Inpatient and Outpatient Technologies to Assist in the Management of Insulin Dosing

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Several new technologies use computer algorithms to analyze a person's blood glucose response to insulin treatment, calculate the person's next recommended insulin dose, advise the person regarding when to check blood glucose next, and provide alerts regarding glucose control for the individual patient or across a hospital system. This article reviews U.S. Food and Drug Administration (FDA)-approved products designed to help manage insulin dosing for inpatients, as well as those available to provide people with insulin-requiring diabetes support in making adjustments to their basal and/or mealtime insulin doses. Many of these products have a provider interface that allows for remote monitoring of patients' glucose readings and insulin doses. By alleviating some of the burdens of insulin initiation and dose adjustment, these products may facilitate improved glycemic management and patient outcomes.

The Centers for Disease Control and Prevention (CDC) estimates that 34.2 million people, or 10.5% of the U.S. population, have diabetes, and its prevalence has been steadily increasing (1). Complications of diabetes include cardiovascular disease, nephropathy, retinopathy, and neuropathy. Diabetes and its complications result in a heavy economic burden on the U.S. health care system. Several studies have shown that improved diabetes management decreases the likelihood of these complications (2–4).

The American Diabetes Association (ADA) recommends A1C goals of <7% for most adults, but also emphasizes the importance of individualization of glycemic goals. According to the CDC's National Diabetes Statistics Report, crude estimates for 2013–2016 showed that half of all people with diabetes had an A1C ≥7.0% (1). The mean A1C among people with diabetes increased from 7.3% in the 2005–2008 period to 7.5% in 2013–2016 based on data from the National Health and Nutrition Examination Survey (NHANES) (5). Despite significant advances in drug development, efforts to deliver affordable medications, better methods of glucose monitoring, and newer insulin pump technologies, the achievement of recommended A1C goals remains elusive for many people with diabetes and their medical care providers.

In this article, we review several inpatient and outpatient insulin titration and calculation technology-based solutions. We focus on products approved by the U.S. Food and Drug Administration (FDA), although many others have been approved in other countries, and new systems are approved frequently.

Challenges of Inpatient Hyperglycemia Management

The CDC has reported 7.8 million hospital discharges with a diagnosis of diabetes among U.S. adults in 2016 (1). Guidelines from the ADA and the Endocrine Society recommend a target blood glucose range of 140–180 mg/dL for the majority of critically ill and noncritically ill hospital inpatients, with more stringent goals for selected patients (e.g., those having cardiac surgery) and less strict goals for older or terminally ill patients (6,7). Inpatient hyperglycemia and hypoglycemia in people with or without diabetes are associated with increased risks of complications, longer hospital stays, and increased mortality rates (8–10).

In most instances, insulin is the preferred treatment for hyperglycemia in hospitalized patients. In the critical care setting, continuous intravenous (IV) insulin is the most effective method for achieving glycemic targets. Outside of critical care units, a regimen of basal, prandial, and

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correctional subcutaneous (SQ) insulin is the preferred treatment. Use of only a correctional insulin regimen (i.e., sliding-scale insulin [SSI], or scheduled short- or rapid-acting insulin given in response to elevated glucose levels) is strongly discouraged but is frequently still used in many hospitals as the primary treatment for hyperglycemia (6).

Many factors can make inpatient hyperglycemia management challenging, including a patient's illness severity, nutritional status, or kidney dysfunction; changes in diabetes medications or concomitant medications that might affect glucose levels (e.g., glucocorticoids); reliance on an SSI regimen; and insufficient knowledge regarding evidence-based glycemic management and risks of hypoglycemia (11).

Patients can have day-to-day, or even hour-to-hour, variability in oral intake depending on their clinical course. Conditions that cause increased insulin resistance (e.g., glucocorticoid therapy, stress, pain, infection, or surgery) will necessitate an increase in both basal and prandial insulin doses, whereas other conditions (e.g., worsening kidney function, decreased oral intake, improvement in clinical condition, or frequent hypoglycemia) may require a decrease in insulin doses. Ideally, the prandial insulin should be adjusted based on the timing of meals and the amount of carbohydrates consumed, but such calculations are often extremely difficult in inpatient settings where meal timing and nutrition intake are variable.

One of the biggest concerns related to insulin management is the risk of iatrogenic hypoglycemia. The Institute for Safe Medication Practices has identified insulin as a high-alert medication that is commonly involved in medication errors in inpatient settings (12). Insulin-related medication errors can cause serious harm, including fatalities, in all hospital settings. However, this concern leads many providers to err on the side of avoiding hypoglycemia at all costs, which can result in persistent hyperglycemia, which can also cause harm.

