COLLEGE OF PHARMACY
UNIVERSITY OF UTAH

L. S. SKAGGS PHARMACY INSTITUTE

UTAH MEDICAID PT REPORT
SEPTEMBER 2023

AMBULATORY INSULIN PUMPS FOR CONTINUOUS SUBCUTANEOUS INSULIN DELIVERY

iLet Bionic Pancreas
MiniMed 630G
MiniMed 770G
MiniMed 780G
Omnipod 5
Omnipod DASH
Omnipod Insulin Management System (Omnipod Eros)
t:slim X2 (with Basal-IQ or Control-IQ)
V-Go

Report finalized: August 2023
Report presented: September 2023

Drug Regimen Review Center

Lauren Heath, PharmD, MS, Clinical Pharmacist
Valerie Gonzales, PharmD, Clinical Pharmacist
Monet Luloh, PharmD, Clinical Pharmacist
Kristin Knippenberg, MFA, Administrator and Editor
Joanne LaFleur, PharmD, MSPH, Director and Associate Professor

University of Utah College of Pharmacy, Drug Regimen Review Center

CONTENTS

LIST OF FIGURES

LIST OF TABLES

ABBREVIATIONS

A1c	Hemoglobin A1c (glycated hemoglobin)
AACE	American Association of Clinical Endocrinology
ACE	Alternate controller enabled
ADA	American Diabetes Association
ADIP	Algorithm-driven insulin pumps
AHCL	Advanced hybrid closed loop
AID	Automated insulin delivery
BG	Blood glucose
BGM	Blood glucose monitor
BMI	Body mass index
CGM	Continuous glucose monitor
CI	Confidence interval
CSII	Continuous subcutaneous insulin infusion
DKA	Diabetes ketoacidosis
DM	Diabetes mellitus
ES	Endocrine Society
FDA	United States Food and Drug Administration
GDM	Gestational diabetes mellitus
HCL	Hybrid closed loop
I:C	Insulin to carbohydrate ratio
IP	Insulin pump
IPS	Insulin pump system
ISPAD	International Society for Pediatric and Adolescent Diabetes
IST	Insulin-suspend technology
LGS	Low-glucose suspend
MDI	Multiple daily insulin injections
P&T	Pharmacy and Therapeutics
PDM	Personal Diabetes Manager
PLGS	Predictive low-glucose suspend
PwD	People (living) with diabetes mellitus
RA	Rapid acting
RCT	Randomized controlled trial
rtCGM	Real-time continuous glucose monitor
SAP	Sensor-augmented insulin pump
SG	Sensor glucose
SMBG	Self-monitor blood glucose
SR	Systematic review
T1D	Type 1 diabetes mellitus
T2D	Type 2 diabetes mellitus
TAR	Time above range
TBR	Time below range
TDD	Total daily dose
TIR	Time in range

EXECUTIVE SUMMARY

Background

Intensive insulin therapy with multiple daily injections (MDI; ie, basal-bolus insulin therapy) or continuous subcutaneous infusion of insulin (CSII) by insulin pump is required for patients with type 1 diabetes (T1D), as well as patients with other forms of insulin-deficit diabetes.[1,2] Compared to MDI, CSII with an insulin pump increases lifestyle flexibility and optimizes insulin dosing while requiring fewer daily injections.[2,3] This report reviews characteristics, clinical guideline recommendations, and head-to-head (H-H) comparative randomized controlled trial (RCT) evidence for commercially available United Stated (US) Food and Drug Administration (FDA)-cleared insulin pumps. See **Table EX1** for pumps addressed by this report.

Table EX1. Overview of Insulin Pumps/Pump Systems Addressed in This Report

Pump/Pump System	Tubed Pump	Compatible CGM for Integration	Labeled Population[a]	Maximal Pump System Type[b]
iLet Bionic Pancreas[4]	Y	Dexcom G6	DM age ≥ 6 (pump); T1D age ≥ 6 (as AID)	Advanced AID
MiniMed 630G[5c]	Y	Guardian 3	DM age ≥ 14	SAP with LGS
MiniMed 770G[6c]	Y	Guardian 3	T1D age ≥ 2	AID
MiniMed 780G[7,8c]	Y	Guardian 3 or 4	T1D age ≥ 7	Advanced AID
Omnipod 5[9c]	N, patch	Dexcom G6	DM on insulin (pump); T1D age ≥ 2 (as AID)	AID
Omnipod DASH[10]	N, patch	--	DM on insulin	Conv. IP or SAP
Omnipod Insulin Management System (Eros)[11]	N, patch	--	DM on insulin	Conv. IP or SAP
t:slim X2 with Basal-IQ[12c]	Y	Dexcom G6	DM age ≥ 6	SAP with LGS and PLGS
t:slim X2 with Control-IQ[13c]	Y	Dexcom G6	DM age ≥ 6 (pump); T1D age ≥ 6 (as AID)	Advanced AID
V-Go[14]	N, patch	--	Adults w/ DM	Conv. IP or SAP

[a] Per pump user guide. Some pumps have separate indicated populations for the pump and insulin delivery algorithms.

[b] Refers to the most advanced insulin delivery system mode usable by a given pump.

[c] Also useable in non-automated mode as a conventional insulin pump or SAP. The MiniMed 770G and 780G are uniquely able to be used as a conventional pump, SAP with LGS/PLGS, or (advanced) AID.

Abbreviations: AID, automated insulin delivery; Conv, conventional; DM, diabetes mellitus; IP, insulin pump; LGS, low-glucose suspend; PLGS, predictive low-glucose suspend; N, no; T1D, type 1 diabetes mellitus; SAP, sensor-augmented pump; Y, yes;

Ambulatory insulin pumps are available as (1) single-use patches that attach directly to the skin (patch-pumps or tubeless pumps)[9,10,15] or (2) reusable, wearable digital devices that deliver insulin via a tube with a cannula (infusion set) that attaches to the skin (tubed pumps).[4-6,8,16] Pumps deliver fast-acting

insulin continuously (basal insulin), covering insulin needs between meals, and as intermittent insulin boluses, covering meals or correcting for hyperglycemia.[17]

Ambulatory insulin pumps can be classified as insulin pump systems based on use with a continuous glucose monitor (CGM) and software algorithm that augments pump insulin delivery. Conventional (stand-alone) insulin pumps and basic sensor-augmented pumps (SAPs) are open-loop systems that cannot automatically augment insulin delivery based on CGM sensor glucose (SG) values.[17,18] Advanced insulin pump systems, SAPs with insulin-suspend technology (IST) and automated insulin delivery (AID) systems, are closed-loop systems. In closed-loop insulin delivery systems, SG CGM readings feed back to a software algorithm (controller) to augment pump insulin delivery.[18]

- Basic SAPs are insulin pumps used with stand-alone CGM. Conventional insulin pumps and basic SAPs require all bolus doses and insulin rate adjustments to be manually carried out by the patient.[3,18]
- SAP with IST either pause insulin delivery for a low SG value (low-glucose suspend [LGS]) and/or when SG is predicted to become too low (predicted LGS [PLGS]). People with diabetes mellitus (PwD) using SAP with IST are still responsible for programming/adjusting the basal insulin infusion rate and manually initiating bolus doses.[5,12]
- AID systems autonomously adjust basal insulin delivery rates based on SG values.[3,18,19] A subtype of AID systems, advanced AID systems, autonomously deliver insulin boluses to correct hyperglycemic SG values in addition to adjusting basal insulin rates.[19] PwD using AID systems are responsible for manually announcing meals or delivering meal boluses.[19]

All pumps except for the Omnipod pumps and V-Go are tubed pumps.[4-14,16] Most reviewed pumps that function as a SAP with IST and/or AID system are compatible with the Dexcom G6 CGM[4,9,12,13]; the exceptions are Medtronic MiniMed pumps that use Medtronic CGMs.[5-8] There are some differences between integrable CGMs. The Dexcom G6 CGM requires less frequent sensor changes than Medtronic sensors,[5-8,20,21] and the Guardian 3 sensor by Medtronic requires frequent calibration with self-monitoring blood glucose (SMBG) testing,[5-7] unlike the Dexcom G6 and Guardian 4 sensor.[8,20,21]

Labeled populations indicated for insulin pumps and/or insulin delivery controller vary as shown in Table EX1. All insulin pumps except for the MiniMed 770G and 780G are indicated for PwD or PwD requiring insulin, including SAPs with IST.[4-14,16] Omnipod pumps indications are not specific to particular age ranges,[9-11] whereas the V-go is indicated only for adults,[14] and other pumps are indicated for pediatric and adult populations, with specific age ranges for approved use (refer to Table EX1). Pumps used as an AID system (ie, with AID software) are indicated specifically for T1D.[4,6-9,13] The Omnipod 5 and MiniMed 770G AID systems are indicated for people ≥ 2 years old with T1D.[6,9] Pump systems functional as an advanced AID system are indicated for patients with T1D age 6 years or older (t:slim X2 with Control-IQ and iLet Bionic Pancreas),[4,13] or age 7 or older (MiniMed 780G).[7,8]

Below are a few unique characteristics of insulin pumps. Refer to section 5 for additional information.

- Conventional insulin pumps and basic SAPs (ie, when used with viewable CGM data only):
  - The mechanical V-go patch-pump delivers CSII at a single pre-set rate (3 patch formulations are available, each with a different pre-set rate ranging from 0.83 to are 1.25 insulin Units/hour) with optional 2-unit manual insulin boluses.[14] Electronic pumps functional as conventional insulin pumps, which includes all pumps except for the iLet Bionic Pancreas,[4] allow the user to

program personalized basal and bolus delivery, and offer safety alarms and bolus dose calculators,[5-11,16] unlike the V-Go.[14]

- SAP with IST:
  - Of pump systems with maximal functionality as a SAP with IST, the t:slim X2 with Basal-IQ offers both PLGS and LGS,[12] whereas the MiniMed 630G only offers LGS.[5] Although, an advantage of the MiniMed 630G is the ability to customize the low glucose threshold.[5]

- AID systems:
  - AID systems change insulin delivery to target different SG values. Omnipod 5 offers the most flexibility by allowing the user to set up to 8 different SG targets throughout the day.[9] The MiniMed 780G can target the lowest SG value of 100 mg/dL.[7,8] AID systems other than the Bionic Pancreas[4] offer a temporarily higher SG target or specific mode for exercise.[6-9,13]
  - Advanced AID systems vary in the number and manner of corrective and meal insulin boluses. Control-IQ only delivers up to 1 automated corrective bolus per hour,[13] whereas the MiniMed 780G and iLet Bionic Pancreas can deliver up to 12 automated boluses per hour.[4,7,8] With regard the user-initiated meal boluses, the iLet Bionic Pancreas is the most automated system, requiring only user announcement of a meal without strict carbohydrate counting.[4]

US or International Guideline Insulin Pump Therapy Recommendations

Primary guidelines reviewed include recent technology-focused guidelines from the American Diabetes Association (ADA; 2023),[22] American Association of Clinical Endocrinology (AACE; 2021),[23] and the International Society for Pediatric and Adolescent Diabetes (ISPAD; 2022).[24] In RCTs among people with T1D, AID systems have been shown to improve glycemic control compared to other insulin pump systems, including improvement of time-in-range (TIR; ie, SG readings between 70-180 mg/dL) by about 10-15%.[24] To achieve optimal glycemic outcomes, patients using AID systems should maximize time spent in the automated dosing mode.[19] Guidelines do not distinguish between AID systems and advanced AID systems in formal recommendations.[22-24] In general, guidelines encourage individualizing insulin pump selection based on patient preferences and needs.[22-24] Continued access to the same insulin pump therapy after changes in insurance coverage is encouraged by the ADA.[22]

For most children and adults with T1D, guidelines prefer an AID system over other modes of intensive insulin therapy. Other pump-based insulin delivery systems (ie, conventional pump, SAP, or SAP with IST) are also options for people with T1D who prefer one of these options to an AID system or who are unable to use an AID system.[22-24] SAP with IST, with PLGS preferred over LGS, is recommended by ISPAD for youth with T1D if an AID system is not available.[24] Experts consider AID systems an option for very young children (eg, <7 years) with T1D[19]; however, very young children with low daily insulin needs may not be able to use some AID systems due to the minimal threshold insulin requirements.[25]

Evidence supporting use of AID systems in **people without T1D** is limited.[22-24] While ISPAD and the AACE formally recommend or suggest AID systems for all youth with DM[24] or PwD with characteristics that might benefit from automated dosing (eg, significant glycemic variability),[23] cited evidence supporting these recommendations is only among people with T1D. It is unclear to what extent these recommendations apply to people without T1D. The ADA specifically recommends AID systems for people with insulin-deficient DM based on low-level evidence (expert opinion),[22] which is consistent with AID system expert consensus recommendations.[19] Conventional insulin pumps for people with

T2D,[22] or basic SAP for insulin-deficient PwD,[23] who require MDI are options based on high-quality evidence. Non-AID insulin pump delivery systems are also options for people with any type of DM (per ADA based on expert opinion)[22]; the AACE recommends SAP with IST for people with any type of DM who have significant problems with hypoglycemia.[23]

Direct Comparative Evidence

We reviewed RCTs comparing insulin pumps or advanced pump system software (ie, IST or AID technology) addressed by this report* to one another (H-H) for the management of PwD. Three H-H RCTs were included: MiniMed 780G vs MiniMed 670G, t:slim X2 with Control-IQ vs t:slim X2 with Basal-IQ, and t:slim X2 with Basal-IQ vs t:slim X2 with stand-alone CGM. No H-H trials were found† for V-Go, iLet Bionic Pancreas, MiniMed 630G, MiniMed 770G, or any Omnipod pumps. All trials enrolled patients with T1D who were not pregnant; patient ages ranged between 6 and 72 years old.[26-28] Below is an overview of the primary outcome results from these RCTs organized by the pump used and pump system type.

Advanced AID (MiniMed 780G) versus AID (MiniMed 670G)*: Open-label, cross-over RCT

Patients (n=113) ages 14-29 years old with T1D previously treated with MDI or an insulin pump were randomized to the order of using the MiniMed 670G or 780G (both with the Guardian 3 sensor) in automated mode for 12 weeks each. The trial achieved co-primary endpoints, demonstrating significantly reduced time in daytime hyperglycemia (glucose >180 mg/dL) without increasing time in hypoglycemia (glucose <54 mg/dL) with 780G compared to the 670G. The mean proportion of TIR, glucose between 70-180 mg/dL, was significantly greater with the 780G (67%) than the 670G (63%), with both systems demonstrating numerically improved TIR compared to baseline (57%). Time spent in automated insulin dosing mode was significantly higher during treatment with 780G (86%) compared to 670G (75%), likely due to fewer forced automation exits. The safety profile appeared similar between pump systems.[28]

Advanced AID (t:slim X2 with Control-IQ) versus SAP with LGS and PLGS (t:slim X2 with Basal-IQ): Parallel-group, switch RCT

Patients (n=109) ages 14 years or older with long-standing T1D who had just completed an RCT using the t:slim X2 with Control-IQ were randomized to either switch to Basal-IQ or continued Control IQ, both with the Dexcom G6 CGM, for 13 weeks. The primary efficacy outcome, risk-adjusted difference in mean percent TIR (5.9; 95% CI 3.6–8.3), significantly favored continuing Control-IQ (mean % TIR 67.6) to Basal-IQ (mean % TIR 60.4). There was not a different difference in hypoglycemic outcomes between study arms, but hyperglycemic outcomes (eg, percent of time >180 mg/dL) significantly favored Control-IQ. Other than worsened glycemic control (>0.5%) by hemoglobin A1c, which occurred significantly more frequently in patients who switched to Basal-IQ than patients who continued Control-IQ, the pump systems exhibited a similar safety profile.[27]

---

* Comparisons with the MiniMed 670G were also allowed since this pump is highly similar to the MiniMed 770G.
† Our literature search targeted systematic reviews published since 2018, so only RCTs included in a review article that clearly stated which pumps were used in an RCT were identified.

SAP with LGS and PLGS (t:slim X2 with Basal-IQ) versus basic SAP (t:slim X2 with CGM): Cross-over RCT

Patients (n=103) between 6 and 72 years old with diagnosed T1D for at least 1 year were randomized to the order of using the t:slim X2 with Basal-IQ or t:slim X2 with non-integrated CGM (SAP with viewable CGM data), both with the Dexcom G5, for 3 weeks each. The primary outcome of the difference in proportion of hypoglycemic readings between each 3-week period significantly favored Basal-IQ, –0.8 (95%CI –1.1 to –0.5). Overall glucose control by TIR was also significantly greater in the Basal-IQ period (65%) compared to the SAP period (63%). One severe hypoglycemic event occurred during the SAP treatment period compared to none in the Basal-IQ period.[26]

Safety

Primary risks of insulin pump therapy include hypo- or hyper-glycemia due to over- or under-delivery of insulin, as well as irritation, infection, or other reaction at the site of insulin infusion and/or CGM sensor insertion.[4-14] Because frequent small doses of fast-acting insulin is used by insulin pumps, ketosis or diabetic ketoacidosis can develop relatively quickly if insulin delivery is interrupted,[17,24] which can occur due to technical issues (eg, hardware or software error) or user error. Direct comparative evidence between specific insulin pump models (and components such as infusion sets for tubed pumps) appears to be limited, but generally, the safety profile of insulin pumps themselves is comparable. A possible exception is the risk of blocked insulin delivery (occlusion) that might be greater with tubed pumps than tubeless pumps.[29] Compared to conventional insulin pump therapy, therapy with automated insulin adjustment technology that reduces or suspends insulin delivery for low or predicted low glucose mitigates hypoglycemia.[19,22-24] Nonetheless, likely due to greater complexity, advanced insulin pump systems carry comparatively more precautions or warnings for use than conventional-only insulin pumps; the V-go carries the fewest warnings of all pumps.[14]

Some patients are either contraindicated or would not be good candidates for treatment with one or more insulin pumps.

- Insulin pumps other than the V-go are either contraindicated or carry warnings to avoid use in people who cannot maintain adequate contact with their healthcare provider or who have impaired vision or hearing (unable to see/hear pump signals).[4-13]
- The MiniMed 630G, 770G, and 780G, when integrated with the Guardian 3 sensor (which requires calibration with a blood glucose meter at least twice daily), are contraindicated in people unwilling to self-monitor blood glucose at least 4 times daily.[5-7]
- Omnipod pumps are not recommended for people who are allergic to acrylic adhesives or who have skin easily damaged by adhesives.[9-11]
- Automated dosing technologies for AID systems (other than the iLet Bionic Pancreas[4]) carry warnings for a minimum and/or maximum total daily insulin dose (TDD) to safely use the technology, as follows:
  - TDD ≥ 5 Units for Omnipod 5,[9]
  - TDD of 8-250 Units for MiniMed 770G and 780G,[6-8] and
  - TDD of 10-100 Units for Control-IQ.[13]
  - The t:slim X2 pump with Control-IQ also requires that patients weigh between 25 and 140 kilograms.[13]

All AID systems carry warnings/precautions for a lack of data or recommendation against their use in pregnancy.[4,6-9,13] Omnipod 5 (when using the AID technology), iLet Bionic Pancreas, and t:slim X2 with Basal- or Control-IQ (when used with Dexcom G6) are specifically recommended to not be used during pregnancy.[4,9,12,13] Refer to section 8 for additional insulin pump safety information.

Utah Medicaid Preferred Drug List (PDL) Recommendations

The Utah Medicaid Pharmacy and Therapeutics (P&T) Committee may consider recommending one or both of the following options for the PDL. Factors to consider for each recommendation are listed below the recommendations. Insulin pumps and pump system characteristics vary, and some patients may require certain pump characteristics for safe and effective use. If either recommendation below is implemented, Utah Medicaid should accommodate reasonable requests for a non-preferred pump.

1. **Recommend that at least 1 insulin pump other than the V-Go be PDL-preferred.**
   - Conventional insulin pump therapy or SAP therapy are options per guidelines for people with T2D or other insulin-dependent DM who require intensive insulin therapy based on high-quality evidence. SAP with LGS/PLGS is also a recommended option for adults or youth with insulin-deficient DM on MDI based on low-quality evidence (expert opinion), or for anyone with DM who has significant issues with hypoglycemia. AID systems are considered more effective than other pumps systems for people with T1D. Evidence for the safety and efficacy of AID systems in people with T2D (or other DM) is limited, and AID systems are yet to be FDA-cleared for patients without T1D. Utah Medicaid could prefer on the PDL any pump usable as a conventional pump or SAP to meet the needs of people with insulin-dependent DM, while allowing patients to access non-preferred pumps via prior authorization and/or including a preferred AID system for patients with T1D as described in recommendation 2.
   - V-Go is the only insulin pump whose users cannot customize insulin delivery rates, and it is indicated only for adults with diabetes. Experts consider it an option primarily for people with T2D based on clinical evidence for its use.[29,30] Given these limitations, another pump may be preferred.

2. **Recommend that at least 1 insulin pump maximally capable of being used as an AID system be PDL-preferred for patients with T1D.**
   - AID systems have demonstrated improved glycemic control compared to other types of intensive insulin therapy in patients with T1D. Evidence supporting at least some type of AID system is available for patients with T1D as young as 2 years old.[19] Guidelines strongly recommend AID systems for people with T1D. The ADA also considers AID systems an option for people with other types of insulin-deficit diabetes based on expert opinion only (lacking clinical trial support). A consensus statement does cite 1 RCT supporting an AID system in the ambulatory setting for patients with T2D and 2 clinical trials in patients with cystic fibrosis-related diabetes.[19]
   - There is limited comparative evidence among commercial AID systems. Generally, the efficacy and safety profiles appear similar. One RCT demonstrated reduced hyperglycemia without increased hypoglycemia among people using the MiniMed 780G (which is an advanced AID system with automatic corrective insulin boluses) compared to the MiniMed 670G (a non-advanced AID system that uses a similar algorithm to the 770G for basal insulin adjustment only).[6]

1.0 INTRODUCTION

Patients living with type 1 diabetes mellitus (T1D) require intensive insulin therapy with either multiple daily insulin injections (MDI) or continuous subcutaneous infusion of insulin (CSII) delivered by an insulin pump. Many patients with advanced type 2 diabetes mellitus (T2D) also require intensive insulin therapy.[1,2] Compared to MDI, CSII with an insulin pump increases lifestyle flexibility and delivers insulin more precisely while requiring fewer daily injections.[2,3] Insulin pump therapy is a popular treatment choice for people living with diabetes mellitus (PwD); over 50% of patients with T1D and increasing numbers of patients with T2D use pump therapy.[3] Historically, insulin pumps have been underutilized among people with lower socioeconomic status compared to people with higher socioeconomic status.[22]

Insulin pumps, especially those with technology capable of automating insulin delivery, are important options for improving glycemic control, thus reducing the risk of chronic complications. Additionally, the systems may improve quality of life and reduce distress associated with the burden of managing DM.[23]

Conventional insulin pump therapy, involving continuous insulin infusion at user-programmed rates and intermittent patient-activated insulin boluses delivered via an ambulatory pump,[17] has been available since the 1970s.[3] Today, insulin pumps are available as single-use patches that attach directly to the skin (patch-pumps or tubeless pumps)[9,10,15] or reusable, wearable digital devices that deliver insulin via a tube with a cannula (ie, infusion set) that attaches to the skin (tubed pumps).[4-6,8,16] **Table 1** shows insulin pumps addressed in this report, with pumps categorized by the most advanced pump operation mode. Conventional insulin pumps are usable as a sensor-augmented pump (SAP) when used alongside a continuous glucose monitor (CGM).[18] With the exception of the t:slim X2 pump,[12,13] conventional pumps cannot directly integrate with CGM to make automatic insulin adjustments per CGM sensor glucose (SG) values. Except for the iLet Bionic Pancreas,[4] pumps maximally functional as advanced pump systems capable of augmenting insulin delivery based on SG values (ie, SAPs with insulin-suspend technology [IST]) or automated insulin delivery (AID) systems) are useable as conventional insulin pumps.[6-9,12,13] See **Appendix A** for select insulin pump component definitions.

Insulin pumps vary in physical characteristics, labeled indications, compatibility with software algorithms, and which CGM integrates with the pump and algorithm. **Table 1** summarizes key factors affecting selection of an insulin pump. All pumps except for the Omnipod pumps and V-Go are tubed pumps.[4-14,16] Most reviewed pumps that function as a SAP with IST and/or AID system are compatible with the Dexcom G6 CGM[4,9,12,13]; the exceptions are Medtronic MiniMed pumps that use Medtronic CGMs.[5-8] Labeled populations indicated for insulin pumps and/or insulin delivery controller vary as shown in **Table 1**. All insulin pumps except for the MiniMed 770G and 780G are indicated for PwD or PwD requiring insulin, including SAPs with IST.[4-14,16] Omnipod pump indications are not specific to particular age ranges,[9-11] whereas the V-go is indicated only for adults,[14] and other pumps are indicated for pediatric and adult populations, with specific age ranges for approved use (refer to **Table 1**). Pumps used as an AID system (ie, with AID software) are indicated specifically for T1D.[4,6-9,13] The Omnipod 5 and MiniMed 770G AID systems are indicated for people ≥ 2 years old with T1D.[6,9] Pump systems functional as an advanced AID system are indicated for patients with T1D age 6 years or older (t:slim X2 with Control-IQ and iLet Bionic Pancreas),[4,13] or age 7 or older (MiniMed 780G).[7,8]

Table 1. Overview of Insulin Pump System Types[18,31-33]

Type of Insulin Pump/Pump System	Loop System Type	Characteristics	Pump System *by Maximal Operation Mode*[a]	Select User Requirements
Conventional insulin pump alone	Open	• IP only • No CGM	V-Go[14] Omnipod DASH[10] Omnipod Insulin Management System (Eros)[11] t:slim X2 (pump only)[16]	• User pre-programs/ determines all insulin delivery
Sensor-augmented pump (SAP)[b]	Open	• IP and viewable (stand-alone) CGM data • No automated insulin changes per CGM value		
Advanced Pump Systems Combining a Pump, CGM, and Software Algorithm				
SAP with insulin-suspend technology (LGS or PLGS)[c]	Closed	• IP with integrated CGM data • Pauses insulin on low threshold (LGS) or when a low is anticipated (PLGS) • No automated insulin dosing	MiniMed 630G[5] t:slim X2 with Basal-IQ[12]	• User pre-programs all insulin delivery, except for triggered suspension for (predicted) low glucose
Automated insulin delivery (AID) system	Closed[d]	• IP with integrated CGM data • Pauses insulin delivery (LGS and/or PLGS) • Automated basal insulin dosing	Omnipod 5[9] MiniMed 770G[6]	• User delivers meal and corrective insulin bolus
Advanced AID system	Closed[d]	• IP with integrated CGM data • Pauses insulin delivery (LGS and/or PLGS) • Automated basal insulin dosing and corrective (non-meal) bolus doses	MiniMed 780G[7,8] t:slim X2 with Control-IQ[13] iLet Bionic Pancreas[4]	• User announces or delivers meal insulin bolus • May require delivery of corrective insulin bolus

[a] *Classified based on how the pump/system would be classified when operated using the most advanced software algorithm. Most advanced systems are also usable in non-automated (manual) modes which would be equivalent to a conventional pump or basic SAP.*

[b] *A basic SAP system is when an insulin pump is used in parallel with a stand-alone CGM device; the CGM values do not directly feedback to the pump to affect insulin delivery. For both SAPs and conventional insulin pumps, there is not a software algorithm controlling insulin delivery per CGM SG values.*

[c] *Sometimes classified as an advanced SAP system*

[d] *Although these systems are closed loop by the scientific definition (ie, a system with feedback from one part to another), AID systems are often called "hybrid" closed loop to emphasize that the user must still interact with the system to manage some aspects of insulin delivery. Users must manually determine insulin doses for SAP with LGS or PLGS systems.*

Abbreviations: AID, automated insulin delivery; CGM, continuous glucose monitor; CSII, continuous subcutaneous insulin infusion; IP, insulin pump; LGS, low-glucose suspend; PLGS, predictive low-glucose suspend; SAP, sensor-augmented pump; SG, sensor glucose

Most insulin pumps and systems are billed as durable medical equipment (DME) through medical coverage; exceptions are Omnipod pumps and the V-Go (tubeless pumps), which are billable or must be billed through the pharmacy insurance benefit.[34,35]

As of August 2023, no insulin pumps are included on the Utah Medicaid Preferred Drug List (PDL).[36] Pump-compatible rapid-acting (RA) insulins and CGM are on the PDL.[36] Humalog U-100 (insulin lispro) and Novolog (insulin aspart) are PDL-preferred;[36] these insulins are compatible with every pump reviewed by this report.[4-6,8-14] Apidra (insulin glulisine) is also PDL-preferred,[36] and it is compatible with a couple pumps (Omnipod DASH and Omnipod Eros).[10,11] PDL-preferred CGM devices include the Dexcom G6 (receiver, sensor, and transmitters) and Dexcom G7 (receiver, sensor).[36] Reviewed insulin pumps that can integrate with CGMs to form advanced pump systems (ie, SAP with IPT or AID system) are compatible with the Dexcom G6,[4,9,12,13] except for the Medtronic MiniMed pumps.[5-8] While pumps are not yet compatible with Dexcom G7, it is anticipated that pumps compatible with the Dexcom G6 will eventually become compatible with the G7.[37,38] Of the Medtronic CGM components, currently the Guardian Sensor 3 is non-preferred, and the Guardian Sensor 4 is not listed on the PDL.[36]

This report addresses commercially available insulin pumps and pump systems (SAP, SAP with IST, and AID devices). Do-It-Yourself (DIY) AID systems, which are systems combining commercially available insulin pumps and CGM with an open-source software algorithm, are not addressed.[39] Other pump devices not included in this report are listed in **Appendix B.** The Omnipod Eros (Omnipod Insulin Management System) insulin pump is addressed in less detail than other commercial ambulatory pumps because it will be discontinued from the US market by December 31, 2023.[40]

The **objective** of this report is to evaluate the comparative efficacy and safety of FDA-cleared commercial ambulatory insulin pumps and closed-loop pump systems (see Table 1) to assist the Utah Medicaid Pharmacy and Therapeutics Committee. Recent US or International guideline recommendations for using ambulatory insulin pump technology are reviewed, along with insulin pump characteristics described in user guides/manuals. Additionally, evidence from head-to-head randomized controlled trials (RCTs) of included insulin pumps is reviewed.

2.0 METHODS

Websites for the following major US organizations with clinical practice guidelines for diabetes mellitus were queried for technology-focused guidelines addressing use of insulin pumps in an outpatient setting: American Diabetes Association (ADA), American Association of Clinical Endocrinology (AACE), Endocrine Society (ES), Pediatric Endocrine Society (PES), and the International Society for Pediatric and Adolescent Diabetes (ISPAD). Additionally, on January 3, 2023, the TRIP database (https://www.tripdatabase.com/) was searched for relevant guidelines using the term “insulin pump” with results restricted to US guidelines.

A literature search for systematic reviews (SRs) published between 2018-2023 was performed in Ovid-Medline and Embase using SR-targeted filters. Search filters used were a SR filter developed by McMaster University for Ovid-Medline[41] and an independently-derived SR filter for Embase. Search terms include both controlled vocabulary and keyword phrases. See **Appendix C** for details of the bibliographic databases literature searches.

Insulin pump manufacturer websites and the FDA device database (Devices@FDA) were searched for user guides or guidance about insulin pumps. Websites of expert groups providing insulin pump guidance, including the PANTHER Program (https://www.pantherprogram.org/), DiabetesWisePro (https://pro.diabeteswise.org/) and danatech Diabetes Technology (https://www.diabeteseducator.org/danatech/insulin-pumps) were also searched for pump information.

2.1 Screening of Bibliographic Databases Searches

Literature search results were uploaded to Covidence software (Melbourne, Australia), and study titles and abstracts were screened by a single reviewer to identify possible SRs or SRs with meta-analysis (SRMAs) of RCTs with head-to-head (H-H) comparisons between ambulatory insulin pumps/pump systems in PwD. Full-text screening was also completed by a single reviewer. Individual RCTs from SRs, published from 2018 and onward, were considered for inclusion because most reviewed SRMAs pooled heterogenous pump system RCT data, making meta-analysis results unrepresentative of individual pump comparisons of interest. For example, many SRMAs pooled RCT data for non-applicable AID systems (eg, including dual-hormone or other non-FDA-cleared AID systems) or used comparator arms including heterogeneous types of insulin delivery (eg, any comparator including CSII, MDI, SAP, SAP with LGS). To select evidence most applicable to making H-H comparisons between the reviewed pumps addressed by this report, SRMAs and RCTs selected for inclusion must have clearly described the types of pumps used (ie, pump model).

For feasibility purposes, our search approach was limited to identifying RCTs among SRs published from 2018 onward. It is possible that relevant RCTs were missed if they were not captured by published SRs over the last 5 years. Moreover, for feasibility, screening of citations among SRs was targeted/limited to identifying relevant RCTs based on details provided by review authors about the pump used in primary studies.

