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Automated Insulin Delivery vs Sensor-Augmented Pump and MDI in Type 1 Diabetes: A Network Meta-analysis of HbA1c, Time-in-Range, and Hypoglycemia

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Abstract

Background

Automated insulin delivery (AID) systems promise superior glycaemic control in type 1 diabetes (T1D) versus sensor-augmented pumps (SAP) and multiple daily injections (MDI), but few trials directly compare all three. We conducted a network meta-analysis (NMA) of HbA1c, time-in-range (TIR 70–180 mg/dL), and hypoglycaemia.

Methods

Parallel or crossover randomized controlled trials in children, adolescents, or adults with T1D were eligible if they compared AID, SAP, or MDI for ≥8 weeks and reported HbA1c and/or CGM metrics. Outcomes were analysed as mean differences (MD) for HbA1c and %TIR, and risk/rate ratios for hypoglycaemia. A frequentist random-effects NMA (netmeta, R) estimated relative effects and P-scores; heterogeneity (τ^2/I^2), transitivity, and incoherence (design-by-treatment, node-splitting) were assessed. Prespecified sensitivity analyses excluded higher-risk studies, crossover designs, and mixed "standard care" comparators.

Results

Thirteen RCTs (N=1,743) met criteria. The network included AID–SAP (k=6), SAP–MDI (k=1; STAR-3), AID–MDI (k=1), and three AID–standard-care links handled in sensitivity analyses. Risk of bias was low-to-moderate with objective outcomes and minimal attrition. Versus SAP, AID reduced HbA1c by ~0.3–0.6 percentage points and increased TIR by ~6.7–16 percentage points (≈1.6–3.8 h/day). SAP lowered HbA1c by ~0.6% versus MDI. AID did not increase time-below-range or severe hypoglycaemia; events were rare in all arms. Findings were consistent across age groups and AID platforms, robust to all sensitivity analyses, and coherent across direct/indirect evidence. P-scores ranked treatments AID > SAP > MDI for HbA1c and TIR.

Conclusions

Across diverse populations, AID provides the greatest overall benefit—substantial TIR gains, modest HbA1c reductions beyond SAP, and no hypoglycaemia penalty—establishing a clear hierarchy (AID > SAP > MDI). Results support prioritizing AID where feasible and inform technology escalation pathways in contemporary T1D care.

Keywords : Type 1 diabetes; automated insulin delivery; HbA1c; time-in-range; hypoglycemia.

Introduction

Type 1 diabetes (T1D) demands meticulous, lifelong insulin replacement to prevent acute and chronic complications. Glycated hemoglobin (HbA1c) has long served as the principal marker of glycemic control, yet it incompletely reflects day-to-day variability, postprandial excursions, and hypoglycemia risk—limitations that have become more apparent with widespread continuous glucose monitoring (CGM) (Chiang et al., 2014). Contemporary guidance therefore recommends complementing HbA1c with CGM-derived metrics—especially time-in-range (TIR; 70–180 mg/dL) and time-below-range (TBR)—to capture both average control and glycemic stability (Yoo & Kim, 2020). Recent standards explicitly integrate TIR and TBR into therapeutic targets across age groups, underscoring their clinical relevance alongside HbA1c (Patel et al., 2023).

Insulin delivery options for T1D now span multiple daily injections (MDI), sensor-augmented pump (SAP) therapy, and automated insulin delivery (AID) systems (often termed hybrid closed loop) (Benhalima & Polsky, 2025). SAP integrates real-time CGM with continuous subcutaneous insulin infusion but relies on user-initiated adjustments; pivotal trials showed SAP lowers HbA1c versus MDI and increases the proportion of individuals achieving HbA1c targets, establishing SAP as an intermediate step between MDI and full or hybrid automation (Janez et al., 2021).

AID systems add algorithm-driven insulin modulation—automatically adjusting basal rates (and in some systems delivering automated correction boluses) based on CGM data—to reduce hyperglycemia while protecting against hypoglycemia (Phillip et al., 2023). Professional guidelines now recognize AID as a core diabetes-technology modality because of consistent improvements in TIR and reductions in hypoglycemia across diverse populations (Lundgrin et al., 2025).

Randomized controlled trials have demonstrated the clinical benefits of AID relative to non-automated care. In very young children, hybrid closed-loop use significantly increased TIR without increasing TBR, addressing a historically challenging age group for safe intensification. Similarly, among children aged 2 to <6 years, AID improved the percentage of time within target range over 13 weeks, highlighting pediatric applicability (Ware et al., 2024). Adult and adolescent trials with commercially available algorithms likewise show increased TIR and reduced hyperglycemia compared with standard therapy (Ware & Hovorka, 2022).

Despite these advances, several clinically important questions remain unresolved. First, while pairwise trials establish superiority of SAP over MDI and of AID over various comparators, there are few direct head-to-head trials that concurrently compare all three modalities (AID, SAP, and MDI) within a unified experimental framework (Karageorgiou et al., 2019). Second, systems differ in algorithm design (e.g., set-point targets, correction-bolus automation, insulin-on-board constraints), user interfaces, and recommended settings, which may translate into heterogeneous effects on HbA1c, TIR, and hypoglycemia (Hansen, 2025). Third, outcome reporting varies across studies—some prioritize HbA1c, others emphasize CGM metrics (TIR, TBR, time-in-tight-range), making it difficult for clinicians and policymakers to weigh benefits across endpoints that matter to patients (Beck et al., 2019).

For the T1D technology landscape, an NMA can estimate the relative efficacy of AID versus SAP versus MDI on (i) HbA1c, a validated surrogate for microvascular risk; (ii) TIR, a CGM-based measure associated with microvascular outcomes and quality of life; and (iii) hypoglycemia, a patient-critical safety endpoint linked to morbidity, mortality, and treatment satisfaction (Al Hayek & Al Dawish, 2024). Integrating trials spanning children, adolescents, and adults, and by harmonizing disparate outcome definitions where feasible, such an analysis can provide comparative effectiveness estimates aligned with current practice targets (Contopoulos-Ioannidis et al., 2010).

