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Comparative Efficacy and Safety of Automated Insulin Delivery Systems in Children and Adolescents with Type 1 Diabetes: A Systematic Review and Network Meta-Analysis

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ADMINISTRATIVE INFORMATION

Support - Self-funded. Supported by University of Hail College of Pharmacy academic resources. No pharmaceutical industry or commercial funding was received for this review.

Review Stage at time of this submission - The review has not yet started.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202660110

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 23 June 2026 and was last updated on 23 June 2026.

INTRODUCTION

Review question / Objective n children and adolescents (aged under 19 years) with type 1 diabetes mellitus, what is the comparative efficacy and safety of different automated insulin delivery (AID) systems — versus one another and versus non-AID therapies — with respect to Time in Range and related glycaemic, safety, and patient-reported outcomes, ranked within a network meta-analysis?

Rationale Automated insulin delivery has become the preferred insulin-delivery modality for type 1 diabetes, and randomised trials consistently show that AID improves Time in Range versus sensor-augmented pump, pump, or injection therapy. However, in children and adolescents the comparative efficacy and safety of different AID platforms remains poorly characterised: most paediatric pivotal trials compared a single system against a non-AID comparator rather than against each other, and the only paediatric head-to-head trial (FLAIR) compared just two systems. Existing network meta-analyses (Di Molfetta 2024 and 2026; Stahl-Pehe 2025) are dominated by adults and report only low-certainty paediatric subgroups in which no system reached the recommended Time-in-Range target of over 70%; they also exclude open-source DIY systems that are widely used by paediatric families. A dedicated paediatric network meta-analysis that incorporates all eligible randomised trials, includes DIY and emerging fully-closed-loop systems, optionally uses adult-inclusive trials as connecting comparison arms to strengthen the network, performs age-stratified analyses, and grades certainty with CINeMA/GRADE would close a clear and clinically important evidence gap and inform device selection in children. This record is at protocol-registration stage; database searches have not yet been executed and no screening, extraction, or analysis has begun.

Condition being studied Type 1 diabetes mellitus in children and adolescents, managed with automated insulin delivery (closed-loop) systems.

METHODS

Search strategy MEDLINE (via PubMed), Embase (via Elsevier), the Cochrane Central Register of Controlled Trials (CENTRAL), Web of Science Core Collection, ClinicalTrials.gov, and the WHO International Clinical Trials Registry Platform (ICTRP), plus conference abstracts (ISPAD, ADA, EASD; 2022–2026), grey-literature sources (OpenGrey, ProQuest Dissertations), and backward and forward citation searching of included studies and prior systematic reviews and network meta-analyses. Publication-date coverage 01 January 2015 to the search date; no language restriction. A sensitivity-maximising randomised-trial filter will be applied. The full Boolean strategy combines controlled vocabulary (MeSH/Emtree) and free text for: type 1 diabetes; automated insulin delivery; closed loop; artificial pancreas; hybrid closed loop; advanced hybrid closed loop; MiniMed 670G; MiniMed 780G; Control-IQ; Omnipod 5; CamAPS FX; iLet; bionic pancreas; OpenAPS; AndroidAPS; Loop; DBLG1; time in range; HbA1c; hypoglycaemia; continuous glucose monitoring; children; adolescents. The PubMed/MEDLINE strategy will be self-audited against the PRESS 2015 checklist and cross-checked by the second reviewer; searches have not yet been executed.

Participant or population Children and adolescents aged 1 to 18 years (under 19 years) with a confirmed diagnosis of type 1 diabetes mellitus, of any diabetes duration. Pre-specified age subgroups: very young children (1–6 years), children (7–11 years), and adolescents (12–18 years). Trials enrolling mixed paediatric and adult populations will be eligible when paediatric data are reported separately, or when more than 50% of participants are aged under 19 years; eligible adult-inclusive trials may additionally be entered as comparison arms to strengthen the connected network and the precision of indirect estimates, with their adult proportion recorded and examined in sensitivity analysis. Studies of type 2, monogenic, gestational, or cystic-fibrosis-related diabetes, and adult-only studies that cannot serve as a connecting comparison arm, are excluded.

