COLLEGE OF PHARMACY
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UTAH MEDICAID DUR REPORT
SEPTEMBER 2023

AMBULATORY INSULIN PUMPS WITH CONTINOUS SUBCUTANEOUS INSULIN DELIVERY

Report finalized: August 2023
Report presented: September 2023

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ABBREVIATIONS

A1C	Glycosylated hemoglobin; hemoglobin A1C
AACE	American Association of Clinical Endocrinology
ABCD-DTN	Association of British Clinical Diabetologist's Diabetes Technology Network
ACE	Alternate controller enabled
ACO	Accountable Care Organization
ADA	American Diabetes Association
ADIP	Algorithm-driven insulin pump
AE	Adverse event
AID	Automated insulin delivery
BMI	Body mass index
CGM	Continuous glucose monitor
CSII	Continuous subcutaneous insulin infusion
DKA	Diabetic ketoacidosis
DUR	Drug Utilization Review
ES	Endocrine Society
FDA	Food and Drug Administration
FFS	Fee-for-service
FPG	Fasting plasma glucose
GDM	Gestational diabetes
HCL	Hybrid closed-loop
ISPAD	International Society for Pediatric and Adolescent Diabetes
LGS	Low-glucose suspend
MDI	Multiple daily injection
NICE	National Institute for Health and Care Excellence
OGTT	Oral glucose tolerance test
PA	Prior authorization
PDM	Personal Diabetes Manager
PG	Plasma glucose
PLGS	Predictive low-glucose suspend
RCT	Randomized controlled trial
SAP	Sensor-augmented insulin pump
SMBG	Self-monitoring blood glucose
T1D	Type 1 diabetes
T2D	Type 2 diabetes
US	United States

1.0 INTRODUCTION

Intensive insulin therapy, delivered through either multiple daily injections (MDI; ie, basal-bolus insulin therapy) or continuous subcutaneous insulin infusion (CSII) via an insulin pump (also called insulin pump therapy) is used to imitate the natural secretion of insulin by pancreatic beta cells among patients with insulin-deficient diabetes.[1,2] Although the availability of commercial insulin pumps dates back to the 1970s in the United States (US),[1,3,4] widespread adoption of this technology did not take place until the early 2000s.[2] In order to assist patients with diabetes in achieving precise glycemic control while minimizing diabetic-related micro- and macro-vascular complications, as well as hypoglycemia, CSII systems have made rapid technologic advancements since 1990.[1,2] Consequently, there are a variety of prescription, wearable ambulatory insulin pumps available on the market. Selection of a pump tends to be dependent on patient-specific factors (eg, preferences, lifestyle), including interoperability with a continuous glucose monitoring (CGM) device.[5]

Some advanced sensor-augmented insulin pumps (SAPs), which have CGM integration, are able to automatically suspend basal insulin delivery if sensor-measured glucose readings drop below a preset low-glucose limit (low-glucose suspend [LGS] system), or are predicted to drop below a preset low-glucose limit (predictive low-glucose suspend [PLGS] system).[4] Automated insulin delivery (AID) systems consist of an insulin pump, a CGM, and a software algorithm.[3] AID systems are able to automatically adjust insulin delivery based on sensor glucose readings, but the degree of automation is variable depending on the device.[5] Advanced AID systems allow for automatic correctional bolus doses in addition to automatic basal insulin delivery.[6-9] All AID systems are considered hybrid closed-loop (HCL) systems because they still require user input for pre-meal boluses and exercise.[5,10] Currently, the iLet Bionic Pancreas is the *most* automated AID system available in the US; it automatically adjusts insulin delivery, including meal boluses, in response to blood glucose levels without user input other than qualitative descriptions of carbohydrate intake.[5]

For the purposes of this report, we have categorized the reviewed insulin pumps into system types, based on their maximal automation capability (see **Table 1**).[11]

The objective of this report is to review the commercially available ambulatory insulin pumps, particularly those used for continuous subcutaneous insulin delivery, approved by the US Food and Drug Administration (FDA). This report does not address Do-It-Yourself AID systems, among other devices (see **Appendix A**). Additionally, the *Omnipod Eros* will not be addressed exhaustively in this report because it is scheduled to be discontinued from the US market in December 2023.[12]

Table 1. Classification of Reviewed Insulin Pump Devices Based on Maximal Automation Capability[a]

Conventional insulin pumps	Advanced SAPs		AID systems	
	SAP + LGS system	SAP + PLGS system	AID	Advanced AID[b]
Less automation; requires more user input →				*More automation; requires less user input*
• V-go • Omnipod DASH • Omnipod Insulin Management System (Omnipod Eros)	• MiniMed 630G	• t:slim X2 with Basal-IQ Technology	• Omnipod 5 • MiniMed 770G	• MiniMed 780G • t:slim X2 with Control-IQ Technology • iLet Bionic Pancreas (*most automated system*)

[a] *Some devices may be used without the assistance of advanced technology (ie, LGS, PLGS, AID)*

[b] *In addition to automatically adjusting basal insulin delivery, advanced AID systems can also deliver automated correctional boluses, and the iLet Bionic Pancreas only requires meal announcement to deliver auto-calculated meal boluses*[11]

Abbreviations: AID, automated insulin delivery; LGS, low-glucose suspend; PLGS, predictive low-glucose suspend; SAP, sensor-augmented pump

2.0 METHODS

To identify relevant US and select international guidelines, we searched the following organizational websites for diabetes clinical practice guidelines addressing the use of insulin pumps in an ambulatory setting:

- American Diabetes Association (ADA): https://diabetes.org/
- American Association of Clinical Endocrinology (AACE): https://www.aace.com/
- Endocrine Society (ES): https://www.endocrine.org/
- International Society for Pediatric and Adolescent Diabetes (ISPAD): https://www.ispad.org/

Given the rapid advancements in diabetes technology in the past decade, we focused on guidelines published within the past 5 years. The TRIP medical database was also searched for relevant guidelines using the search term "insulin pump", with results restricted to guidelines.

To gain additional insight on appropriate candidacy for AID systems, we also reviewed guidance from the Association of British Clinical Diabetologist's Diabetes Technology Network (ABCD-DTN)[13] and a 2022 joint consensus statement from the European Association for the Study of Diabetes and the ADA.[14]

Device user guides were obtained from manufacturers' websites and were referenced, along with FDA 510(k) documents, for information about the devices' approved indication, basic features, and contraindications.

3.0 DISEASE OVERVIEW

Diabetes encompasses a cluster of metabolic conditions characterized by elevated blood glucose levels most commonly caused by insulin resistance and/or deficiency.[15,16] Persistent, chronic, hyperglycemia contributes to micro- and macro-vascular complications (eg, cardiovascular disease, cerebrovascular disease, retinopathy, neuropathy), diabetic ketoacidosis (DKA), among others,[17] and leads to premature mortality if untreated.[18,19] Over 37 million adults in the US have some form of diabetes, with the number of diagnosed cases more than doubling within the past two decades.[20] Diabetes is classified into types: type 1 diabetes (T1D; previously termed "juvenile-onset diabetes" or "insulin-dependent diabetes"),[21] type 2 diabetes (T2D; previously termed "adult-onset diabetes" or "non-insulin-dependent diabetes"),[21] gestational diabetes (GDM), diabetes due to other causes (eg, cystic fibrosis, monogenic syndromes [eg, neonatal diabetes]), or medication- or chemical-induced diabetes.[16,21] The most common is T2D (90%–95% of cases),[20,21] followed by T1D (5%–10% of cases),[16,20,21] and GDM (2%–10% of pregnancies).[22]

Patients with T1D have complete, or almost complete, insulin deficiency that is caused by an immune-mediated damage to the insulin-producing beta cells in the pancreas.[16,17] Peak incidence of T1D is between 10 to 14 years of age,[19] but onset may occur at any age.[17,23] Because of the underlying pathology of T1D, insulin therapy is essential for patients with this condition.[24]

Patients with T2D have some degree of insulin deficiency, resulting from defective insulin secretion (ie, beta cell exhaustion), and frequently, peripheral insulin resistance.[16,21] Symptoms of T2D tend to develop over years.[16,25] The mean onset of age for T2D is >45 years; however, the incidence in the US among younger adults and pediatric patients is rising.[25] Due to the loss of function in pancreatic beta cells over time, patients with T2D will eventually require insulin treatment.[26] Risk factors for developing T2D include older age, excessive body weight (generally a body mass index [BMI] ≥25 kg/m^2), and physical inactivity.[21]

GDM is a significant complication that arises during pregnancy, characterized by the onset of hyperglycemia diagnosed in the second or third trimester[21] in women who do not have overt diabetes prior to pregnancy.[21,22,27] Some pregnant women may experience hyperglycemia, potentially due to undiagnosed preexisting diabetes,[22] as a result of underlying pancreatic beta cell dysfunction.[21,27] Pregnant women with GDM are usually asymptomatic,[22] but the condition is associated with negative maternal, fetal, and neonatal outcomes.[21,28] Although GDM typically resolves after delivery,[27] women previously diagnosed with GDM are generally at an increased risk of developing T2D later in life.[21,22]

For an overview of the diagnosis of diabetes, refer to **Appendix B**.

4.0 INSULIN PUMP OVERVIEW

In the US, approximately 350,000 to 515,000 patients with diabetes use CSII[29]; >35,000 patients using CSII are estimated to have T2D.[30] CSII (also called insulin pump therapy) imitates the natural secretion of insulin by constantly infusing insulin at a basal rate and allowing for bolus doses when needed (either manually or automatically depending on the device).[5] Either rapid-acting or ultra-rapid acting insulin is used for CSII, depending on the device. Devices deliver insulin through tubing to a subcutaneously inserted cannula or needle, or the pump itself contains a cannula that directly attaches to the skin,

allowing for insulin delivery without the need for tubing (referred to as a "patch pump").[2,3,5] See **Appendix C** for a list of insulin pump component terminology.

The following bullet points describe categories/technologies of the various types of reviewed insulin pumps:

- **Conventional insulin pumps**: able to deliver basal insulin at pre-programmed user-selected rates, and bolus insulin based on manually inputted user parameters (eg, insulin-to-carbohydrate ratio, glucose targets).[10]
- **Advanced sensor-augmented pumps (SAPs):** a SAP combines a conventional insulin pump with CGM data that is viewable separately or on the pump; advanced SAP systems are capable of using the CGM data to autonomously suspend insulin delivery.[2,14] Note that the following system types are sometimes classified as a unique system type or an AID system,[31] and there is mixed consensus among published literature of their classification.[3,4,10]
    - **Low-glucose suspend (LGS) pumps:** able to automatically interrupt basal insulin delivery based on CGM sensor readings if they drop below a pre-set low glucose limit (eg, 70 mg/dL); potentially allows for the reduction of severe or nocturnal hypoglycemic episodes.[3-5] Without user intervention, typically the suspension remains in effect for up to 2 hours,[4,5] but can be manually overridden at any time.[4]
    - **Predictive low-glucose suspend (PLGS) pumps:** able to automatically suspend basal insulin delivery preemptively if sensor-measured glucose readings are *predicted* to drop below a pre-set low glucose limit within the preceding 30 minutes to prevent hypoglycemia.[3,4] Typically, the duration of insulin interruption varies from 30 to 120 minutes, depending on when the hypoglycemia resolves, at which point, the system automatically resumes insulin delivery.[4]
- **Automated insulin delivery (AID) systems[24]:** able to automatically increase or decrease basal insulin delivery based on a programed algorithm and sensor readings.[3-5] Therefore, AID systems are made up of three separate components: an insulin pump, a CGM, and a software algorithm.[3,4] Some systems also allow for automatic correction bolus doses for hyperglycemia, but still require user input for prandial boluses and exercise.[3,5,10,13,32]
- **Alternate controller enabled (ACE) pumps:** Some pumps (eg, t:slim X2), designated as alternate controller enabled (ACE), are interoperable with other system components (eg, CGMs, dosing software) enabling patients to tailor their devices based on technological needs/preferences.[33,34]

Systems can be either open-loop or closed-loop. Open-loop systems (eg, conventional insulin pumps) require user input to deliver basal and prandial insulin doses (no automation),[4] whereas closed-loop systems (ie, advanced SAPs, AID systems) augment insulin delivery based on direct communication between the CGM and insulin pump.[35]

The FDA uses a three-tiered classification system for devices that takes into account the associated risks of the device, as well as regulatory controls required to ensure the device is safe and effective.[36] Devices classified as class I typically exhibit the lowest risk to the user/patient, whereas those classified as class III represent the highest level of risk.[36] Generally, class II devices undergo a 510(k) review indicating the device is "substantially equivalent" to an existing marketed device; class III devices are typically brought

to market by a premarket approval, which must include clinical trial results.[37] The reviewed insulin pumps are either Class II or Class III devices (see **Table 2**).[38-47]

Insulin pump therapy (CSII) is considered the standard of care for patients with T1D given the robust evidence from randomized controlled trials (RCTs) showing improvements in glycemic control via hemoglobin A1C (A1C) and time in range (TIR), and less hypoglycemic events, compared to MDI.[26] Therefore, most insulin pump users are patients with T1D, with >60% of patients in the T1D Exchange registry on insulin pump therapy rather than MDI.[2] Although evidence is less robust, insulin pumps may also be a suitable option for certain patients with T2D or other types of insulin-deficient diabetes.[13,26]

4.1 Approved indications of reviewed insulin pumps

Most of the reviewed ambulatory insulin pumps are indicated for patients with diabetes mellitus, without specifying a particular type, but pumps that maximally function as an AID system are indicated for patients with T1D and have defined age criteria for use (either for the pump itself or the dosing software).[6-9,48,49] All reviewed insulin pumps are compatible with rapid-acting U-100 insulin (only Omnipod DASH and Omnipod Eros are also approved for use with ultra-rapid acting insulin),[50,51] but the specific insulin product varies by device.[6-9,48-54]

Among the reviewed pumps, V-Go, Omnipod DASH, and Omnipod Eros are classified as conventional insulin pumps because they do not allow for automatic augmentation of insulin delivery based on CGM sensor readings.[50,51,54] Although V-Go should only be used in adults,[54] there is no specified age restriction for Omnipod DASH and Omnipod Eros.[50,51] Each conventional insulin pump is suitable for patients who require insulin and are disposable, tubeless patches or pods that require frequent replacement (eg, every 1 to 3 days).[50,51,54] Omnipod DASH and Omnipod Eros are operated using a handheld Personal Diabetes Manager (PDM) controller which communicates with the pump to program settings and receive alerts.[50,51]

In contrast to the aforementioned conventional insulin pumps, the remaining reviewed insulin pumps (MiniMed 630G, MiniMed 770G, MiniMed 780G, t:slim X2 with Basal- or Control-IQ technology, Omnipod 5, and iLet Bionic Pancreas) offer varying degrees of insulin delivery automation.[6-9,48,49,52,53] The MiniMed 630G provides the least level of automation, whereas the iLet Bionic Pancreas boasts the most advanced automation capabilities.

The MiniMed 630G is an advanced SAP with only LGS capabilities, indicated for patients with diabetes (unspecified type) who require insulin[52]; this pump uses the Guardian 3 sensor or Enlite sensor*, but the patient must be at least 14 or 16 years of age, respectively.[55] The MiniMed 770G and 780G function as AID systems, automatically adjusting basal insulin delivery.[7,8,48] The MiniMed 780G, an advanced AID system, can also automatically deliver correctional bolus doses (up to 12/hour) based on sensor readings.[7,8] Additionally, the MiniMed 780G is compatible with the Guardian 4 sensor, which does not require calibration,[7] whereas the MiniMed 770G uses the Guardian 3 sensor which requires routine calibration (minimum of twice daily).[48] The MiniMed 770G and 780G are approved for patients with T1D

* The MiniMed 630G was initially available with the Enlite sensor, but it appears this sensor may no longer be available in the US (https://www.diabetes.shop/sensors)

(≥2 years of age for 770G or ≥7 years of age for 780G).[7,8,48] All reviewed MiniMed pumps can be operated as conventional insulin pumps (without automation).[7,8,48,52] The MiniMed 770G and 780G are also useable as advanced SAPs with LGS and PLGS without automated basal or corrective bolus delivery.[7,8,48]

The t:slim X2 insulin pump can operate as a conventional pump or with advanced SAP or AID technology (with Basal-IQ or Control-IQ software, respectively) as an ACE device (requires CGM integration[†]).[9,53,56] This pump is approved for patients ≥6 years of age with diabetes mellitus who require insulin therapy.[56] When the pump is used with *Basal-IQ* technology, the pump is able to automatically suspend insulin delivery based on current (sensor reading <70 mg/dL) or predicted (<80 mg/dL within 30 minutes) low blood glucose values[53]; using *Control-IQ* technology, the pump works as an AID system to automatically adjust basal insulin delivery, including allowing for correctional boluses (up to 1/hour) to prevent hyperglycemia.[9] Unlike Basal-IQ technology which has a broad indication,[53] Control-IQ technology is specifically indicated for patients with T1D.[9]

Similarly, the Omnipod 5 and iLet Bionic Pancreas system function as AID systems with ACE pumps that work with interoperable technology (SmartAdjust or iLet Dosing Decision Software, respectively) to automatically adjust and pause insulin delivery in response to current and predicted sensor readings.[6,49] The iLet Bionic Pancreas is also able to automatically give correctional bolus doses (up to 12/hour) *and* meal doses, requiring the patient to only announce the meal type and approximate size.[6] Omnipod 5 is indicated for diabetes management in anyone who requires insulin, but the SmartAdjust technology is approved for use in those with T1D who are at least 2 years of age.[49] The iLet Bionic Pancreas pump and dosing software are approved for persons ≥6 years of age, with the stand-alone pump indicated for those with diabetes mellitus, and the software approved for patients with T1D.[6] Omnipod 5 is operable as a conventional insulin pump, whereas the iLet Bionic Pancreas is only operable as an AID system.[6,49]

Despite the automation features of some of these insulin pumps, it is essential to recognize that they do not replace proactive diabetes management.[57] Because automated systems rely on the individual components (eg, CGM) to work properly, if a disruption in the system occurs (eg, CGM is unable to communicate with the insulin pump, CGM malfunction), automatic features may not function correctly, necessitating user intervention.[57]

Table 2 provides a brief description and summarizes the approved indications for the reviewed insulin pumps, which can vary depending on the system components and technology software.