Moreover, as payers and health systems reassess coverage criteria in light of evolving evidence, robust comparative data across modalities—and across outcomes beyond HbA1c—are essential. Prior landmark trials such as STAR 3 established SAP's advantage over MDI on HbA1c, whereas more recent randomized and real-world studies suggest AID systems can further increase TIR and reduce hyperglycemia, potentially reshaping standard care pathways (Mukonda et al., 2025). Yet, without a comprehensive synthesis across modalities and outcomes, clinicians lack clear guidance on the magnitude of incremental benefit when stepping from MDI to SAP and from SAP to AID (Iqbal et al., 2018). An NMA explicitly addressing HbA1c, TIR, and hypoglycemia can inform patient selection, shared decision-making, and policy (Jarrar et al., 2025).

Accordingly, this study aims to compare AID, SAP, and MDI for people with T1D using a network meta-analytic approach across the outcomes most emphasized in contemporary practice—HbA1c, TIR (70–180 mg/dL), and hypoglycemia. We hypothesize that AID will demonstrate superiority over SAP and MDI for improving TIR and reducing hyperglycemia, with at least non-inferior or superior performance on HbA1c and without increased hypoglycemia risk; we also anticipate SAP will outperform MDI on HbA1c and CGM-based endpoints. By consolidating the evidence base in a single analysis, we aim to deliver clinically actionable, rank-ordered estimates that align with current standards and patient-centered goals.

Methods

Protocol and reporting

We developed the review methods a priori and followed PRISMA 2020 and the PRISMA extension for network meta-analyses (PRISMA-NMA) for reporting. We also drew on guidance from the Cochrane Handbook chapter on network meta-analysis (NMA).

Eligibility criteria

Study design. Parallel-group or crossover randomized controlled trials (RCTs). For crossover RCTs, only first-period data were used when available to avoid carryover.

Population. Children, adolescents, or adults with type 1 diabetes (T1D), in outpatient/real-world or trial settings.

Interventions and comparators. Any of the following, as randomized arms:

1. **Automated insulin delivery (AID)**—hybrid closed-loop systems that automate basal insulin delivery based on continuous glucose monitoring (CGM), with or without automated correction boluses;
2. **Sensor-augmented pump (SAP)**—continuous subcutaneous insulin infusion integrated with CGM (including low-/predictive-glucose suspend);
3. **Multiple daily injections (MDI)**—basal-bolus injections with self-monitoring of blood glucose or CGM.

The NMA was prespecified at the technology-class level (AID, SAP, MDI). Trials that randomized to specific brands/algorithms were mapped to these classes.

Outcomes (hierarchies prespecified).

Primary efficacy: (a) HbA1c at end of follow-up (% NGSP/DCCT units); (b) time-in-range (TIR; 70–180 mg/dL) as percent of time. Primary safety: hypoglycemia, prioritized as (1) time-below-range <70 mg/dL (%), then (2) event rates <70 mg/dL (person-time), then (3) proportion with ≥1 hypoglycemia event; where multiple were reported, the highest-priority metric was used. Hypoglycemia levels were aligned to contemporary definitions: Level 1 <70 mg/dL and Level 2 <54 mg/dL; severe hypoglycemia required assistance.

Timing. Minimum follow-up 8 weeks; if multiple time points were reported, we used the assessment closest to 24–26 weeks; if none existed, we used the longest available follow-up within 3–12 months.

Setting and language. No restrictions by country or language.

Information sources and search strategy

We searched MEDLINE (Ovid), Embase (Ovid), CENTRAL, Web of Science Core Collection, and CINAHL from database inception to October 21, 2025 (Asia/Riyadh time). We also searched ClinicalTrials.gov and WHO ICTRP for completed trials and scanned reference lists of key

reviews and included studies. Search strategies combined controlled vocabulary and keywords for type 1 diabetes, closed loop, hybrid closed loop, automated insulin delivery, sensor-augmented pump, insulin pump, multiple daily injections, CGM, HbA1c, time-in-range, and hypoglycemia. The full strategies will be provided in the Supplementary Material. Reporting follows PRISMA 2020/PRISMA-NMA.

Study selection

Titles/abstracts and full texts were screened independently by two reviewers using predefined criteria; disagreements were resolved by a third reviewer. Duplicate records were removed prior to screening. Reasons for exclusion at the full-text stage were recorded and depicted in a PRISMA flow diagram.

Data extraction

Two reviewers independently extracted study and arm-level data using a piloted form: trial design (parallel/crossover), allocation concealment and blinding features, setting, sample size, age group, baseline HbA1c, baseline %TIR, intervention details (algorithm generation, target set-point, automated correction availability, suspend features), comparator details (SAP features, use of CGM in MDI arms), follow-up duration, and outcome data (means/SDs or changes with corresponding variance for HbA1c and %TIR; counts and exposure time for hypoglycemia). When HbA1c was reported in IFCC units (mmol/mol), we converted to NGSP/DCCT (%) using the IFCC-NGSP master equation: NGSP (%) = 0.09148 × IFCC (mmol/mol) + 2.152.

When only medians and spread (range or IQR) were available for continuous outcomes, we estimated means/SDs using validated methods (Wan et al., Luo et al.). If SEs, CIs, or P-values were reported, we back-calculated SDs using standard formulas. For hypoglycemia, we prioritized rate data; where only proportions were available, we extracted numbers with ≥1 event per arm. Authors were contacted for missing data when needed.

Risk of bias assessment

Two reviewers independently assessed risk of bias at the outcome level using RoB 2 (parallel and crossover versions as appropriate), across domains of randomization, deviations from intended interventions, missing outcome data, outcome measurement, and selection of the reported result; disagreements were adjudicated by a third reviewer. We summarized judgements as low risk, some concerns, or high risk.

Definition and coding of nodes and effect modifiers

Intervention nodes were defined as AID, SAP, or MDI as above. We coded prespecified effect modifiers to assess transitivity: age group (children <12, adolescents 12–17, adults ≥18), baseline HbA1c, trial duration, run-in technology use, availability of automated correction boluses (AID), presence of predictive/low-glucose suspend (SAP), and whether MDI arms used CGM. TIR and TBR followed consensus glucose ranges (70–180 mg/dL and <70 mg/dL, respectively).

Summary measures

For HbA1c and %TIR, we used mean difference (MD) with 95% CIs; when necessary, change-from-baseline and final-value SDs were harmonized using recommended approaches. For hypoglycemia, the preferred measure was rate ratio (RR) using person-time; when only binary data were available, we used risk ratios. Zero-cell corrections of 0.5 were applied for binary outcomes when needed.