Intervention Any automated insulin delivery (AID) system used in an outpatient or free-living setting, including hybrid closed-loop (HCL), advanced hybrid closed-loop (AHCL), fully closed-loop, bionic-pancreas, and open-source do-it-yourself (DIY) systems. Named systems include MiniMed 670G, MiniMed 780G, Control-IQ (t:slim X2), Omnipod 5, CamAPS FX, DBLG1, iLet Bionic Pancreas, Loop, and AndroidAPS/OpenAPS. Each distinct system (and major algorithm version) forms a separate node in the network.

Comparator Any other AID system (for network ranking) or any non-AID therapy: sensor-augmented pump (SAP), continuous subcutaneous insulin infusion (CSII) without automation, multiple daily injections (MDI) with or without continuous glucose monitoring, or predictive/threshold low-glucose-suspend (PLGS/LGS) systems. The common reference node for relative effects will be sensor-augmented pump therapy (SAP). Comparator type, continuous glucose monitor used, and trial duration will be recorded and examined as potential effect modifiers for the transitivity assessment.

Study designs to be included Randomised controlled trials (parallel-group and crossover) with an outpatient/ambulatory free-living component of at least 3 weeks. Single-arm studies, observational cohorts, and registry analyses are excluded from the primary network meta-analysis (they may inform a separate descriptive synthesis). Inpatient-, hotel-, or camp-only studies without a free-living phase are excluded.

Eligibility criteria Inclusion: children and adolescents under 19 years with type 1 diabetes; an AID system (commercial or open-source) used in the free-living setting; a randomised controlled trial (parallel or crossover) of at least 3 weeks; and at least one reported glycaemic outcome (TIR, TBR, TAR, HbA1c, or hypoglycaemia rate) by CGM or laboratory assay. Adult-inclusive RCTs may be entered as connecting comparison arms when they share a node with paediatric trials.Exclusion: type 1 diabetes managed without AID in all arms; type 2, monogenic, gestational, or cystic-fibrosis-related diabetes; adult-only studies that do not connect the network; non-randomised, single-arm, observational, or registry designs (primary NMA); interventions where AID was used only overnight rather than as the primary modality; inpatient/hotel/camp-only studies; duplicate or overlapping reports (most complete retained); and retracted publications.

Information sources MEDLINE/PubMed, Embase, Cochrane CENTRAL, Web of Science Core Collection (plus ClinicalTrials.gov and WHO ICTRP for trial registries, and ISPAD/ADA/EASD abstracts and OpenGrey/ProQuest for grey literature).

Main outcome(s) Time in Range (TIR): the percentage of time with sensor glucose 70–180 mg/dL (3.9–10.0 mmol/L) per 24 hours, measured by continuous glucose monitoring at the end of the intervention period.

Additional outcome(s) Time below range (250 mg/dL); overnight Time in Range; mean sensor glucose; coefficient of variation; HbA1c; Time in Tight Range (70–140 mg/dL); severe hypoglycaemia events; diabetic ketoacidosis; serious and device-related adverse events; and patient-reported outcomes (diabetes distress, quality of life, fear of hypoglycaemia, treatment satisfaction, sleep) reported with validated instruments. All AID systems will be ranked on each outcome using SUCRA / P-score.

Data management References from all databases will be deduplicated and imported into Rayyan. Two reviewers (A.S.A., B.A.A.) will independently screen titles/abstracts and full texts, with disagreements resolved by consensus or third-party adjudication. Data will be extracted into a pre-piloted standardised form capturing study identifiers, registration and funding, design, randomisation and blinding, population characteristics (age stratum, sex, diabetes duration, baseline HbA1c, baseline TIR, prior therapy), intervention (platform, algorithm version, CGM, glucose target, active insulin time, meal-announcement requirement), comparator, intervention duration, and all primary, secondary, safety, and patient-reported outcomes (baseline, end, change, 95% CI). One reviewer will extract and the second will verify; study authors will be contacted (up to two attempts over four weeks) for missing or unclear data. Retraction status of every included record will be checked against the Retraction Watch database and Crossref before extraction. Crossover trials will use first-period data for the primary analysis.

