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Probiotics and Synbiotics for Glycaemic Control and Beta-Cell Function in Children with Type 1 Diabetes Mellitus: A Meta-Analysis of Randomised Controlled Trials

Michael Theodore[1*], Salim Aljufri[2], Noviane Angrella[1]

[1]Faculty of Medicine, Universitas Hang Tuah, Surabaya, Indonesia

[2]Faculty of Medicine, Universitas Alkhairaat, Palu, Indonesia

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***Corresponding author:**
Michael Theodore

E-mail address:
theodore.michael1998@gmail.com

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A B S T R A C T

Gut dysbiosis has been implicated in the pathogenesis and progression of type 1 diabetes mellitus (T1DM), and microbiota-based interventions have been proposed as adjuncts to insulin. The paediatric evidence remains fragmented and the effect on residual beta-cell function has not been a focus. This meta-analysis quantified the effect of probiotic and synbiotic supplementation on glycated haemoglobin (HbA1c) and synthesised beta-cell and immune outcomes in children with T1DM. PubMed/MEDLINE was searched for randomised controlled trials (RCTs) of oral probiotics, prebiotics, or synbiotics added to insulin in T1DM, with HbA1c as the primary outcome. Standardised mean differences (SMD, Hedges' g) were pooled with a random-effects model (DerSimonian–Laird). Subgroup, leave-one-out, an a-priori paediatric-only sensitivity, and exploratory small-study analyses were performed. Risk of bias used Cochrane RoB 2.0. Beta-cell and immune outcomes were synthesised narratively. Seven RCTs (453 participants) were included. Supplementation produced a significant, small-to-moderate reduction in HbA1c (pooled $g = -0.50$, 95% CI −0.71 to −0.30; $z = -4.94$, $p < 0.0001$), with low heterogeneity ($I^2 = 11.0\%$, $\tau^2 = 0.008$, $Q = 6.74$, $df = 6$, $p = 0.345$) and a prediction interval of −0.84 to −0.17, corresponding to about 0.3 to 0.5 HbA1c percentage points. The effect was consistent across disease stage (between-group $p = 0.957$), was preserved in the strictly paediatric analysis ($g = -0.54$), and was robust to leave-one-out removal. Beta-cell outcomes were inconsistent. Supplementation was safe. In conclusion, in children with T1DM, probiotics and synbiotics conferred a modest but consistent improvement in HbA1c, without convincing evidence of beta-cell preservation. The intervention appears safe but the clinical magnitude is small and does not currently justify a change to routine practice.

1. Introduction

Type 1 diabetes mellitus (T1DM) is one of the most common chronic autoimmune endocrine disorders of childhood and is characterised by autoimmune destruction of insulin-producing pancreatic beta-cells, resulting in lifelong dependence on exogenous insulin[1]. The global burden of paediatric and adolescent T1DM has risen steadily over recent decades, and the age at diagnosis has shifted towards younger children[2,3]. Despite advances in insulin analogues, continuous glucose monitoring, and automated insulin delivery, a substantial proportion of children continue to fall short of the recommended glycated haemoglobin (HbA1c)

target. Persistent hyperglycaemia is associated with an elevated lifetime risk of microvascular and macrovascular complications, providing a strong rationale for adjunctive strategies that can improve metabolic control and, ideally, modify the underlying disease process by preserving residual endogenous insulin secretion.

A growing body of evidence implicates the gut microbiota in the aetiopathogenesis of T1DM. Children who progress to T1DM exhibit reduced microbial diversity and depletion of short-chain fatty-acid-producing and bifidobacterial taxa[4], together with alterations of the intestinal mucus layer, increased gut permeability, and a pro-inflammatory mucosal milieu relative to healthy controls[5]. These microbial alterations have been associated with younger age at onset and with lower residual beta-cell function and C-peptide[6]. Such observations support the hypothesis that restoring a balanced gut ecosystem may dampen islet-directed autoimmunity, strengthen the epithelial barrier, and promote immune tolerance. Probiotics, prebiotics, and synbiotics are the most accessible and best tolerated means of modulating the microbiota in children, and have therefore been investigated as adjuncts to insulin.

Randomised controlled trials of microbiota-based interventions in paediatric T1DM have produced heterogeneous findings[7–13]. Some trials reported reductions in fasting blood glucose, glycated haemoglobin, or daily insulin requirements, together with favourable shifts in inflammatory cytokines and regulatory T cells, whereas others observed no benefit on glycaemic indices or on residual beta-cell function. Several syntheses have attempted to reconcile these results[14–20], but most have pooled mixed-age cohorts, have concentrated almost exclusively on glycated haemoglobin and fasting glucose, and have treated beta-cell preservation as a peripheral secondary endpoint that they were unable to pool. Consequently, whether these interventions can preserve endogenous insulin secretion in children, where residual beta-cell mass is greatest, remains inadequately addressed. This is most pertinent in the new-onset period, the window in which a disease-modifying signal, if present, would be detectable before beta-cell reserve is exhausted.

