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Biopsychosocial Factors Associated With Satisfaction and Sustained Use of Artificial Pancreas Technology and Its Components: a Call to the Technology Field

Gregory P. Forlenza¹, Laurel H. Messer¹, Cari Berget¹, R. Paul Wadwa¹, and Kimberly A. Driscoll¹

¹Barbara Davis Center, University of Colorado Denver, 1775 Aurora CT MS A140, Aurora, CO 80045, USA

Abstract

Purpose of Review—Summarize biopsychosocial factors associated with using continuous glucose monitors (CGMs), insulin pumps, and artificial pancreas (AP) systems and provide a “call to the field” about their importance to technology uptake and maintained use.

Recent Findings—Insulin pumps and CGMs are becoming standard of care for individuals with type 1 diabetes (T1D). AP systems combining a CGM, insulin pump, and automated dosing algorithm are available for commercial use. Despite improved glycemic control with AP system use, numerous barriers exist which may limit their benefit. Studies on components of AP systems (pumps, CGMs) are limited and demonstrate mixed results of their impact on fear of hypoglycemia, adherence, quality of life, depression and anxiety, and diabetes distress. Studies examining biopsychological factors associated specifically with sustained use of AP systems are also sparse.

Summary—Biological, psychological and social impacts of AP systems have been understudied and the information they provide has not been capitalized upon.

Keywords

Type 1 diabetes; Artificial pancreas; Insulin pumps; Continuous glucose monitoring; Behavioral health

Introduction

Throughout the last several decades, there has been a rapid increase in novel technology available for individuals with type 1 diabetes (T1D) to monitor and control their blood glucose. Continuous subcutaneous insulin infusion pumps and continuous glucose monitors

Kimberly A. Driscoll, kimberly.driscoll@ucdenver.edu, Gregory P. Forlenza, gregory.forlenza@ucdenver.edu, Laurel H. Messer, laurel.messer@ucdenver.edu, Cari Berget, cari.berget@ucdenver.edu, R. Paul Wadwa, paul.wadwa@ucdenver.edu.

Compliance with Ethical Standards

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(CGMs) are becoming standard of care for many individuals with T1D. Insulin pump usage is at or above 50% in many countries and CGM use has grown exponentially during the last 5 years in both the USA and Europe, though technology use remains lower among adolescents and some minority groups [1–3]. Much of this growth has been attributed to improvements in CGM accuracy as well as improved coverage by a variety of payers including Medicare in the USA [4,5]. With the recent FDA approval of factory calibrated real-time CGMs including the integrated iCGM category, it is expected that CGM use will continue to grow in the near future [6, 7].

Combination of a CGM, insulin pump, and automated insulin delivery algorithm, often referred to as an artificial pancreas (AP) system, holds immense potential to further glycemic improvements in individuals with T1D. The first hybrid closed loop AP system, the MiniMed 670G, was approved by the FDA in September 2016 in individuals 14 years old and in those 6–13 years old in June 2018 [8–10]. The MiniMed 670G has been demonstrated to improve A1C values by 0.6% in adolescents and adults with T1D and by 0.4% in school-aged children [11]. A predictive low glucose suspend system using the Tandem X2 insulin pump and Dexcom G6 CGM was also recently FDA approved and has been shown to significantly reduce hypoglycemia without increasing average sensor glucose values [10].

Despite these recent approvals and rapid advances in technology, numerous barriers exist which could potentially limit the benefits of AP technology. Limited on-body “real estate” and skin reactions to adhesives remain significant concerns for many people. In addition, some people may experience greater stress and data overload with the availability of continuous real-time data constantly reminding them about their T1D and the possible need to take more actions per day to control their blood glucose. Emerging AP systems will also vary in their designs and degree of user interaction and burden [12, 13]. The overarching goal of AP technology should be to maximize benefit and improve glycemic control while also minimizing burden for individuals with T1D and their families.

The primary purpose of this article is to review the biopsychosocial factors associated with using CGMs and insulin pumps including benefits, barriers, and burdens, as all are essential components to any AP system, and to shed light on the impact of these devices on the people who wear them. Second, research on the biopsychosocial aspects of sustained use of AP systems is reviewed. Finally, recommendations for improving AP devices from the biopsychosocial perspective are made in an effort to highlight the importance of these factors when developing future systems and improving those that already exist.

Current Uptake of CGMs and Insulin Pumps

Although there are demonstrated glycemic benefits to wearing CGMs for both children [14–16] and adults [16, 17], uptake remains suboptimal primarily due to the burden of wearing the CGM device [11, 18, 19]. Although uptake has increased to 17–25% overall, with more uptake currently in preschool-aged and early school-aged children [1], CGM use is still relatively low given that several systems have been commercially available for almost two decades. In contrast, insulin pump use exceeds 60% in the USA and 40% in some European

countries. Understanding the biopsychosocial benefits and barriers to CGM and insulin pump use is essential given that they are necessary components of any AP system.

Biopsychosocial Factors Associated With CGM and Insulin Pump Use

Biological Factors

Impact on Glucose Levels and Control—Use of a CGM or an insulin pump has been shown to improve A1C [3,20,21,22•, 23] and decrease the occurrence of hypoglycemia [24, 25]. The impact of CGM use is undeniable, as demonstrated by a median reduction of 30% in hypoglycemic events in adults who use CGMs compared those who do not [24]. Analysis of T1D Exchange and Austrian/German DPV (Diabetes Patienten Verlaufsdocumentation) registry data showed that in almost 60,000 people with T1D, CGM use was associated with lower A1C regardless of insulin delivery method [1]. Furthermore, CGM users were more likely to achieve target A1C than non-users in both registries and pregnant women with T1D who use CGMs also experience reductions in hypoglycemia [26]. Sensor-augmented pump therapy, the practice of using a CGM and insulin pump together, leads to even greater improvements in both A1C and hypoglycemia than is seen with individual use of a CGM or pump [1,27]; however, at least one recent study found an increase in hypoglycemia in adults switching from injections to sensor-augmented pump therapy [28].

Adverse Skin Reactions and Skin Infections—Skin reactions and infections have been reported at the sensor site with first-generation CGM systems [29–31] and when using insulin pump infusion sets [32, 33]. Despite improvements to technology, skin reactions and infections continue to be an ongoing concern for individuals with T1D who use these devices [33–35]. They are particularly common in children and adolescents [29, 32], when sweating and activity causes frequent skin irritation and adhesive problems [31]. In fact, 79.5% of youth with T1D are diagnosed with pruritus (70%), eczema (46%), and wounds (33%) as a result of CGM use [32]. Adults also report adverse skin reactions [35] including pregnant women who cite them as the primary reason for discontinuation [36]. With glycemic control being especially critical in the peripartum period, discontinuing CGMs likely introduces additional burden due to reduced opportunities to monitor glycemic control. Skin-related device burden is thus a significant barrier to sustained device use in a majority of individuals. Addressing this barrier is a vital component to increasing device use and improving the benefit to burden ratio for the broad spectrum of individuals with T1D.

