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Continuous Glucose Monitor, Insulin Pump, and Automated Insulin Delivery Therapies for Type 1 Diabetes: An Update on Potential for Cardiovascular Benefits

Meghan E. Pauley, DO[1,2], **Kalie L. Tommerdahl, MD**[1,2,3], **Janet K. Snell-Bergeon, PhD**[2], **Gregory P. Forlenza, MD**[2]

[1]Department of Pediatrics, Section of Pediatric Endocrinology, Children's Hospital Colorado and University of Colorado Anschutz Medical Campus, Aurora, Colorado, USA

[2]Barbara Davis Center for Diabetes, University of Colorado School of Medicine, Aurora, Colorado, USA

[3]Ludeman Family Center for Women's Health Research, University of Colorado School of Medicine, Aurora, Colorado, USA

Abstract

Purpose of Review—The incidence of type 1 diabetes (T1D) is rising in all age groups. T1D is associated with chronic microvascular and macrovascular complications but improving glycemic control can delay the onset and slow the progression of these complications. Utilization of technological devices for diabetes management, such as continuous glucose monitors (CGM) and insulin pumps, is increasing, and these devices are associated with improvements in glycemic control. Thus, device use may be associated with long-term prevention of T1D complications, yet few studies have investigated the direct impacts of devices on chronic complications in T1D. This review will describe common diabetes devices and combination systems, as well as review relationships between device use and cardiovascular outcomes in T1D.

Recent Findings—Findings from existing cohort and national registry studies suggest that pump use may aid in improving cardiovascular risk factors such as hypertension and dyslipidemia. Furthermore, pump users have been shown to have lower arterial stiffness and better measures of myocardial function. In registry and case-control longitudinal data, pump use has been associated with fewer cardiovascular events and reduction of cardiovascular disease (CVD) and all-cause mortality.

Corresponding Author: Meghan Pauley, DO, Department of Pediatrics, Section of Endocrinology, University of Colorado Anschutz Medical Campus, 13123 E. 16th Avenue, Box B265, Aurora, CO 80045, Telephone: 720-777-6128 | meghan.pauley@childrenscolorado.org.

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Conflict of Interest

MEP, KLT, and JKSB declare that they have no conflict of interest. GPF reports research support from Medtronic, Dexcom, Abbott, Tandem, Insulet, Beta Bionics, and Lilly; and has been a consultant/speaker/ad board member for Medtronic, Dexcom, Abbott, Tandem, Insulet, Beta Bionics, and Lilly.

Human and Animal Rights and Informed Consent

This article does not contain any studies with human or animal subjects performed by any of the authors.

Summary—CVD is the leading cause of morbidity and mortality in T1D. Consistent use of diabetes devices may protect against the development and progression of macrovascular complications such as CVD through improvement in glycemic control. Existing literature is limited, but findings suggest that pump use may reduce acute cardiovascular risk factors as well as chronic cardiovascular complications and overall mortality in T1D.

Keywords

Type 1 diabetes; continuous glucose monitor; insulin pump; hybrid closed loop; cardiovascular health; diabetes complications

Introduction:

Type 1 diabetes (T1D) is the most common form of diabetes in the pediatric population but is diagnosed in all ages, and incidence rates are continuing to rise. Currently, 1.6 million people are estimated to have T1D in the United States (1) and this figure is predicted to increase to 5 million people by the year 2050 (2). T1D is a result of permanent autoimmune destruction of insulin-producing pancreatic β-cells leading to an absolute insulin deficiency, and thus requires treatment with insulin for the remainder of the lifetime (3). Insulin is administered subcutaneously via injection with a syringe or pen or via infusion with an insulin pump. Injection therapy combines long-acting insulin (LAI, also referred to as basal insulin) and short- or rapid-acting insulin (RAI) to create a multiple daily injection (MDI) regimen. LAI is administered once or twice daily to inhibit gluconeogenesis and ketogenesis and RAI is administered multiple times per day to correct acute hyperglycemia and/or with meals to prevent hyperglycemia from carbohydrate intake (4).