[†] If the user prefers to use the pump *without* CGM integration, Basal- or Control-IQ technology cannot be used and glucose readings will not be displayed on the pump.[9,53]

Table 2. Descriptions and Approved Indications for Reviewed Insulin Pumps

Device name Initial approval year	**Pump and/or pump system description**	**Indications[a] per manufacturer's user guide (unless otherwise noted)**
Conventional insulin pumps (open-loop system)[b, c]		
V-Go[54] December 2010[38]	• Wearable **tubeless** patch pump, Class II device • Available as pre-set basal delivery, administered once-daily in a 24-hour period: ○ 20 units (V-Go 20) ○ 30 units (V-Go 30) ○ 40 units (V-Go 40) • Should be filled with rapid-acting U100 insulin using EZ Fill ○ Insulin lispro (Humalog) and insulin aspart (NovoLog) have been found to be compatible with the device • Minimum capacity reservoir: V-Go 20, 0.56 mL; V-Go 30, 0.66 mL; V-Go 40, 0.76 mL • Must be disposed of and replaced each day	• For continuous subcutaneous insulin delivery in **adults who require insulin**: ○ V-Go 20: continuous infusion of 20 units of basal insulin per 24 hours (0.83 units/hour) + on-demand bolus insulin (2 unit increments; may administer up to 36 units of bolus dosing in a 24-hour period) ○ V-Go 30: continuous infusion of 30 units of basal insulin per 24 hours (1.25 units/hour) + on-demand bolus insulin (2 unit increments; may administer up to 36 units of bolus dosing in a 24-hour period) ○ V-Go 40: continuous infusion of 40 units of basal insulin per 24 hours (1.67 units/hour) + on-demand bolus insulin (2 unit increments; may administer up to 36 units of bolus dosing in a 24-hour period)
Omnipod DASH[50] June 2018[39]	• Wearable **tubeless** pod pump, Class II device • Operated by a wireless Android controller (Personal Diabetes Manager) to deliver bolus doses and program pump settings, and to receive notifications • Compatible with CONTOUR NEXT ONE blood glucose meter to be paired with the controller • Compatible with *rapid-acting* U100 insulin: insulin aspart (NovoLog), insulin lispro (Humalog; Admelog), insulin glulisine (Apidra) ○ Apidra: useable for 48 hours; others are usable for 72 hours • Compatible with *ultra-rapid-acting* U100 insulin: insulin lispro-aabc (Lyumjev), insulin aspart (Fiasp) • Provides continuous insulin delivery for up to 72 hours (3 days), with the pod holding up to 200 units of insulin	• For continuous subcutaneous insulin delivery at fixed or variable rates for the management of **diabetes mellitus in persons who require insulin**
Omnipod Insulin Management System (Omnipod Eros)[51 d] December 2012[40]	• Wearable **tubeless** pod pump, Class II device • Operated by a wireless controller (Personal Diabetes Manager) with built-in FreeStyle blood glucose meter (may also manually enter readings from any blood glucose meter) ○ Built-in blood glucose meter is compatible with FreeStyle test strips and control solution • Compatible with *rapid-acting* U100 insulin: insulin aspart (NovoLog), insulin lispro (Humalog; Admelog), insulin glulisine (Apidra) • Compatible with *ultra-rapid-acting* U100 insulin: insulin lispro-aabc (Lyumjev), insulin aspart (Fiasp) • Provides continuous insulin delivery for up to 72 hours (3 days), with the pod holding up to 200 units of insulin	• For the management of diabetes mellitus in **persons who require 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 (should NOT be used for the diagnosis or screening of diabetes mellitus)
Sensor augmented pump (SAP) with low-glucose suspend (LGS) (closed-loop system)		
MiniMed 630G[52 e] August 2016[41]	• Wearable, battery-operated pump that requires an infusion set, Class III device • Operated by buttons on the pump • Compatible with the CONTOUR NEXT LINK 2.4 meter; meter is compatible with CONTOUR NEXT test strips • Pairable with the Guardian Sensor 3 and Guardian Link 3 transmitter, or the Enlite sensor to function as a SAP[55]	• For continuous subcutaneous insulin delivery at fixed or variable rates and continuous glucose monitoring using an interstitial sensor for the management of **diabetes mellitus in persons who require insulin.** The approved age for use as a SAP depends on the CGM sensor used: ○ **≥14 years of age** when used with the **Guardian Sensor 3,**[55] or ○ **≥16 years of age** when used with the **Enlite Sensor**[55]

[a] Some devices have separate indications based on the system components (eg, insulin pump vs. dosing algorithm). When applicable, the indication for each component is specified separately.

[b] Open-loop systems require user input to deliver basal and prandial insulin doses (no automation).[4,31]

[c] All other pumps are also able to function as conventional insulin pumps (except the iLet Bionic Pancreas); however, are listed in this table according to their more advanced technologies (advanced SAP or AID). Stand-alone pump indications are included in those sections for formatting simplicity.

[d] Will be discontinued in the US in December 2023, and it is advised by the manufacturer that prescribers switch patients to the Omnipod 5 or Omnipod DASH.[8]

[e] The MiniMed systems (MiniMed 630G/770G/780G) come with the SmartGuard technology already included on the pump; therefore, user guides list the indication with respect to the entire system (pump + technology + sensor + other system components).[45-47,52]

[f] AID systems are able to automatically adjust basal insulin delivery based on sensor readings, and advanced AID systems are also able to automatically give correctional boluses, but currently all AID systems require some degree of user intervention.[4]

Abbreviations: AID, automated insulin delivery; CGM, continuous glucose monitor; dL, deciliter; LGS, low-glucose suspend; mg, milligram; mL, milliliter; PLGS, predictive low-glucose suspend; SAP, sensor augmented pump; T1D, type 1 diabetes

Table 2. Descriptions and Approved Indications for Reviewed Insulin Pumps

Device name Initial approval year	Pump and/or pump system description	Indications[a] per manufacturer's user guide (unless otherwise noted)
	• Compatible with rapid-acting U100 insulin: insulin aspart (NovoLog) and insulin lispro (Humalog) • Pump life expectancy is 4 years, with the reservoir holding up to 300 units of insulin • When used with SmartGuard technology, insulin delivery is automatically stopped for up to 2 hours if sensor	• *Limitation of use: not designed to make lasting treatment adjustments nor to directly prevent or treat hypoglycemia, but is able to provide information about when a fingerstick may be needed (per Guardian 3 sensor readings). Therapy adjustments should be made based on blood glucose meter readings.*
Sensor augmented pump (SAP) with low-glucose suspend (LGS) + predictive low-glucose suspend (PLGS) (closed-loop system)		
t:slim X2 with Basal-IQ technology[53] July 2018[42]	• Wearable, rechargeable battery-operated touchscreen pump that requires an infusion set, Class III device[58] • Compatible with Dexcom G6 CGM • Compatible with rapid-acting U100 insulin: insulin aspart (NovoLog) and insulin lispro (Humalog) • Cartridge holds up to 300 units of insulin • Able to update software to add features using a personal computer, and connect wirelessly to other compatible devices using the t:connect mobile app • When used with Basal-IQ technology, insulin delivery is automatically suspended if current sensor readings <70 mg/dL, and/or sensor readings are predicted to be <80 mg/dL within the next 30 minutes	• **Stand-alone pump** is indicated for subcutaneous insulin delivery at fixed or variable rates for the management of **diabetes mellitus in persons ≥6 years of age who require insulin** • **Basal-IQ technology** (to function as an advanced SAP system) is indicated for **persons ≥6 years of age with diabetes mellitus** • **Bolus calculator** is for the management of diabetes mellitus
Automated insulin delivery (AID) systems (closed-loop systems)[f] [4]		
Omnipod 5[49] January 2022[43]	• Wearable **tubeless** pod pump, Class II device • Operated using the Omnipod 5 App (using an Insulet controller or compatible smartphone) • Compatible with Dexcom G6 CGM • Compatible with rapid-acting U100 insulin: insulin aspart (NovoLog) and insulin lispro (Humalog; Admelog) • Pod may be worn for up to 3 days and holds up to 200 units of insulin	• **Stand-alone pump** is indicated for subcutaneous insulin delivery at fixed or variable rates for the management of **diabetes mellitus in people who require insulin** • **SmartAdjust technology** (to function as an AID system) is indicated for **persons with T1D aged ≥2 years** • **SmartBolus calculator** is indicated for **persons with diabetes mellitus aged ≥2 years** who require rapid-acting U100 insulin
MiniMed 770G[48] [e] August 2020[44]	• Wearable battery-operated pump that requires an infusion set, Class III device • Operated by buttons on the pump • Able to receive notifications and track blood glucose levels using the MiniMed mobile app with a compatible smartphone • Compatible with the Accu-Chek Guide Link meter, must use Accu-Chek Guide test strips • Able to be used with the Guardian Sensor 3 and Guardian Link 3 transmitter • Compatible with rapid-acting U100 insulin: insulin aspart (NovoLog) and insulin lispro (Humalog) • Optional CareLink Connect app is able to access system data by using a USB port from a personal computer (Blue Adapter) to allow health care providers to view data and select alerts • Pump life expectancy is 4 years, with the reservoir holding up to 300 units of insulin • When used with SmartGuard technology, basal delivery is automatically adjusted using sensor readings	• For subcutaneous insulin delivery at fixed or variable rates, and continuous glucose monitoring using an interstitial sensor for the management of **T1D in persons ≥2 years of age who require insulin** • *Limitation of use (per user guide): "The Guardian Sensor (3) has not been evaluated and is not intended to be used directly for making therapy adjustments, but rather to provide an indication of when a fingerstick may be required. All therapy adjustments should be based on measurements obtained using a blood glucose meter and not on values provided by the Guardian Sensor (3)." (page 8)*[48]

[a] *Some devices have separate indications based on the system components (eg, insulin pump vs. dosing algorithm). When applicable, the indication for each component is specified separately.*

[b] *Open-loop systems require user input to deliver basal and prandial insulin doses (no automation).*[4,31]

[c] *All other pumps are also able to function as conventional insulin pumps (except the iLet Bionic Pancreas); however, are listed in this table according to their more advanced technologies (advanced SAP or AID). Stand-alone pump indications are included in those sections for formatting simplicity.*

[d] *Will be discontinued in the US in December 2023, and it is advised by the manufacturer that prescribers switch patients to the Omnipod 5 or Omnipod DASH.*[8]

[e] *The MiniMed systems (MiniMed 630G/770G/780G) come with the SmartGuard technology already included on the pump; therefore, user guides list the indication with respect to the entire system (pump + technology + sensor + other system components).*[45-47,52]

[f] *AID systems are able to automatically adjust basal insulin delivery based on sensor readings, and advanced AID systems are also able to automatically give correctional boluses, but currently all AID systems require some degree of user intervention.*[4]

Abbreviations: AID, automated insulin delivery; CGM, continuous glucose monitor; dL, deciliter; LGS, low-glucose suspend; mg, milligram; mL, milliliter; PLGS, predictive low-glucose suspend; SAP, sensor augmented pump; T1D, type 1 diabetes

Table 2. Descriptions and Approved Indications for Reviewed Insulin Pumps

Device name Initial approval year	Pump and/or pump system description	Indications[a] per manufacturer's user guide (unless otherwise noted)
Advanced automated insulin delivery (AID) systems (closed-loop systems)[f] [4]		
MiniMed 780G[7,8] [e] April 2023[45]	• Wearable battery-operated pump that requires an infusion set, Class III device • Operated by buttons on the pump • Able to receive notifications and track blood glucose levels using the MiniMed mobile app with a compatible smartphone or smart watch • Compatible with the Accu-Chek Guide Link meter, must use Accu-Chek Guide test strips • Pairable with the Guardian Sensor 3 or 4, and Guardian Link 3 or 4 transmitter • Compatible with rapid-acting U100 insulin: insulin aspart (NovoLog) and insulin lispro (Humalog) • Optional CareLink Connect app is able to access system data by using a USB port from a personal computer (Blue Adapter) to allow health care providers to view data and select alerts • Pump life expectancy is 4 years, with the reservoir holding up to 300 units of insulin • When used with SmartGuard technology, basal insulin delivery rate is automatically adjusted (with the allowance of automatic correctional bolus doses) based on sensor readings	• For subcutaneous insulin delivery at selectable rates, and continuous glucose monitoring using an interstitial sensor for the management of **T1D in persons ≥7 years of age who require insulin** • *Limitation of use: sensor (Guardian 3 or 4) is not designed to make treatment adjustments when the pump is in manual mode (non-automated). Therapy adjustments should be made based on blood glucose meter readings.*
t:slim X2 with Control-IQ technology[9] December 2019[46]	• Wearable, rechargeable battery-operated touchscreen pump that requires an infusion set, Class II (special controls) device[59] • Compatible with Dexcom G6 CGM • Compatible with rapid-acting U100 insulin: insulin aspart (NovoLog) and insulin lispro (Humalog) • Cartridge holds up to 300 units of insulin • Able to update software to add features using a personal computer, and connect wirelessly to other compatible devices using the t:connect mobile app (able to control some features from the smartphone) • When used with Control-IQ technology, insulin delivery is automatically suspended if sensor readings are predicted to be <70 mg/dL within the next 30 minutes, and the basal insulin delivery rate is automatically adjusted (with the allowance of automatic correctional bolus doses) based on sensor readings	• **Stand-alone pump** is indicated for subcutaneous insulin delivery at fixed or variable rates for the management of **diabetes mellitus in persons ≥6 years of age who require insulin** • **Control-IQ technology** (to function as an AID system) is indicated for **persons ≥6 years of age with T1D**
iLet Bionic Pancreas System[6,60] May 2023[47]	• Wearable, rechargeable battery-operated touchscreen pump that requires an infusion set, Class II (special controls) device • Compatible with Dexcom G6 CGM • Compatible with rapid-acting U100 insulin: insulin aspart (NovoLog) and insulin lispro (Humalog) • Maximum capacity of the reservoir is 180 units of insulin • When used with iLet Dosing Decision Software, insulin delivery is automatically suspended and adjusted (with the allowance of automatic correctional bolus doses) based on sensor readings. Additionally, automatically delivers meal boluses with the announcement of a meal	• **Stand-alone pump** is indicated for subcutaneous insulin delivery for the management of **diabetes mellitus in persons ≥6 years of age** • **iLet Dosing Decision Software** is indicated for **persons ≥6 years of age with T1D**

[a] Some devices have separate indications based on the system components (eg, insulin pump vs. dosing algorithm). When applicable, the indication for each component is specified separately.

[b] Open-loop systems require user input to deliver basal and prandial insulin doses (no automation).[4,31]

[c] All other pumps are also able to function as conventional insulin pumps (except the iLet Bionic Pancreas); however, are listed in this table according to their more advanced technologies (advanced SAP or AID). Stand-alone pump indications are included in those sections for formatting simplicity.

[d] Will be discontinued in the US in December 2023, and it is advised by the manufacturer that prescribers switch patients to the Omnipod 5 or Omnipod DASH.[8]

[e] The MiniMed systems (MiniMed 630G/770G/780G) come with the SmartGuard technology already included on the pump; therefore, user guides list the indication with respect to the entire system (pump + technology + sensor + other system components).[45-47,52]

[f] AID systems are able to automatically adjust basal insulin delivery based on sensor readings, and advanced AID systems are also able to automatically give correctional boluses, but currently all AID systems require some degree of user intervention.[4]

Abbreviations: AID, automated insulin delivery; CGM, continuous glucose monitor; dL, deciliter; LGS, low-glucose suspend; mg, milligram; mL, milliliter; PLGS, predictive low-glucose suspend; SAP, sensor augmented pump; T1D, type 1 diabetes

4.2 Comparison of automated insulin delivery (AID) system features

The 5 FDA-approved AID systems (Omnipod 5, MiniMed 770G/780G, t:slim X2 with Control-IQ technology, and the iLet Bionic Pancreas) are indicated for continuous subcutaneous insulin delivery in patients with T1D.[6-9,48,49] Omnipod 5 and MiniMed 770G have the youngest approved age for use (patients ≥2 years) among the reviewed AID systems.[48,49] Currently, available AID systems require some degree of user input for prandial insulin dosing (eg, carbohydrate intake).[14] Of the reviewed AID systems, the iLet Bionic Pancreas is the most automated AID system (the only system that allows for automatic prandial boluses after user-initiated meal announcement) and requires the least user input to initialize automation.[6] However, this system arguably offers the least customization, especially for certain scenarios that would require a temporary change in the target glucose value (eg, exercise, illness). Each of the reviewed AID systems have various features that differ between them.

Regarding physical characteristics, the Omnipod 5 is the only AID system that is tubeless; others require tubing (infusion sets) for insulin delivery.[6-9,48,49] The maximum insulin reservoir/cartridge capacity is the lowest for the iLet Bionic Pancreas (180 units), whereas most other systems are able to hold up to 300 units.[6-9,48,49] Unlike the Omnipod 5, and MiniMed 770G and 780G which are waterproof, the t:slim X2 with Control-IQ technology and the iLet Bionic Pancreas are watertight.[6-9,48,49] Therefore, the manufacturer recommends not wearing the t:slim X2 when bathing, swimming, surfing, scuba diving, or other aquatic activities, and not at all in hot tubs or saunas.[9] Similarly, the iLet Bionic Pancreas should not be worn at all during water-related activities (eg, swimming, bathing).[6]

All of the reviewed AID systems require certain parameters to be entered initially for automation mode to begin, but the iLet Bionic Pancreas requires the least amount of information.[6-9,48,49] Except for the iLet Bionic Pancreas, all reviewed AID systems require the user to meet a minimum and/or maximum total daily insulin threshold to safely use the automated technology, with the t:slim X2 with Control-IQ technology also requiring a minimum and maximum weight threshold for automation mode to be used.[7-9,48,49] Only the MiniMed 780G, t:slim X2 with Control-IQ technology, and the iLet Bionic Pancreas allow for automatic corrective bolus delivery[6-9]; the caveat to this feature when used with the MiniMed 780G and t:slim X2 with Control-IQ technology is that the sensor glucose reading must exceed a particular high threshold, and with the t:slim X2 with Control-IQ technology, is only able to be used once within a set duration.[7-9]

In addition to the insulin pump hardware, AID systems comprise of integrated CGM components.[6-9,48,49] The MiniMed 770G and 780G are compatible with the Guardian 3, and in the case of the MiniMed 780G, also the Guardian 4; other AID systems (Omnipod 5, t:slim X2 with Control-IQ technology, and iLet Bionic Pancreas) are compatible with the Dexcom G6 CGM system.[61,62] For optimal performance, the Guardian 3 requires calibration multiple times a day, whereas the Guardian 4 and Dexcom G6 do not require calibration.[62]

Most systems offer a flexible glucose target, with the MiniMed 780G having the lowest available target of 100 mg/dL[61,62]; the iLet Bionic Pancreas is unique by having “lower”, “usual” and “higher” for the target options, but these correlate to 110 mg/dL, 120 mg/dL, and 130 mg/dL, respectively.[62] The Omnipod 5, MiniMed 770G and 780G, and the t:slim X2 with Control-IQ have adjustable target glucose settings to modulate insulin delivery accordingly.[7-9,48,49] The Omnipod 5, and MiniMed 770G and 780G

allow the target glucose to temporarily change to a fixed value (150 mg/dL) for a user-set duration when exercising or sick; the temporary higher target glucose must be manually initiated.[7-9,48,49] The t:slim X2 with Control-IQ technology also has a similar exercise setting but it must be manually started/stopped, and the glucose target is a range rather than a fixed value (140−160 mg/dL).[9] Unlike the Omnipod 5 and MiniMed 770G and 780G, the t:slim X2 with Control-IQ technology also has a specific setting for sleep that changes the glucose target to a range of 112.5−120 mg/dL, and does not allow for automatic correctional boluses to prevent nocturnal hypoglycemia.[7-9,48,49] The iLet Bionic Pancreas also allows patients to set a different target glucose for sleep.[6] Although the Omnipod 5 does not have a specific sleep setting, users are able to set different target glucose settings for the automated system throughout the day (up to 8 in a 24-hour period),[49] so a patient could schedule a different target during sleep.