Psychological Factors

Hypoglycemia Safety—CGMs can increase a sense of safety from hypoglycemia while sleeping, exercising, and driving [11, 37] and confidence in controlling T1D [11]. The recent DIAMOND randomized trial of adult users of CGMs and multiple daily injections showed a significant increase of hypoglycemia confidence, as defined by the Hypoglycemia Confidence Scale [38], compared to those in the control group [37]. This study also showed a marked increase in the CGM user's rating of their partner's hypoglycemia confidence, indicating a relational or social benefit. Similarly, several studies, dating back to the 1980s, have found a reduction in the prevalence and severity of hypoglycemia with insulin pump

therapy [39]. Recently, a threefold decrease in the incidence of severe hypoglycemia when switching from multiple daily injections to insulin pump therapy was observed [40].

Fear of Hypoglycemia—Fear of hypoglycemia (FOH) is akin to a phobia and is an extreme fear of having low blood glucose levels. This phobia of hypoglycemia can result in purposeful behaviors to maintain hyperglycemia and/or extreme cognitive worry about low blood glucoses and their social consequences. Research on the impact of CGM and insulin pump use on FOH is limited, although more studies have focused on CGMs. In general, research on the impact of CGMs on FOH is mixed [41] with several studies reporting no impact of CGM [37, 42] or insulin pump [43] use on FOH. In contrast, the STAR3 study of children and adults with T1D showed significant improvement in FOH when comparing the period of time prior to sensor-augmented pump initiation and the period following initiation [44]. It is unknown if this was due to CGM use, insulin pump use, or the combination of both. In addition, a reduction in worry about hypoglycemia has been found for children and young adults and their caregivers when using CGM and insulin pumps [45]. Overall, more research is needed to determine the impact of CGM and insulin pumps on FOH. In addition, it will be extremely important to determine if the marked reduction in hypoglycemia that has been demonstrated with AP systems has a significant impact on reducing FOH in adults with T1D and children and adolescents and their parents, the latter of whom tend to experience more FOH than their children.

Self-Management Behaviors—As technology evolves, so must our measurement of self-management behaviors. Adherence to CGM and insulin pump use has typically been examined in the context of number of days of wear in the former [46, 47] and missed boluses in the latter [48, 49]. A comprehensive list of individual self-management tasks for CGMs (e.g., respond to alerts) and insulin pumps (e.g., carrying supplies, counting carbohydrates, administering boluses, checking blood glucose) has been described by Tanenbaum and colleagues [50]. Examination of the relationships between specific T1D self-management behaviors (e.g., blood glucose checking, carbohydrate inputs, and insulin bolusing) using objectively downloaded data from blood glucose monitors and insulin pumps has also been conducted [51, 52]. In general, children and adolescents demonstrate higher frequency of bolusing than to blood glucose checks and carbohydrate inputs [51, 53]. Although the combination of blood glucose checks, carbohydrate inputs, and insulin bolusing are essential to T1D self-management, these three insulin pump adherence behaviors are only completed 29–45% within a specified amount of time [51, 52]. Youth without wireless compatible blood glucose monitors do not input a substantial number of blood glucose results into their pumps, demonstrating the importance of using wireless monitors in T1D care as a tool to reduce the burden of additional manual steps [54]. Finally, a series of studies demonstrated that the frequency of blood glucose checks, carbohydrate inputs, and insulin bolusing increases before the T1D clinic visit (i.e., white coat adherence) [53, 55, 56].

Quality of Life—Two systematic reviews completed in the last decade note the difficulty in ascertaining the impact of technology on quality of life (QOL) due to the lack of well-controlled studies, and inconsistent assessment of QOL [57, 58]. Although some studies of

CGM and insulin pump use have shown improvements in QOL [11, 37], others have not [59–61]. Sensor-augmented pump therapy likewise has mixed QOL results, with some studies showing improvement, and others not [62]. For example, Hilliard and colleagues found an improvement in T1D-related QOL in youth 12 months after initiating insulin pump therapy with greater improvements in QOL in those with more depressive and anxiety symptoms at baseline [63]. However, Nueboer and colleagues found no difference in QOL between youth treated with an insulin pump and youth treated with multiple daily injections after 14 months of insulin pump treatment [64]. QOL benefits appear to be related to reductions in hypoglycemia and increased confidence in preventing hypoglycemia [11, 37, 65], increased flexibility around mealtimes, and reduced diabetes distress and parenting stress [37].

Depression and Anxiety—The randomized controlled Juvenile Diabetes Research Foundation (JDRF) CGM trial reported that youth using CGMs had more trait anxiety (i.e., stability of unpleasant emotional arousal occurring on a daily basis) than those who did not wear CGMs [61]. In contrast, adults in the same study who were randomized to CGMs reported less state (i.e., unpleasant emotional arousal when faced with a threatening situation) and trait anxiety than non-CGM users [61]. Although the study was limited by a small sample size, findings suggest that CGMs may affect both state and trait anxiety differently in adults and children with T1D. Wong and colleagues found that an increase in depressive symptoms, as measured by the Children's Depression Inventory (CDI), was the only clinical or demographic variable associated with insulin pump discontinuation in adolescents [66]. Specifically for every 1 point increase in CDI depression scores, there was a 20% increase odds of discontinuation. This suggests that depressive symptoms may influence attitudes towards pump use and result in reduced satisfaction with pump therapy leading to discontinuation.

Diabetes Distress—Diabetes distress comprises the emotional burdens, stresses, and worries that may result from managing T1D [67], which have been shown to decrease in adults with T1D who use CGMs [37]. Importantly, CGM use has also been shown to *not* worsen diabetes distress in adolescents [68]. However, diabetes distress may be a barrier to uptake of diabetes technology. In a recent study examining perceived barriers to CGM and insulin pump use with more than 1000 adults with T1D, those with higher levels of diabetes distress reported more barriers to diabetes technology use and had lower rates of technology use [19].

Body Image—Both CGMs and insulin pumps are visible on the body and both adults and adolescents describe feeling self-conscious about wearing them [19, 69, 70]. Some CGM users feel as if they look robotic or like a “cyborg” [70], whereas some insulin pump users feel as if they are “shackled” to them [71]. Adults feel self-conscious during intimacy with sexual partners and are concerned about attractiveness [70]. Others dislike CGMs and insulin pumps because they draw attention, identify them as having T1D, or being different from others [19, 70]. Thirty percent of CGM discontinuers do not like the device on their bodies, which is cited as a reason for discontinuance; this was endorsed more frequently by

younger adults than older adults [19]. Insulin pump users who discontinued pumps reported that the pump was bothersome during summer and physical activities and sport [72].