Computerized physician order entry (CPOE), through which physicians enter orders directly into a computer, has now become the standard of care in most U.S. clinical settings. This process offers many advantages over traditional orders written on paper. A hospital or health care system can create standardized orders based on best evidence and guidelines and offer clinical decision-support tools, including allergy alerts, drug-drug and drug-disease interaction checks, and safe dose ranges and intervals for ordered medications. The National Academy of Medicine recommends using CPOE to prevent medication-related errors and to increase efficiency in medication administration (13).

The Society of Hospital Medicine suggests implementing protocols for discontinuing oral antihyperglycemic medications, prescribing physiologic (i.e., basal, prandial, and correctional) insulin regimens, matching correctional insulin doses with patients' insulin sensitivity, and managing hypoglycemia in a standardized manner (14). These order sets discourage the use of SSI without basal insulin. In addition, IV insulin protocols for patients with diabetic ketoacidosis simplify and standardize insulin infusion rates according to current glucose levels and patterns of glycemic change. Several studies have found that using a computer support system in the hospital lowered average blood glucose levels and significantly increased the percentage of time patients spent in the target glucose range without increasing hypoglycemia (15,16).

Most hospitals have already implemented standardized insulin CPOE, but these systems generally do not provide decision support for setting initial insulin doses or managing changes in the insulin regimen as a hospital stay progresses. In recent years, several advanced software programs using input from electronic medical record (EMR) systems and proprietary algorithms have been developed to help adjust inpatient insulin doses with minimal input from providers.

Inpatient Electronic Glucose Management Systems to Manage Insulin Doses

The ADA recommends consultation with a specialized diabetes or glucose management team when possible for hospitalized patients with diabetes (6). Appropriately trained specialists may help to improve patients' glycemic control and outcomes (17). However, many U.S. hospitals do not have such specialists onsite; rather, blood glucose is managed by the primary inpatient care team. Even among experts, approaches to glycemic management might differ based on their own experience. Using a computer software system could make glycemic management measures more consistent and effective and thereby improve health outcomes.

One inspiration for the development of glucose control computer systems came from an article published in 1982 by White et al. (18), in which the authors presented a complex set of orders for determining the basal insulin requirement of patients using an insulin pump. When the data were graphed, they revealed that a linear regression with an intercept of 60 and a slope, or multiplier, of 0.02 reduced the complexity of the orders to a single formula: (blood glucose − 60) × 0.02 = insulin dose/hour (Figure 1) (19).
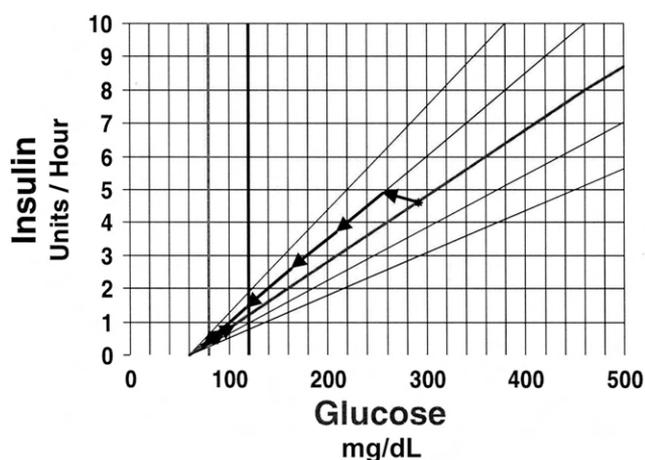
FIGURE 1 Array of slopes representing the multipliers. In this example, the initial blood glucose level (295 mg/dL) is plotted on the 0.02 slope, indicating the initial insulin rate (4.7 units/hour). The second blood glucose level has decreased from 295 to 256 mg/dL. Therefore, the multiplier is increased by 25%, increasing the insulin dose to 4.9 units/hour. Subsequent serially measured blood glucose levels decrease satisfactorily (205 mg/dL followed by 3.6 units/hour, 168 mg/dL followed by 2.7 units/hour, and 115 mg/dL followed by 1.5 units/hour) until the blood glucose level is less than the low target value (69 mg/dL followed by 0.2 units/hour). At that time, the multiplier shifted downward, and the next two blood glucose levels and insulin doses (98 mg/dL followed by 0.8 units/hour and 110 mg/dL followed by 1 unit/hour) centered in the target range. Reprinted with permission from ref. 19.

Simplified systems were initially developed using this construct to help adjust insulin infusions, but more complex software has since been developed to account for a variety of clinical inpatient scenarios. FDA-approved inpatient electronic glycemic management systems include Glucommander (Glytec), EndoTool System (Monarch Medical Technologies), and GlucoStabilizer (Medical Decision Network). Another system is the Cores Diabetes App, which gives practitioners tools to calculate insulin doses but does not adjust insulin automatically and therefore has not required FDA approval.