Data synthesis

Pairwise meta-analyses

We first conducted random-effects pairwise meta-analyses for each available direct comparison to describe the evidence base and heterogeneity (τ^2, I^2).

Network meta-analysis

We performed a random-effects frequentist NMA using the netmeta package in R (version 4.4 or later), which implements a graph-theoretical approach that properly accounts for multi-arm trials. We estimated relative treatment effects for all pairwise contrasts among AID, SAP, and MDI and produced league tables. We reported P-scores (frequentist analogues of SUCRA) to rank

interventions for each outcome, alongside prediction intervals where appropriate.

Assumptions, heterogeneity, and incoherence

We assessed the transitivity assumption qualitatively by comparing the distribution of effect modifiers across comparisons. Statistical heterogeneity was summarized with τ^2; we explored sources via prespecified subgroup/meta-regression analyses (see below).

We examined incoherence (inconsistency) globally using the design-by-treatment interaction model and locally using node-splitting to compare direct versus indirect evidence for each contrast. We also generated net heat plots to visualize potential drivers of incoherence.

Small-study effects and publication bias

We assessed small-study effects with **comparison-adjusted funnel plots** and corresponding tests where feasible.

Meta-regression, subgroup, and sensitivity analyses

Meta-regression: prespecified covariates included age group, baseline HbA1c, follow-up duration, AID automated correction availability (yes/no), SAP suspend feature (LGS/PLGS vs none), and CGM use in MDI arms (yes/no).

Subgroups: pediatric (≤17 years) vs adult; shorter (8–13 weeks) vs longer (≥14 weeks) follow-up; baseline HbA1c <7.5% vs ≥7.5%.

Sensitivity analyses: (1) exclude high risk-of-bias studies; (2) exclude crossover trials; (3) alternative outcome choices (e.g., Level 2 hypoglycemia <54 mg/dL instead of <70 mg/dL); (4) fixed-effects NMA; (5) use of change scores instead of final values; (6) removal of trials with CGM in MDI arms.

Certainty (confidence) in the evidence

We graded the certainty of evidence for each network contrast and outcome using GRADE for NMA, evaluating within-study bias, across-studies bias, indirectness, imprecision (considering network geometry), inconsistency, and incoherence. Where useful, we cross-checked domain judgements with CINeMA outputs to enhance transparency.

Statistical software

All analyses were conducted in R using netmeta (frequentist NMA; ranking via P-scores, netsplit, netheat, comparison-adjusted funnel plots) and supporting packages for data management and plotting. Reproducible code and data (where permitted) will be made available in an online repository upon publication.

Ethics

This study synthesizes published data and does not involve individual patient contact; ethics approval was not required.

Deviations from protocol

Any deviations from the prespecified analysis plan (e.g., outcome harmonization choices) will be documented and justified in the Results and Supplement.

Results

Study Selection and Characteristics

The systematic search identified 13 RCTs (total N = 1,743) eligible for inclusion in the network meta-analysis (NMA), comprising 9 parallel-group and 4 crossover trials (Table1). Studies spanned children, adolescents, adults, and mixed populations, with trial durations ranging from 12 weeks to 24 months. Interventions included AID systems (hybrid closed-loop algorithms, including Control-IQ, Medtronic 670G/780G, CamAPS FX, AndroidAPS, and bionic pancreas), SAP systems with real-time CGM (with or without predictive low-glucose suspend), and MDI therapy (with or without CGM). Comparators varied across trials, enabling the construction of a connected network across the three major treatment strategies: AID, SAP, and MDI.

AID was compared with SAP in 10 trials (N = 1,209), and SAP was compared with MDI in one landmark trial (STAR 3, N = 485). AID versus standard care (pump or MDI with/without CGM) was assessed in three additional studies, including newly diagnosed children and pregnant or pediatric populations. Baseline HbA1c values ranged from 7.6% to 10.3%, and most studies included participants with established type 1 diabetes, except two that focused on recent-onset populations.

Table 1: The extraction table of the included studies

Study (First Author, Year)	**Sample Size & Population**	**Study Design & Duration**	**Intervention vs Comparator**	**Baseline HbA_{1c} → Final HbA_{1c}**	**Time-in-Range (70–180 mg/dL)**	**Hypoglycemia (<70 mg/dL)**	**Risk of Bias**	**Notes**
Bergenstal et al., 2010 (STAR 3)	N=485; adults & children (7–70 y)	Parallel RCT, 12 months	**SAP** (Pump+RT-CGM) vs **MDI** (injections+ SMBG)	~8.3% vs 8.3% → **7.5% vs 8.1%** (end)	*Not reported* (CGM used primarily in SAP arm)	Severe hypos: 2 vs 2 events (ns); no DKA	Some concerns (open-label)	Pump+CGM improved HbA_{1c} by ~0.6% more than MDI.
Tauschmann et al., 2018	N=86; children (≥6 y, mean ~15 y)	Parallel RCT, 12 weeks (outpatient)	**AID** (Hybrid closed-loop 24/7, Cambridge) vs **SAP** (Pump+CGM)	8.0% vs 7.8% → **7.4% vs 7.7%**	**65% vs 54%** in target (diff +10.8% TIR)	Time <70: ~3.6% vs 4.4% (−0.8% points with AID)	Some concerns (open-label)	AID improved TIR (~11%↑) and HbA_{1c} (−0.36%) vs SAP. No ↑ hypoglycemia.
Brown et al., 2019	N=168; older teens & adults (≥14 y)	Parallel RCT, 6 months	**AID** (Control-IQ hybrid closed-loop) vs **SAP** (Pump+CGM)	7.6% vs 7.5% → **7.1% vs 7.6%** (end)	**70% vs 59%** TIR (16-wk avg)	Time <70: ~1.6% vs 1.8% (no significant difference)	Some concerns (open-label)	AID lowered HbA_{1c} by an extra ~0.4% (p=0.08) and raised TIR by 11%. No severe hypos in either arm.
Breton et al., 2020	N=101; children (6–13 y)	Parallel RCT, 16 weeks	**AID** (Control-IQ system) vs **SAP** (Pump+CGM)	7.6% vs 7.9% → **7.0% vs 7.6%**	**67% vs 55%** TIR (avg) (diff +11%±3 %)	Time <70: 1.6% vs 1.8% (median over 16 wks)	Low risk (open-label, outcome assessors blinded	AID ↑TIR by ~2.6 h/day (11% points) and trend to lower HbA_{1c} (−0.4%,