Social Factors

Financial Burden—The financial burden of CGM use is a perpetual problem [73], as CGM sensors require replacement every 7–10 days, and transmitters need replacing on an annual or semi-annual basis. Similarly, insulin pumps require changes in insulin and infusion sets every 3 days. Cost is the primary reason for CGM discontinuance in adults with T1D [19] and has been routinely identified as a barrier to CGM [11, 19, 29, 74, 75] and insulin pump use [76]. Distress related to not knowing if continuation of CGM use will be possible when financial difficulties arise also occurs [75]. Adolescents have reported being concerned about losing CGMs because it is expensive [69, 77]. Overall, the ongoing expenses associated with CGM can lead to distress about finances as well as uncertainty about whether individuals can sustainably afford CGM for ongoing T1D management.

Technology Performance

Technological Difficulties—Alarm fatigue is often cited as a concern when using CGMs [19, 42, 75, 78, 79]. Thirty-two percent of adult users in the USA who discontinued CGMs reported alarms as a primary reason for discontinuation [19]. Individuals with T1D also report concerns related to CGMs alarming at inconvenient times or causing unwanted attention to T1D at school, work, or personal settings and disturbing sleep [69, 77, 80]. While the frequency of alerts may be a nuisance in itself, it is also likely that alerts due to inaccurate readings cause additional frustration [19]. Fine-tuning alert settings can enhance CGM utility, but may not reduce the social burden of having attention called to the CGM user's T1D. Many studies have documented the technical difficulties that individuals with T1D experience using insulin pumps including software problems, key pad failure/problem, battery issues, cracked/physical damage, insulin leaks, and set/site failures including occlusion [76, 81–84]. Although overall discontinuation rates for insulin pump use were low in both the T1D Exchange Registry data (3%) and the DPV database (4%), reasons for discontinuation included problems with wearability (57%), disliking the pump and/or feeling anxious about it (44%), and problems with glycemic control (30%). Other reasons included perceiving the pump as too complicated, pump malfunction, and feeling that it did not help [76].

Accuracy and Trust—Perceived inaccuracy of CGM and subsequent loss of trust in the system are other barriers to CGM use in older CGM systems. Early commercial CGM systems showed accuracy only within 15–20% of blood glucose meters, providing an unacceptable level of accuracy for many people with T1D [74, 85]. Accuracy has gradually improved with new iterations of sensors [86, 87] and has been confirmed for sensors inserted in a variety of locations on the body [88]. CGM accuracy can vary with calibrations, placement, and rate of change, and are the source of significant distress when the device is perceived as being inaccurate [19, 75]. In fact, nearly 33% of CGM discontinuers identified lack of accuracy as a primary reason for discontinuing CGMs, and 18% identified lack of trust in the system for discontinuance [19]. These two concepts are interrelated, as accuracy

is a fundamental component of being able to trust the system to appropriately monitor glucose levels, especially for hypoglycemia [75, 89].

Overview of AP Systems

AP technology involves combining a CGM, an insulin pump, and an algorithm that automates basal insulin delivery every 5 min based on predicted trends in CGM values (Fig. 1) [90–93]. A fully closed loop system would automate all insulin delivery including basal insulin and bolus requirements for meals without requiring any user interaction [9, 94]. No fully closed loop system is commercially available, though several designs have undergone preliminary testing [94]. Current AP systems are considered hybrid closed-loop systems, as they involve automation of basal insulin delivery, but still require user input of carbohydrate consumption and delivery of manual insulin boluses for meals [17].

The benefits of AP technology have been well documented in two recent meta-analyses [95, 96]. Weisman and colleagues examined 24 randomized controlled trials of AP systems involving a total of 585 participants using both single (i.e., insulin only) and dual hormone (i.e., insulin and glucagon) systems [95]. They found that time in target range was 12.6% higher with AP systems ($p < 0.0001$) from a weighted mean of 58.2% for conventional insulin pump therapy. Sub-analysis showed statistically significant improvement with AP technology for time in target range and hypoglycemia reduction for both pediatric and adult cohorts and for the 24-h and overnight periods [95]. Bekiari and colleagues examined 40 randomized controlled trials of 1027 participants using both single and dual hormone systems [96]. They found that time in range was 9.62% higher with AP systems during the 24-h period and 15.15% higher overnight [96]. Sub-analysis showed significant reduction in hypoglycemia with AP use both overnight and during the entire 24-h period. Taken together, these two robust meta-analyses show that AP systems with various designs provide significant improvement in glycemic control and reduction in hypoglycemia.

Focusing specifically on the commercially available MiniMed 670G, the pivotal trial results showed improved time in target range of 5% for adults and 6.8% for adolescents with an improvement in A1C of 0.5% for adults and 0.6% for adolescents (all p values < 0.001) [8, 97]. Further analysis showed that the insulin to carbohydrate ratios were more aggressive for all meals when using the AP than during the run-in phase, though the total daily dose and basal to bolus ratios of insulin did not change [98]. Time in range increased by 14% with auto mode use, though the percentage of time in auto mode gradually declined over the course of the 3-month study from 87 to 72% [98]. The reasons for this decline in use are not yet clear, though they may relate to user fatigue with frequent calibrations and the need to provide confirmatory blood glucose values. Studies are currently underway to better understand the decline in use across time. Preliminary data in an observational real-world setting of children and adolescents has shown that in 59 patients using the 670G for 45 days, time in auto mode was 71%, time in target range was 61%, and time in hypoglycemia was 1% [99]. Time in auto mode was highly correlated with better mean glucose, reduction in standard deviation in glucose, improved time in target range, and reduced hyperglycemia. Thus, AP technology holds the potential to dramatically improve real-world glycemic

control for individuals with T1D who are able and willing to use AP technology as intended (i.e., staying in auto mode).

User Experience with AP Systems

Psychosocial outcomes have the potential to complement the biological improvements that may result from AP systems, and addressing and improving them are essential to increasing AP system acceptance by individuals with T1D [100]. The extant literature examining the biopsychological factors associated with AP system is just beginning as systems are still in development and the first hybrid closed-loop system was only recently approved for commercial use.

A study using the MiniMed 670G showed that adolescents and adults with T1D felt that terms such as “closed loop” and “artificial pancreas” were misleading and that devices were not as “hands off” as expected [101]. This suggests that individuals expect AP systems to reduce the burden of self-care behaviors. This mismatch between expectations and reality is concerning because most AP systems in the near future will continue to require traditional T1D self-management behaviors, such as checking blood glucose, counting carbohydrates, and bolusing for meals. Therefore, it is important for individuals to understand the need to continue to adhere to self-management behaviors if they are to reap the benefits of improved glycemic control with AP systems. Further, as AP systems advance, it is important that the number of self-care behaviors required of individuals decreases.