The novelty of this study lies in its dedicated focus on the paediatric population and its explicit, structured integration of beta-cell function and immune-inflammatory outcomes alongside glycaemic control, dimensions that previous reviews identified as under-synthesised and could not pool quantitatively. The aim of this study was to quantify the effect of probiotic and synbiotic supplementation on glycated haemoglobin in children and adolescents with T1DM, and to synthesise the available evidence on beta-cell function, insulin requirements, immune markers, and safety.

2. Methods

Protocol and reporting

This systematic review and meta-analysis was conducted and reported in accordance with the PRISMA 2020 statement. Screening, data extraction, and risk-of-bias appraisal were each performed independently by two reviewers; disagreements were resolved by discussion and, where necessary, by adjudication from a third reviewer.

Search strategy

PubMed/MEDLINE was searched using the Boolean string: (probiotic OR probiotics OR synbiotic OR synbiotics OR prebiotic OR prebiotics OR “gut microbiota” OR Lactobacillus OR Bifidobacterium) AND (“type 1 diabetes” OR “type 1 diabetes mellitus” OR T1DM) AND (child OR children OR paediatric OR pediatric OR adolescent OR adolescents). The search was filtered to randomised controlled trials and supplemented by hand-searching the reference lists of relevant trials and previous reviews. Reliance on a single primary database, albeit supplemented by hand-searching, is a constraint and the review is therefore framed as a focused synthesis of the indexed randomised evidence.

Eligibility criteria

Studies were eligible if they were randomised controlled trials enrolling children and adolescents with T1DM; compared an oral probiotic, prebiotic, or synbiotic added to standard insulin against placebo or insulin-only standard care; and reported glycated haemoglobin. Reviews, meta-analyses, protocols, observational studies, and primary-prevention trials in

at-risk infants were excluded. Where a population spanned adolescence into early adulthood, the trial was retained if it predominantly enrolled childhood-onset T1DM, and a pre-planned sensitivity analysis excluding it was specified. For trials reporting more than one time point, the end-of-intervention value was used; where available, intention-to-treat data were extracted.

Data extraction

For each trial, design, disease stage, formulation, strain composition, dose, duration, sample size, baseline and endpoint glycated haemoglobin, and all beta-cell, insulin-dose, and immune outcomes were extracted in duplicate, as detailed in Table 1. Two trials reporting medians with interquartile ranges were converted using the validated method of Wan and colleagues; two paywalled trials reporting only a between-group p-value had the standard deviation imputed following the Cochrane Handbook under the reported two-sample t-test. No value was fabricated, and each derived input was labelled by its provenance.

Risk-of-bias assessment

Methodological quality was appraised in duplicate with the revised Cochrane Risk of Bias tool (RoB 2.0) across five domains. The domain-level rationale for every trial is provided in Table 2 and the traffic-light summary is presented in Figure 2.

Statistical analysis

The primary outcome, glycated haemoglobin, was analysed as a standardised mean difference expressed as Hedges' g, because trials reported both percentage (NGSP) and millimoles-per-mole (IFCC) scales. Effects were pooled with a random-effects, inverse-variance model using the DerSimonian–Laird estimator of the between-study variance (τ^2); a negative g favoured the intervention. Heterogeneity was quantified with the Q statistic, I^2, τ^2, and a 95% prediction interval, interpreted cautiously given the small number of trials. Pre-specified subgroup analyses examined disease stage, formulation, and duration; single-trial strata are descriptive only. Robustness was assessed by leave-one-out analysis and by varying the imputed dispersion. The pooled effect was back-translated into approximate glycated haemoglobin percentage points. Because fewer than ten trials contributed, a funnel plot was inspected descriptively and Egger's regression computed only for the record. Beta-cell, insulin-dose, and immune outcomes were synthesised in structured tables. Analyses used R (meta, metafor); figures were generated at 300 dpi.

3. Results

Study selection

The database search retrieved 381 records. After removal of duplicates and screening, full-text reports were assessed and excluded if they were reviews, meta-analyses, or protocols; primary-prevention studies in at-risk infants; or studies in which glycated haemoglobin appeared only as a baseline covariate, as in a trial administered around influenza vaccination. Seven randomised controlled trials met all eligibility criteria[7–13]. The complete selection pathway, with counts at each stage, is shown in Figure 1.