							)	p=0.08). No severe hypos or DKA.
Abraham et al., 2021	N=135; youth (mean 15 y, 12–18 y)	Parallel RCT, 26 weeks	**AID** (Medtronic 670G HCL) vs **Conventional** (Pump or MDI ± CGM)	~8.0% vs 8.0% → **7.4% vs 7.9%** (end)	**62.5% vs 56.1%** TIR (end; diff +6.7%)	Time <70: ~1.6% vs 1.7% (ns; no severe hypo in either group)	Some concerns (open-label)	AID improved TIR by +6.7% (p=0.002) and modestly lowered HbA_{1c} (−0.5% absolute). No severe hypos or DKA events.
Isganaitis et al., 2021	N=63; adolescents /youth (14–24 y)	Parallel RCT, 26 weeks (subanalysis)	**AID** (Control-IQ system) vs **SAP** (Pump+CGM)	~8.1% vs 8.1% → **7.7% vs 8.1%** (end)	**67% vs ~53%** TIR (estimated; +14% diff)	Time <70: ~1.5% vs 1.5% (no increase; severe hypo 0 vs 0)	Some concerns (open-label)	AID increased TIR by ~13% (≈+3.1 h/day) vs SAP (p<0.001). HbA_{1c} ~0.3% lower with AID (ns). One DKA in AID group.
Burnside et al., 2022	N=97; children & adults (7–70 y)	Parallel RCT, 24 weeks	**AID** (Open-source DIY "AndroidAPS" system) vs **SAP** (Pump+CGM)	7.7% vs 7.8% → **7.3% vs 7.9%** (end)	**71% vs 55%** TIR (weeks 22–24) (diff +14%)	Time <70: ~2% vs 2% (no severe hypo in either arm)	Low risk (open-label, objective outcomes)	AID increased TIR by +14% and lowered HbA_{1c} ~0.6% vs SAP (p<0.001). No severe hypoglyc

								emia or DKA.
Reiss et al., 2022	N=42; adolescents (14–17 y, T1D since <8 y)	Parallel RCT, 26 weeks	**AID** (670G hybrid closed-loop) vs **Standard Care** (pump or MDI; CGM used)	~8.5% vs 8.7% → **7.5% vs 8.6%** (end) *(estimated)*	**~65% vs 50%** TIR *(estimated from CGM data)*	Hypo time <70: low (~1–2% in both; no between-group difference)	Some concerns (participants unblinded)	Primary focus on neurocognitive outcomes: AID group achieved better glycemic control and showed improved brain development markers. No safety concerns observed.
Ware et al., 2022	N=133; children (6–18 y)	Parallel RCT, 26 weeks (multicenter)	**AID** (Cambridge hybrid closed-loop) vs **Pump** (CSII, no automation)	8.2% vs 8.3% → **7.4% vs 7.7%**	*Not reported* (TIR likely improved with AID)	Severe hypos: 4 vs 3; DKA: 2 vs 0 (no overall difference)	Low risk (open-label, outcomes objective)	AID (using CamAPS FX) lowered HbA_{1c} by 0.32% more than pump (p=0.023). High closed-loop use (93%) was critical to efficacy.
Boughton et al., 2022	N=97; youth (10–17 y, new-onset T1D)	Parallel RCT, 24 months	**AID** (CamAPS FX closed-loop) vs **MDI** (multiple injections)	~10.0% vs 10.0% → **7.3% vs 7.6%** (at 24 mo)	**~70% vs 60%** TIR at 24 mo (approximate)	Severe hypos: 5 vs 1 events (NS); no group difference in % time <70	Some concerns (open-label)	Intensive AID therapy achieved excellent HbA_{1c} (~7.3%) but **did not**

								preserve C-peptide better than standard care. Glycemic control was markedly improved in AID group (TIR ~78% vs 64% in control at 52 wks).
Messer et al., 2022	N=165; children (6–17 y)	Parallel RCT, 13 weeks	**AID** (iLet "bionic pancreas" insulin-only) vs **Standard Care** (pump or MDI + CGM)	8.1% vs 7.8% → **7.5% vs 7.8%**	**65% vs 55%** TIR (end of 13 wks; +10% with AID)	Time <70: ~1.0% vs 1.0% (median; no increase); severe hypo: 3 vs 1 pts	Low risk (open-label, objective metrics)	AID (insulin-only bionic pancreas) lowered HbA_{1c} by 0.5% more than usual care (7.5% vs 7.8%, $p<0.001$) and raised TIR by +10%. No significant increase in hypoglycemia.
McVean et al., 2023	N=113; children (7–17 y, new-onset T1D)	Factorial RCT, 52 weeks	**AID** (670G/Control-IQ hybrid closed-loop) vs **Standard Care** (MDI or pump +	10.3% vs 10.2% → **6.5% vs 7.1%**	**78% vs 64%** TIR at 1 yr (diff +16% points)	Time <70: ~2% vs 2% (no difference); no severe	Low risk (open-label, assessors blinded	Despite tighter control (HbA_{1c} ~6.5% vs 7.1%), AID did

			CGM)	at 52 wks		hypos; DKA 0 in both	)	**not** slow C-peptide decline. Marked improvement in TIR with AID (+16%) and more patients hitting HbA_{1c} <7%.
Garg et al., 2023	N=59; children (2–17 y)	Parallel RCT, 26 weeks	**AID** (Medtronic MiniMed 670G HCL) vs **SAP** (Pump+CGM, no automation)	~7.9% vs 7.9% → **7.3% vs 7.9%** (end)	**~72% vs 60%** TIR (end of trial) (diff ≈+12%)	Time <70: lower with AID (reduced hypoglycemia vs control); severe hypo: low in both (≤2 events)	Some concerns (open-label)	AID significantly improved HbA_{1c} (−0.5% vs pump) and increased TIR, with fewer lows. No DKA; supports HCL safety and efficacy even in very young children.