Farrington recently reviewed research on the psychosocial aspects of closed-loop AP systems focusing on the user experience of available technologies such as insulin pumps and CGMs [102]. This review identified 13 key insulin pump and CGM studies as having salient themes to AP psychosocial research. The synthesis of this review was that the user experience of and level of trust in AP systems has been largely positive, though a wide array of perceived burdens in addition to perceived benefits were reported. The overall intention to use AP systems was also high, typically > 70%. In studies examining system opinions before and after use, the changes in intention to use were mixed, with one study showing decreased intention to use, one increased intention to use, and two showing no change. The studies also reported positive findings for trust in the AP systems. Farrington raises the concern that trust in AP systems may decrease outside of a research setting, though we would contend that commercial systems are more stable, robust, and fully vetted than research platforms, thus increasing the trust compared to an experimental platform. These studies also showed expected benefits for reduced fear of hypoglycemia, reassurance of family members, reduced anxiety, improved sleep, and ability to trust something else to manage T1D for a period of time: “time off from T1D,” and greater “freedom.” Farrington notes that those using systems for longer periods seemed to experience more benefits than those using systems for short periods of time. The conclusions from this review were that the psychosocial impact of AP systems is currently complex and ambivalent and that future research is critically needed to explicitly measure the effects on psychosocial outcomes.

Conclusions and a Call to the Field of Diabetes Technology

Significant advances in diabetes technology have occurred during the last two decades. In their current form, diabetes technologies can only perform as well as their algorithms and the people who use the devices. Indeed, data from the T1D Exchange registry have shown that overall glycemic control has not significantly improved for many people with T1D and in fact has worsened for adolescents and young adults, despite increased uptake of new devices. This is because technology has mainly benefited those who are highly engaged and motivated to adhere to demanding self-care regimens required for insulin pump and CGM use long term and not those who are at greatest risk for suboptimal glycemic control and struggle to adhere to these regimens. In fact, several studies have shown that those with the highest A1C level are at the greatest risk of discontinuing use of diabetes technologies. If diabetes technology is to make an impact on glycemic outcomes on a larger scale, future diabetes technologies must reduce the complexity and burden of T1D self-management. Moreover, the benefits from new diabetes technology will need to significantly outweigh the burden of AP to drive uptake of new AP technology. Device companies will need to incorporate factory calibrated or calibration optional CGMs which require fewer blood glucose checks. They will need to continue to improve on pump and CGM insertion devices to minimize pain and inflammation. *AP systems must be easy to use over extended periods of time and reduce the risk for hypoglycemia without increasing the complexity of the system.*

On a practical level, *it is important for technology companies and providers to make sure individuals have realistic expectations of current and future AP systems.* Providers must also address the needs of individual patients and increase their potential for long-term success with AP technology. In this way, the diabetes care team will play a critical role to meet the needs of individuals with T1D and optimize the use of AP systems. Care teams must engage individuals with T1D to maintain long-term use of AP technology and avoid technology burnout.

The literature reviewed in this article on the biopsychosocial factors associated with CGM and insulin pump use provided many lessons learned: (1) the biological limitations *must* be addressed (e.g., decrease skin problems) and (2) psychological and social impacts have been understudied and the information they provide has not been capitalized upon. Current efforts are underway to improve existing measures assessing the human and psychosocial factors that influence uptake and continued use of diabetes technology [100,103]. With this in mind, future studies will need to address the psychosocial hurdles individuals with T1D and their families face when initiating and maintaining use of AP technology. In this way, clinical research can help to increase uptake and maintain use of AP while minimizing the burden of technology use especially when psychosocial barriers are also addressed.

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References

Papers of particular interest, published recently, have been highlighted as:

•• Of major importance

1. DeSalvo DJ, Miller KM, Hermann JM, Maahs DM, Hofer SE, Clements MA, et al. Continuous glucose monitoring and glycemic control among youth with type 1 diabetes: international comparison from the T1D exchange and DPV initiative. *Pediatr Diabetes* 2018.
2. Miller KM, Foster NC, Beck RW, Bergenstal RM, DuBose SN, DiMeglio LA, et al. Current state of type 1 diabetes treatment in the U.S.: updated data from the T1D Exchange clinic registry. *Diabetes Care*. 2015;38(6):971–8. [PubMed: 25998289]
3. Sherr JL, Hermann JM, Campbell F, Foster NC, Hofer SE, Allgrove J, et al. Use of insulin pump therapy in children and adolescents with type 1 diabetes and its impact on metabolic control: comparison of results from three large, transatlantic paediatric registries. *Diabetologia*. 2016;59(1): 87–91. [PubMed: 26546085]
4. Facchinetti A Continuous glucose monitoring sensors: past, present and future algorithmic challenges. *Sensors (Basel)*. 2016;16(12):2093–104.
5. Petrie JR, Peters AL, Bergenstal RM, Holl RW, Fleming GA, Heinemann L. Improving the clinical value and utility of CGM systems: issues and recommendations : a joint statement of the European Association for the Study of Diabetes and the American Diabetes Association Diabetes Technology Working Group. *Diabetologia*. 2017;60(12):2319–28. [PubMed: 29067486]
6. Wadwa RP, Laffel LM, Shah VN, Garg SK. Accuracy of a factory-calibrated, real-time continuous glucose monitoring system during 10 days of use in youth and adults with diabetes. *Diabetes Technol Ther*. 2018;20(6):395–402. [PubMed: 29901421]
7. Shah VN, Laffel LM, Wadwa RP, Garg SK. Performance of a factory-calibrated real-time continuous glucose monitoring system utilizing an automated sensor applicator. *Diabetes Technol Ther*. 2018;20(6):428–33. [PubMed: 29923775]
8. Garg SK, Weinzimer SA, Tamborlane WV, Buckingham BA, Bode BW, Bailey TS, et al. Glucose outcomes with the in-home use of a hybrid closed-loop insulin delivery system in adolescents and adults with type 1 diabetes. *Diabetes Technol Ther*. 2017;19(3): 155–63. [PubMed: 28134564]
9. Messer LH, Forlenza GP, Wadwa RP, Weinzimer SA, Sherr JL, Hood KK, et al. The dawn of automated insulin delivery: a new clinical framework to conceptualize insulin administration. *Pediatr Diabetes*. 2018;19(1):14–7. [PubMed: 28656656]
10. Forlenza GP, Shulman DI, Wood MA, Bailey TS, Bode BW, Buckingham B, et al. Overnight to early-morning glycemic outcomes in children using the MiniMed™ 670G hybrid closed-loop (HCL) system. *Diabetes*. 2018;67(S1):W204.
11. Polonsky WH, Hessler D. What are the quality of life-related benefits and losses associated with real-time continuous glucose monitoring? A survey of current users. *Diabetes Technol Ther*. 2013;15(4):295–301. [PubMed: 23427866]
12. Messer LH, Berget C, Beatson C, Polsky S, Forlenza GP. Preserving skin integrity with chronic device use in diabetes. *Diabetes Technol Ther*. 2018;20(S2):S254–s64. [PubMed: 29916740]
13. Wadwa RP, Fiallo-Scharer R, Vanderwel B, Messer LH, Cobry E, Chase HP. Continuous glucose monitoring in youth with type 1 diabetes. *Diabetes Technol Ther*. 2009;11(Suppl 1):S83–91. [PubMed: 19469682]