Chronic hyperglycemia increases risk for microvascular and macrovascular complications, as well as resultant increased morbidity and mortality in T1D. The landmark 1993 Diabetes Control and Complications Trial (DCCT) demonstrated in both pediatric and adult populations alike that intensive insulin treatment and subsequent improvement in glycemic control delays the onset and slows the progression of these complications, but these improvements came at the expense of higher rates of hypoglycemia (5, 6). Hypoglycemia is associated with acute complications such as cognitive impairment and seizures and can contribute to chronic vascular and neurocognitive complications. Consequently, T1D treatment guidelines recommend achievement of >70% time in goal glycemic range (TIR), considered to be between 70 mg/dL and 180 mg/dL), and targeting a hemoglobin A1c (HbA1c) of 7% or less (4, 7-10). Adjunct TIR goals include minimizing the amount of time that blood glucoses exceed goal range and targeting <4% of time per day with glucoses below the goal range (10).

As diabetes technologies continue to undergo rapid advancement, utilization rates are increasing across many national registries, particularly for devices related to glucose monitoring and insulin delivery (11-15). Incorporating devices such as insulin pumps and continuous glucose monitors (CGM) into diabetes management is shown to help persons with diabetes (PwD) reduce risk of hypoglycemia and improve HbA1c and TIR (16-20), and thus may contribute to delaying onset and slowing progression of T1D-associated

complications. This review will provide an overview of commonly utilized diabetes devices and combination systems, as well as review relationships between technology use and T1D-associated cardiovascular outcomes.

Devices:

Continuous Glucose Monitors (CGM)

A subcutaneous CGM estimates blood glucose concentrations by measuring glucose concentration in the interstitial fluid via a sensor inserted directly under the skin. This device serves as an alternative to self-monitoring of blood glucose (SMBG) with a single measurement “fingerstick” glucometer (21). CGM sensors are inserted by the user and adhered directly to the skin with adhesive. In 2000, the Minimed CGM System was the first to obtain United States Food and Drug Administration (FDA) approval (22), and since that time, newer generations have continued to improve upon accuracy, functionality, and ease of use. CGMs can relay glucose values to a designated receiver, cellphone, and/or an insulin pump, and multiple brands now hold FDA approval to replace fingerstick glucose measurements for decision-making in insulin dosing in pediatric and adult populations with diabetes (23). Current devices have varying durations of wear, but typically require removal and replacement every 7 to 14 days. These devices are typically equipped with optional and customizable alerts for hypoglycemia, hyperglycemia, and rapid glycemic change.

CGMs can be divided into two categories based on data type: “real time” and “flash”. Real time CGMs (rtCGM) report glucose s every 1-5 minutes through Bluetooth communication to the designated receiver, cellphone, or insulin pump. Flash CGMs, also referred to as intermittently-scanned CGMs (isCGM), glucose concentrations every 1-15 minutes, but only download the data to the designated reader when the user “flashes” the Near Field Communication tag, at which time the previous 8 hours of data is downloaded (21). In 2018, the first 90-day implantable real-time glucose sensor received FDA approval for use in adults 18 years and older with diabetes, and then in 2019 also received approval for use in insulin dosing decision-making (24). This device is implanted under the skin during an outpatient procedure, requires users to wear a removable transmitter on the skin atop the sensor location, and is replaced every 90-180 days. This CGM glucose concentrations values every 5 minutes and transmits data via Bluetooth to a cellphone app (19, 25). CGMs may also be categorized based on calibration need, including factory-calibrated and calibration-requiring devices. Older CGM devices required 2-3 SMBG values per day to calibrate the sensor value against a reference glucose concentration. Many newer CGM devices are factory calibrated, allowing advanced calibration algorithms to ensure accuracy without the need for user SMBG entry. Table 1 provides an overview of commonly used CGMs.

CGMs are beneficial for all ages of people with T1D, regardless of insulin delivery method. Studies performed around the world utilizing various CGMs have associated CGM use with reductions in hypoglycemia (18, 26-31) and HbA1c (12, 14, 19, 30, 32-34), improvements in TIR (19), fewer episodes of diabetic ketoacidosis (DKA) (14, 35), and improvements in psychosocial outcomes (36-38). Furthermore, early initiation of CGM (i.e., within 1 year of T1D diagnosis) has shown association with lower HbA1c and fewer diabetes-

related emergency visits (39, 40). Few studies have directly compared rtCGM and isCGM, but limited evidence suggests that rtCGM has greater benefit than isCGM in reducing hypoglycemia and improving TIR (41-44). CGM has become standard of care in diabetes management around the world; indeed, United States and international clinical guidelines for both youth and adults with T1D support use of CGM, stating that CGMs are safe and effective in both populations. The American Diabetes Association (ADA) recommends CGM be considered from the time of diagnosis and implementation of insulin therapy (41). The International Society for Pediatric and Adolescent Diabetes (ISPAD) guidelines include that rtCGMs are effective in lowering HbA1c, reducing glucose variability, reducing hypoglycemia, and increasing TIR (45). Similarly, a joint statement by from the ADA and the European Association for the Study of Diabetes (EASD) describes CGM as the standard for glucose monitoring for most adults with T1D and an effective method to improve HbA1c and reduce hypoglycemia (4).