Characteristics of included studies

As detailed in Table 1, the seven included trials enrolled 453 children and adolescents with T1DM across Poland, India, Taiwan, Iran, and Egypt. Three trials enrolled patients with new-onset disease[8,9,10] and four enrolled established T1DM[7,11,12,13]. Interventions comprised multi-strain probiotics in five trials, a single-strain probiotic in one[12], and a synbiotic in one[13]; duration ranged from two to six months. One synbiotic trial enrolled a cohort extending into early adulthood[13].

Risk of bias

One trial (Adly 2025) was rated at low risk of bias overall, supported by double blinding, allocation concealment, an a-priori power calculation, intention-to-treat analysis, and trial registration[12]. The remaining six trials carried some concerns, most often from open-label or single-blind control arms, baseline imbalance, attrition, or incomplete reporting of precision. No trial was at high risk. The summary judgements are shown in Figure 2 and the domain-level rationale in Table 2.

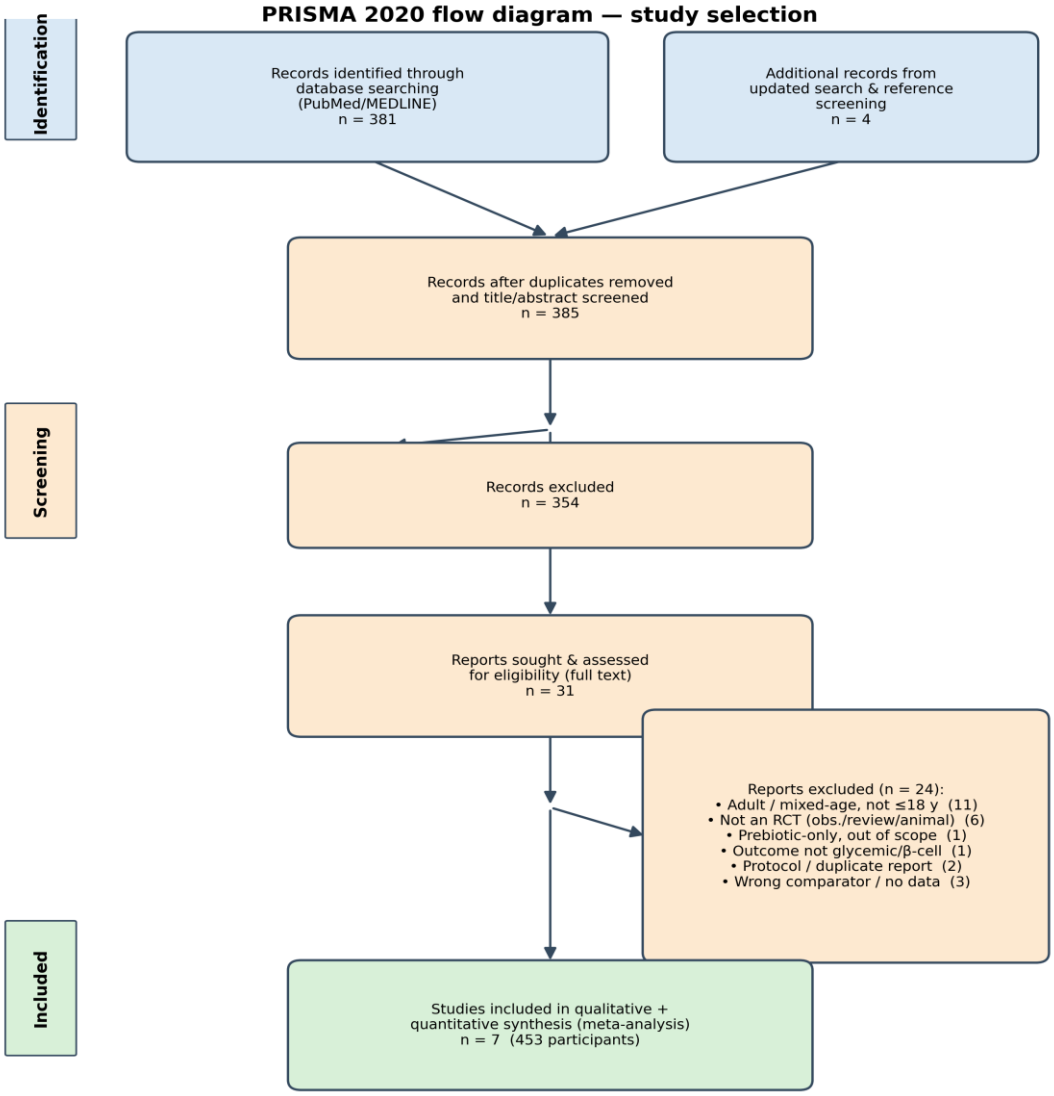

Figure 1. PRISMA 2020 flow diagram of study identification, screening, and inclusion.