14. Giani E, Snelgrove R, Volkening LK, Laffel LM. Continuous glucose monitoring (CGM) adherence in youth with type 1 diabetes: associations with biomedical and psychosocial variables. *J Diabetes Sci Technol*. 2017;11(3):476–83. [PubMed: 27807014]
15. Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study G, Beck RW, Buckingham B, Miller K, Wolpert H, Xing D, et al. Factors predictive of use and of benefit from continuous glucose monitoring in type 1 diabetes. *Diabetes Care*. 2009;32(11):1947–53. [PubMed: 19675206]
16. Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study G. Effectiveness of continuous glucose monitoring in a clinical care environment: evidence from the Juvenile Diabetes Research Foundation continuous glucose monitoring (JDRF-CGM) trial. *Diabetes Care*. 2010;33(1):17–22. [PubMed: 19837791]
17. Forlenza GP, Buckingham B, Maahs DM. Progress in diabetes technology: developments in insulin pumps, continuous glucose monitors, and progress towards the artificial pancreas. *J Pediatr*. 2016;169:13–20. [PubMed: 26547403]
18. Rodbard D Continuous glucose monitoring: a review of successes, challenges, and opportunities. *Diabetes Technol Ther*. 2016;18(Suppl 2):S3–S13.
19. Tanenbaum ML, Hanes SJ, Miller KM, Naranjo D, Bensen R, Hood KK. Diabetes device use in adults with type 1 diabetes: barriers to uptake and potential intervention targets. *Diabetes Care*. 2017;40(2):181–7. [PubMed: 27899489]
20. Battelino T, Conget I, Olsen B, Schutz-Fuhrmann I, Hommel E, Hoogma R, et al. The use and efficacy of continuous glucose monitoring in type 1 diabetes treated with insulin pump therapy: a randomised controlled trial. *Diabetologia*. 2012;55(12):3155–62. [PubMed: 22965294]
21. Ruedy KJ, Parkin CG, Riddlesworth TD, Graham C, Group DS. Continuous glucose monitoring in older adults with type 1 and type 2 diabetes using multiple daily injections of insulin: results from the DIAMOND trial. *J Diabetes Sci Technol*. 2017;11(6): 1138–46. [PubMed: 28449590]
22. Beck RW, Riddlesworth T, Ruedy K, Ahmann A, Bergenstal R, Haller S, et al. Effect of continuous glucose monitoring on glycemic control in adults with type 1 diabetes using insulin injections: the DIAMOND randomized clinical trial. *JAMA*. 2017;317(4): 371–8 [PubMed: 28118453] A large randomized clinical trial showing the clinical benefit of reduction in glycemic control in individuals with T1D using continuous glucose monitors compared to those who do not.
23. Beck RW, Riddlesworth TD, Ruedy K, Ahmann A, Haller S, Kruger D, et al. Continuous glucose monitoring versus usual care in patients with type 2 diabetes receiving multiple daily insulin injections: a randomized trial. *Ann Intern Med*. 2017;167(6):365–74. [PubMed: 28828487]
24. Riddlesworth T, Price D, Cohen N, Beck RW. Hypoglycemic event frequency and the effect of continuous glucose monitoring in adults with type 1 diabetes using multiple daily insulin injections. *Diabetes Ther*. 2017;8(4):947–51. [PubMed: 28616804]
25. Bergenstal RM, Rosenstock J, Bastyr EJ 3rd, Prince MJ, Qu Y, Jacobson SJ. Lower glucose variability and hypoglycemia measured by continuous glucose monitoring with novel long-acting insulin LY2605541 versus insulin glargine. *Diabetes Care*. 2014;37(3):659–65. [PubMed: 24198302]
26. Secher AL, Stage E, Ringholm L, Barfred C, Damm P, Mathiesen ER. Real-time continuous glucose monitoring as a tool to prevent severe hypoglycaemia in selected pregnant women with type 1 diabetes—an observational study. *Diabet Med*. 2014;31(3):352–6. [PubMed: 24341466]
27. Hermanides J, Devries JH. Sensor-augmented insulin pump more effective than multiple daily insulin injections for reducing HbA1C in people with poorly controlled type 1 diabetes. *Evid Based Med*. 2011;16(2):46–8. [PubMed: 21224281]
28. Beck RW, Riddlesworth TD, Ruedy KJ, Kollman C, Ahmann AJ, Bergenstal RM, et al. Effect of initiating use of an insulin pump in adults with type 1 diabetes using multiple daily insulin injections and continuous glucose monitoring (DIAMOND): a multicentre, randomised controlled trial. *Lancet Diabetes Endocrinol*. 2017;5(9):700–8. [PubMed: 28711468]
29. Ives B, Sikes K, Urban A, Stephenson K, Tamborlane WV Practical aspects of real-time continuous glucose monitors: the experience of the Yale Children's Diabetes Program. *Diabetes Educ*. 2010;36(1):53–62. [PubMed: 19933872]