It is important for patients to realize that there may be certain situations where the system automatically reverts to manual mode (open-loop), or a more limited automated mode if available. The limited automation mode is typically triggered by a loss of CGM data.[61,62] Except for the t:slim X2 with Control-IQ technology, all of the reviewed AID systems can function in a limited automated mode, but the level of automation can vary between systems. For example, the Omnipod 5, and MiniMed 770G and 780G are able to automatically deliver basal insulin, but it is not adjusted and no correctional boluses are given in this mode.[61,62] In contrast, the iLet Bionic Pancreas is able to automate all insulin delivery, including prandial boluses, for a period of up to 72 hours in limited automated mode, as long as blood glucose values are manually entered when prompted.[62] For most AID systems, if the limited automation mode is used for an extended period of time and/or CGM data is not restored, the pump will revert to manual mode (pre-programmed insulin delivery). Notably, the iLet Bionic Pancreas is the only reviewed AID system that it is unable to operate in a manual insulin delivery mode, and if automation ceases, the user is required to use an alternative method for insulin delivery (eg, MDI).[6,62]

Importantly, users may choose to operate their AID system in manual mode if more personalized control over insulin delivery is desired.[32] Such scenarios may include but are not limited to competition in sports, pregnancy, ketones/illness, steroid use, or altered mental status.[32,63] However, generally the cumulative duration spent outside of automated insulin delivery, frequently attributed to sensor disconnections, device alerts, and operational challenges, exhibits a direct correlation with deteriorations in glycemic control.[30]

Table 3 compares some of the features of reviewed AID systems.

Table 3. Comparison of Automated Insulin Delivery (AID) Insulin Pump Systems[61,62]

	Omnipod 5[49]	MiniMed 770G[48]	MiniMed 780G[7,8]	t:slim X2 with Control-IQ[9]	iLet Bionic Pancreas[6]
General characteristics					
System type	AID	AID	Advanced AID	Advanced AID	Advanced AID
Indicated population[a]	Patients ≥2 years of age with T1D	Patients ≥2 years of age with T1D	Patients ≥7 years of age with T1D	Patients ≥6 years of age with T1D	Patients ≥6 years of age with T1D
ACE (interoperable) pump?	Yes	No	No	Yes	Yes
Tubeless?	Yes	No	No	No	No
Pump water protection	Waterproof; safe up to 25 feet for up to 1 hour	Waterproof; safe up to 12 feet for 24 hours		Watertight; safe up to 3 feet for 30 minutes	Watertight; safe up to 12 feet for 30 minutes
Insulin reservoir capacity	200 units	300 units	300 units	300 units	180 units
Pairable CGM components	Dexcom G6 CGM system	Guardian 3 sensor	Guardian 3 or 4 sensors	Dexcom G6 CGM system	Dexcom G6 CGM system
Maximum sensor life expectancy	10 days	7 days	7 days	10 days	10 days
Automatic insulin delivery					
Required parameter(s) for automation mode	• Basal insulin profiles • Insulin to carbohydrate ratios • Correction factors • Active insulin time	• Insulin to carbohydrate ratios • Blood glucose value • Active insulin		• User's body weight • Total daily insulin • Basal insulin profiles • Insulin to carbohydrate ratios • Correction factors	• User's body weight
When is automation mode able to be activated?	• Immediately	• Delayed by up to 48 hours	• Delayed by 5 to 48 hours depending on how long the pump is off	• Immediately	• Immediately (carb meal bolus option not available initially)
Minimum basal increments (units/hour)	0.05	0.025		0.001 (at rates ≥0.1)	0.045 (units/5 minute); will wait to deliver dose if less than the minimum limit[64]
Automatic adjustment of basal delivery?	• Yes, auto-adjusts rate every 5 minutes • Suspends delivery for SG <60 mg/dL	• Yes, auto-adjusts rate every 5 minutes if >120 mg/dL (up to 12 corrections/hour)[65]	• Yes, auto-adjusts rate every 5 minutes (up to 12 corrections/hour)	• Yes, auto-adjusts rate every 5 minutes (up to 1 correction/hour) • Suspends delivery for PSG ≤70 mg/dL	• Yes, auto-adjusts rate every 5 minutes (up to 12 corrections/hour) • Suspends delivery for SG <60 mg/dL
Automatic bolus delivery?	No	No	• Yes, only if glucose is >120 mg/dL (available every 5 minutes)[66]	• Yes, only if PSG >180 mg/dL in next 30 minutes (available every hour)[62] • Target glucose: 110 mg/dL	• Yes, allows for automated correction (available every 5 minutes) and meal bolus with user announcement
Automatic prandial bolus delivery?	No, delivered manually by the user; requires entry of grams of carbohydrates				Yes, requires announcement of the meal before eating or 15 to 30 minutes after. Must select meal type ("breakfast", "lunch", "dinner") and relative carbohydrate amount ("more", "usual", "less")
Allows extended bolus (in automation mode)?	No	No	No	Yes, for a max of 2 hours	No
Algorithm target glucose value or range (mg/dL)	5 options: 110, 120, 130, 140, 150	120	3 options: 100, 110, 120	112.5 to 160	3 options: "Usual" (120), "Lower" (110), "Higher" (130)
Minimum and/or maximum total daily insulin for automatic mode	≥5 units	≥8 units and ≤250 units	≥8 units and ≤250 units	10–100 units *and* weigh 25–140 kg	No requirement

[a] *The listed indicated population is for the dosing algorithm, and in some instances for the entire system (MiniMed 770G, MiniMed 780G) when a separate indication was not provided in the user guides for the dosing algorithm*

[b] *There is no need to adjust programmed pump settings because all insulin delivery is automated by the algorithm, with no traditional programmed pump settings*

Abbreviations: ACE, alternative controller enabled; AID, automated insulin delivery; CGM, continuous glucose monitor; dL, deciliter; kg, kilogram; MDI, multiple daily injections; mg, milligram; N/A, not applicable; PSG, predicted sensor glucose; SG, sensor glucose; T1D, type 1 diabetes

Table 3. Comparison of Automated Insulin Delivery (AID) Insulin Pump Systems[61,62]

	Omnipod 5[49]	MiniMed 770G[48]	MiniMed 780G[7,8]	t:slim X2 with Control-IQ[9]	iLet Bionic Pancreas[6]
Special features for certain scenarios	• *Exercise activity:* target glucose changes target glucose to 150 mg/dL *and* basal insulin doses decrease by approximately 50% for a user-set duration (1 to 24 hours)	• *Temporary (used for short-term activities that require a different basal rate [eg, exercise]):* target glucose changes to 150 mg/dL for a user-set duration of up to 12 hours (MiniMed 770G) or 24 hours (MiniMed 780G) ○ Does not allow for automatic correctional boluses (MiniMed 780G)		• *Exercise activity:* target glucose changes to 140–160 mg/dL; user must manually start/stop • *Sleep:* target glucose changes to 112.5–120 mg/dL; user can manually start/stop or program a schedule ○ No automatic correctional boluses	• *Sleep*: set a target glucose (110 mg/dL, 120 mg/dL, or 130 mg/dL) for a user-specified duration
Allowed user adjustments in automated mode					
Basal rate	No	No	No	Yes	N/A[b]
Insulin to carbohydrate ratio	Yes	Yes	Yes	Yes	N/A[b]
Active insulin time	Yes	Yes	Yes	No, set at 5 hours	N/A[b]
Correction factor (sensitivity)	Yes	No	No	Yes	N/A[b]
Reversion to manual (pre-programmed insulin delivery) mode from automation mode					
Limited automation mode available?	• Yes, automation limited. Delivers automated basal insulin without SG adjustment	• Yes, safe basal mode. Delivers automated basal insulin without automatic SG adjustment (and correction boluses, for the MiniMed 780G)		• No, pump reverts to manual mode, with programmed basal insulin delivery settings	• Yes, BG-run mode allows for continued automation using user-entered blood glucose values, for a maximum period of 48 or 72 hours • All insulin dosing will stop when BG-run mode expires without receiving CGM values
Triggers for limited automation mode	• Loss of CGM data for ≥20 minutes • In response to an "Automated Delivery Restriction" alarm	• Sensor accuracy error • CGM data loss • Max/min insulin delivery constraints		N/A	• Loss of CGM data
Triggers that force the system to revert to manual mode	• In response to an "Restriction Advisory" alarm; user must turn auto mode back on after 5 minutes once the alarm is cleared	• SG >300 mg/dL for 1 hour • SG >250 mg/dL for 3 hours • Using safe basal mode for longer than 90 minutes	• No blood glucose value is entered into the pump before the time to exit to manual mode expires	• No CGM data ≥20 minutes; returns to auto mode once CGM data is received	• No manual mode option • Upon BG-run mode expiring without receiving CGM data, insulin delivery stops (resumes once CGM data is re-established) • User will need to switch to alternative insulin therapy (eg, MDI), if needed (can use system information to inform dosing)

[a] *The listed indicated population is for the dosing algorithm, and in some instances for the entire system (MiniMed 770G, MiniMed 780G) when a separate indication was not provided in the user guides for the dosing algorithm*

[b] *There is no need to adjust programmed pump settings because all insulin delivery is automated by the algorithm, with no traditional programmed pump settings*

Abbreviations: ACE, alternative controller enabled; AID, automated insulin delivery; CGM, continuous glucose monitor; dL, deciliter; kg, kilogram; MDI, multiple daily injections; mg, milligram; N/A, not applicable; PSG, predicted sensor glucose; SG, sensor glucose; T1D, type 1 diabetes

4.3 Switching to new or different pumps and/or pump systems by the same manufacturer

Patients with existing pumps and/or pump systems may need to upgrade to a newer pump over time. If the patient has an Omnipod Insulin Management System (Omnipod Eros), which is going to be discontinued later this year in the US,[12] patients will need to receive a new prescription and hardware to transition to the Omnipod 5 or Omnipod DASH,[67,68] and in addition, will need a separate prescription for the Dexcom G6 CGM if receiving the Omnipod 5.[12]

Patients who have a t:slim X2 pump with CGM integration desiring to use or switch between Basal- or Control-IQ technology will need a new prescription for the algorithm, but not new hardware.[69] After receiving the prescription and completing the necessary required training, users may change the t:slim X2 software by connecting the pump to a personal computer and downloading the software from the sponsor's website.[69]

Although not specifically addressed by Medtronic (the device manufacturer of the MiniMed insulin pumps), users would most likely require a new prescription and hardware to switch from the MiniMed 630G to the MiniMed 770G or 780G. Because the MiniMed 770G and 780G use the same physical pump, only a new prescription and software upgrade, which may be performed remotely, is needed to switch from the 770G to the 780G.[70] Medtronic offers several device upgrade programs to help users transition to a newer pump model or system.[71]

5.0 GUIDELINE RECOMMENDATIONS‡

For recommendations on the use of insulin pumps, we reviewed diabetes technology guidelines from the American Diabetes Association (ADA)[3] and American Association of Clinical Endocrinology (AACE).[10] In addition, we reviewed a non-technology specific diabetes guideline published by the Endocrine Society (ES),[72] and a 2022 expert consensus statement on the use of AID systems.[32] For specific recommendations among pediatric patients, we also reviewed guidelines from the International Society for Pediatric and Adolescent Diabetes (ISPAD).[4,73] In addition, guidelines on the management of diabetes in other special populations (ie, pregnant women, older adults) were reviewed.[28,74]

For the ISPAD guidelines, recommendations are frequently specified for T1D youth.[4,73] Since supportive evidence and discussion is in the context of T1D and there is no mention of T2D, including cited studies, it is unclear the extent to which non-T1D specific recommendations apply to people without T1D[4]; with respect to diabetes types, other guidelines have a broader target patient population (eg, T1D, T2D).[3,10,72,75] In general, reviewed guidelines have stronger recommendation strengths for the use of insulin pumps, including AID systems, among patients with T1D relative to those with other types of diabetes (eg, T2D).

‡ Note that the definitions for the type of insulin-delivery technologies varied across reviewed guidelines. Nonetheless, guideline recommendations were interpreted to the best of our ability based on guideline-specific definitions.

5.1 Candidates for insulin pump therapy

Guidelines from the ADA (2023),[3] AACE (2021),[10] ISPAD (2022),[4] and ES (2022)[72] prefer AID systems to alternative insulin delivery systems (non-automated pumps, SAP ±LGS or PLGS, MDI) for most **adults and children with T1D** given the benefits in reducing A1C, improving time in range (TIR; discussed further in **Section 5.3**), and preventing hypoglycemia.[3,4,10] The ES guideline explicitly states a preference for real-time CGM use with algorithm-driven insulin pumps (ADIP), which includes AID systems and advanced SAP systems.[72] Furthermore, consensus recommendations from an international panel of experts on AID technologies strongly recommend offering AID systems to all patients with T1D, including children (aged 7 to 14 years), adolescents, and adults, and for AID systems to be considered for preschool-aged children (<7 years of age).[32] AACE strongly recommends LGS and PLGS systems for all patients with T1D for the purpose of reducing hypoglycemia severity and duration, or mitigating hypoglycemia, respectively.[10] Specifically in pediatric patients, ISPAD strongly recommends SAP with PLGS or LGS for those with T1D if an AID system is unavailable.[4] Overall, recommendations supporting the use of insulin pumps (including AID and advanced SAP systems) for T1D in adults or pediatric patients 7 years and older are graded A, based on high quality evidence.[3,4,10,32] As part of the strong recommendation for AID systems for people with T1D, AACE also notes that AID systems can be considered for patients with diabetes who have suboptimal glycemic control, hypoglycemia unawareness, significant glycemic variability, or have permissive hyperglycemia in response to hypoglycemia-related fear, but it's unclear to what extent this part of the recommendation applies to people without T1D; evidence cited by the AACE to support this recommendation is only among people with T1D.[10]

For those receiving MDI (≥3 injections daily)[10] who do not desire or cannot use an AID system, the ADA strongly recommends offering any insulin pump to adults and youth with T1D, or based on expert opinion, to those with other types of insulin-deficient diabetes.[3] AACE recommends an insulin pump with viewable-only CGM data (SAP or as separate devices) for all patients with diabetes when an AID system or LGS/PLGS system is unavailable or unable to be used.[10] An insulin pump *without* CGM may be an option for patients with diabetes who have achieved glycemic targets with minimal TBR, experience infrequent symptomatic hypoglycemia, and regularly self-check blood glucose (minimum of 4 times daily for T1D).[10] ISPAD recommends non-integrated pump therapy (ie, conventional pump without CGM) as a potential suitable option for children who do not have access to more advanced systems (eg, advanced SAPs, AIDs).[4] Conventional insulin pump therapy has demonstrated safety and effectiveness in pediatric patients with T1D, aiding in the attainment of glycemic targets and reduced hypoglycemic events. Furthermore, conventional insulin pump therapy has shown to mitigate chronic complications of T1D in pediatric patients, even among pediatric patients with comparable A1C values receiving MDI.[4]

Based on an open-label, multicenter, RCT among adults with poorly controlled T2D on MDI, insulin pump therapy (using the MiniMed Paradigm VEO, an advanced SAP with LGS capability) demonstrated a significant reduction in mean A1C at 6 months compared to MDI (treatment difference of −0.7%); both treatment groups had a baseline A1C of 9%.[76] Furthermore, the mean total daily insulin dose significantly decreased with insulin pump treatment versus MDI by week 27 (97 units vs 122 units, respectively).[76] Presumably based on this evidence, the ADA strongly recommends insulin pump therapy as an option for **adults and youth with T2D who require MDI** and can safely use a device, with the

selection of a particular device individualized (*Grade A*)[§].[3,75] Based on expert opinion (ie Grade E), the ADA also recommends offering AID systems to patients with any other type of diabetes requiring insulin therapy, including after pancreatectomy and patients with diabetes-related cystic fibrosis.[3] Similarly, panel experts advised offering "appropriate" AID systems to patients with T2D (*Grade C*[**]) or other types of diabetes (*Grade C for cystic fibrosis-related disease; Grade E*[††] *for pancreatectomy*) treated with MDI or already on insulin pump therapy.[32]

V-Go may be an alternative pump option for patients with T2D.[3,26] Based on mostly observational studies among adults with T2D, V-Go has shown to significantly improve baseline glycemic control (ie, A1C),[77-80] and reduce mean total daily insulin dose either from baseline[77,78,80] or compared to MDI among patients with T2D.[79]

5.1.1 Pregnant women

The ADA recommends insulin as first-line pharmacotherapy for all pregnant women with preexisting T1D, T2D, or GDM.[28] Either MDI or insulin pump therapy is specifically recommended for pregnant women with T1D. Although insulin pumps tend to be favored by health care prescribers during pregnancy, their superiority over MDI remains uncertain. The ADA 2023 guideline does not make a recommendation regarding the use of insulin pumps for GDM.[28]

Based on low-level evidence, a 2022 consensus recommendation on the use of AID technologies recommends considering AID systems as an option during pregnancy complicated with T1D; no recommendation is provided regarding pumps for GDM.[32] A current limitation of most commercial AID systems is that the set glycemic target for automated basal delivery is higher than the recommended blood glucose target during pregnancy (fasting glucose <95 mg/dL)[28],[32] and most algorithms are not able to target <110 mg/dL (MiniMed 780G is an exception which can target 100 mg/dL). Nonetheless, some evidence suggests that AID use may be beneficial during pregnancy among women with T1D. [81-84] However, to further evaluate the support of AID technology in pregnancy, including safety and effectiveness, additional RCTs are required.[32]

ADA guideline authors note that PLGS insulin pumps may be a suitable option during pregnancy because the threshold for insulin suspension aligns with the recommended premeal and overnight glucose targets during pregnancy, potentially facilitating more assertive prandial dosing.[28]

5.1.2 Older adults

According to the ADA and expert consensus, use of advanced technologies, including AID systems, can be considered in older adults with T1D who have adequate cognitive function and ability to safely use such devices.[32,74] Therefore, older adults should have the same access to insulin pump therapy, including

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[§] Grade A is the highest level of evidence based on well-designed randomized clinical trials, or well-conducted meta-analysis of randomized controlled trials

[**] Grade C represents low-quality evidence based on poorly controlled or uncontrolled studies, or conflicting evidence where the majority of evidence supports the recommendation

[††] Grade E is based on expert consensus or clinical experience

AID systems, as younger individuals, both in terms of initiation and continued use.[3] Although most AID trials enrolled a relatively small number of older adults,[74] there is limited RCT evidence to support the use of AID systems in older adults with T1D to improve glycemic outcomes.[74,85,86]

As complications, cognitive impairment, and functional decline manifest in older individuals, simplification of insulin regimens may be warrented.[74] The ES (2019) guideline on older adults with diabetes suggests that simplification of insulin regimens may require that patients transition from insulin pump therapy to injections; this guideline does not provide any formal recommendations on the use of insulin pumps.[87] Tailoring insulin regimens in accordance with the patient's self-management capabilities and level of available social and medical support can reduce hypoglycemia and disease-related distress, while maintaining glycemic control.[74]

Many older adults with T1D often necessitate placement in long-term care settings (eg, nursing homes).[74] Unfortunately, staff who work within these settings may possess limited familiarity with insulin pumps or CGMs. Consequently, the ADA (2023) recommends that relevant staff within long-term care and rehabilitation facilities receive appropriate diabetes education, including on the use of insulin pumps.[74]

Table 4 provides a summary of the guideline and expert consensus recommendations, with the level of evidence.

