Cambridge Hybrid Closed-Loop Use in Very Young Children With Type 1 Diabetes: Parental Expectancies During Long-Term Home Use

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Running title: Parental Expectancies During Long-Term HCL Use

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Novelty Statement

- **What is already known?**

  Hybrid closed-loop systems improve glycaemic outcomes in young children with type 1 diabetes, but less is known about how parental trust and expectations evolve during sustained use.

- **What this study has found?**

  Glycaemic benefits were achieved early and sustained, while parental trust and positive expectancies increased gradually over time, particularly during extended home use.

- **What are the implications?**

  Parental trust appears to develop through experience-dependent adaptation, shaped by sustained use alongside stable glycaemic outcomes, and is essential for sustained

engagement with automated insulin delivery, underscoring the need for ongoing clinical support as trust develops over time.

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Abstract

Aims To examine parental expectancies, long-term satisfaction and trust in automated insulin delivery (AID) during extended home use of CamAPS FX hybrid closed-loop (HCL) in very young children with type 1 diabetes (T1D).

Methods Parents of 65 young children with T1D participated in a multinational randomised crossover trial and an 18-month HCL extension phase. Glycaemic outcomes (HbA1c) were recorded, and parental expectancies were assessed using the INSPIRE questionnaire, which evaluates parents' perceptions and expectations of AID systems. Assessments were conducted at baseline, during the HCL clinical trial phase, and after 18 months extension phase in the home environment. Linear mixed models were used to analyse outcomes across time.

Results Initial HCL use improved HbA1c (baseline: 56.03 ± 7.31 mmol/mol [7.3%] vs. clinical trial: 50.78 ± 6.90 [6.8%]; $p < .001$), with benefits sustained over the 18-month extension period (49.00 ± 6.63 [6.8%]; $p = .45$). Parental expectancies did not change during clinical trial (baseline: 44.78 ± 34.70 vs. clinical trial: 42.10 ± 38.11; $p = .629$, $d = 0.05$) but increased markedly after 18 months of home use (89.83 ± 9.35; $p < .001$, $d = 1.14$).

Conclusions Prolonged HCL use supports sustained glycaemic benefits while parental trust and positive expectancies increase over time. These findings suggest that trust develops through experience-dependent adaptation shaped by the combination of stable glycaemic outcomes and sustained use, and is important for continued engagement with automated insulin delivery.

Clinical trial registration: NCT03784027 (clinicaltrials.gov)

Keywords: type 1 diabetes; young children; hybrid closed-loop; automated insulin delivery; parental expectancies; psychological impact

Introduction

Type 1 diabetes (T1D) management in young children is challenging. Early childhood represents a period of heightened biological vulnerability, and poor glycaemic control has been associated with adverse neurocognitive outcomes and increased long-term cardiometabolic risk, underscoring the importance of stable glucose control from diagnosis onward [1–4]. Young children are also fully dependent on caregivers for diabetes management, increasing parental responsibility and potential impact on family well-being [5–9]. As a result, strategies that reduce glycaemic variability while alleviating caregiver demands are particularly relevant in this age group.

Automated insulin delivery (AID) systems have demonstrated consistent metabolic benefits across paediatric and adult populations, including improved time in range and reduced hypoglycemia[10]. Beyond metabolic outcomes, AID use has also been associated with improvements in patient- and family-reported outcomes [11,12]. In paediatric populations, multiple clinical trials and real-world studies have established the safety and efficacy of hybrid closed-loop (HCL) therapy [13,14]. Among these, the KidsAP study - a multinational randomised crossover trial - demonstrated significant metabolic advantages of the CamAPS FX HCL system in children as young as one year compared with sensor-augmented pump therapy [15]. These benefits, including increased time in target range and lower HbA1c, were sustained during continued use for up to 18 months beyond the initial research setting [16].

In caregivers of very young children, psychosocial outcomes of HCL use have been reported [17,18]. Previous KidsAP analyses demonstrated reductions in fear of hypoglycemia and

improvements in parental well-being [19]. However, how parents' expectations, confidence, and trust in AID systems change during prolonged, real-world use remains unclear.

Parental satisfaction with AID, depends not only on glycemic benefits but also on trust in safety, reliability and willingness to transfer elements of diabetes management to an automated system. Studies suggest that experiences with AID evolve over time through ongoing adaptation and negotiation of control, with both benefits and challenges emerging [20–22]. Consistent with this, interview data from the KidsAP study revealed that, while parents gained confidence in remote monitoring during the clinical trial phase, constant access to glucose data could also limit opportunities for respite from monitoring responsibilities [23].

