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ORIGINAL ARTICLE

Performance of an Electronic Diary System for Intensive Insulin Management in Global Diabetes Clinical Trials

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Abstract

Background: This report describes the performance of a wireless electronic diary (e-diary) system for data collection and enhanced patient–investigator interactions during intensive insulin management in diabetes clinical trials.

Materials and Methods: We implemented a customized electronic communication system featuring an e-diary and a Web portal in three global, randomized, controlled Phase 3 clinical trials testing basal insulin peglispro compared with insulin glargine, both combined with prandial insulin lispro, in patients with type 1 or type 2 diabetes mellitus (T1DM and T2DM, respectively). We collected data during 28 weeks of study e-diary use for the report.

Results: Patients ($n = 2,938$) in 31 countries used e-diaries to transmit 2,439,087 blood glucose (BG) values, 96% of which were associated by the patient with a protocol time point during the 72-h response window. Of 208,192 hypoglycemia events captured, 96% had a BG value, and 95% had treatments and outcomes entered by patients within the 72-h window. Patients recorded administration of 1,964,477 insulin doses; 93% of basal insulin doses were adherent with the investigator prescription. Investigators adjusted 13 basal and 92 bolus insulin prescriptions per patient-year using the e-diary system. After 26 weeks of treatment and e-diary use in the combined study arms, hemoglobin A1c values decreased by 0.6% or 1.6% and fasting BG decreased by 7.8 or 28 mg/dL in patients with T1DM or T2DM, respectively.

Conclusions: The e-diary system enabled comprehensive data collection and facilitated communication between investigators and patients for intensive insulin management in three global clinical trials testing basal insulins.

Background

MOBILE COMMUNICATIONS DEVICES, including mobile phones and personal digital assistants, are being used to a greater extent in clinical medicine, especially for the care of patients with diabetes.[1] Mobile devices, when connected to a system of central servers and remote portals programmed with clinical decision support software, have the potential to enhance diabetes management. Electronic diaries (e-diaries) designed to collect specific information from the patient have been used in diabetes clinical trials with some success, depending on the features available.[2] Newer e-diaries incorporate wireless capability to communicate with both glucose meters and servers. Wireless e-diaries have several

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advantages, including (1) facilitation of real-time data capture, (2) transmitted data can be organized and made available for clinical decision-making, or stored securely for future analyses, and (3) data transfer to a central server is automatic (without patient or staff interaction), increasing integrity and efficiency. These features may have additional value in clinical trials by reducing potential transcribing errors and incomplete data capture, which may affect clinical decisions, patient outcomes, and ultimately study conclusions.

When implementing intensive insulin therapy, the need for close and frequent patient follow-up is particularly critical. To optimize the insulin prescription, investigators require complete, timely, and accurate data on the patient's blood glucose (BG) values, insulin dose, and hypoglycemia events. Possible barriers to the collection of this type of data include (1) the time and resources required, (2) the patient's lack of motivation or social support for diabetes self-management, (3) missed clinic visits, and (4) low numeracy skills.[3–5] A wireless e-diary system may facilitate data collection and patient interaction with investigators and overcome barriers to intensive insulin therapy in clinical trials.

Here we describe the design and implementation of a wireless e-diary system adapted to the specifications for three controlled, randomized clinical trials testing basal insulins (basal insulin peglispro vs. insulin glargine) in combination with insulin lispro in patients with diabetes undergoing intensive insulin therapy. To test the performance and applicability of the system, we collected data during 28 weeks of use in the three global diabetes studies. The primary aim of this report was to assess the system for (1) enabling the comprehensive capture of BG measurements and insulin doses administered by the patient, (2) capturing hypoglycemia events, including symptoms, severity, treatments, and outcomes, (3) facilitating frequent and intensive insulin dose adjustment by the investigator, (4) tracking investigator adherence to the protocol dosing algorithms, and (5) monitoring patient adherence to the prescribed dose during the study. Finally, we examined the combined metabolic outcome data to assess whether the study results were consistent with clinical trials using intensive insulin management, but not using electronic data capture.[6,7]