Insulin Pumps

Increasing numbers of PwD are utilizing insulin pumps, also referred to as continuous subcutaneous insulin infusion (CSII) systems, for insulin delivery (13, 46). The first insulin pump prototype was designed in 1963 and was a large system that was worn by the user similarly to a backpack. Wearable insulin pumps have now been commercially available since 1976 and have continued to undergo reductions in size and advancement in ease of use and capabilities (47). Use of modern CSII replaces the need for insulin injections, as these devices continuously infuse RAI into the subcutaneous tissue via a small cannula and allow for bolus dosing to be administered with carbohydrate intake at meals or to correct hyperglycemia. When utilized as a singular device without associated CGM, insulin dosing parameters for basal and bolus insulin are programmed into the pump. Users then input blood glucoses and carbohydrate counts for the pump to calculate and deliver the appropriate insulin bolus dose. CSII devices can be divided into two categories: tubed and patch. Tubed pumps store insulin in a reservoir within the pump device. Insulin is then delivered through tubing to a small subcutaneous infusion cannula adhered to the skin. Patch pumps are an adhesive patch device that includes an insulin reservoir that is directly connected to an infusion cannula. The cannula is inserted under the skin at the time the device is adhered to the body. Most insulin pumps require the entire patch or the infusion site to be changed every 3 days, though there are now tubed infusion sets approved for 7 days of continuous wear.

CSII is also beneficial for all ages of those with T1D, as it is associated with lower HbA1c (14, 20, 28, 33, 48-52). One pediatric study showed that when compared to MDI users, pump users had lower HbA1cs for 6 years of treatment follow up (53). CSII use is also associated with lower rates of hypoglycemia (33, 48, 54, 55), lower total daily insulin doses (48), less glycemic variability (56), and improved sleep (57) as compared to MDI therapy. In older adults with T1D, people using CSII were less likely to exhibit cognitive dysfunction compared to those using MDI (33). Recent data from diabetes registries and cohort studies also demonstrate associations between insulin pump use and reduced rates of DKA (13, 14, 48, 58), although two meta-analyses analyzing results of clinical trials found higher incidence of DKA in people using CSII when compared to MDI use (28, 52). Like CGMs,

insulin pump use is supported by United States and international T1D clinical treatment guidelines for both pediatric and adult populations. Both ADA and ISPAD guidelines recommend consideration of insulin pump therapy at the time of T1D diagnosis, as CSII is safe and effective and helps to achieve glycemic targets, reduce risk of hypoglycemia and DKA, improve quality of life, and prevent T1D-associated complications (41, 45).

Evolution of Device Collaboration

CGM and CSII devices may be used as independent devices; however, in recent years, technology has advanced to include real-time CGM data as a factor in user-directed and automated pump dosing decisions. Sensor-augmented insulin pump therapy (SAP) describes when a PwD uses CGM data to inform user-driven real-time decisions in insulin dose adjustment via CSII pump. SAP use is associated with a lower HbA1c without increasing rates of hypoglycemia when compared to MDI (59-61) and CSII alone (62). Automated insulin suspension systems allow the insulin pump to suspend basal insulin delivery in response to either a current low glucose concentration or prediction of an impending hypoglycemic event, as identified by CGM. Automated insulin suspension has been shown to reduce HbA1c (63, 64) hypoglycemia (65-68), and patient-reported fear of hypoglycemia (69).

The concept of a completely closed-loop insulin pump and glucose monitoring system has existed since 1974 when Dr. Ernst Friedrich Pfeiffer developed a system that combined an intravenous insulin infusion and continuous glucose monitoring (47, 70). Dr. Pfeiffer's system at that time was too large and complex for commercial use but served as a foundation for advancements in diabetes devices. Current closed-loop systems are termed automated insulin delivery (AID) devices wherein CGM data is incorporated in real time into insulin dosing algorithm software to automatically modulate (i.e., increase or decrease) basal insulin delivery via CSII pump. Some systems also include AID for hyperglycemia correction. The most advanced commercial systems currently available are the hybrid closed loop (HCL) devices, which requires user input of carbohydrate intake at mealtimes as well as some user-initiated correction doses. The first of such devices (Medtronic MiniMed 670G) obtained FDA approval in 2016 (Figure 1). Since the novel MiniMed device's market appearance, multiple other AID systems have obtained FDA approval. Tthese devices continually undergo rapid advancements in functionality and ease of use. Two systematic review and meta-analysis studies from 2017 and 2020, respectively, found AID system use to be the most effective treatment strategy for achieving target range blood glucose concentrations (71, 72). Figure 2 depicts a current HCL system.