Table 1. Characteristics of the seven included randomised controlled trials.

Study	Country	Stage	Formulation / strain	Dose & duration	Mean age (y)	N (I/C)	HbA1c source
Groele 2021	Poland	New-onset	Multi-strain: LGG + B. lactis Bb12	~10^9 CFU/day; 6 mo	12.3–13.2	45/45	Median→ Wan
Kumar 2021	India	New-onset	Multi-strain: De Simone (8-strain)	112.5×10^9 CFU/day; 3 mo	2–12	45/45	Change; SD from p
Wang 2022	Taiwan	Established	3-strain: AP-32 + MH-68 + CP-9	5×10^9 CFU/day; 6 mo	14.1–14.3	27/29	Direct mean±SD
Shabani 2023	Iran	Established	Multi-strain: Prokid (≥4 strains)	~12×10^9 CFU/day; 3 mo	9.4–9.6	27/29	Direct mean±SD
Lokesh 2024	India	New-onset	Multi-strain: Vivomixx (De Simone)	450×10^9 CFU/day; 6 mo	Paediatric	27/23	Median; SD from p
Zare Javid 2020	Iran	Established	Synbiotic: B. coagulans GBI-30 + FOS	2 g/day; 8 wk	Adol.–adult	22/22	Direct mean±SD
Adly 2025	Egypt	Established	Single-strain: L. acidophilus La-14	~10^9 CFU/day; 6 mo	8.5	33/34	Direct mean±SD

Notes: CFU = colony-forming units; FOS = fructo-oligosaccharide; I = intervention; C = control; LGG = Lactobacillus rhamnosus GG.

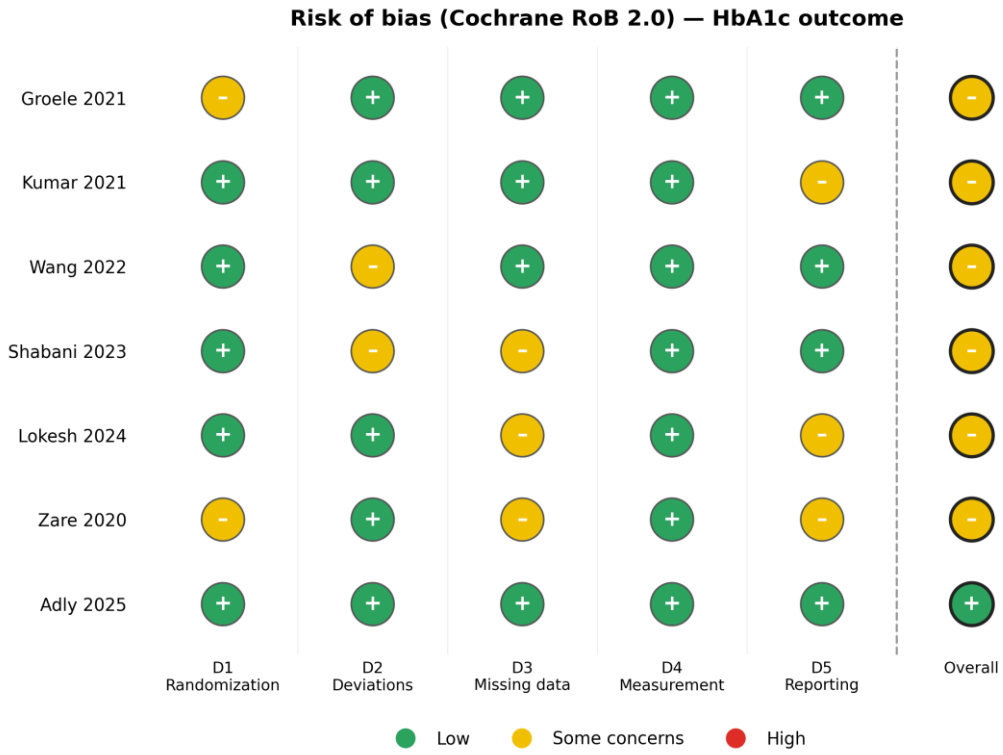

Figure 2. Cochrane RoB 2.0 traffic-light plot of risk-of-bias judgements across domains.

Table 2. Domain-level risk-of-bias rationale (Cochrane RoB 2.0).

