furthermore, SIBO is linked to poorer overall glycemic control and diminished beta-cell function. Cross-sectional analyses have demonstrated that patients with T2DM and SIBO exhibit higher HbA1c levels, impaired insulin responses during oral glucose tolerance testing, and reduced indices of insulin secretion, independent of body mass index and diabetes duration (Yan et al., 2020). Because SIBO generates a state of chronic systemic inflammation and disrupts incretin and bile acid signaling, it may actively contribute to the progressive metabolic deterioration seen in advanced T2DM (Chong et al., 2025; Młynarska et al., 2024; Wicha et al., 2025).

Unsurprisingly, the combination of chronic gastrointestinal distress and worsened metabolic health severely impacts quality of life. Research in general populations and in irritable bowel syndrome (IBS) has shown that chronic bloating, dietary restrictions, and the unpredictable nature of bowel habits associated with SIBO impair social and occupational functioning (Liébana-Castillo et al., 2025). While specific quality-of-life data for the T2DM–SIBO population are limited, it is highly probable that the superimposition of SIBO onto the existing daily burden of diabetes management further diminishes patient well-being and complicates self-care (Martyniak et al., 2025).

4.5. Evidence on SIBO eradication in T2DM

Taken together, the pathophysiological mechanisms described above provide a coherent, if partially speculative, framework for understanding the bidirectional relationship between

T2DM and SIBO. It must be emphasized, however, that most of these links are supported by association data and mechanistic inference rather than by interventional studies demonstrating that SIBO eradication improves glycemic control, beta-cell function, or intestinal permeability in humans with T2DM. This is consistent with the broader critique advanced by Kashyap et al. (2024), who argued that causal relationships between small intestinal dysbiosis and systemic metabolic disorders remain unproven and that current diagnostic tools are insufficient to test these relationships rigorously (Kashyap et al., 2024). Data regarding the clinical and metabolic effects of treating SIBO specifically in patients with T2DM are surprisingly sparse. In the general and IBS populations, meta-analyses demonstrate that non-absorbable antibiotics, particularly rifaximin, are effective in eradicating SIBO and ameliorating symptoms, although long-term recurrence rates are high (Gatta & Scarpignato, 2017; Rao & Bhagatwala, 2019; Takakura et al., 2024), and the overall quality of evidence remains moderate. In the specific context of T2DM, only a few small-scale studies exist. Studies evaluating patients with T2DM and chronic gastroduodenal disorders and H. pylori co-infection found that various H. pylori eradication regimens also successfully reduced the prevalence of SIBO, with the greatest reduction seen in regimens incorporating bismuth and probiotics. This eradication correlated with an improvement in dyspeptic symptoms and a partial normalization of breath test results (Martyniak et al., 2025).

Targeted microbiome interventions also show theoretical promise. A small randomized trial investigating the supplementation of microencapsulated butyrate in patients with T2DM and gastrointestinal symptoms reported a significant decrease in SIBO frequency, alleviation of intestinal symptoms, and slight but statistically significant improvements in BMI and HbA1c compared with placebo (Martyniak et al., 2025; Wei et al., 2022).

Overall, however, there is a critical lack of robust, well-powered randomized controlled trials assessing whether the targeted eradication of SIBO in T2DM yields sustained improvements in hard metabolic endpoints, such as long-term HbA1c reduction, halted MAFLD progression, or improved beta-cell function (Sadagopan et al., 2023; Tarigan et al., 2021; Yan et al., 2020). Available studies are limited by small sample sizes, brief follow-up periods, and confounding co-interventions (e.g., simultaneous H. pylori treatment), precluding definitive causal conclusions.

4.6. Implications for clinical practice

Given the current state of evidence, SIBO in T2DM should be viewed as a common but complex manifestation of diabetic enteropathy, rather than a condition warranting universal population screening. In clinical practice, diagnostic evaluation for SIBO should be considered selectively

in patients with T2DM who present with any of the following (Rana et al., 2011; Rao & Bhagatwala, 2019):

- Chronic, unexplained bloating, excessive flatulence, persistent diarrhea, or unintended weight loss.
- Established cardiovascular autonomic neuropathy, severe gastroparesis, or a history of altered gastrointestinal anatomy (e.g., bariatric surgery).
- MAFLD that progresses aggressively despite optimal standard-of-care management.
- Unexplained, brittle glycemic control despite good adherence to therapy.

Hydrogen or hydrogen-methane breath tests remain the most practical diagnostic tools, but clinicians must be aware of their inherent limitations (Table 2). These tests possess only moderate sensitivity and specificity, and their accuracy is highly dependent on the chosen substrate, sampling intervals, and cut-off values (Martyniak et al., 2025). Notably, the prolonged orocecal transit time commonly seen in patients with diabetes can result in delayed hydrogen peaks, leading to misinterpreted or false-negative results. The gold standard (jejunal aspirate culture) remains invasive and is generally reserved for severe, refractory cases or clinical trials.