AID Systems

The first commercial HCL system, the Medtronic MiniMed 670G, consist of the Medtronic 670G insulin pump paired with the Guardian 3 sensor. It received FDA approval in 2016 based on pivotal trial data demonstrating an average TIR of 68.8% in adults and 67.2% in adolescents with T1D (73). The 670G system was subsequently approved in children with an average TIR of 65% and the updated 770G system later received approval in young children with an average TIR of 63.8% (74, 75). While the 670G and 770G systems brought HCL technology from research to real-world use, the systems were limited by frequent fingerstick

testing requirements, excessive system alerts, and frequent exits from automation (76-79). A 12 month analysis of real-world use of the Medtronic 670G at a single center found a significant decrease in time spent in HCL mode over time, with a decrease from 70.7% at 1 month of use to 49.3% at 12 months of use in children with T1D (77). This same analysis demonstrated showed that adults had a higher time in HCL mode which was maintained in the 78-76% range over 12 months. The updated version of the Medtronic MiniMed design, the advanced hybrid closed loop 780G system, appears to have resolved these issues. This system includes automated basal insulin delivery based upon total daily insulin requirements over previous days as well as automatic correction dose delivery. The approval trial of the 780G system demonstrated a 75.1% average TIR for adults and 72.7% average TIR for adolescents, with adults spending 95.2% time in HCL mode and adolescents spending 93.8% time in HCL mode over 3 months of system use (80). Initial trials were conducted using the Guardian 3 CGM but the commercially available system pairs with the Guardian 4 CGM. At the time of writing, 780G is CE marked in Europe but is still under review by the FDA for approval in the United States.

The second HCL system to come to market was the Tandem Control-IQ (CIQ) HCL system, which includes the Tandem t:slim X2 insulin pump paired with Dexcom G6 CGM (Figure 3). This system expanded on a decade of previous research involving the University of Virginia Diabetes Assistant algorithm and can adjust basal insulin delivery rates as well as administer automatic correction doses according to current and predicted future glucose concentrations (81-83). The National Institute of Health (NIH)-sponsored randomized controlled trial of the CIQ system demonstrated an average 71% TIR for adults and adolescents and a 67% average TIR for children (84, 85). These studies resulted in FDA approval for adults and adolescents in 2019 followed by approval in children in 2020. Pilot testing of the CIQ system in young children demonstrated an average TIR of 71.3% during a brief hotel study with additional at-home use (86). The approval trial of this system in young children has been completed but not yet published.

The European market has several phone-based HCL designs which have received CE mark. The CamAPS FX system demonstrated an average TIR of 65% in adults and was the first system approved to be controlled from the user’s cell phone (87). The algorithm runs on an Android phone and works with the Dexcom G6 CGM and the DANA Diabecare RS insulin pump (88). In an approval trial completed in 2017, the Diabeloop system demonstrated an average TIR of 68.5% in adults (89) and the commercial version of the system is compatible with the Roche Accu-Chek Insight, Vi Centra Kaleido, SOOIL Dana-I and Cellnovo insulin pumps (88).

The most recently approved HCL system is the Insulet Omnipod 5 patch-pump system which pairs the Omnipod tubeless patch pump with the Dexcom G6 CGM (Figure 4). This system can modulate basal insulin delivery rates based upon customizable glucose targets and current and predicted glucoses, with further basal insulin rate automation over the 3-day period of wear as the system recognizes glucose trends (90). The approval trial for Omnipod 5 demonstrated an average 73.9% TIR for adults and adolescents and an average 68% TIR for children over the course of 3 months of use (91). Additional studies completed in the young child age group demonstrated an average 68.1% TIR (92). Table 2 provides an

overview of HCL systems that are currently available and under FDA review in the United States.

