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Hybrid Closed-Loop Insulin Delivery in an Adolescent with Recurrent Diabetic Ketoacidosis: A Narrative Review of Technology, Adherence and Family Support

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Abstract

Adolescence is where type 1 diabetes control reliably deteriorates, and recurrent ketoacidosis in a teenager is rarely a problem of insulin pharmacology. Automated delivery removes some of the daily decisions. It does not remove the adolescent, the household, or the reasons the insulin was not given.

Objectives: *To review the published evidence on hybrid closed-loop insulin delivery in children and adolescents: what it achieves in glycaemic terms, what is known about its effect in those with the poorest control, what it asks of the family, and where the evidence stops.*

Material and Methods: *Narrative review of randomised and crossover trials, meta-analyses, registry analyses and psychosocial studies indexed in PubMed and the major diabetes and paediatric journals. No new patient data were generated; every estimate quoted is one published by the original investigators.*

Results: *Pooled across four randomised trials and 501 children and adolescents, of whom 323 were allocated to closed-loop therapy, time in the target range of 70 to 180 mg/dL improved by a weighted mean difference of 10.89 percentage points (95% CI 8.22 to 13.56), and participants were more likely to reach a glycated haemoglobin below 7 per cent (risk ratio 2.61, 95% CI 1.29 to 5.28). In very young children followed for 18 months, time in target rose 8.7 percentage points to 71 per cent with a fall in glycated haemoglobin of 0.4 per cent.*

Conclusion: *The glycaemic benefit is consistent, of a size that matters clinically, and reproduced across systems and age groups. What the trials do not establish is any effect on ketoacidosis, because trial populations were largely already in reasonable control and adolescents with recurrent ketoacidosis were generally not enrolled. The technology addresses the decisions; recurrent ketoacidosis usually reflects something else.*

Abbreviations: *CGM – Continuous Glucose Monitoring, DKA – Diabetic Ketoacidosis, HbA1c – Glycated Haemoglobin, HCL – Hybrid Closed-Loop, SAP – Sensor-Augmented Pump, TIR – Time in Range, WMD – Weighted Mean Difference.*

Keywords: *Type 1 Diabetes; Hybrid Closed-Loop; Adolescents; Diabetic Ketoacidosis; Family Support*

Introduction

Glycaemic control in type 1 diabetes deteriorates predictably during adolescence and recovers, partially, afterwards. International registry comparisons show the pattern across countries with very different baseline achievement, which suggests it is developmental rather than a failure of any particular health system [1,2]. Diabetic ketoacidosis in an established patient is the sharp end of that deterioration and is associated with insulin omission far more often than with device failure [3,4].

Hybrid closed-loop systems pair a continuous glucose sensor with an algorithm that modulates basal insulin delivery automatically, leaving meal boluses to the user. The premise is that removing most of the moment-to-moment decisions removes most of the opportunities to get them wrong [5,6].

The technology now has substantial randomised support in children and adolescents [7,8,9,10]. This review sets out what that evidence shows, what it does not address, and why an adolescent presenting with recurrent ketoacidosis sits partly outside it.

Material and Methods

Search strategy: PubMed and the archives of the major diabetes, endocrinology and paediatric journals were searched for studies of automated insulin delivery in young people. Search terms combined type 1 diabetes with hybrid closed-loop, automated insulin delivery, artificial pancreas, time in range, adolescent, ketoacidosis and adherence. Reference lists of consensus documents [11,12] were screened by hand for primary sources.

Eligibility: Studies were included if they compared automated insulin delivery with another modality in participants under 21, reported glycaemic or psychosocial outcomes with these systems, or characterised ketoacidosis and adherence in this age group. Trials in adults are cited where they establish the platform and are identified as such.

Data extraction and handling: Design, sample size, age range, comparator, baseline control and reported outcome were extracted as published. Baseline glycated haemoglobin and the trial entry criteria are reported alongside every efficacy figure, because the populations enrolled were mostly in fair control already and that bears directly on whether the results apply to a patient with recurrent ketoacidosis. No pooling or re-analysis was performed. Figures 1 to 4 and Tables 1 and 2 reproduce published values only. This is a narrative synthesis and was not registered as a systematic review.