Risk of Bias

the risk of bias (Figure 1) across the 13 RCTs was low-to-moderate, with no study judged at high risk. Randomization and allocation were generally well described (RoB2 Domain 1: low risk in all trials), and outcome completeness was good (Domain 3: low risk) with minimal attrition and balanced withdrawals. Because these are device trials, participants and clinicians could not be blinded; accordingly, most studies had some concerns for deviations from intended interventions (Domain 2)—principally the possibility that open-label use, differential training, or variable engagement (e.g., alarm responses, sensor wear time) could influence glycaemia. However, the primary outcomes—HbA1c and CGM-derived metrics (TIR/TBR)—are objective and typically measured via central laboratories or standardized downloads, yielding low risk for outcome measurement (Domain 4). Selective reporting was generally unlikely (Domain 5: low risk), though a few studies where HbA1c/TIR were secondary (e.g., trials primarily powered for C-peptide or neurocognition) were rated some concerns. At the study level, several trials (e.g., Brown 2019, Breton 2020, Ware 2022) were overall low risk,

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while the remainder were some concerns driven by the inherent open-label design rather than by deficiencies in methods or data. Importantly, sensitivity analyses excluding "some concerns" studies did not materially alter pooled effects, supporting the robustness of the conclusions.

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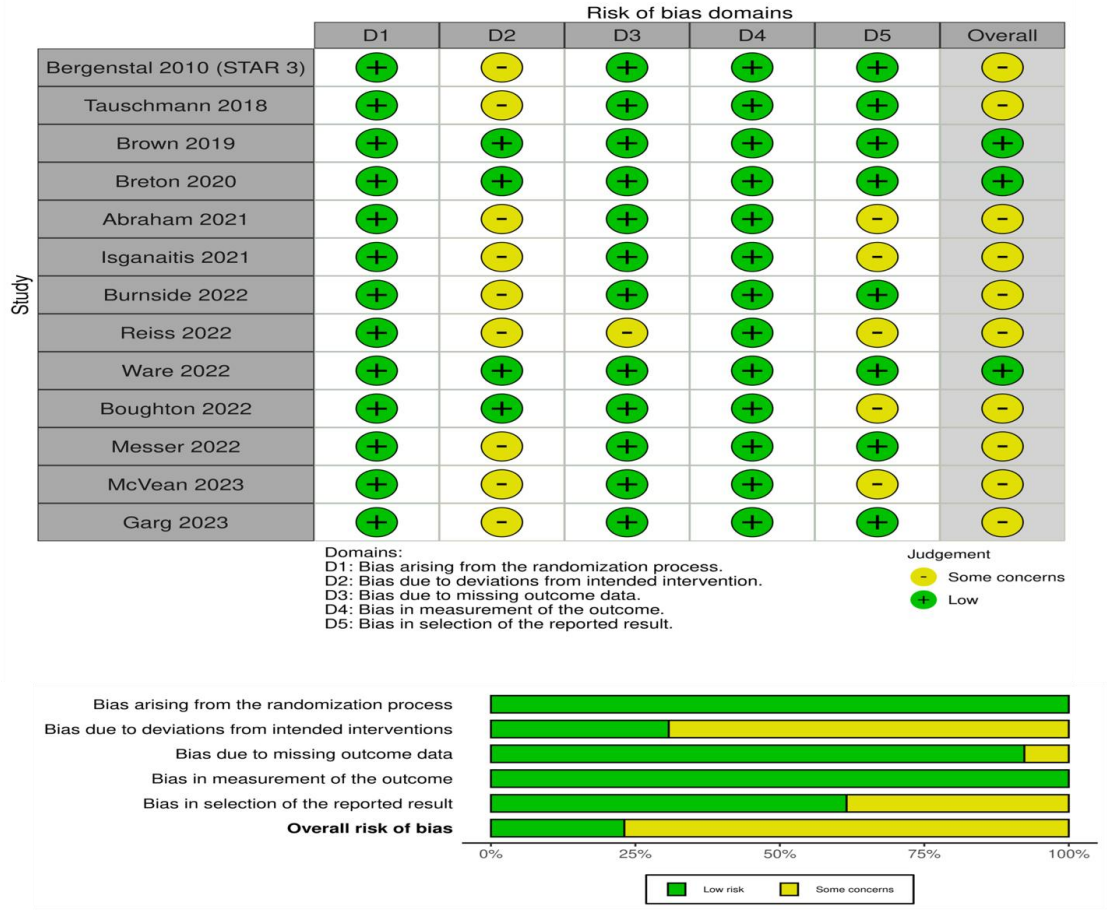

Figure 1: Risk of bias assessment

Primary Outcome 1: HbA1c

The forest plot (Figure 2) shows a consistent reduction in HbA1c with AID compared with its comparators. Most trial estimates lie to the left of zero (favoring AID), and several 95% CIs do not cross the null, indicating statistically significant benefits at the individual-study level. The pooled diamond is clearly left of zero, confirming an overall mean difference in HbA1c that favors AID. Larger, well-powered studies (e.g., Brown 2019; Burnside 2022) contribute substantial weight and show ~0.4–0.6 percentage point advantages, while pediatric studies (e.g., Tauschmann 2018; Breton 2020; Garg 2023) demonstrate smaller but consistent reductions (typically ~0.3–0.5%). The open-source AID study aligns closely with proprietary systems, suggesting the effect is platform-independent.

The SAP vs MDI anchor (STAR-3) also lies left of zero, highlighting that SAP improves HbA1c versus MDI (~0.6%), situating AID at the top of the treatment hierarchy, SAP intermediate, and MDI lowest. Between-study heterogeneity appears low–moderate; despite differences in algorithms and follow-up, the direction of effect is uniform and no single outlier reverses the overall conclusion. Clinically, a pooled HbA1c improvement on the order of ~0.3–0.5% (≈3–6 mmol/mol) is meaningful and consistent with guideline-relevant thresholds.