Glucommander

Glytec's Glucommander system uses evidence-based multivariate algorithms to provide care teams with insulin dosing recommendations that continuously recalculate and dynamically adjust to individual patients' changing conditions, accounting for oral intake, weight, insulin sensitivities, and other clinical variables. It can be used with certain EMR systems, which allows the sharing of patients' data, including blood glucose and laboratory test values. It is cleared by the FDA for use with continuous IV insulin infusion, transition from IV to SQ insulin, SQ insulin, and hospital-to-home transitions. It has also been cleared for outpatient use in pediatric and adult patients with diabetes (20).

To initiate a continuous IV insulin infusion, a bedside fingerstick blood glucose value is entered, and the system calculates an initial insulin infusion rate. Based on the rate of change in glucose level, a system alert notifies a nurse when the next blood glucose value is needed, which may be anywhere from 20 to 120 minutes later. The system continues recommending insulin infusion rates until IV insulin is discontinued (19). When a patient is stable and ready to transition to SQ insulin, the system can calculate basal and prandial insulin doses based on recent infusion rates.

To initiate SQ insulin, a total daily dose (TDD) of insulin can be calculated from the patients' weight or based on previous experience from the outpatient setting (20). The TDD is then divided between basal and prandial insulin doses. Prandial insulin can be a fixed dose or can be based on a patient's insulin-to-carbohydrate (I:C) ratio. The program automatically adjusts prandial doses based on the amount of carbohydrates entered by the nurse and previous responses. The Glucommander's algorithm provides real-time dose changes from meal to meal (prandial insulin dosing) and day to day (basal insulin dosing) without requiring a new order from the provider.

Several safety features are built into the software, including nurse verification of doses, missed dose reminders with alarms, entry of mealtime carbohydrates, and hypoglycemia correction algorithms (20). Theoretically, if the initial dose of insulin initiated by a provider is reasonably close to the dose that a patient actually needs, blood glucose should be well controlled during the entire hospital course without any further provider intervention.

Glytec's software package includes Glucommander to help adjust insulin doses and also offers surveillance, alerting, analytics, and reporting capabilities (20). Studies have shown that Glucommander implementation decreased hyperglycemia, hypoglycemia, time to target blood glucose, average length of stay, 30-day readmissions, and postoperative complications (21–24). In addition, there was an increase in nurses' satisfaction and significant cost saving (25,26).

EndoTool

Monarch Medical Technology's EndoTool system provides insulin dose recommendations based on patient information, blood glucose measurements, and a set of algorithms that includes a nonlinear dosing equation individualized and optimized over time based on blood glucose responses to previously administered doses (27). This system provides clinical decision support for IV insulin, IV-to-SQ transition, and SQ insulin for pediatric and

adult patients. Insulin dose recommendations are personalized based on patient-specific factors, including age, sex, weight, height, diabetes type, blood glucose level, creatinine level, steroid use, insulin/estimated residual extracellular insulin, A1C level, and carbohydrates consumed (27).

Using clinically driven protocols, this tool notifies the provider when a patient has reached an optimal time for safe transition from IV to SQ insulin therapy. EndoTool SubQ is initiated after the provider determines the diet, insulin regimen, and glucose target range. After a nurse enters clinical data (e.g., food intake and scheduled blood glucose readings), the system calculates the next dose of SQ insulin and the next time for a scheduled glucose determination. For the prandial dose, users can input a carbohydrate amount, or the software can calculate and track the carbohydrate intake for patients receiving tube feeding, total parenteral nutrition, and/or IV dextrose (27).

This system can be fully integrated with the majority of EMR systems. It accepts patients' clinical values (height, weight, and diabetes type), laboratory values (creatinine and A1C), and point-of-care glucose readings from an integrated EMR system. EndoTool Analytics provides data reports from EndoTool IV and EndoTool SubQ to help providers identify and analyze trends and track the safety and clinical effectiveness of the insulin regimen (28). Studies have shown that this system helps to achieve *1*) more time in the target glucose range, *2*) immediate and sustained improvement in postoperative glucose control surgical care, and *3*) a reduction in hospital-acquired conditions by 61% over 3 years (28,29).

GlucoStabilizer

The Medical Decision Network's GlucoStabilizer insulin dosing calculator is a network-based software solution that automates calculations to determine the appropriate IV insulin drip rate necessary to manage blood glucose levels for adult and pediatric patients. The pediatric drip setting provides a 3-digit multiplier for more precise calculations (30).

