

International Society for Pediatric and Adolescent Diabetes Clinical Practice Consensus Guidelines 2024: Diabetes Technologies – Insulin Delivery

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Summary of What Is New or Different

This chapter focuses on insulin pump therapy, with a greater emphasis on glucose-responsive integrated technology that is feasible with the use of automated insulin delivery (AID) systems. The chapter also includes connected insulin pens and insulin pump therapy without AID functionality. As behavioral, psychosocial, and educational considerations of insulin delivery devices are a central part of diabetes self-management and use of insulin delivery devices, these topics are also addressed. Updates and changes to previous recommendations include the following:

1. Additional details on automated insulin delivery (AID) incorporating data from clinical trials complemented by real-world evidence.
2. Additional focus and details that delineate the potential benefits of these systems with new data for youth of all ages, from preschoolers to young adults.
3. New data regarding insulin pump therapy that does not involve AID (non-AID).
4. An emphasis on approaches to optimize outcomes for all forms of insulin delivery devices, including insulin pump therapy as well as behavioral, psychosocial, and educational considerations for optimizing the daily use of these devices.
5. A summary of the growing evidence of the technology benefits beyond glycemic outcomes including person-reported outcomes and experience measures and impacts on the quality of life of youth and their caregivers.

Keywords

Pump · Automated insulin delivery · Children · Diabetes

Abstract

The International Society for Pediatric and Adolescent Diabetes (ISPAD) guidelines represent a rich repository that serves as the only comprehensive set of clinical recommendations for children, adolescents, and young adults living with diabetes worldwide. This chapter builds on the 2022 ISPAD guidelines, and summarizes recent advances in the technology behind insulin administration, with special emphasis on insulin pump therapy, especially on glucose-responsive integrated technology that is feasible with the use of automated insulin delivery (AID) systems in children and adolescents.

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List of Abbreviations

AID:	automated insulin delivery
ASPIRE study:	Automation to Simulate Pancreatic Insulin Response
ISPAD:	International Society for Pediatric and Adolescent Diabetes
BGM:	blood glucose monitoring
CGM:	continuous glucose monitoring
CSII:	continuous subcutaneous insulin infusion
DCCT:	Diabetes Control and Complications Trial
DIY:	do it yourself
DKA:	diabetic ketoacidosis
DPV:	Diabetes Patienten Verlaufsdokumentation (Diabetes Prospective Follow-up) a registry from Germany
EDIC study:	Epidemiology of Diabetes Interventions and Complications study (extension of DCCT)
GMI:	glucose management index
HbA1c:	glycated hemoglobin
HCL:	hybrid closed loop
LGS:	low glucose suspension
MDI:	multiple daily injections
PGLM:	predictive glucose low management
PLGS:	predictive low glucose suspension
PWD:	people with diabetes
RCT:	randomized controlled trial
SAP:	sensor augmented pump
SMBG:	self-monitoring of blood glucose
SH:	severe hypoglycemia
STAR study:	Sensor-augmented pump Therapy for A1c Reduction study
TAR:	time above range
TBR:	time below range
TIR:	time in range

T1D:	type 1 diabetes
T1DX:	Type 1 diabetes Exchange (large registry based in the USA).

Introduction

- It is recommended that youth be offered the most advanced insulin delivery technology that is available, accessible and acceptable for them. [A]
- System choice should be based on individual needs and preferences. [A]

In 2018, the International Society for Pediatric and Adolescent Diabetes (ISPAD) created the first consensus guidelines on Diabetes Technology [1]. In 2022, this guideline was divided into two intertwined chapters that continue for this update. Information on Insulin Delivery is covered in the current chapter, and Glucose Monitoring with a discussion of both blood glucose monitoring (BGM) and continuous glucose monitoring (CGM) presented in ISPAD 2024 Consensus Guidelines Chapter on Diabetes technologies: glucose monitoring [2]. This chapter reviews insulin delivery technologies in children, adolescents, and young adults with a focus on practical advice and clinical implementation.

Insulin pump use continues to increase in many diabetes practices. Despite this, disparities persist between the historically most advantaged and disadvantaged groups, even in locales where technology is widely available [3]. Inconsistencies in the availability, cost reimbursement and/or insurance coverage for diabetes technologies contribute to disparities regionally, nationally, and across health systems that are challenging for individuals with low economic status, lower educational attainment, and in lower resource settings [4].

Recognition of these disparities becomes even more important as the systems become more autonomous. Eligibility criteria for treatment based on glycated hemoglobin (HbA1c) value, ability to count carbohydrates, and other self-management factors might exclude users that would benefit most as people with higher baseline HbA1c experience greater glycemic improvements [5].

While diabetes care has traditionally centered on achieving consensus guideline targets for HbA1c, there has been greater adoption of time in range (TIR) and other glucose metrics as CGM-derived or “technology-derived” metrics to guide clinical decision-making and define treatment goals [6, 7]. This greater emphasis on

diabetes technologies has driven important research evaluating how the potential burdens of diabetes technologies can be mitigated by the benefits they may provide, how to set realistic expectations for new device-based therapies to ensure transitions to advanced technologies are associated with shared decision-making alongside appropriate device training.

Aligning with WHO's availability, accessibility, acceptability, and quality "right to health" framework, this guideline mirrors that belief in Recommendations regarding insulin delivery technologies." As all technology, of course, should be tested properly before being used in children, a "Q" for quality is a necessity [8].

Insulin Pumps

Recommendations

- Insulin pump therapy is recommended and appropriate for youth with diabetes, regardless of age [A], baseline glycemia [A], and type 1 diabetes (T1D) duration. [B]
- Infusion set failures may occur with any insulin pump therapy and must be recognized promptly to avoid diabetic ketoacidosis (DKA). [B]

Insulin pump therapy as a platform for insulin delivery provides the basis for more advanced glucose-responsive insulin delivery technologies. While there is a clear benefit to using more advanced technologies, it is also recognized that these systems are currently not available or affordable for all people living with diabetes or do not fit their personal preferences.

The Evidence for Insulin Pump Therapy

Diabetes registry data have demonstrated increased uptake of pump therapy over time in youth with T1D in the USA [9] and Germany [10]. During the periods evaluated, HbA1c trended down in all age groups, except preschoolers (0.5–<7 years old), while TIR increased by ~5 percentage points in all age groups [11]. Additional comparisons of large diabetes registries with nearly 55,000 pediatric people with diabetes (PWD) reported pump use was associated with lower mean HbA1c (pump $8.0 \pm 1.2\%$ [64 ± 14 mmol/mol] vs. injection: $8.5 \pm 1.7\%$ [69 ± 17 mmol/mol], $p < 0.001$) [12]. Similar data from an international network of reference centers reported that pump use was associated with lower HbA1c and daily insulin dose compared to multiple daily injections (MDI) [13]. One prospective exami-

nation of nearly 1,000 youth on either pump or MDI therapy found lower retinopathy and peripheral nerve abnormality rates in the insulin pump-treated group despite similar HbA1c values [14]. Meta-analyses have shown reductions in mean HbA1c [15–17], decreased severe hypoglycemia (SH) rates [17], and a reduction of total daily insulin doses with insulin pump therapy [15, 16]. The long-term benefits of pump therapy have been demonstrated with sustained improvement in glycemia [18–20]. Further data have also shown pump therapy is associated with lower rates of SH and DKA than MDI [20–23].

Baseline glycemia should not preclude insulin pump therapy as those with the highest HbA1c levels (>9.0%) experience the largest decline in HbA1c once pump therapy is initiated [24]. Furthermore, no minimum T1D duration is required before transitioning to this mode of insulin delivery as insulin pump therapy, even from the time of diagnosis, is successful in achieving glycemic targets [25–28]. While availability, costs, and reimbursement or insurance coverage for insulin pumps impact the use of this technology [12, 29], a recent cost-effectiveness analysis performed using IQVIA CORE Diabetes model in China found that pump therapy use equated to lower total lifetime costs when compared to MDI, related to expected delays in the development of diabetes complications [30].

Insulin Pump Therapy: Barriers to Adoption of and Reasons for Discontinuation

Wide variations in the mode of insulin delivery prescribed exist among clinical centers, even those with similar populations [29]. Indeed, US data highlight variability in the frequency of pump adoption related to race and ethnicity (e.g., non-Hispanic White individuals) and socioeconomic status (private or public health insurance) [31]. The Diabetes Patienten Verlaufsdokumentation (DPV) registry also observed an association with sex and migration background in Germany [32]. Variability in pump use between centers may be in part explained by healthcare professional (HCP) preferences, which impact the proportion of people using pumps in a given center [33–39]. In some countries, non-coverage, or incomplete coverage of pump therapy by the health care/insurance system also drives low insulin pump adoption [12, 29].

Besides HCP preferences, barriers to technology among PWDs also impact individual use of technology. Potential barriers to pump use identified include concerns regarding the device's physical footprint of the device on the body, interference of the device in everyday

activities, therapeutic effectiveness, and, to a lesser extent, the financial burdens it may cause [40].

Pump therapy discontinuation is uncommon, with the DPV registry noting a low attrition of just 4% of pump users [41]. Adolescents aged 10–15 years had the highest rate of pump discontinuation, and those who discontinued were more likely to be female [41]. Similar results were noted in a US-based registry analysis, with reasons for discontinuation including problems with wearability (57%), personal dislike or feelings of anxiety toward the pump (44%), and difficulties with glycemic outcomes (30%) [42]. Additionally, higher levels of depressive symptoms have also been reported to precede cessation of pump use [43].

Early studies have documented a 2 to 5-fold higher risk of DKA among individuals using pump therapy. However, recent studies have shown an attenuation in this risk [44, 45]. Therefore, education on the risk of DKA and strategies to manage persistent hyperglycemia are crucial in preventing these complications. The future feasibility of using subcutaneous continuous ketone monitors offers a potential solution to enhance the management of ketone levels [46].

Complications of Insulin Pump Therapy: Infusion Sets, Lipodystrophy, and Skin Irritation

Insulin pump-related adverse events are relatively common, affecting 40–68% of pump users. They include infusion set failures, pump malfunctions and problems with alarms [47–51]. There is no conclusive evidence regarding the optimal choice between steel cannulas and flexible teflon catheters, as well as the suitability of specific infusion sets based on the user's age or individual characteristics. As steel cannulas are less likely to kink or dislodge, they may be ideal for the youngest children. However, the major concern regardless of infusion set type is the potential for full or partial occlusion or dislodgement, thereby interrupting insulin delivery and increasing the risk of DKA. Strategies for identifying failed infusion sets include fault detection algorithms that utilize sensor glucose levels and insulin delivery data to predict potential failures have been described [52, 53].

Lipohypertrophy, or local fat accumulation at the site of insulin administration, is another frequently encountered issue with pump therapy [54]. Lipodystrophy, fat loss at the site of prior insulin infusion sites, is less common and more observed in those with multiple autoimmune conditions [55]. Both conditions are categorized as lipodystrophy. A cross-sectional study of children and adolescents with T1D demonstrated a

greater risk of lipodystrophy in those with higher concomitant circulating insulin autoantibody titers [56]. Lipodystrophy can impact how insulin is absorbed and thus lead to deterioration in glycemia. To avoid lipohypertrophy, it is recommended that infusion set placement be rotated with every new insertion. Once detected, the affected area should be avoided to allow the tissue to heal, which often takes several months. There are reports on the use of special insulin products being beneficial to lipodystrophy [57].

Finally, skin irritation is frequently observed after repeated exposure to adhesives from medical devices. A study involving comprehensive dermatological examinations identified localized eczematous reactions at the site of infusion cannula insertion in 14% of young individuals with diabetes [58]. Additionally, a survey of 143 youth documented that nearly half of the cohort reported non-specific eczema [59]. For more information on skin related issues, please refer to ISPAD 2022 Consensus Guidelines Chapter 19 on “other complications and associated conditions in children and adolescents with type 1 diabetes” [60].

Practical Considerations with Pump Therapy

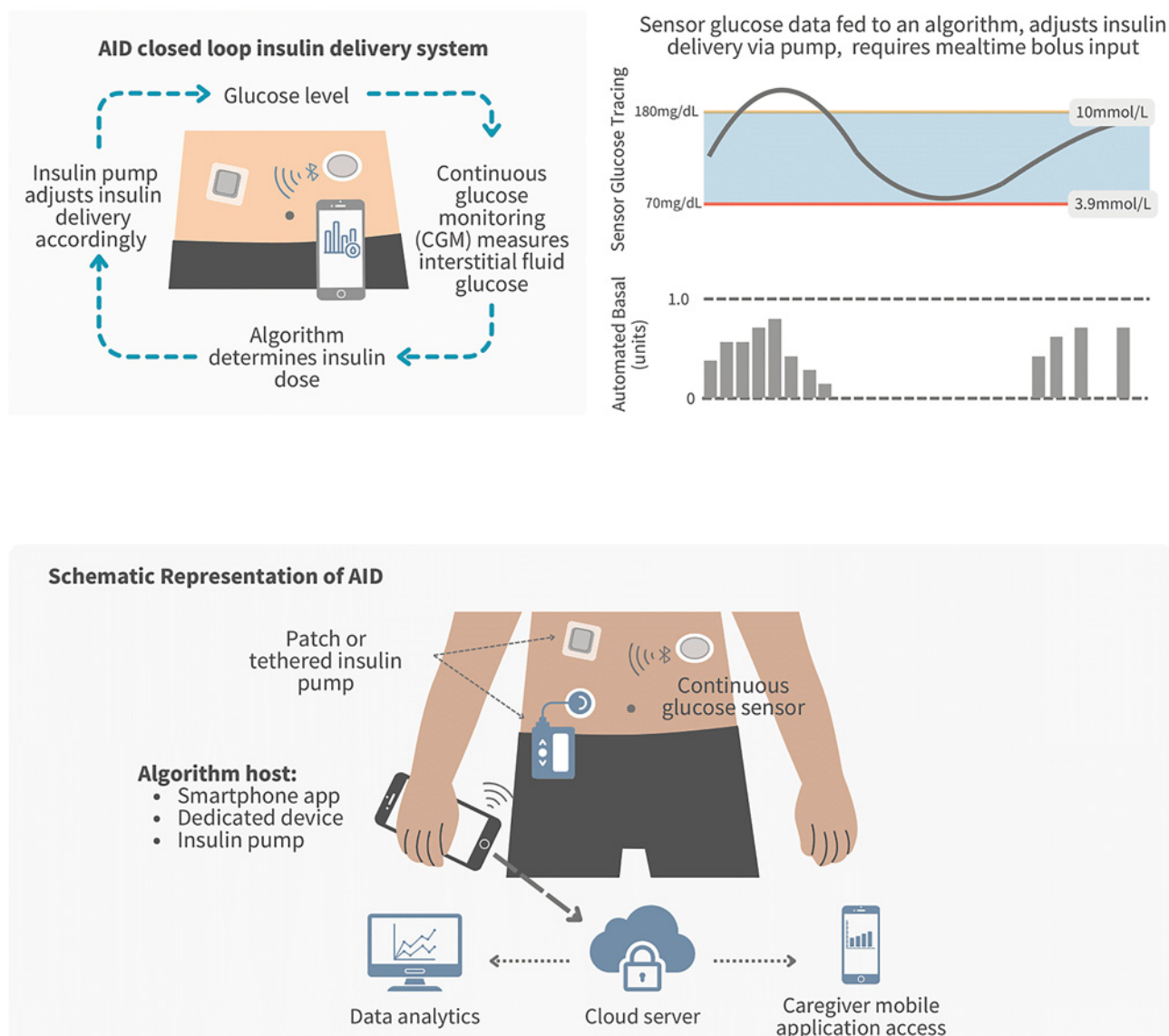
As pump therapy is the basis for other advanced insulin delivery technologies, the benefits and issues mentioned above may also apply to the glucose-responsive technologies discussed in the next sections.

Provider Training. Clinicians must be trained on devices to be competent and comfortable offering diabetes technology. However, a survey of pediatric endocrinology fellows in the USA and Canada revealed that only 14.7% had formal training on pump and CGM use [61]. In a subsequent study, pediatric endocrine fellows ($n = 64$) in North America employed case-based vignettes with 20 multiple-choice questions on either CGM or pump therapy delivered via email or a mobile app [62]. Both curricula increased participants' knowledge base from the pre- to post-test assessment and participants found this method of education engaging [62]. This suggests the potential for providers to be trained in these technologies through user-driven online learning modules. Without keeping abreast of technological advances, clinicians may inadvertently hinder the adoption and optimal use of these devices.

Educational Resources. To help inform families of various insulin delivery modalities, simplified guides can be helpful to supplement in clinic conversations.

When preparing to transition from MDI to insulin pump therapy, one of the first steps is to have the PWD and their family select the insulin pump model they

Automated insulin delivery (AID) or Closed Loop, Artificial Pancreas



(Figure continued on next page.)

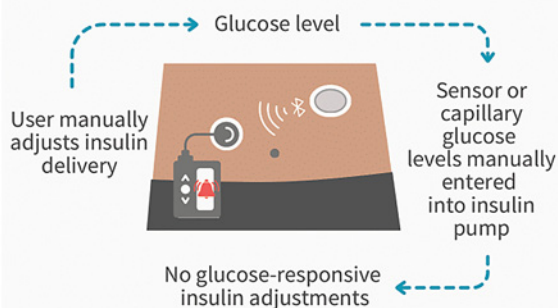
would like to use, unless insurance coverage or regional availability dictates the decision. To accomplish this, charts and literature describing the differences among models are helpful. Pump selection should be based on features desired by the PWD and their family, with guidance provided by the clinical team members. Practical information and a framework for understanding automated insulin delivery (AID) may be found in this

chapter's e-supplement (for all online suppl. material, see <https://doi.org/10.1159/000543034>).