Diabetes Technology and Cardiovascular Outcomes:

Current T1D treatment strategies and goals are largely founded upon results from numerous studies from the DCCT and its epidemiological follow-up study, the Epidemiology of Diabetes Interventions and Complications (EDIC), which demonstrated that intensive insulin therapy aimed at achieving glycemic control approximating normoglycemia is effective at delaying the onset and slowing the progression of microvascular and macrovascular complications seen in T1D (5). Delaying and slowing these chronic complications is critical, as they contribute significantly to morbidity and mortality in T1D.

Macrovascular complications, specifically atherosclerotic cardiovascular disease (ASCVD), are the leading cause of morbidity and mortality in diabetes (93, 94). T1D significantly increases the risk for cardiovascular disease (CVD) and this occurs independently of other common CVD risk factors. Notably, people with T1D are more than twice as likely to exhibit cardiovascular mortality than the general population, even when meeting glycemic targets (95, 96). Known cardiovascular risk factors also contribute to this risk but are not entirely responsible for the excess mortality associated with diabetes (97). Development of atherosclerosis begins in childhood, and youth with T1D may develop subclinical CVD even within the first 10 years of diabetes diagnosis (98). CVD contributes to 25-50% of deaths in those with T1D of less than 20 years diabetes duration, and that percentage increases with longer diabetes duration (93, 99, 100).

Glycemic status is a modifiable risk factor for CVD, and glycemic control has been shown to predict coronary heart disease events independently of other risk factors (101, 102). Chronic hyperglycemia may promote atherosclerosis, endothelial dysfunction, and arterial stiffness (103). Studies also demonstrate associations between glucose variability, CVD, and all-cause mortality, regardless of mean glucose concentration (103-107). Alongside chronic hyperglycemia and glucose variability, hypoglycemia also contributes to cardiovascular complications. Hypoglycemia-induced changes in hemodynamics, hemostasis and coagulation, arterial wall stiffness, and cardiac electrophysiology and autonomic function are postulated to explain the associations seen between hypoglycemia and cardiovascular complications including myocardial ischemia and cardiac arrhythmias (108). Studies have found that a history of recurrent hypoglycemia was associated with reduced survival after a major CVD event such as myocardial infarction or stroke (109), and those with T1D who report history of repeated hypoglycemia events had a higher prevalence of CVD (110). DCCT/EDIC showed that tighter glycemic control can improve cardiovascular risk factors such as hypertension, carotid intima media thickness, and coronary artery calcium scores, and even reduce cardiovascular events (111-114).

As diabetes device use may improve glycemic control and stability, use of diabetes technologies may also have favorable impacts on T1D-associated complications. Indeed, a recent prospective cohort study including 515 adults with T1D utilizing CGMs and insulin pumps found that TIR and HbA1c were independent risk factors for microvascular and

macrovascular complications, respectively (115). Yet, few existing studies have assessed for relationships between technology use and complication onset or severity in T1D. Limited studies suggest that CSII use may reduce microvascular complications seen in T1D, such as retinopathy, neuropathy, and diabetic kidney disease (116-123). There is also evidence suggesting insulin pump use may be beneficial for cardiovascular risk factors and CVD. A large study from the Diabetes-Patienten-Verlaufsdokumentation (DPV) registry involving multiple diabetes centers in Germany, Austria, Switzerland, and Luxembourg found that initiation of insulin pump therapy within 6 months of diagnosis in people with childhood onset T1D was associated with a better cardiovascular risk profile compared to those with delayed CSII initiation within 2-3 years of T1D diagnosis. Specifically, they reported lower mean systolic blood pressure and higher high density lipoprotein cholesterol (HDL-C), although no significant relationships were seen with diastolic blood pressure, low density lipoprotein cholesterol (LDL-C), or triglycerides (124). A 12-month, randomized, multicenter case-control study found that PwD using insulin pumps demonstrated increased HDL-C and decreased total cholesterol, LDL-C, and triglycerides as compared to MDI users. This finding persisted after 8 years of follow up (56, 125). During the follow up study, CSII use was also associated with fewer cardiovascular events, specifically atrial fibrillation, premature ventricular contractions, acute coronary infarction, angina pectoris, peripheral vascular ischemia, and heart failure, as compared to MDI use (125). Similar results were seen in a large T1D Swedish registry, which found pump use was associated with a 45% reduction in fatal coronary heart disease, 42% reduction in fatal CVD, and a 27% reduction in all-cause mortality as compared to MDI use over a mean follow up period of 6.8 years. Authors hypothesize that the reduction in severe hypoglycemic episodes seen with insulin pump use in the study may have contributed to the reduction of cardiovascular mortality (126). Similarly, a 2017 study in participants with T1D utilizing CSII found that longer duration of CSII use was related to longer duration of freedom from chronic diabetes complications, fewer cardiovascular events, and lower mortality (127).