Subjects and Methods

### Components and functions of the electronic system

The electronic patient-recorded outcome (ePRO) system was provided by PHT Corp. (Boston, MA) and programmed to incorporate specific features of the individual clinical trials. In all of the studies, the ePRO system included (1) a MyGlucoHealth® glucose meter (Entra Health Systems, San Diego, CA) with Bluetooth® (Bluetooth SIG, Kirkland, WA) capability for wireless transfer of self-monitored BG (SMBG) measurements with a time and date stamp to the e-diary, (2) a LogPad® (PHT Corp.) hand-held device (e-diary) capable of wireless transmission of data to central servers, and (3) the StudyWorks® (PHT Corp.) software package, implemented on central servers and providing real-time access to all patient-recorded data via a secure online portal at investigational sites. The components and functions of the electronic system are illustrated in Figure 1. It is important that the e-diaries did not function as phones or Internet

portals, but were dedicated for study use only and thus were not an inducement for participation. Patients returned the e-diaries at the completion of the studies.

The data management system collected and stored all SMBG measurements transferred from the glucose meters to the e-diaries. Patients had a response window of 72 h after a measurement to categorize the SMBG value using the e-diary with a protocol-specified time point (pre-morning meal, post-morning meal, pre-midday meal, post-midday meal, pre-evening meal, post-evening meal, bedtime, or 0300 h). The patients could transmit the e-diary data to the central server at any time. Additionally, all e-diaries were programmed to perform a daily automatic transmission to the central servers in the middle of the night. Hypoglycemia event questions were automatically triggered on the e-diary for an SMBG level ≤70 mg/dL; patients were asked to record the signs, symptoms, treatments, and outcomes associated with hypoglycemia events. The e-diary hypoglycemia outcome questionnaire was also accessible to the patient for entry of hypoglycemia events that were not associated with an SMBG measurement.

The e-diary also stored the patient's current insulin doses prescribed by the investigator, including for basal, prandial, and supplemental bolus insulin if indicated. Investigators chose one of three bolus dosing plans for each patient at study entry: (1) carbohydrate (CHO) counting with flexible diet, where bolus insulin dosing was based on the CHO content and provided in units/g of CHO or units/exchange; (2) pre-prandial action plan with fixed diet, where bolus doses in units of insulin were based on planned CHO content for the meal; and (3) pattern adjustment action plan, where bolus insulin doses were fixed for each meal. The SMBG readings, patient administered insulin doses, and hypoglycemia event records needed for determining an insulin dosing regimen were available to investigators and designated clinical staff through the StudyWorks portal. StudyWorks also provided investigators with dosing recommendations based on protocol-specific dosing algorithms (see Supplementary Data [available online at www.liebertonline.com/dia]), which could be modified by the investigator based on an individual patient's clinical circumstances or safety considerations. The doses for basal and bolus insulin were thus ultimately determined by, and the responsibility of, each investigator. The investigator's insulin dosing adjustments were electronically transmitted to the patient's e-diary and were immediately visible when the patient opened the e-diary. Patients had to click on the message to proceed with other e-diary functions, thereby acknowledging receipt of the dosing adjustment.