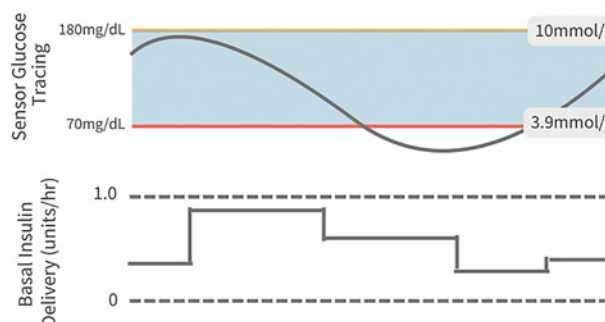
Initiating Pump Therapy. In general, initial pump settings should be derived from an individual's total daily insulin dose. The online supplementary eTable 1 provides some suggestions. Data from the DPV registry highlight differences in basal insulin programs noted by age groups. Youth under the age of 6 had higher basal

Non-automated insulin delivery

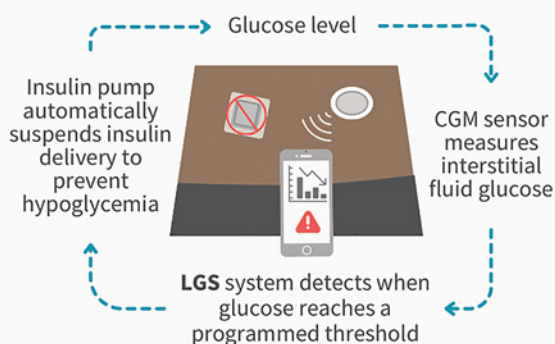
Standalone or Sensor-Augmented Insulin Pump



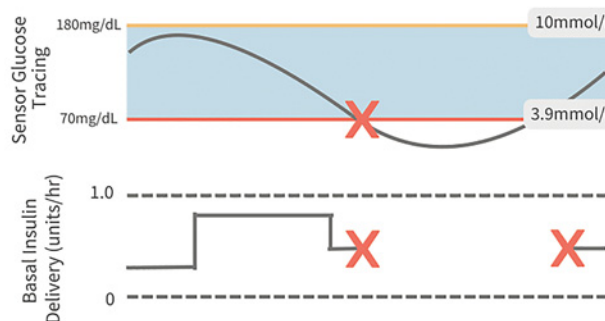
Pre-programmed basal rates delivered regardless of glucose level



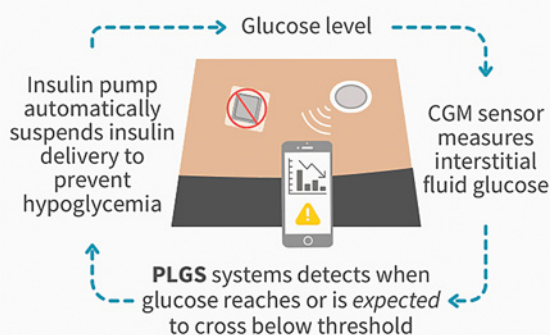
Low Glucose Suspend (LGS)



Basal insulin is interrupted once glucose crosses low threshold



Predictive Low Glucose Suspend (PLGS)



Basal insulin is interrupted once glucose predicted to cross low threshold and automatically restores basal insulin delivery after recovery from hypoglycemia

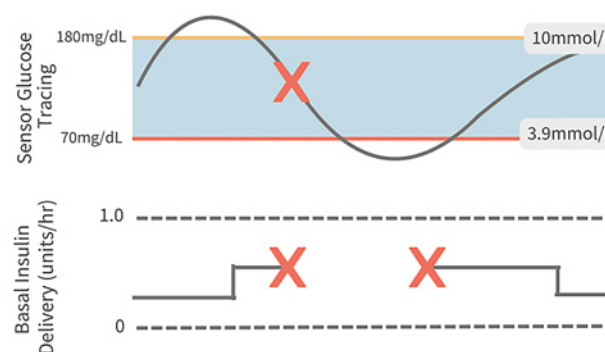


Fig. 1. Schematic representation of automated and non-AID.

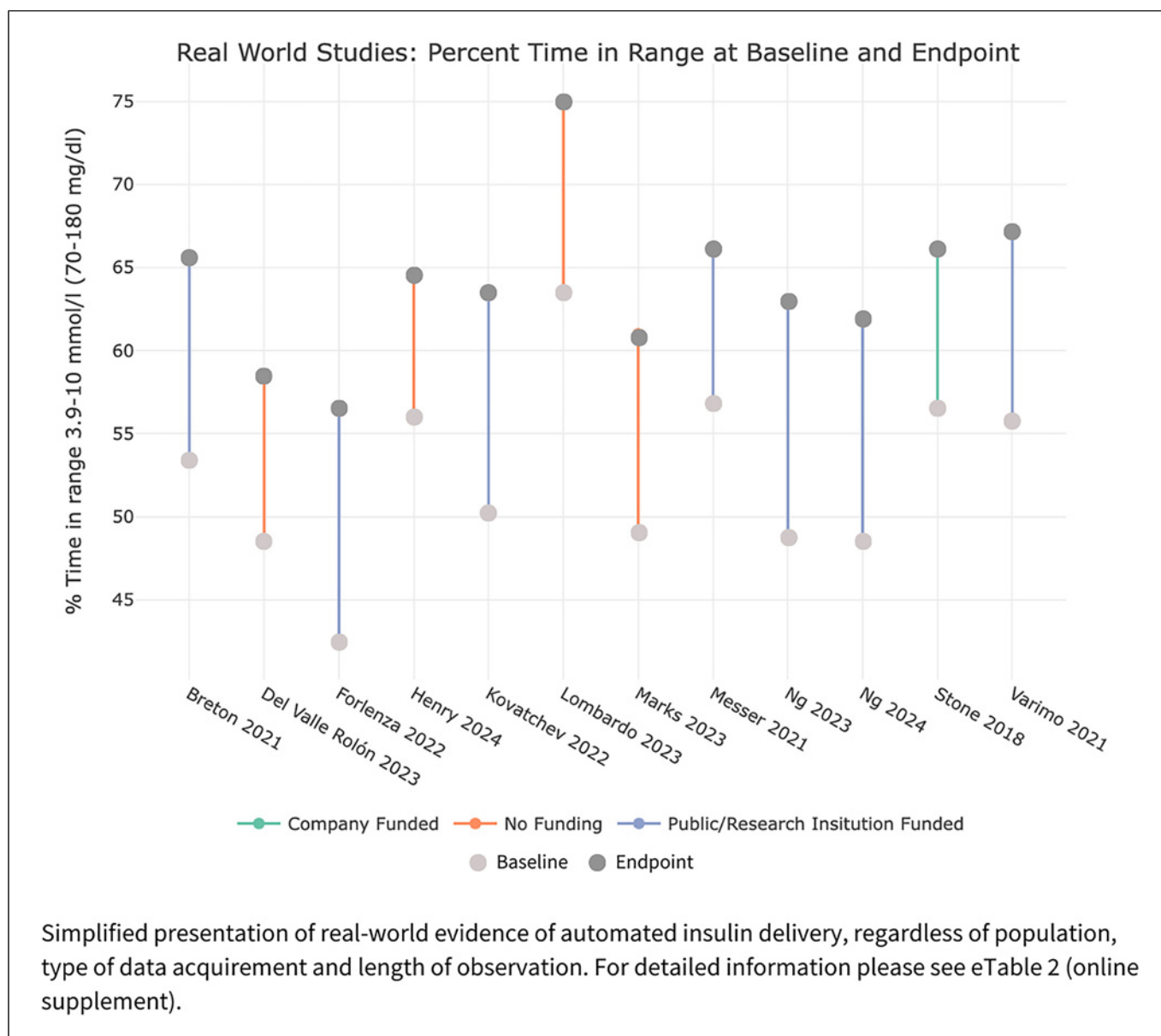


Fig. 2. Real-world studies evaluating AID. Percent TIR at baseline and endpoint.

insulin requirements from 6:00 p.m. to 12:00 a.m., while adolescents (12–18 years of age) and young adults (18–25 years of age) had higher basal insulin needs in the early morning hours (~3:00 a.m. to 8:00 a.m.) [63].

Pumps have integrated bolus calculators allowing users to enter both the number of carbohydrates to be consumed and glucose values, thus allowing the pump to calculate the bolus insulin dose. Current bolus calculators consider not only the glucose reading but also the insulin on board, thereby preventing insulin stacking.

At the time of pump initiation it is critical to advise families about associated risks, particularly that of potential infusion set failure and consequent metabolic decompensation [64]. A useful framework for optimizing the transition is presented by Deiss et al. [65].

In certain circumstances, individual needs may dictate the specific insulin type to be used. For example, in very young children or those with minimal insulin requirements, diluted insulin can be used to accurately deliver very small amounts of insulin, although not all systems

are approved for use of diluted insulin [66–69]. Specific recommendations regarding the need to tailor insulin therapy are reviewed in the updated “Insulin and adjunctive treatment in children and adolescents with diabetes” chapter.

Various factors have been associated with successful pump therapy. These include having more pre-programmed basal rates [70] and a greater total number of boluses delivered daily (both correlate with lower HbA1c levels), with basal insulin delivery accounting for <50% of the total daily dose. It is critical to encourage PWD and their families to be engaged with care [71, 72]. The importance of meal boluses/announcements should be highlighted at each follow-up visit.

Advanced Pump Features. More advanced features of pump therapy include the ability to set temporary basal rates that adjust the usually programmed basal rate for unique day-to-day variations in insulin sensitivity. This includes decreasing delivery before, during and after physical activity or increasing doses for situations like intercurrent illness [73]. Temporary basal rates, including complete suspension of basal insulin delivery can help mitigate hypoglycemia associated with exercise [74]. Similarly, different pre-programmed basal patterns can be utilized for predictable times of differing insulin sensitivity, such as during menstruation.

Insulin boluses can also be delivered in different manners to accommodate differences in food composition: (1) immediately, as a standard or normal bolus, (2) slowly over a specific period of time, an extended or square bolus, or (3) a combination of the two, i.e., a combo or dual wave bolus [73]. Boluses for high-fat foods might be best handled as extended or combo boluses as the rise in blood glucose levels following the meal will be delayed by fat. For the extended bolus, the user sets the duration of the extension; whereas, for combo boluses, the user not only chooses the duration to extend but also the amount to be delivered upfront (e.g., 40% of the bolus immediately and the remaining 60% over 4 h). Pumps can also reduce bolus insulin delivery based on the proportion of insulin that is still “active” from the last bolus, which may decrease the likelihood of post-bolus hypoglycemia and SH.

Reviewing Data to Optimize Management. As insulin pump data can be uploaded or are available through cloud-enabled sharing, clinic visits can be more productive. For more information on care delivery, see ISPAD 2022 Consensus Guidelines Chapter 7 on “The delivery of ambulatory diabetes care to children and adolescents with diabetes” [75].

Automated Insulin Delivery

- AID systems, also known as closed loop (CL), are strongly recommended for youth with diabetes [A] in order to improve TIR by minimizing hypoglycemia and hyperglycemia [A], person-reported outcomes, and reduce burden of care [A], especially in the overnight period. [A]

AID systems, also referred to as CL or artificial pancreas systems, adjust insulin delivery in response to sensor glucose data. AID use is increasing in all age groups [11, 31]. Two recent meta-analyses compared AID to other treatment modalities and demonstrated benefits for HbA1c and all TIRs evaluated [76, 77]. Furthermore, the number and variety of available AID systems are increasing, giving many PWD options to choose a system aligned with personal preferences.

AID systems adjust insulin delivery in response to sensor glucose data. This differs from low glucose suspend (LGS) and predictive low glucose management (PLGM), which both only suspend insulin administration. AID systems consist of three components: (1) an insulin pump (2) a CGM sensor, and (3) an algorithm that determines insulin delivery (Fig. 1). Many algorithms have been widely tested [78–80], and no single “optimal” algorithm has emerged. Comparisons among them [81–83] are difficult to due different study and experimental designs [81].

Besides control mechanisms, AID systems have other differentiating features. Early, fully AID studies (without meal announcements) demonstrated significant postprandial glycemic excursions and led to the use of a “hybrid” approach, meaning the user needs to manually bolus for carbohydrate intake [84]. With hybrid closed loop (HCL) systems, insulin delivery is adjusted based on sensor glucose values. Therefore, the differentiation between “manual or user initiated” and “AID” may be more meaningful than the classic categorization of insulin delivery as being either basal or bolus.

System targets are set in one of two ways; a treat-to-target approach with single target glucose (e.g., 5.8 mmol/L [105 mg/dL]) at a given time or at all times or treat-to-range approach (e.g., 6.2–8.9 mmol/L [112–160 mg/dL]) [80]. Depending on the individual system’s label, there are additional requirements to be met by the user (e.g., minimal amount of insulin, age, or weight).

Data from Large Clinical Trials

Outpatient trials have been conducted using randomized controlled trials (RCTs) [85–93] and single-arm trial designs [94–100]. RCTs have demonstrated that people using different AID systems can achieve ~10–15 percentage point increases in TIR (3.9–10 mmol/L, 70–180 mg/dL) when compared to conventional pump therapy, sensor augmented pump (SAP), predictive low glucose suspension (PLGS), and when upgrading to newer AID versions [85, 86, 88–93, 101]. Similar findings in change in TIR from baseline data collection periods have been noted in single-arm trials [94, 95, 97–100, 102]. Longer outpatient AID studies have also demonstrated concomitant reductions in HbA1c by 0.3–0.7% [85, 88–91, 93–95, 97–102].

These findings hold across all age groups. AID benefits have been demonstrated in very young children aged 2–5 years, children aged 6–13 years, adolescents, and young adults. RCT data from different trials of Tandem Control-IQ® (Tandem Diabetes Care, USA) were used to conduct a meta-analysis, which showed similar benefits including rapid improvement in glycemia after implementation of the system that was sustained over time (adjusted treatment group difference = 11.5 percentage points in TIR) [103]. Since the approval of the first AID systems, recognizing the safety these systems several affords and some of the initial barriers to use, including existing from automation, have been removed.

All Youth with T1D Can Benefit from AID

Real-world data from commercial CL systems demonstrate the performance and acceptance of this technology outside trial settings and are summarized in Figure 2 and online supplementary eTable 2.

A prospective observational multicenter study in the UK, using several different AID systems in youth aged 2–19 years, showed a reduction in HbA1c of 7.7 mmol/mol (0.6%) after 3 months with a 15.8 percentage points increase in TIR. While benefits in TIR stabilized following AID initiation and remained present after another 3 months of system use, HbA1c decreased another 7 mmol/mol (0.6%) [104].

Data from one pivotal trial demonstrated that, while all participants (aged 14–71 years) TIR improved, those with baseline HbA1c >8.5% had the greatest reduction in time above range (TAR). In contrast, those with HbA1c <6.5% also benefited from reductions in time below range (TBR) [105]. Real-world Tandem Control-IQ® system data from those aged >6 years demonstrated that those with a higher initial glucose management index (GMI), which estimates average HbA1c concentration based on mean sensor glucose values, showed substantial improvement

over time [5, 106]. Similarly, real-world use analysis of Medtronic 670G® use in 14,899 PWD (no age demographics provided), demonstrated that for those with a GMI <7%, TIR improved slightly from 76.1% to 78.7%. On the other hand, for the group whose GMI was >8%, improvement of TIR was more substantial, from 34.7% to 58.1% [107]. These data provide compelling evidence that all PWD can benefit from AID, and HCPs should not limit access to this therapy. HCPs should advocate for AID to be safely incorporated into the management plan of youth and young adults with diabetes. Further, they should provide education and support to help children and families use these devices consistently and as intended.

All currently available AID systems provide the ability to access data on insulin delivery and glucose metrics via software available through online portals; in some countries, data transfer is feasible through cloud-enabled transfer from the user's mobile phone. Given the robust nature of this data collection, real-world evidence has surpassed what is feasible in clinical trials. Further, these data highlight that the initial findings in controlled trials are mirrored with real-world use [108, 109]. See online supplementary eTable 2 and Figure 2.

Practical Considerations for AID

Systematic training of individuals with diabetes and their families/caregivers transitioning to AID therapy is essential [110–112]. General aspects of education can be found below.

Frameworks have been developed to teach AID technology use to ensure success with its adoption. The “CARES” strategy (definition see online suppl. eTable 1) has been suggested to help HCP conceptualize the differences and similarities between AID systems [113, 114]. CARES can assist clinicians by summarizing each device's most clinically relevant concepts.

PWD should be generally guided on methods to manage exercise. See ISPAD 2022 Consensus Guidelines Chapter 14 on Exercise in children and adolescents with diabetes [115].

However, carbohydrate intake to treat hypoglycemia may need to be reduced in the context of prolonged basal insulin suspension with integrated systems. A sick day and ketone management training is still important as the way of insulin administration is the same as in former pump therapy.

Tools to assist PWD to compare devices alongside their clinicians are beneficial. Practical information and a framework for understanding AID may be found in the online supplementary material.

AID Systems in Newly Diagnosed Children

- AID systems are recommended for children newly diagnosed with T1D [A] to improve TIR and reduce time in hyperglycemia. [A]

Two recent RCTs have evaluated the safety and efficacy of AID technology from the onset of T1D in children and adolescents [116, 117]. Over a follow-up period of up to 4 years, children and adolescents who used an AID system from diagnosis had more targeted glycemic metrics that sustained over time, with higher TIR and less TAR compared to those using standard insulin therapy. Between-group differences in glucose levels between those using AID and those receiving standard care started to appear 6 to 9 months after diagnosis [116, 118]. This was despite relatively high uptake of other diabetes technologies (insulin pumps and glucose sensors) in the control group, highlighting the important AID role in this population. Of note, neither study showed any beneficial effect of intensive insulin therapy with AID on beta-cell preservation, as measured by stimulated C-peptide secretion in young people recently diagnosed with T1D.

AID systems were safe when used from diagnosis and throughout the “honeymoon period” in children and adolescents with T1D. These glucose-responsive systems can effectively manage the variability of exogenous insulin requirements during the period when there is declining residual endogenous insulin secretion and can achieve stable glycemic levels.

Recent data suggest that use of AID from the time of diagnosis may help mitigate the adverse glycemic effects of DKA at presentation [119, 120]. Participants in the Closed Loop from Onset in Type 1 Diabetes (CLOuD) study presenting with or without DKA who used an AID system from diagnosis had similar glycemic outcomes at 6-, 12-, and 24-months.

Modeling data from the Epidemiology of Diabetes Interventions and Complications (EDIC) study cohort suggests beneficial effects of earlier versus later implementation of intensive therapy in T1D [121]. Earlier implementation was associated with a greater reduction in the risks of kidney and cardiovascular complications compared with later implementation, despite both groups having the same average glycemic exposure over the entire period, highlighting the importance of utilizing therapies that allow tight glycemic management from as early as possible after the diagnosis of T1D.

Preschool Children

- AID systems are strongly recommended for preschool children with T1D for improvement of glycemia. [A]

A variety of AID systems have been tested specifically in young children, with outcomes consistently indicating improved TIR and few episodes of SH or DKA. Specifically, the CamAPS FX[®] (CamDiab, UK) was tested on 74 children between 1 and 7 years old during a 16-week period and compared to a sensor-augmented pump. The study showed that in aggregate users of AID experienced a significant increase in TIR, reduction in TAR, and lowering of average glucose value without a significant increase in TBR. One case of SH was reported during AID use [122]. Using this algorithm, a 3-week outpatient RCT conducted on children aged 1–7 years did not demonstrate any benefit of diluted insulin when compared to a standard U100 rapid-acting analog [123]. Importantly, this study also highlighted that very young children have higher day-to-day variability in insulin requirements compared to other age cohorts [124].

Omnipod 5[®] (Insulet, USA) was evaluated among 80 children between 2 and 6 years of age for 13 weeks. Its use was associated with a significant increase in TIR (10.9 percentage points) and a significant reduction in TBR (0.27 percentage points). No episodes of SH or DKA were reported [100]. Longer term follow-up of this same cohort demonstrated that glycemic improvements attained with use of the Omnipod 5 persisted for up to 2 years of device initiation.

In a study of 46 children between 2 and 6 years old, the MiniMed 670G[®] (Medtronic, USA) system improved TIR and TAR without a significant increase in TBR compared to the run period (Manual Mode). No SH, DKA or serious adverse events were reported [125]. A different randomized crossover study compared a predictive low glucose system to the MiniMed 670G[®] system in 18 young children. TIR was increased from 67.5% to 72.7% ($p = 0.018$) [126]. Finally, an analysis found that off-label use of the MiniMed 780G[®] was safe in 35 children between 2 and 6 years old over a 12-week period. Using this AID led to an 8% increase in TIR ($p < 0.001$) with no significant change in hypoglycemia [127].

A 13-week multicenter randomized trial was conducted on 102 children 2–6 years of age using the Tandem Control-IQ[®] system. TIR significantly increased from 56.7% to 69.3% in the CL arm (68 children), which was accompanied by a significant reduction in TAR

(>250 mg/dL, >13.9 mmol/L) and HbA1c without an increase in TBR. Two cases of SH and one DKA were reported in the CL arm. Benefits were observed over a wide range of demographic and baseline characteristics, including age, race/ethnicity, parental education, income, and baseline glycemia [128].