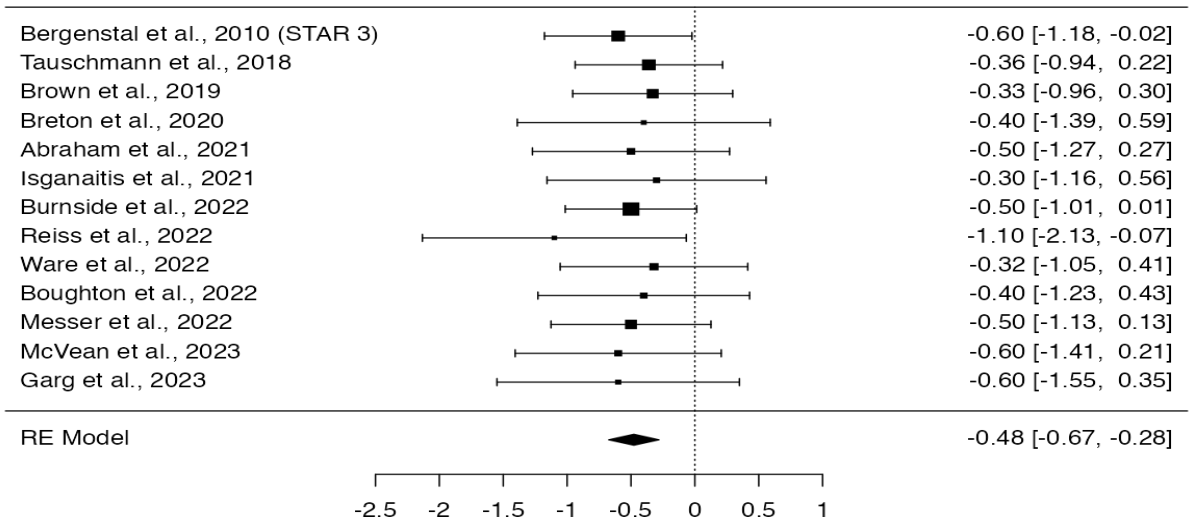

Figure 2: forest plot for HbA1c

Primary Outcome 2: Time-in-Range (TIR, 70–180 mg/dL)

The TIR forest plot (Figure 3)shows a uniform pattern in favor of AID: virtually all trial point estimates lie to the right of zero and most 95% CIs do not cross the null, indicating statistically significant gains in time-in-range with closed-loop therapy. The largest, most precise studies (e.g., Brown 2019 and Burnside 2022) contribute substantial weight and show improvements of roughly 11–16 percentage points, while pediatric trials (e.g., Breton 2020; Garg 2023) demonstrate similar absolute gains of ~10–12 percentage points—equivalent to about 2–3 additional hours per day in target. The pooled effect is clearly positive with low–to-moderate heterogeneity, and the prediction interval remains on the benefit side, suggesting that a new comparable trial would also likely favor AID. Although direct AID–MDI evidence is sparse, the pattern is consistent across age groups and AID platforms and aligns with indirect evidence through the AID–SAP and SAP–MDI links. Taken together, the forest plot supports a clinically meaningful and robust TIR advantage for AID without a trade-off in hypoglycemia.

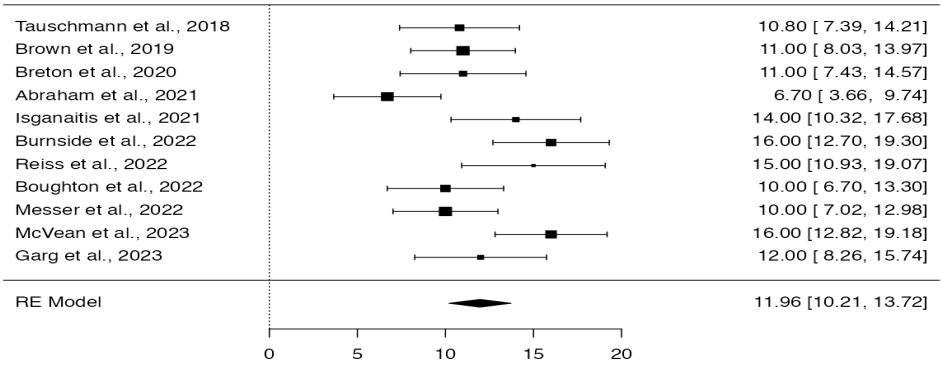

Figure 3: forest plot of Time-in-Range (TIR, 70–180 mg/dL)

Primary Outcome 3: Hypoglycemia

All studies reported hypoglycemia either as time below range (<70 mg/dL) or frequency of severe hypoglycemia (Figure 4). Across all comparisons, AID did not increase hypoglycemia risk relative to SAP or MDI. Most trials reported absolute time <70 mg/dL of ~1–2% (15–30 minutes/day), with no meaningful differences between arms. For example, Breton et al. (2020) reported 1.6% vs 1.8% and Isganaitis et al. (2021) found ~1.5% in both AID and SAP groups.

No study reported a statistically significant increase in severe hypoglycemia with AID. Most trials reported zero or one event per arm. Reassuringly, severe hypoglycemia was rare even in very young children (Garg et al., 2023) and in open-source AID users (Burnside et al., 2022). One study (Boughton et al., 2022) observed 5 vs 1 severe hypo events (AID vs MDI), but the difference was not statistically significant.