2.2 Comparative Evidence Inclusion and Exclusion Criteria

We searched for comparative evidence meeting the criteria below to supplement information from clinical practice guidelines, insulin pump user guides, and expert guidance.

Included studies were SRMAs or RCTs among PwD meeting one of the following criteria:

- SRMA with a direct meta-analysis comparing pumps or pump systems addressed by this report.
    - To meet this criterion, we allowed studies to perform meta-analysis using pooled data for multiple pumps together if the data was pooled as a pump system addressed by this report (eg, all single-hormone, insulin-only, AID systems, or all sensor-augmented pumps with insulin-suspend technology).
- Individual RCTs identified among SRs with an H-H comparison between 2 different pumps from the report. One exception is that RCTs of the MiniMed 670G (a discontinued pump) were allowed if the comparator was another pump addressed by this report. Cross-over or parallel group RCTs were allowed.
    - The exception to include RCTs using MiniMed 670G was made because the MiniMed 670G insulin-dosing software is very similar to the MiniMed 770G. According to the MiniMed 770G

user guide, "The MiniMed 770G system used the same SmartGuard Auto Mode technology as the MiniMed 670G system. Therefore, this clinical data also applies to the MiniMed 770G" (page 325).[6]

Excluded studies met one of more of the following criteria:

- SR or RCT without a H-H comparison between pumps/pump system addressed by this report. For example, studies with comparisons between insulin pumps and multiple daily insulin injections were excluded. Studies exclusively examining systems not commercially available in the US were also excluded.
- Non-randomized controlled studies, post-hoc analyses of RCTs, or extensions of RCTs including only a subset of the original trial population.
- Network meta-analyses that did not report direct comparisons MA results meeting other inclusion criteria.
- Studies that failed to describe details about the type of pump used in the primary text. For example, an RCT identifying the intervention or comparator only as a SAP without stating the pump model.
- RCTs with an intervention or comparator that potentially included pumps not addressed by this report (eg, studies allowing patients to use their own study pump that did not name the pump used).

3.0 DISEASE OVERVIEW

Diabetes mellitus (DM) is a chronic metabolic condition characterized by elevated blood glucose that is associated with serious acute (eg, hypoglycemia, diabetic ketoacidosis [DKA]) and chronic (eg, microvascular and macrovascular disease) complications and excess mortality.[1,42,43] An estimated 37 million people in the US have DM.[44] T1D and T2D are the most common DM types, comprising 5-10%[1] and 90-95% of all DM diagnoses,[45] respectively. Other types of DM include monogenic diabetes (~0.4% of all DM diagnoses), exocrine pancreatic dysfunction, medication-induced diabetes, and gestational diabetes mellitus (GDM).[1]

Patients with T1D exhibit absolute insulin deficiency that is usually due to autoimmune damage to pancreatic insulin-producing cells.[45] Peak incidence of T1D is between 10-14 years old,[46,47] but onset may occur at any age.[48] In contrast, patients with T2D typically have a relative insulin deficiency due to impaired insulin secretion, and frequently, cellular insulin resistance.[45] Increasing age, obesity, and physical inactivity are risk factors for T2D.[45] Onset of T2D diabetes is most common after 45 years old,[49] but the incidence among younger populations is rising.[50] Elevated plasma glucose (eg, by fasting, post 2-hour oral glucose tolerance test, or glycosylated hemoglobin [A1c] glycemic tests) exceeding the hyperglycemic threshold is diagnostic for DM.[45]

4.0 TREATMENT AND MONITORING OVERVIEW

4.1 Treatment Options

Management of DM includes diet, exercise, and pharmacotherapy, including medications to lower blood glucose and for managing comorbidities.[1] Goals of anti-hyperglycemic DM treatments are to facilitate reaching glycemic goals (eg, A1c ≤ 6.5% or <7% for most non-pregnant adults[1,51]) while minimizing short-term complications like hypoglycemia, and to prevent long-term complications associated with DM.[1,2]

Patients with T1D require insulin therapy. T2D may be treated with oral or injectable non-insulin anti-hyperglycemic medications with or without insulin therapy.[1,2] However, since T2D is a progressive condition, many patients with T2D eventually require insulin therapy due to beta cell exhaustion.[2,52] Outpatient insulin delivery options include intermittent administration by injection with syringes, pens, smart pens, or patches; inhalation by inhaler; or continuous subcutaneous RA insulin infusion (CSII) by insulin pump.[2]

To mimic physiologic insulin release, people with T1D receiving intermittently administered insulin require both long-acting insulins to cover between-meal and overnight insulin needs (basal insulin) and short-acting insulin to cover meals (meal/prandial bolus insulin) and daytime hyperglycemia (corrective insulin bolus).[2] Intermittently administered insulin including both basal and bolus insulin is called MDI therapy, which is a type of intensive insulin therapy typically requiring the patient to perform at least 4 injections daily.[1,2] People with T2D requiring insulin may be treated with only basal insulin or with MDI basal-bolus therapy, depending on treatment needs.[1,2] During pregnancy, insulin is the preferred pharmacotherapy option for people with pre-existing T1D or T2D, and for GDM.[1,53]

Total daily insulin dose (TDD) needs vary by factors such as DM type, carbohydrate intake, and weight. For people with T1D, TDD needs typically range between 0.4 to 1.0 Units/kg/day (ie, 28 to 70 units daily for a 70 kg person).[2] People with T2D tend to have increased resistance to insulin with higher TDD needs (eg, ≥ ~1 Unit/kg) compared to people with T1D. Rates of hypoglycemia also tend to be lower in people with T2D.[2]

Evidence for using insulin pumps in people with T2D is limited compared to the robust evidence in people with T1D. Experts suggest that insulin pumps could be a cost-effective therapy in people with T2D, especially for patients who fail to achieve glycemic control goals with MDI. A challenge for using some insulin pumps in people with T2D is the amount of insulin that can be held in the pump reservoir. Ekanayake and Edelman report that few studies of conventional insulin pumps included people requiring over 200 units/day of insulin and opinionate that “Any patch pump designed for use in people with T2D needs to hold a minimum of 300 units for a 3-day period” (page 18).[52]

Today, PwD requiring intensive insulin therapy have many insulin delivery options to choose from. **Table 2** shows descriptive rankings for the level of flexibility and hypoglycemia risks, and advantages/ disadvantages of various intensive insulin delivery approaches for T1D, according to the ADA. The ADA considers AID systems to have the greatest flexibility, lowest risk for hypoglycemia, and highest cost relative to other CSII regimens (SAP with LGS/PLGS or non-automated insulin pump therapy). Conventional non-automated CSII pump therapy was ranked similarly to MDI for flexibility and hypoglycemic risk but may carry higher costs. Major advantages of pump therapy compared to MDI include the ability to deliver very small insulin doses and easily adjust insulin doses throughout the day. However, insulin pumps can be technically complex and require the patient to wear their treatment.[2]

Table 2. Comparison of Subcutaneous Insulin Regimens for T1D, per the ADA[2]

Regimen/ Insulin Delivery Method	Flexibility Rating[a]	Hypoglycemia Risk Rating[a]	Advantages[b]	Disadvantages[b]
HCL AID system	5+	1+	• May adjust insulin doses to account for varying needs • Increased dose precision • Flexible to meal timing	• Cost (most) • Must wear device • Increased DKA risk if insulin delivery stops • Technical complexity (varies among pumps/insulin regimens) • Sensitivity to adhesives
SAP with LGS/PLGS	4+	2+		
Conventional insulin pump alone (or as a SAP with stand-alone continuous glucose monitor)	3+	3+		
Optimal MDI regimen[c] that includes LA basal + RA or UA bolus	3+	3+	• Ability to use insulin pens for all doses • Flexible to meal timing	• Multiple daily injections • Larger incremental insulin units (minimum 0.5 to 1 Unit) • Possibly less effective than pumps for treating glucose rise in early morning

[a] *Ratings are on a scale of 1-5, with 5 being the most flexible and carrying the highest risk of hypoglycemia.*

[b] *Some advantages/disadvantages will depend on the pump/system.*

[c] *The optimal MDI regiment (ie, preferred MDI regimen) for T1D includes LA basal insulin plus RA or UA bolus insulin. Alternative MDI regimens (less preferred) include regimens using intermediate-acting NPH or short-acting insulin in place of the other insulins. These regimens carry less flexibility and a higher risk for hypoglycemia compared to the preferred regimen but tend to be less costly.*

Abbreviations: AID, automated insulin delivery; DKA, diabetic ketoacidosis; HCL, hybrid closed loop; LA, long-acting insulin analog; LGS, low-glucose suspend; MDI, multiple daily injections of insulin; PLGS, predictive low-glucose suspend; RA, rapid-acting insulin analog; SAP, sensor-augmented pump; UA, ultra-RA insulin analog

4.2 Monitoring Options and Glycemic Targets

Glycemic control is assessed by measuring blood glucose concentration and A1c, which is representative of the average blood glucose concentration over approximately 3 months.[1,51] A1c is a gold-standard glycemic metric that correlates well with long-term risks of cardiovascular disease and mortality[1]; however, as an average, it provides little information about daily glycemic variability.[54] To monitor daily glucose fluctuations, PwD receiving insulin should self-monitor glucose with a blood glucose monitor (BGM) or CGM.[1] CGM devices measure interstitial glucose with a subcutaneous sensor (the measured value is called sensor glucose [SG]), providing an approximate measurement of plasma glucose.[22] People using CGM devices should also have access to a BGM,[22] since self-monitoring with a BGM may be needed to verify CGM readings or if a CGM device is unavailable. All CGM devices that can communicate with commercial insulin pumps to form advanced pump systems are real-time CGMs (rtCGM) with disposable sensors.[5-8,20]

It is recommended that PwD receiving insulin and with good glycemic control monitor their blood glucose (BG) at least 2 times daily; more frequent monitoring before each insulin dose is preferred.[1] CGM (as [rtCGM] or intermittently scanned CGM [isCGM]) is recommended by the AACE for all T1D patients and for T2D patients on insulin therapy, or with risk factors for hypoglycemia or observed hypoglycemia unawareness.[1]

Glycemic targets and A1c goals are individualized based on patient-specific factors such as age, co-morbidities, diabetes duration, cognitive status, hypoglycemia risk, and preferences.[1,51] The ADA recommends an A1c goal of <7% for most adults and children/adolescents with DM, and more stringent (≤ 6.5%) or less stringent (up to <8%) goals, depending on the patient's clinical profile and tolerability.[51,55] Similarly, the AACE recommends an A1c goal of ≤ 6.5% for most adults without multiple comorbidities or limited life expectancy, as long as it can be achieved without significant hypoglycemia.[1] Glycemic targets during pregnancy should be individualized, but typically, are stricter (eg, fasting glucose ≤ 95 mg/dL and 1-h post-prandial glucose ≤ 140 mg/dL) if they can be achieved without significant hypoglycemia.[1,53] If tolerated, an A1c of <6% may be targeted during pregnancy.[53]

Multiple CGM metrics, including time in range (TIR), time below range (TBR) and time above range (TAR), are useful for evaluating glycemic control and guiding insulin therapy adjustments.[51,54] TIR is the proportion of time (or proportion of total glucose readings) that the patient maintains glycemic readings within the target glucose range.[1,51,54] TIR is correlated with A1c and is associated with the risk of microvascular complications.[51] An A1c target of ≤7% or ≤ 6.5% corresponds to a TIR target of ≥65% or ≥70%, respectively. An improvement in A1c of ≥0.4% is usually considered clinically significant; the corresponding change in %TIR is approximately 5%.[56] An advantage of TIR compared to A1c is it provides more rapid feedback about glycemic levels, and when combined with other CGM metrics, provides information regarding glycemic variability.[54] An overarching goal is for patients is to maximize their TIR and minimize TBR.[54] Refer to **Table 3** for typical CGM glycemic targets for non-pregnant adults with T1D or T2D. Stricter goals are suggested for pregnant patients with DM.[54]

Table 3. Adult Continuous Glucose Monitor (CGM) Glycemic Control Metrics from 2019 Expert Consensus[54]

Metric[a, b,c]	Non-Pregnant Adults[d] with T1D and T2D
Time in range (TIR) % readings or time between 70-180 mg/dL	>70% (>16 hours, 48 min)
Time below range (TBR) % readings or time below <70 mg/dL and <54 mg/dL	<4% (<1 hour) at <70 mg/dL <1% (<15 min) at <54 mg/dL
Time above range (TAR) % readings or time above 180 and <250 mg/dL and >250 mg/dL	<25% (<6 hours) at >180 mg/dL <5% (<1 hour, 12 min) at >250 mg/dL
Glycemic Variability (percent coefficient of variation)	≤ 36%

[a] Expressed as a percentage of sensor readings or time per day

[b] Stricter goals are recommended during pregnancy. For example, a target range defined as 63-140 mg/dL, with below range considered <63 mg/dL and above range considered >140 mg/dL. Pregnancy TIR goals are mostly based on studies of people with pre-existing T1D. For pregnant women with T2D or CGM, a higher TIR of >90% is suggested.[1]

[c] For patients <25 years of age who have an A1C target of 7.5%, the suggested %TIR is lower, at approximately >60%. For older patients or those high-risk for hypoglycemia, low %TIR of >50%, and <10% for TAR (for >250 mg/dL) may be used.

[d] Due to limited evidence, the target TIR for children is uncertain. The ADA defines the target range for children as a glucose of 70-180 mg/dL.[55] Targets should be individualized, but a similar TIR goals as adults once in remission may be acceptable for children <7 years old.[25]

Abbreviations: ADA, American Diabetes Association; CGM, continuous glucose monitor; dL, deciliter; mg, milligram; min, minutes; T1D, type 1 diabetes; T2D, type 2 diabetes; TAR, time above range; TBR, time below range; TIR, time in range

Failure to achieve glycemic targets is associated with increased medical complications and costs.[23] Insulin pumps and insulin pumps systems may improve glycemic control in PwD. Based on cumulative evidence, the ADA ranked insulin delivery and monitoring approaches according to highest TIR and lowest TBR achievement as follows: "…hybrid closed-loop > low-glucose suspend > CGM-augmented open-loop > BGM-augmented open-loop" (page S144).[2]

5.0 INSULIN PUMP AND PUMP SYSTEMS OVERVIEW

This section provides an overview of different insulin pumps and insulin pumps systems (IPS), defines system components, and compares details about pump functionality. IPSs are the combination of an insulin pump ± CGM ± software algorithm used for different operational modes (ie, conventional insulin pump, SAP, or AID).

5.1 Insulin Pump System Components and Select Terminology

Each insulin pump/system includes different components (see **Appendix A** for select definitions). Prescribers must write separate prescriptions for the necessary components of each system (eg, pump, reservoir set, sensor, transmitter, and infusion set).[57] The duration that an insulin pump can be used

varies by product. Patch-based pumps are replaced daily[14] or every few days,[9-11] whereas other pumps are reusable and most are estimated to last 1-3 years.[58-60] Additionally, individual components used with the pump (eg, infusion sets, CGM sensors) also have various durations of use limits, requiring replacement (refills).[7,20,21,61-63]

Insulin pumps control insulin delivery via various methods or modes. In this report we continue to use "basal" to describe ongoing continuous insulin infusion and "bolus" to describe intermittent insulin infusions. Most programmable pumps require the user to enter personalized information to calculate automatically-delivered or suggested doses optimally.[5,6,8-13] Throughout this report, we distinguish between when AID systems are adjusting insulin delivery according to software algorithms (automated mode) and when AID systems are adjusting insulin according to user-programmed rates or values (manual mode).[64] Refer to **Appendix A** for select additional insulin delivery terminology definitions.

5.2 Insulin Pump System Types

All insulin pumps addressed by this report continuously deliver insulin by subcutaneous infusions (CSII).[17] Table 1 categorizes and describes insulin pump products addressed in this report by the most advanced operating mode (ie, maximal function type). Advanced pump systems integrate with CGM components and execute software algorithms to automate insulin delivery/adjustments (ie, automated pumps). Automated pumps other than the iLet Bionic Pancreas are capable of multiple modes of operation, including a non-automated, manual mode that functions like a conventional stand-alone insulin pump.[6-8,12,13] Generally, it is encouraged for users to run advanced system pumps in automated mode since automated insulin delivery has been shown to improve glycemic control compared to conventional CSII with non-automated pumps[19,22-24]; however, the flexibility to run in both manual and automated modes may appeal to some patients. The medical literature uses many terms for these systems; for the purposes of this report, we will refer to IPSs using the terminology in Table 1.

Conventional insulin pumps deliver CSII using user-programmed (or pre-set) insulin delivery rates.[10,11,14,16] People using stand-alone conventional pumps may self-monitor their blood glucose (SMBG) using a BGM or CGM.[1,2] When CGM is used with a conventional insulin pump, this system is called a sensor-augmented pump (SAP). Notably, readings from the BGM and CGM do not provide feedback to autonomously change insulin delivery with conventional insulin pumps or basic SAP systems.[18] Thus, conventional insulin pumps and basic SAPs are *open-loop* insulin delivery systems. PwD using conventional insulin pumps and SAPs who require different insulin delivery rates throughout their day must self-manage bolus insulin delivery and manually adjust (eg, by pre-programming different rates throughout the day) the pump basal insulin delivery rate.[18]

Over time, IPSs evolved to alter insulin delivery using advanced software algorithms, creating dynamic systems that adjust insulin delivery based on a patient's glucose levels: these advanced IPSs include SAPs with insulin-suspend technology (IST) and automated insulin delivery (AID) systems. Both SAPs with IST and AID systems respond to rtCGM SG readings to alter insulin delivery, and thus are closed-loop systems. While SAPs with IST stop insulin delivery when the SG is at or below a low glucose threshold (called low-glucose suspend [LGS]) or if the SG is predicted to become low (predictive LGS [PLGS]), the user is still responsible for managing all aspects of insulin delivery. AID systems are the most advanced systems, capable of automatically increasing, decreasing, or pausing continuous (basal) insulin delivery rates in reaction to SG values according to a software algorithm.[3,18,32] Advanced AID systems are a

subtype of AID system which offer automated corrective insulin (bolus) doses (ie, higher insulin doses than what would be given per the basal insulin software algorithm alone) in addition to automated basal insulin delivery. Experts often call AID systems "hybrid" closed-loop (HCL) systems because the user must still interact with the system to initiate or manage aspects of insulin delivery (eg, meal boluses), manage insulin delivery during exercise, and manage insulin dosing during other scenarios that might augment insulin sensitivity (eg, illness).[19]

Commercially available AID systems all automate a single hormone (insulin). Dual-hormone systems (eg, also automating pramlintide or glucagon) are being evaluated in clinical trials.[19] One of the pumps addressed in this report usable as an insulin-only advanced AID system, the iLet Bionic Pancreas, is also being studied as a dual-hormone system with glucagon. [65,66]

5.3 Factors for Selecting an Insulin Pump

Insulin pumps and IPSs differ by many factors that might drive selection by a patient, caregiver, or provider. While it is not possible to list all factors influencing preference for a particular pump, below are some ideas to help contrast the pump characteristics.

Refer to **Table 4** for a comparison of characteristics of all pumps, including some additional factors that might influence pump selection for a patient. **Table 5** provides additional details about the automated insulin algorithm used by AID and advanced AID systems. Sections 5.3.1 to 5.3.3 elaborate on this section to contrast select features of pumps with the same maximal IPS type.

***Examples* of factors to consider for pump selection:**

- **Indication** (see Table 4 and **Appendix D**) and/or supportive evidence for use. While the V-go is indicated generally for adults with DM, it is usually intended for people with T2D, which is the population with evidence for its use.[29,30] When used as an AID system, pumps are indicated for patients with T1D only.[4,6-9,13]
- **Type of insulin pump system.** Section 5.2 contrasts different types of IPSs. While guidelines prefer an AID system for most patients with T1D,[22-24] an AID system may not be appropriate for all patients based on patient preference, insulin delivery limitations (eg, maximal or minimum insulin requirement), or system complexity.
- **Automated abilities.** Major considerations for automated systems are the ability to run LGS, PLGS, automated basal adjustment, and/or automated corrective boluses.
    - The V-Go offers the least flexibility of all insulin pumps because users cannot change basal insulin delivery rates throughout the day,[14] but it is the least technically complex pump.
    - AID systems are the most technically complex. See Table 5 and Section 5.3.3 for information contrasting AID systems.
- **Presence of infusion sets** (tubed versus tubeless system). Tubeless systems require the user to wear the pump on their skin, but since they lack lengthy infusion sets, they are less prone to impaired insulin delivery from kinks in the infusion tube.[29] Lack of tubes might appeal to very young and/or active patients.
- **CGM compatibility and capabilities**. Medtronic systems use a Medtronic CGM[5-8] whereas other SAP IPT or AID systems pair with the Dexcom G6 CGM.[4,9,12,13] The older Medtronic CGM (Guardian 3), the only CGM compatible with the MiniMed 630G and 770G, requires calibration with a BGM at least 2 times daily.[5,6] Daily calibration is not required by the Dexcom G6 or Medtronic Guardian 4

(compatible with the MiniMed 780G).[20,21] Medtronic sensors must also be replaced more frequently than the Dexcom G6.[7,20,21]

- **Insulin compatibility.** Most insulin pumps are only compatible with the same U-100 RA insulins (Humalog and Novolog).[4-8,12-14] Exceptions are the Omnipod 5 which is also compatible with the U-100 RA insulin, Admelog,[9] Omnipod DASH and Eros that are compatible with several RA and ultra-RA U-100 insulins,[10,11] and iLet Bionic Pancreas that is also compatible with Fiasp Pumpcart (a prefilled insulin cartridge not yet available in the US).[67]
- **Infusion set type and required frequency for changing the infusion set.** Most tubed insulin pumps offer similar types of cannulas (eg, steel or soft and with different administration angles) and infusion set lengths‡.[4,62,68,69] One notable difference is the MiniMed pumps are pairable with an extended insulin reservoir and infusion set, which is wearable for a longer duration (up to 7 days) compared to the standard 2-3 days.[61]
- **Minimum basal or bolus insulin delivery limit**. Pre-school age patients with T1D have low insulin delivery needs (ie, median of 10 Units daily), and thus may require low basal rates and small boluses.[25] There are small differences in infusion rate minimums between pumps (see Table 4).
- **Ability to control pump with a smartphone and smartphone compatibility.** Not all smartphones are compatible with a pump's designated mobile device applications (see Table 4). Most advanced system pumps offer a smartphone app, which allows the user to view pump and/or CGM data but cannot be used to directly control the pump. The Omnipod 5 can be completely controlled with a smartphone app.[9] People using the t:slim X2 pump and t:connect mobile app have the option to start or stop insulin boluses remotely.[70] Although not a smartphone device, the BGM integrated with the MiniMed 630G can also be used to initiate insulin boluses without using the pump directly.[5]
- **Interoperability.** Some pumps are also approved as alternate controller enabled (ACE) pumps, theoretically enabling them to be interoperable with other insulin dosing software. For example, the Tidepool Loop is an FDA-cleared automated dosing algorithm that could be paired with an ACE pump. However, Tidepool has not yet formally released which pumps it will be compatible with to create a unique AID system.[71] ACE pumps that could become compatible with other insulin dosing algorithms include the Omnipod 5, iLet Bionic Pancreas, and t:slim X2.[4,9,16]

5.3.1 Comparison of Conventional Insulin Pumps: V-Go, Omnipod DASH, and Omnipod Eros

Pumps maximally functional as conventional insulin pumps or basic SAPs (when used with a stand-alone CGM) include the V-Go, Omnipod DASH, and the Omnipod Insulin Management system (Omnipod Eros). Pumps other than the iLet Bionic Pancreas are also usable as conventional insulin pumps when users disable automated insulin dosing software.

All three systems are tubeless patch-pumps worn directly on the skin that deliver insulin through a cannula or needle embedded in the patch.[10,11,14] Unlike the Omnipod pumps that are controlled by the Personal Diabetes Manager (PDM) hand-held device,[10,11]allowing the user to deliver RA insulin at user-selected fixed or variable rates, V-Go is a mechanical pump that delivers RA insulin at a single pre-set rate.[14] Select similarities and differences between these systems are discussed below.

‡ We did not systematically compare all infusion sets offered by insulin pump manufacturers. There may be additional differences in what is offered by different companies.

- **Insulin reservoir and pump replacement:**
  - V-Go patches should be replaced daily[14] whereas the Omnipod patch-pumps (Pods) should be replaced every 48–72 hours.[10,11]
  - V-Go is available as 3 options: V-Go 20, which delivers 20 Units of insulin/24 hr (0.83 U/hr); V-Go 30, which delivers 30 Units of insulin/24 hr (1.25 U/hr); and V-Go 40, which delivers 40 Units of insulin/24 hr (1.67 U/hr). At a maximum, the V-Go can deliver 76 units of U-100 insulin daily (40 Units of basal insulin and 36 Units of bolus insulin in 2-Unit increments).[14] Both Omnipod systems require a minimum of 85 inulin Units to operate and can hold up to 200 Units.[10,11]

- **Insulin delivery settings:**
  - Insulin delivery rates are pre-set for the V-go,[14] whereas insulin delivery by Omnipod pumps can be customized.[10,11] Patients can program up to 12 different basal rates per 24 hours with the Omnipod DASH and up to 7 different basal rates per 24 hours using the Omnipod Eros. In addition, the Omnipod pumps allow the user to switch to temporary basal rates (eg, for exercise) and deliver on-demand boluses at doses suggested by a Bolus calculator. Unlike the Omnipod Eros, Omnipod DASH offers the option to program a basal insulin rate of 0 Units/hr (minimum of 0.05 Units/hr for Eros). Extended duration boluses are possible using the Omnipod DASH or Omnipod Eros.[10,11]

- **BGM Integration:**
  - V-go does not integrate with any BGM device.[14] The Omnipod DASH is compatible with the Contour Next One BGM, and readings from this meter can be sent to the DASH PDM using Bluetooth technology.[10] The Omnipod Eros PDM has a built-in BGM (Freestyle).[11]

- **Other features of note:**
  - V-Go is relatively easily to handle and offers a simple option for basal-bolus insulin therapy in people with DM that can be managed effectively using a single fixed basal rate and 2-Unit on-demand boluses.
  - Omnipod systems offer safety alarms not available with the V-Go. For example, alarms for stopped insulin delivery, detected occlusions, and system errors.[10,11]
  - Omnipod system PDMs can be used to view insulin usage and settings.[10,11] Omnipod DASH offers more advanced technology options than the Eros. DASH users can use an Omnipod DISPLAY app on Apple smartphones to view pump data.[10] Although the Dexcom G6 sensor readings cannot integrate and affect insulin delivery by the Omnipod DASH, users can view pump data and Dexcom G6 sensor readings simultaneously (using an Apple iOS widget).[72]

5.3.2 Comparison of Sensor-augmented Pumps with Insulin-suspend Technology: MiniMed 630G and t:slim X2 with Basal-IQ

Two tubed pump systems, MiniMed 630G and t:slim X2 with Basal-IQ, are maximally functional as SAP (ie, pump paired with CGM) with IST. Both systems allow the user to program personalized basal insulin patterns (at set rates) and require the patient to manage meal and correctional boluses.[5,12] Major differences between these pump systems are the indications, IST characteristics, paired rtCGM, ability to view pump data by mobile device, and ability to easily upgrade to an AID system. These differences are discussed below.

- **Insulin-suspend technology (IST):**
  - Both systems can use IST to stop insulin delivery based on low or predicted low SG values,[5,12] to either prevent or minimize time the patient spends in hypoglycemia.[23] Neither technology is a treatment for hypoglycemia, and the patient should treat low glucose according to directions from their healthcare provider.[5,12] Patients using the MiniMed 630G should also confirm the low SG value with a self-monitoring BGM.[5]
  - The MiniMed 630G has LGS called "SmartGuard Suspend on low," which will stop insulin delivery when the SG reaches or drops below a value (between 60 and 90 mg/dL) set by the user. The patient has the option to set up to 8 different low limit values throughout the day. This safety feature is intended to minimize the time spent with low glucose and protect the patient when they cannot respond to low glucose alarms. When a Suspend on low event occurs, the pump sends an alert and insulin delivery will cease for 2 hours unless it is manually restarted by the patient. Basal insulin delivery automatically resumes 2 hours after the Suspend on low. Once a Suspend on low event occurs, the ability to automatically pause insulin delivery (ie, for a second time) will be temporarily unavailable for a maximum of 4 hours; the amount of time it is unavailable depends on how soon the patient responds to the insulin suspension alert and user settings. The system will also alert patients when the SG is approaching the low glucose threshold.[5]
  - Basal-IQ has more sophisticated IST than the MiniMed 630G, incorporating suspension of insulin for predicted low SG values (PLGS) and LGS.[12] However, the low SG target is not customizable, unlike the MiniMed 630G.[5]
    - Basal-IQ stops and restarts insulin based on current and predicted sensor readings using the following rules[12]:
      1. Suspend insulin if current SG <70 mg/dL
      2. Suspend insulin if SG reading in 30 minutes is predicted to be <80 mg/dL
      3. Restart insulin if next SG increased *or* restart insulin if SG reading in 30 minutes is predicted to be >80 mg/dL despite a lack of increase in the immediate SG value
      4. Restart insulin if insulin suspended for 2 hours over a 2.5-hour period (eg, once insulin stops for 2 hours, it automatically restarts for at least 30 minutes; insulin delivery may be automatically stopped again if any of the Basal-IQ suspend rules apply at that time).

- **Remote bolus options:**
  - A unique feature of the BGM paired with the MiniMed 630G is it can be used to deliver an insulin bolus without interacting with the pump ("Remote Bolus").[5] Manual boluses can also be delivered remotely (without touching the pump) by the t:slim X2 using the t:connect mobile app that is compatible with several Apple and Android devices.[12]

- **Ability to view data on a mobile device:**
  - Pump and CGM data are viewable on the MiniMed 630G and t:slim X2 pumps.[5,12] The MiniMed 630G is not compatible with mobile apps for viewing data on a smartphone,[5] unlike the t:slim X2 (using the t:connect mobile app).[12] To view 630G pump data on CareLink software (software that summarizes pump data and glucose readings for viewing on the Web or sharing with a healthcare provider), patients must upload data manually using a USB device.[5] MiniMed 630G's paired BGM, Contour Link 2.4, can upload BG data directly to CareLink.[73]

- **Ability to upgrade technology to AID system:**
  - To change to an AID system, people using the MiniMed 630G require new hardware (different pump) and new software (new insulin management algorithm). In contrast, people already using the t:slim X2 pump with Basal-IQ can switch to the Control-IQ AID system by connecting to a desktop computer and running a software update (authorized by a new prescription for Control-IQ).[74] However, once the pump incorporates Control-IQ, the patient cannot revert the pump back to running Basal-IQ.[75]

Note that other insulin pumps maximally functional as AID systems also offer IST. Uniquely, the MiniMed 770G and 780G are also functional as SAPs with IST (LGS and PLGS) in manual mode (running pre-programmed basal insulin delivery without dose-adjustment by SG value).[6-8] Both systems suspend insulin delivery if the SG is predicted within 30 minutes to reach 20 mg/dL above the user-selected low limit, and they restart insulin delivery within 30 to 120 minutes, depending in the patient's hypoglycemia recovery rate.[6-8] AID systems suspend insulin delivery while using the automated insulin delivery mode (see Table 5).[4,6-9,13]

5.3.3 Comparison of Automated Insulin Delivery Systems: t:slim X2 with Control-IQ, MiniMed 770G and 780G, Omnipod 5, and iLet Bionic Pancreas

There are 5 commercially available AID systems: MiniMed 770G and MiniMed 780G with SmartGuard technology, Omnipod 5 with SmartAdjust technology, t:slim X2 with Control-IQ and the iLet Bionic Pancreas. When running the automated software, each of these systems automatically adjust basal insulin delivery toward a target SG value or range.[4,6-9,13] Advanced AID systems, MiniMed 780G, t:slim X2 with Control-IQ, and iLet Bionic Pancreas, also automatically deliver corrective insulin boluses for SG values exceeding a threshold or predicted to exceed a threshold while maintaining ongoing continuous basal delivery.[4,7,8,13] All AID systems still require the user to manage some aspects of insulin delivery (eg, meal insulin boluses and acute changes in insulin needs like exercise).[4,6-9,13] The iLet Bionic Pancreas is the only AID system that semi-automates meal insulin boluses, only requiring the user to announce when they are about to eat a meal/snack with carbohydrates.[4] All AID systems employ safety measures to ensure automated insulin doses do not exceed certain parameters.[4,6-9,13]

AID systems offer variable features that appeal to different patients. Below is a discussion of some AID system characteristics highlighting key differences.