To initiate IV insulin infusion for adult patients, providers select and enter the target glucose range and the initial multiplier. For the pediatric population, the same applies, although the initial multiplier is derived from the patient's weight. After the initial multiplier is entered, the computerized hospital insulin protocol (CHIP) calculates subsequent multipliers based on each blood glucose level entered. The CHIP determines the insulin infusion rate and the timing of the next fingerstick blood glucose, and

the system notifies a nurse when the next blood glucose reading should be entered. Testing intervals are configurable by the hospital, but the default testing interval is every 60 minutes, and 55-minute reminder alarms are preprogrammed. In the event of hypoglycemia, the software reverts to a hypoglycemia recovery mode and calculates an appropriate dose of 5% dextrose in water to be given subcutaneously or via IV. An audible and visual alarm alerts the nurse to the next scheduled blood glucose check every 15 minutes until recovery from the hypoglycemic event to the target blood glucose range is complete. All drip run information and insulin doses are electronically saved in the system's database (30).

Studies comparing data before and after implementation of this system showed improvement in mean blood glucose, decreased time to reach target blood glucose, increased time in the blood glucose target range, and less variation in blood glucose readings without an increase in hypoglycemia events (31,32).

Core Diabetes App

Unlike the technologies described above, TransformativeMed's Core Diabetes App helps ordering providers calculate insulin doses, but does not automatically change insulin doses without a provider's order. The insulin order is adjusted only after a provider reviews and confirms it. The app, which can be built into certain EMR systems, provides help with IV insulin rates, IV-to-SQ transitions, and SQ insulin initial doses.

For patients on an IV insulin drip, the app will show the current blood glucose, previous blood glucose, recommended infusion rate, and time of the next recommended blood glucose check. To transition from IV to SQ insulin, the app recommends an SQ insulin dose based on the IV insulin rate and patient's nutritional status. To initiate SQ insulin, the system can automatically calculate initial TDD, basal doses, and prandial doses based on a provider-selected multiplier, listing the factors that might affect a patient's insulin sensitivity, including age, weight, creatinine, steroid use, and nutritional status.

These programs, summarized in Table 1, support clinical reasoning but do not substitute for it. Their software algorithms are particularly helpful to hospital systems that do not have expertise (i.e., endocrinology or specialized glucose management teams) readily available to manage inpatient diabetes.

However, insufficient education before and after implementation of these systems can be a major barrier to their effective use. Without adequate training, there will be a

TABLE 1 Comparison of Inpatient Electronic Glucose Management Systems

Product	Recommends IV Insulin Doses?	Supports IV-to-SQ Transitions?	Recommends SQ Insulin Doses?	Available Software Additions for Data Management	Additional Notes
Glucommander	Yes	Yes	Yes	GlucoMetrics, GlucoSurveillance, GlucoView, GlyCloud, SmartClick	Also approved for outpatient SQ insulin management
EndoTool	Yes	Yes	Yes	EndoTool Analytics	Supports parenteral carbohydrate calculation
GlucoStabilizer	Yes	Yes	Developing	GlucoStabilizer Reports: inbound admit, transfer, discharge; outbound patient information integration in EMR; carbohydrate coverage for patients who are eating	
Core Diabetes App	Yes	Yes	Yes	Core Work Manager App, Core Notify App, Core Messaging App	Does not adjust the insulin dose automatically

lack of understanding regarding the mechanisms and utility of these systems. To make best use of these tools, all patient-care staff, such as nurses, pharmacists, and providers, need to understand the benefits and limitations of the systems in improving patients' health outcomes.

Challenges of Outpatient Hyperglycemia Management

All patients with type 1 diabetes and many patients with longstanding type 2 diabetes need insulin therapy. In patients with type 2 diabetes, the ADA recommends early introduction of insulin if there is evidence of ongoing catabolism (weight loss), symptoms of hyperglycemia are present, A1C is >10%, or blood glucose levels are very elevated (≥300 mg/dL) (33). Patients with diabetes on insulin either alone or in combination with other diabetes medications comprised 29.1% of the total diabetes population based on 2005–2012 NHANES data (34).

Despite the effectiveness of insulin and its potential to improve glucose control, many providers and patients find it extremely difficult to initiate and adjust insulin doses. Barriers include complex insulin therapy regimens, concern about hypoglycemia, inadequate health literacy, lack of experience with insulin on the part of the provider, and limited insulin self-management training.

A survey of 600 primary care physicians and specialists who treat patients with diabetes indicated that the lack of experience in initiating insulin and the limited time available to educate patients pose challenges to insulin intensification (35). More than 20% of the primary care providers had never initiated or modified insulin therapy.

In addition, one-third of all providers felt that administering intensified insulin therapy was difficult (35).

Hypoglycemia is a primary safety concern for both clinicians and patients, representing another major challenge to insulin use and glycemic control. Patients who experience hypoglycemia may be reluctant to maintain or self-adjust their insulin regimen, resulting in chronic hyperglycemia.