An optional bolus dosing feature was available as an algorithm on the e-diary that allowed the patient to generate a premeal bolus insulin dose if using CHO counting or to make optional adjustments, including a correction factor for SMBG levels above study target, stress (e.g., fever), or exercise. The e-diary provided a recommended basal and bolus insulin unit dose based on the investigator prescription, the bolus dosing plan, and any adjustments. The patient entered the actual insulin dose administered into the e-diary and categorized it as basal or bolus, and for bolus insulin as morning meal, midday meal, evening meal, or other bolus. If the dose administered did not match the recommendation given by the e-diary, the patient was asked to choose one of five
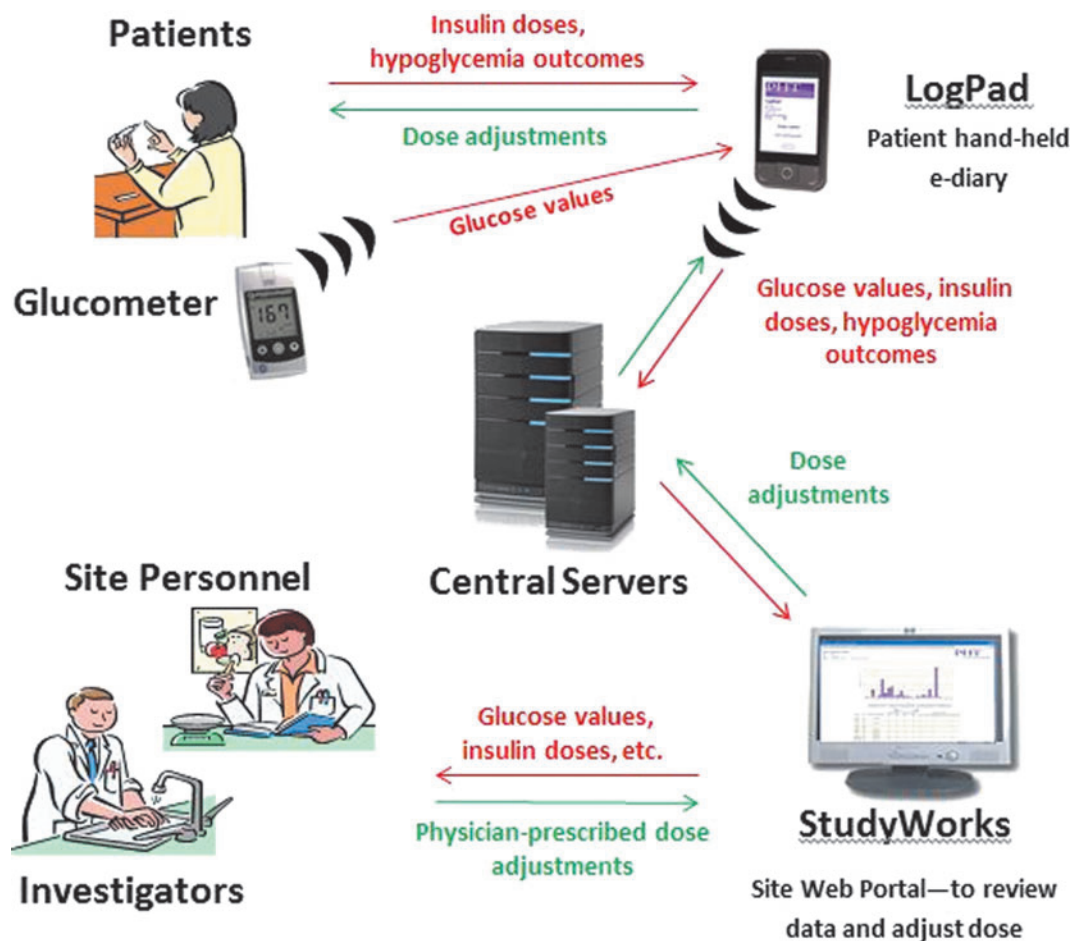
FIG. 1. Insulin management with the electronic system. Using the glucose meter, the patient determines blood glucose and transfers the value to the electronic diary (e-diary). Using the e-diary, the patient enters the meal (breakfast, lunch, or dinner) and the carbohydrate to be consumed. On request, the e-diary recommends a dose based on the prescription (units/g of carbohydrate and units/blood glucose deviation). The patient enters the actual dose administered. On the StudyWorks site portal, the investigator receives the data as they are transferred from the e-diary. The site evaluates the insulin prescription weekly and determines if an adjustment is needed in basal or bolus insulin. The investigator uses the insulin algorithms programmed in StudyWorks to make the changes, and the system notifies the patient via a message on the e-diary. The patient responds that the message was read.

options indicating why the recorded dose differed from the recommended dose. This provided a measure of patient adherence to the investigator prescription.