- **Target glucose:**
  - The SG target for *automated basal* insulin varies between systems. Most systems (MiniMed 770G/780G, Omnipod 5, and iLet Bionic Pancreas) target a certain SG value.[4,6-9] Only the t:slim X2 with Control-IQ targets a SG range (112.5–160 mg/dL), which cannot be adjusted.[13] MiniMed 770G offers only 1 non-adjustable SG target of 120 mg/dL.[6] The MiniMed 780G, Omnipod 5, and iLet Bionic Pancreas offer adjustable target SG values[§] (see Table 5).[4,7-9] MiniMed 780G can target the lowest glucose value of all AID systems (100 mg/dL).[7,8] Omnipod 5 is the most flexible,

[§§] This excludes special automated modes (eg, for sleep and exercise). See separate discussion about special modes with other target glucose values, which require the user to manage the duration of that temporary target glucose.

offering the widest variety of target SG values, and option to set up 8 different target SG values within 24 hours.[9]

- Systems also target different SG for corrective boluses (for either automated or system-suggested doses) as shown in Table 5. MIniMed 770G is the least aggressive.[6]
- Exercise or temporary SG targets (special automated modes):
  - Insulin needs often change during and directly following exercise, depending on the type and intensity of exercise.[76,77] To prevent hypoglycemia, it is recommended for most patients with T1D to temporarily target a higher SG before or during exercise.[76] All AID systems require user interaction to manage exercise.[4,6-9,13]
  - Except for the iLet Bionic Pancreas,[4] AID systems allow users to either set a temporary higher SG target (MiniMed 770G/780G) or an exercise/activity target (Omnipod 5 and t:slim X2 with Control-IQ). To use these temporary targets, the user must interact with the system to either manually turn it on/off (required for t:slim X2 with Control-IQ) or set it for a user-programmed duration.[6-9,13]
  - With the iLet Bionic Pancreas, users may opt to temporarily disconnect from the iLet before, during/after exercise, or remain connected; with all options requiring monitoring SG by CGM to detect significant SG excursions.[4] Although other AID systems do offer higher temporary SG targets, depending on the patient's needs, exercise may still be managed similarly to what is recommended for the iLet Bionic Pancreas.[78]
- Sleep targets (special automated mode):
  - Both t:slim X2 with Control-IQ and the iLet Bionic Pancreas allow patients to set a scheduled different TG target intended for sleep.[4,13] Although Omnipod 5 does not have a designed 'sleep' mode, patients may program a different target for sleep (since users may set up to 8 different daily SG targets).[9] Patients using the 770/780G may manually set the temporary target if hypoglycemia during sleep is a problem[6-8]; or for the 780G, manually switch to a different target SG for sleep, since users may only set 1 algorithm target SG per 24 hours.[7,8]

- **Ability to adjust insulin parameters:**
  - Insulin use factors (eg, insulin to carbohydrate ratio, correction factors) cannot be adjusted for the iLet Bionic Pancreas like they can for some other AID systems (see Table 5).[4]

- **Insulin dosing algorithm types and adaptivity:**
  - Although all AID systems share the goal of improving a patient's TIR,[31] each algorithm uses a unique approach. AID systems other than MiniMed 770G/780G use MPC (Model Predictive Controller) algorithms which consider SG trends when adjusting basal insulin doses.[19] Omnipod 5 predicts SG values further into the future than the Control-IQ (60 minutes vs 30 minutes).[9,13] MiniMed systems use a PID (Proportional Integrative Differential) algorithm.[19] Refer to **Appendix E** for an overview of AID algorithm types.
  - Only the iLet Bionic Pancreas, MiniMed 780G, and t:slim X2 with Control-IQ automatically give corrective insulin boluses. t:slim X2 with Control-IQ can only deliver 1 auto-correction bolus per hour whereas the other 2 systems may deliver up to 12 corrective boluses per hour.[4,7,8,13]
  - The iLet Bionic Pancreas simplifies bolus insulin for meals. All other AID systems require the user to enter the carbohydrate amount for the system to suggest a bolus dose,[6-9,13] necessitating full carbohydrate counting skills. While some systems might compensate for user error in estimating carbohydrate content (eg, the 780G may deliver an auto-correction bolus[7,8]), the iLet Bionic

Pancreas only requires the user to estimate the carbohydrate content relative to other meals of the same type (breakfast, lunch, or dinner). The iLet system will begin to learn how much bolus insulin is needed, customized to each meal type.[4]
    - Limited information is provided by AID system user guides, but it appears that all systems adapt (or "learn") to improve insulin delivery based on prior insulin delivery to some extent.[4,19,64] Adaptation by the Omnipod 5 with each Pod change, every 48 to 72 hours, (ie, basal insulin is auto-adjusted using prior total daily insulin, which updates with each new Pod) is a frequently advertised feature of the system.[64,79]

- **Forced exit from automated mode:**
    - An important consideration for selecting and using an AID system is ability to stay in the automated mode. Achievement of improved glycemic outcomes is correlated with increased time in automated mode.[19] MiniMed systems have comparatively more factors (see Table 5) that could trigger a switch to manual mode[80] and require the user to enter a BG value to return to automated mode.[6-8] If CGM connectivity is lost, the iLet Bionic Pancreas will initially continue running in a limited safety mode using user-entered SMBG values; however, if CGM connectivity ceases for more than 48 to 72 hours, insulin delivery ceases and the user must administer insulin with a back-up method.[4]

- **Unique bolus calculator settings**[81]:
    - AID systems requiring user-delivered meal or corrective boluses have bolus calculators,[4] which can suggest a bolus dose.[6-9,13] Although exact specifications vary, most bolus calculators consider similar factors such as SG value, grams of carbohydrate in a meal, correction factor, and the amount of insulin active in the patient's body. The Omnipod 5 bolus calculator also incorporates the SG trend to meal and corrective boluses, increasing the suggested dose for an upward trend or decreasing the dose for a downward trend.[9] For meal boluses, the MiniMed 780G will adjust the suggested bolus dose down if hypoglycemia is predicted.[7,8] The iLet Bionic Pancreas also reports using the glucose trend and past 24 hour glucose profile for corrective automatic boluses.[4]

- **Water exposure:**
    - Neither the t:slim X2[13] nor the iLet Bionic Pancreas are waterproof.[4,13] It is not recommended for patients to wear the t:slim X2[13,82] or iLet Bionic Pancreas in water (eg, while swimming or bathing).[4,83] The Omnipod 5 (but not the controller) is waterproof up to 25 feet depth for up to 60 minutes.[9] Although the Minimed 770G and 780G pumps are waterproof at up to 12 feet depth for 24 hours,[6-8] Medtronic recommends inspecting the 770G for pump damage before exposing it to water. Additionally, other MiniMed 770G system components (sensor and transmitter) are only water-resistant at up to 8 feet depth for 30 minutes and CGM readings may not be transmitted during time in water.[84]

- **Controller location and privacy:**
    - Omnipod 5 is the only AID system that is fully operable with a smart phone controller (for Android phones).[9] Other systems are primarily controlled by inputs on the pump, requiring the user to interact with the pump. When using the t:slim X2 with Control-IQ and running the t:connect mobile app on select devices, bolus doses can be initiated within the app instead of using the pump.[70]

Table 4. Overview of Insulin Pump Characteristics[a]

Characteristic	Insulin Pump Brand, Manufacturer, and Model							
	MannKind Corporation	**Medtronic: MiniMed**			**Insulet Corporation: Omnipod**[b]		**Beta Bionics:**	**Tandem Diabetes Care**
	V-Go 20, V-Go 30, V-Go 40[14]	**MiniMed 630G**[5]	**MiniMed 770G**[6]	**MiniMed 780G**[7,8]	**Omnipod DASH**[10]	**Omnipod 5**[9]	**iLet Bionic Pancreas**[4]	**T:slim X2**[12,13]
Maximal function system type[c]	Conventional insulin pump or basic SAP	SAP with LGS	HCL AID	Advanced HCL AID	Conventional insulin pump or basic SAP	HCL AID	Advanced HCL AID[d]	Advanced HCL AID
Pump indication	Adults with DM	DM age ≥ 14 (with Guardian 3 sensor) or ≥ 16 (with Enlite sensor)[5]	T1D age ≥ 2	T1D age ≥ 7	DM requiring insulin	DM requiring insulin	DM age ≥ 6	DM age ≥ 6
Advanced system (pump + algorithm) indication	--				--	T1D age ≥ 2	T1D age ≥ 6	DM age ≥ 6 (Basal-IQ) T1D age ≥ 6 (Control-IQ)
Pump description	• Tubeless mechanical patch pump • Disposable: discard after 24 hours • Continuous pre-set basal (20-40 units daily) • On-demand 2-unit bolus (up to 36 units daily) by pressing a button	• Battery-operated tubed pump with color screen • Operated with buttons on the pump • Customize basal and bolus delivery • LGS option • Built-in CGM option, readings viewable on pump	• Battery-operated tubed pump with color screen • Operated with buttons on the pump • Customize basal and bolus delivery • LGS or PLGS options • Automatic basal insulin adjustment option • Built-in CGM, readings viewable on pump	• Battery-operated tubed pump with color screen • Operated with buttons on the pump • Customize basal and bolus delivery • LGS or PLGS options • Automatic basal and correctional bolus insulin adjustment option • Built-in CGM, readings viewable on pump	• Rechargeable battery-operated tubeless patch-pump (Pod) • Operated with PDM (small smartphone-like device) using a touchscreen • Customize basal and bolus delivery • Bluetooth connection to CONTOUR NEXT ONE BGM	• Rechargeable battery-operated tubeless patch-pump (Pod) • Operated with touchscreen on PDM or smartphone • Customize basal and bolus delivery • LGS and PLGS option • Automatic basal insulin adjustment option • Paired CGM readings viewable on PDM or smartphone	• Rechargeable battery-operated tubed pump • Operated with black-and-white touchscreen • Customize basal and bolus delivery • LGS and PLGS • Automatic basal, correctional bolus, and meal bolus (with announcement) • Paired CGM readings viewable on pump screen	• Rechargeable battery-operated tubed pump • Operated with color touchscreen • Customize basal and bolus delivery • LGS and PLGS option (Basal-IQ) • Automatic basal and correctional bolus with PLGS option (Control-IQ) • Paired CGM readings viewable on pump screen
ACE (interoperable) pump?	No	No	No	No	Yes (with BGM only)	Yes	Yes	Yes
Pump size (length x width x depth) and weight	• 2.4 x 1.3 x 0.5 inches • 20 to 50 grams	• 3.8 x 2.11 x 0.98 inches • 106 grams	• 3.78 x 2.11 x 0.96 inches • 106 grams	• 3.81 x 2.18 x 1.01 inches • 106 grams	• 2.05 x 1.53 x 0.57 inches • 26 grams	• 2.05 x 1.53 x 0.57 inches • 26 grams	• 3.6 x 2.3 x 0.59 inches • 110 grams	• 3.13 x 2.0 x 0.6 inches • 112 grams
Insulin reservoir capacity	56 – 76 Units	300 Units			200 Units (with required minimum 85 Units)		180 Units	300 Units
Cannula size and insertion, infusion sets, and maximum duration of infusion set use	• 4.6 mm, 30 gauge • Needle within patch, no infusion set • Auto-insertion by pressing button after patch placed	• Multiple Medtronic infusion sets available with variable cannula characteristics[62] • Insertable manually and/or with serter device (depending on the infusion set)[62] • Extended infusion set with extended insulin reservoir wearable for 7 days[61]			• Cannula is embedded in Pod • Cannula auto-inserts during Pod set up • Pod is wearable for 48-72 hours		• 3 compatible infusion sets with variable cannula sizes (6-13 mm) and cannula types (Teflon or steel) • Option to insert with device • Wearable for 1-3 days (depends on set)	• Multiple Tandem infusion sets available with variable cannula characteristics • Insert manually or with device (depends on set) • Wearable for 2-3 days (depends on set)[63]

[a] *This table provides an overview of insulin pump characteristics, including basic automated features, with a focus on fixed characteristics of the insulin pumps. Refer to Table 5 for details about automation features.*

[b] *The Omnipod Insulin Management System (Omnipod Eros) pump will be discontinued from production in December 2023. For simplicity, this device is not included in this detailed product table.*

[c] *Classified based on how the pump/system would be classified when operated using the most advanced computer algorithm (see Table 1). Most advanced systems are also usable in manual modes which would be equivalent to a conventional pump or SAP.*

[d] *The iLet Bionic Pancreas is sometimes considered a fully closed-loop system since the system autonomously determines all insulin doses; we consider it an HCL system since it still requires user interaction (eg, for meal announcement, exercise).*

[e] *Refers to insulin delivery rates programmed by the user. Pumps used as AID systems adjust basal insulin per sensor glucose values; some also use these programmed basal rates to help tune the automated dosing algorithm.*

[f] *Viewable means pump and/or CGM sensor glucose value data can be reviewed on a smartphone device, whereas controllable means that the user can alter insulin delivery/pump settings using a smartphone. Viewability/controllability is focused on pump manufacturer-specific options. People using the Dexcom G6 CGM may also use the Dexcom G6 mobile app which shows real-time CGM data on a user's or caregiver's mobile device.*

Abbreviations: AID, automated insulin delivery system; app, application; auto, automatic(ally); BGM, blood glucose meter; CGM, continuous glucose monitor; DM, diabetes mellitus; HCL, hybrid closed-loop; LGS, low-glucose suspend; NA, not applicable; PDM, Personal Diabetes Manager; PLGS, predictive low-glucose suspend; SAP, sensor-augmented pump; T1D, type 1 diabetes mellitus; temp, temporary; US, United States of America; USB, Universal Serial Bus (connects computer to peripheral device)

Table 4. Overview of Insulin Pump Characteristics[a]

Characteristic	Insulin Pump Brand, Manufacturer, and Model							
	MannKind Corporation	**Medtronic: MiniMed**			**Insulet Corporation: Omnipod**[b]		**Beta Bionics:**	**Tandem Diabetes Care**
	V-Go 20, V-Go 30, V-Go 40[14]	**MiniMed 630G**[5]	**MiniMed 770G**[6]	**MiniMed 780G**[7,8]	**Omnipod DASH**[10]	**Omnipod 5**[9]	**iLet Bionic Pancreas**[4]	**T:slim X2**[12,13]
Water exposure	IPX8 certified: safe in up to 1 meter of water for 24 hours	Pump is waterproof: safe at depth of 12 ft for 24 hours			IP28 certified: safe in up to 25 ft for up to 1 hour		IPX8 certified: safe in up to 12 ft for 30 min	IPX7 certified: water-resistant in up to 3 feet for 30 min
Compatible U-100 insulin(s)	Insulin lispro, insulin aspart (Humalog and NovoLog)	Insulin lispro, insulin aspart (Humalog and NovoLog)	Insulin lispro, insulin aspart (Humalog and NovoLog)	Insulin lispro, insulin aspart (Humalog and NovoLog)	Insulin lispro (Humalog and Admelog), Insulin aspart (Novolog and Fiasp), insulin lispro-aabc (Lyumjev), Insulin glulisine (Apidra) Apidra: usable for 48 hr; others: usable for 72 hrs	Insulin lispro, insulin aspart (Humalog, Novolog or Admelog)	Insulin lispro (Humalog), insulin aspart (Novolog and Fiasp PumpCart [as a prefilled insulin cartridge, which is not available in the US yet])[67]	Insulin lispro, insulin aspart (Humalog and NovoLog)
Minimum basal increments (Units/hr)	Pre-set: 0.83, 1.25, or 1.67	0.025			0.05	0.05	0.045; will wait to deliver if dose < limit[83]	0.001 (at rates ≥ 0.1)
Maximum number of programmed basal patterns (used in *manual mode* for automated systems[e])	1 (pre-set)	8 (each covers 24 hours and may include up to 48 rates) Allows temp basal rates in manual mode			12 (each covers 24 hours and may include up to 24 rates). Allows temp basal rates (for Omnipod 5, this is allowed in manual mode only)		None	6 (each covers 24 hours and may include up to 16 rates). Allows temp basal rates in manual mode
Minimum bolus increments (Units)	Pre-set: 2 Units per button press	0.025			0.05	0.05	0.045 (will wait to deliver until dose > limit)	0.05 (0.01 increments at volumes > 0.05)
Extended bolus feature?	No	Yes	Yes, in manual mode only		Yes	Yes, in manual mode only	No, all doses are automated	Yes, in manual and auto mode
Built-in bolus dose calculator option	No	Yes, Bolus Wizard	Yes, Bolus Wizard or SmartGuard Auto bolus.		Yes, Bolus Calculator. Also has Food Library with carb content (English only).	Yes, SmartBolus Calculator.	No, all bolus is automated. User must announce any meals.	Yes, Bolus Calculator
Compatible CGM with integration	No	Yes, with Guardian 3, or Enlite sensor (630G)[85]		Yes, with Guardian 3 or Guardian 4	No, but iOS widget allows viewing Dexcom G5/6 data next to DASH data[72]	Yes, with Dexcom G6		

[a] *This table provides an overview of insulin pump characteristics, including basic automated features, with a focus on fixed characteristics of the insulin pumps. Refer to Table 5 for details about automation features.*

[b] *The Omnipod Insulin Management System (Omnipod Eros) pump will be discontinued from production in December 2023. For simplicity, this device is not included in this detailed product table.*

[c] *Classified based on how the pump/system would be classified when operated using the most advanced computer algorithm (see Table 1). Most advanced systems are also usable in manual modes which would be equivalent to a conventional pump or SAP.*

[d] *The iLet Bionic Pancreas is sometimes considered a fully closed-loop system since the system autonomously determines all insulin doses; we consider it an HCL system since it still requires user interaction (eg, for meal announcement, exercise).*

[e] *Refers to insulin delivery rates programmed by the user. Pumps used as AID systems adjust basal insulin per sensor glucose values; some also use these programmed basal rates to help tune the automated dosing algorithm.*

[f] *Viewable means pump and/or CGM sensor glucose value data can be reviewed on a smartphone device, whereas controllable means that the user can alter insulin delivery/pump settings using a smartphone. Viewability/controllability is focused on pump manufacturer-specific options. People using the Dexcom G6 CGM may also use the Dexcom G6 mobile app which shows real-time CGM data on a user's or caregiver's mobile device.*

Abbreviations: AID, automated insulin delivery system; app, application; auto, automatic(ally); BGM, blood glucose meter; CGM, continuous glucose monitor; DM, diabetes mellitus; HCL, hybrid closed-loop; LGS, low-glucose suspend; NA, not applicable; PDM, Personal Diabetes Manager; PLGS, predictive low-glucose suspend; SAP, sensor-augmented pump; T1D, type 1 diabetes mellitus; temp, temporary; US, United States of America; USB, Universal Serial Bus (connects computer to peripheral device)

Table 4. Overview of Insulin Pump Characteristics[a]

Characteristic	Insulin Pump Brand, Manufacturer, and Model							
	MannKind Corporation	Medtronic: MiniMed			Insulet Corporation: Omnipod[b]		Beta Bionics:	Tandem Diabetes Care
	V-Go 20, V-Go 30, V-Go 40[14]	MiniMed 630G[5]	MiniMed 770G[6]	MiniMed 780G[7,8]	Omnipod DASH[10]	Omnipod 5[9]	iLet Bionic Pancreas[4]	T:slim X2[12,13]
About compatible CGM	--	The Guardian 3 characteristics: • Fingerstick required for treatment decisions • Initially requires approximately 4 calibrations in 1 day, then at least 2 calibrations daily thereafter • Sensor duration: 7 days		The Guardian 4 characteristics: • SG usable for treatment decisions in automated mode only • Pre-calibrated • Sensor duration: 7 days	--	• May use data for treatment decisions • Pre-calibrated • Sensor duration: 10 days[20]		
Paired BGM	No	Contour Next Link 2.4 • Used for CGM calibration and insulin dosing • Remote manual bolus option	Accu-Check Guide Link • Sends glucose results to pump for CGM calibration and insulin dosing	Accu-Check Guide Link • Sends glucose results to pump for CGM calibration (required for Guardian 3 sensor) and insulin dosing	Contour Next One • Used for BG monitoring	No	No	No
Pump safety alerts/alarms?	No	Yes, multiple			Yes, multiple	Yes, multiple	Yes, multiple	Yes, multiple
Pump data viewable, or controllable in real-time with compatible smartphone?[f]	No	No	Yes, viewable (pump and CGM data) • Uses the MiniMed Mobile app for Android or Apple • App may send data to Carelink	Yes, viewable (pump and CGM data) • Uses the MiniMed Mobile app for Android or Apple • App may send data to Carelink	Yes, viewable (pump data) • Uses Omnipod DISPLAY app for Apple[72]	Yes, viewable, and controllable (pump and CGM data) • Uses Omnipod 5 app for Android (or PDM)[86]	Unclear, some data may be viewable • Uses iLet mobile app for Apple or Android[4]	Yes, viewable (pump and CGM data); also controllable for manual remote bolus only • Uses t:connect app for Apple or Android
Pump data reports electronically viewable by HCP?	No	Yes, but requires manual transfer of report after uploading data to computer CareLink software by USB.[87]	Yes, data is sharable via CareLink, with auto-upload option.[87]	Yes, data is shareable via CareLink, with auto-upload option.[87]	Yes, data is shareable with Insulet-provided Glooko with auto-upload option.[88]	Yes, data is shareable with Insulet-provided Glooko with auto-upload option.[88]	Unknown	Yes, via the t:connect mobile app with auto-upload or via t:connect web application by directly connecting to pump[89]
Allows remote software updates	No	No[90]	Yes[90], and can be updated to 780G software	Yes, using Diabetes Updater app on compatible smartphone	Yes (per Danatech)[15]	Yes, using controller/mobile app	Yes, using mobile app[83]	Yes, by connecting to desktop computer[74]
Language options	Unknown; user guide published in English and Spanish	English, Spanish, and Simplified Chinese[91]			English and Spanish	English and Spanish[92]	Unknown; pump does allow user to select a language	Depends on region; may offer English, Spanish and other European languages

[a] This table provides an overview of insulin pump characteristics, including basic automated features, with a focus on fixed characteristics of the insulin pumps. Refer to Table 5 for details about automation features.

[b] The Omnipod Insulin Management System (Omnipod Eros) pump will be discontinued from production in December 2023. For simplicity, this device is not included in this detailed product table.

[c] Classified based on how the pump/system would be classified when operated using the most advanced computer algorithm (see Table 1). Most advanced systems are also usable in manual modes which would be equivalent to a conventional pump or SAP.

[d] The iLet Bionic Pancreas is sometimes considered a fully closed-loop system since the system autonomously determines all insulin doses; we consider it an HCL system since it still requires user interaction (eg, for meal announcement, exercise).

[e] Refers to insulin delivery rates programmed by the user. Pumps used as AID systems adjust basal insulin per sensor glucose values; some also use these programmed basal rates to help tune the automated dosing algorithm.

[f] Viewable means pump and/or CGM sensor glucose value data can be reviewed on a smartphone device, whereas controllable means that the user can alter insulin delivery/pump settings using a smartphone. Viewability/controllability is focused on pump manufacturer-specific options. People using the Dexcom G6 CGM may also use the Dexcom G6 mobile app which shows real-time CGM data on a user's or caregiver's mobile device.

Abbreviations: AID, automated insulin delivery system; app, application; auto, automatic(ally); BGM, blood glucose meter; CGM, continuous glucose monitor; DM, diabetes mellitus; HCL, hybrid closed-loop; LGS, low-glucose suspend; NA, not applicable; PDM, Personal Diabetes Manager; PLGS, predictive low-glucose suspend; SAP, sensor-augmented pump; T1D, type 1 diabetes mellitus; temp, temporary; US, United States of America; USB, Universal Serial Bus (connects computer to peripheral device)

Table 5. Comparison of AID System Indications, Automations, and Customizations, by Model

	MiniMed 770G[6]	MiniMed 780G[7,8]	Omnipod 5[9]	t:slim X2 with Control-IQ[13]	iLet Bionic Pancreas[4,83]
System type	HCL AID	Advanced HCL AID	HCL AID	Advanced HCL AID	Advanced HCL AID[a]
Algorithm indication and insulin or weight requirement	• T1D ≥ 2 years • TDD between 8–250 Units/day	• T1D ≥ 7 years • TDD between 8–250 Units/day	• T1D ≥ 2 years • TDD ≥ 5 Units/day	• T1D ≥ 6 years • TDD 10–100 Units/day *and* weight 25–140 kg	• T1D ≥ 6 years • No TDD requirement
Automated insulin delivery	• Auto-adjust basal every 5 min • Pauses insulin delivery when SG values trend low	• Auto-adjust basal every 5 min • Auto-correction bolus (max 12/hr) • Pauses insulin delivery when SG values trend low[93]	• Auto-adjust basal every 5 min • Pauses insulin delivery for SG <60 mg/dL • Pauses insulin delivery for low PSG	• Auto-adjust basal every 5 min • Auto-correction bolus (max 1/hr) • Pauses insulin delivery for PSG ≤ 70 mg/dL or ≤ 80 mg/dL (during exercise mode only)	• Auto-adjust basal every 5 min • Auto-correction bolus (max 12/hr) • Auto-meal bolus with user announcement • Pauses insulin delivery for rapidly declining SG and/or SG < 60 mg/dL
Algorithm target sensor glucose/range	120 mg/dL	*Options:* 100, 110, 120 mg/dL	• *Options:* 110, 120, 130, 140, 150 mg/dL • May set up to 8 different targets per 24 hours	*Range:* 112.5–160 mg/dL	*Options:* "lower" (110 mg/dL), "usual" (120 mg/dL), "higher" (130 mg/dL)
Controller location	Pump	Pump	• Phone app or PDM. Pump automation occurs without pump being next to controller.	Pump May deliver bolus from phone app.	Pump
Initialization Steps					
Required input(s) to initiate auto mode	Actual TDD during 48-hr run-in (insulin is delivered per programmed basal profile); I:C ratio, active insulin time, BG value		Basal insulin profiles, I:C ratios, correction factors, active insulin time	User's body weight, TDD, basal insulin profiles, I:C ratios, correction factors	User's body weight
When does auto mode start?	Delayed 48 hrs. Manual run-in mode must be used during warm up		Immediately	Immediately (with limited automation during the 2-hr CGM sensor warm-up period)	Immediately. "Less carb" meal bolus option not available initially.
Additional Automation Characteristics					
Adaptivity	TDD needs (for max/min basal limits[73]) and CF updated daily (at midnight) using TDD and fasting glucose/insulin concentration data from up to the prior 6 days[33]		TDD needs update with each Pod change (~ every 72 hr)	Tracks actual TDD. Six-day average used to adjust algorithm aggression.[19]	Continuously adapts basal and corrective bolus. Meal adaptations based on carb content and are specific to each meal.
Auto-corrective bolus parameters[b]	• NA, no auto-corrective bolus. System suggests bolus for BG >150 mg/dL. • Bolus calculator suggests doses using TG of 150 mg/dL	• Delivers ≤ 12 x/hr for SG > 120 mg/dL • User may turn off auto-correction • Uses TG of 120 mg/dL	• NA, no auto-corrective bolus • Bolus calculator suggests doses using overall algorithm TG	• Delivers 1x/hr (at 60% of calculated dose[19]) for PSG >180 mg/dL in 30 min • Uses TG of 110 mg/dL	• Delivers ≤ 12x/hr based on SG, SG trend, and IOB • Uses overall algorithm TG
Meal bolus and/or manual bolus parameters	Meal bolus manually delivered by user; system suggests a bolus doses based on user entry of grams of carbohydrates User also has the option to give manual correction boluses.				User announces meal, and selects meal type (breakfast, lunch, dinner) and relative carb amount (more, usual, or less).
Special auto modes	• *Temp mode:* TG 150 mg/dL, reduced basal delivery for user-set duration (0.5-12 hr).	• *Temp mode:* TG 150 mg/dL, reduced basal delivery for user-set duration (0.5-24 hr), and no auto-correction bolus.	• *Activity mode:* TG 150 mg/dL and basal insulin doses decreased 50% for user-set duration (1-24 hr). Auto-restarts automated mode after manual stop or upon expiration of set duration.	• *Exercise mode*: TG 140–160 mg/dL. User must manually start/stop. • *Sleep mode*: TG 112.5–120 mg/dL. No auto-correction bolus. Set as a schedule or manually start/stop.	• Sleep mode: set a scheduled sleep mode TG (of 110, 120 or 130 mg/dL) • Set "CGM target" or "CGM sleep target" (up to 2/24 hr) and select "usual," "lower" or "higher" for each CGM target.
Select Allowed User Adjustments to Insulin Settings while in Automated Mode[78,94]					
Basal rate	No (in automated mode)	No (in automated mode)	No (in automated mode)	Yes	No
I:C ratio	Yes	Yes	Yes	Yes	No
Active insulin time	Yes	Yes	Yes	No, set at 5 hr (in automated mode)	No
Correction factor	No	No (not for auto-correction bolus)	Yes	Yes	No
Extended bolus (in auto mode)	No	No	No	Yes, for 2 hr maximum	No

[a] *The iLet Bionic Pancreas is sometimes considered a fully closed-loop system since the software automatically calculates all insulin doses. However, we consider it to be a HCL system because patients still must announce meals and manage insulin delivery during exercise.*

[b] *Note that systems still adjust basal insulin in response to elevated SG, and some systems may use more aggressive basal insulin corrections despite lacking automated corrective boluses.*

Abbreviations: AID, automated insulin delivery; auto, automated or automatic; BG, blood glucose; CF, correction factor; CGM, continuous glucose monitor; HCL, hybrid closed-loop; hr, hour; I:C, insulin to carbohydrate ratio; IOB, insulin on board; max, maximum; MPC, model predictive algorithm; NA, not applicable; PDM, Personal Diabetes Manager; PID, proportional integrative derivative; PSG, predicted sensor glucose (sensor glucose reading in the future); SG, sensor glucose; T1D, type 1 diabetes mellitus; TDD, total daily insulin dose; TG, target sensor glucose;

Table 5. Comparison of AID System Indications, Automations, and Customizations, by Model

	MiniMed 770G[6]	MiniMed 780G[7,8]	Omnipod 5[9]	t:slim X2 with Control-IQ[13]	iLet Bionic Pancreas[4,83]
Reversion to Manual or Limited Automation Mode[78,94]					
Limited auto mode	Yes; Safe Basal mode. Pump delivers static basal rate using insulin use history.	Yes; fixed basal mode. Pump delivers static basal rate without correction bolus using insulin use history.	Yes; Automated Limited mode. Pump delivers automated dynamic basal rate without SG adjustment using user-programmed settings and recent history.	No; pump reverts to manual mode insulin delivery settings	Yes; Continued automation in BG-run mode for max of 72 hrs using user-entered BG values and past 7-day basal insulin use.
Limited auto mode triggers	• CGM data loss for ≥ 5 min • Min insulin delivery limit for 2.5 hr • Max insulin delivery limit for 4 hr • Sensor accuracy errors To prevent switching to manual mode, user usually must enter a BG value.	• CGM data loss for ≥ 5 min • Min insulin delivery for 3–6 hr • Max insulin delivery for 7 hr • Sensor accuracy error To prevent switching to manual mode, user usually must enter a BG value.	• Loss of CGM data for ≥ 20 min; auto restarts upon return of CGM data. • "Automated Delivery Restriction" alarm due suspending insulin for too long or running max insulin delivery for too long. User must clear it.	NA	• Loss of CGM data for an extended period (duration not provided)
What events force reversion to manual (ie, mode?	• SG >300 mg/dL for 1 hr • SG > 250 mg/dL for 3 hr • User failed to clear a suspend event message within 4 hrs of the message • Running Safe Basal mode for 90 min • Sensor manually turned off or transmitter disconnected User must enter BG to restart auto mode.	• Running fixed basal mode for 4 hr • Insulin delivery manually suspended for 4 hr • Sensor turned off or transmitter disconnected User must enter BG to restart auto mode.	User is prompted to switch to manual mode if an "Automated Delivery Restriction" alarm occurs. User must manually switch on auto mode (after ≥ 5 min in manual mode).	Loss of CGM data for ≥ 20 min; automatically restarts insulin delivery upon return of CGM data.	NA; no manual mode. After 48 or72 hr of BG-run mode, insulin delivery stops. Use system information (eg, TDD) to switch to back-up insulin therapy.

[a] The iLet Bionic Pancreas is sometimes considered a fully closed-loop system since the software automatically calculates all insulin doses. However, we consider it to be a HCL system because patients still must announce meals and manage insulin delivery during exercise.

[b] Note that systems still adjust basal insulin in response to elevated SG, and some systems may use more aggressive basal insulin corrections despite lacking automated corrective boluses.