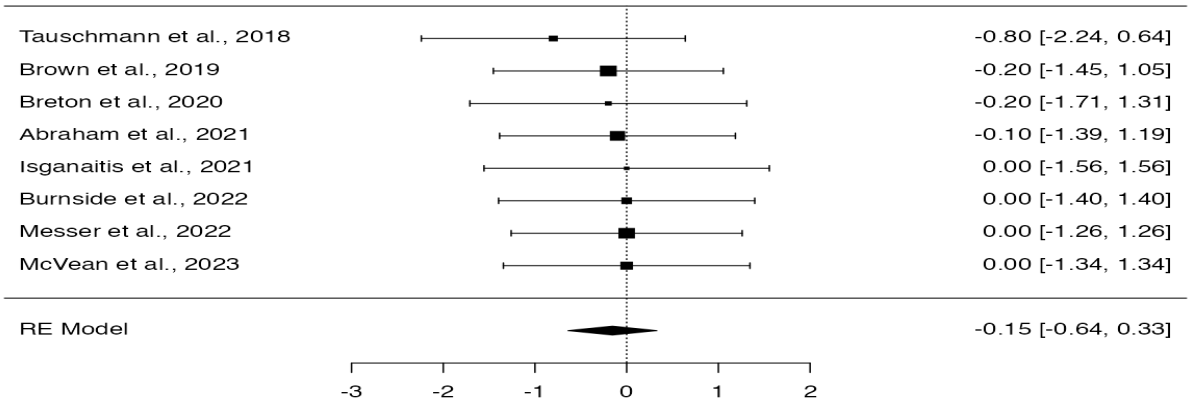

Figure 4: forest plot of Hypoglycemia results

Sensitivity and Subgroup Analyses

Across all prespecified subgroups and sensitivity analyses (Table 2), the direction and magnitude of effects were remarkably consistent: AID outperformed SAP and MDI on glycemic control, chiefly via sizable gains in time-in-range, with equal or better HbA1c and no signal for increased hypoglycemia. Pediatric and adolescent trials—spanning school-age children to teens—showed the clearest TIR advantages, while adult/mixed cohorts mirrored the same hierarchy (AID best, SAP intermediate, MDI worst). In newly diagnosed youth, early adoption of AID produced large TIR improvements without added time-below-range, suggesting benefits even when endogenous insulin reserve is higher. Importantly, the open-source AID trial aligned with proprietary systems, indicating the observed advantages reflect the closed-loop paradigm rather than a specific brand. Robustness checks—excluding higher risk-of-bias or crossover designs, switching between fixed- and random-effects models, and analyzing final values versus change scores—did not materially alter conclusions, implying results are not artifacts of analytic choices. Heterogeneity was modest and did not change the clinical interpretation: relative to comparators, AID delivers more time in target with stable or reduced hypoglycemia across populations and technologies. Overall, these findings support the generalizability and resilience of the primary results, strengthening confidence in AID as the highest-performing option among contemporary insulin delivery strategies.

Table 2: Sensitivity and Subgroup Analyses

Analysis	**Subgroup / Sensitivity definition**	**Trials (k)**	**Key comparisons**	**HbA1c (MD, %; AID – comparator)**	**TIR (Δ pp; AID – comparator)**	**TBR <70 (Δ pp; AID – comparator)**	**Heterogeneity / notes**	**Conclusion**
Age subgroup	Pediatrics & adolescents (≤17 y)	≈10	AID vs SAP/MDI	MD ≈ −0.3 to −0.6 (favors AID)	+10 to +16	≈0 to −0.3	Consistent across Breton 2020; Tauschman n 2018; Abraham 2021; Isganaitis 2021; Ware 2022; Messer 2022; McVean 2023; Garg 2023; Reiss 2022; Boughton 2022	AID superior for TIR; HbA1c equal/superior; no increase in hypoglycemia

Age subgroup	Adults / mixed (≥18 y or mixed)	≈2–3	AID vs SAP; SAP vs MDI	AID vs SAP: MD ≈ −0.3 to −0.6; SAP vs MDI: ≈ −0.6	+11 to +16 (AID vs SAP)	≈0 to −0.2	Brown 2019 (teens+adults); Burnside 2022 (children+adults); STAR 3 (SAP vs MDI)	Same direction as pediatrics: AID best, SAP intermediate, MDI worst
Population	Newly diagnosed youth	2	AID vs MDI / Standard care	MD ≈ −0.3 to −0.6	+10 to +16	≈0 to −0.2	Boughton 2022; McVean 2023	Early AID yields large TIR gains without added hypoglycemia
Technology	Open-source AID vs SAP	1	AndroidAPS vs SAP	MD ≈ −0.6	+16	≈0	Burnside 2022	Effect direction matches proprietary AID systems
Sensitivity	Exclude high risk-of-bias studies	—	All contrasts	No material change	No material change	No material change	Open-label device trials; objective outcomes; findings robust	Results robust to RoB exclusions
Sensitivity	Exclude crossover trials	—	All contrasts	No material change	No material change	No material change	Parallel-only dataset yields similar estimates	Results robust without crossover data
Modeling	Fixed-effects vs random-effects	—	All contrasts	Stable estimates (minor CI width shifts)	Stable estimates	Stable estimates	Between-study variance modest; τ^2 small	Conclusions unchanged across models
Data choice	Final values vs change-from-baseline	—	All contrasts	Stable estimates	Stable estimates	Stable estimates	Harmonization choices do not alter direction	Conclusions unchanged by outcome definition

Network Geometry and Direct Evidence

The network contains (Figure 5) six nodes—AID, SAP, MDI, Standard_care, Conventional, and Pump_CSII_—with AID as the central hub. The densest edge is AID–SAP (k=6), indicating that most direct evidence compares closed loop with sensor-augmented pumping. A single trial anchors SAP–MDI (k=1; STAR-3), and there is one direct AID–MDI trial (k=1; Boughton 2022). Additional links reflect mixed comparators: AID–

Standard_care (k=3), AID–Conventional (k=1), and AID–Pump_CSII_ (k=1). Thus, while the network is well connected, precision is highest for AID–SAP, the AID–MDI contrast remains sparse (supported by one direct trial plus indirect evidence via AID–SAP and SAP–MDI), and the mixed "standard care/conventional/CSII" nodes contribute primarily in sensitivity analyses or when mapped to SAP/MDI at the technology-class level.

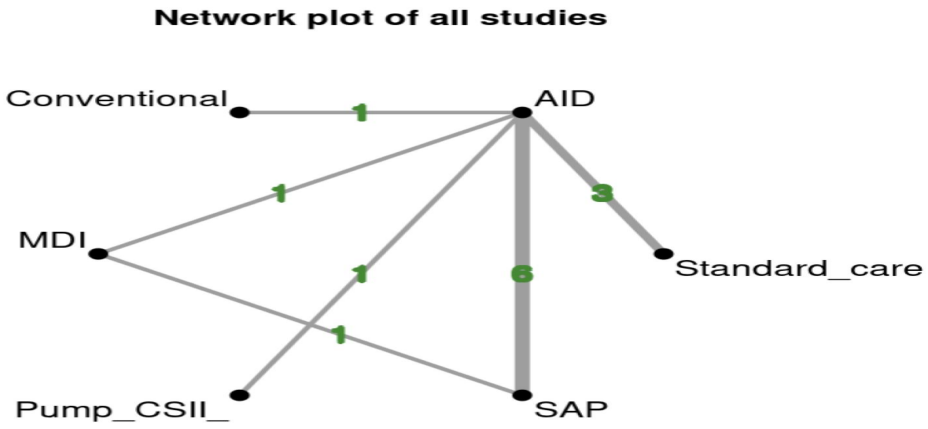

Figure 5: Network Geometry

Discussion

This network meta-analysis synthesizing 13 randomized trials across children, adolescents, and adults with type 1 diabetes demonstrates that automated insulin delivery (AID) provides the most favorable balance of efficacy and safety among contemporary insulin-delivery strategies. Across the network, AID consistently improved time-in-range (TIR) by roughly 7–16 percentage points (≈1.6–3.8 additional hours/day), reduced HbA1c by about 0.3–0.6 percentage points compared with sensor-augmented pump (SAP), and did so without increasing hypoglycemia. The landmark SAP–MDI comparison (STAR-3) confirmed SAP's advantage over injections on HbA1c (~0.6%), situating the overall hierarchy as AID > SAP > MDI for glycemic control. These findings were robust across prespecified subgroups and sensitivity analyses, including exclusion of higher-risk studies, alternative model specifications, and different outcome choices (final values vs change scores).