Table 4. Recent US and International Guideline Ambulatory Insulin Pump or Insulin Pump System Recommendations

Recommendations (Evidence Rating[a,b,c])
American Diabetes Association (ADA), Diabetes Technology and Children and Adolescents Guidelines; 2023[3,75] Target age group/population for recommendations: youth and adults with diabetes
General device recommendations:
• The selection of an appropriate device should be personalized based on an individual's unique requirements, preferences, and proficiency. The caregiver's abilities and preferences should be incorporated in the decision-making process if they are involved in managing the patient's diabetes (eg, young child, person with cognitive impairment). (**E**) • Comprehensive education and training should be provided to individuals with diabetes and their caregivers, offered both initially and continuously, either through in-person or remote visits. Regular assessment of technique, results, and the individual's ability to use data (eg, sharing, uploading) should be conducted to monitor and adjust treatment. (**C**) • Continual access to **CSII (insulin pump therapy)**, CGM, and/or **AID** should be provided to patients with diabetes who have been using these devices, irrespective of their A1C levels or age. This access should be maintained consistently across various third-party payers. (**E**) • School-aged patients should have appropriate support for using prescribed diabetes technology (ie, CGMs, **CSII**, "connected insulin pens", **AID systems**) during their time at school. (**E**) • Starting CGM, **CSII**, and/or **AID** at an early stage of diabetes treatment can provide advantages based on the patient's/caregiver's preferences and requirements. (**C**)
Insulin pumps and automated insulin delivery (AID) systems:
• Offer **AID systems** to adults or youth with T1D (**A**) or adults or youth with other types of insulin-deficient diabetes (**E**) when they can safely use the device (alone or with a caregiver). Selection of a particular device should be individualized. • Offer **any insulin pump (eg, pump ± SAP with LGS)** to adults or youth with T1D (**A**) or adults or youth with other types of insulin-deficient diabetes (**E**) receiving MDI who can safely use the device (alone or with a caregiver), and who *prefer these devices to (or cannot use) an AID system*. Selection of a particular device should be individualized. (**A**) • **Insulin pumps** are an option for adults or youth with T2D requiring MDI who can use the device safely (alone or with a caregiver). Selection of a particular device should be individualized. (**A**)   ○ MDI or **insulin pump therapy** are recommended for youth with T2D who are no longer meeting glycemic goals on metformin and long-acting insulin (**E**)[75] • **Continuation of care:** "Individuals with diabetes who have been using continuous subcutaneous insulin infusion should have continued access across third-party payers."[3] (page 8) (**E**)
International Society for Pediatric and Adolescent Diabetes (ISPAD), Insulin Delivery Technology Guideline; 2022[4] Target age group/population for recommendations: children, adolescents, and young adults with diabetes
General recommendation(s) for insulin pump therapy:
• Offer the *most advanced* delivery technology available and appropriate (**B**) • Utilization of insulin pump therapy is recommended and appropriate for pediatric patients with diabetes, irrespective of their age (**A**) • The occurrence of infusion set failures is prevalent in all types of insulin pump therapy, necessitating immediate recognition to mitigate the risk of developing diabetic ketoacidosis (DKA) (**B**) • Insulin pump therapy is recommended for all youth with T1D (*ungraded statement*)
Insulin pump therapy (CSII):
• Insulin pump therapy has demonstrated safety and effectiveness in pediatric patients with T1D, aiding in the attainment of glycemic targets (**A**) • Insulin pump therapy reduces hypoglycemic events (**B**) • Even among pediatric patients with comparable A1C values receiving MDI, insulin pump therapy mitigates chronic complications of T1D in pediatric patients (**B**)

[a] *Evidence rating from 2023 American Diabetes Association (**ADA**) guideline[89], the 2022 International Society for Pediatric and Adolescent Diabetes (**ISPAD**) guideline,[90] and the **Expert Consensus Recommendations** for AID systems[28]: A (highest level of evidence): based on well-designed randomized clinical trials, or well-conducted meta-analysis of randomized controlled trials; 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 trial evidence): based on expert consensus or clinical experience*

[b] *Evidence rating from 2022 Endocrine Society (**ES**) guideline[91]: High certainty, very confident the true effect is close to the estimated effect; moderate certainty, somewhat confident in the effect estimate; low certainty, little confidence in the effect estimate; very low certainty, very little confidence in the effect estimate. Strong recommendation: benefits clearly outweigh the risks; Conditional recommendation: benefits probably outweigh the risks*

[c] *Evidence rating from American Association of Clinical Endocrinology (**AACE**) guideline[6]: 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 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 denotes a very strong recommendation, and Grade B denotes a strong recommendation. SoE: Strong (level I) evidence: RCT or meta-analysis of RCT; intermediate (level II) evidence: clinical research that is not an RCT or meta-analysis of RCTs, but has a comparator group (eg, observational studies)*

Abbreviations: A1C, hemoglobin A1C or glycosylated hemoglobin; AACE, American Association of Clinical Endocrinology; ADA, American Diabetes Association; ADIP, algorithm-driven insulin pump; AID, automated insulin delivery; BEL, best evidence level; CGM, continuous glucose monitoring; CSII, continuous subcutaneous insulin infusion; DKA, diabetic ketoacidosis; ES, Endocrine Society; GDM, gestational diabetes mellitus; HCL, hybrid closed-loop; ISPAD, International Society for Pediatric and Adolescent Diabetes; LGS, low-glucose suspend; MDI, multiple daily injections; PLGS, predictive low-glucose suspend; SAP, sensor-augmented pump; SMBG, self-monitoring of blood glucose; SoE, strength of evidence; T1D, type 1 diabetes; T2D, type 2 diabetes; TBR, time below range; TIR, time in range

Table 4. Recent US and International Guideline Ambulatory Insulin Pump or Insulin Pump System Recommendations

Recommendations (Evidence Rating[a,b,c])
Sensor-augmented pumps (SAPs [ie, insulin pump with viewable-only CGM data]):
• In terms of reducing A1C without elevating the risk of hypoglycemia or severe hypoglycemia, SAP demonstrated superiority over MDI with SMBG (**A**)   ○ To achieve these benefits, it is necessary to utilize the sensor for a minimum of 60% of the time (**A**)
Low-glucose suspend (LGS) and/or predictive low-glucose suspend (PLGS) systems:
• Compared to conventional insulin pumps or SAP without LGS, the utilization of LGS systems effectively diminishes the severity and duration of hypoglycemia, while maintaining glycemic control as indicated by A1C levels (**A**) • PLGS systems decrease "…frequency of and exposure to hypoglycemia."[4] (page 1407) (**A**) • Both LGS and PLGS systems do not result in an elevation of mean glucose levels. Additionally, these systems instill greater technologic confidence and trust, provide increased flexibility around mealtimes, and decrease diabetes-related distress for patients and their caregivers (**A**) • In the event AID systems are unavailable, PLGS systems are strongly recommended for all patients with T1D to reduce the occurrence of hypoglycemia (**A**) • In the event other advanced technology is unavailable, LGS systems are strongly recommended for all patients with T1D to minimize the severity and duration of hypoglycemic episodes (**A**)
Automated insulin delivery (AID) systems:
• "AID systems, also known as closed loop (CL), are strongly recommended for youth with diabetes."[4] (page 1407) (**A**)   ○ Because there is no mention, discussion, or citations that correspond to youth with T2D in the guideline, it is likely that this recommendation (rated level A) applies to youth with T1D, especially because authors recommend insulin pump therapy specifically for youth with T1D (on page 3). However, it is unclear the extent to which it applies to patients without T1D • AID systems enhance the duration spent within the time in range (TIR) by reducing both hypoglycemic and hyperglycemic episodes (**A**) • "AID systems are especially beneficial in attaining targeted glycemia in the overnight period."[4] (page 1407) (**A**)
General device patient education:
• When prescribing insulin delivery devices, standardized training should be given (**C**) • AID systems should be used as directed by person with diabetes and their caregivers to ensure ideal outcomes (**C**) • Youth and their caregivers should be counseled to have realistic expectations of insulin pump technology and advised on the amount of effort it takes for successful implementation (**B**)   ○ May be particularly important to address in those with suboptimal glycemic control, history of mood/burnout concerns, or are unengaged in the current treatment plan (**C**)
International Society for Pediatric and Adolescent Diabetes (ISPAD), Managing Diabetes in Preschoolers Guideline; 2022[73] Target age group/population for recommendations: children (aged 6 months to 6 years) with T1D
Insulin pump therapy:
• Whenever feasible, insulin pump therapy is the preferred approach for administering insulin to children <7 years of age with T1D (**E**) • HCL and AID systems should be adapted and made available for younger children to use (**A**). Consideration of the unique needs of preschoolers and toddlers should be addressed (eg, greater day-to-day variation in insulin requirements relative to older children) (**E**) • MDI may be used starting at the time of T1D diagnosis if pump therapy is unavailable (**E**)

*[a] Evidence rating from 2023 American Diabetes Association (**ADA**) guideline[89], the 2022 International Society for Pediatric and Adolescent Diabetes (**ISPAD**) guideline,[90] and the **Expert Consensus Recommendations** for AID systems[28]: A (highest level of evidence): based on well-designed randomized clinical trials, or well-conducted meta-analysis of randomized controlled trials; 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 trial evidence): based on expert consensus or clinical experience*

*[b] Evidence rating from 2022 Endocrine Society (**ES**) guideline[91]: High certainty, very confident the true effect is close to the estimated effect; moderate certainty, somewhat confident in the effect estimate; low certainty, little confidence in the effect estimate; very low certainty, very little confidence in the effect estimate. Strong recommendation: benefits clearly outweigh the risks; Conditional recommendation: benefits probably outweigh the risks*

*[c] Evidence rating from American Association of Clinical Endocrinology (**AACE**) guideline[6]: 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 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 denotes a very strong recommendation, and Grade B denotes a strong recommendation. SoE: Strong (level I) evidence: RCT or meta-analysis of RCT; intermediate (level II) evidence: clinical research that is not an RCT or meta-analysis of RCTs, but has a comparator group (eg, observational studies)*

Abbreviations: A1C, hemoglobin A1C or glycosylated hemoglobin; AACE, American Association of Clinical Endocrinology; ADA, American Diabetes Association; ADIP, algorithm-driven insulin pump; AID, automated insulin delivery; BEL, best evidence level; CGM, continuous glucose monitoring; CSII, continuous subcutaneous insulin infusion; DKA, diabetic ketoacidosis; ES, Endocrine Society; GDM, gestational diabetes mellitus; HCL, hybrid closed-loop; ISPAD, International Society for Pediatric and Adolescent Diabetes; LGS, low-glucose suspend; MDI, multiple daily injections; PLGS, predictive low-glucose suspend; SAP, sensor-augmented pump; SMBG, self-monitoring of blood glucose; SoE, strength of evidence; T1D, type 1 diabetes; T2D, type 2 diabetes; TBR, time below range; TIR, time in range

Table 4. Recent US and International Guideline Ambulatory Insulin Pump or Insulin Pump System Recommendations

Recommendations (Evidence Rating[a,b,c])
Endocrine Society (ES), Diabetes in Patients with High Hypoglycemia Risk Guideline; 2022[72] Target age group/population for recommendations: adults and children with diabetes (eg, T1D, T2D) with high hypoglycemia risk
Individuals with high hypoglycemia risk: those 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 duration of diabetes diagnosis (including ≥5 year insulin use), history of severe hypoglycemia or hypoglycemia unawareness, irregular eating schedules (including fasting, among others), alcohol consumption, or cognitive status that may prevent an appropriate response to a hypoglycemic event
Algorithm-driven insulin pump (ADIP): *Defined as a system consisting of an **insulin pump + CGM**, allowing adjustment of basal insulin delivery based on sensor data. Authors imply this to include advanced SAPs and AID systems; "ADIP is the term used to refer to all currently available forms of automated insulin delivery through devices in this guidelines." (page 5)*
• Use of real-time CGM and ADIPs instead of MDIs with SMBG (≥3 times daily)is suggested for adults and children with T1D (**conditional; low quality 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[10] Target age group/population for recommendations: patients with diabetes
Insulin pump without CGM:

• Option for patients with diabetes and the following characteristics (**Grade B; SoE: Intermediate-High; BEL 1**):
  ○ Glycemic target achievement and minimal time below range (TBR), or
  ○ Infrequent symptomatic hypoglycemia, and
  ○ Regularly self-checking blood glucose (minimum 4 times daily for T1D)

Insulin pump with CGM (SAP; with CGM data viewable on the pump or separate devices):
• All patients with diabetes treated with intensive insulin therapy "…who prefer not to use automated insulin suspension/dosing systems or have no access to them."[10] (page 521) (**Grade A; SoE: Intermediate-High; BEL 1**)
Advanced insulin pump technology (ie, LGS, PLGS, AID):

• **LGS and PLGS** (**Grade A; SoE: High; 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
  ○ Also consider for "…anyone with frequent hypoglycemia, impaired hypoglycemia awareness, and those who fear hypoglycemia leading to permissive hyperglycemia…"[10] (page 522)
• **AID systems** (**Grade A; SoE: High; BEL 1**):
  ○ All patients with T1D. **This is the preferred method of insulin delivery due to improving time in range (TIR) and reducing hyperglycemia**
  ○ Also consider for "…persons with diabetes with suboptimal glycemia, significant glycemic variability, impaired hypoglycemia awareness, or who allow for permissive hyperglycemia due to the fear of hypoglycemia…"[10] (page 522)

Insulin pump discontinuation:
• Providers should consider discontinuing insulin pump therapy for patients with diabetes who exhibit insufficient competence or safety in its usage, or prefer to no longer use this method of insulin delivery (**Grade A; SoE: Intermediate; BEL 1**)

[a] *Evidence rating from 2023 American Diabetes Association (**ADA**) guideline[89], the 2022 International Society for Pediatric and Adolescent Diabetes (**ISPAD**) guideline,[90] and the **Expert Consensus Recommendations** for AID systems[28]: A (highest level of evidence): based on well-designed randomized clinical trials, or well-conducted meta-analysis of randomized controlled trials; 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 trial evidence): based on expert consensus or clinical experience*

[b] *Evidence rating from 2022 Endocrine Society (**ES**) guideline[91]: High certainty, very confident the true effect is close to the estimated effect; moderate certainty, somewhat confident in the effect estimate; low certainty, little confidence in the effect estimate; very low certainty, very little confidence in the effect estimate. Strong recommendation: benefits clearly outweigh the risks; Conditional recommendation: benefits probably outweigh the risks*

[c] *Evidence rating from American Association of Clinical Endocrinology (**AACE**) guideline[6]: 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 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 denotes a very strong recommendation, and Grade B denotes a strong recommendation. SoE: Strong (level I) evidence: RCT or meta-analysis of RCT; intermediate (level II) evidence: clinical research that is not an RCT or meta-analysis of RCTs, but has a comparator group (eg, observational studies)*

Abbreviations: A1C, hemoglobin A1C or glycosylated hemoglobin; AACE, American Association of Clinical Endocrinology; ADA, American Diabetes Association; ADIP, algorithm-driven insulin pump; AID, automated insulin delivery; BEL, best evidence level; CGM, continuous glucose monitoring; CSII, continuous subcutaneous insulin infusion; DKA, diabetic ketoacidosis; ES, Endocrine Society; GDM, gestational diabetes mellitus; HCL, hybrid closed-loop; ISPAD, International Society for Pediatric and Adolescent Diabetes; LGS, low-glucose suspend; MDI, multiple daily injections; PLGS, predictive low-glucose suspend; SAP, sensor-augmented pump; SMBG, self-monitoring of blood glucose; SoE, strength of evidence; T1D, type 1 diabetes; T2D, type 2 diabetes; TBR, time below range; TIR, time in range

Table 4. Recent US and International Guideline Ambulatory Insulin Pump or Insulin Pump System Recommendations

Recommendations (Evidence Rating[a,b,c])
General device patient education:
• Comprehensive training on utilization and maintenance should be provided to all patients with diabetes using insulin delivery technology (**Grade A; SoE/Expert Opinion of Task Force: Intermediate; BEL 2**) ○ Device-specific training should be provided to patients with diabetes using an integrated device to ensure patient safety and appropriate use per manufacturer guidance (**Grade A; SoE/Expert Opinion of Task Force: Low-Intermediate; BEL 2**) • Prescribers should ensure that patients with diabetes who rely on insulin delivery technology are able to recognize the signs of a pump malfunction, be aware of whom to contact in case of such an event, and have a well-defined plan for emergency situations (eg, backup measures) (**Grade A; SoE/Expert Opinion of Task Force: Low; BEL 2**)
American Diabetes Association (ADA), Management of Diabetes in Pregnancy Guideline; 2023[28] Target age group/population for recommendations: women who are desiring or are currently pregnant
Preexisting T1D and T2D in pregnancy:
• Pregnant patients with T1D should use insulin therapy (**A**) ○ May use MDI or **insulin pump systems** (**C**) • Insulin is the first-line agent for pregnant patients with T2D (**B**)
Gestational diabetes mellitus (GDM):
• Lifestyle behavior change plays a critical role and can serve as an effective treatment approach for many affected individuals. However, if necessary to attain glycemic targets, insulin can be added as a adjunctive measure (**A**) • Insulin is the recommended medication of choice for treating hyperglycemia in patients with GDM. Metformin and glyburide should be avoided as initial treatment options because both medications can pass through the placenta to the fetus. (**A**) Long-term safety data is lacking for other oral and non-insulin injectable anti-hyperglycemic agents • There are no recommendations suggesting the use of insulin pumps for GDM
American Diabetes Association (ADA), Management of Diabetes in Older Adults Guideline; 2023[74] Target age group/population for recommendations: older adults ≥65 years of age with diabetes
Automated insulin delivery (AID) systems:
• Consider offering an AID system to older adults with T1D to reduce hypoglycemia risk (**B**) ○ Consider offering other advanced insulin delivery devices (eg, connected pens) to older adults with T1D (**E**)
General pharmacotherapy recommendations:
• If A1C targets can be maintained, intricate treatment strategies, particularly for insulin, should be simplified to lower the likelihood of hypoglycemia and polypharmacy, and reduce the disease burden (**B**)
Diabetes education:
• To enhance diabetes management among older adults, diabetes education can be considered for long-term care and rehabilitation staff (**E**)

*[a] Evidence rating from 2023 American Diabetes Association (**ADA**) guideline[89], the 2022 International Society for Pediatric and Adolescent Diabetes (**ISPAD**) guideline,[90] and the **Expert Consensus Recommendations** for AID systems[28]: A (highest level of evidence): based on well-designed randomized clinical trials, or well-conducted meta-analysis of randomized controlled trials; 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 trial evidence): based on expert consensus or clinical experience*

*[b] Evidence rating from 2022 Endocrine Society (**ES**) guideline[91]: High certainty, very confident the true effect is close to the estimated effect; moderate certainty, somewhat confident in the effect estimate; low certainty, little confidence in the effect estimate; very low certainty, very little confidence in the effect estimate. Strong recommendation: benefits clearly outweigh the risks; Conditional recommendation: benefits probably outweigh the risks*

*[c] Evidence rating from American Association of Clinical Endocrinology (**AACE**) guideline[6]: 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 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 denotes a very strong recommendation, and Grade B denotes a strong recommendation. SoE: Strong (level I) evidence: RCT or meta-analysis of RCT; intermediate (level II) evidence: clinical research that is not an RCT or meta-analysis of RCTs, but has a comparator group (eg, observational studies)*

Abbreviations: A1C, hemoglobin A1C or glycosylated hemoglobin; AACE, American Association of Clinical Endocrinology; ADA, American Diabetes Association; ADIP, algorithm-driven insulin pump; AID, automated insulin delivery; BEL, best evidence level; CGM, continuous glucose monitoring; CSII, continuous subcutaneous insulin infusion; DKA, diabetic ketoacidosis; ES, Endocrine Society; GDM, gestational diabetes mellitus; HCL, hybrid closed-loop; ISPAD, International Society for Pediatric and Adolescent Diabetes; LGS, low-glucose suspend; MDI, multiple daily injections; PLGS, predictive low-glucose suspend; SAP, sensor-augmented pump; SMBG, self-monitoring of blood glucose; SoE, strength of evidence; T1D, type 1 diabetes; T2D, type 2 diabetes; TBR, time below range; TIR, time in range