Abbreviations: AID, automated insulin delivery; auto, automated or automatic; BG, blood glucose; CF, correction factor; CGM, continuous glucose monitor; HCL, hybrid closed-loop; hr, hour; I:C, insulin to carbohydrate ratio; IOB, insulin on board; max, maximum; MPC, model predictive algorithm; NA, not applicable; PDM, Personal Diabetes Manager; PID, proportional integrative derivative; PSG, predicted sensor glucose (sensor glucose reading in the future); SG, sensor glucose; T1D, type 1 diabetes mellitus; TDD, total daily insulin dose; TG, target sensor glucose;

5.4 Glycemic Benefits of Insulin Pump Systems

Compared to MDI, conventional CSII (with a stand-alone insulin pump) may reduce A1c slightly more and reduce the occurrence of hypoglycemia. In youth, conventional CSII reduces the risk of DM complications (ie, DKA, retinopathy, and neuropathy) over MDI.[22] Using a SAP (with or without integrated CGM) improves glycemic control compared to MDI therapy in children and adults with T1D, and people with T2D.[23] SAPs with IST significantly reduced hypoglycemia without worsening overall glycemic control in patients with T1D.[22] While PLGS may reduce the frequency of hypoglycemia by stopping insulin delivery before a low threshold, LGS reduces the severity and length of time within the low glycemic range.[23] According to the AACE, IST are also advantageous for many PwD because they "…lead to increased confidence and trust in the technology, more flexibility around mealtimes, and reduced diabetes distress for both persons with diabetes and caregivers" (page 522).[23]

Compared to alternative insulin delivery options (ie, MDI, CSII, or SAP), single-hormone HCL AID systems may improve glycemic control among people with T1D as measured by A1c and TIR.[95,96] Clinical trials among youth over age 2 years old with T1D demonstrated improved TIR by about 10-15% with AID and advanced AID systems compared to less advanced pump systems.[24] Glycemic benefits of AID systems are especially apparent overnight.[23,24] Additionally, AID systems may offer increased psychosocial benefits.[22] Although AID systems tend to improve TIR overall, postprandial hyperglycemia is a challenge for some patients.[18] One RCT comparing an advanced AID system with auto-corrective boluses up to every 5 minutes to an AID system with only automated basal insulin only demonstrated significantly reduced time in daytime hyperglycemia in people with T1D.[28]

5.5 Potential Limitations of Insulin Pumps/Systems

Disadvantages of insulin pump therapy of any type compared to alternative insulin delivery methods (eg, MDI) include the potentially higher costs, discomfort (eg, requirement to wear the device constantly, adhesive sensitivity), complexity, and risk for rapid development of ketosis or DKA if insulin delivery is interrupted.[2] Disrupted insulin therapy can occur relatively easily from physical problems with infusion sets (eg, dislodgment or occlusions) or problems at the infusion site (eg, lipodystrophy, infection), making prevention and early recognition essential.[22,24] Technological issues can also lead to malfunction and interrupted insulin delivery, particularly with automated pump systems that require uninterrupted communication (eg, via Bluetooth technology) between the pump, controller, and CGM.[23] See **Section 8** for additional safety information about contraindications, warnings or precautions, and adverse events with insulin pumps or pump systems.

Even the most advanced IPSs available (eg, AID systems) are still not full pancreatic replacements.[18] Physiologic limitations of AID systems include sensor lag times and the time required for subcutaneous insulin absorption.[18] Patients must either announce carbohydrate intake (ie, for the iLet Bionic Pancreas,[4] the most automated AID system) or administer meal boluses (as with other AID systems).[6-9,13] Additionally, as glucose levels change rapidly during exercise making SG values potentially less reliable,[77] patients must actively monitor their glucose or modify AID system settings for exercise.[18,97] Options for changing algorithm glucose targets for exercise are available for most AID systems (see Section 5.3.3 and Table 5).[6-9,13]

Importantly, insulin pumps, including HCL AID systems, do not replace proactive diabetes management. Patients using insulin pumps should be familiar with diabetes management principles (eg, carbohydrate counting and management of hypoglycemia).[18,19] Patients using insulin pumps also require back-up methods of insulin delivery and blood-glucose monitoring in case of insulin pump and/or CGM failure.[19]

Computer-operated pumps are potentially vulnerable to cyber-attacks that could compromise pump functions.[18] In 2022, the FDA issued a device recall for a potential cybersecurity risk with Medtronic MiniMed 600-series pumps,[98] which was identified and corrected by the manufacturer.[98,99] Recent federal regulations active as of March 2023 require manufacturers of new devices susceptible to cyberattacks to submit plans for mitigating cyber risks, and to make any post-market security patches available to users.[100] Manufacturers of multiple computer-operated insulin pumps recommend that users take steps to protect their devices physically and electronically. For example, avoid leaving the pump unattended, follow good cyber-security practices (eg, do not download suspicious software to device controllers), and Bluetooth-pair pump system components away from other people/devices to avoid accidentally pairing the pump with another person's device (a concern per Medtronic specifically).[6-9,13]

Discontinuation of pump therapy is relatively uncommon (estimated median incidence of 7% and up to 30% in people with T1D). The most frequent reason for discontinuation is issues with pump wearability, including concerns such as discomfort or poor body image. Discontinuation may also be attributed to suboptimal glycemic outcomes, problems following therapy recommendations, side effects, or complications.[101]

5.6 Switching to Pumps/Systems by the Same Manufacturer

- **Insulet systems (Omnipod):**
  - A new prescription and hardware are required to switch from Omnipod DASH or Omnipod Insulin Management System (Omnipod Eros) to Omnipod 5. Omnipod 5 Pods differ from the Pods used from the other Omnipod systems.[102]
  - Omnipod DASH and Omnipod Insulin Management System components are not compatible. Neither the Pods nor the Omnipod Eros PDM can be used with the other system.[72]

- **Tandem Diabetes (t:slim X2):**
  - A new prescription is required to run other Tandem software (ie, to add Basal-IQ or Control-IQ); however, new hardware is not required. After receiving a prescription and completing the required training, users may update t:slim X2 software by connecting the pump to a desktop computer.[74] Of note, it is not possible to switch back to Basal-IQ after switching to Control-IQ.[75]

- **Medtronic (Minimed):**
  - MiniMed 770G and 780G systems use the same pump. To switch from the 770G to the 780G system, users must update the software after obtaining a new prescription and completing training. The 780G software update may be performed with a Medtronic update app running on a mobile phone with Wi-Fi internet connection.[103]
  - Hardware and software for the Minimed 630G and earlier pump models (eg, MiniMed 530G and 670G) differ from the Minimed 770G/780G. Although not specifically addressed by Medtronic, we assume users would require a new prescription along with new hardware to switch between

these systems. Medtronic does offer "upgrade programs" (ie, monetary credits) for eligible users to switch to the newest models[104]; see https://www.medtronicdiabetes.com/products/device-upgrading for information about upgrade programs.

6.0 GUIDELINE RECOMMENDATIONS

We reviewed insulin delivery, technology-focused guideline recommendations from US or combined US and international organizations. Recent guidelines from the American Diabetes Association (ADA; 2023)[22] and American Association of Clinical Endocrinology (AACE; 2021)[23] provide insulin pump/system recommendations for both youth and adults. The International Society for Pediatric and Adolescent Diabetes (ISPAD; 2022) guideline provides recommendations specific to children, adolescents, and young adults.[24] Insulin pump recommendations from the 2023 Endocrine Society (ES) guideline is specific for PwD at high risk for hypoglycemia; the ES has not published a recent technology-specific guideline.[105]

Information below discusses relative preferences for insulin pump technologies based on type of DM, age, or pregnancy. In general, guidelines suggest individualizing insulin pump selection based on patient's preferences and requirements.[22-24] Because advanced AID systems that offer automated corrective insulin boluses are only recently available in the US, **recent guidelines do not distinguish between AID systems and advanced AID systems in formal recommendations.**

When implementing AID systems, experts recommend starting PwD without prior experience with insulin delivery technologies on an insulin pump and/or CGM before starting the AID system.[19] Once a PwD begins using an insulin delivery device, the ADA recommends allowing continued access if that patient's insurance coverage changes, based on expert consensus.[22] The AACE strongly recommends discontinuation of insulin pump therapy based on patient preference for an appropriate alterative therapy, or if patients are unable to use the device safely or effectively.[23]

In 2022, the ADA and the European Association for the study of Diabetes released a joint "Consensus Report" on AID systems. Included in this report are non-graded statements on the best candidates for AID systems. Like guidelines, they suggest the ideal patient for AID systems should be capable of using the technology (eg, able to understand and trouble-shoot the system), including having current mental capacity, and desire to use the system (eg, desire to achieve better glucose control). Furthermore, good candidates for an AID system include those with realistic expectations of the system's capabilities, and those who can undergo the training for appropriate use and continue communicating with their provider about the system. Patients with the following characteristics may face additional challenges with an AID system: 1) patients with very high or very low insulin requirements (system is less effective); 2) patients with visual impairment; and 3) patients with diabetes complications. Nevertheless, patients with visual impairment or complications of diabetes may still be able to use an AID system effectively.[18]

Refer to **Table 6** for a summary of guideline recommendations for use of conventional pumps, SAPs, or advanced insulin pump systems in children and adults with diabetes. Note that reviewed guidelines use different definitions to refer to types of insulin-delivery technologies. To the best of our ability, we interpreted how different recommendations might apply to various technologies based on guideline-specific definitions, as shown in Table 6.

Table 6. Recent US or International Guideline Ambulatory Insulin Pump or Insulin Pump System Recommendations

Recommendations (Evidence Rating[a,b,c])
American Diabetes Association (ADA), Diabetes Technology Guideline; 2023[22] Target age group for recommendations: youth and adults
Insulin pumps and automated insulin delivery (AID) systems

• Offer **AID systems** to patients (populations and LOE below) when they can safely use the device. Selection of a particular device should be individualized.
  ○ Adults or youth with T1D (**A**)
  ○ Adults or youth with other types of diabetes with insulin deficiency (**E**)
• Offer an **insulin pump (eg, pump ± SAP with LGS)** to patients (population and LOE below) receiving MDI who can safely use the device, and who *prefer these devices to (or cannot use) an AID system.* Selection of a particular device should be individualized.
  ○ Adults or youth with T1D (**A**)
  ○ Adults or youth with other types of diabetes with insulin deficiency (**E**)
• **Insulin pumps** are an option for adults or youth with T2D requiring MDI that can use the device safely. Selection of a particular device should be individualized. (**A**)
• **Continuation of care:** "Patients with diabetes who have been using continuous glucose monitoring, continuous subcutaneous insulin infusion, and/or automated insulin delivery for diabetes management should have continued access across third-party payers, regardless of age of A1c levels.." (page S112) (**E**)

Do-it-Yourself closed-loop systems *Non FDA-approved systems that combine a CGM, insulin pump, and insulin delivery algorithm (directions may be provided on the internet). Some of these systems are seeking regulatory approval.*
• These systems cannot be prescribed by providers; providers should assist patients using these systems to maintain patient safety. (**E**)
Endocrine Society, Diabetes in Patients with High Hypoglycemia Risk Guideline; 2023[105] Target age group/population: adults and children with T1D or T2D with high hypoglycemia risk
High hypoglycemia risk: includes individuals taking high risk medications (including insulin), very young or old age, certain comorbidities (eg, renal or liver dysfunction; untreated pituitary, adrenal or thyroid deficiency; eating disorders), longer diabetes diagnosis duration (≥ 5 y insulin use), history of severe hypoglycemia or hypoglycemia unawareness, irregular eating schedules (including fasting, among others), consumption of alcohol, or whose cognitive status prevents appropriate response to low blood glucose.
Algorithm-driven insulin pumps (ADIP) *Defined as use of an insulin pump + CGM, with automatic adjustment of basal insulin delivery based on sensor readings. Authors imply this to include SAPs with insulin-suspend technology and AID systems: "ADIP is the term used to refer to all currently available forms of automated insulin delivery through devices in this guideline." (page 5)*
• Use of rtCGM and ADIPs instead of MDIs with SMBG (≥3x daily) suggested for adults and children with T1D (**Suggested, lower recommendation; weak; low quality of evidence)**   ○ Guideline authors noted that patients using CGMs and/or ADIPs will still require some SMBG monitoring for validation of CGM readings
American Association of Clinical Endocrinology (AACE), Advanced Technology Guideline; 2021[23] Target age group for recommendations: not specified
Populations that would benefit from the following devices (listed below each device heading)
Insulin pump without CGM

• Option for patients with diabetes with the following characteristics (**Grade B; SOE, I-H; BEL 1**)
  ○ Glycemic target achievement and minimal time below range (TBR), or
  ○ Infrequent symptomatic hypoglycemia, and

[a] *Evidence rating from ADA 2023 guidelines and 2022 ISPAD guideline[105]: A (highest level of evidence): based on well-designed randomized clinical trials, well-conducted meta-analysis of randomized controlled trials, or very strong nonexperimental evidence; B (moderate level of evidence): based on well-conducted observational studies (cohort or case-control), or meta-analysis of observational studies; C (low level of evidence): based on poorly controlled or uncontrolled studies, or conflicting evidence where the majority of evidence supports the recommendation; E (No clinical evidence): based on expert consensus or clinical experience*

[b] *LOE rating per GRADE criteria and recommendation interpretation for ES 2022 guideline: low certainty, little confidence in the effect estimate; Suggested recommendation: benefits probably outweigh the risks*

[c] *Evidence rating from AACE 2022 guideline: recommendations provided for evidence grade (ie, A or B), SOE for the evidence grade, and BEL. BEL and evidence grade: Recommendation achieved >66% consensus and received evidence lacked positive qualifiers and either lacked negative subjective evidence factors (and is assigned evidence Grade A) or had predominant negative subjective factors (and is downgraded to Grade B); Grade A = very strong recommendation and Grade B = strong recommendation. SOE: Strong (level I) evidence = RCT or meta-analysis of RCT evidence; Intermediate (level II) evidence = clinical research that is non-RCT or meta-analysis of RCTs and that has a comparator group (eg, observational studies)*

[d] *It is unclear whether ISPAD recommendations are intended for patients with T1D only. Evidence cited by the guideline is for people with T1D, yet some formal recommendations by ISPAD are not written as being only for people with T1D.*

Abbreviations: A1c, hemoglobin A1c or glycosylated hemoglobin; AID, automated insulin delivery; BEL, best evidence level; CGM, continuous glucose monitoring; CSII, continuous subcutaneous insulin infusion; H, high SOE; HCL, hybrid closed-loop; I-H, intermediate-high SOE; LGS, low glucose suspend; PLGS, predictive low glucose suspend; LOE, level of evidence; MDI, multiple daily insulin injections; rtCGM, real-time continuous glucose monitoring; SAP, sensor augmented pump; SOE, strength of evidence; T1D, type 1 diabetes mellitus; T2D, type 2 diabetes mellitus; x, times; y, year(s);

Table 6. Recent US or International Guideline Ambulatory Insulin Pump or Insulin Pump System Recommendations

Recommendations (Evidence Rating[a,b,c])
○ Regularly self-checking blood glucose (minimum 4x daily for T1D)
Insulin pump with CGM (ie, as basic SAP)
• Everyone with diabetes treated with intensive insulin therapy "…who prefer not to use automated insulin suspension/dosing systems or have no access to them" (page 521) (**Grade A; SOE, I-H; BEL 1**)
Advanced insulin pump technology (ie, LGS, PLGS, HCL)
• **LGS and PLGS:** (**Grade A; SOE, H; BEL 1**) ○ LGS: All patients with T1D, for the purpose of reducing hypoglycemia severity and duration ○ PLGS: All patients with T1D, for the purpose of mitigating hypoglycemia ○ An option for: "…anyone with frequent hypoglycemia, impaired hypoglycemia awareness, and those who fear hypoglycemia leading to permissive hyperglycemia" (page 521)
• **AID systems**: (**Grade A; SOE, H; BEL 1**) ○ All patients with T1D. **"Given the improvement in TIR and the reduction in hyperglycemia with AID, this method is preferred above other modalities."** (page 509) ○ An option for: "…persons with diabetes with suboptimal glycemia, significant glycemic variability, impaired hypoglycemia awareness, or who allow for permissive hyperglycemia due to fear of hypoglycemia…" (page 509)
Insulin pump discontinuation
• Providers should consider insulin pump discontinuation for patients with diabetes who exhibit insufficient competence or safety in its usage or prefer an alternative method for insulin delivery (**Grade A; SoE: Intermediate; BEL 1**)
International Society for Pediatric and Adolescent Diabetes (ISPAD), Insulin Delivery Diabetes Technology Guideline; 2022[24] Target age group for recommendations: children, adolescents, and young adults with diabetes[d]
Overarching principle for selecting an insulin delivery technology
• Offer youth *the most advanced delivery technology* available and appropriate for them **(B)**
Insulin pump therapy (CSII)
• Recommended for youth of all ages with diabetes **(A)** ○ Note that infusion set failures, which can cause DKA, with CSII are common and should be recognized promptly **(B)** ○ Patient-driven factors should drive pump selection (ie, based on what pump features interest them)
Sensor augmented pump (SAP) with or without LGS/PLGS
• **SAP:** Basic SAP alone is superior to MDI with SMBG for A1c reduction **(A)** but requires at least 60% CGM sensor use to realize the A1c reduction **(A)** • **LGS:** Strongly recommended for people with T1D when other advanced technology is not available • **PLGS:** Strongly recommended for people with T1D when AID is not available ○ LGS systems reduce hypoglycemia severity/duration compared to CSII or SAP without LGS **(A)** and PLGS systems reduce hypoglycemia frequency **(A);** both LGS and PLGS allow greater user flexibility and have evidence showing reduced diabetes-related distress **(A)**
Automated insulin delivery (AID) systems (closed loop systems)
• **AID:** Strongly recommended for all youth with diabetes **(A)** ○ AID systems improve TIR **(A)**, especially overnight **(A)** ○ Greater increase in TIR over other insulin delivery systems have been demonstrated in in all age groups, starting with children as young as 2-5 years ○ Clinicians should support patients who choose DIY systems **(E)**

[a] *Evidence rating from ADA 2023 guidelines and 2022 ISPAD guideline[105]: A (highest level of evidence): based on well-designed randomized clinical trials, well-conducted meta-analysis of randomized controlled trials, or very strong nonexperimental evidence; B (moderate level of evidence): based on well-conducted observational studies (cohort or case-control), or meta-analysis of observational studies; C (low level of evidence): based on poorly controlled or uncontrolled studies, or conflicting evidence where the majority of evidence supports the recommendation; E (No clinical evidence): based on expert consensus or clinical experience*

[b] *LOE rating per GRADE criteria and recommendation interpretation for ES 2022 guideline: low certainty, little confidence in the effect estimate; Suggested recommendation: benefits probably outweigh the risks*

[c] *Evidence rating from AACE 2022 guideline: recommendations provided for evidence grade (ie, A or B), SOE for the evidence grade, and BEL. BEL and evidence grade: Recommendation achieved >66% consensus and received evidence lacked positive qualifiers and either lacked negative subjective evidence factors (and is assigned evidence Grade A) or had predominant negative subjective factors (and is downgraded to Grade B); Grade A = very strong recommendation and Grade B = strong recommendation. SOE: Strong (level I) evidence = RCT or meta-analysis of RCT evidence; Intermediate (level II) evidence = clinical research that is non-RCT or meta-analysis of RCTs and that has a comparator group (eg, observational studies)*

[d] *It is unclear whether ISPAD recommendations are intended for patients with T1D only. Evidence cited by the guideline is for people with T1D, yet some formal recommendations by ISPAD are not written as being only for people with T1D.*

Abbreviations: A1c, hemoglobin A1c or glycosylated hemoglobin; AID, automated insulin delivery; BEL, best evidence level; CGM, continuous glucose monitoring; CSII, continuous subcutaneous insulin infusion; H, high SOE; HCL, hybrid closed-loop; I-H, intermediate-high SOE; LGS, low glucose suspend; PLGS, predictive low glucose suspend; LOE, level of evidence; MDI, multiple daily insulin injections; rtCGM, real-time continuous glucose monitoring; SAP, sensor augmented pump; SOE, strength of evidence; T1D, type 1 diabetes mellitus; T2D, type 2 diabetes mellitus; x, times; y, year(s);

6.1 Patients with T1D

Recent guidelines from the ADA, AACE, and ISPAD **prefer AID systems** to other methods of insulin delivery (ie, MDI, convention insulin pumps, or SAP with or without IST) **youth and adults with T1D**[23,24] who can safely and effectively use these devices.[22] The preference for the most advanced insulin delivery technology in patients with T1D is based on high-quality evidence showing AID systems improve TIR and reduce time with hyperglycemia compared to other types of insulin delivery technology.[23,24] The ES suggests, based on low-quality evidence (in contrast to previous organization's ratings), rtCGM be used with an AID system (or SAP with IST) **instead of MDI with SMBG** for patients with T1D.[105]

Alternative modes of insulin pump delivery including conventional insulin pump, SAP, or SAP with IST are also options for non-pregnant youth and adults with T1D based on high-quality evidence.[22-24] Although recent guidelines by ADA, AACE and ISPAD emphasize offering the most advanced technology (AID systems), less advanced pump systems are options for patients who prefer another modality to AID systems,[23,24] or who are not able to use an AID system.[22] ISPAD strongly recommends that youth with T1D use a SAP with PLGS if an AID system is not available, or alternatively, use a SAP with LGS if other advanced technology is not available.[24]

Selection of a particular insulin pump device should be individualized, including considering caregiver's preferences when applicable.[22]

6.2 Patients with Other Types of DM

Patients without T1D may also benefit from use of AID systems; however, there is little high-quality evidence supporting AID use in people without T1D.[22] Based on expert consensus (level E evidence unlike level A for people with T1D), the ADA suggests offering an AID system to youth or adults with insulin-deficient diabetes using MDI who can safely use the device.[22] Unlike the ADA, the extent to which formal recommendations for AID systems by the AACE and ISPAD apply to people without T1D is unclear. Despite wording in formal recommendations suggesting AID systems might be considered for some patients with types of DM other than T1D, supporting evidence cited by the AACE and ISPAD is among patients with T1D only and evidence quality is rated as high, suggesting recommendations for AID systems are intended for people with T1D. Nonetheless, the AACE might consider AID systems to be an option for PwD who are likely to benefit from an AID system (ie, lack of glycemic control, large glycemic variability, or demonstrated hypoglycemia concerns).[23] ISPAD's formal recommendation is worded without specifying a recommended type of DM: AID systems are "…strongly recommended for youth with diabetes" (page 1407).[24] Like the ADA, recent (2022) consensus recommendations for AID systems support AID system use in patients with other types of DM who require intensive insulin therapy (ie, MDI or CSII), including T2D (grade C evidence), post-pancreatectomy (expert opinion), or diabetes secondary to cystic fibrosis (grade C evidence).[19]

Conventional insulin pumps or SAP (with LGS/PLGS per the ADA) are recommended by the ADA and AACE for people with DM on intensive insulin therapy who prefer one of these delivery options to an SAP with IST system (AACE) or AID system (ADA and AACE).[22,23] High-quality evidence supports use of insulin pumps instead of MDI therapy for adults and youth with T2D who can safely use a pump.[22] While the ADA recommends SAP with IST for people with insulin-deficient DM on MDI who prefer it to an AID

system,[22] the AACE more specifically recommends SAP with LGS or PLGS for people with DM and demonstrated hypoglycemia concerns.[23]

Selection of a particular insulin pump device should be individualized, including considering caregiver's preferences when applicable.[22]

6.3 Guideline Considerations for Special Populations

Refer to the Diabetes technology guideline recommendations in Table 6 above, which apply to children and adults. The extent to which the technology guideline recommendations apply to pregnant people is unclear.

6.3.1 Children and Adolescents

As indicated above, recommendations from the ADA and AACE consider conventional insulin pumps, SAP with or without IST, or AID systems as options for youth with DM.[22,23] AID systems are a preferred option for youth with T1D based on high-quality evidence, [22-24] and may be preferred for some patients with other DM based on expert opinion or low-level evidence.[19,22] Similarly, ISPAD recommends SAP with IST for youth with T1D when they cannot use/access an AID system.[24] Conventional insulin pumps are recommended by ISPAD for youth of all ages with DM.[24]

Neither the ADA and AACE nor the pediatric-focused ISPAD technology guidelines specifically state a minimum age for insulin delivery device recommendations.[22-24] By expert consensus, ISPAD prefers CSII with insulin pumps over MDI for children <7 years old with T1D because pumps offer increased insulin dose precision and flexibility.[25] Pre-school age children (ie, ages 6 months to 6 years) with T1D face age-specific challenges to using AID systems including low total insulin needs (often <10 Units daily) and significant within-day and day-to-day variation in insulin needs.[25] Both ISPAD and AID system expert consensus guidelines point out that commercial HCL AID systems have been studied in children with T1D as young as 2 years old, and similar benefits have been achieved in people with T1D of all ages.[19,24] Fewer studies evaluated AID systems for younger children (age <6 years) with T1D, so experts assigned a lower evidence rating and recommendation to the younger population (B; consider recommending) versus older children age 7-14 years with T1D (A; strongly recommend).[19]

Very low insulin needs in preschool children with T1D may be a barrier to using some AID systems.[25] Other barriers to pump use among all youth include "…concerns regarding the physical interference of the device, discomfort with the idea of having a device on the body, therapeutic effectiveness, and financial burden" (ADA, page S119).[22]

6.3.2 Pregnancy

ADA and AACE recommend insulin as first-line for all pregnant women with preexisting T1D or T2D, or GDM (when lifestyle therapy is insufficient).[1,53] Insulin delivery as MDI or by insulin pump are options for pregnant women with T1D per the ADA (grade C evidence).[53] The AACE considers CSII with RA insulin an option for basal insulin delivery for pregnant women with DM (grade B; BEL 1); cited evidence for insulin pump therapy during pregnancy is among women with T1D.[1] Conventional insulin pump therapy without CGM has not demonstrated superior outcomes to MDI during pregnancy in women with T1D, but insulin pumps may improve glycemic control during labor and delivery.[23]

Other technology-specific guidelines from the ADA and AACE[22,23] do not specifically address pregnant patients. Expert consensus considers AID systems an option for pregnant people with T1D based on low-level evidence (C; consider recommending).[19] Historically, one barrier to using AID systems during pregnancy is the glycemic targets used by the dosing algorithms target a glucose level higher than what is recommended during pregnancy.[22,31] Recently, the MiniMed 780G systems was approved, which offers the lowest target glucose of all systems, 100 mg/dL.[7,8] The ADA points out that insulin-suspend thresholds used by systems with PLGS may be theoretically suitable for pregnancy, and the ability to suspend insulin when glucose values trend low may allow more aggressive meal-time insulin doses.[22]

Only one AID system, CamAPS FX, has received regulatory approval in other countries for pregnancy.[31] Experts report there are off-label case reports of use of an older MiniMed AID system (670G) during pregnancy.[31]

6.3.3 Older Adults

Most evidence for using SAP with IST or AID systems is among people with T1D, though such trials have included comparatively fewer older adults.[106] Nonetheless, the ADA recommends insulin pump therapy, including AID systems, for older adults as they recommend them for younger adults, as long the patient can safely and effectively use the device.[22] The benefits of using any device should be weighed against the burden of its use.[106]

Older adults are at higher risk for hypoglycemia than younger adults.[105,106] A formal recommendation by the ADA is provided for the use of AID systems in older adults with T1D to reduce hypoglycemia risk (Grade B). Other advanced delivery devices (including non-pump technologies like connected pens) are also recommended to reduce hypoglycemia risk in older adults based on expert opinion.[106]

7.0 DIRECT COMPARATIVE EFFICACY AND SAFETY EVIDENCE

Forty-six possible SRs were screened in full-text review, but none of these studies met our strict inclusion and exclusion criteria. Refer to **Appendix F** for a flow diagram of the screening process and reasons for exclusion and **Appendix G** for excluded citations by reason for exclusion. Three RCTs[26-28] were identified from 2 of the screened review studies, Moon et al 2021[32] and Alotaibi et al 2020.[107] The number of trials per insulin pump is as follows: MiniMed 780G (1),[28] MiniMed 670G (1),[28] and t:slim X2 (2).[26,108] The 2 t:slim X2 studies (Brown et al 2020 and Forlenza 2018) compared system algorithms (Control-IQ versus Basal-IQ, or Basal-IQ versus no algorithm).[26,108] The 3rd trial (Bergenstal et al 2021) used 2 different pumps (MiniMed 670G vs 780G) that were also running different insulin dose-adjustment algorithms.[28]

Each RCT included patients with T1D.[28,108] Ages of patients in trials ranged from 6 years to 72 years old. The trial comparing an AID and advanced AID system (MiniMed 670G and 780G) enrolled adolescents and adults 14 to 29 years old,[28] and the trial comparing the advanced AID t:slim X2 with Control-IQ to SAP with PLGS (t:slim X2 with Basal-IQ) also enrolled patients at least 14 years old.[108] The 3rd trial comparing a SAP with PLGS (Basal-IQ) to SAP, both with the t:Slim X2 pump, enrolled the widest age range of 6 to 72 years old.[26]

Consistent with the results of our literature search for SRs, a recent expert opinion editorial reported a lack of head-to-head comparisons between HCL AID systems for glycemic outcomes.[109] Though, we did

find an RCT comparing HCL AID systems from the same manufacturer (MiniMed 670G, the first HCL AID, vs MiniMed 780G, Medtronic's newest HCL AID system).[28] Because there is a lack of direct comparisons between current HCL AID systems and generally AID systems have each demonstrated TIR improvement by 9-12% (with the magnitude of improvement dependent on the study population's percent TIR at baseline), experts suggested that selection of an HCL AID system should be individualized. "The best HCL system is the one the person wants to use" (Messer and Berget, Page 92).[109]

7.1 Advanced AID (MiniMed 780G) versus AID (MiniMed 670G)

The FLAIR (Fuzzy Logic Automated Insulin Regulation) randomized, crossover, open-label, multinational trial by Bergenstal et al 2021[28] compared an advanced AID system, MiniMed 780G, to an older AID system, MiniMed 670G[**], among adolescent and adults (ages 14-29 years) with T1D. First, patients completed a run-in period where they received training on use of the pump and CGM in non-automated mode. To be included in the experimental trial period, patients were required to complete at least 80% of all possible CGM readings over 2 weeks and at least 3 BGM tests per day during the run-in period. Patients were randomized to the order of 12-week treatment with either the 670G or 780G, both with the Medtronic Guardian Sensor 3 CGM and Contour Next 2.4 BGM. Patients received training on the automated mode of each pump at the start of each 12-week period (running manual mode for the first 6-10 days unless they were an experienced 670G user), with no washout between study periods. Both pumps operated similarly except for key differences in their insulin dosing software: auto-correction boluses by the 780G and a lower glucose target for the 780G. During the 780G arm, the automated insulin-dosing algorithm glucose target could be reduced to 100 mg/dL at week 2 from the initial target of 120 mg/dL for patients without increased hypoglycemia risk[††] (83% of patients used the lower goal at 12 weeks), whereas the 670G algorithm always targeted 120 mg/dL. Patients using the 670G self-delivered boluses (system-suggested boluses for a targeted glucose <150 mg/dL) whereas auto-correction boluses by the 780G targeted a glucose <120 mg/dL[‡‡]. Both systems require user-initiated meal insulin boluses.[28]

Included patients were 113 non-pregnant adolescents and adults (mean age 19 years) who had diagnosed T1D for at least 1 year (mean duration of 12 years) with a A1c between 7-11% despite use of either basal-bolus MDI or an insulin pump. Key exclusion criteria were use of non-insulin medications for diabetes, a history of ≥ 1 severe hypoglycemia episode or ketoacidosis requiring hospitalization in the 6 months before enrollment, or significant renal disease (eGFR <45 mL/min or on dialysis). At baseline, the mean patient A1c level was 8.1%, 80% of patients had been using an insulin pump, and only 12% had not been using a pump or CGM.[28]

[**] MiniMed 670G was the first FDA-cleared insulin-only AID system in the US. Its insulin-dosing software is highly similar to the MiniMed 770G; Medtronic considers them to be clinically similar.

[††] To switch to the lower glucose target, users must have had ≤1% of past 24-hour sensor readings <54 mg/dL and either no night (midnight-6 AM) hypoglycemia (<54 mg/dL) or ≤3% of past 24-hour sensor readings <70 mg/dL.

[‡‡] In the 780G study period, active insulin time (initially set at 3-4 hr) could be adjusted in 30 min increments every 2 weeks by the study investigator–shorter times lead to increased corrective and meal bolus aggressiveness.