Despite increasing use of AID in young children, little is known about how parental expectancies and confidence in these systems change during sustained (home) use. To address this gap, we examined parental expectancies regarding AID during the KidsAP trial and throughout an extension phase beyond the research setting in which HCL was continued.

Methods

This work is embedded in the KidsAP02 study, a multinational, multicentre investigation of the HCL insulin delivery system in very young children with T1D. The study comprised two phases. The initial phase, conducted in a research setting, consisted of an open-label, randomised, two-period crossover trial (16 weeks per arm separated by a 1-4 week washout period) comparing HCL with sensor-augmented pump (SAP) therapy [15]. This was followed by an optional, single-arm extension phase in which participants continued HCL use in a free-living, home setting for an additional 18 months [16].

A total of 65 children aged 1-7 years with T1D for at least 6 months and using insulin pump therapy for a minimum of 3 months were included in the present analysis. Exclusion criteria for participation included: (i) current use of closed-loop therapy; (ii) glycated hemoglobin (HbA1c) >11% (97 mmol/mol); and (iii) comorbid conditions affecting metabolic control.

Eligible participants were randomly assigned to one of two treatment orders: SAP-HCL or HCL-SAP. All families completed baseline assessments relevant to the present study. One participant withdrew during the randomised trial phase after completing the SAP arm but before crossover to HCL. Follow-up data were unavailable for a subset of participants due to withdrawal or transition to another treatment system. Availability of INSPIRE questionnaire data across study phases was documented. Adverse events, including severe hypoglycaemia and diabetic ketoacidosis, were prospectively monitored during both the randomised trial and extension phases in accordance with study protocols. Occurrence of adverse events is summarised in the Results section.

For the present analyses, metabolic and psychosocial outcomes were analysed using all available data from participants who completed the KidsAP clinical trial, excluding one participating centre (Germany; N=10) that did not collect psychosocial data during follow-up. Glycaemic outcomes (HbA1c) were summarised for all participants with available metabolic data at each study phase. Parental expectancies were analysed using INSPIRE data from participants

with available questionnaire data at each corresponding time point. Metabolic and psychosocial outcomes were analysed independently[1].

Closed-loop insulin delivery was provided using the CamAPS FX system, running on an unlocked Android smartphone and wirelessly linked to an insulin pump and continuous glucose monitoring system. The algorithm was initialised using total daily insulin dose and body weight and applied adaptive learning to adjust insulin delivery based on daily glucose patterns, meal information, and insulin action. Caregivers were able to administer boluses via the smartphone application and remotely view glucose data using a follower function with real-time alerts. A detailed technical description of the CamAPS FX system and algorithm has been reported previously [16,19].

Measures

Glycaemic control. Glycaemic control was assessed using glycated haemoglobin (HbA1c), which was measured repeatedly throughout the study. For the purposes of the present analysis, HbA1c values at baseline, at the end of the randomised trial HCL phase, and after 18 months of HCL use during the extension phase were analysed. Analyses were performed using methods aligned with the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) and standardised according to the National Glycohemoglobin Standardisation Program (NGSP) [24,25], ensuring cross-centre comparability.

[1] The sample size reported in the present study differs from that in previous publications from the KidsAP trial, as analyses were restricted to participants with available INSPIRE data and excluded centres where psychosocial measures were not collected. In addition, differences in data availability across centres during the extension phase mean that the present analytic sample does not fully correspond to the cohort included in prior reports of longer-term safety and efficacy of hybrid closed-loop therapy in very young children with type 1 diabetes (Ware J, Allen JM, Boughton CK, et al. Diabetes Care. 2024;47(12):2189–2195).

Parental expectancies. Parental expectancies regarding AID were assessed using the INSPIRE (INsulin Dosing Systems: Perceptions, Ideas, Reflections and Expectations) questionnaire, a validated patient-reported outcome instrument developed to capture the psychosocial impact of hybrid closed-loop and related AID systems on people with type 1 diabetes and their caregivers [26]. The INSPIRE measure is qualified by the U.S. Food and Drug Administration as a Medical Device Development Tool (clinical outcome assessment; Q191073)[27]. The parent version was administered at baseline, during the randomised crossover trial after each treatment arm and at the conclusion of the 18-month extension phase.

The INSPIRE instrument evaluates parents' perceptions, beliefs, and expectations about AID, including trust in the technology, perceived safety and efficacy, and anticipated effects on family life and caregiving burden. Items are rated on Likert-type response scales, with higher scores indicating more positive expectancies. Prior psychometric evaluations have demonstrated strong internal consistency, construct validity, and responsiveness to change, supporting its use as a sensitive measure of caregiver attitudes in longitudinal studies [28].