A qualitative study in preschool children assessed parent's experience with remote monitoring for glycemic values. While remote monitoring of glucose data helped, parents noted that access to the insulin delivery data was even more helpful [129, 130].

Real-World Studies. Although there is limited real-world evidence on the use of AID in very young children, data from clinical trials are supported by real-world evidence (online supplementary eTable 2). A prospective real-world observational study of people who used Loop Open Source included 67 children <7 years of age. This age group benefited from AID and had a significant increase in TIR (67%–73%) over 6 months without a significant increase in TBR [131].

Real-world use of the Omnipod 5[®] system has been reported in 376 children between 2 and 6 years of age. When focusing on those with a time-weighted average target of 110 mg/dL, 68.8% of the children met the AID consensus target of less than 4% TBR, and 57% met the target of >70% TIR [132].

As a part of the National Health Service pilot initiative in England, (1) Medtronic MiniMed 780G[®], (2) Tandem t:slim X2[®] insulin pump with Control-IQ[®] with the Dexcom G6[®] CGM (Dexcom, USA) sensor, and (3) CamAPS FX[®] were studied. The participants were between 1 and 19 years of age. Overall, AID use led to an improvement in glycemic outcomes. Data from young children with T1D are shown separately [104].

School-Aged Children

- AID systems are strongly recommended for school-aged children with T1D. [A]

School age represents a relevant threshold for AID therapy as the Tandem Control-IQ[®] system is approved for children aged 6 years and older, while the Medtronic MiniMed 670G/780G[®] systems are approved for those aged 7 years and above. In a 16-week RCT involving 78 children aged 6–14 years in the intervention group, using the Tandem Control-IQ[®] system resulted in an 11% higher TIR and a 0.4% (4 mmol/mol) lower HbA1c compared to a control group using sensor-augmented pump ($n = 23$). While no SH was observed, 4 cases of

DKA occurred in the intervention group. TBR did not differ [133]. A post hoc analysis showed a high baseline TIR as predictor for greater success in AID use, while those with a lower baseline TIR experienced the most significant improvement [134].

The iLet[®] (Beta Bionics, USA) system operates differently from all other AID systems as it does not require or allow manual entry of meal carbohydrate amounts (discrete grams of carbs to be consumed). Instead, a qualitative approach to meal announcement is employed. Additionally, system initiation is solely based on an individual's weight. In a large multicenter trial, 219 participants 6–73 years old showed a 0.5% (6 mmol/mol) lower HbA1c compared to the control group (entire study population) and 11 percentage points more TIR with the same TBR after 13 weeks [135]. The 165 pediatric participants (6–17 years) showed benefits in all CGM metrics and HbA1c. The group with higher baseline HbA1c demonstrated the highest reduction in glycemia [136]. In a subsequent 13-week extension phase, the pediatric group showed an additional 0.55% (6.0 mmol/mol) reduction in HbA1c and 12.3 percentage points more TIR compared to baseline [137]. While no DKA occurred and 10 SH events were reported in the overall population during the initial RCT, no SH was found in the pediatric extension phase, with one DKA case reported that was associated with catheter occlusion.

A 4-week RCT with 60 participants aged 7–80 years compared the MiniMed 780G[®] AID system to PLGM. In a cohort aged 7–13 years ($n = 19$), TIR was increased 11.8% when using the AID mode, with no difference in TBR between the study groups. This effect was more pronounced during the night. No severe hypoglycemic events were observed throughout the entire population, with one mild DKA occurring during the PLGM phase. Not surprisingly, more targeted glycemic results were observed when the target was set to the lowest permissible in the system (100 mg/dL; 5.6 mmol/L) lower [86].

In a single-arm trial involving 112 children using Omnipod 5[®] pump for 3 months, data were compared to a 2-week baseline phase where participants used their usual insulin regimen. HbA1c decreased by 0.71% (8 mmol/mol), with a TIR increase of 15.6% without differences in TBR. One DKA case and one SH occurred in the pediatric group, with infusion site failure and delayed meal consumption after bolusing identified as the reasons, respectively. Children with higher baseline HbA1c showed a greater reduction, when compared to those with HbA1c levels <8% at baseline [5].

The Diabeloop system has the algorithm installed on a hand-held device, and is not prescriptive in terms of insulin pump utilized in the system. In a small crossover RCT with 21 participants, a pediatric version of the commercially available adult system was investigated. After an inpatient period, the system was used for 6-weeks at home. No severe events occurred (SH or DKA). Compared to the control condition, where participants used an insulin pump and a sensor without predictive function, the intervention with the AID system led to higher TIR (66.2% vs. 58.7%) and reduced hypoglycemic events (25.5 vs. 48 during the period) and TBR (2.6% vs. 5.2%) nearly 2-fold. Surprisingly, mean glycemia did not differ significantly with 8.82 mmol/L (158 mg/dL) in the intervention and 9.05 mmol/L (162 mg/dL) in the control group [138].

In a 12-week multicenter, crossover RCT with 25 children and adolescents, the CamAPS FX[®] System showed 8.9% more TIR with a 24.7% nocturnal difference in TIR when comparing AID use to SAP therapy. There were 2 hyperglycemic events without acidosis due to catheter occlusion in the AID intervention period compared to SAP [139].

All systems provide improvements in glycemia in terms of TIR and HbA1c without increasing the risk for severe hyper- or hypoglycemic events in this age group. These data from clinical trials are supported by real-world evidence (online supplementary eTable 2).

Adolescents

- AID systems are strongly recommended for adolescents with T1D. [A]

Adolescence is typically characterized as the most challenging period for maintaining optimal glucose levels throughout a PWD's lifespan [140]. An early study in this age group, including adolescents with suboptimal glucose management, showed early improvement of glycemia after initiation of AID [141], with 10.8 percentage points more TIR compared to the control group using SAP.

The Fuzzy Logic Automated Insulin Regulation (FLAIR) study compared the first-generation Medtronic 670G with the second-generation Medtronic 780G in a randomized crossover design trial in adolescents and young adults aged 14–29 years old and [142]. Compared to 670G, the second-generation Medtronic system incorporates new features including selectable target glucose set-points (100, 110, and 120 mg/dL–5.6/6.1/6.7 mmol/L), autobolus functionality that delivers correction doses automatically if sensor glucose rises above

120 mg/dL (6.7 mmol/L) and maximal automated basal insulin delivery has been reached, and an automated meal-detection algorithm, which when triggered, enables the system to deliver more aggressive autocorrection boluses. Twenty percent of the study cohort were using MDI at baseline, and almost one-third (27%) of the study participants had suboptimal glycemia (defined as HbA1c >8.5% [70 mmol/mol]) at baseline. Each study period lasted 12 weeks, TIR improved from 57% at baseline on their usual insulin delivery modality to 63% during the 12-week period of 670G[®] use and to 67% during the 3 months using the 780G[®]. Improved TIR was attained because of reduced TAR; hypoglycemia exposure remained similar between treatments and was minimal. There was a significant reduction in HbA1c between CL periods in favor of the 780G[®] system. Importantly, glycemic benefits were observed irrespective of baseline treatment modality and baseline HbA1c. Some of the improvement in glucose management between the CL systems may be attributable to increased time when the system was in automated mode (75% with 670G and 86% with the 780G), due to fewer exits per week from automation with the advanced system. From a safety perspective in this population, there was one episode of SH while using the 780G[®] system and none while using the 670G[®] system. No cases of DKA were reported.

Compared to PLGM, one study showed TIR improvement of 14.4 percentage points with 780G[®] [86], and another small RCT observed a 10 percentage points increase in TIR compared to a run-in phase with PLGM [143]. This improvement was associated with significantly higher bolus insulin amounts, which were delivered as auto-corrections by the system, which accounted for approximately 69.9% of the total bolus dose in the trial.

Forty adolescents (above age 14) and young adults up to the age of 25 participated in a 6-month RCT of the Tandem Control-IQ[®] system compared to those on sensor-augmented pump therapy [88]. In this age group, AID use led to TIR that was 13.3 percentage points higher in the intervention group with no difference in TBR. HbA1c was 0.35 percentage points (4 mmol/mol) higher in the control group who used sensor-augmented pump therapy. Compared to other study participants, this age group had fewer user-initiated boluses observed [103].

Data from adolescents using the Omnipod 5[®] system were reported collectively with the 124 participants aged 14–70 years. The cohort as a whole demonstrated increased TIR by 9.8 percentage points, accompanied by a 0.38 percentage points (4 mmol/mol) reduction in HbA1c. TBR was also reduced from 2% to 1%, with two events of SH after manual bolus administration. People

with higher baseline HbA1c (defined as HbA1c >8%) showed a greater reduction in HbA1c by the end of the 3-month study [5].

Similar to both the school-aged and preschool age groups, all systems studied appear to improve glycemia (TIR, HbA1c) without increasing the risk for severe hyper- or hypoglycemic events in the adolescent age group. The data derived in clinical trials are echoed in real-world evidence (online supplementary eTable 2).

Young Adults

- AID systems are strongly recommended for young adults with type 1 diabetes. [A]

Ease of use of AID technology is an important consideration to realizing the clinical benefits, particularly in the young adult population. Improvements in glycemic outcomes are highly correlated with greater time spent in automation; AID system use greater than 70% is associated with attaining $\geq 70\%$ TIR [144–146].

Many RCTs have now demonstrated the safety and efficacy of AID systems, both commercially available and open-source systems, compared to non-automated insulin therapies, SAP therapy, and systems that interrupt insulin delivery based on either a threshold or in a predictive fashion, both in young adults with T1D [86, 135, 141, 147–151].

Two studies discussed above, the FLAIR study and one Tandem Control-IQ study, included both adolescents and young adults. In another Control-IQ[®] study, a subgroup of 40 participants aged 14–24 years using the Control-IQ[®] system had a mean TIR from 51% at baseline to 64% after 6 months [152]. Similar glycemic benefits have been observed when other commercially available AID systems have been used in young adults. A subgroup of 11 participants aged 13–21 years using the Cambridge CL algorithm showed a 14% increase in TIR over 12 weeks [141].

Real-world data parallel the findings from clinical research trials (online suppl. eTable 2), where sub-analyses by age group are presented [132, 145, 153, 154]. In young adults, competing priorities and psychosocial challenges are important factors in self-management and glycemic outcomes [155]. AID system user data in this age group show the lowest engagement in therapy with the fewest user-initiated boluses and the most automated corrections compared to other age groups [156, 157]. Despite this, the beneficial effect of AID on TIR is statistically similar across all age

groups [103]. Further supporting the use of AID in this population, both trial data and real-world data have consistently shown that the greatest clinical benefits occur in those with the highest HbA1c or lowest TIR at the time of initiation of the AID system [5, 103, 134, 157, 158].

Non-AID

Practical Considerations for Non-AID Use

Critical to the integration of SAP, LGS, PLGS, and even AID is successful adoption of sensor therapy. For evidence on sensor therapy, please refer to the ISPAD 2024 Consensus Guidelines Chapter on Diabetes technologies: glucose monitoring [2]. Topics that should be considered when initiating these therapies may include expected frequency of sensor use, and how treatment may vary when interruptions from sensor therapy occur [159].

Predictive LGS Systems

- PLGS is strongly recommended for all people with T1D who do not have access to AID systems as these systems can mitigate hypoglycemia. [A]

PLGS systems interrupt basal insulin delivery to prevent hypoglycemia (Fig. 1). Different systems are available; however, not all provide published evidence for successful use, and therefore, only systems with published peer-reviewed data are recommended for use [160].

Two RCTs of the Medtronic PLGS approach (MiniMed 640 G[®]) have shown reductions in hypoglycemia with PLGS use [161, 162], with one study demonstrating no concomitant increase in mean glucose, as measured by HbA1c, in the PLGS group [162]. These results have also been echoed during real-world use [163].

A RCT of the Tandem system (Basal-IQ[®]) found that PLGS use led to a 31% reduction in sensor time <3.9 mmol/L (<70 mg/dL) [164]. Real-world registry data from adults using the Tandem systems show a significant reduction in TBR after PLGS started [165], with no change in mean glucose [166].

A meta-analysis including data on 493 children in 5 RCTs concluded that there is high quality evidence to support PLGS' superiority to SAP in decreasing TBR and nocturnal hypoglycemia [160]. This was accomplished without increasing the percentage of time spent on hyperglycemia or episodes of DKA [160]. Another meta-analysis concluded that the use of PLGS during the

overnight period was associated with an 8.8% lower risk of hypoglycemia when compared with non-PLGS use overnight [167].

LGS Systems

- When AID and PLGS systems are not available, LGS systems are recommended to reduce the severity and duration of hypoglycemia as compared to non-integrated pump and SAP [A] by increased confidence and trust in the technology, more flexibility around mealtimes, and reduced diabetes distress for both PWD and caregivers compared to CSII. [A]

With CGM data integrated into an algorithm on an insulin pump, altering insulin delivery based on sensor glucose readings is possible. An LGS system can suspend insulin delivery when the sensor glucose reaches a programmed low threshold (Fig. 1). An LGS feature is optional, and the pump functions normally if the feature is switched off, if sensor glucose data are not available, or if the sensor glucose value is above the predetermined threshold value [168, 169]. LGS systems reduce the risk of hypoglycemia, which may facilitate user engagement with bolusing.

In the Automation to Simulate Pancreatic Insulin Response (ASPIRE) study, hypoglycemia was detected by sensor readings. They were significantly reduced with the use of the LGS system without any deterioration in glycemia as measured by HbA1c [170, 171]. Real-world observational studies have substantiated the RCT findings showing benefits of LGS over SAP [163].

While more advanced insulin pump therapies are now available and include PLGS and AID systems, advanced pumps are not available in all countries and may not be covered by certain health/insurance plans. In such circumstances, LGS systems are strongly recommended over other types of pumps. Studies have shown that LGS is cost-effective and should be particularly considered where there is a high risk of hypoglycemia, impaired hypoglycemia awareness or fear of hypoglycemia, which may lead to difficulty with achievement of glycemic targets [172–174].

Sensor-Augmented Pump

- Sensor-augmented pump (SAP) therapy is recommended over MDI with sensor wear of $\geq 60\%$ of the time. [A]

SAP therapy is defined as the combination or augmentation of a conventional insulin pump with CGM (Fig. 1),

without the presence of an algorithm. For more details on CGM, please see ISPAD 2024 Consensus Guidelines on Diabetes technologies: glucose monitoring [2].

The benefits of SAP have been demonstrated in RCTs [175–178], including the Sensor-augmented pump Therapy for A1c Reduction (STAR) 3 study that compared SAP with MDI and SMBG checks over 1 year in device-naïve participants with T1D including children [176–178]. The SAP group had a sustained greater reduction in HbA1c, less time in hyperglycemia, and reduced glucose variability [178]. Rates of SH and DKA were relatively low and did not differ between groups. Achievement of glycemic targets was directly linked to sensor wear duration and was more prominent in the children's cohort (aged 7–12 years) who had sensor use that was 1.5 times higher than adolescents (aged 13–18 years) [178]. The crucial impact of regular sensor use has been echoed in other trials [179]. For every 10% increase in sensor use frequency there is an associated 1.1 percentage point increase in TIR and a 1.0 percentage point decrease in TAR >10 mmol/L (180 mg/dL) [180].

Although SAP is more expensive than insulin pump therapy with fingerstick glucose monitoring, the additional clinical benefits and quality-adjusted life years SAP affords justification for considering this treatment good value for the money spent, provided sensor use is persistent [181, 182].

Connected Insulin Pens

- Connected pens, if available and affordable, may be offered to interested youth who prefer not to have an on-body device. [C]

Connected insulin pens, also known as smart insulin pens, are an emerging option for youth with T1D to access some of the benefits of diabetes technology when AID use is not feasible or desired. Connected pens can be used with or without a CGM and can either be in the form of a non-disposable pen device or a pen cap that is placed on a disposable pen. Connected pens link to an app on a smartphone, which aids users in dose calculation and helps prevent insulin stacking by tracking insulin on board. Connected pens also capture important data on insulin dose and timing, generating reports that clinicians can use for dose optimization.

Literature supporting the efficacy of connected pens in youth with T1D remains limited. Most studies done to

date are on adults and only a few are RCTs; however, overall evidence suggests that connected pens may improve outcomes as noted in a recent systematic review [183].

A recent RCT on a smart pen cap that included adolescents with T1D reported a 5.2 percentage point increase in TIR as well as an increase in on-time injections with connected pen use [184]. A real-world observational study in children and adults demonstrated a 13% reduction in sensor-detected prolonged hypoglycemia (≥ 10 min) with connected pen use [185]. This finding was echoed by another observational study of connected pen use in youth with T1D, where hypoglycemia was reduced, but not hyperglycemia [186].

Currently, the use of connected pens among youth with T1D is not widespread. A recent study identified several barriers to connected pen use from providers at select centers in the T1D Exchange Quality Improvement Collaborative consortium [187]. Barriers included low provider awareness and lack of training on these devices, lack of insurance coverage, high out-of-pocket costs, need for user education and training on the device, and lack of smartphone availability for younger children. Facilitators of connected pen use that were identified included generating reports with improved quality of clinic visits, providing an alternative to an insulin pump, and improved diabetes management and adherence. More research is needed to determine whether connected pen use should be encouraged in youth with T1D who choose not to use AID.

Behavioral, Psychosocial, and Educational Considerations of Insulin Delivery Devices

- AID is recommended to reduce burden, improve perceived sleep quality, and improve treatment satisfaction. [B]
- Youth and their caregivers should be educated and counseled about realistic expectations for glycemic outcomes and the effort required for successful use of all insulin pump technologies. [C]
- A standardized, structured training program with early follow-up within the first few weeks after the device starts is recommended to optimize device use. This training can take place in-person or remotely. [C]

Behavioral and Psychosocial Outcomes

Initiating and sustaining the use of insulin delivery devices is associated with behavioral and psychosocial considerations, including self-management demands, emotional experiences, family diabetes management, and

social factors. These issues may promote or be barriers to optimal engagement in self-management using insulin delivery devices. ISPAD 2022 Consensus Guidelines Chapter 15 on Psychological Care of Children and Adolescents with Type 1 Diabetes and Other Clinical Practice Guidelines [188, 189] highlight the importance of recognizing and addressing the psychosocial and behavioral needs of youth with diabetes and their families, which have implications for supporting their use of insulin delivery devices.

Youth with T1D who use insulin pumps tend to experience benefits in health-related quality of life compared to MDI [190–192] and may have lower depressive symptoms [193]. Parents may also experience improved quality of life [193, 194]. Specific perceived benefits of pump therapy include increased autonomy in diabetes management, a greater sense of control over one's life and diabetes, decreased diabetes burdens, greater flexibility in social activities and eating, improved sleep, and higher treatment satisfaction [191, 195–199]. However, these results are not universally reported [197, 200, 201] and psychosocial factors, such as depressive symptoms, may increase the risk of pump use discontinuation [43].