Arterial stiffness is a marker of cardiovascular events, and pulse wave velocity (PWV) is the gold standard measure of arterial stiffness (128). A prospective study found young adults with T1D of 10 or more years duration had increased PWV compared to healthy controls. After 5 years of follow up, CSII use was associated with reduced PWV compared to MDI users (129). These results align with previous literature which showed lower PWV in those with T1D using CSII as compared to MDI (130). Endothelial dysfunction is suggested to play a role in development of atherosclerosis (131), and a recent study including 123 youth and adults with T1D found that pump use may impart cardiac benefit through improvements in endothelial function and overall myocardial performance. As compared to MDI use, CSII users had lower measures of carotid intima-media thickness and anteroposterior diameter of the infrarenal abdominal aorta via ultrasound assessment, and lower left and right Tei index and left E/e’ ratio (132).

Expert Commentary and Conclusions:

For over 3 decades, the primary barometer for diabetes control has been HbA1c, based on established correlations between HbA1c and vascular complications. Over the past several years, however, TIR has emerged as a viable alternative to HbA1c. Analysis within the

DCCT demonstrated that TIR derived from frequent SMBG measurements can hold similar correlations to T1D outcomes as those seen with HbA1c (133). Additional analyses of correlations between HbA1c and average glucose concentrations have demonstrated wide ranges of average glucose at each HbA1c percentage, with potential bias for HbA1c tendencies across racial/ethnic groups (134, 135). These observations have driven diabetes assessment to move “beyond HbA1c” to include use of other measures such as TIR, glucose management index (GMI), and glycemia risk index (GRI) (10, 136, 137). During the quarantine period due to COVID-19, many practices managed PwD using CGM, with an emphasis on TIR and other CGM-derived metrics as patients were unable to obtain HbA1c measurements in a medical office or laboratory. With growth of telemedicine practices, it is expected that virtual visits will continue to require glycemic assessment via TIR.

AID research uses both HbA1c and TIR as prespecified endpoints, though there is interest in the field to consider TIR as a primary glycemic outcome. Technology research moves at a rapid pace with new devices developed every year. Technology development studies frequently last 1-4 weeks and thus require a valid metric of glycemic control that can be assessed within that timeframe. Even within pivotal trials, the need for laboratory HbA1c assessments necessitates in-person visits and venipuncture, which may limit clinical trial participation for some populations. For these reasons, it is desirable for TIR and CGM-based metrics to gain acceptance as valid endpoints.

A concern with fully equating CGM-derived metrics with established HbA1c targets is that little research exists to definitively correlate soft outcomes such as TIR, GMI, and GRI with hard outcomes such as diabetes-associated retinopathy, nephropathy, neuropathy, and cardiovascular disease. While HbA1c is clearly correlated with vascular hard endpoints, associations between CGM-derived metrics and vascular endpoints are limited to inferences made through associations with HbA1c rather than direct comparisons. This has been a major limitation for both regulatory agencies and payers accepting CGM-derived endpoints as fully validated surrogates for change in rates of vascular disease.

Next steps include combining data from large multicenter studies, registries, and national databases to clearly demonstrate these relationships with CGM metrics obtained over the past 5-10 years. Additionally, prospective longitudinal studies are needed to examine CGM-derived metrics, CGM and AID use, and the rates of vascular disease in order to move beyond dependence on HbA1c as the primary indicator of glycemic control in T1D.

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Figure 1.
Medtronic 670G insulin pump (**left**) with Guardian Sensor 3 continuous glucose monitor (**right**).