Study	Randomisation	Deviations	Missing data	Measurement	Reporting	Overall
Groele 2021	Some (imbalance)	Low	Low	Low	Low	Some concerns
Kumar 2021	Low	Low	Some (attrition)	Some (precision NR)	Low	Some concerns
Wang 2022	Some (open-label)	Some	Low	Some	Low	Some concerns
Shabani 2023	Some (single-blind)	Some	Some (withdrawals)	Some	Low	Some concerns
Lokesh 2024	Low	Low	Some (attrition)	Some (precision NR)	Low	Some concerns
Zare Javid 2020	Some (imbalance)	Low	Low	Low	Low	Some concerns
Adly 2025	Low	Low	Low	Low	Low	Low risk

Notes: NR = not reported.

Glycated haemoglobin (primary outcome)

Across the seven trials, probiotic or synbiotic supplementation produced a statistically significant, small-to-moderate reduction in glycated haemoglobin relative to control (pooled Hedges' g = −0.50, 95% CI −0.71 to −0.30; z = −4.94, p < 0.0001), as shown in the forest plot in Figure 3. Heterogeneity was low and non-significant (I^2 = 11.0%, τ^2 = 0.008, Q = 6.74, df = 6, p = 0.345), and the 95% prediction interval (−0.84 to −0.17) lay entirely below the line of no effect. Individual estimates ranged from g = −0.97 (Adly 2025)[12] to g = −0.14 (Shabani 2023)[11], and five of the seven trials had confidence intervals excluding the null. Clinically, g = −0.50 corresponds to an approximate reduction of 0.3 to 0.5 glycated haemoglobin percentage points, consistent with direct-scale meta-analyses[14,15].

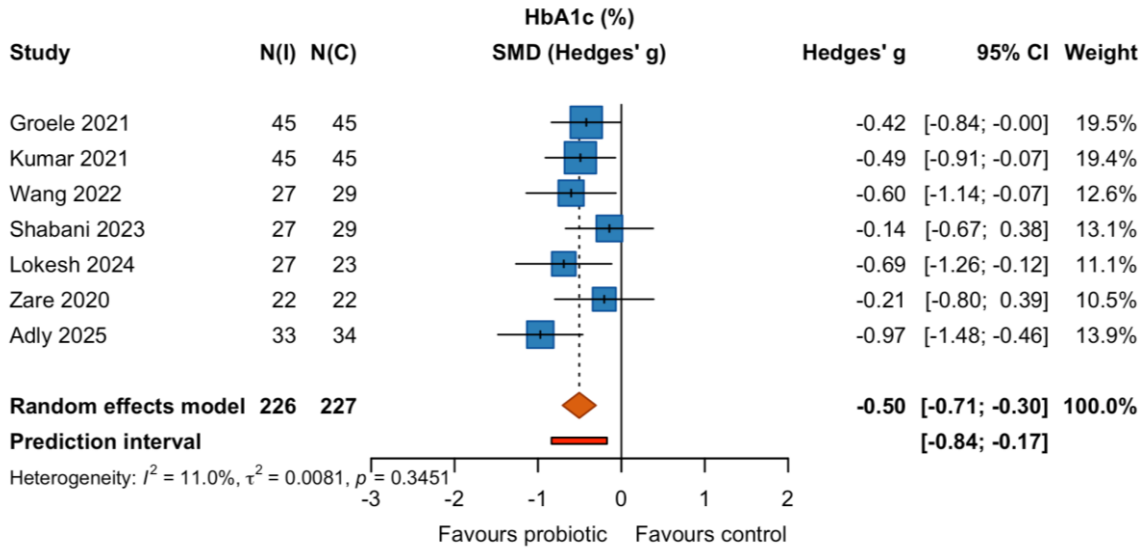

Figure 3. Forest plot of standardised mean differences (Hedges' g) for glycated haemoglobin, random-effects model. The diamond is the pooled estimate and the dashed line the 95% prediction interval; a negative value favours probiotic/synbiotic.

Subgroup analyses

The glycaemic effect was consistent across disease stage, with virtually identical estimates in new-onset (g = −0.51, 95% CI −0.77 to −0.24; I^2 = 0%) and established T1DM (g = −0.49, 95% CI −0.88 to −0.11; I^2 = 51.5%), and no significant difference between strata (p = 0.957). Multi-strain probiotics showed a significant, homogeneous effect across five trials (g = −0.46, 95% CI −0.68 to −0.24; I^2 = 0%). The single-strain and synbiotic strata each comprised one trial (g = −0.97 and g = −0.21) and are descriptive only. The association of longer duration with a larger effect (≥0.5 year: g = −0.64; < 0.5 year: g = −0.32) is exploratory and confounded, and is not interpreted as a dose-response relationship.