The study achieved the co-primary endpoints[§§] in the intention-to-treat (ITT) population[***], demonstrating superiority of the 780G to the 670G for reduced time in daytime hyperglycemia (glucose > 180 mg/dL) [37% vs 34%, mean adjusted difference –3% (95% CI –3.97 to –2.04); P<0.0001] without increased 24-hour time in hypoglycemia (glucose < 54 mg/dL) [0.5% vs 0.46%, mean adjusted difference –0.06% (95% CI — 0.11 to –0.02); P<0.0001 for non-inferiority[†††]]. At baseline, 42% of daytime CGM readings exceeded 180 mg/dL and 0.46% of readings were hypoglycemic; thus, numerically, both pumps slightly improved time in hyperglycemia with similar rates of hypoglycemia. Time-in-range[TIR] (percent of CGM glucose readings between 70-180 mg/dL) for 24 hours was significantly (P<0.0001) higher during the 780G period (67%) compared to the 680G period (63%). Both systems numerically improved TIR compared to the baseline rate of 57%. Other pre-specified secondary glycemic outcomes favored the 780G except for time in hypoglycemia (<70 mg/dL) that was not statistically different between study periods. Mean user-reported satisfaction scores slightly favored the 780G to the 670G (P=0.0030).[28]

Mean CGM usage was around 85% in each study arm. Trial participants using the 670G spent significantly less time in automated mode (75%) compared to the MiniMed 780G participants (86%), consistent with other data showing numerically more frequent exits from automated mode for the 680G vs 780G (mean 5.7 vs 1.7 times per week).[28]

Adverse events (AEs) reported for people who used each pump (n=112 each), were comparable during use of each device. The proportion of patients with ≥1 reportable AE was 6% in the 670G period and 5% in the 780G period. Key safety outcomes were severe hypoglycemia, diabetic ketoacidosis (DKA), or other serious AE. Severe hypoglycemia occurred in 1 patient during 780G use (patient gave a meal bolus 1 hour after dinner and snack bolus 1-2 hours later) and no patients during 670G use. No patients experienced DKA with either pump. Other serious AEs considered non-device related occurred for 2 patients during the 670G period (1 patient hospitalized for suicidal ideation and the other hospitalized for a ruptured appendix) and no patients during the 780G period. Other reported specific events were skin reactions at the infusion site (1 patient using 780G) and skin reactions at the CGM site (2 patients, with 1 each running the 670G or 780G).[28]

7.2 Advanced AID (t:slim X2 with Control-IQ) versus SAP with LGS/PLGS (t:slim X2 with Basal-IQ)

A randomized, multi-site, controlled, parallel-group, switch trial by Brown et al 2020[27] compared continuation with an advanced AID system (t:slim X2 with Control-IQ) to switching to a SAP with LGS and PLGS (t:slim X2 with Basal-IQ). Prior to this trial, participants had completed a 6-month RCT demonstrating superiority of the Control-IQ system to a basic SAP system (ie, stand-alone pump with stand-alone CGM) for improving TIR[108]; 109 patients of the original 112 (97.3%) who had received Control-IQ participated in this secondary switching trial.[27] Patients in both study arms used the Dexcom G6 CGM. Follow up was for 13 weeks after the prior 6-month trial. Notably, due to a temporary Control-

[§§] Co-primary endpoints were assessed with CGM readings after the automated mode started in each pump study period until 84 days or hour 23:59 the day before the 12-week visit. Daytime was defined as between 06:00 and 23:59 daily.

[***] All participants with ≥72 hours of CGM readings and who used each pump's automated mode at least 80% of the time. Only 2 patients were lost to follow-up, 1 each from each pump arm during the 1st study period.

[†††] Non-inferiority margin was 2%

IQ software error, apparently during the 13-week trial, 50 (92.6%) patients in the Control-IQ arm were required to stop Control-IQ for approximately 4 weeks.[108] This impacted median time in automated mode for the t:slim X2 with Control-IQ; time in automation was 67% overall, or 88% when the 4-week suspension is excluded.[108]Though, median CGM use was high at about 97% during the trial.[108]

Trial patients, including 54 in in the Control-IQ continuation arm and 55 in the Basal-IQ switch arm, were at least 14 years old (mean age of 33 years) with T1D for a median duration of 16-18 years.[27] Patients using non-insulin agents for diabetes were excluded.[110] During the prior 6-month trial, the mean percent TIR ± standard deviation (SD) was 71.6 ± 12.7 and 71.6 ± 10.7 for patients now assigned to the Basal-IQ and Control-IQ arms of the secondary study, respectively. [27]

In the ITT population,[‡‡‡] 13-week TIR (mean [SD] percent time with CGM-measured glucose 70-180 mg/dL) was significantly greater among patients continuing Control-IQ (67.6 ± 12.6) compared to patients who switched to Basal-IQ (60.± 12.6). The risk-adjusted[§§§] difference in mean percent TIR between arms over 13 weeks, the study's primary efficacy outcome, was 5.9 (95%CI 3.6–8.3), P<0.001 favoring Control-IQ. Other 13-week CGM data showed similar hypoglycemia outcomes with Control-IQ and Basal-IQ, and worse hyperglycemia outcomes in the group that switched to Basal-IQ compared to the group continuing Control-IQ. Regarding hyperglycemia, mean percent time above 180 mg/dL was 31 in the Control-IQ continuers arm compared to 38 in the Basal-IQ arm (adjusted difference [95%CI], –6.04 [–8.40 to –3.63]; P<0.001).[27]

Regarding safety over 13 weeks, 3 hyperglycemia/ketosis events (2 events due to infusion set failure and 1 due to illness) occurred in the Basal-IQ arm compared to no events in the Control-IQ arm. No DKA or severe hypoglycemia events occurred.[27] A numerically higher percentage of patients in the Basal-IQ arm experienced worsened A1c by >0.5% (36%) compared to the Control-IQ continuers (15%).[110]

7.3 SAP with LGS/PLGS (t:slim X2 with Basal-IQ) versus SAP (t:slim X2 with stand-alone CGM)

The PROLOG (PLGS for Reduction of Low Glucose) multi-site, randomized, cross-over trial by Forlenza et al 2018[26] compared SAP with PLGS system (t:slim X2 with Basal-IQ) to SAP using the t:slim X2 pump. Patients were randomized to 3 weeks of treatment with either the SAP with LGS/PLGS or the basic SAP. Both study arms used the Dexcom G5 sensor. Basal-IQ automatically suspended insulin delivery for predicted low glucose (<80 mg/dL) or observed low glucose <70 mg/dL, whereas all insulin delivery adjustments or pauses in the basic SAP system arm was controlled by the user. Prior to the study period, patients received pump and CGM training during a run-in period; demonstration of daily pump use and CGM use during 85% of possible days during the run-in period was required for participation in the experimental period. Since participants used the Dexcom G5, patients used the Accu-Check BGM for calibration during both 3-week study periods.[26]

Included patients were 103 adults and children ≥ 6 years old (mean age 24 years, range 6-72 years) who had diagnosed T1D for at least 1 year (median duration of 8 years). Prior to the trial, most patients were

[‡‡‡] Authors report that most participants (92.6%) in the Control-IQ had to discontinue use of the algorithm for about 4 weeks due to a software error. Authors reported a per-protocol analysis excluding this 4-week period, showing a slightly higher percent TIR (~69.1%) in the Control-Q arm.
[§§§] Adjusted for baseline TIR value, age, and clinical study site

using an insulin pump (83%) and only 2% had never used CGM. At enrollment, the mean ± SD patient A1c was 7.3± 0.9. At baseline, the median percent of glucose readings <70 mg/dL was 3.6% and the mean ± SD percent of CGM glucose readings between 70-180 mg/dL was 64 ± 15.[26]

CGM usage was high (about 95%) during the trial, and glycemic efficacy outcomes were assessed using CGM readings. During the 3-week Basal-IQ period, patients spent significantly less time in hypoglycemia (glucose <70 mg/dL), a median of 2.6% of glucose readings, compared to a median of 3.2% during the 3-week basic SAP period. The primary outcome of the difference in proportion of hypoglycemic readings significantly favored SAP with Basal-IQ compared to the basic SAP (–0.8 [95%CI –1.1 to –0.5; P<0.001]). Overall percent TIR (mean ± SD percent glucose between 70-180 mg/dL) was also greater with Basal-IQ treatment (65 ± 15) compared to basic SAP treatment (63 ± 15), with a difference of +2 (95% CI 1–4; P adjusted for multiple comparisons <0.001). A significant benefit for time in hyperglycemia favoring Basal-IQ to basic SAP was demonstrated for very high glucose excursions (percent glucose >250 mg/dL) but not for all hyperglycemia excursions (percent glucose >180 mg/dL). Participants felt the Basal-IQ system was usable (composite mean score of 88 out of 100) per the System Usability Questionnaire.[26]

Regarding safety, during the basic SAP period, 1 severe hypoglycemic event occurred compared to no events during the Basal-IQ period. One other severe AE, a bowel obstruction, occurred during the SAP period. There was no difference in the rate of significant ketone elevations between study periods.[26]

8.0 SAFETY

The following subsections provide an overview of contraindications, and warnings and precautions per insulin pump user guides, and summarize risks associated with insulin pumps or pump systems.

8.1 Contraindications and Select Warnings/Precautions

Most insulin pumps/systems have numerous warnings and precautions for safe and effective use. Compared to all other reviewed pumps/systems that are computer-operated, the V-Go patch-pump carries fewer warnings. Generally, AID systems, which are the systems with the greatest complexity, have the most warnings and precautions for use. **Table 7** shows all contraindications and select warnings or precautions by device. **Refer to user guides for *all* warnings and precautions for use.**

Unlike other insulin pumps/systems, there are no **contraindications** to using the V-Go[14] or the iLet Bionic Pancreas.[4] Yet, the iLet bionic pancreas carries warnings to avoid use in populations similar to contraindicated populations for other devices. All other devices are contraindicated (or should not be used per the iLet Bionic Pancreas) among people unwilling to maintain contact with a healthcare provider, or who are unable to hear or see device alarms.[4-10,12,13,16] Most devices should not be used by patients who are unwilling or unable to SMBG as recommended.[4-10,12,13,16] The MiniMed 770G/780G carry unique contraindications for use of the Serter (a device for sensor placement), and use of the parts as intended (ie, for subcutaneous delivery of insulin).[6-8] Although not a contraindication, all devices are indicated as insulin delivery systems.[4,9,10,12-14,16] MiniMed 780G is contraindicated for people under 7 years old.[7,8] Some devices used with the Dexcom G6 CGM sensor are contraindicated for use in patients receiving hydroxyurea[9]; nonetheless, this is concern for all systems using a CGM as taking hydroxyurea can falsely elevate sensor readings.[5,6,20,21] Tandem t:slim X2 systems are uniquely contraindicated in people unable to practice adequate diabetes self-care skills,[12,13,16] and in people with insufficient carbohydrate-counting skills (for the Control-IQ only).[13] See Table 6 for the list of contraindications by

device. Omnipod 5 is contraindicated near radiation devices or strong magnets[9]; other pumps also should not be used near radiation or magnetic fields.[4-8,10,12-14,16]

Most insulin pumps/systems share similar warnings/precautions, including but not limited to the following:

- All patients should receive insulin pump/system training before starting to use the system.[4-14] It is important that patients are prepared to use the system, and that a healthcare provider is consulted for programming necessary clinical information for use (eg, selecting basal insulin rates, and/or parameters for automated dosing).
- Patients should carry an emergency kit with back-up supplies, including supplies for the pump/system such as batteries and new infusion sets as applicable, and for manual insulin administration in case of pump/system failure.[4-14]
- Users should only use compatible system components (eg, pump, insulin reservoir, infusion sets, insulin, CGM).[4-14] Generally, this means that users are using disposable components (eg, reservoir, infusion sets) produced by the same manufacturer as the pump. Disposable components should be used as directed, including for the recommended duration of use.[4-6,8-13]
- Electronic devices (ie, all pumps except V-go) performance may be reduced when used within 12 inches of portable radio frequency communications equipment that is unpaired with a system component.[4-13] It is important that users ensure IPS components communicate with each other as intended.

Warnings unique to the Omnipod systems are they should be avoided in people with acrylic adhesive allergies or skin easily damaged by adhesive.[9,10] User manuals for AID systems warn of a minimum and/or maximum daily insulin dosage for use of the automated dosing algorithms. To use MinIMed 770G/780G SmartGuard Auto Mode, users must use between 8 and 250 insulin Units daily.[6-8] Omnipod 5 SmartAdjust technology is not recommended for people who require fewer than 5 insulin Units daily.[9] Tandem t:slim X2 with Control-IQ is not recommended for people who require fewer than 10 insulin Units daily or who weigh less than 55 pounds (25 kg).[13]

All commercial AID systems addressed by this report carry warnings/precautions for a lack of data or recommendation against their use in pregnancy.[4,6-9,13] Omnipod 5 (when using the SmartAdjust AID technology), iLet Bionic Pancreas, and t:slim X2 with Basal- or Control-IQ (when used with Dexcom G6) are specifically recommended to not be used during pregnancy.[4,9,12,13]

Refer to Table 7 for additional select warnings by device.

Table 7. Contraindications and Select Warnings/Precautions[a] per Insulin Pump/System User Guide

V-go[14]
Contraindications: None per the "Instructions for Patient Use"
Key warnings/precautions:

• People with the following characteristics may experience hypoglycemia:
  ○ make frequent adjustments to the basal rate within 24 hours
  ○ require less than 2-Units of insulin bolus at meals
• MRI, X-ray, CT scan (or similar procedure): remove V-go before these procedures.
• Avoid exposure of V-go to direct sunlight or very hot temperatures. V-go should be removed before hot tub or sauna use.

Most Medtronic MiniMed Systems[5-8] (concern specific to a particular insulin pump system, as applicable)
Contraindications:

• Pump therapy is NOT recommended for people:
  ○ who are unwilling or unable to perform at least 4 BG tests daily (*630G, 770G, and 780G with guardian 3 sensor*); or unwilling to perform BG meter readings (*780G with guardian 4 sensor*)
  ○ who are unwilling or unable to keep contact with their HCP
  ○ whose vision or hearing does not recognize pump signals or alarms

Key warnings/precautions:
• Bolus dosing wizard does not account for manual insulin injections; avoid using this feature for a certain period (consult HCP for duration to wait) after a manual insulin injection to prevent hypoglycemia • LGS or PLGS are not intended to prevent or treat low BG; these features only stop insulin delivery. Use BG meter readings (*for 630G only*) and follow HCP instructions for treating low BG (*for 770G, 780G-3, 780G-4*).   ○ LGS usually suspends insulin delivery for a maximum of 2 hours, but it is possible for it to suspend again prolonging the time without insulin and risks of hyperglycemia, or DKA. • Pump should not be used in environments containing flammable anesthetic with air, oxygen, or nitrous oxide (risk of serious injury) • Strong magnetic fields and radiation (eg, MRI, diathermy, X-ray, CT scan) unsafe; remove system components before entering rooms with this equipment. Additionally, do not use pump cases containing magnets to prevent pump malfunction. • SMBG at least 4 times daily; if an abnormal BG reading occurs, ensure insulin is infusing properly (*for 630G and 770G only*) • Pump is safe to use up to 12 ft underwater for 24 hrs (this applies to the pump only) • High temperatures, and some skin products (eg, lotion, sunscreen, bug repellent) can damage the insulin pump. Following use of skin products, hands should be washed before touching the plastic pump case. • Check Daily History for insulin already delivered when restarting insulin delivery after suspending insulin delivery to prevent hyperglycemia; planned boluses prior to insulin delivery suspension will not resume automatically • Reservoir and infusion set should not be used if liquid gets trapped at the reservoir top or inside the tubing connector to prevent errors in insulin delivery • Do not make therapy decisions using SG values; verify SG readings with a SMBG value if SG values are outside of desired range or when feeling symptoms of low or elevated BG (*630G, 770G, and 780G when used in manual mode or with G-3 sensor*)
Additional for Minimed 630G[5]
Key warnings/precautions:
• Sensor-related features (eg, LGS) will not operate properly when the pump is in Airplane Mode, which should be used during a flight (unless the airline allows for operating medical devices during the flight) • Insulin delivery stops if the pump alarms (alarms are specifically for detecting problems with insulin delivery); do not ignore pump alarms
Additional for Minimed 770G and MiniMed 780G[6-8]
Additional contraindications:
• The Serter sensor application device is only for use with Medtronic sensor used with the devices (ie, Guardian Sensor 3 or Guardian 4 sensor, depending on the pump) • System insulin reservoir should not be used to infuse blood or blood products • Infusion sets are indicated for subcutaneous use only
Key warnings/precautions:
• SmartGuard Auto Mode (for automated dosing) should not be used by people: ○ who require <8 or >250 daily insulin Units daily (required for safe operation) • There is a lack of data for use of the MiniMed 770G and 780G systems among people:

[a] *This table is not comprehensive for all labeled warnings/precautions; please refer to the specific user guide for all labeled warnings and precautions.*

[b] *Listed contraindications are for the t:slim X2 insulin pump itself. User guides specific to Basal- and Control-IQ technology do not include any contraindications (listed contraindications are labeled as warnings).*

Abbreviations: CGM, continuous glucose monitor(ing); CT, computerized tomography; DKA, diabetic ketoacidosis; G-3, Guardian Sensor 3; G-4, Guardian Sensor 4; HCP, healthcare professional; kg, kilograms; LGS, low-glucose suspend; MRI, magnetic resonance imaging; PDM, Personal Diabetes Manager; PET, positron emission tomography; PLGS, predicted low-glucose suspend; SG, sensor glucose; SMBG, self-monitor blood glucose; T2D, type 2 diabetes mellitus

Table 7. Contraindications and Select Warnings/Precautions[a] per Insulin Pump/System User Guide

- who are pregnant, have T2D, have impaired renal function, or who are using non-insulin anti-hyperglycemic therapies; a HCP should determine if the benefits from using this system outweigh the potential risks for people with ≥1 of these characteristics
- Sensor is NOT recommended to be used by people:
  - who are critically ill
- Automated insulin dosing mode (Auto Mode) does not account for insulin administered manually; avoid using this feature for a certain period (consult HCP for duration to wait) after a manual insulin injection to prevent hypoglycemia
- For users ages 2-13 (*or ages 7-13 for 780G*): Low SG alerts function is separate from the automated insulin delivery function; users should not rely on SG alert to identify hypoglycemia
- Avoid contact of perfumes, deodorants and disinfects with the infusion sets.
- There is a lack of experience using automated insulin dosing (*770G only*), LGS, or PLGS among people without established insulin pump settings (ie, basal rate, insulin: carbohydrate ratio, insulin sensitivity); users should discuss use of these advanced features with a HCP before using them

Additional for Minimed 780G[7,8]

Additional Contraindications:

- Pump therapy is NOT recommended for people:
  - who are under 7 years old (labeled as a contraindication for the 780G with G-4 only)

Key warnings/precautions:

- There is a lack of data for use in people:
  - who are <7 years old
- SG readings should not be used for treatment decisions when the pump is running manual (non-automated dosing) mode; failure to confirm the SG with a BG reading could result in hypo- or hyperglycemia.
- Perform SMBG meter reading for higher or lower than expected SG readings, when experiencing signs/symptoms of hypo- or hyperglycemia or DKA, and before giving a correction bolus in manual mode
- Monitor SMBG levels ≥ every 12 hours (*780 with G-3 only*); if an abnormal BG reading occurs, ensure insulin is infusing properly
- Pump should be used with a manually programmed basal rate (basal pattern); users should consult a HCP to set a basal pattern
- Monitor for diabetic retinopathy, which is associated with rapid reductions in BG that have occurred with 780G systems (*780G with G-4 only*)

Omnipod DASH[10]

Contraindications:

- Pump therapy is NOT recommended for people:
  - who are unable to follow glucose monitoring recommendations from their HCP
  - who are unwilling or unable to maintain contact with their HCP
  - who are unable to use the device according to instructions

Key warnings/precautions:

- Pump therapy is NOT recommended for people:
  - who are unable to hear device alarms/notifications
  - who have allergies to acrylic adhesives or fragile skin easily damaged by adhesive
- Do not use the device at low atmospheric pressures (eg, at ≥ 10,000 feet) or high oxygen (>25%) environments (eg, hyperbaric chambers). Check BG frequently when flying to mitigate hypoglycemia.
- Check BG as directed by HCP, and contact HCP for symptoms that do not match BG readings
- Advisory alarms for Pod Expired, Low Reservoir, and Auto-off will stop insulin delivery if user does not respond
- Do not expose the Pod to extended direct sunlight. Remove the pod before hot tub or sauna use.
- Do not expose the device to water greater than 25 feet depth for more than 60 minutes
- MRI, X-ray, CT scan (or similar procedure) unsafe. Remove Pod and PDM before these procedures and follow HCP directions for temporary Pod removal.
- Do not expose the Pod to strong detergents or solvents, including sunscreen or bug spray, to prevent Pod or infusion site damage

Omnipod 5[9]

Contraindications:

- Pump therapy is NOT recommended for people:

[a] *This table is not comprehensive for all labeled warnings/precautions; please refer to the specific user guide for all labeled warnings and precautions.*

[b] *Listed contraindications are for the t:slim X2 insulin pump itself. User guides specific to Basal- and Control-IQ technology do not include any contraindications (listed contraindications are labeled as warnings).*

Abbreviations: CGM, continuous glucose monitor(ing); CT, computerized tomography; DKA, diabetic ketoacidosis; G-3, Guardian Sensor 3; G-4, Guardian Sensor 4; HCP, healthcare professional; kg, kilograms; LGS, low-glucose suspend; MRI, magnetic resonance imaging; PDM, Personal Diabetes Manager; PET, positron emission tomography; PLGS, predicted low-glucose suspend; SG, sensor glucose; SMBG, self-monitor blood glucose; T2D, type 2 diabetes mellitus

Table 7. Contraindications and Select Warnings/Precautions[a] per Insulin Pump/System User Guide

- who are unable to follow glucose monitoring recommendations from their HCP
- who are unwilling or unable to maintain contact with their HCP
- who are unable to use the device according to instructions
- who are taking hydroxyurea (falsely increases Dexcom G6 SG values)
- whose vision or hearing does not recognize pump signals or alarms

- Before MRI, X-ray, CT scan and diathermy: remove Pod and controller/phone, placing them outside the procedure area.

Key warnings/precautions:

- Pump therapy is NOT recommended for people:
  - who have allergies to acrylic adhesives or fragile skin easily damaged by adhesive
- SmartAdjust technology (for automated dosing) should NOT be used for patients who are:
  - under 2 years old, pregnant, critically ill, or receiving dialysis (lack of data for use)
  - requiring <5 Units of insulin daily (lack of data for use)
- Do not use the device at low atmospheric pressures (eg, at ≥ 10,000 feet) or high oxygen (>25%) environments (eg, hyperbaric chambers). Check BG frequently when flying and during sudden gravity/atmosphere changes (eg, rollercoaster) to mitigate hypoglycemia.
- Do not expose the Pod to extended direct sunlight. Remove the pod before hot tub or sauna use.
- Do not expose the Pod to water greater than 25 feet depth for more than 60 minutes.
- Do not expose the Pod to strong detergents or solvents, including sunscreen or bug spray, to prevent Pod or infusion site damage
- Avoid administering insulin by means other than the Omnipod 5 while wearing the Omnipod 5 Pod to prevent hypoglycemia
- Monitor BG according HCP instructions, and check BG meter reading if SG values does not match symptoms. Monitor for hypoglycemia when using the Activity feature (an automated mode with a higher target glucose setting); hypoglycemia may still occur.
- User should respond to Hazard Alarms, which indicate insulin delivery has stopped, right away to mitigate hyperglycemia. Pod Expired, Low Pod Insulin and Pod Shut-Off alarms escalate to Hazard Alarms if ignored.
- When using the SmartBolus Calculator for bolus doses, avoid entering BG readings >10 minutes old to prevent improper insulin dose delivery

iLet Bionic Pancreas[4]

Contraindications: None per the patient or health care provider user guides

Key warnings/precautions:

- Use of the iLet Bionic Pancreas pump and Dosing Decision Software is NOT recommended for people:
  - who are unwilling or unable to perform SMBG testing
  - who cannot recognize and/or respond to safety alerts
  - who are taking hydroxyurea (falsely increases SG values)
  - who are less than 6 years old
  - who are pregnant, receiving dialysis, critically ill, or hospitalized
- Device components should not be exposed to X-ray, MRI, CT, or PET scans. Remove device components before radiation therapy, MRI, CT scan, diathermy, or laser surgery.
- Do not expose components to equipment used during procedures for automatic defibrillator or pacemaker placement, cardiac catheterization, or Nuclear stress test.
- Temporarily disconnect tubing before sudden altitude or gravity changes (eg, amusement park rides, unpressurized airplane cabins)
- To maintain functionality, the iLet device should be within 20 unobstructed feet of the CGM transmitter.
- Avoid administering insulin by means other than the iLet device while using the iLet system to prevent hypoglycemia
- Check SMBG before disconnecting or reconnecting to the iLet system; treat BG as directed by HCP when disconnected.
- If the CGM is offline, iLet will switch to BG-run mode, which should only be temporarily used. Automated dosing will stop if CGM is offline for an extended amount of time (ie, 48-72 hours); user should administer treatment by an alternative means until the CGM connection is reestablished.

[a] *This table is not comprehensive for all labeled warnings/precautions; please refer to the specific user guide for all labeled warnings and precautions.*

[b] *Listed contraindications are for the t:slim X2 insulin pump itself. User guides specific to Basal- and Control-IQ technology do not include any contraindications (listed contraindications are labeled as warnings).*

Abbreviations: CGM, continuous glucose monitor(ing); CT, computerized tomography; DKA, diabetic ketoacidosis; G-3, Guardian Sensor 3; G-4, Guardian Sensor 4; HCP, healthcare professional; kg, kilograms; LGS, low-glucose suspend; MRI, magnetic resonance imaging; PDM, Personal Diabetes Manager; PET, positron emission tomography; PLGS, predicted low-glucose suspend; SG, sensor glucose; SMBG, self-monitor blood glucose; T2D, type 2 diabetes mellitus

Table 7. Contraindications and Select Warnings/Precautions[a] per Insulin Pump/System User Guide

t:slim X2 (pump alone or with Basal-IQ/Control-IQ)[12,13,16]
Contraindications[b]:

• Pump therapy is NOT recommended for people:
  ○ who are unable to following BG level testing recommended by their HCP
  ○ who are unable to adequately practice DM self-care skills
  ○ who are unable to unwilling to see their HCP regularly
  ○ who are without adequate hearing/vision to follow pump alerts or instructions, etc.
  ○ who have insufficient carbohydrate-counting skills (*for Control-IQ; this is preferred according to t:Slim X2 ± Basal-IQ*)

Key warnings/precautions:

• *Pump therapy* with Basal-IQ or Control-IQ is NOT recommended for people[12,13]:
  ○ who are unable to use system components according to instructions (*per Basal-IQ only*)
  ○ who have conditions or circumstances that would place them at risk when using this device or its components by HCP judgement
  ○ who have uncontrolled thyroid disease, renal failure, hemophilia or major bleeding disorder, unstable CVD
• *Dexcom G6* CGM, used with Basal-IQ or Control-IQ, should NOT be used by people[12,13]:
  ○ who are pregnant, receiving dialysis, or critically ill (lack of data, sensor readings may be inaccurate)
  ○ who are taking hydroxyurea (falsely elevates sensor readings); persons taking this mediation should use a BGM for treatment decisions, and consult their HCP for alterative monitoring options
• MRI, X-ray (including full body screening at airports), Positron Emission Tomography (PET), and other radiation unsafe. Pump, transmitter, and sensor should be removed and left outside the MRI room
• Unsafe for several cardiac procedures (pacemaker/automatic implantable cardioverter defibrillator, cardiac catheterization, nuclear stress test). Pump, transmitter, and sensor should be removed and left outside the room before these procedures
• Do not use the insulin pump in areas with flammable anesthetics or explosive gases to prevent an explosion
• Wear the device cautiously during laser surgery (some lasers trigger system alarms) and consult a HCP about wearing the device during general anesthesia
• Avoid submersion of the pump into liquid of >3 ft for more than 30 minutes. Do not wear pump in hot tubs or saunas
• Temporarily disconnect tubing before sudden altitude or gravity changes (eg, amusement park rides, unpressurized airplane cabins)
• Check BG using a meter following 1,000 ft elevation changes (delivery accuracy is affected).

Additional for t:slim X2 with Basal-IQ[12]
Key warnings/precautions:
• Basal-IQ technology has not been studied in people: ○ who are pregnant, receiving dialysis, or critically ill • Basal-IQ technology will be unavailable "…if a sensor session is ended, either automatically or manually…" • Basal-IQ technology is not a replacement for active diabetes management and will not prevent all hypoglycemia episodes. Low BG is not treated by Basal-IQ technology. • Do not administer insulin by means other than this device while using the pump to prevent hypoglycemia • To maintain functionality, the pump should be within 20 unobstructed feet of the CGM transmitter. If CGM is out of range, Basal-IQ will not suspend insulin delivery, and if insulin delivery was suspended, insulin will resume at the set rate in the user's profile. User may set the "Out of range" alert to be notified when the CGM communicated is interrupted. • Do not cover vent holes (6 holes) at the back of the insulin pump to prevent errors in insulin delivery • The insulin pump should be used for therapy decisions if smartphone controller is either incompatible, lost, or damaged, or disconnected from Bluetooth Check SMBG if symptoms do not match SG readings.
Additional for t:slim X2 with Control-IQ[13]
Key warnings/precautions:

• Control-IQ technology should NOT be used for people:
  ○ under age 6
  ○ who require <10 insulin Units daily
  ○ who weigh <55 pounds (25 kg)

[a] *This table is not comprehensive for all labeled warnings/precautions; please refer to the specific user guide for all labeled warnings and precautions.*

[b] *Listed contraindications are for the t:slim X2 insulin pump itself. User guides specific to Basal- and Control-IQ technology do not include any contraindications (listed contraindications are labeled as warnings).*

Abbreviations: CGM, continuous glucose monitor(ing); CT, computerized tomography; DKA, diabetic ketoacidosis; G-3, Guardian Sensor 3; G-4, Guardian Sensor 4; HCP, healthcare professional; kg, kilograms; LGS, low-glucose suspend; MRI, magnetic resonance imaging; PDM, Personal Diabetes Manager; PET, positron emission tomography; PLGS, predicted low-glucose suspend; SG, sensor glucose; SMBG, self-monitor blood glucose; T2D, type 2 diabetes mellitus

Table 7. Contraindications and Select Warnings/Precautions[a] per Insulin Pump/System User Guide

○ who require hydroxyurea therapy • Control-IQ technology has not been studied in people: ○ who are pregnant, receiving dialysis, or critically ill • To maintain functionality, the pump should be within 20 unobstructed feet of the CGM transmitter • If a CGM reading is not received for 20 minutes while using Control-IQ technology, basal insulin delivery is restricted to 3 Units/hr. Insulin delivery is also restricted to 3 Units/hr during sensor start-up; Control-IQ should be disabled when starting the sensor if a higher insulin delivery rate is required. User may set the "Out of range" alert to be notified when the CGM communicated is interrupted. • Control-IQ will stop adjusting insulin "If a sensor session is ended, either automatically or manually…" • Suspend insulin delivery by Control-IQ if the pump will be removed for ≥ 30 minutes • Do not administer insulin by means other than this device while using the pump to prevent hypoglycemia • Do not cover vent holes (6 holes) at the back of the insulin pump to prevent errors in insulin delivery • The insulin pump should be used for therapy decisions if smartphone controller is either incompatible, lost, damaged, or disconnected from Bluetooth • Check BG if symptoms do not match SG readings • Low BG is not treated by Control-IQ technology; ensure BG is managed according to directions from a HCP

[a] This table is not comprehensive for all labeled warnings/precautions; please refer to the specific user guide for all labeled warnings and precautions.

[b] Listed contraindications are for the t:slim X2 insulin pump itself. User guides specific to Basal- and Control-IQ technology do not include any contraindications (listed contraindications are labeled as warnings).

Abbreviations: CGM, continuous glucose monitor(ing); CT, computerized tomography; DKA, diabetic ketoacidosis; G-3, Guardian Sensor 3; G-4, Guardian Sensor 4; HCP, healthcare professional; kg, kilograms; LGS, low-glucose suspend; MRI, magnetic resonance imaging; PDM, Personal Diabetes Manager; PET, positron emission tomography; PLGS, predicted low-glucose suspend; SG, sensor glucose; SMBG, self-monitor blood glucose; T2D, type 2 diabetes mellitus

8.2 Adverse Events and Risks of Insulin Pumps/Systems

Insulin pumps/systems carry the risk for similar adverse events. Refer to **Appendix H** for a summary of adverse events from clinical trials per pump user guides, and **Appendix I** for details about the safety concerns listed below. Blocked insulin delivery (ie, occlusion) can prevent insulin delivery leading to hyperglycemia. **Appendix J** summarizes average time to occlusion alarms for all electronic insulin pumps.

Safety concerns during use of insulin pumps/systems[4-13]:

- Hypoglycemia, hyperglycemia, and associated sequelae (eg, DKA, seizures, coma, death)
- Infection, skin irritation, bleeding, bruising, pain, rash, or other reactions at the insulin infusion or CGM sensor sites
- Sensor (wire) fracture or infusion set cannula fracture
- Small part choking hazard for young children

Insulin pumps also vary slightly by reported insulin delivery accuracy as shown in **Appendix K**.