Current clinical guidelines from major gastroenterological societies strongly caution against indiscriminate testing. The American College of Gastroenterology (ACG) and recent position papers from the Brazilian Federation of Gastroenterology (FBG) and Spanish societies (ASENEM-SEPD) recommend breath testing for SIBO only in symptomatic patients, specifically those with unexplained chronic diarrhea, flatulence, or bloating, and explicitly advise against testing asymptomatic individuals (Gatta & Scarpignato, 2017; Liébana-Castillo et al., 2025; Pimentel et al., 2020; Silva et al., 2025). These consensus documents also highlight the moderate diagnostic accuracy of breath tests and warn against the overprescription of antibiotics based on borderline results or functional symptoms alone. The recommendations are further supported by the ESNM/ANMS 2024 clinical practice update (Kashyap et al., 2024), which, as noted in the pathophysiological framework above, explicitly cautioned against the use of breath tests in non-structural gastrointestinal conditions and against antibiotic prescribing based on borderline or unvalidated results. Importantly, the same document recognized that SIBO retains clinical validity in patients with predisposing structural or autonomic conditions, precisely the phenotype most relevant to T2DM with established neuropathy, thereby supporting a selective rather than universal approach to diagnostic evaluation in this population. While Tarigan et al. (2021) suggested that breath testing may be warranted in patients with

T2DM and disease duration exceeding five years, this recommendation was based on a small number of predominantly cross-sectional studies with extreme heterogeneity (I^2 = 97%) and was not endorsed by major gastroenterological guidelines (Tarigan et al., 2021). On balance, routine population-level screening for SIBO in T2DM cannot yet be justified; however, targeted testing appears reasonable in patients presenting with unexplained deterioration of glycemic control, refractory gastrointestinal symptoms, suspected autonomic enteropathy, or established MAFLD. If SIBO is highly suspected clinically and anatomical causes (e.g., strictures) are ruled out, a short course of a non-absorbable antibiotic such as rifaximin is a reasonable symptomatic intervention (Gatta & Scarpignato, 2017; Liébana-Castillo et al., 2025; Pimentel et al., 2020). However, pharmacological eradication must be paired with the management of underlying risk factors (such as optimizing glycemic control, managing dysmotility, and rationalizing the use of proton-pump inhibitors or opioids) to mitigate the high risk of recurrence. Future management paradigms will require high-quality trials to determine whether SIBO eradication can move beyond symptom control to become a disease-modifying intervention in T2DM.

4.7. Research gaps

Several important gaps limit current understanding. First, there is a lack of large, population-based epidemiological studies using standardized diagnostic protocols to quantify SIBO prevalence in unselected T2DM cohorts. Second, breath-test methodology is not tailored to populations with diabetes, despite known differences in transit time and motility, leading to uncertainty about optimal substrates, sampling intervals, and diagnostic thresholds. Third, little is known about the natural history of SIBO in T2DM or about the long-term metabolic effects of recurrent or chronic SIBO. Randomized controlled trials are also lacking. Studies testing whether treatment of SIBO (using non-absorbable antibiotics, probiotics, dietary interventions, or prokinetic agents) can improve glycemic control, reduce MAFLD progression, or ameliorate gastrointestinal symptoms in T2DM would be highly informative. Finally, mechanistic work integrating small-bowel microbiome sequencing, metabolomics, host genetics, and detailed phenotyping of neuropathy, MAFLD, and medication exposure is needed to disentangle causal pathways. Future research in this field should prioritize prospective interventional design, preferably randomized controlled trials, that use validated, T2DM-specific diagnostic protocols and pre-specified metabolic outcomes to determine whether correction of intestinal dysbiosis translates into clinically meaningful benefit in this population.

4.8. Limitations

Several limitations of this narrative review should be acknowledged. First, the literature search, although comprehensive, was selective by design and did not follow a formal systematic

protocol; consequently, the possibility of overlooking relevant studies cannot be excluded. Second, no formal risk-of-bias assessment of included primary studies was performed, and the overall quality of the primary evidence base is variable, with most studies being small, cross-sectional, and conducted in tertiary referral settings. Third, the considerable methodological heterogeneity in SIBO diagnosis across studies (including differences in breath-test substrates, sampling intervals, and positivity thresholds) limits the comparability of prevalence estimates and the strength of derived conclusions (Table 1). Fourth, the predominance of studies from Eastern European and East Asian centers may limit generalizability to other populations with different dietary patterns and healthcare contexts. Fifth, as a narrative review, the synthesis reflects the authors' interpretive judgment, and the conclusions should be read in this light.

5. Conclusions

Current evidence indicates that small intestinal bacterial overgrowth is common in individuals with type 2 diabetes mellitus, with prevalence estimates in observational and meta-analytic studies of approximately one quarter when actively investigated. Elevated risk appears to be driven by a combination of autonomic neuropathy-related dysmotility, broader gut microbial dysbiosis, increased intestinal permeability, MAFLD, and the use of medications that modulate gastrointestinal motility and the luminal environment.

SIBO in T2DM has been associated with worse glycemic control, impaired beta-cell function, and more advanced liver disease, suggesting that it may contribute to the burden of diabetic complications, although available data are predominantly cross-sectional and do not prove causality.

At present, evidence is insufficient to justify universal screening for SIBO in all patients with T2DM; however, clinicians should consider it in those with prominent gastrointestinal symptoms, autonomic neuropathy, MAFLD, or unexplained metabolic deterioration.

The distinction between hydrogen-predominant SIBO and intestinal methanogen overgrowth (IMO) is clinically important in T2DM, given the frequency of constipation-predominant diabetic enteropathy and the differing therapeutic strategies required. In particular, the eradication of IMO typically requires the addition of neomycin or metronidazole to rifaximin for methane suppression, although the efficacy of this approach specifically in T2DM remains to be confirmed in prospective trials.

Future research priorities include population-based prevalence studies with standardized diagnostic criteria, trials assessing whether SIBO eradication improves metabolic and hepatic outcomes, and integrative mechanistic studies exploring the small-bowel microbiome–diabetes

axis. Clarifying these issues will help determine the role of SIBO as a potential therapeutic target in type 2 diabetes mellitus.

Disclosure

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The authors used Claude Sonnet 4.6 AI model by Anthropic for the purpose of language editing, grammar checking, text formatting and basic data analysis. AI did not contribute to the conception of the study. All intellectual content, including the critical appraisal of evidence and final conclusions, was determined exclusively by the authors. Human oversight was maintained throughout the entire preparation of this manuscript.

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