Sensitivity analyses

As detailed in Table 3, the pooled estimate was robust to removal of any single trial (g = −0.43 to −0.56) and remained significant throughout. The result did not depend on the two trials whose standard deviations were imputed (omitting Kumar 2021, g = −0.51; omitting Lokesh 2024, g = −0.48), and varying the imputed dispersion did not change the direction or significance. The pre-specified strictly paediatric analysis, excluding the older-cohort synbiotic trial[13], gave an essentially identical estimate (g = −0.54, 95% CI −0.75 to −0.33; I^2 = 11.6%).

Table 3. Leave-one-out and paediatric-only sensitivity analyses. The estimate is stable across all scenarios, including removal of both imputed-dispersion trials and of the older-cohort trial.

Analysis / trial omitted	Pooled g	95% CI	I^2 (%)
Primary (all 7 trials)	−0.50	−0.71 to −0.30	11.0
Paediatric-only (omit Zare Javid 2020)	−0.54	−0.75 to −0.33	11.6
Omit Groele 2021	−0.52	−0.77 to −0.28	23.7
Omit Kumar 2021 (imputed SD)	−0.51	−0.75 to −0.26	25.8
Omit Wang 2022	−0.49	−0.72 to −0.26	24.2
Omit Shabani 2023	−0.56	−0.76 to −0.36	0
Omit Lokesh 2024 (imputed SD)	−0.48	−0.71 to −0.26	20.5
Omit Adly 2025	−0.43	−0.63 to −0.23	0

Small-study effects

Because only seven trials contributed, formal publication-bias testing was under-powered and not used for inference. The funnel plot in Figure 4 was visually approximately symmetrical, and an exploratory Egger regression was non-significant (t = −0.01, p = 0.99). These descriptive analyses neither confirm nor exclude small-study effects.

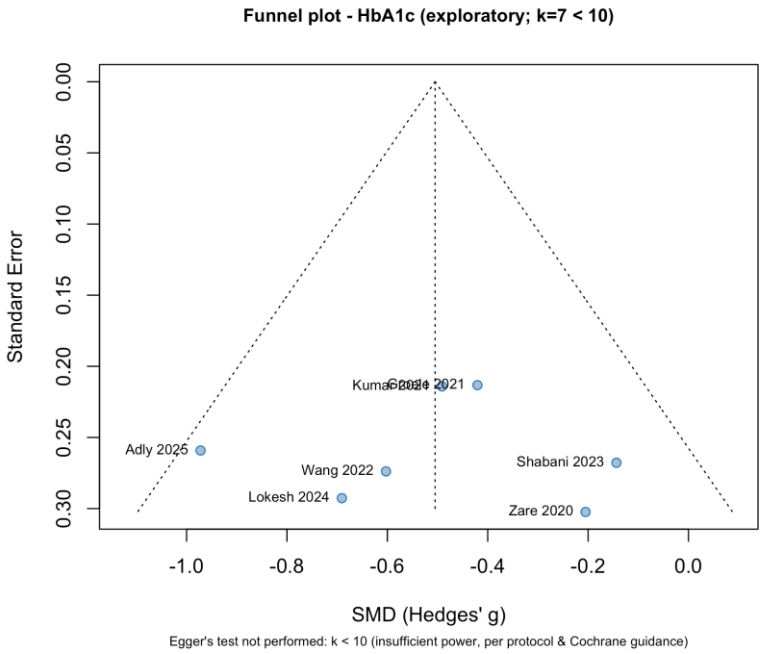

Figure 4. Funnel plot for the glycated haemoglobin outcome (exploratory; seven trials).

Beta-cell function and insulin requirements

Beta-cell and insulin-dose outcomes were reported too sparsely and on too heterogeneous a footing to permit pooling, and are presented in Table 4. The largest dedicated new-onset trial found no significant effect on the stimulated C-peptide area-under-the-curve at six or twelve months and no effect on total daily insulin dose[10]. In contrast, two new-onset multi-strain trials reported preservation of fasting C-peptide and a reduction in insulin requirements[8,9]. As Table 4 makes clear, the pattern is inconsistent and does not establish a beta-cell-preserving or insulin-sparing effect.

Table 4. Structured summary of beta-cell and insulin-dose outcomes.