Additionally, the e-diary incorporated study-specific reminders to patients to measure SMBG and to record insulin doses administered. Protocol-specified SMBG measurements included four readings on most days and either a 5-point SMBG profile or a 9-point SMBG profile on specific days, such that each patient was asked to provide approximately 830 SMBG measurements, categorized by meal or time point, during the 28-week period.

Implementation in diabetes clinical studies

The e-diary system was used as the primary method of SMBG and insulin dosing data collection and diabetes management monitoring (at both patient and investigative site levels) in three Phase 3 multicenter, international, controlled, randomized clinical trials (registered at ClinicalTrials.gov with clinical trial registration numbers NCT01481779, NCT01454284, and NCT01468987) comparing basal insulin peglispro with insulin glargine in combination with insulin lispro. In patients with T1DM, two studies were conducted as parallel-arm trials and included male or female patients diagnosed with T1DM for at least 1 year, who were over the age of 18 years, and had been treated with basal-bolus insulin therapy for at least 90 days prior to the first visit. In patients with T2DM, a parallel-arm study included male or female patients diagnosed with T2DM for at least 1 year, who were over the age of 18 years, and had been treated with one or more injections of insulin daily with or without oral antihyperglycemic medications.

Data were collected during the 2-week lead-in period and the first 26 weeks of treatment for each study; the treatment period comprised 12 weeks of intensive insulin adjustment, with protocol-recommended weekly interactions via e-diary, and a 14-week maintenance period, requiring interactions every 4–6 weeks. Scheduled clinic visits were at randomization and at weeks 2, 4, 8, 12, 16, and 26; all other visits were via the e-diary communication.

In addition to the scheduled reviews of patient data, investigators could initiate a review at any time to access the patient's data in real time, for example, to respond to a hypoglycemia episode. A "click and run" report format in the StudyWorks software assisted with this type of review. Investigators then had the option to call the patient for more information or send a new insulin dose recommendation to the patient's e-diary.

The studies were conducted in accordance with the International Conference on Harmonization Guidelines for Good Clinical Practice and the Declaration of Helsinki and were approved by ethical review boards. All patients signed an informed consent document prior to study entry.

Statistical analyses

The data are presented for the overall study population combining both basal insulin treatment groups (basal insulin peglispro and insulin glargine) by type of diabetes (T1DM or T2DM). For continuous variables, summary statistics included sample size, mean, SD, median, and range (minimum, maximum). For categorical variables, summary statistics included sample size, frequency, and percentages. SAS version 9.1 or higher software (SAS Institute, Cary, NC) was used to perform all statistical analyses. Demographics and baseline clinical characteristics were summarized for all randomized patients by type of diabetes. The number of patients was summarized by continent and country. Histograms of the frequency of SMBG values were created. Investigator adherence to a protocol-suggested algorithm of basal insulin dose adjustment, as well as patient adherence to the investigator-prescribed basal insulin dose, was calculated and summarized. For hemoglobin A1c (HbA1c) and fasting BG (FBG), summary statistics are presented for baseline (last nonmissing observation at or before the randomization visit) and for selected postbaseline visits.

Results

Data were collected from a total of 2,938 subjects from three studies, encompassing 342 investigational sites in 31 countries on six continents (Table 1). Languages available on the e-diary are given in Supplementary Table S1. Patient demographic and baseline clinical data are provided in Supplementary Table S2. The patients were diverse in age, ethnicity, and duration of diabetes. Approximately 57% of patients were male.

During the 28 weeks of study, 2,439,087 SMBG values were captured, representing an average of 4.6 values per patient per day transmitted from the e-diary (Table 2). Approximately 0.3% of SMBG values were outside of the measuring range of the glucose meter (30–600 mg/dL). The frequency histograms for the SMBG values for patients with either T1DM or T2DM demonstrated a right-skewed distribution (Fig. 2).