Technologies to Assist in Outpatient Insulin Dosing

Several FDA-cleared technologies are available to help providers and patients adjust insulin in the outpatient setting (Table 2). Generally, these products can be divided into three categories: basal insulin titration algorithms, mealtime insulin dose calculators, and tools that adjust both basal and bolus insulin. Although some are intended for people with either type 1 or type 2 diabetes, others should only be used by people with type 2 diabetes. Providers must activate the systems and configure the patient-specific parameters. These systems are not intended to be used as a substitute for professional medical advice.

Basal Insulin Titration Systems

Certain systems, including the Insulia (Voluntis), iSage Rx (Amalgam), Mobile Insulin Dosing System (Glooko), and My Dose Coach (Sanofi), are intended to adjust long-acting insulins for patients with type 2 diabetes. They are not to be used by people with NPH or premixed insulin regimens.

After reviewing patients' information, medical history, comorbidities, and current medications, providers formulate initial insulin dose and titration plans. These titration plans

TABLE 2 Comparison of Outpatient Electronic Glycemic Management Systems

Product	Supports Long-Acting Insulin Dosing?	Supports Rapid-Acting Insulin Dosing?	Format	For Use With Which Type(s) of Diabetes?	Information Input	Other Functions
Insulia	Yes	No	Mobile app with Web-based portal	Type 2 diabetes	Manually entered	Shares reports with providers; patients receive educational coaching messages; safety rules for hypoglycemia management
iSage Rx	Yes	No	Mobile app with Web-based portal	Type 2 diabetes	Manually entered	Shares reports with providers
Glooko's Mobile Insulin Dosing System	Yes	No	Mobile app with Web-based platform	Type 2 diabetes	Majority of meters use the Glooko MeterSync Blue device to transmit; data transits automatically from Dexcom CGM; no manual entry†	Shares reports with providers
My Dose Coach	Yes	No	Mobile app with Web-based portal	Type 2 diabetes	Manually entered	Shares reports with providers
InPen	No	Yes (Humalog, Novolog, Fiasp)	Pen connected with app by Bluetooth	Type 1 and type 2 diabetes	Manually entered; transmitted automatically from some Bluetooth-enabled blood glucose meters through Apple iHealth*; transmitted automatically from Dexcom CGM	Shares reports with providers; sends reminders to check blood glucose, inject insulin, and change cartilage after 28 days; displays last dose and current IOB; monitors insulin temperature
Accu-Chek Bolus Advisor	No	Yes	Mobile app with Web-based portal	Type 1 and type 2 diabetes	Manually entered; wirelessly transmitted from Accu-Chek Guide Me, Guide, and Aviva Connect; transferred from other Accu-Chek meters into the Accu-Chek Connect online portal	Shares reports with providers
Go Dose system (approved but not on the market)	No	Yes (Humalog only)	Mobile app	Type 2 diabetes	—	—
BlueStar Rx	Pending	Yes	Mobile-app with Web-based portal	Type 1 and type 2 diabetes	Manually entered; automatically transmitted from OneTouch Verio Flex, Accu-Check Aviva, Accu-Check Guide, TrueMatrix, Relion Premier Blu, Contour Next One, and Dexcom CGM	Shares reports with providers; stores personal health record; sends educational coaching messages; reminds user to take medication; communicates with providers

TABLE 2 Comparison of Outpatient Electronic Glycemic Management Systems (continued)

Product	Supports Long-Acting Insulin Dosing?	Supports Rapid-Acting Insulin Dosing?	Format	For Use With Which Type(s) of Diabetes?	Information Input	Other Functions
d-Nav System	Yes	Yes	Mobile app with Web-based portal	Type 2 diabetes	Manually entered; BioTel and iGlucose meters automatically upload data to the phone app; pending new Cloud-based glucose meter and CGM will also transmit data automatically	Shares reports with providers
Glucommander	Yes	Yes	Web-based	Type 1 and type 2 diabetes	Cellular-enabled glucose meters	Shares reports with providers
DreaMed	Yes	Yes	Mobile app with Web-based portal	Type 1 diabetes	All meters, pumps, and CGM systems with regulatory approval can transmit via the Tidepool Diabetes Management System	Gives personalized diabetes management tips

*Compatible systems include AgaMatrix Jazz Wireless 2, Ascensia Contour Next One, iHealthSmart, LifeScan OneTouch Verio Flex, LifeScan OneTouch Verio Sync, One Drop Chrome, Roche Accu-Chek Aviva Connect, and Roche Accu-Chek Guide. †A full list of compatible devices can be accessed at https://www.glooko.com/compatibility.

individualize a target blood glucose range, adjustment period, low blood glucose threshold, and maximum TDD. Patients log their fasting blood glucose readings and episodes of hypoglycemia events or administered insulin doses. Based on these inputs, the system calculates and recommends the subsequent dose of basal insulin.