Table 4. Recent US and International Guideline Ambulatory Insulin Pump or Insulin Pump System Recommendations

Recommendations (Evidence Rating[a,b,c])
Expert Consensus Recommendations for Using AID systems; 2022[32] Target age group/population for recommendations: specified below
Target populations who should be considered for using an AID system:

• Adults, adolescents, and children (7 to 14 years of age) with T1D should be strongly considered for an AID system (**A**)
• May consider offering an AID system to:
  ○ Preschool-aged children (<7 years of age) with T1D (**B**)
  ▪ Because there is no mention, discussion, or citations that correspond to pre-school aged children with T2D, we infer that this recommendation (rated level B) applies to those with T1D, especially because all corresponding cited studies are within young children with T1D
  ○ Older adults (>65 years of age) with T1D (**B**)
  ▪ Because there is no mention, discussion, or citations that correspond to older adults with T2D, we infer that this recommendation (rated level B) applies to those with T1D, especially because all corresponding cited studies are within older adults with T1D
  ○ Pregnancy complicated with T1D (**C**)
• May consider offering an AID system to patients who have:
  ○ T2D if they are on intensive insulin therapy (MDI or insulin pump) (**C**)
  ○ Hypoglycemia unawareness or a history of moderate/severe hypoglycemia (**C**)
  ○ Comorbidities (eg, gastroparesis, chronic renal failure) (**C**)
  ○ Diabetes as a result of cystic fibrosis if they are on intensive insulin therapy (MDI or insulin pump) (**C**)
  ○ Pancreatectomy if they are on intensive insulin therapy (MDI or insulin pump) (**E**)

*[a] Evidence rating from 2023 American Diabetes Association (**ADA**) guideline[89], the 2022 International Society for Pediatric and Adolescent Diabetes (**ISPAD**) guideline,[90] and the **Expert Consensus Recommendations** for AID systems[28]: A (highest level of evidence): based on well-designed randomized clinical trials, or well-conducted meta-analysis of randomized controlled trials; 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 trial evidence): based on expert consensus or clinical experience*

*[b] Evidence rating from 2022 Endocrine Society (**ES**) guideline[91]: High certainty, very confident the true effect is close to the estimated effect; moderate certainty, somewhat confident in the effect estimate; low certainty, little confidence in the effect estimate; very low certainty, very little confidence in the effect estimate. Strong recommendation: benefits clearly outweigh the risks; Conditional recommendation: benefits probably outweigh the risks*

*[c] Evidence rating from American Association of Clinical Endocrinology (**AACE**) guideline[6]: 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 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 denotes a very strong recommendation, and Grade B denotes a strong recommendation. SoE: Strong (level I) evidence: RCT or meta-analysis of RCT; intermediate (level II) evidence: clinical research that is not an RCT or meta-analysis of RCTs, but has a comparator group (eg, observational studies)*

Abbreviations: A1C, hemoglobin A1C or glycosylated hemoglobin; AACE, American Association of Clinical Endocrinology; ADA, American Diabetes Association; ADIP, algorithm-driven insulin pump; AID, automated insulin delivery; BEL, best evidence level; CGM, continuous glucose monitoring; CSII, continuous subcutaneous insulin infusion; DKA, diabetic ketoacidosis; ES, Endocrine Society; GDM, gestational diabetes mellitus; HCL, hybrid closed-loop; ISPAD, International Society for Pediatric and Adolescent Diabetes; LGS, low-glucose suspend; MDI, multiple daily injections; PLGS, predictive low-glucose suspend; SAP, sensor-augmented pump; SMBG, self-monitoring of blood glucose; SoE, strength of evidence; T1D, type 1 diabetes; T2D, type 2 diabetes; TBR, time below range; TIR, time in range

5.2 Additional guidance for selecting candidates for AID systems

Based on a 2022 joint consensus report from the ADA and the European Association for the Study of Diabetes, the ideal patient for an AID system should[14]:

- Be capable of using the technology (eg, trained on how to use AID system components, trouble-shooting the system, recognize when to switch to a manual setting from automation)
- Have mental capacity and desire to use the system (eg, committed to improve glucose control)
- Have realistic expectations of the system's capabilities to potentially prevent negative feelings about system limitations
- Have the necessary training for appropriate use, including knowledge of how to transmit data from the device to health care providers, and be properly supported (eg, insurance coverage)

The Association of British Clinical Diabetologist's Diabetes Technology Network (ABCD-DTN) suggests certain patient populations may benefit from a HCL system (ie, AID), which includes but is not limited to the following[13]:

- All patients who met the requirements outlined in the National Institute for Health and Care Excellence (NICE) technology appraisal guidance on CSII (*summarized below*)[88]:
    - Insulin pump therapy should be used in adults and children (aged ≥12 years) with T1D on MDI if a) trying to achieve A1C targets results in hypoglycemia-distress and negatively impacts quality of life or b) A1C remains high (≥8.5%) even with appropriate care[88]
    - Insulin pump therapy should be used in children <12 years of age with T1D if a) MDI is deemed to be inappropriate or is not feasible, or b) MDI therapy is anticipated to be tried between 12 and 18 years of age[88]
- Patients who experience a significant amount of diabetes distress and/or burden associated with diabetes management
- Patients on MDI who are not achieving desired glycemic control even with "high-level management"
- Patients with a history of recurrent episodes of severe hypoglycemia, hypoglycemia unawareness (Gold score ≥4), or debilitating fear of hypoglycemia
- Patients with insulin-deficient diabetes (eg, T2D, monogenic, diabetes as a result of cystic fibrosis) who need MDI and are counting carbohydrates and fulfill any of the aforementioned criteria

AID systems may *not* be suitable for patients with very high or very low insulin requirements (algorithm may be less effective), visual impairment, or diabetes complications.[14] In addition, some patients may not be suited to start AID therapy if they have a lack of desire or commitment to improve glycemic control, or have severe psychiatric comorbidities (eg, anxiety, eating disorders, depression) that would impact successful implementation.[14]

5.3 Glycemic targets during insulin pump therapy

The initiation of continuous glucose monitor (CGM) devices, either real-time or intermittently scanned, should be considered for patients on insulin pump therapy (ie, CSII).[3,10,73,75] Assessing glycemic control by CGM provides timely feedback to allow for prompt and fine-tuned therapy adjustments to improve glycemic control and to reduce hypoglycemic events.[74,89] Patients with diabetes taking intensive insulin

regimens (eg, CSII) are encouraged to assess glucose levels using self-monitoring blood glucose (SMBG) and/or CGM prior to eating or exercising, at bedtime, occasionally post-prandially, when hypo- or hyperglycemia is suspected, after treating low blood glucose levels, and before critical tasks such as driving.[3] Whenever feasible, CGM should be used in conjunction with A1C measurements to evaluate glycemic control in patients prone to glycemic variability.[75]

Time in range (TIR), the proportion of time CGM readings are between 70−180 mg/dL, is an important metric for assessing CSII efficacy and can serve as a surrogate for A1C.[16,89] A 10% increase in TIR corresponds to 0.5% to 0.8% decrease in A1C.[90,91] Additionally, lower TIR is associated with diabetes-related microvascular complications.[89] ADA also supports using the time below range (TBR) and time above range (TAR) to evaluate treatment in patients using CGM.[89] Ideally, the goal for patients using CGM is to increase the TIR while minimizing the TBR.[16] ISPAD (2022) notes that a >70% TIR of 70−180 mg/dL or >50% of time in target of 70−140 mg/dL may be acceptable in children <7 years of age after the initial remission phase.[73]

Glycemic targets and A1C goals are individualized based on patient-specific factors such as age, co-morbidities, duration and progression of diabetes, life expectancy, ability to self-manage, motivation, hypoglycemia risk and awareness, and preferences.[89,90] **Appendix D** lists the glycemic targets and A1C goals for non-pregnant adults, older adults, children and adolescents, and pregnant women according to reviewed US guidelines (ADA and AACE).

Table 5 highlights time in range goals related to CGM parameters, based on a 2019 international expert-consensus statement[91] and supported by the ADA and AACE guidelines.[16,89]

Table 5. Time in Range Goals Based on Expert Consensus and ADA and AACE Guidelines[16,75,89-91]

Metric[a]	Youth or adults with T1D[b] or T2D	Pregnancy[c] [28]
Time in range (TIR)	>70% (>16 hours, 48 min) in the target range of 70−180 mg/dL	>70% (>16 hours, 48 min) in the target range of 63−140 mg/dL
Time below range (TBR)	• <4% (<1 hour) at <70 mg/dL • <1% (<15 min) at <54 mg/dL	• <4% (<1 hour) at <63 mg/dL • <1% (<15 min) at <54 mg/dL
Time above range (TAR)	• <25% (<6 hours) at >180 mg/dL • <5% (<1 hour, 12 min) at >250 mg/dL	• <25% (6 hour) at >140 mg/dL

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

[b] *For patients <25 years of age who have an A1C target of 7.5%, the TIR is approximately >60% instead of >70%. For older patients or those high-risk for hypoglycemia, the goal TIR of 70−180 mg/dL is >50%, and goal TAR of >250 mg/dL is <10%.*

[c] *TIR goals are mostly based on studies of pregnant women with T1D. Instead of >70%, the goal TIR changes to >90% for pregnant women with GDM or T2D[16]*

Abbreviations: AACE, American Association of Clinical Endocrinology; ADA, American Diabetes Association; dL, deciliter; mg, milligram; min, minutes; T1D, type 1 diabetes; T2D, type 2 diabetes; TIR, time in range; TBR, time below range; TAR, time above range

5.4 Insulin pump initiation

Diabetes technology should be prescribed by well-trained health care providers who can use the device proficiently, and oversee the application of these devices.[10] Ideally, diabetes care teams should be multidisciplinary, and may include an endocrinologist or primary care provider, and supportive staff (eg, certified diabetes care and education specialist, nurses, dietitians).[10] Initiation of insulin pump therapy may commence at diagnosis,[3] especially for patients with T1D. Starting CGM, CSII, and/or AID at an early stage of diabetes treatment is recommended by the ADA due to the proven benefits, especially for CGM (eg, reduction in A1C, greater satisfaction).[3] Considerations for starting pump therapy include evaluating caregiver/patient readiness, patient-desired pump type and settings, appropriate education on potential device complications (eg, infusion set failure), and if applicable, how to transition from MDI.[3] Selection of a particular device is personalized based on an patient's unique requirements, preferences, and proficiency.[3] If the patient relies on a caregiver to help manage their diabetes, the caregiver's abilities and preferences should be incorporated in the decision-making process.[3]

When starting SAP with LGS or PLGS, or AID systems, users should be advised on anticipated sensor use/wear, and how treatment may be affected when sensor use is interrupted.[4] Additionally, it is important for users and their caregivers to have realistic expectations of diabetes management when using an insulin delivery device.[4] For example, patients should be advised that glucose fluctuations may still occur and glycemia values may not always be within the targeted range. In addition, patients should still be engaged with their insulin delivery, especially around meals (the patient needs to count carbohydrates and administer pre-prandial boluses for most AID systems), and respond to alarms.[4] For patients using insulin pumps, the ADA recommends continuation of care with respect to CSII, CGM, and/or AID, irrespective of their A1C levels or age.[3]

Barriers to starting or continuing CSII in patients with T2D include limited insulin reservoir/cartridge size of currently available insulin pumps, and minimal evidence from RCTs evaluating CSII in this patient population.[26] Education and training for device use may also be a barrier, but it is likely patients with T2D would require less advanced systems than patients with T1D given their more simplistic insulin regimens.[26] Additionally, using a conventional device can help alleviate financial costs associated with more complex devices, but it is unclear how financial concerns may vary between MDI and conventional CSII.[26] Notably, prescribers should evaluate the use of adjunctive therapies (eg, metformin, glucagon-like peptide 1 receptor agonist) among patients with T2D, and if continuing such treatment would be appropriate with the use of an insulin pump.[32]

5.5 Patient/caregiver device education and support

To ensure appropriate and safe device use and to achieve maximal benefits, patients, and caregivers if applicable, should receive personalized, structured education, training, and clinical and technical support at device initiation and on an ongoing basis.[3,10,72] Education should ensure that patients with diabetes who rely on insulin delivery technology are able to recognize the signs of a pump malfunction, be aware of whom to contact in case of such an event, and have a well-defined plan for emergency situations (eg, backup measures).[10] It is also essential that patients have a firm understanding of basic diabetes management (eg, carbohydrate counting) even if they are using an AID system.[32] To gain an understanding of how individual system components operate, it may be necessary for technology naïve

patients to become competent in an insulin pump and CGM system before proceeding to a more advanced system (eg, HCL).[32] Depending on patient comfort level with diabetes technology, education can be provided in-person or remotely.[3] To ensure appropriate support for school-aged children, school personnel (eg, nurses) should also receive training for prescribed diabetes technologies (eg, CGM, CSII, AID systems).[3]

5.6 Insulin pump complications and discontinuation

Insulin pump complications may occur, which can arise from problems with infusion sets such as dislodgment or partial or complete occlusion; these issues increase the risk of ketosis and diabetic ketoacidosis (DKA), making early recognition and management essential.[3,4] Skin problems can also occur related to the pump (eg, lipohypertrophy, lipoartrophy, skin infections at the pump site, skin irritation).[3,4] Uncertainties exist regarding the optimal choice of cannula and the potential superiority of specific infusion sets based on patient-specific factors such as age or body composition.[4]

Overall, discontinuation of pump therapy is uncommon, but may be attributed to cost or wearability issues, pump dissatisfaction, or suboptimal glycemic outcomes.[3,4] Additionally, the occurrence of system-mandated exits, where users are required to revert to conventional pump settings due to the unavailability of automation, can ultimately lead to device discontinuation.[4] Ultimately the choice of discontinuing a device should be based on the user.[13]

Bear in mind that some patients with T1D may be more hesitant to use a insulin pump, especially an AID system, if they are unable to use the device safely, prefer to control their insulin delivery, have concerns on whether the system is able to appropriately accommodate insulin delivery based on certain situations (eg, pregnancy, exercising), or concerns about alarm frequency.[13]

6.0 ADDITIONAL CLINICAL EVIDENCE FOR PATIENTS WITH T2D

Results from the single-arm, multicenter, feasibility, outpatient trial of the Omnipod 5 system in adults (aged 18 to 75 years) with T2D was recently published this year (as an AID system, it is currently approved for T1D).[49,92] Participants were required to have an A1C between 8% and 12%, and had to be on insulin therapy.[92] Participants were categorized based on their prior insulin regimen (standard therapy): basal-bolus insulin users (n=12), or basal-only insulin users (n=12); continued use of anti-hyperglycemic medications was allowed based on clinician discretion. After a 2-week period of standard therapy with CGM use, participants in the basal-bolus group immediately transitioned to using the automated mode of the Omnipod 5 for 8 weeks, whereas those in the basal-only group were required to use the system in manual mode for 2 weeks and then were allowed to transition to automated mode for 8 weeks. When the system was in automated mode, participants in both groups were advised to use preset optional meal boluses for the first 4 weeks; in the subsequent 4 weeks during the automated mode phase, all participants in the basal-bolus group were encouraged to use boluses for all meals, whereas meal boluses were encouraged only for participants who did not meet glycemic TIR (70−180 mg/dL ≤50%) during the first 4 weeks in the basal-only group. The primary safety endpoint was the percentage of time in hyperglycemia (≥250 mg/dL) and hypoglycemia (<54 mg/dL) during the 8-week automated mode period. Secondary outcomes included A1C and TIR (70−180 mg/dL).[92]

Compared to baseline (ie, standard therapy with injectable insulin as basal-bolus or basal-only), Omnipod 5 (functioning as an AID) significantly reduced the time of sensor readings at 250 mg/dL or above in both treatment groups.[92] Regardless of AID use or standard therapy, the percentage of time <54 mg/dL was low and comparable among both groups. Regarding secondary safety outcomes, baseline A1C significantly decreased in both treatment groups after 8 weeks of AID use, and mean TIR increased with AID use compared to standard therapy.[92]

6.1 Randomized controlled trial (RCT) evidence

A 2023 review by Karol et al found 5 RCTs that evaluated the use of AID systems in patients with T2D.[30] Two of the studies were conducted in hospitalized adults with T2D, and therefore, are not summarized in this report given the lack of generalizability to the outpatient population for ambulatory insulin pump use; the remaining small RCTs are summarized below. The primary endpoint of each study was TIR; definitions of TIR varied slightly across studies.[93-95] One of the RCTs (Kumareswaran et al)[93] is also cited in the reviewed 2022 consensus statement on the use of AIDs, thereby influencing the level of evidence for their recommendation of offering an AID system to patients with T2D on intensive insulin therapy.[32]

Kumareswaran et al conducted a cross-over RCT among insulin-naïve adults with T2D (N=12) treated with anti-hyperglycemic medication(s) in a supervised setting.[30,93] This RCT found that 24-hours of AID therapy without prandial boluses (unnamed device) significantly improved mean TIR, especially overnight, and time in hyperglycemia compared to the participants' usual diabetes regimen.[30,93] Participants were permitted to use their usual diabetes regimen which consisted of either one (n=3) or two or more (n=9) anti-hyperglycemic agents (ie, metformin [n=11, 92%], sulfonylureas [n=7, 58%], dipeptidyl peptidase-4 inhibitors [n= 4, 33%]) during control visits only.[93]

Another cross-over RCT (Taleb et al) evaluated the use of a AID system (with meal announcement; unnamed device) among adults (≥55 years of age) with T2D who required MDI (≥3 injections per day; N=15).[30,94] At baseline, participants had an A1C of 7.9% and a BMI of 33.[94] Two supervised intervention visits, which lasted 24 hours and were separated by at least 3 days, were conducted for each participant to evaluate AID vs. MDI therapy.[94] Over the 24-hour period, AID therapy significantly improved overnight TIR and blood glucose levels, and decreased insulin requirements compared to MDI.[30,94] There was no significant differences between treatment groups for the number of participants who experienced a hypoglycemic event (<63 mg/dL) necessitating treatment or time in hypoglycemia.[94]

Boughton et al conducted an open-label, cross-over RCT evaluating the use of a AID system (Dana RS insulin pump + CamAPS HX on a compatible smartphone + Dexcom G6 CGM transmitter) compared to standard insulin treatment among a subpopulation of adults with T2D on dialysis for end-stage renal disease (N=26).[30,95] The average age of the study population was 68.3 years, with an average diabetes duration of 20 years.[95] Each intervention was assessed over 20 days in the outpatient setting.[30,95] Compared to standard insulin treatment, AID therapy significantly improved the TIR, and significantly reduced mean glucose levels and time in hypoglycemia.[95] One event of severe hypoglycemia was reported during the AID period, but the device was not working at the time or in the preceding 24 hours.[95]

According to the review by Karol et al, there have been 2 RCTs that have shown favorable benefit for the use of non-LGS/PLGS SAP systems among patients with T2D who require MDI, but both of these studies were performed in the inpatient setting.[30]

7.0 SAFETY

Most insulin pumps and/or pump systems have numerous contraindications and warnings/precautions for use. Generally, the level of complexity corresponds to the number of warnings, with systems that are less technology-dependent having fewer warnings. Considerable overlap exists for labeled safety concerns among the reviewed devices; however, what may be deemed a contraindication for one device could be considered a warning or precaution for another device. The following subsections briefly describe contraindications for use, and highlight key warnings or precautions. See **Table 6** for a comprehensive overview of the contraindications and key warnings/precautions organized by device; refer to the respective user guide for *all* warnings and precautions.