Statistical analyses

Linear mixed-effects models were used to evaluate changes in outcomes across three study time points (baseline, end of the randomised hybrid closed-loop phase, and end of the 18-month extension). Models included participant as a random intercept to account for repeated measures within individuals, and time as a categorical fixed effect. Pre-specified pairwise contrasts compared (i) baseline versus the trial hybrid closed-loop phase and (ii) trial hybrid closed-loop versus the 18-month extension phase. Multiplicity was addressed using a Bonferroni

correction, with the significance threshold adjusted according to the number of planned comparisons (α = 0.05 divided by three).

Parameter estimates were obtained using maximum likelihood estimation, which provides unbiased inference under a missing-at-random assumption. All available data were included; no ad-hoc imputation was performed. Analyses were performed using IBM SPSS Statistics, version 29 [29]

Results

Caregivers of 64 children with T1D aged 1-7 years were included in the present analysis. Forty children were male (62.5%) and 24 were female (37.5%). Age at diagnosis was 0-<2 years in 18 children (28.1%), 2-3 years in 37 children (57.8%), 4-5 years in 8 children (12.5%), and 6-7 years in 1 child (1.6%). Thirty-four participants (53.1%) were randomised to the HCL-SAP treatment sequence and 30 (46.9%) to the SAP-HCL sequence. Of the 64 participants, 53 continued into the extension phase. During the extension phase, adverse events occurred in 5 of 53 participants (9.4%), while no adverse events were reported in the remaining 48 participants (90.6%).

INSPIRE questionnaire data were available for 63/64 participants at baseline. During the randomised trial phase, INSPIRE data were missing for three participants, and during the extension phase for 12 participants. Baseline characteristics and psychosocial outcomes were compared between families who entered the extension phase and those who did not, with no significant differences observed (all $p > 0.05$). Rates of adverse events did not differ between groups; however, a higher proportion of boys than girls did not continue into the extension phase ($p = 0.008$).

Glycemic Control (HbA1c)

Descriptive statistics, including medians, interquartile ranges, and model-based mean differences with 95% confidence intervals, are summarised in Table 1. HbA1c improved significantly from baseline to the end of the clinical HCL phase, with a significant overall effect of time ($F(2,180) = 18.49$, $p < 0.001$ for HbA1c mmol and $F(2,180) = 18.75$, $p < 0.001$ for HbA1c %). Glycemic control was sustained during the extension phase, with no significant change between the end of the clinical HCL phase and 18 months of continued HCL use.

-Insert Table 1 around here-

Parental Expectancies (INSPIRE)

Descriptive and model-based INSPIRE outcomes, including medians, interquartile ranges, and mean differences with 95% confidence intervals, are summarised in Table 2. Parental expectancies (INSPIRE scores) regarding AID did not change significantly between baseline and the end of the clinical HCL phase. In contrast, INSPIRE scores increased markedly after 18 months of continued HCL use during the extension phase, resulting in a significant overall effect of time ($F(2,174) = 41.04$, $p < 0.001$).

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Discussion

In this multinational cohort of very young children with T1D, prolonged use of a HCL was associated with sustained improvements in glycemic control and a marked increase in parental expectancies regarding AID. While parental expectancies did not change during the initial clinical trial phase, substantial gains were observed after extended home use, indicating that trust in and perceived benefits of AID develop over time through continued real-world experience.

These findings complement previous KidsAP reports demonstrating short-term psychosocial benefits of HCL, as well as durable metabolic benefits during extended HCL use in real-world settings, indicating that glycemic benefits are sustained across participating centres despite differences in data availability [16,19] . Whereas earlier work focused on clinical efficacy and short-term caregiver reported outcomes under controlled or early extension conditions, the present study extends this evidence by showing that parental confidence and positive expectancies towards AID continue to evolve over time, beyond the research setting. This distinction is clinically relevant, as sustained engagement with diabetes technology depends not only on metabolic effectiveness but also on long-term acceptability, perceived safety, and the development of parental trust through sustained use and stable outcomes over time.

The observed pattern of stable glycaemic outcomes alongside increasing parental confidence highlights the importance of experience-dependent adaptation to automated systems. Rather than being driven by glycaemic outcomes or duration of use alone, our findings suggest that parental trust emerges through the combination of sustained use and consistent metabolic outcomes over time. For parents of very young children, transferring elements of diabetes management to an algorithm represents a substantial shift in responsibility and control. Our findings suggest that, as families gain familiarity with HCL systems and experience consistent metabolic outcomes over time, confidence in system reliability and safety increases, potentially reducing the cognitive and emotional burden of ongoing diabetes management. This process may be critical for enabling sustained engagement with automated insulin delivery in early childhood.