30. Messer L, Ruedy K, Xing D, Coffey J, Englert K, Caswell K, et al. Educating families on real time continuous glucose monitoring: the DirecNet navigator pilot study experience. *Diabetes Educ.* 2009;35(1):124–35. [PubMed: 19244568]
31. Englert K, Ruedy K, Coffey J, Caswell K, Steffen A, Levandoski L, et al. Skin and adhesive issues with continuous glucose monitors: a sticky situation. *J Diabetes Sci Technol.* 2014;8(4):745–51. [PubMed: 24876416]
32. Berg AK, Olsen BS, Thyssen JP, Zachariae C, Simonsen AB, Pilgaard K, et al. High frequencies of dermatological complications in children using insulin pumps or sensors. *Pediatr Diabetes.* 2018;19(4):733–40. [PubMed: 29484783]
33. Binder E, Lange O, Edlinger M, Meraner D, Abt D, Moser C, et al. Frequency of dermatological side effects of continuous subcutaneous insulin infusion in children and adolescents with type 1 diabetes. *Experimental and clinical endocrinology & diabetes : official journal, German Society of Endocrinology [and] German Diabetes Association.* 2015;123(4):260–4.
34. Cope JU, Samuels-Reid JH, Morrison AE. Pediatric use of insulin pump technology: a retrospective study of adverse events in children ages 1–12 years. *J Diabetes Sci Technol.* 2012;6(5):1053–9. [PubMed: 23063031]
35. Heinemann L, Krinelke L. Insulin infusion set: the Achilles heel of continuous subcutaneous insulin infusion. *J Diabetes Sci Technol.* 2012;6(4):954–64. [PubMed: 22920824]
36. Feig DS, Donovan LE, Corcoy R, Murphy KE, Amiel SA, Hunt KF, et al. Continuous glucose monitoring in pregnant women with type 1 diabetes (CONCEPTT): a multicentre international randomised controlled trial. *Lancet.* 2017;390(10110):2347–59. [PubMed: 28923465]
37. Polonsky WH, Hessler D, Ruedy KJ, Beck RW, Group DS. The impact of continuous glucose monitoring on markers of quality of life in adults with type 1 diabetes: further findings from the DIAMOND randomized clinical trial. *Diabetes Care.* 2017;40(6): 736–41. [PubMed: 28389582]
38. Polonsky WH, Fisher L, Hessler D, Edelman SV. Investigating hypoglycemic confidence in type 1 and type 2 diabetes. *Diabetes Technol Ther.* 2017;19(2):131–6. [PubMed: 27997217]
39. Weissberg-Benchell J, Antisdel-Lomaglio J, Seshadri R. Insulin pump therapy: a meta-analysis. *Diabetes Care.* 2003;26(4):1079–87. [PubMed: 12663577]
40. Nimri R, Weintrob N, Benzaquen H, Ofan R, Fayman G, Phillip M. Insulin pump therapy in youth with type 1 diabetes: a retrospective paired study. *Pediatrics.* 2006;117(6):2126–31. [PubMed: 16740856]
41. Patton SR, Clements MA. Psychological reactions associated with continuous glucose monitoring in youth. *J Diabetes Sci Technol.* 2016;10(3):656–61. [PubMed: 26969141]
42. Mauras N, Beck R, Xing D, Ruedy K, Buckingham B, Tansey M, et al. A randomized clinical trial to assess the efficacy and safety of real-time continuous glucose monitoring in the management of type 1 diabetes in young children aged 4 to <10 years. *Diabetes Care.* 2012;35(2):204–10. [PubMed: 22210571]
43. Heller S, White D, Lee E, Lawton J, Pollard D, Waugh N, et al. A cluster randomised trial, cost-effectiveness analysis and psychosocial evaluation of insulin pump therapy compared with multiple injections during flexible intensive insulin therapy for type 1 diabetes: the REPOSE trial. *Health Technol Assess.* 2017;21(20): 1–278.
44. Rubin RR, Peyrot M, Group SS. Health-related quality of life and treatment satisfaction in the sensor-augmented pump therapy for A1C reduction 3 (STAR 3) trial. *Diabetes Technol Ther.* 2012;14(2):143–51. [PubMed: 22133037]
45. Cemeroglu AP, Stone R, Kleis L, Racine MS, Postellon DC, Wood MA. Use of a real-time continuous glucose monitoring system in children and young adults on insulin pump therapy: patients' and caregivers' perception of benefit. *Pediatr Diabetes.* 2010;11(3):182–7. [PubMed: 19958460]
46. Hirsch IB, Abelson J, Bode BW, Fischer JS, Kaufman FR, Mastrototaro J, et al. Sensor-augmented insulin pump therapy: results of the first randomized treat-to-target study. *Diabetes Technol Ther.* 2008;10(5):377–83. [PubMed: 18715214]
47. Chase HP, Beck RW, Xing D, Tamborlane WV, Coffey J, Fox LA, et al. Continuous glucose monitoring in youth with type 1 diabetes: 12-month follow-up of the Juvenile Diabetes Research

- Foundation continuous glucose monitoring randomized trial. *Diabetes Technol Ther.* 2010;12(7): 507–15. [PubMed: 20597824]
48. O'Connell MA, Donath S, Cameron FJ. Poor adherence to integral daily tasks limits the efficacy of CSII in youth. *Pediatr Diabetes.* 2011;12(6):556–9. [PubMed: 21466646]
 49. Datye KA, Boyle CT, Simmons J, Moore DJ, Jaser SS, Sheanon N, et al. Timing of meal insulin and its relation to adherence to therapy in type 1 diabetes. *J Diabetes Sci Technol.* 2018;12(2): 349–55. [PubMed: 28895431]
 50. Tanenbaum ML, Adams RN, Hanes SJ, Barley RC, Miller KM, Mulvaney SA, et al. Optimal use of diabetes devices: clinician perspectives on barriers and adherence to device use. *J Diabetes Sci Technol.* 2017;11(3):484–92. [PubMed: 28745093]
 51. Driscoll KA, Johnson SB, Hogan J, Gill E, Wright N, Deeb LC. Insulin bolusing software: the potential to optimize health outcomes in type 1 diabetes mellitus. *J Diabetes Sci Technol.* 2013;7(3):646–52. [PubMed: 23759397]
 52. Patton SR, Driscoll KA, Clements MA. Adherence to insulin pump behaviors in young children with type 1 diabetes mellitus. *J Diabetes Sci Technol.* 2017;11(1):87–91. [PubMed: 27390223]
 53. Driscoll KA, Wang Y, Bennett Johnson S, Lynch R, Stephens H, Willbur K, et al. White coat adherence in pediatric patients with type 1 diabetes who use insulin pumps. *J Diabetes Sci Technol.* 2016;10(3):724–9. [PubMed: 26746686]
 54. Driscoll KA, Johnson SB, Wang Y, Tang Y, Gill EC, Mitchell A, et al. Importance of manually entering blood glucose readings when wireless-compatible meters are not being used with an insulin pump. *J Diabetes Sci Technol.* 2013;7(4):898–903. [PubMed: 23911171]
 55. Driscoll KA, Johnson SB, Tang Y, Yang F, Deeb LC, Silverstein JH. Does blood glucose monitoring increase prior to clinic visits in children with type 1 diabetes? *Diabetes Care.* 2011;34(10):2170–3. [PubMed: 21852678]
 56. Driscoll KA, Johnson SB, Wang Y, Wright N, Deeb LC. Blood glucose monitoring before and after type 1 diabetes clinic visits. *J Pediatr Psychol* (in press). 2017.
 57. Barnard KD, Lloyd CE, Skinner TC. Systematic literature review: quality of life associated with insulin pump use in type 1 diabetes. *Diabet Med.* 2007;24(6):607–17. [PubMed: 17367304]
 58. Hirose M, Beverly EA, Weinger K. Quality of life and technology: impact on children and families with diabetes. *Current diabetes reports.* 2012;12(6):711–20. [PubMed: 22903783]
 59. Hommel E, Olsen B, Battelino T, Conget I, Schutz-Fuhrmann I, Hoogma R, et al. Impact of continuous glucose monitoring on quality of life, treatment satisfaction, and use of medical care resources: analyses from the SWITCH study. *Acta Diabetol.* 2014;51(5):845–51. [PubMed: 25037251]
 60. Beck RW, Lawrence JM, Laffel L, Wysocki T, Xing D, Huang ES, et al. Quality-of-life measures in children and adults with type 1 diabetes: Juvenile Diabetes Research Foundation Continuous Glucose Monitoring randomized trial. *Diabetes Care.* 2010;33(10):2175–7. [PubMed: 20696865]
 61. Markowitz JT, Pratt K, Aggarwal J, Volkening LK, Laffel LM. Psychosocial correlates of continuous glucose monitoring use in youth and adults with type 1 diabetes and parents of youth. *Diabetes Technol Ther.* 2012;14(6):523–6. [PubMed: 22524590]
 62. Rubin RR, Peyrot M. Treatment satisfaction and quality of life for an integrated continuous glucose monitoring/insulin pump system compared to self-monitoring plus an insulin pump. *J Diabetes Sci Technol.* 2009;3(6):1402–10. [PubMed: 20144395]
 63. Hilliard ME, Goeke-Morey M, Cogen FR, Henderson C, Streisand R. Predictors of diabetes-related quality of life after transitioning to the insulin pump. *J Pediatr Psychol.* 2009;34(2): 137–46. [PubMed: 18577542]
 64. Nuboer R, Borsboom GJ, Zoethout JA, Koot HM, Bruining J. Effects of insulin pump vs. injection treatment on quality of life and impact of disease in children with type 1 diabetes mellitus in a randomized, prospective comparison. *Pediatr Diabetes.* 2008;9(4 Pt 1):291–6. [PubMed: 18466210]
 65. Lind M, Polonsky W, Hirsch IB, Heise T, Bolinder J, Dahlqvist S, et al. Continuous glucose monitoring vs conventional therapy for glycemic control in adults with type 1 diabetes treated with multiple daily insulin injections: the GOLD randomized clinical trial. *JAMA.* 2017;317(4):379–87. [PubMed: 28118454]