Insulia

Patients can download Voluntis' Insulia mobile application (app) on their smartphone but cannot activate it until their provider prescribes and creates a specific treatment plan. This is done on a Web-based portal where the provider can also monitor patients' progress. Patient-specific parameters include target blood glucose range, insulin brand, starting long-acting insulin dose, injection timing, interval for adjustment, dose adjustment (from +1 to +8 units), low blood glucose threshold, and maximum TDD. A patient manually enters glucose readings and hypoglycemia events into the app. The algorithm provides the next appropriate insulin dose to attempt to bring glucose into the target range. In addition, patients will receive coaching messages to further their education about diabetes (36). Franc et al. (37) reported on the TeleDiab-2 trial of a predecessor device to Insulia called Diabeo-Basal and showed that, at month 4, twice as many patients in the Diabeo-Basal group as in the control group achieved an A1C <7% (29.8 vs. 12.5%).

iSage Rx

After a provider prescribes the Amalgam's iSage Rx, patients can activate the app on their smartphone with an activation code. Similar to the Insulia app, the iSage product has a Web-based portal where providers can set up initial patient profiles and choose which algorithm to use for titration. These algorithms are taken from various published insulin titration studies and range from adjusting by 1 unit daily to adjusting by 2–8 units weekly. A patient enters glucose readings and current insulin dose into the app, which then recommends the next dose of insulin. The app also includes educational videos and trivia challenges (38). One study showed that patients using iSage Rx had an A1C reduction of 1.04% after ~3 months and required almost no unexpected visits or phone consultations to manage their insulin doses (39).

Mobile Insulin Dosing System

Glooko's Mobile Insulin Dosing System (MIDS), which is one component of the Glooko mobile app, also assists patients with type 2 diabetes in adjusting basal insulin. Glooko offers Web- and mobile-based solutions for patients and for providers. Patients and clinics can use the Glooko platform to sync data from most glucose meters, continuous glucose monitoring (CGM) systems, smart pens, health/fitness apps, and insulin pumps. Providers set up individualized plans by specifying the starting dose,

titration period, minimum required fasting glucose reading, fasting target range, and specific dose adjustments based on fasting glucose values. After the provider prescribes this treatment plan from the Glooko system, the patient will be able to self-adjust basal insulin using MIDS via the Glooko mobile app (40).

My Dose Coach

Patients can download Sanofi's My Dose Coach app to their smartphone, and, once their provider has created an individualized dose plan on a separate Web-based provider portal, they can activate the app with a verification code received via text message. For the app to provide dose guidance, users must manually input their fasting blood glucose levels and insulin dosing once daily, along with any incidences of hypoglycemia. Based on that information, the app tells users whether and by how much to adjust their dose.

Mealtime Insulin Calculators

Whereas the process for titrating basal insulin is relatively straightforward, managing mealtime insulin can be quite difficult for both patients and providers. Adjustment of mealtime insulin is based on several factors, including a patient's premeal blood glucose value, carbohydrate amount, I:C ratio, and insulin sensitivity factor. The I:C ratio tells how many grams of carbohydrate will be adequately covered by 1 unit of insulin. For example, if a patient's I:C ratio is 10, 1 unit of insulin will cover 10 g carbohydrates, so that patient would need 3 units of mealtime insulin for a meal containing 30 g carbohydrates. The insulin sensitivity factor helps determine how much extra insulin a person needs to correct an elevated blood glucose level. For example, a patient with an insulin sensitivity factor of 50 could expect 1 extra unit of insulin to reduce blood glucose by 50 mg/dL; thus, that person would need to take an extra 4 units of insulin to decrease their glucose by 200 mg/dL. Many patients find carbohydrate counting and calculating insulin doses with complicated formulas to be demanding and difficult. Thus, providers often prescribe fixed doses of mealtime insulin and do not fully educate patients about the complex factors that need to be considered to calculate appropriate doses.

A few technologies have been developed to simplify these mealtime and correctional dose calculations, provide more accurate doses each time, and lessen patients' and providers' burden while improving blood glucose levels. Several free and subscription services are available, but here we highlight three that must be initiated by a health care provider: InPen (Companion Medical), Accu-Chek Bolus Advisor (Roche), and Go Dose (Eli Lilly). All of these products can be used for patients with type 2 diabetes. Inpen and Accu-Chek Bolus Advisor also can be used in patients with type 1 diabetes.