Strengths of this study include the longitudinal design, extended follow-up duration, multinational setting, and the use of INSPIRE, an FDA-qualified patient-reported outcome

measure specifically developed to assess perceptions and expectations of AID. Limitations include the voluntary nature of the extension phase, which may introduce selection bias; however, INSPIRE scores did not differ between baseline and the end of the randomised clinical HCL phase, suggesting that the observed increase in parental expectancies was unlikely to be attributable to pre-existing differences among families who continued participation. In addition, parental expectancies were assessed via self-report and may be influenced by contextual factors not directly measured. Together, these findings underscore the importance of parental trust as a key factor in the sustained use of automated insulin delivery, highlighting the need to support families as this trust develops over time.

Author Contributions (CRediT)

C.d.B., J.W., J.M.A., C.K.B., M.E.W., A.T., F.M.C., E.F.-R., S.E.H., T.M.K., B.R.-M., and R.H. codesigned the study. C.d.B., A.T., F.M.C., E.F.-R., S.E.H., T.M.K., and B.R.-M. are the lead clinical investigators. C.d.B., J.W., J.M.A., C.K.B., M.E.W., S.H., F.M.C., E.F.-R., S.E.H., T.M.K., B.R.-M., and M.T. screened and enrolled participants, provided patient care, and/or took study samples. A.V., I.M.P.C., C.d.B., conceptualised the specific study reported in this manuscript. I.M.P.C. and A.V. carried out and supported the data analysis, including the statistical analyses and A.V., I.M.P.C., C.d.B., were involved in the interpretation of the results. A.V. and I.M.P.C. wrote the manuscript and the co-authors critically reviewed and edited the document.

The authors submit this Original Article on behalf and with the approval of the KidsAp consortium.

Statements and Declarations

Ethical Considerations

The study protocol was reviewed and approved by national and local research ethics committees in all participating countries: the Cambridge East Research Ethics Committee (UK), the Ethics Committee of the University of Innsbruck (Austria), the Ethics Committee of the University of Vienna (Austria), the Ethics Committee of the University of Graz (Austria), the Ethics Committee of the Medical Faculty of the University of Leipzig (Germany), and the Comité National d'Éthique de Recherche (Luxembourg). Written informed consent was obtained from parents or legal guardians of all participants, with assent obtained from children.

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Data availability

The data underlying this study are subject to data sharing agreements within the KidsAP consortium and are not publicly available. Requests for data access may be directed to the

corresponding author and will be considered in accordance with institutional and regulatory requirements (Mauras, Buckingham, White, et al., 2021).

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Table 1: Descriptive statistics for glycemic control (HbA1c) and comparisons of mean differences over time

	Baseline (N=64) Mean ± SD; Median (IQR)	**HCL trial (N=63)** Mean ± SD; Median (IQR)	**HCL extension (N=53)** Mean ± SD; Median (IQR)	**Mean difference (95% CI) baseline vs. HCL trial**	**Mean difference (95% CI) baseline vs. HCL extension**	**Mean difference (95% CI) HCL trial vs. HCL extension**
HbA1c (mmol/mol)	56.03 ± 7.31; 56.00 (51.00 - 60.75)	50.78 ± 6.90; 51.00 (45.00 – 56.00)	49.00 ± 6.63; 50.00 (44.50 - 52.00)	−5.25 (−8.08 - −2.43)[a]	−7.03 (−9.99 - −4.07)[a]	−1.78 (−4.75 – 1.19)[b]
HbA1c (%)	7.28 ± 0.66; 7.30 (6.80 - 7.68)	6.78 ± 0.64; 6.80 (6.30 - 7.30)	6.63 ± 0.49; 6.70 (6.25 – 6.90)	−0.50 (−0.71 - −0.28)[a]	−0.64 (−0.86 - −0.42)[a]	−0.15 (−0.37 - 0.08)[c]

[a]p<.001, [b]p=.450, [c]p=.193

Table 2: Descriptive statistics of parental expectancies (INPSIRE score) and comparisons of mean differences over time

	Baseline (N=63) Mean ± SD; Median (IQR)	**CL trial (N=60)** Mean ± SD; Median (IQR)	**CL extension (N=51)** Mean ± SD; Median (IQR)	**Mean difference (95% CI) vs baseline vs. HCL trial**	**Mean difference (95% CI) baseline vs HCL extension**	**Mean difference (95% CI) HCL trial vs HCL extension**
INSPIRE score	44.78 ± 34.70; 31.58 (15.79 - 80.26)	42.10 ± 38.11; 23.69 (5.92 - 83.55)	89.83 ± 9.35; 92.11 (84.21 - 98.68)	-2.68 (−16.10 – 1073)[a]	45.05 (31.04 - 59.06)[b]	47.74 (36.20 - 59.27)[b]

[a]*p*=.629; [b]*p*<.001