Results

The pooled glycaemic effect: A meta-analysis of four randomised trials including 501 children and adolescents, of whom 323 were allocated to closed-loop therapy, found time in the target range of 70 to 180 mg/dL improved by a weighted mean difference of 10.89 percentage points (95% CI 8.22 to 13.56) against control therapies (Figure 1) [13]. Roughly eleven percentage points is around two and a half hours more each day within range, which is a clinically substantial difference rather than a statistical one.

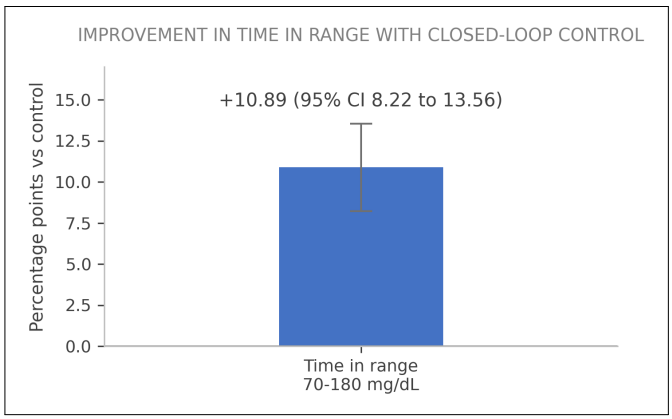

Figure 1: Improvement in time in range with hybrid closed-loop against control therapy, pooled across four randomised trials [13]

Reaching target: The same analysis found participants using closed-loop therapy more than twice as likely to achieve a glycated haemoglobin below 7 per cent (risk ratio 2.61, 95% CI 1.29 to 5.28) (Figure 2) [13]. The confidence interval is wide, reflecting the modest number of trials, but excludes no effect.

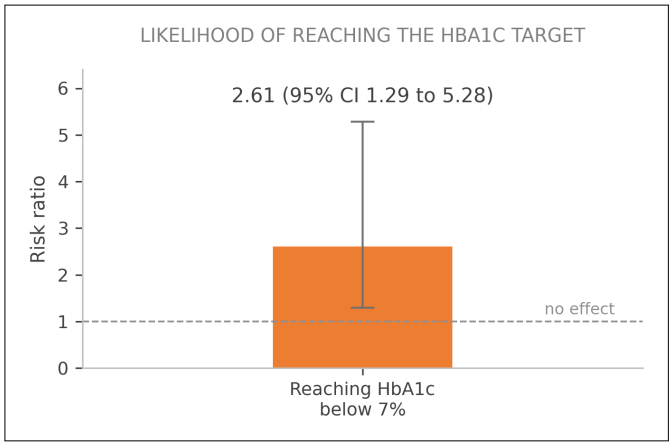

Figure 2: Likelihood of achieving glycated haemoglobin below 7 per cent with closed-loop therapy [13]

Durability and the youngest patients: Benefit is not confined to short trial periods or to older children. In very young children studied over 18 months, time in target rose by 8.7 percentage points to 71 per cent against sensor-augmented pump therapy, with a reduction in glycated haemoglobin of 0.4 per cent (Figure 3) [14,15,16]. Randomised trials of the Cambridge algorithm in participants aged 6 to 18 with baseline glycated haemoglobin around 8.2 per cent showed a lower value at six months in the closed-loop group [17], and trials of other systems in children aged 6 to 12 and in adolescents report the same direction [7,8,18], as do trials comparing activation schedules and advanced systems [33,35] and a wider meta-analysis including adults [34].

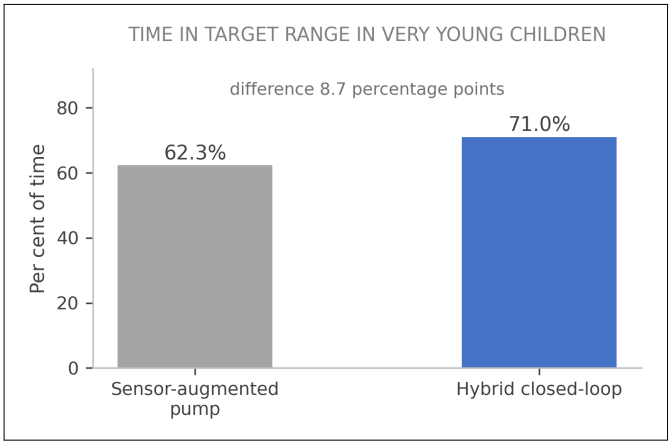

Figure 3: Time in target range over 18 months of hybrid closed-loop use in very young children [14]