9.0 PHARMACOKINETICS

Most insulin pumps are compatible with RA U-100 insulins, which have a similar onset of effect and duration of action.[111] Ultra-rapid U-100 insulins (ie, faster-acting insulin aspart [Fiasp] and insulin lispro-aabc [Lyumjev]) are absorbed faster than RA insulins resulting in a slightly faster onset of effect (eg, by ~5-10 minutes).[112] Ultra-rapid insulins may lead to improved post-prandial glucose control compared to their rapid-acting counterparts,[112] as was demonstrated in at least 1 clinical trial of adults with T1D using non-automated insulin pumps.[113] Use of ultra-rapid insulins by closed-loop AID systems might improve the ability of these systems to address post-prandial glycemia while minimizing hypoglycemia compared to RA insulin; however, clinical evidence of this is limited and inconsistent.[114] Among insulin pumps addressed by this report, only the Omnipod DASH, Omnipod Eros, and iLet Bionic Pancreas are cleared for use with an ultra-rapid acting insulin[10,11]; the iLet Bionic Pancreas is narrowly cleared for use with Fiasp pre-filled cartridges, which are not yet available in the US.[67]

10.0 CONTINUOUS GLUCOSE MONITORING (CGM) DRUG INTERACTIONS

Some medications interfere with sensor glucose readings from CGM devices, affecting use of SAP or AID systems.

- Dexcom G6[20]:
  - **Hydroxyurea** falsely elevates SG readings, which could result in hypoglycemia when used with automated insulin delivery systems. Users should not rely on Dexcom G6 SG values when taking hydroxyurea.
  - **Acetaminophen (at doses >1 gram every 6 hours**): Large doses of acetaminophen may falsely elevate SG readings. Dexcom G6 SG values should not be used for treatment decisions if the user takes a large dose of acetaminophen.

- Guardian sensor 3 and Guardian sensor 4:
  - **Hydroxyurea** falsely elevates SG readings, which may result in hypoglycemia when used with automated insulin delivery systems. Users should not rely on SG values when taking hydroxyurea.[7,8] Information about the interaction with hydroxyurea was only provided in the MiniMed 780G user guide; however, the interaction likely applies when using the Guardian sensor 3 with any pump.
  - **Acetaminophen** may falsely elevate SG readings, depending on the amount taken (MiniMed insulin pump user guides do not specify a safe amount).[5-8] SG readings should not be used for treatment decisions (when used with the MiniMed 780G[7,8]; SG readings are not recommended for treatment decisions when used with the Minimed 630G and 770G[5,6]) after taking acetaminophen. Medtronic recommends that users program a temporary SG target for up to 8 hours when running SmartGuard mode after taking acetaminophen when using MiniMed 780G.[7,8] For the 770G, it's recommended that users consider switching to manual mode after taking acetaminophen.[6]

REFERENCES

1. Blonde L, Umpierrez GE, Reddy SS, et al. American Association of Clinical Endocrinology Clinical Practice Guideline: Developing a Diabetes Mellitus Comprehensive Care Plan-2022 Update. *Endocr Pract*. 2022;28(10):923-1049. doi:10.1016/j.eprac.2022.08.002

2. ElSayed NA, Aleppo G, Aroda VR, et al. 9. Pharmacologic Approaches to Glycemic Treatment: Standards of Care in Diabetes-2023. *Diabetes Care*. 2023;46(Supplement_1):S140-s157. doi:10.2337/dc23-S009

3. Berget C, Messer LH, Forlenza GP. A Clinical Overview of Insulin Pump Therapy for the Management of Diabetes: Past, Present, and Future of Intensive Therapy. *Diabetes Spectr*. 2019;32(3):194-204. doi:10.2337/ds18-0091

4. iLet Bionic Pancreas. User Guide. Beta Bionics; 2023. Accessed June 27, 2023. Available at https://www.betabionics.com/wp-content/uploads/LA000039_J-iLet-User-Guide-LAUNCH.pdf

5. MiniMed 630G. System User Guide. Medtronic; 2017. Accessed January 12, 2023. Available at https://www.medtronicdiabetes.com/sites/default/files/library/download-library/user-guides/MiniMed%20630G%20System%20User%20Guide%20-%2020-Mar-2018.pdf

6. MiniMed 770G. System User Guide. Medtronic; 2020. Accessed January 11, 2023. Available at https://www.medtronicdiabetes.com/sites/default/files/library/download-library/user-guides/MiniMed_770G_System_User_Guide.pdf

7. MiniMed 780G with the Guardian Sensor(3). User Guide. Medtronic; 2023. Accessed June 27, 2023. Available at https://www.medtronicdiabetes.com/sites/default/files/library/download-library/user-guides/MiniMed-780G-system-user-guide-with-Guardian-sensor-3.pdf

8. Minimed 780G with the Guardian 4 Sensor. User Guide. Medtronic; 2023. Accessed June 27, 2023. Available at https://www.medtronicdiabetes.com/sites/default/files/library/download-library/user-guides/MiniMed-780G-system-user-guide-with-Guardian-4-sensor.pdf

9. Omnipod 5. User Guide. Insulet Corporation; 2022. Accessed June 29, 2023. Available at https://www.omnipod.com/sites/default/files/Omnipod-5_User-guide.pdf

10. Omnipod DASH Insulin Management System. User Guide. Insulet Corporation; 2021. Accessed January 17, 2023. Available at https://www.omnipod.com/sites/default/files/2021-04/Omnipod-DASH_User-Guide_English.pdf

11. Omnipod Insulin Management System, . User Guide. Insulet Corporation; 2021. Accessed January 17, 2023. Available at https://www.omnipod.com/sites/default/files/2021-04/Omnipod-System_User-Guide_English.pdf

12. t:slim X2 Insulin Pump with Basal-IQ technology. User Guide. Tandem Diabetes Care; 2023. Accessed July 6, 2023. Available at https://www.tandemdiabetes.com/docs/default-source/product-documents/t-slim-x2-insulin-pump/aw-1007707_a_user-guide-mobile-bolus-tslim-x2-basal-iq-6-6-mgdl-artwork_web.pdf?sfvrsn=9feae2d7_18

13. t: slim X2 Insulin pump with Control-IQ technology. User Guide. Tandem Diabetes Care; Accessed January 13, 2023. Available at https://www.tandemdiabetes.com/docs/default-source/product-documents/t-slim-x2-insulin-pump/aw-1007704_b-user-guide-mobile-bolus-tslim-x2-control-iq-7-6-mgdl-artwork-web.pdf?sfvrsn=71e5e2d7_32

14. V-Go Wearable Insulin Delivery. Instructions for Patient Use. MannKind Corporation; 2022. Accessed April 25, 2023. Available at https://www.go-vgo.com/hcp

15. Danatech diabetes technology. Omnipod DASH from Insulet. Omnipod DASH. Diabeteseducator.org; 2022. Accessed July 17, 2023. Available at https://www.diabeteseducator.org/danatech/insulin-pumps/find-and-compare-insulin-pumps/product-detail/omnipod-dash

16. t:Slim X2 Insulin Pump. User Guide. Tandem Diabetes Care; Accessed May 1, 2023. Available at https://www.tandemdiabetes.com/docs/default-source/product-documents/tslim-insulin-pump/updated-t-slim-user-guide.pdf?sfvrsn=fd4d3bd7_22

17. Pickup JC. Insulin-pump therapy for type 1 diabetes mellitus. *N Engl J Med*. 2012;366(17):1616-1624. doi:10.1056/NEJMct1113948

18. Sherr JL, Heinemann L, Fleming GA, et al. Automated Insulin Delivery: Benefits, Challenges, and Recommendations. A Consensus Report of the Joint Diabetes Technology Working Group of the European Association for the Study of Diabetes and the American Diabetes Association. *Diabetes Care*. 2022;45(12):3058-3074. doi:10.2337/dci22-0018

19. Phillip M, Nimri R, Bergenstal RM, et al. Consensus Recommendations for the Use of Automated Insulin Delivery (AID) Technologies in Clinical Practice. *Endocrine reviews*. 2023;44(2):254-280. doi:10.1210/endrev/bnac022

20. Dexcom G6 Continous Glucose Monitoring System. User Guide. Dexcom I; Accessed January 23, 2023. Available at https://s3-us-west-2.amazonaws.com/dexcompdf/G6-CGM-Users-Guide.pdf

21. Guardian 4. User Guide. Medtronic; 2023. Accessed August 7, 2023. Available at https://www.medtronicdiabetes.com/sites/default/files/library/download-library/user-guides/Guardian_4_sensor_user_guide.pdf

22. ElSayed NA, Aleppo G, Aroda VR, et al. 7. Diabetes Technology: Standards of Care in Diabetes-2023. *Diabetes Care*. 2023;46(Supplement_1):S111-s127. doi:10.2337/dc23-S007

23. Grunberger G, Sherr J, Allende M, et al. American Association of Clinical Endocrinology Clinical Practice Guideline: The Use of Advanced Technology in the Management of Persons With Diabetes Mellitus. *Endocr Pract*. 2021;27(6):505-537. doi:10.1016/j.eprac.2021.04.008

24. Sherr JL, Schoelwer M, Dos Santos TJ, et al. ISPAD Clinical Practice Consensus Guidelines 2022: Diabetes technologies: Insulin delivery. *Pediatr Diabetes*. 2022;23(8):1406-1431. doi:10.1111/pedi.13421

25. Sundberg F, deBeaufort C, Krogvold L, et al. ISPAD Clinical Practice Consensus Guidelines 2022: Managing diabetes in preschoolers. *Pediatr Diabetes*. 2022;23(8):1496-1511. doi:10.1111/pedi.13427

26. Forlenza GP, Li Z, Buckingham BA, 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):2155-2161. doi:10.2337/dc18-0771

27. Brown SA, Beck RW, Raghinaru D, et al. Glycemic Outcomes of Use of CLC Versus PLGS in Type 1 Diabetes: A Randomized Controlled Trial. *Diabetes Care*. 2020;43(8):1822-1828. doi:10.2337/dc20-0124

28. Bergenstal RM, Nimri R, Beck RW, 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):208-219. doi:10.1016/s0140-6736(20)32514-9

29. Kulzer B, Freckmann G, Heinemann L, Schnell O, Hinzmann R, Ziegler R. Patch Pumps: What are the advantages for people with diabetes? *Diabetes Res Clin Pract*. 2022;187:109858. doi:10.1016/j.diabres.2022.109858

30. Heinemann L, Waldenmaier D, Kulzer B, Ziegler R, Ginsberg B, Freckmann G. Patch Pumps: Are They All the Same? *J Diabetes Sci Technol*. 2019;13(1):34-40. doi:10.1177/1932296818795150

31. Templer S. Closed-Loop Insulin Delivery Systems: Past, Present, and Future Directions. *Frontiers in Endocrinology*. 2022;13doi:10.3389/fendo.2022.919942 https://www.frontiersin.org/articles/10.3389/fendo.2022.919942

32. Moon SJ, Jung I, Park CY. Current Advances of Artificial Pancreas Systems: A Comprehensive Review of the Clinical Evidence. *Diabetes Metab J*. 2021;45(6):813-839. doi:10.4093/dmj.2021.0177

33. Phillip M, Nimri R, Bergenstal RM, et al. Consensus Recommendations for the Use of Automated Insulin Delivery Technologies in Clinical Practice. *Endocrine reviews*. 2023;44(2):254-280. doi:https://dx.doi.org/10.1210/endrev/bnac022

34. Insulet Corporation. Pharmacy Coverage. Omnipod.com. 2023. Accessed August 7, 2023. Available at https://www.omnipod.com/is-omnipod-right-for-me/coverage/pharmacy

35. MannKind Corporation. Basal and Bolus Insulin Delivery with V-Go Requires Only 2 Co-Pays. Go-Vgo.com. 2023. Accessed August 14, 2023. Available at https://www.go-vgo.com/prescribing/

36. Utah Department of Health & Human Services. *Utah Medicaid Preferred Drug List - Effective August 1, 2023*. 2023: 113 pages. Last Updated August 1, 2023. Accessed August 8, 2023. Available at https://medicaid.utah.gov/pharmacy/preferred-drug-list/

37. Tandem Diabetes Care. t:slim X2 insulin pump and Dexcom G7. TandemDiabetes.com. 2023. Accessed August 8, 2023. Available at https://www.tandemdiabetes.com/support/company-update/dexcom-g7

38. Insulet Corporation. Omnipod 5 FAQs: Dexcom G7 Integration. Omnipod.com. 2023. Accessed August 8, 2023. Available at https://www.omnipod.com/current-podders/resources/omnipod-5/faqs/dexcom-g7

39. Braune K, Lal RA, Petruželková L, 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. doi:10.1016/s2213-8587(21)00267-9

40. Insulet Corporation. Discontiniation of the Omnipod Insulin Management System. Omnipod.com. 2023. Accessed July 26, 2023. Available at https://www.omnipod.com/discontinuation

41. McMaster University Health Information Research Unit. Search filters for Medline in Ovid syntax and the PubMed translation. hiru.mcmaster.ca; 2016. Last Updated February 9, 2016. Accessed November 7, 2022. Available at https://hiru.mcmaster.ca/hiru/hiru_hedges_medline_strategies.aspx

42. Rosenquist KJ, Fox CS. Mortality Trends in Type 2 Diabetes. In: Cowie CC, Casagrande SS, Menke A, et al, eds. National Institute of Diabetes and Digestive and Kidney Diseases (US); 2018.

43. Secrest AM, Washington RE, Orchard TJ. Mortality in Type 1 Diabetes. In: Cowie CC, Casagrande SS, Menke A, et al, eds. National Institute of Diabetes and Digestive and Kidney Diseases (US); 2018.

44. Centers for Disease Control and Prevention. Prevalence of Both Diagnosed and Undiagnosed Diabetes. CDC.gov. 2022. Last Updated September 30, 2022. Accessed January 10, 2023. Available at https://www.cdc.gov/diabetes/data/statistics-report/diagnosed-undiagnosed-diabetes.html

45. ElSayed NA, Aleppo G, Aroda VR, et al. 2. Classification and Diagnosis of Diabetes: Standards of Care in Diabetes-2023. *Diabetes Care*. 2023;46(Supplement_1):S19-s40. doi:10.2337/dc23-S002

46. Imperatore G, Mayer-Davis EJ, Orchard TJ, Zhong VW. Prevalence and Incidence of Type 1 Diabetes Among Children and Adults in the United States and Comparison With Non-U.S. Countries. In: Cowie CC, Casagrande SS, Menke A, et al, eds. National Institute of Diabetes and Digestive and Kidney Diseases (US); 2018.

47. McCullough ML, Wan N, Pezzolesi MG, et al. Type 1 Diabetes incidence among youth in Utah: A geographical analysis. *Soc Sci Med*. 2021;278:113952. doi:10.1016/j.socscimed.2021.113952

48. DiMeglio LA, Evans-Molina C, Oram RA. Type 1 diabetes. *Lancet*. 2018;391(10138):2449-2462. doi:10.1016/s0140-6736(18)31320-5

49. Cowie CC, Casagrande SS, Geiss LS. Prevalence and Incidence of Type 2 Diabetes and Prediabetes. In: Cowie CC, Casagrande SS, Menke A, et al, eds. National Institute of Diabetes and Digestive and Kidney Diseases (US); 2018.

50. Centers for Disease Control and Prevention. Rates of New Diagnosed Cases of Type 1 and Type 2 Diabetes Continue to Rise Among Children, Teens. CDC.gov. 2020. Last Updated February 11, 2020. Accessed January 10, 2023. Available at https://www.cdc.gov/diabetes/research/reports/children-diabetes-rates-rise.html

51. ElSayed NA, Aleppo G, Aroda VR, et al. 6. Glycemic Targets: Standards of Care in Diabetes-2023. *Diabetes Care*. 2023;46(Supplement_1):S97-s110. doi:10.2337/dc23-S006

52. Ekanayake P, Edelman S. Identifying patients with type 2 diabetes who might benefit from insulin pump therapy: Literature review, clinical opportunities, potential benefits and challenges. *Diabetes Obes Metab*. 2023;25 Suppl 2:3-20. doi:10.1111/dom.15059

53. ElSayed NA, Aleppo G, Aroda VR, et al. 15. Management of Diabetes in Pregnancy: Standards of Care in Diabetes-2023. *Diabetes Care*. 2023;46(Suppl 1):S254-s266. doi:10.2337/dc23-S015

54. Battelino T, Danne T, Bergenstal RM, et al. Clinical Targets for Continuous Glucose Monitoring Data Interpretation: Recommendations From the International Consensus on Time in Range. *Diabetes Care*. 2019;42(8):1593-1603. doi:10.2337/dci19-0028

55. ElSayed NA, Aleppo G, Aroda VR, et al. 14. Children and Adolescents: Standards of Care in Diabetes-2023. *Diabetes Care*. 2023;46(Supplement_1):S230-s253. doi:10.2337/dc23-S014

56. Vigersky RA, McMahon C. The Relationship of Hemoglobin A1C to Time-in-Range in Patients with Diabetes. *Diabetes Technol Ther*. 2019;21(2):81-85. doi:10.1089/dia.2018.0310

57. DiabetesWisePro. Device Library. Pro.DiabetesWise.org. Accessed January 23, 2023. Available at https://pro.diabeteswise.org/#/en/devices/device-library

58. DiabetesWisePro. Medtronic 780G. Pro.DiabetesWise.org; Accessed August 7, 2023. Available at https://pro.diabeteswise.org/devices/device-library/automated-systems/overview/overall/device:medtronic-780g

59. DiabetesWisePro. Beta Bionics ILet. Accessed August 7, 2023. Available at https://pro.diabeteswise.org/devices/device-library/automated-systems/overview/overall/device:beta-bionics-ilet

60. DiabetesWisePro. Medtronic 770G. Pro.DiabetesWise.org; Accessed August 7, 2023. Available at https://pro.diabeteswise.org/devices/device-library/automated-systems/overview/overall/device:medtronic-770g

61. Medtronic. Medtronic Extended Infusion Set and Extended Reservoir. Medtronicdiabetes.com. 2023. Accessed January 19, 2023. Available at https://www.medtronicdiabetes.com/products/infusion-sets/extended-infusion-set

62. Medtronic. Comparing Medtronic infusion sets. Medtronicdiabetes.com. 2023. Accessed May 2, 2023. Available at https://www.medtronicdiabetes.com/customer-support/infusion-set-support/compare-set

63. Tandem Diabetes Care. Insulin Infusion Sets to Meet your Unique Needs. TandemDiabetes.com. 2023. Accessed July 18, 2023. Available at https://www.tandemdiabetes.com/products/infusion-sets

64. Berget C, Sherr JL, DeSalvo DJ, et al. Clinical Implementation of the Omnipod 5 Automated Insulin Delivery System: Key Considerations for Training and Onboarding People With Diabetes. *Clin Diabetes*. 2022;40(2):168-184. doi:10.2337/cd21-0083

65. Drug Development and Delivery. Beta Bionics Receives IDE Approval from the FDA to Begin a Home-Use Clinical Trial Testing the New Bionic Pancreas System. Drug-Dev.com. Accessed August 3, 2023. Available at https://drug-dev.com/beta-bionics-receives-ide-approval-from-the-fda-to-begin-a-home-use-clinical-trial-testing-the-a-new-bionic-pancreas-system

66. Juvenile Diabetes Cure Alliance. FDA approves Beta Bionics' insulin only device. What about dual-hormone? TheJDCS.org. 2023. Last Updated June 5, 2023. Accessed August 3, 2023. Available at https://www.thejdca.org/article/2023/06/05/fda-approves-beta-bionics-insulin-only-device-what-about-dual-hormone-

67. Beta Bionics Announces FDA Clearance for the use of a Prefilled Insulin Cartridge with the iLet Bionic Pancreas. Press release. BetaBionics.com. June 22, 2023, 2023. Accessed August 30, 2023. Available at https://www.betabionics.com/beta-bionics-announces-fda-clearance-for-the-use-of-a-prefilled-insulin-cartridge-with-the-ilet-bionic-pancreas/

68. Care TD. Infusion sets. Select from a variety of options to meet your unique needs. . TandemDiabetes.com. 2023. Accessed January 23, 2023. Available at https://www.tandemdiabetes.com/products/infusion-sets

69. Medtronic. Infusion Sets. Medtronic.com/. 2022. Last Updated November 2022. Accessed January 23, 2023. Available at https://www.medtronic.com/us-en/healthcare-professionals/products/diabetes/infusion-sets.html

70. Care TD. T:connect mobile app. Bolus directly from your smartphone. TandemDiabetes.com. 2023. Accessed August 11, 2023. Available at https://www.tandemdiabetes.com/products/software-apps/tconnect-mobile

71. Tidepool. Groudbreaking: Tidepool Loop receives FDA clearance. Tidepool.org. 2023. Accessed June 28, 2023. Available at https://www.tidepool.org/tidepool-loop

72. Insulet Corporation. Omnipod DASH System - Frequently Asked Questions. Omnipod.com. 2023. Accessed July 3, 2023. Available at https://www.omnipod.com/current-podders/resources/omnipod-dash/faq

73. Frequently Asked Questions Carelink Personal Software. Frequently Asked Questions Fact Sheet. Medtronic. 2019. Accessed July 26, 2023. Available at https://www.medtronicdiabetes.com/sites/default/files/library/download-library/workbooks/CareLink-Personal-Software-FAQ.pdf

74. Tandem Diabetes Care. How to Update your Pump Software. TandemDiabetes.com. 2023. Accessed July 3, 2023. Available at https://www.tandemdiabetes.com/support/software-updates/how-to-update

75. Tandem Diabetes Care. I already have Basal-IQ software on my pump. Once I update my software to the Control-IQ, will i still have access to the Basal-IQ feature? TandemDiabetes.com. 2022. Accessed July 26, 2023. Available at https://support.tandemdiabetes.com/hc/en-us/articles/1500011451201-I-already-have-Basal-IQ-software-on-my-pump-Once-I-update-my-software-to-Control-IQ-will-I-still-have-access-to-the-Basal-IQ-feature-

76. Moser O, Riddell MC, Eckstein ML, et al. Glucose management for exercise using continuous glucose monitoring (CGM) and intermittently scanned CGM (isCGM) systems in type 1 diabetes: position statement of the European Association for the Study of Diabetes (EASD) and of the International Society for Pediatric and Adolescent Diabetes (ISPAD) endorsed by JDRF and supported by the American Diabetes Association (ADA). *Diabetologia*. 2020;63(12):2501-2520. doi:10.1007/s00125-020-05263-9

77. Eckstein ML, Weilguni B, Tauschmann M, et al. Time in Range for Closed-Loop Systems versus Standard of Care during Physical Exercise in People with Type 1 Diabetes: A Systematic Review and Meta-Analysis. *J Clin Med*. 2021;10(11)doi:10.3390/jcm10112445

78. Device Comparison Chart. Fact sheet. 2023. Accessed July 20, 2023. Available at https://www.pantherprogram.org/_files/ugd/71a2f0_619d8ceb4c2c4b0bb8feb7cce3eeb6ba.pdf

79. Corporation I. Simply Life with Omnipod 5. Omnipod.com. 2023. Accessed July 25, 2023. Available at https://www.omnipod.com/what-is-omnipod/omnipod-5

80. Nwokolo M, Hovorka R. The Artificial Pancreas and Type 1 Diabetes. *J Clin Endocrinol Metab*. 2023;108(7):1614-1623. doi:10.1210/clinem/dgad068

81. ADCES Staff and Subject Matter Faculty. Automated Insulin Delivery, a Quick Overview. DiabetesEducator.org. 2023. Last Updated January 2023. Accessed January 18, 2023. Available at https://www.diabeteseducator.org/danatech/insulin-pumps/insulin-pumps-101/automated-insulin-devices-faq

82. Tandem Diabetes Care. Is the t:slim X2 insulin pump waterproof? Support.tandemdiabetes.com. Accessed January 18, 2023. Available at https://support.tandemdiabetes.com/hc/en-us/articles/1500011481601-Is-the-t-slim-X2-insulin-pump-waterproof-#

83. iLet Bionic Pancreas System. Guide for Health Care Providers. Beta Bionics; 2023. Accessed June 27, 2023. Available at https://www.betabionics.com/wp-content/uploads/LA000079-A-iLet-Bionic-Pancreas-System-HCP-Guide-v1.0-3.

84. Medtronic. Our best answer: Can I go swimming with my pump? Medtronicdiabetes.com. Accessed January 18, 2023. Available at https://www.medtronicdiabetes.com/search?t=8&cq=Can%20I%20go%20swimming%20with%20my%20pump?

85. Medtronic. MiniMed 630G Insulin Pump System. MedtronicDiabtes.com. 2023. Accessed August 17, 2023. Available at https://www.medtronicdiabetes.com/products/minimed-630g-insulin-pump-system

86. Insulet Corporation. Omnipod 5 App Compatible Smartphones. Omnipod.com. 2023. Accessed July 17, 2023. Available at https://www.omnipod.com/current-podders/resources/omnipod-5/device-compatibility

87. Medtronic. *Frequently asked questions CareLink system software*. 2022: 8 pages. Accessed August 22, 2023. Available at https://carelink.medtronic.com/crs/pow/3.9/media/FAQ-CLS-US-EN-002.pdf

88. Insulet Corporation. Insulet Provided Glooko. Omnipod.com. 2023. Accessed July 17, 2023. Available at https://www.omnipod.com/hcp/clinical-resources/insulet-provided-glooko

89. Tandem Diabetes Care. Doctor's Office Reports. 2022. Accessed July 18, 2023. Available at https://support.tandemdiabetes.com/hc/en-us/articles/360039443193-Doctor-s-Office-Reports

90. Medtronic. The MiniMed 770G System. Medtronicdiabetes.com. 2023. Accessed May 2, 2023. Available at https://www.medtronicdiabetes.com/products/minimed-770g-insulin-pump-system

91. Danatech diabetes technology. MiniMed 780G System from Medtronic. Diabetes educator.org. 2023. Accessed July 14, 2023. Available at https://www.diabeteseducator.org/danatech/insulin-pumps/find-and-compare-insulin-pumps/product-detail/minimed-780g

92. Insulet Corporation. Omnipod 5 FAQs: Apps and Phone Control. Omnipod.com. 2023. Accessed August 30, 2023. Available at https://www.omnipod.com/current-podders/resources/omnipod-5/faqs/phone-control-mobile-apps

93. Medtronic. MiniMed 780G system Insulin pump technology. Medtronic.com/. 2023. Accessed August 30, 2023. Available at https://www.medtronic.com/us-en/healthcare-

professionals/products/diabetes/insulin-pump-systems/minimed-780g.html?cmpid=DSP_MIX_NA_consumer780g

94. Panther Program. *Device Comparison Chart*. Panther Program; 2022: 5 pages. Last Updated August 2022. Accessed January 12, 2023. Available at https://www.pantherprogram.org/_files/ugd/29eb34_ea40831c6cc54760bcfd10a554cdd5aa.pdf

95. Pease A, Lo C, Earnest A, Kiriakova V, Liew D, Zoungas S. Time in Range for Multiple Technologies in Type 1 Diabetes: A Systematic Review and Network Meta-analysis. *Diabetes Care*. 2020;43(8):1967-1975. doi:10.2337/dc19-1785

96. Pease A, Lo C, Earnest A, Kiriakova V, Liew D, Zoungas S. The Efficacy of Technology in Type 1 Diabetes: A Systematic Review, Network Meta-analysis, and Narrative Synthesis. *Diabetes Technol Ther*. 2020;22(5):411-421. doi:10.1089/dia.2019.0417

97. Griffin TP, Gallen G, Hartnell S, et al. UK's Association of British Clinical Diabetologist's Diabetes Technology Network (ABCD-DTN): Best practice guide for hybrid closed-loop therapy. *Diabet Med*. 2023;40(7):e15078. doi:10.1111/dme.15078

98. U.S. Food & Drug Administration. Class 2 Device Recall Medtronic MiniMed 600 Series. FDA.gov. 2022. Accessed May 2, 2023. Available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfres/res.cfm?id=196205

99. Medtronic. Urgent Medical Device Correction Medtronicdiabetes.com. 2022. Last Updated September 2022. Accessed May 2, 2023. Available at https://www.medtronicdiabetes.com/customer-support/product-and-service-updates/notice19-letter

100. U.S. Food & Drug Administration. Cybersecurity in Medical Devices Frequently Asked Question. FDA.gov. 2023. Last Updated March 29, 2023. Accessed May 2, 2023. Available at https://www.fda.gov/medical-devices/digital-health-center-excellence/cybersecurity-medical-devices-frequently-asked-questions-faqs

101. Dekker P, Aanstoot HJ, Sas T, et al. Prevalence of and Reasons for Discontinuation of Continuous Subcutaneous Insulin Infusion in People with Type 1 Diabetes: A Systematic Review. *Diabetes Technol Ther*. 2023;25(8):559-570. doi:10.1089/dia.2023.0038

102. Insulet Corporation. Omnipod 5 FAQs: About Omnipod 5. Omnipod.com. 2023. Accessed July 3, 2023. Available at https://www.omnipod.com/current-podders/resources/omnipod-5/faqs/about-omnipod-5

103. Medtronic. How to Remotely Upgrade the Minimed 780G System. Medtronicdiabetes.com. 2023. Last Updated May 17, 2023. Accessed July 3, 2023. Available at https://www.medtronicdiabetes.com/loop-blog/upgrade-to-the-minimed-780g-system/

104. Medtronic. Simple upgrade. Medtronicdiabetes.com. 2023. Accessed July 3, 2023. Available at https://www.medtronicdiabetes.com/products/device-upgrading

105. McCall AL, Lieb DC, Gianchandani R, et al. Management of Individuals With Diabetes at High Risk for Hypoglycemia: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab*. 2023;108(3):529-562. doi:10.1210/clinem/dgac596

106. ElSayed NA, Aleppo G, Aroda VR, et al. 13. Older Adults: Standards of Care in Diabetes-2023. *Diabetes Care*. 2023;46(Supplement_1):S216-s229. doi:10.2337/dc23-S013

107. 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):1256-1267. doi:10.1111/pedi.13088

108. Brown SA, Kovatchev BP, Raghinaru D, et al. Six-Month Randomized, Multicenter Trial of Closed-Loop Control in Type 1 Diabetes. *N Engl J Med*. 2019;381(18):1707-1717. doi:10.1056/NEJMoa1907863

109. Messer LH, Berget C. Hybrid Closed-Loop Systems to Date: Hype Versus Reality. *Diabetes Technol Ther*. 2023;25(1):91-94. doi:10.1089/dia.2022.0375

110. Brown SA, Kovatchev BP, Raghinaru D, et al. Six-Month Randomized, Multicenter Trial of Closed-Loop Control in Type 1 Diabetes. Supplementary appendix. . *N Engl J Med*. 2019;381(18):1707-1717. doi:10.1056/NEJMoa1907863 Accessed August 1, 2023. https://www.nejm.org/doi/suppl/10.1056/NEJMoa1907863/suppl_file/nejmoa1907863_appendix.pdf.