As AID systems become more accessible, youth and parent trust in the system is of central importance for uptake, but factors may depend on users, device or context [202]. Studies have reported children and adolescents emphasized concerns related to use at school and with peers, while parents' concerns prioritized accuracy and ensuring that systems stabilize glucose levels and reduce risk for long-term complications [203, 204]. Evidence from qualitative research and self-report surveys suggests that caregivers are motivated for their children to use AID systems (including open-source or do-it-yourself [DIY] systems) primarily to improve glycemic outcomes, lower the risk of complications, reduce diabetes care burdens, interact with diabetes technology less, and improve sleep [205–208].

In recent years, substantial data have been reported regarding the benefits of AID systems for quality of life and well-being for youth and caregivers, in both clinical trial and real-world settings. Advantages include reduced diabetes burden/distress (especially around meals) and mood concerns, reduced fear of hypoglycemia, and worries about glycemic excursions. Additional benefits include greater confidence related to diabetes management, increased autonomy for the child, ability to participate in social activities, and improved treatment satisfaction [104, 127, 191, 207–221]. At the time of T1D diagnosis, AID has also been shown to assist in adapting to this chronic medical diagnosis as compared to MDI [217].

There are also indications of perceived improvements in sleep for both youth and parents, though significant differences in objectively measured sleep are not typically observed [104, 204, 208, 213, 214, 216, 222–224].

Though the psychosocial and behavioral benefits of AID use are not universally reported [223–226], the consistent conclusion is that advanced insulin delivery devices do not increase the burden or lead to psychological or behavioral distress, and in many cases, these devices reduce the burden and improve quality of life [215, 222, 227–229].

Limited data describe specific benefits of particular AID devices when compared to others [104, 230], but some specific features are valued by youth and families. Qualitative data regarding experiences with remote monitoring suggest a number of specific benefits (e.g., greater access to therapy data, increased comfort being away from the child or relying on other caregivers, fewer disruptions to play, sleep, and social activities) [231], especially for parents of young children [129].

While the evidence regarding positive psychosocial impacts of AID is growing, psychosocial barriers to optimal self-management remain. Notable barriers include perceived high workload required to maintain AID function and frustrations with technical glitches (e.g., frequent exits from automated delivery modes), as well as concerns about device size/visibility and stigma. Physical discomforts have also been reported, as well as burdens related to alarms causing sleep disruptions, limitations in remote monitoring access for parents, and difficulties with the required calibration of some devices [211, 217, 232, 233]. Notably, these concerns were more common with first-generation HCL systems compared to newer systems [234, 235]. Newer AID devices that use factory-calibrated CGM, which eliminate/minimize the need for capillary blood glucose checks with a glucometer have been found to reduce many of the burdens associated with AID devices and improve sustainability of use, especially in youth [236]. Indeed, data suggest improvements in burden and satisfaction for adolescents, young adults, and parents using advanced HCL devices compared to sensor-augmented pumps and earlier HCL systems [223, 234, 237].

Education and Training for Insulin Delivery Devices

Education and device training are important to ensure effective pump use and to promote sustained device use and ongoing success [111, 112, 238, 239]. Structured training programs with early follow-up within the first few weeks of use can optimize device use. Evidence indicates that virtual training is similar in effectiveness to

in-person training and may facilitate more rapid AID uptake and reduce training burdens for both families and HCPs [240–243]. The training program should emphasize education on the basics of CGM use, required diabetes self-management tasks to optimize the device (i.e., pre-meal bolusing), and common troubleshooting for the specific device. This education also helps ensure new users have realistic expectations of their device and understand the self-management behaviors needed for optimal outcomes. It is imperative that users understand the safety principles of managing persistent hyperglycemia and infusion site failure (i.e., when to check ketones, change infusion site, and/or give insulin by injection). These principles are vital for the safe use of any insulin pump therapy to prevent DKA and are equally applicable to the use of AID technologies [244]. Users who discontinue insulin delivery devices are most likely to discontinue within the first 1–3 months of use [144, 245]. Therefore, follow-up within the first month of use is helpful to assess system use and glucose trends, to allow the provider or diabetes educator an opportunity to identify early any challenges the user may be experiencing, and to provide an opportunity for targeted re-education to help the user overcome challenges and improve outcomes. Furthermore, youth may benefit from adjustments to any modifiable pump settings (i.e., insulin-to-carbohydrate ratios) to improve glycemic outcomes when transitioning from MDI or a conventional insulin pump to AID. A follow-up call or visit in the first month provides the opportunity for the clinician to make these changes [246].

Practical Considerations for Behavioral, Psychosocial, and Educational Considerations of Insulin Delivery Devices

When integrating diabetes technology into the care of youth with diabetes, families of all backgrounds (socio-economic, racial, etc.) should be informed about the spectrum of insulin delivery devices from conventional pumps to AID systems. Clinicians should portray insulin delivery devices as an option that can be a good fit for all youth and families, provide education, and encourage youth and families to review vetted websites and device informational materials. Further, it is critical for the diabetes team to recommend the most advanced device technology available that the person with diabetes is interested in and to not make assumptions about interest or capability. Clinicians should refrain from having youth and families “earn” the right to use devices (i.e., achieve a certain HbA1c before considering starting a device). If payers/insurance companies require logging or other documentation before device approval, convey that

directly to the family and advise that this is not a requirement of the diabetes care practice/team. Further, while counting carbohydrates and delivering boluses consistently for all meals and snacks is the optimal way to use most AID devices, carb counting or a history of consistent bolusing should not be a pre-requisite for AID use. Significant benefits using AID can still be obtained for those who struggle to count carbohydrates or deliver meal boluses consistently. Even those who do not bolus consistently can experience significant improvement in glycemic outcomes, and alternative bolus strategies, such as using fixed meal doses instead of carbohydrate counting, can improve TIR [103, 105, 247–249].

Assessing youth or family concerns and other barriers to device uptake and use should be part of routine clinical practice. Providers should seek to work with the youth and their families on ways to break down barriers and increase facilitators of device use. This may require referral to a psychological or behavioral/mental health professional, who can teach problem-solving skills and other strategies to support device uptake and sustained use [250].

Non-Certified Open-Source AID Approaches

- If PWD choose to use open-source AID systems, support from care providers is encouraged. [E]

Recognizing the inherent delays in conducting clinical trials and obtaining regulatory approval for new technologies, the past decade has seen the creation of open-source AID systems. Through an online community, the DIY approach has been adopted by several thousand PWD and their families. In silico, studies have demonstrated the relative safety of the system through simulations with both meal bolus over- and underestimation as well as what might occur with delayed bolusing [251]. Additionally, a real-world prospective observational study of 558 users, more than half <25 years old, showed improvement in TIR and reductions in the incidence of SH events with system use, suggesting these systems can be used safely and effectively [131]. As these systems do not have regulatory approval, healthcare professionals should be cautious about recommending these devices in preference to commercially available systems. Yet, when PWD choose to use an open-source system, a consensus statement endorsed by some organizations suggests that providers should support them [252]. One RCT in those aged 7–70 years compared the use of an open-source developed algorithm to a control group using SAP. The AID group showed an increase in TIR of 10%, leading to

an adjusted difference between groups of 14%. However, it is important to note that the setting of this clinical study differed from the typical daily open-source use as it was a preset device with support from a clinical team [253].

While PWD may independently build their DIY AID systems, the diabetes care team remains essential for core diabetes self-management education and support for DIY AID use. Clinicians should consider learning the key system characteristics to facilitate supporting PWD in optimizing settings to help them meet glycemic and personal goals safely and effectively.

Conclusion

AID is an established therapy and has become the standard of care in jurisdictions and healthcare settings where it is available and accessible. Just as our everyday lives have vastly changed with the integration of new technologies, with increased connectivity, the technological revolution has had an enormous effect on the management of diabetes and modes of insulin delivery. This reality means that individuals of all ages with diabetes can carry a smartphone with CGM or AID application and that glycemic data can be monitored in a cloud-based manner from everywhere.

The true test of new technologies, reducing glycemic variability while achieving greater TIR and improving quality of life, is passed. It is reasonable to expect that in the years ahead, there will be significant growth in this aspect of diabetes care and that progressive technological solutions will allow PWD, and their families, an improved ability to attain glycemic targets while reducing the burdens of daily diabetes care and improving the quality of life. In the long term, the integration of more physiologic insulin delivery afforded by AID systems will further minimize the risk of diabetes complications. Long-term data to prove its additional benefits for secondary conditions and cardiovascular risk are yet to come.

Clinicians engaged in the care of PWD have an obligation to remain abreast of new technology developments to optimize uptake and use. Broader implementation of technology into clinical care will also require an understanding of the cost-benefit of therapies to justify payer coverage, as many of these technologies are expensive and consideration of total lifetime costs alongside reductions in overall healthcare expenditures require further evaluation [30]. Additionally, interoperable approaches should provide options to interchange separate components, which would allow users to customize treatment through their diabetes management devices along with appropriate data

sharing. Updates are anticipated in this rapidly evolving area of research and practice to further the ISPAD's aim: "a better world for children, adolescents, and young adults with diabetes."

Methodology

A literature search was conducted to gather updated evidence, using a combination of relevant medical subject headings (MeSH, Emtree) and free text terms specific to each chapter's focus. Studies published from 2021 to 2022 onward, related to children and young adults, were retrieved from MEDLINE. The Project Officer, in collaboration with chapter leads and co-authors, performed the literature searches. The resulting articles (with search terms summarized in online suppl. material) were then uploaded to Covidence for screening and review. Two authors/experts involved in drafting this guideline version independently screened the articles. Any disagreements were resolved by a third reviewer. Where relevant, further literature was included. The draft chapter was posted on the ISPAD forum to allow feedback from the greater ISPAD membership. Modifications were made with authorship consensus, with the chapter receiving endorsement from the ISPAD editorial team. Literature search terms are summarized in the online supplementary material.

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Conflict of Interest Statement

T.B. received research support from Dexcom, VitalAire, and Ypsomed and speakers honoraria from DexCom, Insulet, Lilly, Medtronic, NovoNordisk, Sanofi, Synlab, and Ypsomed; participated in advisory boards from DexCom, Insulet, Medtronic, Tandem, and Ypsomed; and serves as chair in the EXPAMED-Panel Diabetes/Endo of EMA for new medical devices. C.B. re-

ceived speaking and consulting fees for Medtronic, Tandem, Insulet, and Emecta. Ch.B. received consultancy fees from CamDiab and speaker honoraria from Ypsomed and the Association of British Clinical Diabetologists. L.C. received speakers' fee from NovoNordisk. L.E. has served on the advisory board of Diabetes Center Berne, Sequel, Abbot, and Medtronic; has received consulting fees from Tandem Diabetes Care; and has received honorarium fees from Medtronic and Insulet. Her institution has received research support from Breakthrough T1D, Medtronic, Mannkind, and Abbot. L.E. has received travel accommodations for conferences from Medtronic and Insulet; has served as a consultant to Jaeb; has received honorarium fees from Tandem Diabetes Care; and has received an honorarium for a grand round presentation/CME event sponsored by Sanofi. M.E.H. and S.S.N.U. report no conflict of interest. L.R. reports speakers' fee from Medtronic. M.S. received research support and paid to the University of Virginia from Tandem and Insulet. J.L.S. works as a consultant for the following entities with all compensation being <10K per year: Abbott Diabetes, Insulet, Medscape, Medtronic Diabetes, Vertex, and Ypsomed; served on advisory boards for the following entities with all compensation being <10K per year: Cecelia Health, Insulet, Mannkind, Medtronic Diabetes, StartUp Health T1D Moonshot, and Vertex; research contracts for which payment is rendered to Yale for work, completed from Abbott Diabetes, Dexcom, JDRF/Breakthrough T1D, Insulet, Medtronic, NIH, and Provention Bio; and participated in advisory boards by Insulet, Medtronic, and Ypsomed. K.D. received honoraria for participation in the speaker's bureau of Abbott, Eli Lilly, Medtronic, NovoNordisk A/S, and Pfizer and served on the advisory board for Medtronic and NovoNordisk.

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Author Contributions

T.B., C.B., Ch.B., L.C., L.E., M.E.H., L.R., S.S.N.U., M.S., J.L.S., and K.D. reviewed the literature, provided drafts of sections, attended the online meetings, discussed the content, voted on recommendations, and edited the manuscript. T.B. oversaw completion of the first draft of the guidelines and edited the manuscript. K.D. outlined the guidelines, reviewed the literature, edited the manuscript, and served as the senior author.

References

- Sherr JL, Tauschmann M, Battelino T, de Bock M, Forlenza G, Roman R, et al. ISPAD clinical practice consensus guidelines 2018: diabetes technologies. *Pediatr Diabetes*. 2018;19(Suppl 27):302–25. <https://doi.org/10.1111/pedi.12731>
- Martin Tauschman RC-H, DeSalvo DJ, Hood K, Laptev DN, Lindholm Olinder A, Wheeler BJ, et al. ISPAD clinical practice consensus guidelines 2024 diabetes technologies: glucose monitoring. *Horm Res Pediatr*. 2024; In preparation.
- Everett EM, Wright D, Williams A, Divers J, Pihoker C, Liese AD, et al. A longitudinal view of disparities in insulin pump use among youth with type 1 diabetes: the SEARCH for diabetes in youth study. *Diabetes Technol Ther*. 2023;25(2):131–9. <https://doi.org/10.1089/dia.2022.0340>

- 4 Stanley JR, Clarke ABM, Shulman R, Mahmud FH. Mediating effects of technology-based therapy on the relationship between socioeconomic status and glycemic management in pediatric type 1 diabetes. *Diabetes Technol Ther.* 2023; 25(3):186–93. <https://doi.org/10.1089/dia.2022.0388>
- 5 Brown SA, Forlenza GP, Bode BW, Pinsker JE, Levy CJ, Criego AB, et al. Multicenter trial of a tubeless, on-body automated insulin delivery system with customizable glycemic targets in pediatric and adult participants with type 1 diabetes. *Diabetes Care.* 2021;44(7):1630–40. <https://doi.org/10.2337/dc21-0172>
- 6 Battelino T, Danne T, Bergenstal RM, Amiel SA, Beck R, Biester T, et al. Clinical targets for continuous glucose monitoring data interpretation: recommendations from the international consensus on time in range. *Diabetes Care.* 2019;42(8):1593–603. <https://doi.org/10.2337/dci19-0028>
- 7 Agiostratidou G, Anhalt H, Ball D, Blonde L, Gourgari E, Harriman KN, et al. Standardizing clinically meaningful outcome measures beyond HbA1c for type 1 diabetes: a consensus report of the American Association of Clinical Endocrinologists, the American Association of Diabetes Educators, the American Diabetes Association, the Endocrine Society, JDRF International, the Leona M. and Harry B. Helmsley Charitable Trust, the Pediatric Endocrine Society, and the T1D Exchange. *Diabetes Care.* 2017;40(12):1622–30. <https://doi.org/10.2337/dci17-1624>
- 8 Nations U. General comment no. 14. Committee on economic, social and cultural rights. The right to the highest attainable standard of health (article 12 of the International Covenant on Economic, Social and Cultural Rights). Geneva: UN; 2000.
- 9 Foster NC, Beck RW, Miller KM, Clements MA, Rickels MR, DiMeglio LA, et al. State of type 1 diabetes management and outcomes from the T1D Exchange in 2016–2018. *Diabetes Technol Ther.* 2019;21(2):66–72. <https://doi.org/10.1089/dia.2018.0384>
- 10 van den Boom L, Karges B, Auzanneau M, Rami-Merhar B, Lilienthal E, von Sengbusch S, et al. Temporal trends and contemporary use of insulin pump therapy and glucose monitoring among children, adolescents, and adults with type 1 diabetes between 1995 and 2017. *Diabetes Care.* 2019;42(11):2050–6. <https://doi.org/10.2337/dc19-0345>
- 11 van den Boom L, et al. Use of continuous glucose monitoring in pump therapy sensor augmented pump or automated insulin delivery in different age groups (0.5 to <26 years) with type 1 diabetes from 2018 to 2021: analysis of the German/Austrian/Swiss/Luxembourg DPV registry. *J Diabetes Sci Technol.* 2023;19322968231156601.
- 12 Sherr JL, Hermann JM, Campbell F, Foster NC, Hofer SE, Allgrove J, et al. Use of insulin pump therapy in children and adolescents with type 1 diabetes and its impact on metabolic control: comparison of results from three large, transatlantic paediatric registries. *Diabetologia.* 2016;59(1):87–91. <https://doi.org/10.1007/s00125-015-3790-6>
- 13 Szypowska A, Schwandt A, Svensson J, Shalitin S, Cardona-Hernandez R, Forsander G, et al. Insulin pump therapy in children with type 1 diabetes: analysis of data from the SWEET registry. *Pediatr Diabetes.* 2016;17(Suppl 23):38–45. <https://doi.org/10.1111/pedi.12416>
- 14 Zabeen B, Craig ME, Virk SA, Pryke A, Chan AKF, Cho YH, et al. Insulin pump therapy is associated with lower rates of retinopathy and peripheral nerve abnormality. *PLoS One.* 2016;11(4):e0153033. <https://doi.org/10.1371/journal.pone.0153033>
- 15 Jeitler K, Horvath K, Berghold A, Gratz TW, Neeser K, Pieber TR, et al. Continuous subcutaneous insulin infusion versus multiple daily insulin injections in patients with diabetes mellitus: systematic review and meta-analysis. *Diabetologia.* 2008;51(6):941–51. <https://doi.org/10.1007/s00125-008-0974-3>
- 16 Pankowska E, Błazik M, Dziechciarz P, Szypowska A, Szajewska H. Continuous subcutaneous insulin infusion vs. multiple daily injections in children with type 1 diabetes: a systematic review and meta-analysis of randomized control trials. *Pediatr Diabetes.* 2009;10(1):52–8. <https://doi.org/10.1111/j.1399-5448.2008.00440.x>
- 17 Pickup JC, Sutton AJ. Severe hypoglycaemia and glycaemic control in type 1 diabetes: meta-analysis of multiple daily insulin injections compared with continuous subcutaneous insulin infusion. *Diabet Med.* 2008; 25(7):765–74. <https://doi.org/10.1111/j.1464-5491.2008.02486.x>
- 18 Jakisch BI, Wagner VM, Heidtmann B, Lepler R, Holterhus PM, Kapellen TM, et al. Comparison of continuous subcutaneous insulin infusion (CSII) and multiple daily injections (MDI) in paediatric type 1 diabetes: a multicentre matched-pair cohort analysis over 3 years. *Diabet Med.* 2008; 25(1):80–5. <https://doi.org/10.1111/j.1464-5491.2007.02311.x>
- 19 Scrimgeour L, Cobry E, McFann K, Burdick P, Weimer C, Slover R, et al. Improved glycaemic control after long-term insulin pump use in pediatric patients with type 1 diabetes. *Diabetes Technol Ther.* 2007;9(5):421–8. <https://doi.org/10.1089/dia.2007.0214>
- 20 Johnson SR, Cooper MN, Jones TW, Davis EA. Long-term outcome of insulin pump therapy in children with type 1 diabetes assessed in a large population-based case-control study. *Diabetologia.* 2013;56(11):2392–400. <https://doi.org/10.1007/s00125-013-3007-9>
- 21 Karges B, Schwandt A, Heidtmann B, Kordonouri O, Binder E, Schierloh U, et al. Association of insulin pump therapy vs insulin injection therapy with severe hypoglycemia, ketoacidosis, and glycaemic control among children, adolescents, and young adults with type 1 diabetes. *JAMA.* 2017;318(14):1358–66. <https://doi.org/10.1001/jama.2017.13994>
- 22 Birkebaek NH, Drivvoll AK, Aakeson K, Bjarnason R, Johansen A, Samuelsson U, et al. Incidence of severe hypoglycemia in children with type 1 diabetes in the Nordic countries in the period 2008–2012: association with hemoglobin A1c and treatment modality. *BMJ Open Diabetes Res Care.* 2017;5(1):e000377. <https://doi.org/10.1136/bmjdr-2016-000377>
- 23 Phillip M, Battelino T, Rodriguez H, Danne T, Kaufman F, European Society for Paediatric Endocrinology, et al. Use of insulin pump therapy in the pediatric age-group: consensus statement from the European Society for Paediatric Endocrinology, the Lawson Wilkins Pediatric Endocrine Society, and the International Society for pediatric and adolescent diabetes, endorsed by the American Diabetes Association and the European Association for the Study of diabetes. *Diabetes Care.* 2007;30(6):1653–62. <https://doi.org/10.2337/dci07-9922>
- 24 Botros S, Islam N, Hursh B. Insulin pump therapy, pre-pump hemoglobin A1c and metabolic improvement in children with type 1 diabetes at a tertiary Canadian children's hospital. *Pediatr Diabetes.* 2019;20(4):427–33. <https://doi.org/10.1111/pedi.12834>
- 25 Ramchandani N, Ten S, Anhalt H, Sinha S, Ching J, Finkelstein A, et al. Insulin pump therapy from the time of diagnosis of type 1 diabetes. *Diabetes Technol Ther.* 2006;8(6):663–70. <https://doi.org/10.1089/dia.2006.8.663>
- 26 Berghaeuser MA, Kapellen T, Heidtmann B, Haberland H, Klinkert C, Holl RW, et al. Continuous subcutaneous insulin infusion in toddlers starting at diagnosis of type 1 diabetes mellitus. A multicenter analysis of 104 patients from 63 centres in Germany and Austria. *Pediatr Diabetes.* 2008;9(6):590–5. <https://doi.org/10.1111/j.1399-5448.2008.00416.x>
- 27 de Beaufort CE, Houtzagers CM, Bruining GJ, Aarsen RS, den Boer NC, Grose WF, et al. Continuous subcutaneous insulin infusion (CSII) versus conventional injection therapy in newly diagnosed diabetic children: two-year follow-up of a randomized, prospective trial. *Diabet Med.* 1989;6(9):766–71. <https://doi.org/10.1111/j.1464-5491.1989.tb01276.x>
- 28 Kamrath C, Tittel SR, Kapellen TM, von dem Berge T, Heidtmann B, Nagl K, et al. Early versus delayed insulin pump therapy in children with newly diagnosed type 1 diabetes: results from the multicentre, prospective diabetes follow-up DPV registry. *Lancet Child Adolesc Health.* 2021;5(1):17–25. [https://doi.org/10.1016/S2352-4642\(20\)30339-4](https://doi.org/10.1016/S2352-4642(20)30339-4)
- 29 Dos Santos TJ, Dave C, MacLeish S, Wood JR. Diabetes technologies for children and adolescents with type 1 diabetes are highly dependent on coverage and reimbursement: results from a worldwide survey. *BMJ Open Diabetes Res Care.* 2021;9(2):e002537. <https://doi.org/10.1136/bmjdr-2021-002537>