InPen

A novel approach to dosing insulin at meals is provided by Companion Medical's InPen system. This is a prescription insulin pen injector that can be used with Humalog (insulin lispro), Novolog (insulin aspart), or Fiasp (faster-acting insulin aspart) brand insulin cartridges. The InPen is a durable, nonrechargeable, Bluetooth-enabled device that delivers insulin in 0.5-unit increments and records doses in the InPen app. This app can be downloaded to a smartphone and then paired with the InPen. The InPen battery lasts for 1 year. It can be used for patients with type 1 or type 2 diabetes.

Clinicians provide the settings, which include patients' I:C ratio, insulin sensitivity factor, glucose target range, predictive active insulin duration, and maximum calculated dose. When patients need to decide on a dose of insulin, they enter their current glucose level and carbohydrates to be eaten. The dose calculator then recommends the insulin dose and records how much insulin they actually take. The app also helps to avoid stacking of insulin (delivering insulin without regard to previous doses that may still be active) by taking into account any remaining active insulin on board (IOB) from previous doses. This information is displayed prominently on the app. If patients are not as skilled with carbohydrate-based dosing, there is an option for fixed-meal dosing or three dose options for small, medium, or large meals. Reports can be sent to clinicians and incorporated with data from a Dexcom CGM device for patients who use one (41).

Accu-Chek Bolus Advisor

The Accu-Chek Bolus Advisor from Roche is a prescription insulin calculator built into the Accu-Chek Connect diabetes management app that provides mealtime insulin dose recommendations for patients with type 1 or type 2 diabetes. The system must be configured by a provider to include a patient's I:C ratio, blood glucose target ranges, and insulin sensitivity factor. Once set up, the app provides personalized dosing advice based on the patient's current blood glucose level, carbohydrates to be consumed, and IOB. Patients can choose either an assigned meal dose or a calculated dose based on carbohydrate counting. This app also helps to prevent insulin stacking by calculating IOB.

Blood glucose values can be transmitted wirelessly from Accu-Chek Guide Me, Accu-Chek Guide, and Accu-Chek

Aviva Connect meters; transferred from other Accu-Chek meters into the Accu-Chek Connect online portal; or manually entered. The software stores and then transfers the data to a provider. The provider can then access these reports and help patients make the appropriate adjustments to their insulin regimen to achieve better control (42).

Go Dose System

The Go Dose system from Eli Lilly was approved by the FDA in 2017 but it has not yet been brought to market. This mobile app is intended to help patients with type 2 diabetes who are also on basal insulin in adjusting mealtime Humalog (insulin lispro) U100 insulin doses based on the algorithm used in the Autonomy Study (43). This algorithm uses the insulin dose and postmeal glucose level from the same meal on the previous day and the current blood glucose level to recommend the next dose of lispro insulin. As of this writing, this product was not available to patients.

Basal and Bolus Insulin Titration Systems

For patients on a basal/bolus insulin regimen, the ultimate solution is a product that will help them adjust both their basal and mealtime doses. Four FDA-approved systems do so: the BlueStar Rx app (WellDoc), the d-Nav system (Hygieia), the Glucommander Outpatient system (Glytec), and the DreaMed Advisor Pro (DreaMed Diabetes).

Bluestar Rx

WellDoc's BlueStar app has multiple functions such as storing a patient's personal health record and logbook entries, providing diabetes education materials with health tips, sending educational coaching messages based on real-time blood glucose values and trends, reminding patients to take the correct medication at the scheduled time, communicating with providers through a message center, and providing clinician decision support. In a 12-month prospective study, patients using the BlueStar app had a 1.9% reduction in A1C compared with a 0.7% decrease in the control group (44). Within the app, patients can activate the BluStar Rx insulin dosing calculator after the provider sends the prescription. BlueStar Rx uses a patient's individualized prescribed regimen to calculate a dose of mealtime insulin for a given amount of carbohydrates and/or blood glucose value, with flexibility based on I:C ratio, insulin sensitivity factor, programmed sliding scale, or any combination of these calculations. Based on personalized A1C targets of either <7.0% or <8.0%, different blood glucose targets are displayed for a variety of time periods, including when fasting, before meals, after meals, and at bedtime.

Recently, BlueStar was also approved for titration of long-acting insulin. Based on the prescriber-directed titration plan, the approved function in the BlueStar app will recommend the next long-acting insulin dose based on a patient's target blood glucose, hypoglycemia events, and other factors.