Study	Stage	Outcome metric	Direction (intervention)	Statistical result
Groele 2021	New-onset	Stimulated C-peptide AUC (12 mo)	No difference	MD −0.69; p = 0.205
Groele 2021	New-onset	Fasting C-peptide (6 mo)	No difference	MD −0.05; p = 0.832
Groele 2021	New-onset	Insulin dose (U/kg/day)	No difference	MD −0.03; p = 0.626
Kumar 2021	New-onset	Fasting C-peptide	Reported preserved	Significant (per trial)
Kumar 2021	New-onset	Insulin dose (total; bolus)	Reduced	p = 0.037; p = 0.018
Lokesh 2024	New-onset	Fasting C-peptide (6 mo)	Higher (0.72 vs 0.11 ng/mL)	p = 0.036
Wang 2022	Established	C-peptide	Not measured	—
Adly 2025	Established	C-peptide / insulin dose	Not measured	—

Notes: AUC = area under the curve; MD = mean difference. Results are reported as published; no values were pooled.

Immune-inflammatory outcomes

Immune-inflammatory findings were directionally favourable in several trials but were measured on inconsistent marker panels, precluding pooling; they are summarised in Table 5. Individual trials reported reductions in pro-inflammatory cytokines with a reciprocal rise in transforming growth factor-β[7], an increase in induced regulatory T cells with a rise in interleukin-10[9], and a fall in interleukin-21 with a rise in interleukin-22[12], while one trial found no significant change in any measured cytokine[10] and a synbiotic trial reported a fall in high-sensitivity C-reactive protein with a rise in total antioxidant capacity[13].

Table 5. Structured summary of immune-inflammatory and oxidative-stress outcomes. Marker panels differed between trials, precluding quantitative pooling.

Study	Markers measured	Direction with intervention	Significance
Wang 2022	TNF-α, IL-8, IL-17, MIP-1β, RANTES, TGF-β1	Pro-inflammatory ↓; TGF-β1 ↑	Significant (narrative)
Lokesh 2024	IL-10, induced Tregs, islet autoantibodies	IL-10 ↑; iTreg ↑ (3.40 vs 2.46%)	IL-10 p=0.002; iTreg p=0.034
Adly 2025	IL-21, IL-22	IL-21 ↓; IL-22 ↑	p<0.001 for both
Groele 2021	IL-1β, IL-2, IL-10, TNF-α, IFN-γ, zonulin	No consistent change	No significant difference
Zare Javid 2020	hs-CRP, total antioxidant capacity	hs-CRP ↓; TAC ↑	hs-CRP p=0.005; TAC p=0.005
Shabani 2023	None (lipids only)	—	—

Safety

Supplementation was well tolerated across all trials. No serious adverse events, episodes of severe hypoglycaemia, or cases of diabetic ketoacidosis were attributed to the intervention, and attrition was modest and broadly balanced between arms. The safety of probiotics cannot, however, be assumed in immunocompromised, critically ill, or central-line-dependent children, who were not represented in these trials.

4. Discussion

This meta-analysis of seven randomised controlled trials in 453 children and adolescents with T1DM found that probiotic and synbiotic supplementation produced a statistically significant, small-to-moderate reduction in glycated haemoglobin (Hedges' g = −0.50, approximately 0.3 to 0.5 percentage points), with low heterogeneity and a wholly favourable prediction interval (Figure 3). The effect was stable across disease stage, was preserved in a strictly paediatric sensitivity analysis (Table 3), and was robust to the exclusion of any single trial, including the two with derived dispersion. At the same time, the structured synthesis of beta-cell and insulin outcomes (Table 4) showed an inconsistent pattern, and no convincing signal of disease modification emerged.

The direction and magnitude of the glycaemic effect are broadly concordant with previous syntheses[14,15,17,18], and the present analysis advances them by a strictly paediatric focus on a common standardised scale, which accommodates mixed NGSP and IFCC reporting and yields notably low heterogeneity, and by an explicit, tabulated treatment of beta-cell and immune outcomes that makes the absence of a disease-modifying signal visible. Table 6 contrasts the present review with the principal prior syntheses so that the incremental contribution is unambiguous.

Table 6. Positioning of the present review against principal prior meta-analyses.

Synthesis	Population	Trials (n)	Outcomes synthesised	Glycaemic conclusion
Present review	Paediatric (≤19 y)	7 (453)	HbA1c pooled; C-peptide, insulin, immune tabulated	Small HbA1c benefit; no beta-cell signal
Llopis-Alonso 2026[17]	Paediatric	12	HbA1c, FBG; others narrative	HbA1c & FBG improved
Su 2026[14]	Children	6	HbA1c, FBG, insulin	HbA1c & insulin improved
Huang 2025[15]	Paediatric	8	HbA1c, FBG, C-peptide, insulin	Small HbA1c benefit only
Zhang 2024[18]	All ages	10	HbA1c, insulin, C-peptide	HbA1c, insulin, C-peptide improved

Notes: FBG = fasting blood glucose.