- 30 Zhang L, Leng X, Tian F, Xiao D, Xuan J, Yang H, et al. Cost-effectiveness analysis of continuous subcutaneous insulin infusion versus multiple daily insulin for treatment of children with type 1 diabetes. *Postgrad Med.* 2022;134(6):627–34. <https://doi.org/10.1080/00325481.2022.2088938>
- 31 Ebekozien O, Mungmode A, Sanchez J, Rompicherla S, Demeterco-Berggren C, Weinstock RS, et al. Longitudinal trends in glycemic outcomes and technology use for over 48,000 people with type 1 diabetes (2016–2022) from the T1D Exchange quality improvement collaborative. *Diabetes Technol Ther.* 2023;25(11):765–73. <https://doi.org/10.1089/dia.2023.0320>
- 32 Auzanneau M, Rosenbauer J, Maier W, von Sengbusch S, Hamann J, Kapellen T, et al. Heterogeneity of access to diabetes technology depending on area deprivation and demographics between 2016 and 2019 in Germany. *J Diabetes Sci Technol.* 2021; 15(5):1059–68. <https://doi.org/10.1177/19322968211028608>
- 33 Blackman SM, Raghinaru D, Adi S, Simmons JH, Ebner-Lyon L, Chase HP, et al. Insulin pump use in young children in the T1D Exchange clinic registry is associated with lower hemoglobin A1c levels than injection therapy. *Pediatr Diabetes.* 2014; 15(8):564–72. <https://doi.org/10.1111/pedi.12121>
- 34 Lipman TH, Hawkes CP. Racial and socioeconomic disparities in pediatric type 1 diabetes: time for a paradigm shift in approach. *Diabetes Care.* 2021;44(1):14–6. <https://doi.org/10.2337/dci20-0048>
- 35 Lipman TH, Smith JA, Patil O, Willi SM, Hawkes CP. Racial disparities in treatment and outcomes of children with type 1 diabetes. *Pediatr Diabetes.* 2021;22(2):241–8. <https://doi.org/10.1111/pedi.13139>
- 36 O'Connor MR, Carlin K, Coker T, Zierler B, Pihoker C. Disparities in insulin pump therapy persist in youth with type 1 diabetes despite rising overall pump use rates. *J Pediatr Nurs.* 2019;44:16–21. <https://doi.org/10.1016/j.pedn.2018.10.005>
- 37 Majidi S, Ebekozien O, Noor N, Lyons SK, McDonough R, Gandhi K, et al. Inequities in health outcomes in children and adults with type 1 diabetes: data from the T1D Exchange quality improvement collaborative. *Clin Diabetes.* 2021;39(3):278–83. <https://doi.org/10.2337/cd21-0028>
- 38 Addala A, Auzanneau M, Miller K, Maier W, Foster N, Kapellen T, et al. A decade of disparities in diabetes technology use and HbA1c in pediatric type 1 diabetes: a transatlantic comparison. *Diabetes Care.* 2021;44(1):133–40. <https://doi.org/10.2337/dc20-0257>
- 39 Mönkemöller K, Müller-Godeffroy E, Lilienthal E, Heidtmann B, Becker M, Feldhahn L, et al. The association between socioeconomic status and diabetes care and outcome in children with diabetes type 1 in Germany: the DIAS study (diabetes and social disparities). *Pediatr Diabetes.* 2019; 20(5):637–44. <https://doi.org/10.1111/pedi.12847>
- 40 Commissariat PV, Boyle CT, Miller KM, Mantravadi MG, DeSalvo DJ, Tamborlane WV, et al. Insulin pump use in young children with type 1 diabetes: sociodemographic factors and parent-reported barriers. *Diabetes Technol Ther.* 2017;19(6):363–9. <https://doi.org/10.1089/dia.2016.0375>
- 41 Hofer SE, Heidtmann B, Raile K, Fröhlich-Reiterer E, Lilienthal E, Berghaeuser MA, et al. Discontinuation of insulin pump treatment in children, adolescents, and young adults. A multicenter analysis based on the DPV database in Germany and Austria. *Pediatr Diabetes.* 2010;11(2): 116–21. <https://doi.org/10.1111/j.1399-5448.2009.00546.x>
- 42 Wong JC, Boyle C, DiMeglio LA, Mastrandrea LD, Abel KL, Cengiz E, et al. Evaluation of pump discontinuation and associated factors in the T1D Exchange clinic registry. *J Diabetes Sci Technol.* 2017; 11(2):224–32. <https://doi.org/10.1177/1932296816663963>
- 43 Wong JC, Dolan LM, Yang TT, Hood KK. Insulin pump use and glycemic control in adolescents with type 1 diabetes: predictors of change in method of insulin delivery across two years. *Pediatr Diabetes.* 2015; 16(8):592–9. <https://doi.org/10.1111/pedi.12221>
- 44 Hanas R, Lindgren F, Lindblad B. A 2-yr national population study of pediatric ketoacidosis in Sweden: predisposing conditions and insulin pump use. *Pediatr Diabetes.* 2009;10(1):33–7. <https://doi.org/10.1111/j.1399-5448.2008.00441.x>
- 45 Brorsson AL, Viklund G, Örtqvist E, Lindholm Olinder A. Does treatment with an insulin pump improve glycaemic control in children and adolescents with type 1 diabetes? A retrospective case-control study. *Pediatr Diabetes.* 2015;16(7):546–53. <https://doi.org/10.1111/pedi.12209>
- 46 Alva S, Castorino K, Cho H, Ou J. Feasibility of continuous ketone monitoring in subcutaneous tissue using a ketone sensor. *J Diabetes Sci Technol.* 2021;15(4):768–74. <https://doi.org/10.1177/19322968211008185>
- 47 Wheeler BJ, Heels K, Donaghue KC, Reith DM, Ambler GR. Insulin pump-associated adverse events in children and adolescents—a prospective study. *Diabetes Technol Ther.* 2014;16(9):558–62. <https://doi.org/10.1089/dia.2013.0388>
- 48 Guenego A, Bouzillat G, Breitel S, Esvant A, Poirier JY, Bonnet F, et al. Insulin pump failures: has there been an improvement? Update of a prospective observational study. *Diabetes Technol Ther.* 2016;18(12):820–4. <https://doi.org/10.1089/dia.2016.0265>
- 49 Heinemann L, Walsh J, Roberts R. We need more research and better designs for insulin infusion sets. *J Diabetes Sci Technol.* 2014; 8(2):199–202. <https://doi.org/10.1177/1932296814523882>
- 50 Heinemann L, Krinkel L. Insulin infusion set: the Achilles heel of continuous subcutaneous insulin infusion. *J Diabetes Sci Technol.* 2012;6(4):954–64. <https://doi.org/10.1177/193229681200600429>
- 51 Heinemann L. Insulin infusion sets: a critical reappraisal. *Diabetes Technol Ther.* 2016;18(5):327–33. <https://doi.org/10.1089/dia.2016.0013>
- 52 Cescon M, DeSalvo DJ, Ly TT, Maahs DM, Messer LH, Buckingham BA, et al. Early detection of infusion set failure during insulin pump therapy in type 1 diabetes. *J Diabetes Sci Technol.* 2016;10(6):1268–76. <https://doi.org/10.1177/1932296816663962>
- 53 Forlenza GP, et al. Application of zone model predictive control artificial pancreas during extended use of infusion set and sensor: a randomized crossover-controlled home-use trial. *Diabetes Care.* 2017;dc170500.
- 54 Kordonouri O, Lauterborn R, Deiss D. Lipoatrophy in young patients with type 1 diabetes. *Diabetes Care.* 2002;25(3):634. <https://doi.org/10.2337/diacare.25.3.634>
- 55 Kordonouri O, Biester T, Schnell K, Hartmann R, Tsioli C, Fath M, et al. Lipoatrophy in children with type 1 diabetes: an increasing incidence? *J Diabetes Sci Technol.* 2015;9(2):206–8. <https://doi.org/10.1177/1932296814558348>
- 56 Raile K, Noelle V, Landgraf R, Schwarz HP. Insulin antibodies are associated with lipoatrophy but also with lipohypertrophy in children and adolescents with type 1 diabetes. *Exp Clin Endocrinol Diabetes.* 2001; 109(8):393–6. <https://doi.org/10.1055/s-2001-18991>
- 57 Kordonouri O, Biester T, Weidemann J, Ott H, Remus K, Grothaus J, et al. Lipoatrophy in children, adolescents and adults with insulin pump treatment: is there a beneficial effect of insulin glulisine? *Pediatr Diabetes.* 2020;21(7):1285–91. <https://doi.org/10.1111/pedi.13094>
- 58 Burgmann J, Biester T, Grothaus J, Kordonouri O, Ott H. Pediatric diabetes and skin disease (PeDiSkin): a cross-sectional study in 369 children, adolescents and young adults with type 1 diabetes. *Pediatr Diabetes.* 2020;21(8):1556–65. <https://doi.org/10.1111/pedi.13130>
- 59 Berg AK, Olsen BS, Thyssen JP, Zachariae C, Simonsen AB, Pilgaard K, et al. High frequencies of dermatological complications in children using insulin pumps or sensors. *Pediatr Diabetes.* 2018;19(4):733–40. <https://doi.org/10.1111/pedi.12652>
- 60 Fröhlich-Reiterer E, Elbarbary NS, Simmons K, Buckingham B, Humayun KN, Johannsen J, et al. ISPAD Clinical Practice Consensus Guidelines 2022: other complications and associated conditions in children and adolescents with type 1 diabetes. *Pediatr Diabetes.* 2022;23(8):1451–67. <https://doi.org/10.1111/pedi.13445>

- 61 Marks BE, Wolfsdorf JJ, Waldman G, Stafford DE, Garvey KC. Pediatric endocrinology trainees' education and knowledge about insulin pumps and continuous glucose monitors. *Diabetes Technol Ther.* 2019;21(3):105–9. <https://doi.org/10.1089/dia.2018.0331>
- 62 Marks BE, Waldman G, Reardon K, Terrio S, Kumar A, Stafford DEJ, et al. Improving pediatric endocrinology trainees' knowledge about insulin pumps and continuous glucose monitors with online spaced education: technology Knowledge Optimization in T1D (TeKnO T1D). *Pediatr Diabetes.* 2020; 21(5):814–23. <https://doi.org/10.1111/pedi.13010>
- 63 Biester T, Eckert A, Becker M, Boettcher C, Golembowski S, Heidtmann B, et al. Expected basal insulin requirement during continuous subcutaneous insulin infusion therapy by age group, sex, and body mass index, based on 25,718 young people with type 1 diabetes in the DPV registry. *Diabetes Technol Ther.* 2023;25(11):774–81. <https://doi.org/10.1089/dia.2023.0283>
- 64 Wolfsdorf JJ, Allgrove J, Craig ME, Edge J, Glaser N, Jain V, et al. ISPAD Clinical Practice Consensus Guidelines 2014. Diabetic ketoacidosis and hyperglycemic hyperosmolar state. *Pediatr Diabetes.* 2014; 15(Suppl 20):154–79. <https://doi.org/10.1111/pedi.12165>
- 65 Deiss D, Adolfsson P, Alkemade-van Zomeren M, Bolli GB, Charpentier G, Cobelli C, et al. Insulin infusion set use: European perspectives and recommendations. *Diabetes Technol Ther.* 2016;18(9):517–24. <https://doi.org/10.1089/dia.2016.07281.sf>
- 66 Elleri D, Allen JM, Tauschmann M, El-Khairi R, Benitez-Aguirre P, Acerini CL, et al. Feasibility of overnight closed-loop therapy in young children with type 1 diabetes aged 3–6 years: comparison between diluted and standard insulin strength. *BMJ Open Diabetes Res Care.* 2014;2(1):e000040. <https://doi.org/10.1136/bmjdr-2014-000040>
- 67 Del Favero S, Boscarì F, Messori M, Rabbone I, Bonfanti R, Sabbion A, et al. Randomized summer camp crossover trial in 5- to 9-year-old children: outpatient wearable artificial pancreas is feasible and safe. *Diabetes Care.* 2016;39(7):1180–5. <https://doi.org/10.2337/dc15-2815>
- 68 Ruan Y, Elleri D, Allen JM, Tauschmann M, Wilinska ME, Dunger DB, et al. Pharmacokinetics of diluted (U20) insulin aspart compared with standard (U100) in children aged 3–6 years with type 1 diabetes during closed-loop insulin delivery: a randomised clinical trial. *Diabetologia.* 2015;58(4): 687–90. <https://doi.org/10.1007/s00125-014-3483-6>
- 69 Mianowska B, Fendler W, Tomasik B, Młynarski W, Szadkowska A. Effect of insulin dilution on lowering glycemic variability in pump-treated young children with inadequately controlled type 1 diabetes. *Diabetes Technol Ther.* 2015;17(9):605–10. <https://doi.org/10.1089/dia.2014.0392>
- 70 Nabhan ZM, Rardin L, Meier J, Eugster EA, Dimaggio LA. Predictors of glycemic control on insulin pump therapy in children and adolescents with type 1 diabetes. *Diabetes Res Clin Pract.* 2006;74(3):217–21. <https://doi.org/10.1016/j.diabres.2006.03.020>
- 71 Danne T, Battelino T, Jarosz-Chobot P, Kordonouri O, Pánkowska E, Ludvigsson J, et al. Establishing glycaemic control with continuous subcutaneous insulin infusion in children and adolescents with type 1 diabetes: experience of the PedPump Study in 17 countries. *Diabetologia.* 2008;51(9): 1594–601. <https://doi.org/10.1007/s00125-008-1072-2>
- 72 Rasmussen VF, Vestergaard ET, Schwandt A, Beltrand J, Rami-Merhar B, O'Riordan SMP, et al. Proportion of basal to total insulin dose is associated with metabolic control, body mass index, and treatment modality in children with type 1 diabetes-A cross-sectional study with data from the International SWEET registry. *J Pediatr.* 2019;215:216–22 e1. <https://doi.org/10.1016/j.jpeds.2019.06.002>
- 73 Adolfsson P, Ziegler R, Hanas R. Continuous subcutaneous insulin infusion: special needs for children. *Pediatr Diabetes.* 2017; 18(4):255–61. <https://doi.org/10.1111/pedi.12491>
- 74 Diabetes Research in Children Network DirecNet Study Group; Tsalikian E, Kollman C, Tamborlane WB, Beck RW, Fiallo-Scharer R, et al. Prevention of hypoglycemia during exercise in children with type 1 diabetes by suspending basal insulin. *Diabetes Care.* 2006;29(10):2200–4. <https://doi.org/10.2337/dc06-0495>
- 75 Limbert C, Tinti D, Malik F, Kosteria I, Messer L, Jalaludin MY, et al. ISPAD Clinical Practice Consensus Guidelines 2022: the delivery of ambulatory diabetes care to children and adolescents with diabetes. *Pediatr Diabetes.* 2022;23(8):1243–69. <https://doi.org/10.1111/pedi.13417>
- 76 Zeng B, Gao L, Yang Q, Jia H, Sun F. Automated insulin delivery systems in children and adolescents with type 1 diabetes: a systematic review and meta-analysis of outpatient randomized controlled trials. *Diabetes Care.* 2023;46(12):2300–7. <https://doi.org/10.2337/dc23-0504>
- 77 Michou P, Gkiourtzis N, Christoforidis A, Kotanidou EP, Galli-Tsinopoulou A. The efficacy of automated insulin delivery systems in children and adolescents with type 1 diabetes mellitus: a systematic review and meta-analysis of randomized controlled trials. *Diabetes Res Clin Pract.* 2023;199: 110678. <https://doi.org/10.1016/j.diabres.2023.110678>
- 78 Mauseth R, Wang Y, Dassau E, Kircher R Jr, Matheson D, Zisser H, et al. Proposed clinical application for tuning fuzzy logic controller of artificial pancreas utilizing a personalization factor. *J Diabetes Sci Technol.* 2010;4(4):913–22. <https://doi.org/10.1177/193229681000400422>
- 79 Bequette B. Algorithms for a closed-loop artificial pancreas: the case for model predictive control. *J Diabetes Sci Technol.* 2013; 7(6):1632–43. <https://doi.org/10.1177/193229681300700624>
- 80 Boughton CK, Hovorka R. New closed-loop insulin systems. *Diabetologia.* 2021;64(5): 1007–15. <https://doi.org/10.1007/s00125-021-05391-w>
- 81 Pinsker JE, Lee JB, Dassau E, Seborg DE, Bradley PK, Gondhalekar R, et al. Randomized crossover comparison of personalized MPC and PID control algorithms for the artificial pancreas. *Diabetes Care.* 2016; 39(7):1135–42. <https://doi.org/10.2337/dc15-2344>
- 82 Pinsker JE, Lee JB, Dassau E, Seborg DE, Bradley PK, Gondhalekar R, et al. Randomized crossover comparison of personalized MPC and PID control algorithms for the artificial pancreas. *Diabetes Care.* 2016;39(7): 1135–42. <https://doi.org/10.2337/dc15-2344>
- 83 Pinsker JE, Lee JB, Dassau E, Seborg DE, Bradley PK, Gondhalekar R, et al. Randomized crossover comparison of personalized MPC and PID control algorithms for the artificial pancreas. *Diabetes Care.* 2016; 39(7):1135–42. <https://doi.org/10.2337/dc15-2344>
- 84 Weinzimer SA, Steil GM, Swan KL, Dziura J, Kurtz N, Tamborlane WV. Fully automated closed-loop insulin delivery versus semi-automated hybrid control in pediatric patients with type 1 diabetes using an artificial pancreas. *Diabetes Care.* 2008;31(5):934–9. <https://doi.org/10.2337/dc07-1967>
- 85 Ware J, Hovorka R. Closed-loop control in very young children with type 1 diabetes. Reply. *N Engl J Med.* 2022;386(15):1482–3. <https://doi.org/10.1056/NEJMc2202163>
- 86 Collins OJ, Meier RA, Betts ZL, Chan DSH, Frampton C, Frewen CM, et al. Improved glycemic outcomes with medtronic MiniMed advanced hybrid closed-loop delivery: results from a randomized crossover trial comparing automated insulin delivery with predictive low glucose suspend in people with type 1 diabetes. *Diabetes Care.* 2021; 44(4):969–75. <https://doi.org/10.2337/dc20-2250>
- 87 Tauschmann M, Thabit H, Bally L, Allen JM, Hartnell S, Wilinska ME, et al. Closed-loop insulin delivery in suboptimally controlled type 1 diabetes: a multicentre, 12-week randomised trial. *Lancet.* 2018; 392(10155):1321–9. [https://doi.org/10.1016/S0140-6736\(18\)31947-0](https://doi.org/10.1016/S0140-6736(18)31947-0)
- 88 Brown S, Kovatchev BP, Raghinaru D, Lum JW, Buckingham BA, Kudva YC, et al. Six-month randomized, multicenter trial of closed-loop control in type 1 diabetes. *N Engl J Med.* 2019;381(18):1707–17. <https://doi.org/10.1056/NEJMoa1907863>