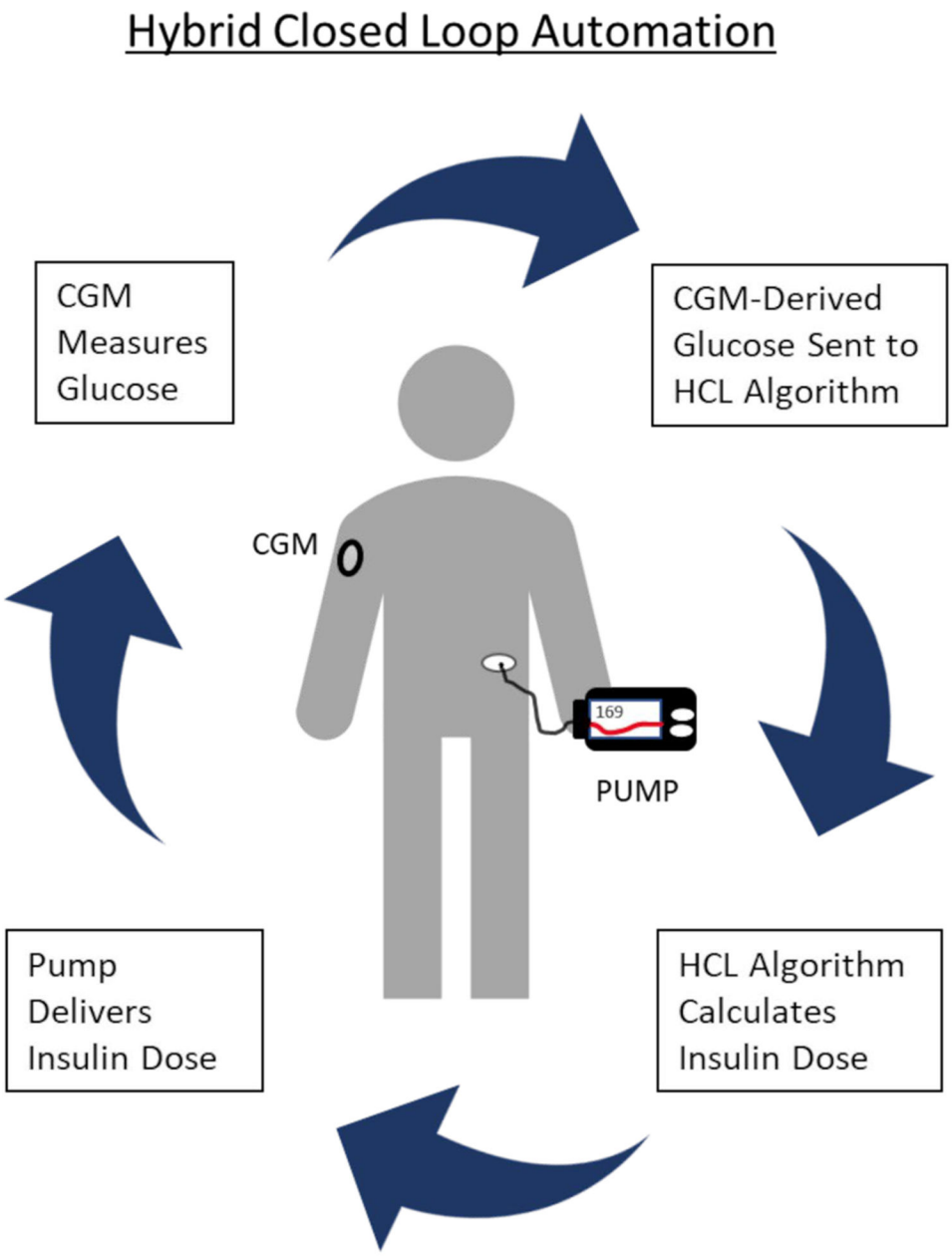

Figure 2.

Illustration of Hybrid Closed Loop System. A continuous glucose monitor measures the interstitial glucose concentration and sends the glucose measurement to the control algorithm. The algorithm calculates the dose of insulin required based on the glucose received. The insulin pump then delivers the insulin dose. The cycle repeats.

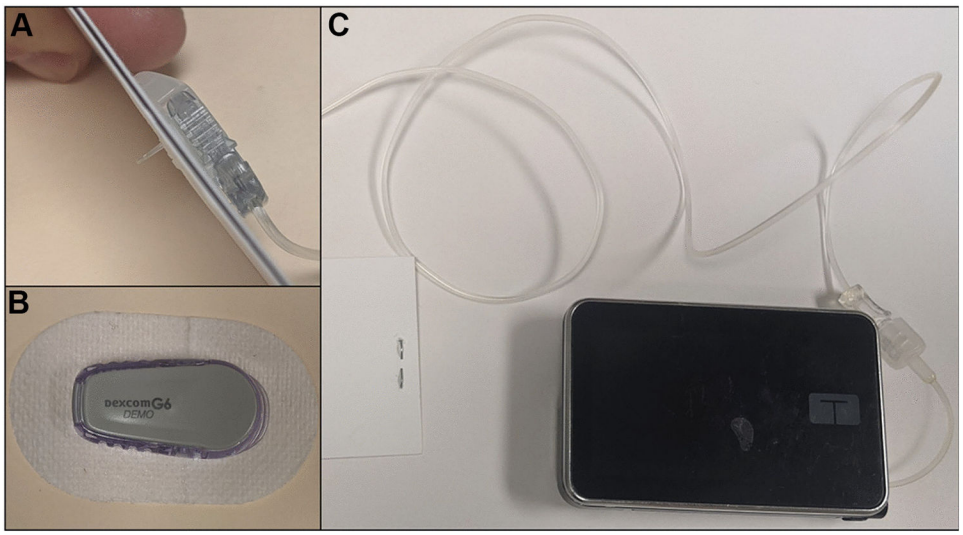

Figure 3.