Quality assessment / Risk of bias analysis Risk of bias will be assessed independently by two reviewers using the Cochrane Risk of Bias 2 tool (RoB 2) for randomised trials, across the five domains (randomisation process; deviations from intended interventions; missing outcome data; measurement of the outcome; selection of the reported result). AID trials are open-label by necessity, so the deviations domain is expected to carry the greatest risk for behaviour-mediated and patient-reported outcomes, whereas CGM-derived glycaemic outcomes are objective and at lower measurement risk. Manufacturer sponsorship and selective reporting will be tabulated. Certainty of evidence for the primary outcome will be rated with CINeMA (Confidence in Network Meta-Analysis), and with GRADE for network evidence for selected secondary outcomes. Disagreements will be resolved by discussion or a third reviewer.

Strategy of data synthesis A random-effects network meta-analysis will be performed to compare all AID systems and comparators on each outcome, synthesising direct and indirect evidence within a connected network. The effect measure will be the mean difference (continuous outcomes: TIR, TBR, TAR, HbA1c, mean glucose, CV) or the risk ratio (binary outcomes: severe hypoglycaemia, DKA), each with 95% confidence intervals, estimated relative to a common reference node (sensor-augmented pump). The frequentist NMA will be run in R using the netmeta package; between-study heterogeneity (tau-squared) will be estimated by REML, with I-squared and 95% prediction intervals reported. Transitivity will be assessed by tabulating effect modifiers (age stratum, baseline HbA1c, diabetes duration, comparator type, CGM device, trial duration, run-in use) across comparisons. Global inconsistency will be tested with the design-by-treatment interaction model and local inconsistency by node-splitting. Treatments will be ranked using SUCRA and P-scores with rankograms and a league table. If the network is disconnected or intransitive, a pairwise random-effects meta-analysis with subgroup analysis by platform will be performed instead. A network graph (nodes proportional to participants, edges to direct comparisons) will be presented. Comparison-adjusted funnel plots will assess publication bias where at least 10 trials inform a comparison.

Subgroup analysis Age stratum (very young 1–6 years vs children 7–11 years vs adolescents 12–18 years); baseline HbA1c (optimally controlled <8% vs suboptimally controlled ≥8%); prior therapy (prior MDI vs prior CSII/SAP); sex; trial duration (≥12 weeks vs shorter); system class (HCL vs AHCL vs FCL vs DIY vs bionic). Age-stratified NMAs will be run where at least three trials inform a stratum.

Sensitivity analysis Restriction to low-risk-of-bias and some-concerns studies; exclusion of manufacturer-funded trials; parallel-group-only (excluding crossover); first-period-only data for crossover trials; ≥12-week interventions only; exclusion of single-study network nodes; and the network with versus without DIY/open-source nodes and with versus without adult-inclusive connecting arms.

Language restriction No language restriction at the screening stage; non-English full texts will be translated where feasible.

Country(ies) involved Saudi Arabia.

Other relevant information Paediatric Endocrinology; Diabetes Technology; Clinical Pharmacy; Evidence Synthesis

Keywords type 1 diabetes; automated insulin delivery; artificial pancreas; hybrid closed loop; time in range; hypoglycaemia; children; adolescents; network.

Dissemination plans Peer-reviewed publication in a paediatric, diabetes-technology, or diabetology journal; open-access preferred. Findings may also be presented at relevant scientific meetings (e.g., ISPAD, ADA, EASD).

Contributions of each author
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Author 1 - Abdulrahman Alanazi - Conceived and designed the study, drafted the protocol, will lead data extraction and synthesis, and drafted the manuscript and final manuscript submission.
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