- 89 Breton M, Beck RW, Wadwa RP; iDCL Trial Research Group. A randomized trial of closed-loop control in children with type 1 diabetes. *Reply*. *N Engl J Med*. 2020;383(25):2484. <https://doi.org/10.1056/NEJMc2030417>
- 90 Bergenstal R, Nimri R, Beck RW, Criego A, Laffel L, Schatz D, et al. A comparison of two hybrid closed-loop systems in adolescents and young adults with type 1 diabetes (FLAIR): a multicentre, randomised, cross-over trial. *Lancet*. 2021;397:208–19. [https://doi.org/10.1016/S0140-6736\(20\)32514-9](https://doi.org/10.1016/S0140-6736(20)32514-9)
- 91 Benhamou P, Franc S, Reznik Y, Thivolet C, Schaepelynck P, Renard E, et al. Closed-loop insulin delivery in adults with type 1 diabetes in real-life conditions: a 12-week multicentre, open-label randomised controlled crossover trial. *Lancet Digit Health*. 2019;1(1):e17–25. [https://doi.org/10.1016/S2589-7500\(19\)30003-2](https://doi.org/10.1016/S2589-7500(19)30003-2)
- 92 Kariyawasam D, Morin C, Casteels K, Le Tallec C, Sfez A, Godot C, et al. Hybrid closed-loop insulin delivery versus sensor-augmented pump therapy in children aged 6–12 years: a randomised, controlled, cross-over, non-inferiority trial. *Lancet Digit Health*. 2022;4(3):e158–68. [https://doi.org/10.1016/S2589-7500\(21\)00271-5](https://doi.org/10.1016/S2589-7500(21)00271-5)
- 93 von dem Berge T, Remus K, Biester S, Reschke F, Klusmeier B, Adolph K, et al. In-home use of a hybrid closed loop achieves time-in-range targets in preschoolers and school children: results from a randomized, controlled, crossover trial. *Diabetes Obes Metab*. 2022;24(7):1319–27. <https://doi.org/10.1111/dom.14706>
- 94 Forlenza G, Ekhlaspour L, DiMeglio LA, Fox LA, Rodriguez H, Shulman DI, et al. Glycemic outcomes of children 2–6 years of age with type 1 diabetes during the pediatric MiniMed™ 670G system trial. *Pediatr Diabetes*. 2022;23(3):324–9. <https://doi.org/10.1111/pedi.13312>
- 95 Brown S, Forlenza GP, Bode BW, Pinsker JE, Levy CJ, Criego AB, et al. Multicenter trial of a tubeless, on-body automated insulin delivery system with customizable glycemic targets in pediatric and adult participants with type 1 diabetes. *Diabetes Care*. 2021;44(7):1630–40. <https://doi.org/10.2337/dc21-0172>
- 96 Carlson AL, Sherr JL, Shulman DI, Garg SK, Pop-Busui R, Bode BW, et al. Safety and glycemic outcomes during the MiniMed advanced hybrid closed-loop system pivotal trial in adolescents and adults with type 1 diabetes. *Diabetes Technol Ther*. 2022;24(3):178–89. <https://doi.org/10.1089/dia.2021.0319>
- 97 Bergenstal RM, Garg S, Weinzimmer SA, Buckingham BA, Bode BW, Tamborlane WV, et al. Safety of a hybrid closed-loop insulin delivery system in patients with type 1 diabetes. *JAMA*. 2016;316(13):1407–8. <https://doi.org/10.1001/jama.2016.11708>
- 98 Garg SK, Weinzimmer SA, Tamborlane WV, Buckingham BA, Bode BW, Bailey TS, et al. Glucose outcomes with the in-home use of a hybrid closed-loop insulin delivery system in adolescents and adults with type 1 diabetes. *Diabetes Technol Ther*. 2017;19(3):155–63. <https://doi.org/10.1089/dia.2016.0421>
- 99 Forlenza GP, Pinhas-Hamiel O, Liljenquist DR, Shulman DI, Bailey TS, Bode BW, et al. Safety evaluation of the MiniMed 670G system in children 7–13 years of age with type 1 diabetes. *Diabetes Technol Ther*. 2019;21(1):11–9. <https://doi.org/10.1089/dia.2018.0264>
- 100 Sherr JL, Bode BW, Forlenza GP, Laffel LM, Schoelwer MJ, Buckingham BA, et al. Safety and glycemic outcomes with a tubeless automated insulin delivery system in very young children with type 1 diabetes: a single-arm multicenter clinical trial. *Diabetes Care*. 2022;45(8):1907–10. <https://doi.org/10.2337/dc21-2359>
- 101 Tauschmann M, Thabit H, Bally L, Allen JM, Hartnell S, Wilinska ME, et al. Closed-loop insulin delivery in suboptimally controlled type 1 diabetes: a multicentre, 12-week randomised trial. *Lancet*. 2018;392(10155):1321–9. [https://doi.org/10.1016/S0140-6736\(18\)31947-0](https://doi.org/10.1016/S0140-6736(18)31947-0)
- 102 Carlson A, Sherr JL, Shulman DI, Garg SK, Pop-Busui R, Bode BW, et al. Safety and glycemic outcomes during the MiniMed™ advanced hybrid closed-loop system pivotal trial in adolescents and adults with type 1 diabetes. *Diabetes Technol Ther*. 2022;24(3):178–89. <https://doi.org/10.1089/dia.2021.0319>
- 103 Beck RW, Raghinaru D, Calhoun P, Bergenstal RM. A meta-analysis of randomized trial outcomes for the tslim X2 insulin pump with control-IQ technology in youth and adults from age 2 to 72. *Diabetes Technol Ther*. 2024;26(3):151–5. <https://doi.org/10.1089/dia.2023.0380>
- 104 Ng SM, Wright NP, Yardley D, Campbell F, Randell T, Trevelyan N, et al. Real world use of hybrid-closed loop in children and young people with type 1 diabetes mellitus—a National Health Service pilot initiative in England. *Diabet Med*. 2023;40(2):e15015. <https://doi.org/10.1111/dme.15015>
- 105 Ekhlaspour L, Town M, Raghinaru D, Lum JW, Brown SA, Buckingham BA. Glycemic outcomes in baseline hemoglobin A1C subgroups in the international diabetes closed-loop trial. *Diabetes Technol Ther*. 2022;24(8):588–91. <https://doi.org/10.1089/dia.2021.0524>
- 106 Forlenza GP, Breton MD, Kovatchev BP. Candidate selection for hybrid closed loop systems. *Diabetes Technol Ther*. 2021;23(11):760–2. <https://doi.org/10.1089/dia.2021.0217>
- 107 Da Silva J, Bosi E, Jendle J, Arrieta A, Castaneda J, Grossman B, et al. Real-world performance of the MiniMed 670G system in europe. *Diabetes Obes Metab*. 2021;23(8):1942–9. <https://doi.org/10.1111/dom.14424>
- 108 Kovatchev B, Breton M. Response to Comment on “One year real-world use of the Control-IQ advanced hybrid closed-loop technology” by Goran Petrovski et al. *Diabetes Technol Ther*. 2021;23(10):729. <https://doi.org/10.1089/dia.2021.0209>
- 109 Da Silva J. Real-world performance of the MiniMed™ 780G system: first report of outcomes from 4'120 users. *Diabetes Technol Ther*. 2021.
- 110 Boughton CK, Hartnell S, Allen JM, Fuchs J, Hovorka R. Training and support for hybrid closed-loop therapy. *J Diabetes Sci Technol*. 2022;16(1):218–23. <https://doi.org/10.1177/1932296819835183>
- 111 Berget C, Thomas SE, Messer LH, Thivener K, Slover RH, Wadwa RP, et al. A clinical training program for hybrid closed loop therapy in a pediatric diabetes clinic. *J Diabetes Sci Technol*. 2020;14(2):290–6. <https://doi.org/10.1177/1932296819835183>
- 112 Petrovski G, Al Khalaf F, Campbell J, Fisher H, Umer F, Hussain K. 10-Day structured initiation protocol from multiple daily injection to hybrid closed-loop system in children and adolescents with type 1 diabetes. *Acta Diabetol*. 2020;57(6):681–7. <https://doi.org/10.1007/s00592-019-01472-w>
- 113 Messer LH, Forlenza GP, Wadwa RP, Weinzimmer SA, Sherr JL, Hood KK, et al. The dawn of automated insulin delivery: a new clinical framework to conceptualize insulin administration. *Pediatr Diabetes*. 2018;19(1):14–7. <https://doi.org/10.1111/pedi.12535>
- 114 Messer LH, Berget C, Forlenza GP. A clinical guide to advanced diabetes devices and closed-loop systems using the CARES paradigm. *Diabetes Technol Ther*. 2019;21(8):462–9. <https://doi.org/10.1089/dia.2019.0105>
- 115 Adolfsson P, Taplin CE, Zaharieva DP, Pemberton J, Davis EA, Riddell MC, et al. ISPAD clinical practice consensus guidelines 2022: exercise in children and adolescents with diabetes. *Pediatr Diabetes*. 2022;23(8):1341–72. <https://doi.org/10.1111/pedi.13452>
- 116 Boughton CK, Allen JM, Ware J, Wilinska ME, Hartnell S, Thankamony A, et al. Closed-loop therapy and preservation of C-peptide secretion in type 1 diabetes. *N Engl J Med*. 2022;387(10):882–93. <https://doi.org/10.1056/NEJMoa2203496>
- 117 McVean J, Forlenza GP, Beck RW, Bauza C, Bailey R, Buckingham B, et al. Effect of tight glycemic control on pancreatic beta cell function in newly diagnosed pediatric type 1 diabetes: a randomized clinical trial. *JAMA*. 2023;329(12):980–9. <https://doi.org/10.1001/jama.2023.2063>
- 118 Ware J, Boughton CK, Allen JM, Wilinska ME, Hartnell S, Thankamony A, et al. Effect of 48 months of closed-loop insulin delivery on residual C-peptide secretion and glycemic control in newly diagnosed youth with type 1 diabetes: a randomized trial. *Diabetes Care*. 2024;47(8):1441–8. <https://doi.org/10.2337/dc24-0360>

- 119 Zaharieva DP, Ding VY, Addala A, Prahalad P, Bishop F, Hood KK, et al. Diabetic ketoacidosis at diagnosis in youth with type 1 diabetes is associated with a higher hemoglobin A1c even with intensive insulin management. *Diabetes Technol Ther.* 2024;26(3):176–83. <https://doi.org/10.1089/dia.2023.0405>
- 120 Lakshman R, Najami M, Hovorka R, Boughton CK. Contrasting glycemic outcomes in young people with diabetic ketoacidosis at onset of type 1 diabetes. *Diabetes Technol Ther.* 2024;26(9):686–7. <https://doi.org/10.1089/dia.2024.0147>
- 121 Lachin JM, Bebu I, Nathan DM; DCCT/EDIC Research Group. The beneficial effects of earlier versus later implementation of intensive therapy in type 1 diabetes. *Diabetes Care.* 2021;44(10):2225–30. <https://doi.org/10.2337/dc21-1331>
- 122 Ware J, Allen JM, Boughton CK, Wilinska ME, Hartnell S, Thankamony A, et al. Randomized trial of closed-loop control in very young children with type 1 diabetes. *N Engl J Med.* 2022;386(3):209–19. <https://doi.org/10.1056/NEJMoa2111673>
- 123 Tauschmann M, Allen JM, Nagl K, Fritsch M, Yong J, Metcalfe E, et al. Home use of day-and-night hybrid closed-loop insulin delivery in very young children: a multicenter, 3-week, randomized trial. *Diabetes Care.* 2019;42(4):594–600. <https://doi.org/10.2337/dc18-1881>
- 124 Dovc K, Boughton C, Tauschmann M, Thabit H, Bally L, Allen JM, et al. Young children have higher variability of insulin requirements: observations during hybrid closed-loop insulin delivery. *Diabetes Care.* 2019;42(7):1344–7. <https://doi.org/10.2337/dc18-2625>
- 125 Forlenza GP, Ekhlaspour L, DiMeglio LA, Fox LA, Rodriguez H, Shulman DI, et al. Glycemic outcomes of children 2–6 Years of age with type 1 diabetes during the pediatric MiniMed™ 670G system trial. *Pediatr Diabetes.* 2022;23(3):324–9. <https://doi.org/10.1111/pedi.13312>
- 126 von dem Berge T, Remus K, Biester S, Reschke F, Klusmeier B, Adolph K, et al. In-home use of a hybrid closed loop achieves time-in-range targets in preschoolers and school children: results from a randomized, controlled, crossover trial. *Diabetes Obes Metab.* 2022;24(7):1319–27. <https://doi.org/10.1111/dom.14706>
- 127 Pulkkinen MA, Varimo TJ, Hakonen ET, Harsunen MH, Hyvönen ME, Janér JN, et al. MiniMed 780G™ in 2- to 6-year-old children: safety and clinical outcomes after the first 12 weeks. *Diabetes Technol Ther.* 2023;25(2):100–7. <https://doi.org/10.1089/dia.2022.0313>
- 128 Wadwa RP, Reed ZW, Buckingham BA, DeBoer MD, Ekhlaspour L, Forlenza GP, et al. Trial of hybrid closed-loop control in young children with type 1 diabetes. *N Engl J Med.* 2023;388(11):991–1001. <https://doi.org/10.1056/NEJMoa2210834>
- 129 Hart RI, Kimbell B, Rankin D, Allen JM, Boughton CK, Campbell F, et al. Parents' experiences of using remote monitoring technology to manage type 1 diabetes in very young children during a clinical trial: qualitative study. *Diabet Med.* 2022;39(7):e14828. <https://doi.org/10.1111/dme.14828>
- 130 Musolino G, Dovc K, Boughton CK, Tauschmann M, Allen JM, Nagl K, et al. Reduced burden of diabetes and improved quality of life: experiences from unrestricted day-and-night hybrid closed-loop use in very young children with type 1 diabetes. *Pediatr Diabetes.* 2019;20(6):794–9. <https://doi.org/10.1111/pedi.12872>
- 131 Lum J, Bailey RJ, Barnes-Lomen V, Naranjo D, Hood KK, Lal RA, et al. A real-world prospective study of the safety and effectiveness of the loop open source automated insulin delivery system. *Diabetes Technol Ther.* 2021;23(5):367–75. <https://doi.org/10.1089/dia.2020.0535>
- 132 Forlenza GP, DeSalvo DJ, Aleppo G, Wilmot EG, Berget C, Huyett LM, et al. Real-world evidence of Omnipod® 5 automated insulin delivery system use in 69,902 people with type 1 diabetes. *Diabetes Technol Ther.* 2024;26(8):514–25. <https://doi.org/10.1089/dia.2023.0578>
- 133 Breton MD, Kanapka LG, Beck RW, Ekhlaspour L, Forlenza GP, Cengiz E, et al. A randomized trial of closed-loop control in children with type 1 diabetes. *N Engl J Med.* 2020;383(9):836–45. <https://doi.org/10.1056/NEJMoa2004736>
- 134 Schoelwer MJ, Kanapka LG, Wadwa RP, Breton MD, Ruedy KJ, Ekhlaspour L, et al. Predictors of time-in-range (70–180 mg/dL) achieved using a closed-loop control system. *Diabetes Technol Ther.* 2021;23(7):475–81. <https://doi.org/10.1089/dia.2020.0646>
- 135 Bionic Pancreas Research Group, Russell SJ, Beck RW, Damiano ER, El-Khatib FH, Ruedy KJ, et al. Multicenter, randomized trial of a bionic pancreas in type 1 diabetes. *N Engl J Med.* 2022;387(13):1161–72. <https://doi.org/10.1056/NEJMoa2205225>
- 136 Messer LH, Buckingham BA, Cogen F, Daniels M, Forlenza G, Jafri RZ, et al. Positive impact of the bionic pancreas on diabetes control in youth 6–17 Years old with type 1 diabetes: a multicenter randomized trial. *Diabetes Technol Ther.* 2022;24(10):712–25. <https://doi.org/10.1089/dia.2022.0201.pub>
- 137 Lynch J, Kanapka LG, Russell SJ, Damiano ER, El-Khatib FH, Ruedy KJ, et al. The insulin-only bionic pancreas pivotal trial extension study: a multi-center single-arm evaluation of the insulin-only configuration of the bionic pancreas in adults and youth with type 1 diabetes. *Diabetes Technol Ther.* 2022;24(10):726–36. <https://doi.org/10.1089/dia.2022.0341>
- 138 Kariyawasam D, Morin C, Casteels K, Le Tallec C, Sfez A, Godot C, et al. Hybrid closed-loop insulin delivery versus sensor-augmented pump therapy in children aged 6–12 years: a randomised, controlled, crossover, non-inferiority trial. *Lancet Digit Health.* 2022;4(3):e158–e168. [https://doi.org/10.1016/S2589-7500\(21\)00271-5](https://doi.org/10.1016/S2589-7500(21)00271-5)
- 139 Thabit H, Tauschmann M, Allen JM, Leelarthana L, Hartnell S, Wilinska ME, et al. Home use of an artificial beta cell in type 1 diabetes. *N Engl J Med.* 2015;373(22):2129–40. <https://doi.org/10.1056/NEJMoa1509351>
- 140 Hermann JM, Miller KM, Hofer SE, Clements MA, Karges W, Foster NC, et al. The Transatlantic HbA1c gap: differences in glycaemic control across the lifespan between people included in the US T1D exchange registry and those included in the German/Austrian DPV registry. *Diabet Med.* 2020;37(5):848–55. <https://doi.org/10.1111/dme.14148>
- 141 Tauschmann M, Thabit H, Bally L, Allen JM, Hartnell S, Wilinska ME, et al. Closed-loop insulin delivery in suboptimally controlled type 1 diabetes: a multicentre, 12-week randomised trial. *Lancet.* 2018;392(10155):1321–9. [https://doi.org/10.1016/S0140-6736\(18\)31947-0](https://doi.org/10.1016/S0140-6736(18)31947-0)
- 142 Bergenstal RM, Nimri R, Beck RW, Criegio A, Laffel L, Schatz D, et al. A comparison of two hybrid closed-loop systems in adolescents and young adults with type 1 diabetes (FLAIR): a multicentre, randomised, crossover trial. *Lancet.* 2021;397(10270):208–19. [https://doi.org/10.1016/S0140-6736\(20\)32514-9](https://doi.org/10.1016/S0140-6736(20)32514-9)
- 143 Carlson AL, Sherr JL, Shulman DI, Garg SK, Pop-Busui R, Bode BW, et al. Safety and glycemic outcomes during the MiniMed advanced hybrid closed-loop system pivotal trial in adolescents and adults with type 1 diabetes. *Diabetes Technol Ther.* 2022;24(3):178–89. <https://doi.org/10.1089/dia.2021.0319>
- 144 Lal RA, Basina M, Maahs DM, Hood K, Buckingham B, Wilson DM. One year clinical experience of the first commercial hybrid closed-loop system. *Diabetes Care.* 2019;42(12):2190–6. <https://doi.org/10.2337/dc19-0855>
- 145 Berget C, Akturk HK, Messer LH, Vigers T, Pyle L, Snell-Bergeon J, et al. Real-world performance of hybrid closed loop in youth, young adults, adults and older adults with type 1 diabetes: identifying a clinical target for hybrid closed-loop use. *Diabetes Obes Metab.* 2021;23(9):2048–57. <https://doi.org/10.1111/dom.14441>
- 146 Ware J, Boughton CK, Allen JM, Wilinska ME, Tauschmann M, Denvir L, et al. Cambridge hybrid closed-loop algorithm in children and adolescents with type 1 diabetes: a multicentre 6-month randomised controlled trial. *Lancet Digit Health.* 2022;4(4):e245–55. [https://doi.org/10.1016/S2589-7500\(22\)00020-6](https://doi.org/10.1016/S2589-7500(22)00020-6)
- 147 Burnside MJ, Lewis DM, Crockett HR, Meier RA, Williman JA, Sanders OJ, et al. Extended use of an open-source automated insulin delivery system in children and adults with type 1 diabetes: the 24-week continuation phase following the CREATE randomized controlled trial. *Diabetes Technol Ther.* 2023;25(4):250–9. <https://doi.org/10.1089/dia.2022.0484>