111. Home PD. The pharmacokinetics and pharmacodynamics of rapid-acting insulin analogues and their clinical consequences. *Diabetes Obes Metab*. 2012;14(9):780-788. doi:10.1111/j.1463-1326.2012.01580.x

112. Wong EY, Kroon L. Ultra-Rapid-Acting Insulins: How Fast Is Really Needed? *Clinical Diabetes*. 2021;39(4):415-423. doi:10.2337/cd20-0119 Accessed 7/17/2023. Available at https://doi.org/10.2337/cd20-0119

113. Klonoff DC, Evans ML, Lane W, et al. A randomized, multicentre trial evaluating the efficacy and safety of fast-acting insulin aspart in continuous subcutaneous insulin infusion in adults with type 1 diabetes (onset 5). *Diabetes, Obesity and Metabolism*. 2019;21(4):961-967. doi:https://doi.org/10.1111/dom.13610 https://dom-pubs.onlinelibrary.wiley.com/doi/abs/10.1111/dom.13610

114. Thabit H, Lal R, Leelarathna L. Automated insulin dosing systems: Advances after a century of insulin. *Diabet Med*. 2021;38(12):e14695. doi:10.1111/dme.14695

115. Danatech diabetes technology. Insulin Pump Glossary. Diabeteseducator.org. Accessed August 7, 2023. Available at https://www.diabeteseducator.org/danatech/insulin-pumps/insulin-pumps-101/insulin-pump-glossary

116. Medtronic. MiniMed Reservoir. Medtronicdiabetes.com. 2015. Accessed August 7, 2023. Available at https://www.medtronicdiabetes.com/sites/default/files/library/download-library/user-guides/MiniMed-Reservoir.pdf

117. FDA Clears New Insulin Pump and Algorithm-Based Software to Support Enhanced Automatic Insulin Delivery News Release. FDA.gov. May 19, 2023, 2023. Accessed June 27, 2023. Available at https://www.fda.gov/news-events/press-announcements/fda-clears-new-insulin-pump-and-algorithm-based-software-support-enhanced-automatic-insulin-delivery

118. Zhang G, Romo-Anselmo E, Kwa T, Cohen O, Vigersky R, Chattaraj S. Advances in Insulin Infusion Set in the New Era of Automated Insulin Delivery: A Systematic Review. *J Diabetes Sci Technol*. 2023;17(2):302-313. doi:10.1177/19322968221145731

119. Guardian Sensor(3). User Guide. Medtronic; 2023. Accessed August 7, 2023. Available at https://www.medtronicdiabetes.com/sites/default/files/library/download-library/user-guides/Guardian_Sensor_3_User_Guide_Jun-2023.pdf

120. Lewis DM, Hussain S. Practical Guidance on Open Source and Commercial Automated Insulin Delivery Systems: A Guide for Healthcare Professionals Supporting People with Insulin-Requiring Diabetes. *Diabetes Ther*. 2022;13(9):1683-1699. doi:10.1007/s13300-022-01299-9

121. Insulet Announces FDA Clearance of Omnipod GO, a First-of-its-Kind Basal-Only Insulin Pod, Further Simplifying Life for People with Type 2 Diabetes. Press Release. Investors.Insulet.Com. April 24, 2023, 2023. Accessed June 28, 2023. Available at https://investors.insulet.com/news/news-details/2023/Insulet-Announces-FDA-Clearance-of-Omnipod-GO-a-First-of-its-Kind-Basal-Only-Insulin-Pod-Further-Simplifying-Life-for-People-with-Type-2-Diabetes/default.aspx

122. Tandem Diabetes Care. Tandem Mobi receives FDA clearance! TandemDiabetes.com. 2023. Accessed July 11, 2023. Available at https://www.tandemdiabetes.com/products/tandem-mobi

123. Tandem Diabetes Care. Tandem Mobi System. Support.tandemdiabetes.com. 2023. Accessed July 11, 2023. Available at https://support.tandemdiabetes.com/hc/en-us/sections/15929038635415-Tandem-Mobi-System

124. U.S. Food & Drug Administration. Re: K203689 Trade/Device Name: Tidepool Loop. Accessdata.fda.gov; 2023. Accessed June 28, 2023. Available at https://www.accessdata.fda.gov/cdrh_docs/pdf20/K203689.pdf

125. CeQur Simplicity 3-Day Insulin Patch. User Guide. CeQur Corportation; 2020. Accessed August 17, 2023. Available at https://myceqursimplicity.com/wp-content/uploads/User-Guide.pdf

126. U.S. Food & Drug Administration. *510(k) Summary for Valeritas V-Go Insulin Delivery Device*. 2010: 10 pages. Last Updated December 1, 2010. Accessed April 25, 2023. Available at https://www.accessdata.fda.gov/cdrh_docs/pdf10/K100504.pdf

127. U.S. Food & Drug Administration. *K180045 Trade/Device Name: Omnipod DASH Insulin Management System*. 2018: 14 pages. Last Updated June 1, 2018. Accessed April 25, 2023. Available at https://www.accessdata.fda.gov/cdrh_docs/pdf18/K180045.pdf

128. U.S. Food & Drug Administration. Omnipod Insulin Management System. K122953. Devices@FDA; 2012. Accessed June 28, 2023. Available at https://www.accessdata.fda.gov/scripts/cdrh/devicesatfda/index.cfm?db=pmn&id=K122953

129. U.S. Food & Drug Administration. *Re: P15001 MiniMed 630G System with SmartGuard*. 2016: 8 pages. Last Updated August 12, 2016. Accessed April 25, 2023. Available at https://www.accessdata.fda.gov/cdrh_docs/pdf15/P150001a.pdf

130. Tandem Diabetes Care. Introducting the t:slim X2 Insulin pump with Basal-IQ Technology Tandemdiabetes.com. 2018. Last Updated July 21, 2018. Accessed June 28, 2023. Available at https://www.tandemdiabetes.com/resources/blog/post/introducing-the-t-slim-x2-insulin-pump-with-basal-iq-technology#

131. U.S. Food & Drug Administration. Omnipod 5 ACE Pump (Pod). K203768. Accessdata.fda.gov; 2022. Accessed June 28, 2023. Available at https://www.accessdata.fda.gov/scripts/cdrh/devicesatfda/index.cfm?db=pmn&id=K203768

132. U.S. Food & Drug Administration. MiniMed 770G System - P160017/S076. FDA.gov. 2020. Last Updated December 23, 2020. Accessed June 28, 2023. Available at https://www.fda.gov/medical-devices/recently-approved-devices/minimed-770g-system-p160017s076

133. FDA Roundup: April 21, 2023. News Release. FDA.gov. April 21, 2023, 2023. Accessed April 25, 2023. Available at https://www.fda.gov/news-events/press-announcements/fda-roundup-april-21-2023

134. Tandem Diabetes Care. FDA announces clearance of Control-IQ technology as first in new category! TandemDiabetes.com. 2020. Accessed June 28, 2023. Available at https://www.tandemdiabetes.com/resources/blog/post/fda-announces-clearance-of-control-iq-as-first-in-new-category

135. Ware J, Hovorka R. Recent advances in closed-loop insulin delivery. *Metabolism*. 2022;127:154953. doi:10.1016/j.metabol.2021.154953

136. Cinar A. Automated Insulin Delivery Algorithms. *Diabetes Spectr*. 2019;32(3):209-214. doi:10.2337/ds18-0100

137. Pinsker JE, Lee JB, Dassau E, et al. Randomized Crossover Comparison of Personalized MPC and PID Control Algorithms for the Artificial Pancreas. *Diabetes Care*. 2016;39(7):1135-1142. doi:10.2337/dc15-2344

138. Forlenza GP. Ongoing Debate About Models for Artificial Pancreas Systems and In Silico Studies. *Diabetes Technol Ther*. 2018;20(3):174-176. doi:10.1089/dia.2018.0038

139. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. *J Clin Epidemiol*. 2021;134:178-189. doi:10.1016/j.jclinepi.2021.03.001

140. Dovc K, Mutlu GY, Philippov YI, et al. Free-living use of artificial pancreas for children with type 1 diabetes: Systematic review. *Diabetes Mellitus*. 2018;21(3):206-216. doi:10.14341/DM9714

141. Medtronic. Insertion Site Rotation. MedtronicDiabetes.com. 2023. Accessed July 13, 2022. Available at https://www.medtronicdiabetes.com/customer-support/insertion-site-management/site-rotation

142. Dexcom I. Where can I insert by Dexcom G6 sensor? Dexcom.com. Accessed July 13, 2023. Available at https://www.dexcom.com/en-us/faqs/where-can-i-insert-my-dexcom-g6-sensor

APPENDIX A – SELECT DEFINITIONS OF INSULIN PUMP SYSTEM COMPONENTS AND INSULIN PUMP DELIVERY TERMINOLOGY

Common insulin pump system components

- **Insulin pump:** Reviewed insulin pumps are small digital or mechanical devices that deliver a continuous infusion of rapid-acting (RA) insulin to meet basal insulin needs; most also deliver intermittent bolus doses (automatically and/or manually) to meet meal-time or rapid glucose adjustment needs.[18,115] Most pumps are digital devices that can be programmed to deliver insulin at variable rates,[5-11,16] and some simple mechanical pumps only deliver insulin at a set rate (eg, V-Go).[14] When combined with CGM and a software algorithm, some insulin pumps automatically adjust insulin delivery based on CGM SG values.[4,6-9,13,33] The pumps house an **insulin reservoir or cartridge**,[13,116] which holds insulin available for infusion. Some insulin pumps are patches that attach directly to the skin with adhesive (tubeless pumps),[9-11,14] and others are wearable devices (such as clipped to the patient's belt) that deliver insulin though an infusion set that attaches to the patient's skin (tubed pumps).[5-8,13]
    - **ACE (alternate controller enabled) pumps:** ACE is a special designation given to insulin pumps that can be paired with more than 1 pump system components of the same type (eg, different software algorithms or CGM devices). Also called *interoperable* pumps.[117]

- **Infusion sets:** Infusion sets are tubing and cannula which connect to the insulin pump with the cannula inserted in the patient's subcutaneous tissue for insulin delivery.[3] Most systems are compatible with multiple infusion sets with variable characteristics (eg, insertion tools, angle of insertion, tubing length, soft or steel cannula), which are selected based on the patient's unique needs.[68,69] Infusion sets are replaced frequently, usually every 2-3 days.[57,118] Replacement of infusion sets at the manufacturer- or healthcare provider-recommended frequency is important to prevent occlusions and insulin delivery interruptions.[19] Infusion sets adhere to the patient's skin with adhesive.[62,68,69] Patients should follow instructions for use of each infusion set, but generally, infusion sets can be placed anywhere on the body where one can inject insulin (eg, stomach, back of arms, thighs).[5,6,8,13] Patch-based insulin pumps are tubeless and the cannula or needle is housed within the patch (or Pod) so the pump adheres to the skin directly.[3]

- **Continuous glucose monitoring system (CGM)** parts**:**
    - A **sensor** is a device that detects glucose values (often called sensor glucose [SG] values) and is usually inserted under the skin.[22] Sensors must be replaced at manufacturer-recommended frequency, for example up to every 7 days for Medtronic sensors[21,119] and up to 10 days for the Dexcom G6 sensor.[20]
    - **Transmitter**: The transmitter communicates SG data to another component (ie, receiver or controller device).[6,20,22]

- **Controller:** A controller is a software algorithm housed within a pump or external component that sends commands to insulin pump to control advanced insulin delivery functions.[33]

Insulin pump delivery terminology

- **Types of insulin delivery:** All insulin pumps can deliver RA insulin continuously (or as micro boluses), which serves to meet basal insulin needs (so in this context, it is usually called basal insulin). Intermittent administered RA insulin (ie, called bolus doses, or boluses) are used to cover meals (meal/prandial bolus) or correct hyperglycemia (correctional bolus); meal boluses are user-initiated and depending on the pump/system, correctional boluses may be user- or algorithm-initiated.[17,19] Recently, experts suggested that "basal" and "bolus" terminology is not useful for AID systems since both types of insulin infusions (basal and bolus) play a role in managing hypo- and hyperglycemia and covering carbohydrate intake. Instead, for AID systems, experts suggest distinguishing between insulin delivered by the algorithm and by user request, using "user-initiated" and "algorithm-modulated."[33] While this terminology is suggested by experts, in this report we continue to use "basal" to describe ongoing continuous insulin infusion and "bolus" to describe intermittent insulin infusions.
- **Extended bolus:** The time over which the bolus dose is delivered is extended so some of the dose is delivered immediately and part of the dose delivered later. Extended bolus delivery may be useful when the user anticipates eating a high-fat meal (which delays carbohydrate absorption) or among individuals with gastroparesis to mitigate hypergycemia.[3]
- **Active insulin (or insulin on board):** This is the amount of insulin expected to be present and working in the body.[6] The length of time active insulin is anticipated to be in effect (active insulin time)[6] can be used by some insulin pump systems to estimate how much additional insulin should be delivered and mitigate hypoglycemia risk.[120]
- **Insulin: carbohydrate (I:C) ratio:** The grams of carbohydrates covered per 1 Unit of insulin.[10] This is often a pump setting that is set by the user (in consultation with a healthcare provider).
- **Correction factor (or insulin sensitivity factor):** The amount blood glucose is reduced per 1 Unit of insulin.[10] This is often a pump setting that is set by the user (in consultation with a healthcare provider).

APPENDIX B – OTHER INSULIN PUMPS OR PUMP SYSTEMS NOT ADDRESSED BY THIS REPORT

Insulin delivery technologies are rapidly developing, with several devices recently cleared by the FDA. Insulin pump-related devices not addressed by this report are the following:

- **Omnipod Go:**
  - Omnipod Go is a wearable patch-pump for subcutaneous insulin delivery at fixed rates (10-40 units per day). It is indicated for adults (≥18 years) with T2D who require long-acting insulin therapy. Compatible U-100 insulins include Novolog, Fiasp, Humalog, Admelog, and Lyumjev. The manufacturer, Insulet, plans to "commercialize" the device in 2024.[121]

- **Tandem Mobi:**
  - The Tandem Mobi is an interoperable (ACE) subcutaneous insulin delivery pump with a 200-Unit insulin cartridge for use with Control-IQ technology as an AID system. As a pump, it is indicated for PwD requiring insulin.[122] The Mobi is half the size of the T:Slim X2 pump and it is fully controllable with a user's iPhone. A shorter infusion set (5 inches) for on-body wear was developed as a more flexible option to be paired with the Mobi (other Tandem infusion sets will also be compatible). Tandem has not announced the compatible CGM. Full commercial availability of Tandem Mobi is anticipated in early 2024.[123]

- **Tidepool Loop:**
  - Tidepool loop is a mobile-application algorithm for automated insulin delivery (ie, automated glycemic controller) which is interoperable with select other FDA-cleared insulin pump system components.[71,124] The algorithm automates basal insulin delivery and recommends correctional insulin bolus doses. It is indicated for people with T1D ages 6 or older.[124] Tidepool Loop is not yet available[71]; see www.tidepool.org/tidepool-loop for updates about compatibility with other devices.

- **CeCur Simplicity:**
  - The CeCur Simplicity is a wearable single-use patch-pump that delivers intermittent 2-Unit subcutaneous boluses of RA acting insulin upon patient request (activated by pressing a button on the pump). It was excluded from this report because it does not provide continuous insulin delivery. Cecur Simplicity is indicated for adults with DM who require insulin treatment. Like pumps addressed by this report, it is compatible with U-100 insulin lispro (Humalog) and U-100 insulin aspart (Novolog).[125]

This report focused on commercial devices and does not include details about DIY AID systems. Interested readers may refer to Lewis et al 2022[120] and Braune 2022[39] for guidance on alternative AID systems using open-source technology.

APPENDIX C – LITERATURE SEARCHES

Ovid-Medline SR Search Conducted June 26, 2023

Database(s): Ovid MEDLINE(R) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations and Daily 1946 to June 22, 2023
Search Strategy:

#	Searches	Results
1	exp Diabetes Mellitus/	506,013
2	(diabet* or type 1 DM or type 2 DM or T1DM or T2DM or T1D or T2D or IDDM).ti,ab,kw,kf.	778,266
3	(insulin adj2 (pump* or patch or infusion-system* or infusion-device)).ti,ab,kw,kf.	4327
4	(sensor-augment* adj2 pump).ti,ab,kw,kf.	397
5	automat* insulin delivery.ti,ab,kw,kf.	425
6	closed-loop.ti,ab,kw,kf.	13,728
7	(t:slim or tslim or t-slim or control-iq or basal-iq).ti,ab,kw,kf.	92
8	V-go.ti,ab,kw,kf.	32
9	minimed.ti,ab,kw,kf.	419
10	(Medtronic and pump).ti,ab,kw,kf.	451
11	Omnipod.ti,ab,kw,kf.	68
12	exp Insulin Infusion Systems/	6407
13	exp Pancreas, Artificial/	1006
14	((bionic or artificial) adj1 pancreas).ti,ab,kw,kf.	1648
15	1 or 2	838,782
16	3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14	22,152
17	(MEDLINE or Embase or PubMed or systematic review).tw. or meta analysis.pt.	490,998
18	meta-analysis/ or (metaanaly$ or meta-analy$).ti,ab,kw,kf. or "Systematic Review"/ or ((systematic* adj3 review*) or (systematic* adj2 search*) or cochrane$ or (overview adj4 review)).ti,ab,kw,kf. or (cochrane$ or systematic review?).jw.	523,826
19	17 or 18	608,958
20	15 and 16 and 19	250
21	limit 20 to yr="2018 -Current"	133

Embase SR Search Conducted June 26, 2023

Database(s): Ovid MEDLINE(R) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations and Daily 1946 to June 22, 2023
Search Strategy:

#	Searches	Results
1	'diabetes mellitus'/exp	1,252,893
2	diabet*:ti,ab,kw OR 'type 1 dm':ti,ab,kw OR 'type 2 dm':ti,ab,kw OR t1dm:ti,ab,kw OR t2dm:ti,ab,kw OR t1d:ti,ab,kw OR t2d:ti,ab,kw OR iddm:ti,ab,kw	1,198,718
3	(insulin NEAR/2 (pump* OR patch OR 'infusion system*' OR 'infusion device')):ti,ab,kw	8,861
4	('sensor augment*' NEAR/2 pump):ti,ab,kw	876
5	'automat* insulin delivery':ti,ab,kw	751
6	'closed-loop':ti,ab,kw	17,870
7	'sensor augmented pump'/exp OR 'sensor augmented pump therapy'/exp	138
8	'closed loop system'/exp OR 'closed loop insulin delivery system'/exp OR 'closed loop insulin delivery'/exp OR 'hybrid closed loop system'/exp OR 'advanced hybrid closed loop system'/exp	195
9	'automated insulin delivery system'/exp	18
10	tslim:ti,ab,kw OR 't-slim':ti,ab,kw OR 't:slim':ti,ab,kw OR 'control iq':ti,ab,kw OR 'basal iq':ti,ab,kw OR 'control-iq'	288
11	'v go'/exp OR 'v-go':ti,ab,kw	98
12	'minimed'/exp OR 'minimed 780g'/exp OR minimed:ti,ab,kw	1,050
13	medtronic:ti,ab,kw AND pump:ti,ab,kw	1,227
14	'omnipod 5'/exp OR omnipod:ti,ab,kw	274
15	'insulin pump'/exp OR 'insulin infusion'/exp	18,308
16	'medication system'/exp AND (pump:ti,ab,kw OR 'closed loop':ti,ab,kw)	86
17	'artificial pancreas'/exp	2,863
18	((bionic OR artificial) NEAR/1 pancreas):ti,ab,kw	2,661
19	'bionic pancreas'/exp	11
20	#1 OR #2	1,466,413
21	#3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19	39,035
22	cochrane*:jt OR 'systematic review*':jt OR 'meta analysis'/exp OR 'systematic review'/exp OR ((systematic* NEAR/3 review*):ti,ab,kw) OR ((systematic* NEAR/2 search*):ti,ab,kw) OR 'meta analys*':ti,ab,kw OR metaanalys*:ti,ab,kw OR ((overview NEAR/4 (review OR reviews)):ti)	706,350
23	#20 AND #21 AND #22	493
24	#20 AND #21 AND #22 AND [2018-2023]/py	264
25	#24 NOT ('conference abstract'/it OR 'conference review'/it)	203

APPENDIX D – INSULIN PUMP AND PUMP SYSTEM INDICATIONS

Table D1. Insulin Pump Components and Indications for Use

Name *Initial Approval Date*	Primary System Components	Pump and Pump System Indications[a] (per FDA Approval and/or Manufacturer's User Guide)
Insulin Pumps or Sensor-Augmented Pumps (if used with stand-alone CGM)		
V-go[14] December 2010[126]	Conventional insulin delivery system via wearable patch: • V-Go wearable patch; available as V-Go 20, V-Go 30, or V-Go 40, • EZ-Fill (1 per 30 days of V-go prescription for filling V-go with insulin)	For continuous subcutaneous insulin delivery in **adults** • V-Go 20: continuous infusion of 20 Units of insulin/24 hr (0.83 U/hr) and on-demand bolus (2 U increments to max 36 Units/24 hours) • V-Go 30: continuous infusion of 30 Units of insulin/24 hr (1.25 U/hr) and on-demand bolus doses (2 U increments max 36 Units/24 hours) • V-Go 40: continuous infusion of 40 Units of insulin/24 hr (1.67 U/hr) and on-demand bolus doses (2 U increments to max 36 Units/24 hours)
Omnipod DASH[9] June 2018[127]	Conventional insulin delivery system via wearable pod: • Tubeless insulin delivery pod and Personal Diabetes Manager controller (PDM; handheld device like a smart phone) • Compatible with CONTOUR NEXT ONE BG meter, for delivery of BG data to the Omnipod DASH PDM using Bluetooth connectivity.	DASH insulin management system is for management of **DM in persons requiring insulin** using: • Continuous subcutaneous insulin delivery at fixed or variable rates • Interoperable with a compatible BG meter
Omnipod Insulin Management System[11] (Omnipod Eros) December 2012[128]	Conventional insulin delivery system via wearable pod: • Tubeless insulin delivery pod and Personal Diabetes Manager controller (PDM; handheld device like a smart phone) with a built-in FreeStyle BGM • BGM is compatible with FreeStyle test strips and control solution	Omnipod Insulin Management system is for management of **DM in persons requiring insulin and for measurement of blood glucose**, using: • Continuous subcutaneous insulin delivery at fixed or variable rates • Glucose measurements using whole blood from the finger. These measurements are NOT for the diagnosis or screening of DM.
Sensor Augmented Pumps with Insulin-Suspend Technology		
MiniMed 630G[5] August 2016[129]	SAP system with LGS: • MiniMed 630G IP, Guardian Link 3 transmitter, Guardian Sensor 3, one-press serter (for sensor insertion), Contour Next link 2.4 wireless meter, CareLink USB, and Contour Next test strips	630G system is for management of **DM in persons ≥ 14 years (Guardian 3 sensor) or ≥ 16 years (Enlite sensor)[85] requiring insulin and CGM**, using: • Continuous basal insulin delivery (user may select rate) • Insulin bolus delivery (user may select amount) When used with SmartGuard technology, it: • Stops insulin delivery for up to 2 hours if sensor glucose readings fall below a low threshold • Limitation of use: The 630G system is NOT designed for direct treatment adjustments but to provide information about when a fingerstick may be needed. Use BGM readings for making therapy decisions. The system is not intended to directly prevent or treat hypoglycemia.
t:slim X2a with Basal-IQ Technology[12] July 2018[130]	SAP system with PLGS: • t:slim X2 IP, Basal-IQ algorithm, t:slim X2 cartridge, compatible CGM (Dexcom G6)	t:slim X2 ACE pump is for management of **DM in persons ≥ 6 years**: • For subcutaneous insulin delivery at set or variable rates • Communicates with other devices (eg, AID software) and executes demands from those devices Basal-IQ technology is for **persons with DM ≥ 6 years**, it: • Automatically suspends insulin delivery based on current or predicted low BG values Bolus calculator technology is for management of DM in people with DM, it:

[a] *Some systems have separate indications for system parts (eg, IP versus dosing algorithm). When available, the indication for each part is specified separately.*

Abbreviations: ACE, alternate controller-enabled; AID, automated insulin delivery; BGM, blood glucose meter; CGM, continuous glucose monitor/monitoring; DM, diabetes mellitus; HCL, hybrid closed-loop ; I:C, insulin: carbohydrate; IP, insulin pump; RA, rapid-acting; SMBG, self-monitor(ing) blood glucose;

Table D1. Insulin Pump Components and Indications for Use

Name *Initial Approval Date*	Primary System Components	Pump and Pump System Indications[a] (per FDA Approval and/or Manufacturer's User Guide)
		• Uses information entered by the user to predict insulin doses or carbohydrate intake
Automated Insulin Delivery Systems		
Omnipod 5[9] January 2022[131]	HCL AID system: • Tubeless insulin pod, Omnipod 5 App (using an Insulet controller or smartphone), and compatible CGM (Dexcom G6)	Omnipod 5 ACE pump for management of **DM in people requiring insulin**: • Delivers continuous subcutaneous insulin at set or variable rates • Communicates with other devices (ie, AID software) and executes commands from those devices SmartAdjust Technology: for persons with **T1D ages ≥ 2 years**, in combination with ACE pumps • Automatically adjusts insulin delivery rate using sensor reading SmartBolus Calculator: for persons with **DM ages ≥ 2 years** requiring RA U-100 insulin • Calculates insulin bolus dose using sensor readings including the rate of change, patient-entered carbohydrates, and programmed factors (I:C ratio, target glucose, correction factor)
MiniMed 770G[6] December 2020[132]	HCL AID system: • MiniMed 770G IP, Guardian Link 3 transmitter, Guardian Sensor 3, One-press serter (for sensor insertion), MiniMed Mobile app, CareLink Connect app, Blue adapter, Accu-Check Guide link BGM, and Accu-check Guide test strips	770G system is for management of **T1D in persons ≥ 2 years requiring insulin**, using: • Continuous basal insulin delivery (user may select rate) • Insulin bolus delivery (user may select amount) • Continuous glucose monitoring using an interstitial sensor When used with SmartGuard technology, it: • Automatically adjusts basal insulin delivery rate using sensor readings • May stop insulin delivery if sensor glucose readings fall below a low threshold or are predicted to fall below a threshold ***Limitation of use:*** The CGM sensor (Guardian 3) is NOT designed for direct treatment adjustments but to provide information about when a fingerstick may be needed. Use BGM readings for making therapy decisions.
MiniMed 780G April 2023[133]	Advanced HCL AID system: • MiniMed 780G IP, Guardian Link 3 or 4 transmitter, Guardian 3 or 4 sensor, One-press serter (for sensor insertion), Accu-Check Guide link BGM, and Accu-check Guide test strips	780G system is for management of **T1D in persons ≥ 7 years requiring insulin**, using: • Continuous basal insulin delivery (user may select rate) • Insulin bolus delivery (user may select amount) • Continuous glucose monitoring using an interstitial sensor When used with SmartGuard technology, it: • Automatically adjusts insulin delivery rate using sensor readings • May stop insulin delivery if sensor glucose readings fall below a low threshold or are predicted to fall below a threshold **Limitation of use**: The CGM sensor (Guardian 3 or 4) is NOT designed for direct treatment adjustments when the 780G is used in manual (non-automated) mode. Use BGM readings for making therapy decisions.
t:slim X2a with Control-IQ Technology[13] December 2019[134]	Advanced HCL AID system: • t:slim X2 IP, Control-IQ algorithm, t:slim X2 cartridge, compatible CGM (Dexcom G6)	t:slim X2 ACE pump is for management of **DM in persons ≥ 6 years**: • For subcutaneous insulin delivery at set or variable rates • Communicates with other devices (eg, AID software) and executes demands from those devices Control-IQ technology is for **persons with T1D ≥ 6 years**, it: • Automatically adjusts insulin delivery rate using sensor reading • Stops insulin delivery if sensor glucose readings are predicted to fall below a threshold • Delivers correctional insulin bolus for elevated sensor glucose readings predicted to exceed a particular threshold

[a] *Some systems have separate indications for system parts (eg, IP versus dosing algorithm). When available, the indication for each part is specified separately.*

Abbreviations: ACE, alternate controller-enabled; AID, automated insulin delivery; BGM, blood glucose meter; CGM, continuous glucose monitor/monitoring; DM, diabetes mellitus; HCL, hybrid closed-loop ; I:C, insulin: carbohydrate; IP, insulin pump; RA, rapid-acting; SMBG, self-monitor(ing) blood glucose;

Table D1. Insulin Pump Components and Indications for Use

Name ***Initial Approval Date***	**Primary System Components**	**Pump and Pump System Indications[a]** **(per FDA Approval and/or Manufacturer's User Guide)**

iLet Bionic Pancreas System[4]
May 2023[117]
	Advanced AID system:
	• iLet Device (ie, ACE pump and iLet Dosing Decision Software), iLet cartridge, icompatible CGM (Dexcom G6)
		iLET ACE pump is for **management of DM in persons ≥ 6 years**:
		• For insulin delivery for a single person when used with in integrated CGM and interoperable automated glycemic controller
		iLET Dosing Decision Software is for management of **T1D in persons ≥ 6 years**:
		• For insulin delivery for a single person with a prescription when used with in integrated CGM (or temporary SMBG meter) and ACE pump
		• The software automatically:
		  ○ Adjusts or suspends insulin delivery using sensor readings
		  ○ Delivers correctional insulin boluses based on sensor readings
		  ○ Delivers meal insulin boluses after a meal announcement

[a] Some systems have separate indications for system parts (eg, IP versus dosing algorithm). When available, the indication for each part is specified separately.

Abbreviations: ACE, alternate controller-enabled; AID, automated insulin delivery; BGM, blood glucose meter; CGM, continuous glucose monitor/monitoring; DM, diabetes mellitus; HCL, hybrid closed-loop ; I:C, insulin: carbohydrate; IP, insulin pump; RA, rapid-acting; SMBG, self-monitor(ing) blood glucose;

APPENDIX E – COMPARISONS BY TYPE OF AUTOMATED DOSING ALGORITHM

AID systems algorithms try to keep sensor glucose (SG) values within the ideal range, which they accomplish using different approaches. Most commercial AID systems use Model Predictive Control (MPC) algorithms, whereas MiniMed pumps (770G and 780G) use a Proportional Integrative Derivative (PID) algorithm with insulin limit adaptations to minimize hypoglycemia.[33,81]

PID algorithms adjust insulin based on 3 components (proportional, derivative, and integral), corresponding to the distance from the current SG to the target glucose, how fast the SG values are changing, and the area under a graph of the difference between actual and target glucose values. MPC algorithms predict future SG values and adjust insulin by trying to match the predicted SG trajectory to the target SG trajectory.[135,136] Constraints on the MPC algorithm adjust for various parameters (eg, active insulin time, or variation in glucose after eating).[135] Some algorithms also use "fuzzy logic," which is when the algorithm follows conditional (If-Then) rules based on how a clinician would respond to glucose values.[19]

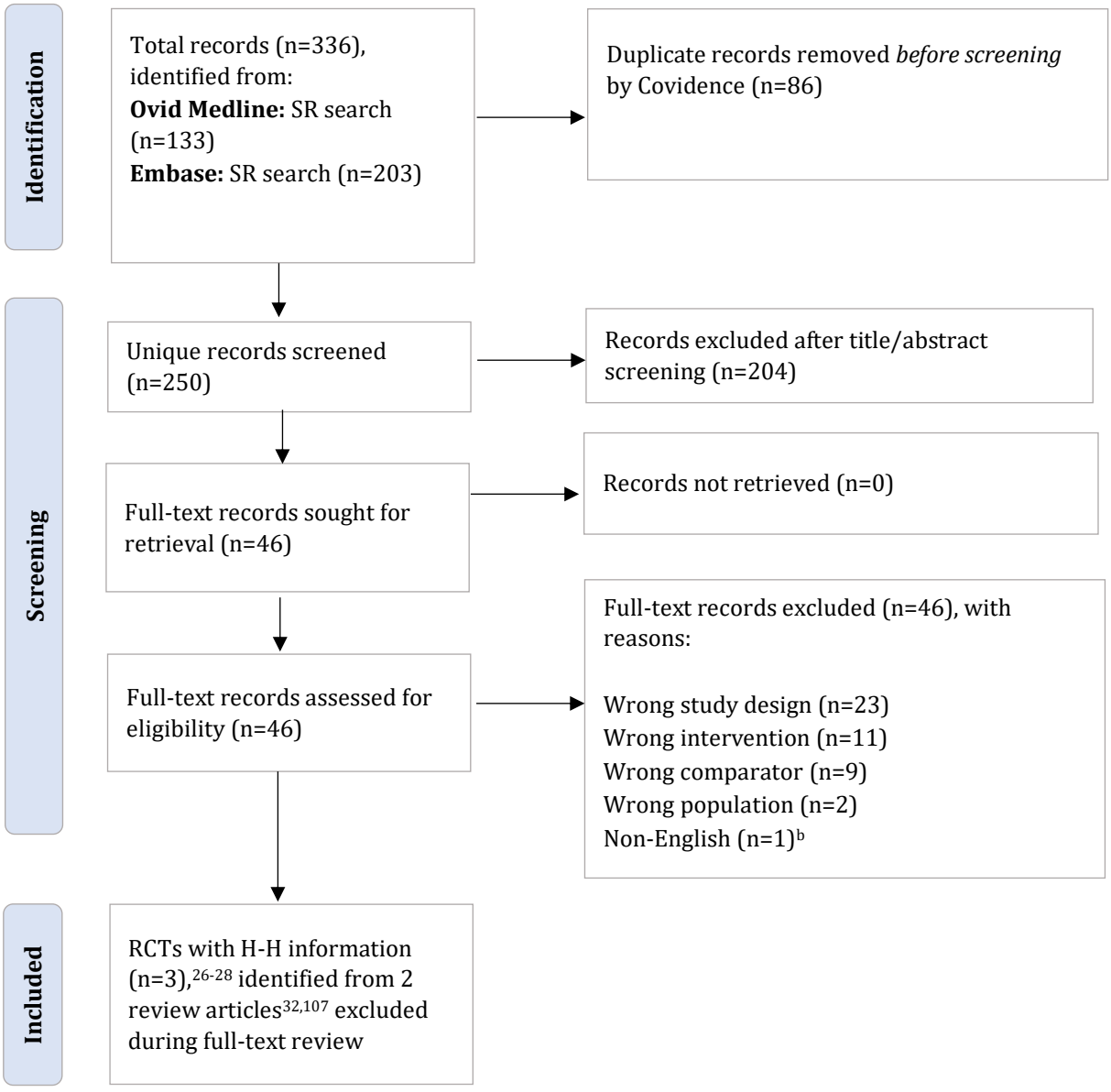
In a clinical trial comparing MPC and PID controllers with identical other system components under non-ideal conditions (eg, no setting optimization or unannounced meal), both algorithms performed well, but the MPC statistically outperformed the PID for most glucose control measures including TIR.[137] Nonetheless, the algorithms in the aforementioned study are not identical to those used by commercial AID systems, so the relevance to comparisons between AID systems is unclear. According to expert commentary in 2018, there is considerable debate about whether a particular type of algorithm model (eg, MPC versus PID) should be preferred.[138]

From the clinical perspective, differences between PID and MPC algorithms lead to differences in required user input(s) for the algorithm to run, and how the system adapts. According to one expert, an advantage of MPC algorithms is system aggressiveness adjusts using programmed basal rates (eg, user-programmed basal insulin rates for different times of the day), allowing the system to be responsive to changes in insulin needs throughout the day. In contrast, generally, PID algorithms rely on total daily insulin needs (not accounting for within-day variability).[138]

APPENDIX F –PRISMA FLOW DIAGRAM

Figure F1 outlines the literature screening process including the number of records identified from searches of each database, and the number of included and excluded records.