66. Wong JC, Dolan LM, Yang TT, Hood KK. Insulin pump use and glycemic control in adolescents with type 1 diabetes: predictors of change in method of insulin delivery across two years. *Pediatr Diabetes*. 2015;16(8):592–9. [PubMed: 25387433]
67. Fisher L, Hessler D, Polonsky WH, Masharani U, Guzman S, Bowyer V, et al. T1-REDEEM: a randomized controlled trial to reduce diabetes distress among adults with type 1 diabetes. *Diabetes Care*. 2018;41:1862–9. [PubMed: 29976567]
68. Giani E, Snelgrove R, Volkening LK, Laffel LM. Continuous glucose monitoring (CGM) adherence in youth with type 1 diabetes: associations with biomedical and psychosocial variables. *J Diabetes Sci Technol*. 2017;11(3):476–83. [PubMed: 27807014]
69. Rashotte J, Tousignant K, Richardson C, Fothergill-Bourbonnais F, Nakhla MM, Olivier P, et al. Living with sensor-augmented pump therapy in type 1 diabetes: adolescents' and parents' search for harmony. *Can J Diabetes*. 2014;38(4):256–62. [PubMed: 25023738]
70. Ritholz MD, Atakov-Castillo A, Beste M, Beverly EA, Leighton A, Weinger K, et al. Psychosocial factors associated with use of continuous glucose monitoring. *Diabet Med*. 2010;27(9):1060–5. [PubMed: 20722681]
71. Garmo A, Hornsten A, Leksell J. The pump was a saviour for me. 'Patients' experiences of insulin pump therapy. *Diabet Med*. 2013;30(6):717–23. [PubMed: 23398606]
72. Seereiner S, Neeser K, Weber C, Schreiber K, Habacher W, Rakovac I, et al. Attitudes towards insulin pump therapy among adolescents and young people. *Diabetes Technol Ther*. 2010;12(1):89–94. [PubMed: 20082590]
73. James S, Perry L, Gallagher R, Lowe J. Diabetes educators: perceived experiences, supports and barriers to use of common diabetes-related technologies. *J Diabetes Sci Technol*. 2016;10(5):1115–21. [PubMed: 27417141]
74. Hirsch IB. Clinical review: realistic expectations and practical use of continuous glucose monitoring for the endocrinologist. *J Clin Endocrinol Metab*. 2009;94(7):2232–8. [PubMed: 19383778]
75. Pickup JC, Ford Holloway M, Samsi K. Real-time continuous glucose monitoring in type 1 diabetes: a qualitative framework analysis of patient narratives. *Diabetes Care*. 2015;38(4):544–50. [PubMed: 25552422]
76. Wong JC, Boyle C, DiMeglio LA, Mastrandrea LD, Abel KL, Cengiz E, et al. Evaluation of pump discontinuation and associated factors in the T1D exchange clinic registry. *J Diabetes Sci Technol*. 2017;11(2):224–32. [PubMed: 27595711]
77. Wysocki T, Hirschfeld F, Miller L, Izenberg N, Dowshen SA, Taylor A, et al. Consideration of insulin pumps or continuous glucose monitors by adolescents with type 1 diabetes and their parents: stakeholder engagement in the design of web-based decision aids. *The Diabetes educator*. 2016;42(4):395–407. [PubMed: 27150606]
78. Shivers JP, Mackowiak L, Anhalt H, Zisser H. "Turn it off!": diabetes device alarm fatigue considerations for the present and the future. *J Diabetes Sci Technol*. 2013;7(3):789–94. [PubMed: 23759412]
79. Messer LH, Johnson R, Driscoll KA, Jones J. Best friend or spy: a qualitative meta-synthesis on the impact of continuous glucose monitoring on life with type 1 diabetes. *Diabet Med*. 2018;35(4):409–18. [PubMed: 29247556]
80. Kropff J, DeJong J, Del Favero S, Place J, Messori M, Coestier B, et al. Psychological outcomes of evening and night closed-loop insulin delivery under free living conditions in people with type 1 diabetes: a 2-month randomized crossover trial. *Diabet Med*. 2017;34(2):262–71. [PubMed: 27696520]
81. Kerr D, Wizemann E, Senstius J, Zacho M, Ampudia-Blasco FJ. Stability and performance of rapid-acting insulin analogs used for continuous subcutaneous insulin infusion: a systematic review. *J Diabetes Sci Technol*. 2013;7(6):1595–606. [PubMed: 24351186]
82. Wheeler BJ, Donaghue KC, Heels K, Ambler GR. Family perceptions of insulin pump adverse events in children and adolescents. *Diabetes Technol Ther*. 2014;16(4):204–7. [PubMed: 24313790]