Tandem Control-IQ Hybrid Closed Loop System: (**A**) Insulin infusion set with subcutaneous cannula. (**B**) Dexcom G6 continuous glucose monitor. (**C**) Tandem t:slim X2 insulin pump with infusion tubing.

Figure 4.
Omnipod patch pump (**top right**) with personal diabetes manager (**left**) and Dexcom G6 continuous glucose monitor (**bottom right**).

Table 1.

Comparison of Select Continuous Glucose Monitors

	Medtronic Guardian Sensor 3	Medtronic Guardian Sensor 4*	Senseonics Eversense	Dexcom G6	Abbott Freestyle Libre 2	Abbott Freestyle Libre 3
Sensor Type	**rtCGM**	**rtCGM**	**rtCGM**	**rtCGM**	**isCGM**	**rtCGM**
Age of Approval (years)	2+	7+	18+	2+	4+	4+
Subcutaneous or Implanted	Subcutaneous	Subcutaneous	Surgically Implanted Transmitter adhered to skin over implanted sensor	Subcutaneous	Subcutaneous	Subcutaneous
Duration of Wear (days)	7	7	Maximum 180	10	14	14
Calibration Status	User calibration with blood glucose meter at least 2x/day	Factory calibrated	User calibration with blood glucose meter 2x/day	Factory calibrated	Factory calibrated	Factory calibrated
Approved for Use for Insulin Dosing	No	Yes	Yes	Yes	Yes	Yes
Compatible in HCL System	MiniMed 670G, 770G	MiniMed 780G	No	Tandem t:slim X2 CIQ Omnipod 5 CamAPS ** Diabeloop **	No	No
References for Table 1 information: (25, 138-140)						

* At the time of writing, CE marked in Europe but still under review for United States FDA approval.

** System not available in the United States.

Abbreviations: rtCGM, real-time continuous glucose monitor; isCGM, intermittently scanned continuous glucose monitor; HCL, hybrid closed loop; CIQ, Control IQ.

Table 2.

Comparison of Select Hybrid Closed Loop Systems

	Medtronic 670G/770G	Medtronic 780G*	t:slim X2 Control IQ	Omnipod 5
Term for Automated Insulin Delivery	"Auto Mode"	"Smart Guard"	"Control-IQ"	"Automated Mode"
Age of Approval (years)	7+ (670G) 2+ (770G)	7+	6+	6+
Basal Rate Automation	"Auto Basal" Basal rates based on total daily insulin from previous 2-6 days	"Auto Basal" Basal rates based on total daily insulin from previous 2-6 days	"Control IQ" Can increase or decrease the programmed basal rates	"Adaptive Basal" Basal rates determined from total daily insulin since last pump change
Correction Bolus Dose Automation	No	Yes, IF: Glucose >120 mg/dL AND at maximum "auto basal" delivery	Yes, IF: Glucose predicted to reach >180 mg/dL Maximum 1 dose per hour Delivers 60% of calculated dose from programmed settings	No
Algorithm Target Glucose	120 mg/dL	Select 100, 110, or 120 mg/dL	112.5-160 mg/dL range	Select 110, 120, 130, 140, or 150 mg/dL
Special Features	"Temporary Target": changes target glucose to 150 mg/dL (30 minutes-12 hours)	"Temporary Target": changes target glucose to 150 mg/dL (30 minutes-24 hours) Extended wear (7 day) insulin infusion set	"Exercise Activity": changes target glucose range to 140-160 mg/dL "Sleep Activity": changes target range to 112.5-120 mg/dL and prevents automated correction bolus	"Activity Feature": changes target glucose to 150 mg/dL and reduces insulin delivery (1-24 hours) User can control basal or bolus dosing remotely from cell phone

References for Table 2 information: (138, 139)

*At the time of writing, system CE marked in Europe but under review for United States FDA approval.