- 148 Benhamou P-Y, Franc S, Reznik Y, Thivolet C, Schaepelynck P, Renard E, et al. Closed-loop insulin delivery in adults with type 1 diabetes in real-life conditions: a 12-week multicentre, open-label randomised controlled crossover trial. *Lancet Digit Health*. 2019;1(1):e17–25. [https://doi.org/10.1016/S2589-7500\(19\)30003-2](https://doi.org/10.1016/S2589-7500(19)30003-2)
- 149 Choudhary P, Kolassa R, Keuthage W, Kroeger J, Thivolet C, Evans M, et al. Advanced hybrid closed loop therapy versus conventional treatment in adults with type 1 diabetes (ADAPT): a randomised controlled study. *Lancet Diabetes Endocrinol*. 2022; 10(10):720–31. [https://doi.org/10.1016/S2213-8587\(22\)00212-1](https://doi.org/10.1016/S2213-8587(22)00212-1)
- 150 Garg SK, Grunberger G, Weinstock R, Lawson ML, Hirsch IB, DiMeglio LA, et al. Improved glycemia with hybrid closed-loop versus continuous subcutaneous insulin infusion therapy: results from a randomized controlled trial. *Diabetes Technol Ther*. 2023;25(1):1–12. <https://doi.org/10.1089/dia.2022.0421>
- 151 Brown SA, Kovatchev BP, Raghinaru D, Lum JW, Buckingham BA, Kudva YC, et al. Six-month randomized, multicenter trial of closed-loop control in type 1 diabetes. *N Engl J Med*. 2019;381(18):1707–17. <https://doi.org/10.1056/NEJMoa1907863>
- 152 Isganaitis E, Raghinaru D, Ambler-Osborn L, Pinsker JE, Buckingham BA, Wadwa RP, et al. Closed-loop insulin therapy improves glycemic control in adolescents and young adults: outcomes from the International diabetes closed-loop trial. *Diabetes Technol Ther*. 2021;23(5):342–9. <https://doi.org/10.1089/dia.2020.0572>
- 153 Pinsker JE, Müller L, Constantin A, Leas S, Manning M, McElwee Malloy M, et al. Real-world patient reported outcomes and glycemic results with initiation of control-IQ technology. *Diabetes Technol Ther*. 2021; 23(2):120–7. <https://doi.org/10.1089/dia.2020.0388>
- 154 Alwan H, Wilinska ME, Ruan Y, Da Silva J, Hovorka R. Real-world evidence analysis of a hybrid closed-loop system. *J Diabetes Sci Technol*. 2023;19322968231185348. <https://doi.org/10.1177/19322968231185348>
- 155 Monaghan M, Helgeson V, Wiebe D. Type 1 diabetes in young adulthood. *Curr Diabetes Rev*. 2015;11(4):239–50. <https://doi.org/10.2174/1573399811666150421114957>
- 156 Arrieta A, Battelino T, Scaramuzza AE, Da Silva J, Castañeda J, Cordero TL, et al. Comparison of MiniMed 780G system performance in users aged younger and older than 15 years: evidence from 12 870 real-world users. *Diabetes Obes Metab*. 2022;24(7):1370–9. <https://doi.org/10.1111/dom.14714>
- 157 Castaneda J, Mathieu C, Aanstoot HJ, Arrieta A, Da Silva J, Shin J, et al. Predictors of time in target glucose range in real-world users of the MiniMed 780G system. *Diabetes Obes Metab*. 2022;24(11):2212–21. <https://doi.org/10.1111/dom.14807>
- 158 Arunachalam S, Velado K, Vigersky RA, Cordero TL. Glycemic outcomes during real-world hybrid closed-loop system use by individuals with type 1 diabetes in the United States. *J Diabetes Sci Technol*. 2023; 17(4):951–8. <https://doi.org/10.1177/19322968221088608>
- 159 Scaramuzza AE, Arnaldi C, Cherubini V, Piccinno E, Rabbone I, Toni S, et al. Recommendations for the use of sensor-augmented pumps with predictive low-glucose suspend features in children: the importance of education. *Pediatr Diabetes*. 2017;18(8):883–9. <https://doi.org/10.1111/pedi.12503>
- 160 Alotaibi A, Al Khalifah R, McAssey K. The efficacy and safety of insulin pump therapy with predictive low glucose suspend feature in decreasing hypoglycemia in children with type 1 diabetes mellitus: a systematic review and meta-analysis. *Pediatr Diabetes*. 2020; 21(7):1256–67. <https://doi.org/10.1111/pedi.13088>
- 161 Battelino T, Nimri R, Dovc K, Phillip M, Bratina N. Prevention of hypoglycemia with predictive low glucose insulin suspension in children with type 1 diabetes: a randomized controlled trial. *Diabetes Care*. 2017;40(6): 764–70. <https://doi.org/10.2337/dc16-2584>
- 162 Abraham MB, Nicholas JA, Smith GJ, Fairchild JM, King BR, Ambler GR, et al. Reduction in hypoglycemia with the predictive low-glucose management system: a long-term randomized controlled trial in adolescents with type 1 diabetes. *Diabetes Care*. 2018;41(2):303–10. <https://doi.org/10.2337/dc17-1604>
- 163 Choudhary P, de Portu S, Arrieta A, Castañeda J, Campbell FM. Use of sensor-integrated pump therapy to reduce hypoglycaemia in people with type 1 diabetes: a real-world study in the UK. *Diabet Med*. 2019;36(9):1100–8. <https://doi.org/10.1111/dme.14043>
- 164 Forlenza GP, Li Z, Buckingham BA, Pinsker JE, Cengiz E, Wadwa RP, et al. Predictive low-glucose suspend reduces hypoglycemia in adults, adolescents, and children with type 1 diabetes in an at-home randomized crossover study: results of the PROLOG trial. *Diabetes Care*. 2018;41(10):2155–61. <https://doi.org/10.2337/dc18-0771>
- 165 Pinsker JE, Leas S, Müller L, Habif S. Real-world improvements in hypoglycemia in an insulin-dependent cohort with diabetes mellitus pre/post Tandem Basal-iq technology remote software update. *Endocr Pract*. 2020;26(7):714–21. <https://doi.org/10.4158/EP-2019-0554>
- 166 Muller L, Habif S, Leas S, Aronoff-Spencer E. Reducing hypoglycemia in the real world: a retrospective analysis of predictive low-glucose suspend technology in an ambulatory insulin-dependent cohort. *Diabetes Technol Ther*. 2019;21(9):478–84. <https://doi.org/10.1089/dia.2019.0190>
- 167 Chen E, King F, Kohn MA, Spanakis EK, Breton M, Klonoff DC. A review of predictive low glucose suspend and its effectiveness in preventing nocturnal hypoglycemia. *Diabetes Technol Ther*. 2019;21(10): 602–9. <https://doi.org/10.1089/dia.2019.0119>
- 168 Shah VN, Rewers A, Garg S. Low glucose suspend systems. In: C Fabris, Kovatchev B, editors. *Glucose monitoring devices: measuring blood glucose to manage and control diabetes*. 525 B Street, Suite 1650, San Diego, CA, United States: Elsevier; 2020. Vol. 92101. p. 257–74. <https://doi.org/10.1016/b978-0-12-816714-4.00013-2>
- 169 Cengiz E, Sherr JL, Weinzier SA, Tamborlane WV. Clinical equipoise: an argument for expedited approval of the first small step toward an autonomous artificial pancreas. *Expert Rev Med Devices*. 2012; 9(4):315–7. <https://doi.org/10.1586/erd.12.33>
- 170 Bergenstal RM, Klonoff DC, Garg SK, Bode BW, Meredith M, Slover RH, et al. Threshold-based insulin-pump interruption for reduction of hypoglycemia. *N Engl J Med*. 2013;369(3):224–32. <https://doi.org/10.1056/NEJMoa1303576>
- 171 Ly TT, Nicholas JA, Retterath A, Lim EM, Davis EA, Jones TW. Effect of sensor-augmented insulin pump therapy and automated insulin suspension vs standard insulin pump therapy on hypoglycemia in patients with type 1 diabetes: a randomized clinical trial. *JAMA*. 2013;310(12):1240–7. <https://doi.org/10.1001/jama.2013.277818>
- 172 Conget I, Martín-Vaquero P, Roze S, Elías I, Pineda C, Álvarez M, et al. Cost-effectiveness analysis of sensor-augmented pump therapy with low glucose-suspend in patients with type 1 diabetes mellitus and high risk of hypoglycemia in Spain. *Endocrinol Diabetes Nutr*. 2018;65(7):380–6. <https://doi.org/10.1016/j.endinu.2018.03.008>
- 173 Roze S, Smith-Palmer J, Valentine W, Payet V, de Portu S, Papo N, et al. Cost-effectiveness of sensor-augmented pump therapy with low glucose suspend versus standard insulin pump therapy in two different patient populations with type 1 diabetes in France. *Diabetes Technol Ther*. 2016;18(2):75–84. <https://doi.org/10.1089/dia.2015.0224>
- 174 National Institute for Health and Care Excellence. Integrated sensor-augmented pump therapy systems for managing blood glucose levels in type 1 diabetes (the MiniMed Paradigm Veo system and the Vibe and G4 PLATINUM CGM system). 2016. [cited 2021; Available from: <https://www.nice.org.uk/guidance/dg21>
- 175 Hirsch IB, Abelson J, Bode BW, Fischer JS, Kaufman FR, Mastrototaro J, et al. Sensor-augmented insulin pump therapy: results of the first randomized treat-to-target study. *Diabetes Technol Ther*. 2008; 10(5):377–83. <https://doi.org/10.1089/dia.2008.0068>

- 176 Bergenstal RM, Tamborlane WV, Ahmann A, Buse JB, Dailey G, Davis SN, et al. Effectiveness of sensor-augmented insulin-pump therapy in type 1 diabetes. *N Engl J Med*. 2010;363(4):311–20. <https://doi.org/10.1056/NEJMoa1002853>
- 177 Buse JB, Kudva YC, Battelino T, Davis SN, Shin J, Welsh JB. Effects of sensor-augmented pump therapy on glycemic variability in well-controlled type 1 diabetes in the STAR 3 study. *Diabetes Technol Ther*. 2012;14(7):644–7. <https://doi.org/10.1089/dia.2011.0294>
- 178 Slover RH, Welsh JB, Criego A, Weinzimer SA, Willi SM, Wood MA, et al. Effectiveness of sensor-augmented pump therapy in children and adolescents with type 1 diabetes in the STAR 3 study. *Pediatr Diabetes*. 2012;13(1):6–11. <https://doi.org/10.1111/j.1399-5448.2011.00793.x>
- 179 Kordonouri O, Pankowska E, Rami B, Kappellen T, Coutant R, Hartmann R, et al. Sensor-augmented pump therapy from the diagnosis of childhood type 1 diabetes: results of the Paediatric Onset Study (ONSET) after 12 months of treatment. *Diabetologia*. 2010;53(12):2487–95. <https://doi.org/10.1007/s00125-010-1878-6>
- 180 Abraham MB, Smith GJ, Nicholas JA, Fairchild JM, King BR, Ambler GR, et al. Effect of frequency of sensor use on glycaemic control in individuals on sensor-augmented pump therapy with and without predictive low glucose management system. *Diabetes Res Clin Pract*. 2020;159:107989. <https://doi.org/10.1016/j.diabres.2019.107989>
- 181 Roze S, Smith-Palmer J, de Portu S, Özdemir Saltik AZ, Akgül T, Deyneli O. Cost-effectiveness of sensor-augmented insulin pump therapy versus continuous insulin infusion in patients with type 1 diabetes in Turkey. *Diabetes Technol Ther*. 2019;21(12):727–35. <https://doi.org/10.1089/dia.2019.0198>
- 182 Roze S, Payet V, Debroucker F, de PS, Cucherat M. Projection of long term health economic benefits of sensor augmented pump (sap) versus pump therapy alone (csi) in uncontrolled type 1 diabetes in France. *Value Health*. 2014;17(7):A348. <https://doi.org/10.1016/j.jval.2014.08.715>
- 183 Cranston I, Jamdade V, Liao B, Newson RS. Clinical, economic, and patient-reported benefits of connected insulin pen systems: a systematic literature review. *Adv Ther*. 2023;40(5):2015–37. <https://doi.org/10.1007/s12325-023-02478-1>
- 184 Gomez-Peralta F, Abreu C, Fernández-Rubio E, Cotovad L, Pujante P, Gaztambide S, et al. Efficacy of a connected insulin pen cap in people with noncontrolled type 1 diabetes: a multicenter randomized clinical trial. *Diabetes Care*. 2023;46(1):206–8. <https://doi.org/10.2337/dc22-0525>
- 185 Chien A, Thanasekaran S, Gaetano A, Im G, Wherry K, MacLeod J, et al. Potential cost savings in the United States from a reduction in sensor-detected severe hypoglycemia among users of the InPen smart insulin pen system. *J Manag Care Spec Pharm*. 2023;29(3):285–92. <https://doi.org/10.18553/jmcp.2023.22283>
- 186 Adolfsson P, Björnsson V, Hartvig NV, Kaas A, Möller JB, Ogionwo Lange E. Improved glycemic control observed in children with type 1 diabetes following the introduction of smart insulin pens: a real-world study. *Diabetes Ther*. 2022;13(1):43–56. <https://doi.org/10.1007/s13300-021-01177-w>
- 187 Ospelt E, Noor N, Sanchez J, Nelson G, Rioles N, Malik FS, et al. Facilitators and barriers to smart insulin pen use: a mixed-method study of multidisciplinary stakeholders from diabetes teams in the United States. *Clin Diabetes*. 2022;41(1):56–67. <https://doi.org/10.2337/cd22-0068>
- 188 American Diabetes Association Professional Practice Committee. 14. Children and adolescents: standards of care in diabetes-2024. *Diabetes Care*. 2024;47(Suppl 1):S258–81. <https://doi.org/10.2337/dc24-S014>
- 189 American Diabetes Association Professional Practice Committee. 5. Facilitating positive health behaviors and well-being to improve health outcomes: standards of care in diabetes-2024. *Diabetes Care*. 2024;47(Suppl 1):S77–110. <https://doi.org/10.2337/dc24-S005>
- 190 Blair J, McKay A, Ridyard C, Thornborough K, Bedson E, Peak M, et al. Continuous subcutaneous insulin infusion versus multiple daily injections in children and young people at diagnosis of type 1 diabetes: the SCIPRI RCT. *Health Technol Assess*. 2018;22(42):1–112. <https://doi.org/10.3310/hta22420>
- 191 Papadakis JL, Anderson LM, Garza K, Feldman MA, Shapiro JB, Evans M, et al. Psychosocial aspects of diabetes technology use: the child and family perspective. *Endocrinol Metab Clin North Am*. 2020;49(1):127–41. <https://doi.org/10.1016/j.ecl.2019.10.004>
- 192 Lukács A, Mayer K, Sasvári P, Barkai L. Health-related quality of life of adolescents with type 1 diabetes in the context of resilience. *Pediatr Diabetes*. 2018;19(8):1481–6. <https://doi.org/10.1111/pedi.12769>
- 193 Chen CW, Tinsley LJ, Volkening LK, Anderson BJ, Laffel LM. Observed characteristics associated with diabetes device use among teens with type 1 diabetes. *J Diabetes Sci Technol*. 2023;17(1):186–94. <https://doi.org/10.1177/19322968211050069>
- 194 Rosner B, Roman-Urrestarazu A. Health-related quality of life in paediatric patients with type 1 diabetes mellitus using insulin infusion systems. A systematic review and meta-analysis. *PLoS One*. 2019;14(6):e0217655. <https://doi.org/10.1371/journal.pone.0217655>
- 195 Mueller-Godeffroy E, Vonthein R, Ludwig-Seibold C, Heidtmann B, Boettcher C, Kramer M, et al. Psychosocial benefits of insulin pump therapy in children with diabetes type 1 and their families: the pumpkin multicenter randomized controlled trial. *Pediatr Diabetes*. 2018;19(8):1471–80. <https://doi.org/10.1111/pedi.12777>
- 196 Hitt TA, Hershey JA, Olivos-Stewart D, Forth E, Stuart F, Garren P, et al. The impact of fear of hypoglycaemia on sleep in adolescents with type 1 diabetes. *Diabet Med*. 2023;40(5):e15066. <https://doi.org/10.1111/dme.15066>
- 197 Nivet E, Lo G, Nivot-Adamiak S, Guitteny MA, De Kerdanet M. Impact of OMNIP-OD® on the quality of life of adolescents with type 1 diabetes. *Arch Pediatr*. 2022;29(1):21–6. <https://doi.org/10.1016/j.arcped.2021.10.001>
- 198 Prigge R, McKnight JA, Wild SH, Haynes A, Jones TW, Davis EA, et al. International comparison of glycaemic control in people with type 1 diabetes: an update and extension. *Diabet Med*. 2022;39(5):e14766. <https://doi.org/10.1111/dme.14766>
- 199 Lawton J, Blackburn M, Rankin D, Allen J, Campbell F, Leelarathna L, et al. The impact of using a closed-loop system on food choices and eating practices among people with Type 1 diabetes: a qualitative study involving adults, teenagers and parents. *Diabet Med*. 2019;36(6):753–60. <https://doi.org/10.1111/dme.13887>
- 200 Bratke H, Biringer E, Margeisdottir HD, Njølstad PR, Skrivvarhaug T. Relation of health-related quality of life with glycemic control and use of diabetes technology in children and adolescents with type 1 diabetes: results from a National Population Based Study. *J Diabetes Res*. 2022;2022:8401328. <https://doi.org/10.1155/2022/8401328>
- 201 Ilter Bahadur E, Özalkak Ş, Özdemir AA, Çetinkaya S, Özmert EN. Sleep disorder and behavior problems in children with type 1 diabetes mellitus. *J Pediatr Endocrinol Metab*. 2022;35(1):29–38. <https://doi.org/10.1515/jpem-2021-0523>
- 202 Tanenbaum ML, Iturralde E, Hanes SJ, Suttiratana SC, Ambrosino JM, Ly TT, et al. Trust in hybrid closed loop among people with diabetes: perspectives of experienced system users. *J Health Psychol*. 2020;25(4):429–38. <https://doi.org/10.1177/1359105317718615>
- 203 Naranjo D, Suttiratana SC, Iturralde E, Barnard KD, Weissberg-Benchell J, Laffel L, et al. What end users and stakeholders want from automated insulin delivery systems. *Diabetes Care*. 2017;40(11):1453–61. <https://doi.org/10.2337/dc17-0400>
- 204 Kimbell B, Rankin D, Hart RI, Allen JM, Boughton CK, Campbell F, et al. Parents' experiences of using a hybrid closed-loop system (CamAPS FX) to care for a very young child with type 1 diabetes: qualitative study. *Diabetes Res Clin Pract*. 2022;187:109877. <https://doi.org/10.1016/j.diabres.2022.109877>