BlueStar Rx connects via Bluetooth to many glucose meters, including OneTouch, Accu-Chek, and Contour, as well as the Dexcom CGM system. This connectivity allows users to transmit their glucose monitoring data to the app (45,46).

d-Nav

The d-Nav system by Hygieia can be used by patients with type 2 diabetes who are on any insulin therapy regimen: basal only, premixed insulin, or multiple daily injections. Patients use the d-Nav software on either a cellular phone or the proprietary d-Nav glucose meter. Based on glucose readings and insulin doses during the past 7 days, the software provides the next recommended basal or bolus insulin dose. It can also be used with premixed insulins. The algorithm increases or decreases insulin doses from meal to meal to avoid hypoglycemia and hyperglycemia. Providers and patients can review the history of glucose readings and insulin doses on a Web-based portal. In addition, this company offers periodic follow-up with specialists to review the patient's progress and consider escalation of therapy. A study by Bergenstal et al. (47) found a significant reduction in A1C of 1.0% in the group using d-Nav compared with a reduction of 0.3% in the group not using d-Nav.

Glucommander Outpatient

Glucommander Outpatient, by Glytec, uses similar logic as the company's inpatient system described above. It is intended to be used by a medical system or large office to manage multiple patients on complex insulin regimens. The provider has a dashboard and sets a patient's profile with starting insulin doses. The patient will need to have a cellularly enabled glucose meter that can automatically send data to the dashboard. The Glucommander algorithm analyzes trends in glucose and make recommendations to the provider to adjust basal and mealtime insulin doses. It also alerts the provider to extremes in glucose readings. The provider then communicates to the patient to make changes in the insulin regimen.

DreaMed

DreaMed Advisor Pro by DreaMed Diabetes is a decision-support software intended to assist health care providers in titrating insulin pump setting for patients with type 1 diabetes who use an insulin pump and either a CGM system or blood glucose monitoring via a glucose meter.

Insulin pump settings that can be programmed include I:C ratio, insulin sensitivity factor, and basal infusion rates. The system is not intended for use with patients who use an automated insulin delivery system.

After a patient's data from insulin pump, CGM device, and/or glucose meter are downloaded to the DreaMed software, the system analyzes patterns of high and low glucose and insulin dosing events to create a personalized recommendation for insulin titration. It also provides the patient with personalized management tips based on the data to help improve glucose-related behaviors and outcomes. The provider reviews DreaMed recommendations and discusses changes with the patient or simply sends the approved recommended changes via e-mail.

Conclusion

Outpatient and inpatient glucose management can be extremely challenging given daily and even hourly changes in a patient's condition. In the hospital, insulin dosing technology that is integrated into the EMR can provide support to busy clinicians. For patients trying to determine appropriate insulin doses at home, app-based systems provide needed support with titration and dose adjustments.

In academic settings, these inpatient and outpatient digital solutions can also serve as educational tools, especially at crucial decision points such as when initiating basal and bolus insulin, transitioning from IV to SQ insulin, and titrating an insulin regimen. Supervising providers can use these tools to teach trainees about evidence-based use of basal and bolus insulin, the rationale behind recommended dose titration, and the newest technologies available to help both clinicians and patients who are managing diabetes.

Insulin therapy is essential for people with diabetes that is not managed by lifestyle modification and appropriate use of noninsulin pharmacologic therapies. However, numerous barriers impede the timely initiation and intensification of insulin therapy. Clinicians typically have only 15–30 minutes with each patient every 3 months, even when their blood glucose is not well managed. This lack of time to communicate with and educate patients, coupled with concerns about hypoglycemia from insulin therapy, may delay initiation or intensification of insulin therapy when indicated. Technological systems can provide patients and providers with tools to overcome some of the barriers associated with insulin initiation, titration, and adherence and thereby improve health outcomes.

Many insulin dosing systems are relatively new, and others are still in development. The technologies they use are rapidly evolving, and providers have limited time to stay up to date on available options. Availability and accessibility of these systems also remains an open question. Implementation of the programs designed for inpatient use requires a large investment from the hospital, and the financial benefits from their use are not realized immediately. Outpatient apps have variable insurance coverage, and providers need to be familiar with the specific process to obtain approval for each one.

In 2020, medical systems around the world have been forced to adapt quickly to the novel coronavirus pandemic. This experience has pushed everyone to reimagine the ways in which patients and clinicians interact. Most clinical settings now include some aspect of virtual or remote care. With the availability of these connected apps for insulin management and others that remotely transmit glucose monitoring results, diabetes care is particularly well suited for this new reality.

These technologies were developed to help clinicians and patients. When used correctly, they will likely have a positive effect on patients' diabetes management, decrease complications, and lessen the economic burden of diabetes while reducing diabetes care providers' workloads and helping them better aid and communicate with their patients with diabetes.

DUALITY OF INTEREST

No potential conflicts of interest relevant to this article were reported.

AUTHOR CONTRIBUTIONS

L.C. wrote the manuscript and researched data. P.R.S. and P.A.S. critically reviewed and approved the manuscript. P.A.S. is the guarantor of this work and, as such, takes responsibility for the integrity and accuracy of this review.

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