The size of the evidence base: The pooled paediatric randomised evidence comprises four trials and 501 participants (Figure 4) [13]. That is a reasonable foundation for a device but a narrow one for extrapolation, and it matters most when considering populations the trials did not enrol.

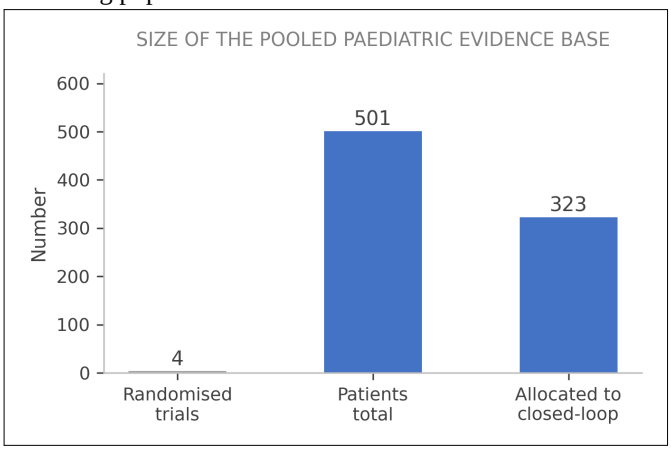

Figure 4: Size of the pooled randomised evidence base in children and adolescents [13]

Study	Design and cohort	Principal reported finding
Meta-analysis, 4 RCTs [13]	501 children and adolescents, 323 on HCL	TIR +10.89 pp (8.22-13.56); HbA1c <7% RR 2.61 (1.29-5.28)
Breton et al. 2020 [7]	RCT, children aged 6-13	Increased time in range over 16 weeks against sensor-augmented pump
Ware et al. 2022 [15]	RCT, very young children	Closed-loop superior to sensor-augmented pump therapy
18-month extension [14]	Very young children, single arm	TIR 71%, +8.7 pp; HbA1c -0.4%; benefit maintained
Boughton et al. 2022 [17]	RCT, aged 6-18, baseline HbA1c 8.2%	Lower HbA1c at 6 months with closed-loop
Australian RCT 2021 [19]	172 children and adolescents, 6 months	Glycaemic and psychosocial outcomes assessed together
Bergenstal et al. 2021 [18]	FLAIR, adolescents and young adults	Compared two closed-loop systems directly

Table 1: Principal studies reviewed, with the finding as reported by the original investigators

What the trials did not study: Entry criteria across these studies generally required established pump use, a glycated haemoglobin within a defined band, and a family able to complete training and study procedures [7,15,17]. The Cambridge trial enrolled participants with screening values between 7.0 and 10.0 per cent [17]. An adolescent presenting with a third episode of ketoacidosis in a year typically has a value well above that range, may not be using a pump, and is often not attending clinic. Almost none of the randomised evidence describes that patient.

Why ketoacidosis happens: Recurrent ketoacidosis in an established patient is predominantly a behavioural and social phenomenon rather than a technical one. Insulin omission is the dominant precipitant, and it is associated with psychological distress, disordered relationship with food, family conflict and socioeconomic adversity [3,4,20,21]. Diabetes distress and depressive symptoms are common in adolescence and track with control [22,23]. A pump that adjusts basal delivery cannot give a bolus that was never requested, and closed-loop systems still require the user to announce meals and to keep the infusion set and sensor in place [5,24].

What technology can and cannot displace: Trials reporting psychosocial outcomes alongside glycaemic ones generally find improvements in sleep, in parental fear of hypoglycaemia and in perceived burden, which are real gains for households organised around overnight glucose checks [19,25,26]. Device discontinuation is nonetheless common in adolescence, driven by alarm fatigue, body image, the visibility of worn devices and the effort of carbohydrate counting [27,28,29]. Structured education, family-based intervention and attention to distress remain necessary alongside the hardware rather than instead of it [30,31,32].