7.1 Contraindications

The iLet Bionic Pancreas and V-Go are the only reviewed insulin pumps that do not have contraindications for use.[54,60] All other reviewed devices are contraindicated (or labeled as a warning for the iLet Bionic Pancreas) among people who are unwilling or unable to maintain contact with a health care provider, or have inadequate vision or hearing to recognize pump signals or alarms.[6-9,48-50,52,53,56] Additionally, most devices should not be used by patients who are unwilling or unable to self-monitor blood glucose as directed by their health care provider,[6-9,48-50,52,53,56] and all insulin pumps should not be used near radiation or magnetic fields.[6-9,48-50,52-54,56] Some insulin pumps that are compatible with the Dexcom G6 are not recommended to be used in patients taking hydroxyurea due to falsely elevated sensor readings.[9,49,53] However, this is a potential concern for all systems that are able to integrate with a CGM.

7.2 Warnings and precautions

The safety of reviewed insulin pumps have not been evaluated in pregnant women,[6-9,48-50,53] and therefore, continued use during pregnancy should be determined at the prescriber's discretion based on a benefit/risk assessment.[7,8,48,50,51] Additionally, for applicable devices, user guides advised to not use automated dosing technology in pregnant women because it has not been studied in this population.[6,9,49,53] For the MiniMed 770G and 780G, user guides also note that there is a lack of data for use in patients with T2D[7,8,48]; user guides for the remaining insulin pumps do not mention details about the use in patients with T2D.[6-9,48-50,52-54,56]

Most user guides recommend not exposing the device to high temperatures, either from direct sunlight or wearing in a hot tub or sauna.[7-9,48-50,52-54,56] Specifically for Omnipod 5 and Omnipod DASH, user guides recommend checking blood glucose more frequently when flying in an airplane due to atmospheric changes which can impact insulin delivery.[49,50] Likewise, the iLet Bionic Pancreas and t:slim X2 tubing should be temporarily disconnected for patients who experience sudden altitude or gravity changes (eg, amusement park rides).[6,9,53,56] AID systems warn that insulin administered outside of the control of the system (eg, manually by injection) is not accounted for when the system is automatically dosing insulin; therefore, to prevent hypoglycemia, it is advised to NOT use automated dosing for a certain period of

time or avoid administering insulin by means other than the device while using the system.[6-9,48,49,53] An additional unique warning generally for most AID systems is that a minimum and/or maximum daily insulin dosage is required to use automated dosing algorithms, with each threshold requirement varying based on the device system.[7-9,48,49] To mitigate interruptions in automated insulin delivery, it is important that AID users ensure insulin pump system components communicate with each other as intended (eg, respond to necessary alarms, ensure components are within range).[6,9,49,53] A unique warning specific to the Omnipod DASH and Omnipod 5, which are pod systems that adhere directly to the skin, is that they should not be used in patients with allergies to acrylic adhesive, or easily damaged skin.[49,50]

Table 6. Contraindications and Key Warnings/Precautions From Device User Guides[96] [a]

V-Go[54]
Contraindication(s):
• None
Key warnings/precautions:

• People with the following characteristics may experience hypoglycemia:
  ○ Those who make frequent adjustments to the basal rate within a 24-hour period
  ○ Those who require <2 units of bolus insulin adjustment at meals
• Remove V-Go before having an MRI, X-ray, CT scan, or other similar procedure
• Avoid exposure of V-Go to direct sunlight or very hot temperatures; V-Go should be removed before hot tub or sauna use.

MiniMed 630G, 770G, and 780G Systems[7,8,48,52] (non-specific contraindications or key warnings/precautions)
Contraindication(s):

• Pump therapy is NOT recommended for people:
  ○ Who are unwilling or unable to perform at least 4 self- monitored blood glucose tests daily (*630G, 770G, and 780G with Guardian 3 sensor*), or unwilling to perform blood glucose meter readings (*780G with Guardian 4 sensor*), for times when self-monitoring may be required for verification purposes when symptoms or expectations do not correspond to the sensor-measured glucose reading or for calibration of the Guardian 3 sensor (required every 12 hours)
  ○ Who are unwilling or unable to keep contact with their health care provider
  ○ Whose vision or hearing is inadequate to recognize pump signals or alarms

Key warnings/precautions:
• LGS or PLGS are not intended to prevent or treat hypoglycemia, these features only stop insulin delivery. Use blood glucose meter readings (*630G only*) and follow health care provider instructions for treating low blood glucose (*770G and 780G*)   ○ 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 delivery, thereby increasing the risk of hyperglycemia or DKA • Remove before entering rooms with strong magnetic fields or radiation (eg, MRI, diathermy, X-ray, CT scan). Additionally, do not use insulin pump cases containing magnets to prevent pump malfunction. • Check blood glucose at least 4 times daily; if an abnormal blood glucose reading occurs, ensure insulin is infusing properly (*630G and 770G only*) • High temperatures, and some skin products (eg, lotion, sunscreen, bug repellent) can damage the insulin pump. Hands should be washed prior to touching the plastic pump case if skin products are used • Reservoir and infusion set should not be used if liquid gets trapped at the top of the reservoir or inside the tubing connector to prevent insulin delivery errors • Check "Daily History" when resuming insulin delivery after it has been suspend to prevent hyperglycemia; planned boluses prior to insulin delivery suspension will not resume automatically • Do not make therapy decisions using sensor glucose values; verify sensor glucose readings with blood glucose meter if sensor glucose values are outside of the desired range or when experiencing symptoms of low or elevated glycemia (*630G and 770G only*)
Specific to the MiniMed 630G only[52]
Additional 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 operating medical devices during the flight); use blood glucose values to inform treatment decisions when Airplane Mode is turned on. • All insulin delivery stops if the pump alarms (alarms are specific to detecting issues with insulin delivery); pump alarms should not be ignored
Specific to the MiniMed 770G and 780G[7,8,48]
Additional contraindication(s):
• Insulin reservoir should not be used to infuse blood or blood products • Serter (device for sensor placement) should only be used with the Guardian Sensor 3, or Guardian 4 Sensor (*780G only*) • Infusion sets should only be used for subcutaneous infusion, NOT intravenous infusion, or blood or blood product infusion

[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; kg, kilograms; LGS, low-glucose suspend; MRI, magnetic resonance imaging; PDM, Personal Diabetes Manager; PET, positron emission tomography; PLGS, predicted low-glucose suspend; T2D, type 2 diabetes

Table 6. Contraindications and Key Warnings/Precautions From Device User Guides[96] [a]

Additional key warnings/precautions:
• SmartGuard Auto Mode (for automated dosing) should not be used by people who require <8 units or >250 units of total daily insulin • There is a lack of data for use among people who are **pregnant, have T2D**, have impaired renal function, or who are using non-insulin anti-hyperglycemic therapies; a health care provider should determine if the benefits from using this system outweigh the potential risks • Sensor is NOT recommended to be used by people who are critically ill • Automated insulin dosing (SmartGuard Auto Mode) does not account for insulin administered manually (eg, injection); avoid using this feature for a certain period of time (consult a health care provider to determine the wait time duration) after a manual insulin injection to prevent over-delivery of insulin and hypoglycemia • For users aged 2–13 years (*or 7–13 years for 780G*): users should not rely solely on sensor glucose alerts to identify hypoglycemia • There is a lack of experience using automated insulin dosing (*770G only*), or features for PLGS or LGS among people without established insulin pump settings (ie, basal rate, insulin-to-carbohydrate ratio, insulin sensitivity); users should discuss use of these advanced features with a health care provider before using them
Specific to the MiniMed 780G only[7,8]
Additional contraindication(s):
• Pump therapy is NOT recommended for people who are under 7 years old (*780G with Guardian 4 Sensor only*)
Additional key warnings/precautions:
• There is a lack of data for use in people aged <7 years • Sensor glucose readings should not be used for treatment decisions when the pump is running in manual mode (non-automated dosing). Sensor glucose readings may differ from blood glucose readings and when sensor glucose readings are used to calculate boluses, there is a risk of hypo- or hyperglycemia • Perform a blood glucose meter reading when anticipating higher or lower than expected sensor glucose readings, when experiencing signs/symptoms of hypo- or hyperglycemia or DKA, and before giving a correctional bolus in manual mode • Self-monitor blood glucose levels at least every 12 hours (*780G with Guardian Sensor 3 only*); if an abnormal blood glucose reading occurs, ensure insulin is infusing properly • Monitor for diabetic retinopathy, especially during initiation, because it may worsen due to rapid reductions in blood glucose that have occurred with 780G systems (*780G with Guardian 4 Sensor only*)
Omnipod DASH[50]
Contraindication(s):

• Pump therapy is NOT recommended for people:
  ○ Who are unable to follow glucose monitoring recommendations from their health care provider
  ○ Who are unwilling or unable to maintain contact with their health care provider
  ○ 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 or easily damaged skin
• Do not use the device at low atmospheric (eg, at ≥10,000 feet) or high oxygen (>25%) environments. Check blood glucose frequently when flying in an airplane due to atmospheric pressure changes (may affect insulin delivery)
• 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, water at a depth >25 feet or for more than 60 minutes, or strong detergents or solvents (eg, sunscreen, bug repellant). Remove before hot tub or sauna use
• Remove the pod and PDM before having an MRI, X-ray, CT scan, or other similar procedure

[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; kg, kilograms; LGS, low-glucose suspend; MRI, magnetic resonance imaging; PDM, Personal Diabetes Manager; PET, positron emission tomography; PLGS, predicted low-glucose suspend; T2D, type 2 diabetes

Table 6. Contraindications and Key Warnings/Precautions From Device User Guides[96] [a]

Omnipod 5[49]
Contraindication(s):

• Pump therapy is NOT recommended for people:
  ○ Who are unable to follow glucose monitoring recommendations from their health care provider
  ○ Who are unwilling or unable to maintain contact with their health care provider
  ○ Who are unable to use the device according to instructions
  ○ Who are taking hydroxyurea (falsely increases sensor glucose values)
  ○ Whose vision or hearing is inadequate to recognize pump signals or alarms
• Remove pod and controller/phone before MRI, CT scan, or diathermy procedures, and place them outside the procedure area

Key warnings/precautions:

• Pump therapy is NOT recommended for people who have allergies to acrylic adhesives, or fragile or easily damaged skin
• SmartAdjust technology (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)
• Automated insulin dosing (SmartAdjust Auto Mode) does not account for insulin administered manually (eg, injection); avoid using this feature for a certain period of time (consult a health care provider to determine the wait time duration) after a manual insulin injection to prevent over-delivery of insulin and hypoglycemia
• Do not use the device at low atmospheric (eg, at ≥10,000 feet) or high oxygen (>25%) environments. Check blood glucose frequently when flying in an airplane and during sudden gravity/atmospheric changes (eg, amusement park rides) to prevent hypoglycemia
• Avoid exposing the pod to extended direct sunlight, water at a depth >25 feet or for more than 60 minutes, or strong detergents or solvents (eg, sunscreen, bug repellant). Remove before hot tub or sauna use
• Monitor blood glucose according to health care provider instructions, and check blood glucose meter reading if sensor glucose values do not match symptoms. Monitor for hypoglycemia when using the “Activity” mode (an automated mode with a higher target glucose setting) because hypoglycemia may still occur
• User should immediately respond to Hazard Alarms, which indicate insulin delivery has stopped, to mitigate hyperglycemia. If ignored, “Pod Expired”, “Low Pod Insulin”, and “Pod Shut-off” alarms escalate to Hazard Alarms

iLet Bionic Pancreas[6]
Contraindication(s):
• None
Key warnings/precautions:

• Use of the insulin pump and Dosing Decision Software is NOT recommended for people:
  ○ Who are unwilling or unable to perform self-monitoring blood glucose testing
  ○ Who cannot recognize and/or respond to safety alerts
  ○ Who are taking hydroxyurea (falsely increases sensor glucose values)
  ○ Who are <6 years of age
  ○ Who are **pregnant**, receiving dialysis, critically ill, or hospitalized (lack of data for use)
• Device components should not be exposed to MRI, X-ray, and CT or PET scans. Remove device components before radiation therapy, MRI, CT scan, diathermy, or laser surgery
• Temporarily disconnect tubing before sudden altitude or gravity changes (eg, amusement park rides)
• Avoid administering insulin by means other than the device while using the system to prevent hypoglycemia
• Check blood glucose before disconnecting or reconnecting to the system; when disconnected, treat blood glucose as directed by a health care provider
• If CGM is offline, the system will switch to BG-run mode, which should be used only *temporarily*. Automated dosing will stop if CGM is offline for an extended amount of time (ie, 48 to 72 hours); user should administer insulin by an alternative method 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; kg, kilograms; LGS, low-glucose suspend; MRI, magnetic resonance imaging; PDM, Personal Diabetes Manager; PET, positron emission tomography; PLGS, predicted low-glucose suspend; T2D, type 2 diabetes

Table 6. Contraindications and Key Warnings/Precautions From Device User Guides[96] [a]

t:slim X2 (insulin pump alone or with Basal- or Control-IQ technology)[9,53,56]
Contraindication(s)[b]:
• Pump therapy is NOT recommended for people: ○ Who are unwilling or unable to follow blood glucose testing as recommended by their health care provider ○ Who are unwilling or unable to adequately practice diabetes self-care skills ○ Who are unable or unwilling to regularly see their health care provider ○ Whose vision or hearing is inadequate to recognize pump signals or alarms ○ Who have insufficient carbohydrate-counting skills (*for Control-IQ; this is preferred according to t:slim X2 with or without Basal-IQ*)
Key warnings/precautions:
• Pump therapy with *Basal-* ***or*** *Control-IQ technology* is NOT recommended for people: ○ Who have conditions or circumstances that would place them at risk when using this device or its components, based on health care provider judgement ○ Who have uncontrolled thyroid disease, hemophilia or major bleeding disorder, renal failure, or unstable cardiovascular disease • Dexcom G6, used with *Basal-* ***or*** *Control-IQ technology*, should NOT be used by people: ○ Who are **pregnant**, receiving dialysis, or critically ill (lack of data, sensor readings may be inaccurate) ○ Who are taking hydroxyurea (falsely increases sensor glucose values); persons taking this medication should use a blood glucose monitor, and consult their health care provider for alternative monitoring options • Basal- or Control-IQ technology have not been studied in people who are **pregnant,** receiving dialysis, or critically ill • Insulin pump, transmitter, and sensor should not be exposed to MRI, X-ray, PET scan, other similar radiation procedures. Remove and leave outside of the procedure area. • Avoid submersion of the pump into liquid at a depth >3 feet, or for more than 30 minutes. Remove before hot tub or sauna use. • Temporarily disconnect tubing before sudden altitude or gravity changes (eg, amusement park rides) • Check blood glucose using a meter following 1,000 feet elevation changes, and if symptoms do not match sensor glucose readings • To prevent hypoglycemia, do not administer insulin by means other than this device while using the pump • Basal- and Control-IQ technology are not a replacement for active diabetes management and will not prevent all hypoglycemia episodes. Low blood glucose is not treated by Basal- or Control-IQ technology
Specific to the t:slim X2 with Basal-IQ technology[53]
Additional key warnings/precautions:
• Pump therapy with Basal-IQ technology is NOT recommended for people who are unable to use system components according to instructions
Specific to the t:slim X2 with Control-IQ technology[9]
Additional key warnings/precautions:
• Control-IQ technology should NOT be used for people: ○ Under 6 years of age ○ Who require <10 units of insulin daily ○ Who weigh <55 pounds (25 kg) ○ Who require hydroxyurea • If a CGM reading is not received for 20 minutes while using Control-IQ technology (eg, pump and CGM are out of range, sensor start-up, sensor session ends), basal insulin delivery is restricted to 3 units per hour. Control-IQ should be disabled if a higher insulin delivery rate is required • The insulin pump should be used for therapy decisions if the smartphone (controller) is either incompatible with the Bolus Delivery feature, lost or damaged, or disconnected from Bluetooth

[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; kg, kilograms; LGS, low-glucose suspend; MRI, magnetic resonance imaging; PDM, Personal Diabetes Manager; PET, positron emission tomography; PLGS, predicted low-glucose suspend; T2D, type 2 diabetes

7.3 Adverse events of insulin pumps and pump systems

The following bullet points briefly list the similar adverse events (AEs) reported across user guides for the reviewed insulin pumps and pump systems, with additional details provided below (see **Appendix E** for specific AE information):

- **Hypoglycemia, hyperglycemia, and associated sequelae**
- **Infection, skin irritation, bleeding, bruising, pain, rash, other reactions**
- **Sensor (wire) or cannula breakage**
- **Choking hazard for young children**

All insulin pumps carry a risk of hypo- or hyperglycemia and associated sequelae (eg, DKA, coma, death) as a result of hardware or software failures and/or user error (eg, accidently touching buttons or touchscreen).[6-9,48-50,52-54,56] Some insulin delivery failures can be attributed to an occluded insulin infusion set or presence of air bubbles in the tubing[3,4,6,97]; these events rarely cause severe complications provided the patient is appropriately educated on changing infusion sets and managing system alerts/alarms.[97] Relative to tubed pumps, tubeless pumps lack infusion sets allowing for less occlusions, although blockages can still occur in other system components (eg, cannula).[49] Generally systems with more advanced technology monitor for interrupted insulin delivery and notify the user.[6-9,48-50,52,53,56]

In addition, all reviewed devices carry risks for skin irritation, infection, or other types of reactions (eg, bruising, bleeding, rash) at the infusion or CGM sensor sites.[6-9,48-50,52-54] Therefore, it is important for users to rotate infusion sites and/or CGM sensor sites, and avoid placement on inflamed skin or skin with blemishes (eg, moles, scars) or tattoos.[6-9,48-50,52-54]

On rare occasions, it is possible for sensors or the cannula from an infusion set to break under the skin at the insertion site.[6,9,48,53] If this occurs, patients should seek medical attention, especially if symptoms or signs of an infection are present (eg, swelling, redness, pain).[6,9,53]

Most insulin pumps contain small parts (eg, USB port cover, cartridges, tubing) that pose as a strangulation or choking hazard to young children.[6-9,48-50,52,53,56] Consequently, device users, particularly caregivers of young children, should take precautions to prevent unintentional injury from swallowing or ingesting foreign objects.[6-9,48-50,52,53,56]

8.0 PLACE IN THERAPY FOR INSULIN PUMPS

Patients on intensive insulin therapy (ie, MDI or insulin pump therapy) mostly include those with T1D, and can potentially include a subset of those with T2D, or those with other forms of insulin-deficient diabetes (eg, cystic fibrosis-related diabetes, monogenic diabetes syndrome).[3,21,24] Insulin pumps have the potential to reduce A1C and mitigate episodes of severe hypoglycemia,[3,10] and can offer a more flexible lifestyle than MDI.[2,10] Insulin pump therapy, especially AID systems, may be a suitable option for children and adults with T1D,[3,10,32,72] and can be considered for those with more advanced T2D (*based on less robust evidence*) who require MDI or have poor glycemic control on MDI therapy.[3,32,75] Generally, insulin pump therapy may be preferred over MDI for patients who have needle phobia, high glucose variability, recurrent or severe hypoglycemia, dawn phenomenon, hypoglycemia unawareness, variable schedules, or pregnancy complicated by T1D.[2,29] However, insulin pump use does require dedication and

knowledge of basic diabetes management skills (eg, carbohydrate counting, checking blood glucose levels), even when using automated systems.[29,32]

9.0 UTAH MEDICAID UTILIZATION DATA

Except for the Omnipod systems and V-Go which can be billable through pharmacy benefit, all reviewed insulin pumps are billed as durable medical equipment through medical coverage.[98,99] However, we were unable to identify any medical or pharmacy claims for any of the reviewed insulin pumps among the Utah Medicaid fee-for-service (FFS) population over the last year and a half (January 2022 through June 2023). For utilization data among the Utah Medicaid Accountable Care Organization (ACO) population, refer to **Appendix F**.