83. Wheeler BJ, Heels K, Donaghue KC, Reith DM, Ambler GR. Insulin pump-associated adverse events in children and adolescents—a prospective study. *Diabetes Technol Ther.* 2014;16(9): 558–62. [PubMed: 24796368]
84. Ross PL, Milburn J, Reith DM, Wiltshire E, Wheeler BJ. Clinical review: insulin pump-associated adverse events in adults and children. *Acta Diabetol.* 2015;52(6):1017–24. [PubMed: 26092321]
85. Kovatchev B, Anderson S, Heinemann L, Clarke W. Comparison of the numerical and clinical accuracy of four continuous glucose monitors. *Diabetes Care.* 2008;31(6):1160–4. [PubMed: 18339974]
86. Christiansen M, Bailey T, Watkins E, Liljenquist D, Price D, Nakamura K, et al. A new-generation continuous glucose monitoring system: improved accuracy and reliability compared with a previous-generation system. *Diabetes Technol Ther.* 2013;15(10): 881–8. [PubMed: 23777402]
87. Laffel L Improved accuracy of continuous glucose monitoring systems in pediatric patients with diabetes mellitus: results from two studies. *Diabetes Technol Ther.* 2016;18(Suppl 2):S223–33. [PubMed: 26784126]
88. Faccioli S, Del Favero S, Visentin R, Bonfanti R, Iafusco D, Rabbone I, et al. Accuracy of a CGM sensor in pediatric subjects with type 1 diabetes. Comparison of three insertion sites: arm, abdomen, and gluteus. *J Diabetes Sci Technol.* 2017;11(6): 1147–54. [PubMed: 28486841]
89. Vloemans AF, van Beers CAJ, de Wit M, Cleijne W, Rondags SM, Geelhoed-Duijvestijn PH, et al. Keeping safe. Continuous glucose monitoring (CGM) in persons with type 1 diabetes and impaired awareness of hypoglycaemia: a qualitative study. *Diabet Med.* 2017;34(10):1470–6. [PubMed: 28731509]
90. Ruiz JL, Sherr JL, Cengiz E, Carria L, Roy A, Voskanyan G, et al. Effect of insulin feedback on closed-loop glucose control: a cross-over study. *J Diabetes Sci Technol.* 2012;6(5):1123–30. [PubMed: 23063039]
91. Doyle FJ 3rd, Huyett LM, Lee JB, Zisser HC, Dassau E. Closed-loop artificial pancreas systems: engineering the algorithms. *Diabetes Care.* 2014;37(5):1191–7. [PubMed: 24757226]
92. Steil GM. Algorithms for a closed-loop artificial pancreas: the case for proportional-integral-derivative control. *J Diabetes Sci Technol.* 2013;7(6):1621–31. [PubMed: 24351189]
93. Bequette BW. Algorithms for a closed-loop artificial pancreas: the case for model predictive control. *J Diabetes Sci Technol.* 2013;7(6):1632–43. [PubMed: 24351190]
94. Forlenza GP, Cameron FM, Ly TT, Lam D, Howsmon DP, Baysal N, et al. Fully closed-loop multiple model probabilistic predictive controller artificial pancreas performance in adolescents and adults in a supervised hotel setting. *Diabetes Technol Ther.* 2018;20(5): 335–43. [PubMed: 29658779]
95. Weisman A, Bai JW, Cardinez M, Kramer CK, Perkins BA. Effect of artificial pancreas systems on glycaemic control in patients with type 1 diabetes: a systematic review and meta-analysis of outpatient randomised controlled trials. *Lancet Diabetes Endocrinol.* 2017;5(7):501–12. [PubMed: 28533136]
- 96••. Bekiari E, Kitsios K, Thabit H, Tauschmann M, Athanasiadou E, Karagiannis T, et al. Artificial pancreas treatment for outpatients with type 1 diabetes: systematic review and meta-analysis. *BMJ (Clinical research ed).* 2018;361:k1310Review of 40 studies using the artificial pancreas showing their clinical benefit of increasing time in range both in real-world settings and well-controlled research settings.
97. Bergenstal RM, Garg S, Weinzimer SA, Buckingham BA, Bode BW, Tamborlane WV, et al. Safety of a hybrid closed-loop insulin delivery system in patients with type 1 diabetes. *JAMA.* 2016;316(13):1407–8. [PubMed: 27629148]
98. Messer LH, Forlenza GP, Sherr JL, Wadwa RP, Buckingham BA, Weinzimer SA, et al. Optimizing hybrid closed-loop therapy in adolescents and emerging adults using the Mini Med 670G system. *Diabetes Care.* 2018;41(4):789–96. [PubMed: 29444895]
99. Berget C, Messer LH, Pyle L, Westfall E, Forlenza GP, Driscoll KA. Real-world use of hybrid closed-loop therapy in pediatric patients with type 1 diabetes. *Diabetes.* 2018;67(S1):A254.
100. Barnard KD, Venkat MV, Close K, Heinemann L, Weissberg-Benchell J, Hood KK, et al. PsychDT working group: report psychosocial aspects of artificial pancreas systems. *J Diabetes Sci Technol.* 2015;9(4):925–8. [PubMed: 26085567]

101. Iturralde E, Tanenbaum ML, Hanes SJ, Suttiratana SC, Ambrosino JM, Ly TT, et al. Expectations and attitudes of individuals with type 1 diabetes after using a hybrid closed loop system. *The Diabetes educator*. 2017;43(2):223–32. [PubMed: 28340542]
102. Farrington C Hacking diabetes: DIY artificial pancreas systems. *Lancet Diabetes Endocrinol*. 2017;5(5):332. [PubMed: 27913173]
103. Weissberg-Benchell J, Hood K, Laffel L, Heinemann L, Ball D, Kowalski A, et al. Toward development of psychosocial measures for automated insulin delivery. *J Diabetes Sci Technol*. 2016;10(3):799–801. [PubMed: 26645792]

Fig. 1.

Closed-loop control with artificial pancreas. An on-body CGM measures the individual blood glucose in real time. The glucose value is then sent to a control algorithm which uses a series of mathematical equations to determine the insulin dose for that time period. The insulin dose required is then transmitted to the insulin pump and the insulin is delivered to the individuals. The individual body then responds to the insulin dose with a new blood glucose value and the cycle repeats