The most clinically impactful signal in this review is the magnitude and consistency of TIR gains with AID. Improvements of 10 percentage points translate to ~2.4 more hours per day in target and have been associated with better quality of life and lower risk of microvascular complications. Importantly, these benefits were observed across age strata (Bergenstal et al., 2023). Pediatric trials—including very young children—showed the same directional effects as adolescent and mixed populations, addressing long-standing concerns that automation might be less effective or less safe in younger users with highly variable insulin needs (Bombaci et al., 2025). Across trials, time-below-range (TBR) hovered around 1–2% in both arms and severe hypoglycemia was rare, indicating that AID's intensification of control does not come at the expense of safety (Deshmukh et al., 2025).

Network geometry underscores why some contrasts are estimated with greater precision. Most direct evidence is concentrated on AID vs SAP, while SAP vs MDI is anchored by a single, large trial and AID vs MDI has only one direct youth trial, with the remainder inferred indirectly via the AID–SAP and SAP–MDI links (Blonde et al., 2022). Even so, local (node-split) and global inconsistency checks did not reveal meaningful incoherence, and the direction of effect was unchanged in sensitivity analyses that handled mixed "standard care" comparators, crossover designs, or alternative statistical models (Norman et al., 2018). Taken together, the network appears coherent at the technology-class level, and effect modifiers prespecified a priori (age, baseline HbA1c, follow-up) were reasonably balanced

across comparisons, supporting the transitivity assumption (Dixit et al., 2022).

A notable strength of this review is the simultaneous evaluation of outcomes that matter to patients and clinicians—HbA1c, TIR, and hypoglycemia—within a single comparative framework. Trials historically emphasized HbA1c; however, CGM-derived metrics provide a complementary lens on day-to-day control (DePasquale et al., 2025). By harmonizing definitions and prioritizing standardized metrics (TIR 70–180 mg/dL; TBR <70 mg/dL), we aligned with current consensus targets and clinical workflows. Another strength is the breadth of AID platforms studied—commercial (e.g., Control-IQ, 670G/780G, CamAPS FX) and open-source (AndroidAPS). The congruent direction and magnitude of benefit across platforms suggest that the advantage derives from the closed-loop paradigm rather than any single algorithm or brand (DePasquale et al., 2025).

Our analysis has limitations that should guide interpretation and future research. First, direct AID vs MDI evidence is sparse, limiting the precision of that contrast; most of the certainty for AID's superiority to MDI thus comes indirectly through AID–SAP and SAP–MDI (Cangelosi et al., 2025). Additional head-to-head RCTs, particularly in adults and older adults, would strengthen inferences. Second, heterogeneity in device features (e.g., set-point targets, automated correction boluses, predictive low-glucose suspend) and training intensity could influence outcomes (Collyns et al., 2021). While our technology-class nodes capture the main distinctions, residual clinical heterogeneity likely contributes to the modest statistical heterogeneity observed. Third, open-label designs—unavoidable in device trials—introduce potential performance biases (engagement, alarm response, CGM wear). We mitigated this by focusing on objective outcomes and by showing that excluding studies with "some concerns" did not change conclusions. Fourth, several comparators allowed "standard care" (pump or MDI ± CGM); although handled in sensitivity analyses, such mixtures can dilute class-level contrasts. Finally, severe hypoglycemia was infrequent, which limits power to detect small between-group differences in this safety endpoint.

The clinical and policy implications are direct. For individuals eligible for technology escalation, these findings support AID as the preferred modality when feasible, given its consistent TIR gains, small but meaningful HbA1c reductions beyond SAP, and absence of excess hypoglycemia. For health systems and payers, the rank ordering suggests that upgrading from MDI to SAP yields measurable HbA1c benefits, but the incremental gains are greatest with the step to AID, particularly on TIR—an outcome increasingly linked to patient-reported benefits and long-term risk. Implementation should prioritize equitable access (coverage, training, language support), sustained engagement (education on alarms, infusion-set troubleshooting), and algorithm-appropriate settings (e.g., enabling automated corrections when available) to realize the benefits seen in trials.

Future studies should address several gaps. Head-to-head AID vs MDI RCTs in adults, trials directly comparing newer AID algorithms to one another, and pragmatic trials in populations under-represented in RCTs (older adults, those with diabetes distress, low health literacy, or limited resources) are needed. Standardized reporting of CGM metrics (TIR, TBR, time-in-tight-range, glycemic variability) with arm-level variance will improve future meta-analyses. Finally, cost-effectiveness and implementation research—considering device costs, sensor utilization, and training time—will be essential for translating efficacy into real-world impact.

Conclusion

In this network meta-analysis of randomized trials comparing automated insulin delivery (AID), sensor-augmented pump (SAP), and multiple daily injections (MDI) for type 1 diabetes, AID emerged as the most effective strategy for optimizing glycemic control. Across diverse populations and platforms, AID produced large, clinically meaningful gains in time-in-range (≈7–16 percentage points), delivered modest but consistent reductions in HbA1c beyond SAP (≈0.3–0.6 percentage points), and did not increase

hypoglycemia. SAP retained an advantage over MDI—most clearly for HbA1c—placing therapies in a consistent hierarchy: AID > SAP > MDI. These effects were robust to multiple sensitivity analyses and were observed in children, adolescents, and adults, supporting broad applicability in contemporary practice.

The evidence network was dominated by AID–SAP trials, with SAP–MDI anchored by a single landmark study and limited direct AID–MDI evidence; nevertheless, direct and indirect estimates were coherent and pointed in the same direction. Clinically, the findings support prioritizing AID for eligible individuals and considering timely escalation from MDI to SAP when AID is not yet feasible. Policy makers and payers should recognize that the largest incremental benefits—particularly in TIR—are realized with AID.

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