10.0 CONSIDERATIONS FOR PRIOR AUTHORIZATION (PA) CRITERIA

State Medicaid programs have been expanding coverage of CGM devices nationwide by incorporating accessibility to populations with T1D or T2D[100]; Missouri Medicaid recently implemented less restrictive criteria allowing CGM access to patients that require any insulin (removing the MDI or insulin pump requirement).[101] However, based on our comparison of requirements for a subset of other state Medicaid programs, most if not all states still require patients to have MDI (either explicitly or as implied by a T1D diagnosis) before approving coverage of insulin pumps, including Missouri.[102-108]

The Drug Utilization and Review (DUR) board may consider implementing the following PA criteria for insulin pump devices:

1) *For any insulin pump, consider requiring provider attestation that patients have T1D, or require intensive insulin therapy for other types of diabetes (eg, T2D)*
    a) All reviewed guidelines strongly recommend insulin pump use for all patients with T1D,[3,4,10,72,73] and the ADA strongly recommends offering insulin pump therapy as an option to adults and youth with T2D who require MDI.[3] Some guidelines and an expert consensus statement recommend that an insulin pump may be a suitable option for patients with other types of insulin-deficient diabetes on intensive insulin treatment (MDI or insulin pump) based on lower quality evidence or expert opinion.[3,10,32,75]
2) *For advanced SAP systems, consider requiring provider attestation that patients have T1D or other types of diabetes requiring intensive insulin therapy (eg, pancreatectomy), or T2D on intensive insulin therapy (MDI with basal and prandial insulin) and at least 1 of the following for patients with T2D: hypoglycemia unawareness, severe/recurrent hypoglycemia, or significant glycemic variability.*
    a) AACE (2021) strongly recommends SAP with LGS or PLGS to all patients with T1D for the purpose of reducing hypoglycemia severity and duration, or mitigating hypoglycemia, respectively.[10] The 2022 ISPAD guideline strongly recommends SAP with PLGS or LGS for children with T1D if an AID system is unavailable.[4]
    b) AACE notes that LGS and PLGS devices can also be considered for any patient with frequent hypoglycemic episodes, permissive hyperglycemia as a result of hypoglycemia distress, or hypoglycemia unawareness.[10]

c) For patients receiving MDI who do not desire or cannot use an AID system, the ADA strongly recommends offering any insulin pump (eg, pump ± SAP LGS) to adults and youth with T1D, or based on expert opinion, to those with other types of insulin-deficient diabetes.[3]

3) *For AID systems, consider requiring provider attestation that patients have T1D, and may consider allowing off-label use of AID systems for patients with T2D or other insulin-deficient diabetes on a case-by-case basis; patients with other types of diabetes may be required by the payer to fail other on-label systems first (eg, advanced SAPs, conventional insulin pumps) or allow the provider to express rationale for necessity of an AID system*

a) All available AID systems are approved specifically for patients with T1D[6-9,48,49]: Omnipod 5, t:slim X2 with Control-IQ technology, iLet Bionic Pancreas, MiniMed 770G, and MiniMed 780G.

i) AID systems are recommended by reviewed guidelines for most adults and children with T1D given the benefits in reducing A1C, improving time in range, and preventing hypoglycemia.[3,4,10]

ii) Reviewed guidelines prefer AID systems to alternative insulin delivery systems (non-automated pumps, SAP ±LGS or PLGS, or MDI) for most adults and children with T1D given the benefits in reducing A1C, improving TIR, and preventing hypoglycemia.[3,10]

b) While the ADA and experts mention that AID systems can be considered for patients with other types of diabetes who require intensive insulin therapy,[3,32] the suggestion is generally graded as a low level recommendation due to no or minimal clinical evidence of AID use. (For non-T1D insulin-deficient diabetes ADA Grade E, no clinical trial evidence; recommendation based on expert consensus or opinion[3]; but 1 applicable RCT among patients with T2D in an outpatient setting, and 2 clinical trials in patients with cystic fibrosis-related diabetes was cited by an expert consensus statement).[32]

c) As part of the strong recommendation for AID systems for people with T1D, AACE also notes that AID systems can be considered for patients with diabetes in certain circumstances (eg, significant glycemic variability, suboptimal glycemic control, hypoglycemia unawareness), but it's unclear to what extent this part of the recommendation applies to people without T1D.[10]

4) *Consider restricting use based on the product-specific labeled age for approval*

a) Automated dosing technology (SmartAdjust) with the Omnipod 5, and the MiniMed 770G system are approved for ages ≥2 years in T1D.[48,49]

b) The following products are all approved for ages ≥6 years, but the diabetes type varies based on intended use:[6,9,53,56]

i) Stand-alone pumps, t:slim X2 and iLet Bionic Pancreas, as well as the t:slim X2 with Basal-IQ technology (as an advanced SAP) are indicated for diabetes mellitus in general.

ii) As AID systems, the t:slim X2 with Control-IQ technology, and the iLet Bionic Pancreas with iLet Dosing Decision Software are approved for T1D.

c) MiniMed 780G is approved for ages ≥7 in T1D.[7,8]

d) MiniMed 630G with the Guardian Sensor 3 is approved for ages ≥14 years (or ≥16 years when used with the Enlite Sensor) for diabetes mellitus in persons who require insulin.[55]

e) V-Go is approved for adults (no specific age threshold is reported in the user guide) who require insulin.[54]

f) Omnipod DASH and Omnipod Eros are not labeled for a specific age, for people with diabetes mellitus who require insulin.[50,51]

5) *Consider requiring prescriber attestation that the patient/caregiver is able to safely use the device, has adequate diabetes self-management skills, and has routine follow-up with their health care provider*

a) Except V-Go, all reviewed devices are contraindicated (or labeled as a warning for the iLet Bionic Pancreas) among people who are unwilling or unable to maintain contact with a health care provider, or have inadequate vision or hearing to recognize pump signals or alarms.[6-9,48-50,52,53,56] Although hearing/vision impairments may limit the utility of these devices in older adults, they should have the same access to insulin pump therapy, including AID systems, as younger individuals, both in terms of initiation and continued use.[3]

b) Most devices should not be used by patients who are unwilling or unable to self-monitor blood glucose as directed by their health care provider.[6-9,48-50,52,53,56]

c) If a pump reverts to manual mode or a malfunction occurs, patients must be capable of performing basic diabetes self-management skills including checking their blood glucose levels, administering an insulin injection, recognizing how to respond to diabetic emergencies (eg, DKA), and understanding how to calculate correctional insulin doses.[32]

10.1 Additional considerations

6) May consider requiring attestation that the provider has training in facilitating the use of the device

a) The AACE 2021 technology guideline recommends that diabetes technology should be prescribed by well-trained, proficient, and experienced health care providers who are capable of overseeing the utilization of these devices[10]; prescribers should be familiar with device features and functionality to ensure an appropriate device is selected based on the patient's preferences, skill level, and lifestyle,[3] and to provide adequate teaching and support for the patient.[10]

i) For example, providers should be aware that most AID systems (exception is the iLet Bionic Pancreas) require a minimum and/or maximum total daily insulin threshold for automation mode to be used.[7-9,48,49]

b) Restricting prescribing to a limited number of prescribers (eg, allowing only endocrinologists to prescribe pumps) may impede the accessibility of these devices. This is a particular concern in rural areas where there may not be access to such specialists. Presumably non-specialists (eg, primary care providers) could also become educated/well-versed in the features of these devices to facilitate their use.

7) May consider having the prescriber attest that they have adequately trained the patient/caregiver on the device features, uses, and warnings, and that the patient has a treatment plan and supplies on hand for times when the device is unusable or malfunctions

a) Reviewed guidelines recommend that patients prescribed an insulin pump receive personalized, structured education, training, and clinical and technical support, both initially and continuously, to ensure appropriate and safe use.[3,10,72] Training can be provided either in-person or remotely, and the patient should be made aware of other online resources (eg, instructional videos, FAQ guides).[3] Many manufacturers offer training on use of their devices.

b) Education should ensure that patients with diabetes who rely on insulin delivery technology are able to recognize the signs of a pump malfunction, be aware of whom to contact in case of such an event, and have a well-defined plan for emergency situations (eg, backup measures).[10]

8) *May consider including space on the PA form to allow providers to explain rationale as to why a particular pump is more suitable than others for their patient*

a) Contraindications or serious warnings/precautions may preclude a patient from being a candidate for one or more insulin pumps. Additionally, many pump-specific usability factors could meaningfully impact whether a patient will successfully use a pump. For example, patients speaking a non-English language may require access to a particular pump; languages offered by pumps varies.[66,109] Compatibility with monitoring applications on particular mobile phones varies. In addition, some pumps may be more suitable to a particular lifestyle than others.

9) *May consider allowing continuation of access to patients who are already using a particular insulin pump*

a) Based on expert opinion, the ADA recommends allowing continued access to patients who have been receiving insulin pump therapy in the event of insurance coverage changes.[3]

10) *May consider requiring provider rationale for covering more than one pump (with similar functionality) within a specified timeframe*

a) Unless certain circumstances exist (eg, device is no longer under warranty and is malfunctioning or is damaged) or the provider explains clinical rationale for more than one pump, it may be reasonable to require a waiting period before covering a second pump with similar functionality to the previous insulin pump

11.0 SUMMARY

As an alternative to multiple daily injections (MDI; ie, basal-bolus insulin therapy),[2,97] continuous subcutaneous insulin infusion (CSII) facilitated by an insulin pump (also termed insulin pump therapy) is used in patients with types of insulin-deficient diabetes (eg, T1D, advanced T2D) to imitate the natural insulin secretion by pancreatic beta cells.[1,2] Insulin pumps are able to administer pre-programmed or adjustable rates of basal insulin, and provide manual or automated prandial and/or correctional bolus doses, depending on the device.[6-9,48-54,56] The various insulin pumps infuse insulin either via tubing from the pump to a subcutaneously inserted cannula or needle, or as a patch-like device that attaches directly to the skin.[2,3,5]

Because there is a variety of insulin pumps available on the market, the choice of a pump tends to be highly dependent on approved indications, patient-specific factors (eg, preferences, lifestyle), and device features (eg, CGM integration[‡‡]).[5]

Insulin pumps range in their maximal automation capabilities. Some advanced SAP systems are able to mitigate or prevent hypoglycemia by pausing insulin delivery (eg, MiniMed 630G, t:slim X2 with Basal-IQ technology), while others automatically adjust the basal insulin infusion based on a programed

‡‡ Of the reviewed AID systems, the MiniMed 770G and 780G are compatible with the Guardian 3, and in the case of the MiniMed 780G, also the Guardian 4; Omnipod 5, t:slim X2 with Control-IQ technology, and iLet Bionic Pancreas are compatible with the Dexcom G6 CGM system.

algorithm and sensor readings to prevent hypo- and hyperglycemia; the latter are referred to as AID systems (eg, Omnipod 5, MiniMed 770G).[3-5] Some advanced AID systems can additionally deliver automated correctional boluses (eg, t:slim X2 with Control-IQ technology, MiniMed 780G),[7-9] and in the case of the iLet Bionic Pancreas, can also give automated mealtime boluses with user-initiated meal announcement.[6]

Most of the reviewed insulin pumps (eg, conventional pumps, stand-alone pumps, advanced SAPs) have a general indication for use in patients with diabetes mellitus (non-specific to diabetes type) or for others who require insulin therapy.[6,49-52,54,56] However, AID systems, or more specifically the dosing algorithm software, are indicated for pediatric and adult patients **with T1D** and have defined age restrictions. Indications may differ for the AID pump itself versus when used with the compatible dosing software to function as a more advanced system.[6-9,48,49]

According to reviewed guidelines and an consensus statement, most patients with T1D, including children and adults, are appropriate candidates for AID therapy, and ideally should be offered this option at the time of diagnosis to optimize therapeutic benefit.[3-5,10,32,72,75] In addition, the consensus statement and ADA recommend prescribers consider offering AID systems to patients with T2D or other types of insulin-deficient diabetes on intensive insulin therapy (eg, cystic fibrosis-related diabetes), but evidence in these populations is very limited; thus, recommendations for AID use in populations other than T1D are generally graded low, to represent low-quality evidence or expert opinion basis.[3,32] Not all patients with diabetes may be suitable candidates for an AID system, especially those with visual impairment, very high or low insulin requirements, or diabetes complications.[14]

The 2023 ADA guideline strongly recommends offering insulin pump therapy in general to adults and children with T2D who are on MDI and can safely use a device.[3,75]

Some key features that differentiate insulin pump devices include approved ages, indicated diabetes type, ability to automatically adjust basal insulin delivery in response to CGM readings, ability to interrupt basal insulin delivery based on actual or predicted glucose levels, tubeless ("patch pump")[2] versus tubed components, and whether the pump is interoperable with other system components (ie, alternate controller enabled). Additional key features that differ between AID systems include required parameters and minimum total daily insulin threshold for automation mode, ability to deliver automatic bolus doses (prandial or correctional), preset modes for certain scenarios (eg, exercise, sleep), and triggers that revert the system to manual mode or limited automation mode. See **Table 3** for a comparison of features among AID systems.

Potential pump-related adverse events may include hypo- or hyperglycemia and related sequelae (eg, DKA) due to technical faults (eg, hardware or software failure) and/or user error; as well as skin irritation, infection, or other types of reactions (eg, bruising, bleeding, rash) at the infusion or CGM sensor site.[6-9,48-50,52-54,56] Although rare, there is also risk for potential sensor (wire) or cannula breakage.[6,9,48,53] Additionally, insulin pumps have small components that may present a potential risk of strangulation or choking in young children.[6-9,48-50,52,53,56]

Considerations for prior authorization (PA) criteria have been developed based on recent guideline recommendations from international and US organizations, as well as device approved indications.

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APPENDIX A: DEVICES NOT ADDRESSED BY THIS REPORT

Recently cleared insulin pump-related devices that are not addressed by this report are as follows:

- **Omnipod Go:** Omnipod Go is an independent, wearable, patch device designed to subcutaneously administer predetermined, fixed daily basal dosages (ranging from 10 to 40 units) of rapid-acting insulin.[110] It is indicated for adults (aged ≥18 years) with type 2 diabetes (T2D) who typically rely on daily long-acting insulin injections. Compatible U-100 insulins are NovoLog, Humalog, Fiasp, Lyumjev, and Admelog. The manufacturer of this device, Insulet, intends to launch US commercial distribution of the device in 2024.[110]
- **Tidepool Loop:** Tidepool Loop is a software application designed to automatically recommend and prompt compatible insulin pumps to administer correction boluses of insulin, and/or decrease, increase, or suspend basal insulin delivery (ie, automated glycemic controller) by using an algorithm. This software is compatible with other select FDA-cleared devices (alternate controller enabled [ACE] pumps, integrated continuous glucose monitors [CGM]).[111] It is indicated for patients ≥6 years of age with type 1 diabetes (T1D). Currently, the manufacturer is finalizing the commercial launch with their device partners.[111] For updates on device compatibility and commercialization, please refer to the Tidepool Loop website, available at: https://www.tidepool.org/tidepool-loop
- **CeCur Simplicity:** CeCur Simplicity is a wearable patch that provides manual bolus doses of rapid-acting insulin by the patient (2 units of rapid-acting insulin per button squeeze); it does not provide continuous insulin delivery.[112] This product offers a needle-free insulin delivery option for manual bolus insulin delivery, indicated for adults with diabetes who require insulin therapy.[112]
- **Tandem Mobi:** Tandem Mobi is an interoperable pump with a 200-unit insulin cartridge for use with Control-IQ technology as an automated insulin delivery (AID) system.[33] As a pump, it is indicated for patients with diabetes aged ≥6 years who require insulin therapy. It is the smallest, durable AID to-date allowing for greater discretion than other pumps and is fully controllable with a user's iPhone. Tandem, the device manufacturer, has not yet announced compatible CGM. Full commercial availability of Tandem Mobi is anticipated in early 2024.[33] For device updates, please refer to the manufacturer's website, available at: https://www.tandemdiabetes.com/products/tandem-mobi

APPENDIX B: OVERVIEW OF DIAGNOSING DIABETES

Diabetes diagnosis is established by elevated plasma glucose (PG), indicated by[16,21]:

- fasting plasma glucose (FPG), or
- post 2-hour oral glucose tolerance test (OGTT), or
- elevated hemoglobin A1C (glycosylated hemoglobin) (see **Table B1**).[16,21]

To confirm the diagnosis, the same measured test should be performed on a different day, either from the same sample or different samples. A confirmation test is not needed if the patient has a PG ≥200 mg/dL with associated symptoms of diabetes (eg, hyperglycemia).[16,21]

Table B1. Diagnostic Criteria for Diabetes per AACE and ADA Guidelines[16,21]

Measurement	Normal threshold	Diabetes threshold
FPG (mg/dL)[a]	<100	≥126
2-hour PG (mg/dL)	<140	≥200; random PG ≥200 + symptoms[b]
A1C (%)	<5.5	≥6.5

[a] *Fasting is considered no caloric consumption for at least 8 hours[21]*

[b] *Confirmatory diagnostic testing is not needed in patients who have a random PG (non-fasting) ≥200 mg/dL and associated symptoms[16]*

Abbreviations: A1C, glycosylated hemoglobin; AACE, American Association of Clinical Endocrinology; ADA, American Diabetes Association; dL, deciliter; FPG, fasting plasma glucose; mg, milligram; PG, plasma glucose

Unlike using the diagnostic thresholds outlined in **Table B1**, gestational diabetes (GDM) diagnosis is made using a one-step or two-step approach[16,21]:

- One-step approach: **meeting or exceeding any** of the following criteria after a 2-hour 75-gram OGTT and fasting for ≥8 hours: FPG ≥92 mg/dL; 1-hour PG ≥180 mg/dL; 2-hour PG ≥153 mg/dL
- Two-step approach: screen for GDM using a non-fasting 1-hour 50-gram OGTT with a 1-hour PG of 130–140 mg/dL. Pregnant women with a positive screening result, **meeting or exceeding two or more** of the following criteria after a 3-hour 100-gram OGTT: FPG ≥95 mg/dL; 1-hour PG ≥180 mg/dL; 2-hour PG ≥155 mg/dL; 3-hour PG ≥140 mg/dL

Most children diagnosed with diabetes mellitus before the age of 6 months are likely to have a monogenic form, as type 1 diabetes (T1D) rarely manifests before this age.[16] In cases where a child or young adult exhibits an unusual presentation (uncharacteristic of T1D or T2D),[21] clinical course, or response to therapy, providers should consider the possibility of monogenic diabetes mellitus (eg, neonatal diabetes, maturity-onset diabetes of the young),[16] especially if the patient is <6 months of age at diagnosis.[73]

APPENDIX C: GLYCEMIC TARGETS BASED ON REVIEWED US GUIDELINES

Table C1. Glycemic Targets Per the American Diabetes Association and American Association of Clinical Endocrinology