Question	What the evidence shows	Caution
Does it improve time in range?	Yes, by about 11 percentage points	Pooled from four trials, 501 participants [13]
Does it lower HbA1c?	Yes; more reach below 7%	RR 2.61 with a wide interval [13]
Does benefit persist?	Maintained to 18 months in young children	Single-arm extension [14]
Does it prevent ketoacidosis?	Not established	Trials were not powered or populated for it [7,15,17]
Does it reduce family burden?	Reported improvements in sleep and fear	Secondary outcomes, unblinded [19,25]
Will an adolescent keep using it?	Discontinuation is common	Alarm fatigue, body image, effort [27,28]

Table 2: Practical questions about closed-loop therapy and what the current evidence supports

Discussion

The glycaemic case is settled. Automated insulin delivery improves time in range by around eleven percentage points and roughly doubles the chance of reaching a glycated haemoglobin

below 7 per cent, and it does so consistently across systems, age groups and trial designs [13,14,17,18]. For a technology, that is about as clean a result as paediatric diabetes has produced. Any child or adolescent who can access one of these systems should be offered it.

The difficulty is that the question posed by a teenager with recurrent ketoacidosis is not the question the trials answered. Those studies enrolled young people already using pumps, already within a defined glycaemic band, and supported by families able to complete study procedures [7,15,17]. Recurrent ketoacidosis in an established patient is associated with insulin omission, and omission is associated with distress, conflict and adversity rather than with the arithmetic of basal rates [3,4,20]. Extrapolating an eleven-point improvement in time in range to that patient assumes the mechanism of their poor control is the one the device addresses.

There is a reasonable counter-argument, and it should be stated. Automation reduces the number of daily actions required, and fewer required actions may mean fewer omitted ones. It also reduces the visibility of diabetes work in the household, which may lower the conflict that drives some omission. Both are plausible; neither has been demonstrated in the population that matters. What would settle it is a trial enrolling adolescents with elevated glycated haemoglobin and a history of ketoacidosis, with ketoacidosis as an endpoint. That trial has not been done, which is understandable, since it is the hardest population to recruit and retain.

The practical implication is not to withhold the technology but to be clear about what it is expected to do. Offering a closed-loop system to an adolescent whose insulin is not being given, without addressing why it is not being given, risks two failures: the ketoacidosis recurs, and the family concludes that the best available technology did not work for them. The psychosocial and family-directed interventions in this literature are less impressive individually than the device trials, and are more likely to be the active ingredient in this specific presentation [30,31,32].

Study limitations

The limitations belong to the underlying literature. The pooled paediatric evidence is four randomised trials and 501 participants, with heterogeneity in systems, comparators and duration [13]. Entry criteria excluded the poorest control and required existing pump use, so the trials are not representative of the population with recurrent ketoacidosis [7,15,17]. Blinding is impossible, and psychosocial outcomes are particularly vulnerable to that [19,25]. Follow-up rarely exceeds six months, with one 18-month single-arm extension [14]. Ketoacidosis is too infrequent for these sample sizes to assess, so its absence from the results is uninformative rather than reassuring. Trial participants receive intensive support that routine care does not provide, and real-world discontinuation rates are higher than trial completion rates suggest [27,28]. And the evidence comes almost entirely from high-income settings with reimbursed device access [1,2].

Conclusion

Hybrid closed-loop delivery is the most effective glycaemic intervention available to children and adolescents with type 1 diabetes, improving time in range by roughly eleven percentage points and doubling the likelihood of reaching target. That case is made. What has not been shown is that it prevents recurrent ketoacidosis in adolescents, and the reason is that the trials enrolled young people who were already doing reasonably well. For a teenager admitted for the third time in a year, the technology is worth offering and is unlikely to be sufficient on its own, because the insulin that was not delivered was usually not delivered for reasons an algorithm cannot reach.

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Conflict of Interest

The authors declare no competing interests.

Ethics Statement

This article reviews previously published studies only. No new patient data were collected and no participants were recruited, so ethical approval was not required.

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