- 205 Garza KP, Jedraszko A, Weil LEG, Naranjo D, Barnard KD, Laffel LMB, et al. Automated insulin delivery systems: hopes and expectations of family members. *Diabetes Technol Ther.* 2018;20(3):222–8. <https://doi.org/10.1089/dia.2017.0301>
- 206 Braune K, Gajewska KA, Thieffry A, Lewis DM, Froment T, O'Donnell S, et al. Why #WeAreNotWaiting-Motivations and self-reported outcomes among users of open-source automated insulin delivery systems: multinational survey. *J Med Internet Res.* 2021;23(6):e25409. <https://doi.org/10.2196/25409>
- 207 Braune K, Krug N, Knoll C, Ballhausen H, Thieffry A, Chen Y, et al. Emotional and physical health impact in children and adolescents and their caregivers using open-source automated insulin delivery: qualitative analysis of lived experiences. *J Med Internet Res.* 2022;24(7):e37120. <https://doi.org/10.2196/37120>
- 208 Nir J, Rachmiel M, Fraser A, Leventhal Y, Brenner A, Pinhas-Hamiel O, et al. Open-source automated insulin delivery systems (OS-AIDs) in a pediatric population with type 1 diabetes in a real-life setting: the AWeSoMe study group experience. *Endocrine.* 2023;81(2):262–9. <https://doi.org/10.1007/s12020-023-03398-4>
- 209 Cobry EC, Hamburger E, Jaser SS. Impact of the hybrid closed-loop system on sleep and quality of life in youth with type 1 diabetes and their parents. *Diabetes Technol Ther.* 2020;22(11):794–800. <https://doi.org/10.1089/dia.2020.0057>
- 210 Lawton J, Blackburn M, Rankin D, Allen JM, Campbell FM, Leelarathna L, et al. Participants' experiences of, and views about, daytime use of a day-and-night hybrid closed-loop system in real life settings: longitudinal qualitative study. *Diabetes Technol Ther.* 2019;21(3):119–27. <https://doi.org/10.1089/dia.2018.0306>
- 211 Farrington C. Psychosocial impacts of hybrid closed-loop systems in the management of diabetes: a review. *Diabet Med.* 2018;35(4):436–49. <https://doi.org/10.1111/dme.13567>
- 212 Forlenza GP, Ekhlaspour L, Breton M, Maahs DM, Wadwa RP, DeBoer M, et al. Successful at-home use of the Tandem control-IQ artificial pancreas system in young children during a randomized controlled trial. *Diabetes Technol Ther.* 2019; 21(4):159–69. <https://doi.org/10.1089/dia.2019.0011>
- 213 Beato-Vibora PI, Gallego-Gamero F, Lázaro-Martín L, Romero-Pérez MDM, Arroyo-Díez FJ. Prospective analysis of the impact of commercialized hybrid closed-loop system on glycemic control, glycemic variability, and patient-related outcomes in children and adults: a focus on superiority over predictive low-glucose suspend technology. *Diabetes Technol Ther.* 2020; 22(12):912–9. <https://doi.org/10.1089/dia.2019.0400>
- 214 Cobry EC, Bisio A, Wadwa RP, Breton MD. Improvements in parental sleep, fear of hypoglycemia, and diabetes distress with use of an advanced hybrid closed-loop system. *Diabetes Care.* 2022;45(5):1292–5. <https://doi.org/10.2337/dc21-1778>
- 215 Franceschi R, Mozzillo E, Di Candia F, Maines E, Leonardi L, Girardi M, et al. A systematic review on the impact of commercially available hybrid closed loop systems on psychological outcomes in youths with type 1 diabetes and their parents. *Diabet Med.* 2023;40(9):e15099. <https://doi.org/10.1111/dme.15099>
- 216 Bisio A, Brown SA, McFadden R, Pajewski M, Yu PL, DeBoer M, et al. Sleep and diabetes-specific psycho-behavioral outcomes of a new automated insulin delivery system in young children with type 1 diabetes and their parents. *Pediatr Diabetes.* 2021;22(3):495–502. <https://doi.org/10.1111/pedi.13164>
- 217 Rankin D, Kimbell B, Hovorka R, Lawton J. Adolescents' and their parents' experiences of using a closed-loop system to manage type 1 diabetes in everyday life: qualitative study. *Chronic Illn.* 2022;18(4):742–56. <https://doi.org/10.1177/1742395320985924>
- 218 Gianini A, Suklan J, Skela-Savič B, Klemencic S, Battelino T, Dovc K, et al. Patient reported outcome measures in children and adolescents with type 1 diabetes using advanced hybrid closed loop insulin delivery. *Front Endocrinol.* 2022;13:967725. <https://doi.org/10.3389/fendo.2022.967725>
- 219 Mingorance Delgado A, Lucas F. The Tandem Control-IQ advanced hybrid system improves glycemic control in children under 18 years of age with type 1 diabetes and night rest in caregivers. *Endocrinol Diabetes Nutr.* 2023;70(Suppl 3):27–35. <https://doi.org/10.1016/j.endien.2023.08.005>
- 220 Knoll C, Schipp J, O'Donnell S, Wäldchen M, Ballhausen H, Cleal B, et al. Quality of life and psychological well-being among children and adolescents with diabetes and their caregivers using open-source automated insulin delivery systems: findings from a multinational survey. *Diabetes Res Clin Pract.* 2023;196:110153. <https://doi.org/10.1016/j.diabres.2022.110153>
- 221 Roberts A, Fried L, Dart J, de Bock M, Fairchild J, King B, et al. Hybrid closed-loop therapy with a first-generation system increases confidence and independence in diabetes management in youth with type 1 diabetes. *Diabet Med.* 2022; 39(9):e14907. <https://doi.org/10.1111/dme.14907>
- 222 Cobry EC, Kanapka LG, Cengiz E, Carria L, Ekhlaspour L, Buckingham BA, et al. Health-related quality of life and treatment satisfaction in parents and children with type 1 diabetes using closed-loop control. *Diabetes Technol Ther.* 2021;23(6):401–9. <https://doi.org/10.1089/dia.2020.0532>
- 223 Wheeler BJ, Collyns OJ, Meier RA, Betts ZL, Frampton C, Frewen CM, et al. Improved technology satisfaction and sleep quality with Medtronic MiniMed® Advanced Hybrid Closed-Loop delivery compared to predictive low glucose suspend in people with Type 1 Diabetes in a randomized crossover trial. *Acta Diabetol.* 2022;59(1): 31–7. <https://doi.org/10.1007/s00592-021-01789-5>
- 224 Wong JJ, Hood KK, Hanes SJ, Lal RA, Naranjo D. Psychosocial effects of the loop open-source automated insulin delivery system. *J Diabetes Sci Technol.* 2023;17(6): 1440–7. <https://doi.org/10.1177/19322968221105288>
- 225 Mameli C, Smylie GM, Galati A, Rapone B, Cardona-Hernandez R, Zuccotti G, et al. Safety, metabolic and psychological outcomes of Medtronic MiniMed 670G in children, adolescents and young adults: a systematic review. *Eur J Pediatr.* 2023; 182(5):1949–63. <https://doi.org/10.1007/s00431-023-04833-4>
- 226 Michaels VR, Boucsein A, Watson AS, Frewen CM, Sanders OJ, Haszard JJ, et al. Glucose and psychosocial outcomes 12 Months following transition from multiple daily injections to advanced hybrid closed loop in youth with type 1 diabetes and suboptimal glycemia. *Diabetes Technol Ther.* 2024;26(1):40–8. <https://doi.org/10.1089/dia.2023.0334>
- 227 Hood KK, Garcia-Willingham N, Hanes S, Tanenbaum ML, Ware J, Boughton CK, et al. Lived experience of CamAPS FX closed loop system in youth with type 1 diabetes and their parents. *Diabetes Obes Metab.* 2022;24(12):2309–18. <https://doi.org/10.1111/dom.14815>
- 228 Kudva YC, Laffel LM, Brown SA, Raghinaru D, Pinsker JE, Ekhlaspour L, et al. Patient-reported outcomes in a randomized trial of closed-loop control: the pivotal International diabetes closed-loop trial. *Diabetes Technol Ther.* 2021;23(10):673–83. <https://doi.org/10.1089/dia.2021.0089>
- 229 Weissberg-Benchell J, Vesco AT, Shapiro J, Calhoun P, Damiano ER, Russell SJ, et al. Psychosocial impact of the insulin-only iLet bionic pancreas for adults, youth, and caregivers of youth with type 1 diabetes. *Diabetes Technol Ther.* 2023;25(10): 705–17. <https://doi.org/10.1089/dia.2023.0238>
- 230 Ng SM, Katkat N, Day H, Hubbard R, Quinn M, Finnigan L. Real-world prospective observational single-centre study: hybrid closed loop improves HbA1c, time-in-range and quality of life for children, young people and their carers. *Diabet Med.* 2022;39(7):e14863. <https://doi.org/10.1111/dme.14863>

- 231 Lawton J, Hart RI, Kimbell B, Allen JM, Besser REJ, Boughton C, et al. Data sharing while using a closed-loop system: qualitative study of adolescents' and parents' experiences and views. *Diabetes Technol Ther.* 2021;23(7):500–7. <https://doi.org/10.1089/dia.2020.0637>
- 232 Forlenza GP, Messer LH, Berget C, Wadwa RP, Driscoll KA. Biopsychosocial factors associated with satisfaction and sustained use of artificial pancreas technology and its components: a call to the technology field. *Curr Diab Rep.* 2018;18(11):114. <https://doi.org/10.1007/s11892-018-1078-1>
- 233 Messer LH, Berget C, Vigers T, Pyle L, Geno C, Wadwa RP, et al. Real world hybrid closed-loop discontinuation: predictors and perceptions of youth discontinuing the 670G system in the first 6 months. *Pediatr Diabetes.* 2020;21(2):319–27. <https://doi.org/10.1111/pedi.12971>
- 234 Hood K, Laffel LM, Danne T, Nimri R, Weinzimer SA, Sibayan J, et al. Lived experience of advanced hybrid closed-loop versus hybrid closed loop: patient-reported outcomes and perspectives. *Diabetes Technol Ther.* 2021;23(12):857–61. <https://doi.org/10.1089/dia.2021.0153>
- 235 DuBose SN, Bauza C, Verdejo A, Beck RW, Bergenstal RM, Sherr J, et al. Real-world, patient-reported and clinic data from individuals with type 1 diabetes using the MiniMed 670G hybrid closed-loop system. *Diabetes Technol Ther.* 2021;23(12):791–8. <https://doi.org/10.1089/dia.2021.0176>
- 236 Messer LH, Berget C, Pyle L, Vigers T, Cobry E, Driscoll KA, et al. Real-world use of a new hybrid closed loop improves glycemic control in youth with type 1 diabetes. *Diabetes Technol Ther.* 2021;23(12):837–43. <https://doi.org/10.1089/dia.2021.0165>
- 237 Sehgal S, De Bock M, Jones S, Frewen C, Wheeler BJ. User experiences during the transition to calibration-free sensors with remote monitoring while using automated insulin delivery: a qualitative study. *Front Endocrinol.* 2023;14:1214975. <https://doi.org/10.3389/fendo.2023.1214975>
- 238 Ehrmann D, Kulzer B, Roos T, Haak T, Al-Khatib M, Hermanns N. Risk factors and prevention strategies for diabetic ketoacidosis in people with established type 1 diabetes. *Lancet Diabetes Endocrinol.* 2020;8(5):436–46. [https://doi.org/10.1016/S2213-8587\(20\)30042-5](https://doi.org/10.1016/S2213-8587(20)30042-5)
- 239 Messer LH, Berget C, Ernst A, Towers L, Slover RH, Forlenza GP. Initiating hybrid closed loop: a program evaluation of an educator-led Control-IQ follow-up at a large pediatric clinic. *Pediatr Diabetes.* 2021;22(4):586–93. <https://doi.org/10.1111/pedi.13183>
- 240 Pinsker JE, Singh H, McElwee Malloy M, Constantin A, Leas S, Kriegl K, et al. A virtual training program for the Tandem t: slim X2 insulin pump: implementation and outcomes. *Diabetes Technol Ther.* 2021;23(6):467–70. <https://doi.org/10.1089/dia.2020.0602>
- 241 Vigersky RA, Velado K, Zhong A, Agrawal P, Cordero TL. The effectiveness of virtual training on the MiniMed 670G system in people with type 1 diabetes during the COVID-19 pandemic. *Diabetes Technol Ther.* 2021;23(2):104–9. <https://doi.org/10.1089/dia.2020.0234>
- 242 Bassi M, Dufour F, Strati MF, Franzone D, Scalas M, Lionetti B, et al. Advanced Hybrid Closed Loop users' satisfaction of telemedicine and telenursing in pediatric and young adult type 1 diabetes. *Front Public Health.* 2023;11:1249299. <https://doi.org/10.3389/fpubh.2023.1249299>
- 243 Gomez AM, Henao D, Parra D, Kerguelen A, Pinilla MV, Muñoz OM, et al. Virtual training on the hybrid close loop system in people with type 1 diabetes (T1D) during the COVID-19 pandemic. *Diabetes Metab Syndr.* 2021;15(1):243–7. <https://doi.org/10.1016/j.dsx.2020.12.041>
- 244 Doyle EA, Weinzimer SA, Tamborlane W. DKA prevention and insulin pumps: lessons learned from a large pediatric pump practice. *Sci Diabetes Self Manag Care.* 2022;26350106221125699.
- 245 Berget C, Messer LH, Vigers T, Frohnert BI, Pyle L, Wadwa RP, et al. Six months of hybrid closed loop in the real-world: an evaluation of children and young adults using the 670G system. *Pediatr Diabetes.* 2020;21(2):310–8. <https://doi.org/10.1111/pedi.12962>
- 246 Petrovski G, Al Khalaf F, Campbell J, Umer F, Almajaly D, Hamdan M, et al. One-year experience of hybrid closed-loop system in children and adolescents with type 1 diabetes previously treated with multiple daily injections: drivers to successful outcomes. *Acta Diabetol.* 2021;58(2):207–13. <https://doi.org/10.1007/s00592-020-01607-4>
- 247 Akturk HK, Snell-Bergeon J, Shah VN. Efficacy and safety of Tandem control IQ without user-initiated boluses in adults with uncontrolled type 1 diabetes. *Diabetes Technol Ther.* 2022;24(10):779–83. <https://doi.org/10.1089/dia.2022.0162>
- 248 Tornese G, Carletti C, Giangreco M, Nisticò D, Faleschini E, Barbi E. Carbohydrate tolerance threshold for unannounced snacks in children and adolescents with type 1 diabetes using an advanced hybrid closed-loop system. *Diabetes Care.* 2022;45(6):1486–8. <https://doi.org/10.2337/dc21-2643>
- 249 Haidar A, Legault L, Raffray M, Gouchie-Provencher N, Jafar A, Devaux M, et al. A randomized crossover trial to compare automated insulin delivery (the artificial pancreas) with carbohydrate counting or simplified qualitative meal-size estimation in type 1 diabetes. *Diabetes Care.* 2023;46(7):1372–8. <https://doi.org/10.2337/dc22-2297>
- 250 Kichler J, Harris M, Weissberg-Benchell J. Contemporary roles of the pediatric psychologist in diabetes care. *Curr Diabetes Rev.* 2015;11(4):210–21. <https://doi.org/10.2174/1573399811666150421104449>
- 251 Toffanin C, Kozak M, Sumnik Z, Cobelli C, Petruzelkova L. In silico trials of an open-source android-based artificial pancreas: a new paradigm to test safety and efficacy of do-it-yourself systems. *Diabetes Technol Ther.* 2020;22(2):112–20. <https://doi.org/10.1089/dia.2019.0375>
- 252 Braune K, Lal RA, Petruželková L, Scheiner G, Winterdijk P, Schmidt S, et al. Open-source automated insulin delivery: international consensus statement and practical guidance for health-care professionals. *Lancet Diabetes Endocrinol.* 2022;10(1):58–74. [https://doi.org/10.1016/S2213-8587\(21\)00267-9](https://doi.org/10.1016/S2213-8587(21)00267-9)
- 253 Burnside MJ, Lewis DM, Crockett HR, Meier RA, Williman JA, Sanders OJ, et al. Open-source automated insulin delivery in type 1 diabetes. *N Engl J Med.* 2022;387(10):869–81. <https://doi.org/10.1056/NEJMoa2203913>