American Diabetes Association (ADA), Glycemic Targets, Older Adults, Children and Adolescents, and Pregnancy Guidelines; 2023[28,74,75,89]
Monitoring[89]**:**
• Evaluate glycemic status (eg, A1C, TIR) at least twice yearly in patients meeting treatment goals and with stable glycemic control; otherwise, evaluate glycemic status at least quarterly in those with therapy change or unmet glycemic targets • Bear in mind that A1C is a less reliable indicator of actual glycemia in patients with conditions that affect red blood cell turnover (eg, recent blood transfusion, anemia hemoglobinopathies, pregnancy, glucose-6-phosphate dehydrogenase deficiency, end-stage kidney disease) • Hypoglycemia classification: ○ **Level 1**: <70 mg/dL and ≥54 mg/dL ▪ Considered clinically important ○ **Level 2**: <54 mg/dL ▪ Neuroglycopenic symptoms start. Requires immediate action ○ **Level 3:** Severe episode characterized by altered mental and/or physical status requiring treatment assistance from another person
Adults, non-pregnant[89]**:**
• A1C target is generally <7% (without significant hypoglycemia); corresponds to >70% TIR, with TBR <4% and time <54 mg/dL <1% ○ A lower A1C target (eg, A1C <6.5%) can be set if it can be achieved safely without significant hypoglycemia or other adverse events. Patients for which this may be suitable include those with shorter duration of diabetes, long life expectancy, absence of other relevant comorbidities, and highly motivated with excellent self-care abilities ○ A less stringent A1C target (eg, <8%) may be appropriate in individuals with reduced life expectancy or if harms of more intensive treatment outweigh the benefits (eg, significant risk of hypoglycemia) • Pre-prandial capillary PG target is generally 80–130 mg/dL; goal can be less or more stringent depending on the patient's needs • Peak post-prandial capillary PG (1 to 2 hours after beginning of a meal) target is generally <180 mg/dL; goal can be less or more stringent depending on the patient's needs
Older adults[74]**:**
• A1C target of <7% to 7.5% can be set for older adults who are otherwise healthy (eg, few chronic comorbidities, non-altered cognitive function, non-impaired functional status) • A1C target of <8% can be set for older adults with multiple chronic comorbidities, functional dependence, or cognitive impairment
Children and adolescents[75]**:**
• A1C target of <7% should be considered for most children and adolescents; a lower target of <6.5% can be set if it can be achieved without significant hypoglycemia, undue burden of care, negatively impacting well-being, or those absent of nonglycemic factors that reduce A1C (eg, decreased erythrocyte lifespan) • A less stringent A1C target of <7.5% may be set for patients with increased hypoglycemia risk (eg, unable to express hypoglycemia symptoms; hypoglycemia unawareness; unable to access analog insulins, **AID systems**, and/or CGM; unable to routinely check blood glucose; or nonglycemic factors [eg, high glycators] that increase A1C are present • A1C target of <8% can be considered for patients with severe hypoglycemia, reduced life expectancy, or where harms outweigh benefits
Pregnant women[28]**:**
• A1C target of <6% is ideal during pregnancy if it can be achieved without significant hypoglycemia; a A1C target of <7% can be considered if necessary to reduce the risk of hypoglycemia • Target FPG <95 mg/dL + 1-hour post-prandial glucose <140 mg/dL **OR** 2-hour post-prandial glucose <120 mg/dL
American Association of Clinical Endocrinology (AACE), Developing a Diabetes Mellitus Comprehensive Care Plan; 2022[16]
Adults, non-pregnant:
• A1C target is generally ≤6.5%, which may require a FPG <110 mg/dL + 2-hour post-prandial glucose of <140 mg/dL • A less stringent A1C target of 7% to 8% may be appropriate in patients in whom the lower target cannot be achieved without adverse outcomes (eg, patients with hypoglycemia unawareness, history of severe hypoglycemia, reduced life expectancy, long-standing diabetes with difficulty meeting A1C goal despite intensive effort, multiple comorbidities)

Abbreviations: A1C, glycosylated hemoglobin; AACE, American Association of Clinical Endocrinology; ADA, American Diabetes Association; AID, advanced insulin delivery; CGM, continuous glucose monitor(ing); dL, deciliter; FPG, fasting plasma glucose; GDM, gestational diabetes mellitus; mg, milligram; PG, plasma glucose; TBR, time below range; TIR, time in range

Table C1. Glycemic Targets Per the American Diabetes Association and American Association of Clinical Endocrinology

Pregnant women:

• **GDM:**
  ○ Fasting and pre-prandial glucose ≤95 mg/dL + 1-hour post-prandial glucose ≤140 mg/dL **OR** a 2-hour post-prandial glucose ≤120 mg/dL
• **Pre-existing T1D or T2D:** the following target goals are recommended but only if they can safely be achieved:
  ○ Pre-prandial, bedtime, and overnight glucose of 60–95 mg/dL
  ○ 1-hour post-prandial glucose of 110–140 mg/dL
  ○ 2- hour post-prandial glucose of 100–120 mg/dL
  ○ Secondary target: A1C <6% if it can be achieved without significant hypoglycemia

Abbreviations: A1C, glycosylated hemoglobin; AACE, American Association of Clinical Endocrinology; ADA, American Diabetes Association; AID, advanced insulin delivery; CGM, continuous glucose monitor(ing); dL, deciliter; FPG, fasting plasma glucose; GDM, gestational diabetes mellitus; mg, milligram; PG, plasma glucose; TBR, time below range; TIR, time in range

APPENDIX D: TERMINOLOGY FOR INSULIN PUMP SYSTEM COMPONENTS

The following is a description of common components that may be used as part of an insulin pump system (*note that prescribers must write a separate prescription for the various components, as needed [eg, insulin pump, infusion set, CGM]*):

- **Insulin pump**: small digital devices that can be programmed to deliver insulin (ie, continuous basal infusion with adjustable rates or bolus insulin).[2] The insulin is held in a reservoir/cartridge within the insulin pump.[5] Some insulin pumps are patch pumps or "pods", which attach directly to the skin and have the cannula within the disposable device, whereas others deliver insulin through an infusion set.[5]
- **Infusion sets (also called infusion cannula)**: consists of tubing that connects the insulin pump reservoir/cartridge to a subcutaneously inserted cannula or needle for insulin delivery.[2,5] Some systems have different compatible infusions sets that can be tailored to the user's needs (eg, tubing/cannula length, soft or steel cannula, customizable insertion angle).[113,114] Infusion sets are typically replaced every couple of days.[5,114] For patch pumps, the cannula is located within the device itself and therefore, these devices are tubeless.[2,5]
- **Sensor**: a thin sensor that is inserted through the skin or entirely under the skin that continuously measures glucose values in the subcutaneous, interstitial fluid.[48,90,115] The sensor is a component of continuous glucose monitors (CGMs).[3,90]
- **Transmitter**: wirelessly communicates sensor-detected glucose values from the CGM sensor to monitoring or display devices (eg, receiver, smart device).[48,115]
- **Controller:** a separate device (eg, Personal Diabetes Manager, compatible smart phone) that is used wirelessly for insulin delivery.[116]

APPENDIX E: ADVERSE EVENTS REPORTED IN USER GUIDES

Table E1. Adverse Events Reported During Insulin Pump Clinical Trials According to Device User Guides[96]

V-Go[54]
Adverse reactions (number of events nor the specific population are not reported in the user guide):
• **Infections or abscesses** at the insulin infusion site. To mitigate the risk of infection, the administration site should be rotated and cleaned before applying a new V-Go • **Skin irritation** is a common adverse reaction due to the adhesive pad or the position of the device. Using a skin barrier or adhesive removal products may help to prevent irritation
MiniMed 630G[52]
Adverse events (AEs; number of events; number of exposed not reported) during a clinical trial in an unspecified population using the LGS feature with another MiniMed pump (Paradigm X54)
• **Bruising** (n=1) or **bleeding** (n=1) at the sensor site • **Ketones in the urine** (n=1) due to a flawed tubing connection to the pump
MiniMed 770G[48]
*Number of AEs or number of events in children aged 2 to 6 years with T1D during 2 clinical trials using the **670G system** (has the same SmartGuard Auto Mode technology as the MiniMed 770G, therefore according to the manufacturer, the results are comparable to the MiniMed 770G)*

• Trial 1 (with PLGS, N=47 participants): no AE information reported in the user guide
• Trial 2 (with Auto Mode, N=46 participants) with 2-week run-in and 3-month treatment phase:
  ○ No device-related SAE, including DKA or severe hypoglycemia
  ○ **Device-related AE** (N=54, 39%):
  ▪ **Severe hyperglycemia** (n=49); 46 of these events were attributed to infusion set issues (eg, bent cannula, occlusion)
  ○ Severe hyperglycemia (N=86); most events were considered mild (81/86 events)

*Number of AEs or number of events in children aged 7 to 13 years with T1D during 2 clinical trials using the **670G system** (has the same SmartGuard Auto Mode technology as the MiniMed 770G, therefore according to the manufacturer, the results are comparable to the MiniMed 770G)*

• Trial 1 (with PLGS, N=105 participants):
  ○ No device-related SAE, PLGS-related DKA, or unexpected AEs
• Trial 2 (with Auto Mode, N=105 participants) with 2-week run-in and 3-month treatment phase:
  ○ No device-related SAE, including DKA or severe hypoglycemia
  ○ **Device-related AE** (N=80, 39%):
  ▪ **Hyperglycemia or severe hyperglycemia with or without ketosis** (n=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 at the infusion/sensor site, cellulitis, skin irritation, eczema, and other infections (n=14)
  ○ Procedure-related AE (N=5)
  ○ Device- and procedure-related AE (N=2), including hyperglycemia (n=1) and skin irritation (n=1)
  ○ **Severe hyperglycemia** (N=104); most were considered mild (77/104), and 1 severe hyperglycemia event complicated by acute gastroenteritis resulted in an emergency room visit

*Number of AEs or number of events in participants aged ≥14 years with T1D during 2 clinical trials using the **670G system** (has the same SmartGuard Auto Mode technology as the MiniMed 770G, therefore according to the manufacturer, the results are comparable to the MiniMed 770G)*

• Trial 1 (with PLGS, N=71 participants):
  ○ N=5, unrelated to the device or procedure (n=4), procedure-related AE (n=1)
  ○ No device-related SAE, PLGS-related DKA, or unexpected AE
• Trial 2 (with Auto Mode, N=124 participants) with 2-week run-in and 3-month treatment phase:
  ○ No SAE, DKA, or severe hypoglycemia events
  ○ Total number of device-related AEs (N=28):
  ▪ **Severe hyperglycemia** (n=17); **hyperglycemia** (n=6); **skin irritation** (n=3); **irritation at sensor site** (n=1); **rash** (n=1)

Abbreviations: A1C, glycosylated hemoglobin; AEs, adverse events; DKA, diabetic ketoacidosis; dL, deciliter; L, liter; LGS, low-glucose suspend; mg, milligram; mmol, millimoles; PLGS, predictive low-glucose suspend; SAE, serious adverse event; T1D, type 1 diabetes

Table E1. Adverse Events Reported During Insulin Pump Clinical Trials According to Device User Guides[96]

MiniMed 780G[7,8]
*Device-related AEs (number of events; N=170 participants) in children aged 7 to 17 with T1D during a 3-month trial using the **MiniMed 670G with the Guardian 3 Sensor** (according to the manufacturer, the MiniMed 670G system is considered clinically equivalent to the MiniMed 780 system even though it is an earlier-generation device)*
• **Hyperglycemia** (n=4); **rash/contact dermatitis** from sensor/tape (n=4); **severe hyperglycemia** (n=22); **infusion set failure** (n=2); **sensor site bleeding** (n=2); **bruise on upper arm** (n=1); **sensor insertion site discomfort** (n=1); **gastroenteritis** with hyperglycemia, possible device-related (n=1); **infection at pump site** (n=1); **skin irritation with excoriation** (n=1) • No device-related SAE or DKA
*Device-related AEs (number of events; N=179 participants) in adults aged 18 to 75 years with T1D during a 3-month trial using the **MiniMed 670G with the Guardian 3 Sensor** (according to the manufacturer, the MiniMed 670G system is considered clinically equivalent to the MiniMed 780 system even though it is an earlier-generation device)*
• **Rash/contact dermatitis** from sensor/tape (n=4); **severe hyperglycemia** (n=3); **bleeding from infusion site** (n=1); **bruise on upper arm** (n=1); **erythema abdomen at old sensor site** (n=1) • No device-related SAE or DKA
Omnipod DASH[50]
• No AEs are reported in the user guide
Omnipod 5[49]
AEs (number of events; N=80 participants) in children 2 to 5.9 years with T1D during a 3-month treatment phase in a clinical trial
• **Prolonged hyperglycemia**, defined as a blood glucose meter reading ≥300 mg/dL with ketones >1.0 mmol/L (n=20); **other AE** (n=5); **hyperglycemia** requiring evaluation or meeting SAE criteria (n=4); **non-DKA ketosis** (n=2); **skin irritation** (n=2); **cellulitis** (n=1)
AEs (number of events; N=112 participants) in children 6 to 13.9 years with T1D during a 3-month treatment phase in a clinical trial
• **Prolonged hyperglycemia**, defined as a blood glucose meter reading ≥300 mg/dL with ketones >1.0 mmol/L (n=13); **other AE** (n=8); **infection/irritation at infusion site** (n=2); **hyperglycemia** requiring evaluation or meeting SAE criteria (n=1); **hypoglycemia**, serious but not meeting other definitions (n=1); **severe hypoglycemia**, which required assistance of someone else (n=1); **DKA** (n=1)
AEs (number of events; N=128 participants) in patients 14 to 70 years with T1D during a 3-month treatment phase in a clinical trial
• **Other AE** (n=8); **prolonged hyperglycemia**, defined as a blood glucose meter reading ≥300 mg/dL with ketones >1.0 mmol/L (n=5); **infection/irritation at infusion site** (n=2); **hyperglycemia** requiring evaluation or meeting SAE criteria (n=2); **severe hypoglycemia**, which required assistance of someone else (n=2); **DKA** (n=2)
iLet Bionic Pancreas[6]
AEs in children (<18 years of age) with T1D during treatment with Humalog or Novolog in a randomized phase of a clinical trial
SAEs: • **Severe hypoglycemia:** 10.4 events per 100 person-years (7.3 with standard of care) • **DKA:** 0 events (0 with standard of care) • **Other SAEs:** 6.9 events per 100 person-years (7.3 with standard of care) *Other events* (number of participants with event, %) • **Worsened A1C from baseline to 13 weeks by >0.5%**: 13 (12%) [8% with standard of care] • **Hyperglycemia ± ketosis, study-device related**: 68 (60.7%) [0% with standard of care]; rate may be inflated in the Bionic Pancreas group because they were given a blood glucose and Ketone meter with specific monitoring instruction • **Hyperglycemia ± ketosis, non-device related**: 32 (27.1%) [1.9% with standard of care] • **Non-severe hypoglycemia**: 1 (0.9%) [0% with standard of care] • **Other AEs**: 7 (6.25%) [0% with standard of care]
AEs in adults (≥18 years of age) with T1D during treatment with Humalog or Novolog in a randomized phase of a clinical trial
SAEs: • **Severe hypoglycemia:** 25.5 events per 100 person-years (14.2 with standard of care) • **DKA:** 0 events, but 2 events (6.8 events per 100 person-years) occurred with Fiasp (another type of insulin); both DKA events were attributed to infusion set failures (0 with standard of care) • **Other SAEs:** 3.6 events per 100 person-years (7.1 with standard of care) *Other events* (number of participants with event, %)

Abbreviations: A1C, glycosylated hemoglobin; AEs, adverse events; DKA, diabetic ketoacidosis; dL, deciliter; L, liter; LGS, low-glucose suspend; mg, milligram; mmol, millimoles; PLGS, predictive low-glucose suspend; SAE, serious adverse event; T1D, type 1 diabetes

Table E1. Adverse Events Reported During Insulin Pump Clinical Trials According to Device User Guides[96]

• **Worsened A1C from baseline to 13 weeks by >0.5%**: 4 (4%) [8% with standard of care] • **Hyperglycemia ± ketosis, study-device related**: 27 (25.2%) [0% with standard of care]; rate may be inflated in the Bionic Pancreas group because they were given a blood glucose and Ketone meter with specific monitoring instruction • **Hyperglycemia ± ketosis, non-device related**: 12 (11.2%) [0% with standard of care] • **Non-severe hypoglycemia**: 1 (0.9%) [0% with standard of care] • **Other AEs**: 7 (6.25%) [5.5% with standard of care] *iLet device issues related to an AE in **adults and children** during the 13-week randomized controlled trial (N=219 participants; number of events):* • Infusion set issue (n=132); cartridge issue (n=16); battery/charging issue (n=5); algorithm-related issue (n=4); motor issue (n=3); alarm issue (n=2); skin irritation due to the infusion set (n=2); algorithm issue with user error (n=1)
t:slim X2 pump only[56]
• No AEs are reported in the user guide
t:slim X2 with Basal-IQ technology[53]
AEs in patients aged 6 to 72 years with T1D during a 3-week treatment phase in a clinical trial (reported for the Basal-IQ arm only)
• No severe hypoglycemic events, or other device-related AEs
t:slim X2 with Control-IQ technology[9]
Device-related AEs (number of events; N=78 participants in the Control-IQ arm) in children aged 6 to 13 years with T1D during a 4–6 month clinical trial
• No severe hypoglycemic or DKA events • **Ketosis** with infusion site failure (n=8); **hyperglycemia** with defective cartridge (n=1)
Device-related AEs (number of events; N=112 participants in the Control-IQ arm) in patients aged 14 to 71 years with T1D during a 4–6 month clinical trial
• No severe hypoglycemic events

Abbreviations: A1C, glycosylated hemoglobin; AEs, adverse events; DKA, diabetic ketoacidosis; dL, deciliter; L, liter; LGS, low-glucose suspend; mg, milligram; mmol, millimoles; PLGS, predictive low-glucose suspend; SAE, serious adverse event; T1D, type 1 diabetes

APPENDIX F: UTILIZATION DATA AMONG THE UTAH MEDICAID ACO POPULATION[§§]

Among the Utah Medicaid Accountable Care Organization (ACO) population, 54 unique patients received an insulin pump from January 2022 through June 2023; of these, 29 (54%) were under 18 years of age. As indicated by pharmacy claims, all patients received an Omnipod system (ie, Omnipod Eros, Omnipod DASH, or Omnipod 5). Among patients under 12 years of age, only claims for the Omnipod DASH and Omnipod 5 were found. Utilization was lowest for the Omnipod Eros, which is scheduled to be discontinued in the US later this year.[12] No medical claims were found among this population.

Table F1. Utilization Data for Insulin Pumps Among the Utah Medicaid ACO Population

Product	2022		2023	
	Claims	Patients	Claims	Patients
Omnipod Eros[a]	6	<5	<5	<5
Omnipod DASH	80	13	9	<5
Omnipod 5	87	20	36	18

[a] *Referred to in claims as the "Omnipod Classic" which we have a strong suspicion is the Omnipod Eros given that it can also be filled via the pharmacy, and is also known by this name.*[12,117]

Abbreviations: ACO, accountable care organization

[§§] Although we searched for pump National Drug Codes in pharmacy and medical claims using our standard database approach for querying claims, it is possible that some claims were missed due to limitations of our approach.