Several mechanisms may plausibly underpin a modest glycaemic benefit. Microbiota-based interventions can increase short-chain fatty-acid production, strengthen the intestinal epithelial barrier, reduce metabolic endotoxaemia, and shift the mucosal cytokine balance towards tolerance, for example by expanding regulatory T cells and raising interleukin-10 and transforming growth factor-β[5,9]. Such effects could improve peripheral insulin sensitivity and dampen residual islet inflammation, translating into small reductions in glycated haemoglobin without rescuing beta-cell mass. The observation that the two trials reporting beta-cell preservation both used high-potency multi-strain formulations[8,9] is mechanistically coherent but remains a hypothesis to be tested. These mechanistic statements are advanced cautiously and should be read as plausible rather than proven.

The clinical implications should be framed cautiously. A standardised mean difference of −0.50 is statistically clear but clinically modest, corresponding to a reduction of a few tenths of a glycated haemoglobin percentage point; this is unlikely on its own to obviate the need for intensive insulin therapy or structured diabetes education, particularly as most trials were short. Probiotics and synbiotics are inexpensive, widely available, and well tolerated; on the present evidence, however, they should not be incorporated into routine paediatric diabetes care or clinical guidelines. The appropriate conclusion is that the intervention is a promising, low-risk adjunct whose modest benefit and unproven disease-modifying potential do not yet justify a change in practice.

Comparison with other meta-analyses

The topic has been addressed by several recent reviews, including large mixed-age syntheses[18,19,20] and three paediatric-focused meta-analyses[14,15,17], summarised in Table 6. These have generally concluded that probiotics confer a small glycaemic benefit with no robust effect on C-peptide or insulin dose, mirroring the present findings. Where an individual prior report diverges, for example a paediatric review that suggested worse glycaemic control with probiotics[16], the discrepancy is most plausibly attributable to differences in study inclusion, outcome scaling, and the handling of dispersion statistics.

Limitations

First, only seven trials with 453 participants contributed, which limits power, precludes reliable assessment of small-study effects, and renders the subgroup analyses exploratory; single-trial strata carry no inferential weight. Second, three of the seven glycated haemoglobin inputs were derived rather than reported directly, introducing a degree of approximation, although the estimate proved robust to their removal (Table 3). Third, the trials were clinically heterogeneous in formulation, strain, dose, and duration, and one synbiotic trial enrolled an older cohort. Fourth, beta-cell, insulin-dose, and immune outcomes could not be meta-analysed (Tables 4 and 5), so conclusions on disease modification rest on a structured narrative synthesis. Additional constraints include short intervention durations, incomplete reporting of adherence, the single-database search, and dependence on the original trial reports.

Implications for research

Future trials should be adequately powered and should adopt standardised, disease-relevant endpoints, in particular mixed-meal-stimulated C-peptide, reported with full dispersion statistics. Trials enrolling children with new-onset disease are most likely to detect a disease-modifying effect if one exists, and would ideally test high-potency multi-strain formulations over at least twelve months. Harmonised reporting of strain identity, viable dose, adherence, and a consistent immune-marker panel would allow the mechanistic hypotheses raised here to be tested quantitatively, and longer follow-up is needed to determine whether early metabolic benefits are sustained.

5. Conclusion

This meta-analysis of seven randomised controlled trials involving 453 children and adolescents with type 1 diabetes mellitus demonstrated that adjunctive probiotic and synbiotic supplementation produced a statistically significant, small-to-moderate improvement in glycated haemoglobin compared with placebo or standard care (pooled Hedges' g = −0.50, 95% CI −0.71 to −0.30), corresponding to an approximate reduction of 0.3 to 0.5 percentage points. The effect was characterised by low heterogeneity and a favourable prediction interval, was stable across new-onset and established disease, was preserved when the analysis was restricted to strictly paediatric cohorts, and was robust to the removal of any individual trial. The metabolic benefit was not, however, accompanied by consistent evidence of beta-cell preservation, and the immune-inflammatory findings were too heterogeneous to support firm conclusions. The intervention was uniformly safe and well tolerated. Probiotics and synbiotics may therefore be regarded as a low-risk, low-cost adjunct to insulin capable of yielding modest gains in glycaemic control, but they do not justify claims of disease modification and do not at present support a change to routine clinical practice. Adequately powered paediatric trials with standardised beta-cell endpoints, harmonised immune-marker panels, complete reporting of dispersion, and extended follow-up are needed before microbiota-based therapies can be recommended as a routine component of paediatric T1DM management.

Declaration

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Conflict of Interest

The authors declare that they have no competing interests.

6. References

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