Figure F1. PRISMA Flow Chart[a] for Literature Screening



Abbreviations: H-H, head-to-head; info, information; RCT, randomized controlled trials; SR, systematic review

[a] Modified from Page et al. 2021[139]

[b] Due to time constraints, we were not able to pursue translation of an article by Dovc K et al 2018[140]

APPENDIX G – CITATIONS OF STUDIES EXCLUDED IN FULL TEXT REVIEW

Wrong Study Design

1. Al-Beltagi M, Saeed NK, Bediwy AS, Elbeltagi R. Insulin pumps in children - a systematic review. World J Clin Pediatr. 2022;11(6):463-484. doi:10.5409/wjcp.v11.i6.463
3. Beck RW, Kanapka LG, Breton MD, et al. A Meta-Analysis of Randomized Trial Outcomes for the t:slim X2 Insulin Pump with Control-IQ Technology in Youth and Adults from Age 2 to 72. Diabetes technology & therapeutics. 2023, https://dx.doi.org/10.1089/dia.2022.0558doi:https://dx.doi.org/10.1089/dia.2022.0558
4. Franceschi R, Mozzillo E, Di Candia F, 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, 10.1111/dme.15099:e15099. doi:10.1111/dme.15099
5. Fuchs J, Hovorka R. Closed-loop control in insulin pumps for type-1 diabetes mellitus: safety and efficacy. Expert Rev Med Devices. 2020;17(7):707-720. doi:10.1080/17434440.2020.1784724
6. Heinemann L, Waldenmaier D, Kulzer B, Ziegler R, Ginsberg B, Freckmann G. Patch Pumps: Are They All the Same? J Diabetes Sci Technol. 2019;13(1):34-40. doi:10.1177/1932296818795150
7. Hernando ME, Garciá-Saéz G, Gómez EJ, Pérez-Gandiá C, Rodríguez-Herrero A. Automated Insulin Delivery: The Artificial Pancreas Technical Challenges. American Journal of Therapeutics. 2020;27(1):E62-E70. doi:10.1097/MJT.0000000000001086
8. Hur KY, Moon MK, Park JS, et al. 2021 Clinical Practice Guidelines for Diabetes Mellitus of the Korean Diabetes Association. Diabetes Metab J. 2021;45(4):461-481. doi:10.4093/dmj.2021.0156
9. Karageorgiou V, Papaioannou TG, Bellos I, et al. Effectiveness of artificial pancreas in the non-adult population: A systematic review and network meta-analysis. Metabolism: Clinical and Experimental. 2019;90:20-30. doi:10.1016/j.metabol.2018.10.002
10. McCall AL, Lieb DC, Gianchandani R, et al. Management of Individuals With Diabetes at High Risk for Hypoglycemia: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2023;108(3):529-562. doi:10.1210/clinem/dgac596
11. Molitch ME. Hyperglycaemia management in non-critical care settings: guidelines in focus. Lancet Diabetes Endocrinol. 2022;10(9):614-616. doi:10.1016/s2213-8587(22)00214-5
12. Moon SJ, Jung I, Park CY. Current Advances of Artificial Pancreas Systems: A Comprehensive Review of the Clinical Evidence. Diabetes Metab J. 2021;45(6):813-839. doi:10.4093/dmj.2021.0177
13. Napoli A. Insulin Therapy and Diabetic Pregnancy. American Journal of Therapeutics. 2020;27(1):E91-E105. doi:10.1097/MJT.0000000000001095
14. Nimri R, Nir J, Phillip M. Insulin Pump Therapy. American Journal of Therapeutics. 2020;27(1):E30-E41. doi:10.1097/MJT.0000000000001097
15. Papadakis JL, Anderson LM, Garza K, et al. Psychosocial Aspects of Diabetes Technology Use: The Child and Family Perspective. Endocrinology and Metabolism Clinics of North America. 2020;49(1):127-141. doi:10.1016/j.ecl.2019.10.004
16. Peacock S, Frizelle I, Hussain S. A Systematic Review of Commercial Hybrid Closed-Loop Automated Insulin Delivery Systems. Diabetes Ther. 2023;14(5):839-855. doi:10.1007/s13300-023-01394-5
17. Pease A, Lo C, Earnest A, Kiriakova V, Liew D, Zoungas S. Time in range for multiple technologies in type 1 diabetes: A systematic review and network meta-analysis. Diabetes Care. 2020;43(8):1967-1975. doi:10.2337/dc19-1785

18. Pease A, Lo C, Earnest A, Kiriakova V, Liew D, Zoungas S. The Efficacy of Technology in Type 1 Diabetes: A Systematic Review, Network Meta-analysis, and Narrative Synthesis. Diabetes Technology and Therapeutics. 2020;22(5):411-421. doi:10.1089/dia.2019.0417
19. Pease A, Zomer E, Liew D, Lo C, Earnest A, Zoungas S. Cost-effectiveness of health technologies in adults with type 1 diabetes: A systematic review and narrative synthesis. Systematic Reviews. 2020;9(1)doi:10.1186/s13643-020-01373-y
20. Rodríguez-Sarmiento DL, León-Vargas F, García-Jaramillo M. Artificial pancreas systems: experiences from concept to commercialisation. Expert Rev Med Devices. 2022;19(11):877-894. doi:10.1080/17434440.2022.2150546
21. Speight J, Choudhary P, Wilmot EG, et al. Impact of glycaemic technologies on quality of life and related outcomes in adults with type 1 diabetes: A narrative review. Diabetic medicine : a journal of the British Diabetic Association. 2023;40(1):e14944. doi:https://dx.doi.org/10.1111/dme.14944
22. Tyler NS, Jacobs PG. Artificial Intelligence in Decision Support Systems for Type 1 Diabetes. Sensors (Basel). 2020;20(11)doi:10.3390/s20113214
23. Wu Z, Lebbar M, Taleb N, Legault L, Messier V, Rabasa-Lhoret R. Comparing dual-hormone and single-hormone automated insulin delivery systems on nocturnal glucose management among children and adolescents with type 1 diabetes: A pooled analysis. Diabetes Obes Metab. 2023;25(1):310-313. doi:10.1111/dom.14850

Wrong Intervention

24. Al Balwi R, Al Madani W, Al Ghamdi A. Efficacy of insulin dosing algorithms for high-fat high-protein mixed meals to control postprandial glycemic excursions in people living with type 1 diabetes: A systematic review and meta-analysis. *Pediatric Diabetes*. 2022;23(8):1635-1646.
25. 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. *Pediatric Diabetes*. 2020;21(7):1256-1267. doi:10.1111/pedi.13088
26. Bekiari E, Kitsios K, Thabit H, et al. Artificial pancreas treatment for outpatients with type 1 diabetes: systematic review and meta-analysis. *Bmj*. 2018;361:k1310. doi:10.1136/bmj.k1310
27. 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 Technology and Therapeutics*. 2019;21(10):589-601. doi:10.1089/dia.2019.0119
28. De Ridder F, den Brinker M, De Block C. The road from intermittently scanned continuous glucose monitoring to hybrid closed-loop systems. Part B: results from randomized controlled trials. *Therapeutic Advances in Endocrinology and Metabolism*. 2019;10doi:10.1177/2042018819871903
29. Fang Z, Liu M, Tao J, Li C, Zou F, Zhang W. Efficacy and safety of closed-loop insulin delivery versus sensor-augmented pump in the treatment of adults with type 1 diabetes: a systematic review and meta-analysis of randomized-controlled trials. *Journal of Endocrinological Investigation*. 2022;45(3):471-481. doi:10.1007/s40618-021-01674-6
30. Kulzer B, Freckmann G, Heinemann L, Schnell O, Hinzmann R, Ziegler R. Patch Pumps: What are the advantages for people with diabetes? *Diabetes Research and Clinical Practice*. 2022;187doi:10.1016/j.diabres.2022.109858
31. Mannucci E, Candido R, Delle Monache L, et al. Italian guidelines for the treatment of type 2 diabetes. *Nutrition, Metabolism and Cardiovascular Diseases*. 2022;32(4):770-814.

32. Metwally M, Cheung TO, Smith R, Bell KJ. Insulin pump dosing strategies for meals varying in fat, protein or glycaemic index or grazing-style meals in type 1 diabetes: A systematic review. *Diabetes Research and Clinical Practice*. 2021;172doi:10.1016/j.diabres.2020.108516
33. Zeng B, Jia H, Gao L, Yang Q, Yu K, Sun F. Dual-hormone artificial pancreas for glucose control in type 1 diabetes: A meta-analysis. *Diabetes, Obesity and Metabolism*. 2022;24(10):1967-1975. doi:10.1111/dom.14781
34. Zhang G, Romo-Anselmo E, Kwa T, Cohen O, Vigersky R, Chattaraj S. Advances in Insulin Infusion Set in the New Era of Automated Insulin Delivery: A Systematic Review. *Journal of Diabetes Science and Technology*. 2023;17(2):302-313. doi:10.1177/19322968221145731

Wrong Comparator

35. Benioudakis E, Karlafti E, Kalaitzaki A, Kaiafa G, Savopoulos C, Didangelos T. Technological Developments and Quality of Life in Type 1 Diabetes Mellitus Patients: A Review of the Modern Insulin Analogues, Continuous Glucose Monitoring and Insulin Pump Therapy. *Current Diabetes Reviews*. 2022;18(7)doi:10.2174/1573399818666211103163208
36. Dai X, Luo ZC, Zhai L, Zhao WP, Huang F. Artificial Pancreas as an Effective and Safe Alternative in Patients with Type 1 Diabetes Mellitus: A Systematic Review and Meta-Analysis. *Diabetes Therapy*. 2018;9(3):1269-1277. doi:10.1007/s13300-018-0436-y
37. Eberle C, Loehnert M, Stichling S. Clinical effectiveness of different technologies for diabetes in pregnancy: Systematic literature review. *Journal of Medical Internet Research*. 2021;23(4)doi:10.2196/24982
38. Eckstein ML, Weilguni B, Tauschmann M, et al. Time in range for closed-loop systems versus standard of care during physical exercise in people with type 1 diabetes: A systematic review and meta-analysis. *Journal of Clinical Medicine*. 2021;10(11)doi:10.3390/jcm10112445
39. Jiao X, Shen Y, Chen Y. Better TIR, HbA1c, and less hypoglycemia in closed-loop insulin system in patients with type 1 diabetes: a meta-analysis. *BMJ Open Diabetes Research and Care*. 2022;10(2)doi:10.1136/bmjdrc-2021-002633
40. Kamusheva M, Tachkov K, Dimitrova M, et al. A Systematic Review of Collective Evidences Investigating the Effect of Diabetes Monitoring Systems and Their Application in Health Care. *Frontiers in Endocrinology*. 2021;12doi:10.3389/fendo.2021.636959
41. Kang SL, Hwang YN, Kwon JY, Kim SM. Effectiveness and safety of a model predictive control (MPC) algorithm for an artificial pancreas system in outpatients with type 1 diabetes (T1D): systematic review and meta-analysis. *Diabetology & Metabolic Syndrome*. 2022;14(1):187. doi:10.1186/s13098-022-00962-2
42. Luo J, Zhang K, Xu Y, Tao Y, Zhang Q. Effectiveness of Wearable Device-based Intervention on Glycemic Control in Patients with Type 2 Diabetes: A System Review and Meta-Analysis. *Journal of Medical Systems*. 2022;46(1)doi:10.1007/s10916-021-01797-6
43. 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 Research and Clinical Practice*. 2023;199doi:10.1016/j.diabres.2023.110678

Wrong Population

44. Helvacı BC, Başer H, Çakır B. Mini-review: pump therapy in endocrinology & metabolism beyond diabetes. *Endocrine*. 2022;76(2):245-252. doi:10.1007/s12020-022-03007-w
45. Torres Roldan VD, Urtecho M, Nayfeh T, et al. A Systematic Review Supporting the Endocrine Society Guidelines: Management of Diabetes and High Risk of Hypoglycemia. *Journal of Clinical Endocrinology and Metabolism*. 2023;108(3):592-603. doi:10.1210/clinem/dgac601

Non-English Language Publication

46. Dovc K, Mutlu GY, Philippov YI, et al. Free-living use of artificial pancreas for children with type 1 diabetes: Systematic review. *Diabetes Mellitus*. 2018;21(3):206-216. doi:10.14341/DM9714

APPENDIX H – ADVERSE EVENTS FROM PUMP USER GUIDES

Table H1. Potential or Observed Adverse Events during Insulin Pump System Clinical Studies per Manufacturer User Guides[a]

V-Go[14]
Adverse Reactions: • Infections or abscesses at the insulin infusion site. Rotating the administration site and using cleaning the site before use minimizes this risk. • Skin irritation is more common. Using a skin barrier or adhesive removal products may help mitigate irritation of sensitive skin.
MiniMed 630G[5]
AE (number of events; number exposed not reported) during a clinical trial in an unspecified population using the LGS with another MiniMed pump (Paradigm X54): • **Bruising** (1) or **bleeding** (1) at sensor site • **Ketones in urine** (1)**,** due to flawed tubing connection to pump
Minimed 770G[6]

Number of AE or AE (number of events) in children ages 2-6 years with T1D during 2 clinical trials using the 670G system:
• Trial 1 (with PLGS, N=47 participants): no AE information reported
• Trial 2 (with AutoMode, included 46 patients) with 2-week run-in and 3-month treatment:
  ○ No device-related SAE, including DKA or severe hypoglycemia
  ○ **Device-related AE** (54, 39%), that included:
  ▪ **severe hyperglycemia** (49); 46 of these events were attributed to infusion set issues (eg, occlusion, bent cannula)
  ○ **Severe hyperglycemia** (86); most events were considered mild
Number of AE or AE (number of events) in children ages 7-13 with T1D during 2 clinical trials using the 670G system:
• Trial 1 (with PLGS, N=105 participants):
  ○ No device-related SAE, PLGS-related DKA, or unexpected AE
• Trial 2 (with AutoMode, N=105 participants) with 2-week run-in and 3-month treatment:
  ○ No device-related SAE, including DKA or severe hypoglycemia
  ○ **Device-related AE** (80, 39%), that included:

[a] *Includes AEs reported in the adverse events or adverse reactions section of device user guides. Both serious and non-serious AEs were included if reported in the adverse event section. Note that all products warn of the potential for hypoglycemia, hyperglycemia, and DKA.*

Abbreviations: A1c, hemoglobin A1c or glycated hemoglobin; AE, adverse event; DKA, diabetic ketoacidosis; LGS, low glucose suspend; No., number; PLGS, predicted low glucose suspend; TID, type 1 diabetes; SAE, serious adverse event; SOC, standard of care (comparator group);

Table H1. Potential or Observed Adverse Events during Insulin Pump System Clinical Studies per Manufacturer User Guides[a]

- **hyperglycemia or severe hyperglycemia with or without ketosis** (65)
  - 51 of 62 device-related severe hypoglycemia events were due to issues with the infusion set (eg, occlusion, bent cannula)
- **Skin issues,** including skin infection or irritation, cellulitis, other infection, eczema (14)

- Procedure-related AE (5)
- Device- and procedure-related AE (2), including hyperglycemia (1) and skin irritation (1)
- **Severe hyperglycemia** (104); most were considered mild, and 1 severe hyperglycemic event complicated by acute gastroenteritis resulted in an ER visit

Number of AE or AE (number of events) in patients age ≥ 14 with T1D during 2 clinical trials using the 670G system:

- Trial 1 (with PLGS, N=71 participants):
  - 5 AEs, 4 considered unrelated to the device or a procedure and 1 procedure-related AE
  - No device-related SAE, DKA events related to PLGS, or unexpected AE
- Trial 2 (with Auto Mode, N=124 participants) total number of device-related AE:
  - **Severe hyperglycemia** (17); **hyperglycemia** (6); **skin irritation** (3); **irritation on sensor site** (1); **rash** (1)
  - No SAE, DKA, or severe hypoglycemia events

Minimed 780G[7,8]

Device-related AE (number of events; N=179 trial participants) in children ages 7-17 with T1D during a 3-month trial using the MiniMed 670G with the Guardian 3 Sensor:

- **Severe hyperglycemia** (22); **rash/contact dermatitis** from sensor/tape (4); **hyperglycemia** (4); **infusion set failure** (2); sensor **site bleeding** (2); **bruise** on upper arm (1); sensor insertion **site discomfort** (1); **gastroenteritis** with hyperglycemia, possibly device-related (1); **infection** at pump site (1); **skin irritation** with excoriation (1)

Device-related AE (number of events; N=179 trial participants) in adults ages 18-75 with T1D during a 3-month trial using the MiniMed 670G with the Guardian 3 Sensor:

- **Rash/contact dermatitis** from sensor/tape (4); **severe hyperglycemia** (3); **sensor site bleeding** (1); **erythema abdomen at old sensor site** (1)

Among children and adults, there were no device-related SAE or DKA. One episode of non-device related severe hypoglycemia occurred.

Omnipod DASH[10]

- No AE reported by user guide

[a] *Includes AEs reported in the adverse events or adverse reactions section of device user guides. Both serious and non-serious AEs were included if reported in the adverse event section. Note that all products warn of the potential for hypoglycemia, hyperglycemia, and DKA.*

Abbreviations: A1c, hemoglobin A1c or glycated hemoglobin; AE, adverse event; DKA, diabetic ketoacidosis; LGS, low glucose suspend; No., number; PLGS, predicted low glucose suspend; TID, type 1 diabetes; SAE, serious adverse event; SOC, standard of care (comparator group);

Table H1. Potential or Observed Adverse Events during Insulin Pump System Clinical Studies per Manufacturer User Guides[a]

Omnipod 5[9]
AE (number of events; N=80 trial participants) in children 2-5.9 years with T1D during 3-month treatment in a clinical trial: • **Severe hypoglycemia**, which required assistance of someone else (0); **hypoglycemia**, serious but not meeting other definitions (0); **DKA** (0); **hyperglycemia r**equiring evaluation or meeting SAE criteria (4); **prolonged hyperglycemia**, defined as BGM reading 300 mg/dL with ketones >1.0 mmol/L (20); other AE (5); **skin irritation** (2); **cellulitis** (1); **non-DKA ketosis** (2) AE (number of events; N=112 trial participants) in children 6-13.9 years with T1D during 3-month treatment in a clinical trial: • **Severe hypoglycemia,** which required assistance of someone else (1); **hypoglycemia**, serious but not meeting other definitions (1); **DKA** (1); **Hyperglycemia** requiring evaluation or meeting SAE criteria (1); **prolonged hyperglycemia**, defined as BGM reading 300 mg/dL with ketones >1.0 mmol/L (13); **other AE** (8); **infection/irritation at infusion site** (2) AE (number of events; N=128 trial participants) in adolescents and adults 14-70 years with T1D during 3-month treatment in a clinical trial: • **Severe hypoglycemia,** which required assistance of someone else (2); **hypoglycemia**, serious but not meeting other definitions (0); **DKA** (2); **hyperglycemia** requiring evaluation or meeting SAE criteria (2); **prolonged hyperglycemia**, defined as BGM reading 300 mg/dL with ketones >1.0 mmol/L (5); **other AE** (8); **infection/irritation at infusion site** (2)
ILet Bionic Pancreas[4]
AE in children (<18 years) with T1D during treatment with Humalog or Novolog in randomized period of clinical trial: *Serious Events* • **Severe hypoglycemia:** 10.4 events per 100 person-years (vs 7.3 with SOC) • **DKA:** 0 events • **Other SAE:** 6.9 events per 100 person-years (vs 7.3 with SOC) *Other Events* (number of participants with event, %) • **Worsened A1c** from BL by >0.5%: 13 (12%) [vs 8% in SOC] • **Hyperglycemia ± ketosis, study-device related:** 68 (60.7%) [vs 0% SOC]; rate may be inflated in the Bionic Pancreas group since they were given a BG and Ketone meter with specific monitoring instruction. • **Hyperglycemia ± ketosis,** non-device related: 32 (27.1%) [vs 1.9% SOC] • **Non-severe hypoglycemia**: 1 (0.9%) [vs 0% SOC] • **Other AEs:** 7 (6.25%) [vs 0% SOC]

[a] *Includes AEs reported in the adverse events or adverse reactions section of device user guides. Both serious and non-serious AEs were included if reported in the adverse event section. Note that all products warn of the potential for hypoglycemia, hyperglycemia, and DKA.*

Abbreviations: A1c, hemoglobin A1c or glycated hemoglobin; AE, adverse event; DKA, diabetic ketoacidosis; LGS, low glucose suspend; No., number; PLGS, predicted low glucose suspend; TID, type 1 diabetes; SAE, serious adverse event; SOC, standard of care (comparator group);

Table H1. Potential or Observed Adverse Events during Insulin Pump System Clinical Studies per Manufacturer User Guides[a]

AE in adults (<18 years) with T1D during treatment with Humalog or Novolog in randomized period of clinical trial: *Serious Events* • **Severe hypoglycemia:** 25.5 events per 100 person-years (vs 14.2 with SOC) • **DKA:** 0 events, although 2 events (6.8 events per 100 person-years) occurred with another insulin (Fiasp); DKA events were attributed to infusion set failures. (vs 0 with SOC) • **Other SAE:** 3.6 events per 100 person-years (vs 7.1 with SOC) *Other Events* (number of participants with event, %) • **Worsened A1c** from BL by >0.5%: 4(4%) [vs 8% in SOC] • **Hyperglycemia ± ketosis, study-device related:** 27 (25.2%) [vs 0% SOC]; rate may be inflated in the Bionic Pancreas group since they were given a BG and Ketone meter with specific monitoring instruction. • **Hyperglycemia ± ketosis**, non-device related: 12 (11.2%) [vs 0% SOC] • **Non-severe hypoglycemia:** 1 (0.9%) [vs 0% SOC] • **Other AEs:** 7 (6.25%) [vs 5.5% SOC] Device Issues in adults or children during 13-week RCT: 472 total events, with 223 (47.2%) of them being associated with an AE • ILet devices issues related to an AE (No. issues reported from 219 participants): infusion set issue (132), cartridge issue (16), battery/charging issue (5), algorithm-related issue (4), motor issue (3), alarm issue (2), skin irritation at infusion set (2), algorithm issue with user error (1)
t:slim X2 pump alone[16]
• No AE reported by user guide
t:slim X2 with Basal-IQ[12]
AE in people with T1D ages 6-72 years in 3-week treatment period of clinical trial: • No severe hypoglycemic events • No other device-related AE in the Basal-IQ study arm

[a] *Includes AEs reported in the adverse events or adverse reactions section of device user guides. Both serious and non-serious AEs were included if reported in the adverse event section. Note that all products warn of the potential for hypoglycemia, hyperglycemia, and DKA.*

Abbreviations: A1c, hemoglobin A1c or glycated hemoglobin; AE, adverse event; DKA, diabetic ketoacidosis; LGS, low glucose suspend; No., number; PLGS, predicted low glucose suspend; TID, type 1 diabetes; SAE, serious adverse event; SOC, standard of care (comparator group);

Table H1. Potential or Observed Adverse Events during Insulin Pump System Clinical Studies per Manufacturer User Guides[a]

t:slim X2 with Control-IQ[13]
Device-related AE (number of events; N=78 participants received Control-IQ) in children 6-13 years with T1D over 4-6 months in a clinical trial: • No severe hypoglycemic events • No DKA events • **Ketosis** with infusion site failure (8); **hyperglycemia** with defective cartridge (1); Device-related AE (number of events; N=112 people received Control-IQ) in adolescents/adults 14-71 years with T1D over 4-6 months in a clinical trial: • No severe hypoglycemic events • **Ketosis** with infusion site failure (3); **hyperglycemia** with infusion site failure (4); hyperglycemia with defective cartridge (1); **DKA** due to infusion set failure (1) Among children and adults, non-device related AE were primarily related to user error.

[a] Includes AEs reported in the adverse events or adverse reactions section of device user guides. Both serious and non-serious AEs were included if reported in the adverse event section. Note that all products warn of the potential for hypoglycemia, hyperglycemia, and DKA.

Abbreviations: A1c, hemoglobin A1c or glycated hemoglobin; AE, adverse event; DKA, diabetic ketoacidosis; LGS, low glucose suspend; No., number; PLGS, predicted low glucose suspend; TID, type 1 diabetes; SAE, serious adverse event; SOC, standard of care (comparator group);

APPENDIX I – ADDITIONAL INFORMATION ABOUT INSULIN PUMP RISKS

The following is a discussion of risks associated with insulin pump with discussion about potential differences between pumps/systems.

- **Hypoglycemia, hyperglycemia, and associated sequelae (eg, DKA, seizures, coma, death)**.
  - Over- or under-delivery of insulin from insulin pumps can result in low or high blood glucose. All insulin pumps carry these risks,[4-10,12-14,16] which can occur due to hardware or software failures (including from the pump, dosing software, or CGM) or user error. Unique features of pumps/systems may contribute to the way system failures occur.
    - Insulin infusion set occlusions or air bubbles that interrupt insulin delivery can cause elevated blood glucose.[4] Tubeless patch-pumps lack infusion sets, limiting the mechanisms for occlusions compared to tubed pumps.[29] However, blockages may still occur with tubeless systems. With Omnipod systems, an occlusion may result from a "…blocked cannula, a Pod malfunction, or from using old or inactive insulin…" (Omnipod 5 user guide, Page 168).[9-11] Electronic pumps (ie, all pumps except V-go) monitor for interrupted insulin delivery and can sound an occlusion alarm.[4-13,16] Time to occlusion alarms vary by type of insulin delivery (basal or bolus) and the basal delivery rate, with time to alarm being longest at low basal infusion rates. See **Appendix J** for a comparison of time to occlusion alarms for all electronic insulin pumps.
    - Unintentional insulin delivery may occur when users accidentally press touchscreens for systems controlled by touchscreen. Users should take steps to prevent accidentally changing insulin delivery. This is especially a concern when insulin pumps/systems are managed by a caregiver. All electronic pumps with buttons/touchscreens on the pump offer caregiver settings to prevent changes to the systems (as described below). Omnipod systems that are controlled by a separate device/phone do not offer these settings.[9,10]
      - Using the iLet Bionic Pancreas Limited Access feature, users can set a passcode preventing access to meal announcements, cartridges, and setting without the passcode.[4] It is recommended that caregivers managing another's diabetes with t:slim X2 with Basal-IQ/Control-IQ activate the security PIN to prevent changes to settings or accidental automatic insulin bolus with the Quick Bolus feature.[12,13] Similarly, the Feature Lock function (including Quick Bolus lock) is available to caregivers using the t:slim X2 pump alone.[16] MiniMed systems offer Block Mode, preventing delivery of a bolus or setting modifications.[5-8] Although, Block mode does not prevent remote boluses from the CONTOUR NEXT LINK 2.4 meter for the MiniMed 630G.[5] The screens of controller devices (eg, smartphone App or PDM) for Omnipod 5 and DASH can be locked and require a PIN for use.[9,10]

- **Infection, skin irritation, bleeding, bruising, pain, rash, or other reactions at the insulin infusion or CGM sensor sites**.
  - All devices carry these risks.[4-10,12-14,16] Insulin pump users should rotate infusion sites[5-10,12-14,16] and CGM sensor sites[141,142], avoid placing system components on red/inflamed skin,[9,10,14] or skin with scars, moles, stretch marks, or tattoos[4,9,10,12,13,16], and remove the device component if skin at the placement site is red or inflamed.[4-10,14]

- When insulin pumps are not used with a CGM, risks associated with CGM sensor placement are avoided. Nonetheless, since all systems require some components be placed on the skin, it is not possible to avoid these risks entirely. Patch-pumps avoid the risks from infusion set placement; however, the entire pump is placed on the skin using adhesive. Omnipod systems are not recommended for people with allergies to acrylic adhesive or fragile skin that may be damaged by adhesive.[9-11]
- Lipodystrophy, including the more frequent lipohypertrophy or less frequent lipoatrophy, can occur at insulin infusion sites. Changes in the body fat at the administration site can interfere with insulin absorption, potentially having deleterious effects.[24]

- **Sensor (wire) fracture or infusion set cannula fracture**
  - Although it seems to be a rare occurrence,[6,12,13] it is possible for sensors (eg, sensor wires)[4-8,12,13] or infusion site cannula[4,12,13,16] to break and become trapped under the skin. Patients should contact a healthcare professional for removal if this occurs.[4,6,12,13]
  - Systems including a CGM are at risk for sensor facture,[4-8,12,13] although this risk is not listed by the Omnipod 5 User guide.[9]
  - Infusion site cannula breakage is formally considered a risk for iLet Bionic Pancreas and t:slim X2 (with or without Basal-IQ/Control-IQ)[4,12,13,16]; as this risk is not listed user guides for other systems, it is unclear if the risks differ between pumps/systems.

- **Small part choking hazard for young children.**
  - All devices other than V-Go warn that small parts associated with the device are choking hazards if swallowed by young children.[4-10,12,13,16] People using these devices, especially caregivers to young children using these devices, should take precautions to prevent choking. There are warnings regarding different parts of accessories being a choking hazard; however, except for differences between systems using a CGM and those without (CGM sensor and transmitter are choking hazards), risks seem similar between devices.

APPENDIX J – TIME TO OCCLUSION DETECTION ALARM BY PUMP

Table J1. Time between Blockage and Insulin Pump/System Occlusion Alarm

Operation	Typical or Average Time	Maximum Time
V-go[14]		
	No information provided by the "Instructions for Patient Use"	
MiniMed 630G, 770G and 780G[5-8]		
10 U bolus, std speed	95 s	136 s
10 U bolus, quick	10 s	14 s
1 U/hr basal	2.5 hr	3.8 hr
0.025 U/hr basal	142.0 hr	178.3 hr
Omnipod DASH and Omnipod 5[9,10]		
5 U bolus	33 min	35 min
1 U/hr basal	3 hr	5.5 hr
0.05 U/hr basal	51 hr	80 hr (expired Pod)
iLet Bionic Pancreas[4]		
≥ 4 U bolus	11 s	15 s
1 U/hr basal	2 hr 51 min	3 hr 52 min
0.1 U/hr basal	29 hr 29 min	39 hr 25 min
t:slim X2 ± Basal-IQ or Control-IQ[12,13]		
≥ 3 U bolus	1 min 2 s	3 min
2 U/hr basal	1 hr 4 min	2 hr
0.1 U/hr basal	19 hr 43 min	36 hr

Abbreviations: hr, hour; min, minutes; s, seconds; U, units of insulin;

APPENDIX K – COMPARISON OF PUMP INSULIN DELIVERY ACCURACY

Table K1. Pump Insulin Delivery Accuracy per User Guides

Insulin Pump/System	Basal Delivery Accuracy	Bolus Delivery Accuracy
V-go[14]	± 10%	± 10%
MiniMed 630G[5] MiniMed 770G[6] MiniMed 780G[7,8]	± 5% (at rates of 1 U/hr) ± 10% (at rates of 0.025 U/hr)	± 5% (for ≥ 0.1 Unit) ± 20% (for <0.1 Unit)
Omnipod DASH[10] Omnipod 5[9]	± 5% (at rates ≥ 0.05 U/hr)	± 5% (for ≥ 1.0 Unit) ± 0.05 Units (for < 1.0 Unit)
iLet Bionic Pancreas[4]	± 5% (at max rate of 10 U/hr and intermediate rate of 1.0 U/hr) ± 15% (at min rate of 0.1 U/hr)	± 5% (for 30 Units, 5 Units, and 0.5 Units)
t:slim X2 ± Basal-IQ or Control-IQ[12,13]	± 5% Delivery rate may vary by up to 15% until delivery of 3 Units following 1,000 ft of elevation change.	± 5%

Abbreviations: U, units of insulin;