Overall, 95.6% of SMBG values were categorized (e.g., pre-morning meal, pre-midday meal, bedtime, etc.) by the patient within the specified response window of 72 h, which enabled the association of the SMBG values and recorded insulin doses with a meal (Table 2). The bolus dosing plan used most frequently by patients with T1DM was the CHO counting plan (50.4%), whereas the plan used most by patients with T2DM was the pattern adjustment plan (60.8%)

TABLE 1. PATIENTS BY CONTINENT AND COUNTRY

Continent/country	n
Africa	
South Africa	24
Asia Pacific	
Japan	112
Russian Federation	59
Taiwan	15
Australia	
Australia	90
New Zealand	14
Americas	
Brazil	54
Canada	52
Mexico	65
Puerto Rico	46
United States	1,248
Europe	
Austria	26
Belgium	36
Croatia	17
Czech Republic	45
Denmark	13
France	56
Germany	170
Greece	46
Hungary	72
Ireland	5
Italy	51
Lithuania	13
The Netherlands	18
Poland	165
Romania	65
Slovakia	52
Spain	139
Sweden	26
United Kingdom	71
Eurasia	
Israel	62
Turkey	11

(Table 3). During 28 weeks, patients recorded 1,964,477 administered insulin doses in the e-diaries (Table 3). Patients used the optional bolus dosing feature on the e-diary to generate an adjusted bolus insulin dose 171,148 times (Table 3).

In 28 weeks, 208,192 hypoglycemia events were captured on the e-diaries; 96% had an associated SMBG value, and 95% had patient self-reported outcomes (Table 2). These records, in addition to the patient SMBG profiles and insulin doses available at the secure site portals, facilitated 199,500 investigator-prescribed doses of basal and bolus insulin in StudyWorks (Table 3). This resulted in averages of 13 basal and 92 individual meal bolus insulin dose adjustments per patient-year.

On average, 53% of the protocol algorithm-recommended basal insulin doses were prescribed by the investigator without adjustment (Table 4). Modifications to the recommended dose generated by the algorithm were greater in number in the first 12 weeks of the study period when the insulin dose was being intensively adjusted. Investigator

TABLE 2. BLOOD GLUCOSE VALUES
AND HYPOGLYCEMIA EVENTS

	T1DM (n = 1,569)	T2DM (n = 1,369)
Total BG values captured (n)	1,360,469	1,078,618
BG values/patient/day (mean)	4.8	4.3
Categorized within 72 h (%)	94.3	97.2
Patient-days of use	283,977	253,153
Out-of-range values [n (%)]		
<30 mg/dL (<1.67 mmol/L)	2,472 (0.18)	2,396 (0.22)
>600 mg/dL (>33.3 mmol/L)	1,298 (0.10)	646 (0.06)
Hypoglycemia events [n (%)]		
With BG value	152,788 (97.0)	48,078 (94.8)
Symptoms only (no BG value)	4,665 (3.0)	2,661 (5.2)
Patient-reported outcomes within 72 h	148,305 (94.2)	49,479 (97.5)

BG, blood glucose; T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus.

dosing discretion was permitted by the protocol, and ''individual patient circumstances'' was the most commonly selected reason for not following the algorithm for basal insulin (60–80% of deviations); ''fear of hypoglycemia'' was the second most selected reason (10–18% of deviations).

The average patient adherence to the basal insulin dose prescribed by the investigator was 93% (Table 4). The most common reason selected by the patient for deviation from the prescribed dose was a circumstance ''other'' than diet, exercise, or fear of hyper- or hypoglycemia, whereas the second most common reason was ''fear of hypoglycemia.''

The patient metabolic outcomes measures, HbA1c and FBG, were determined at randomization and at scheduled postbaseline visits. For each patient, the FBG value was the mean of the pre-breakfast SMBG measures taken during the 7 days prior to the visit; the HbA1c value was one central laboratory measurement from a blood sample collected at the time of the visit. The mean FBG and HbA1c values decreased during treatment in both the T1DM and T2DM populations (Fig. 2). The correlation between the two measures of glycemic control, one obtained via the e-diary (FBG) and one from a similarly timed laboratory measurement (HbA1c), is demonstrated (Fig. 2).
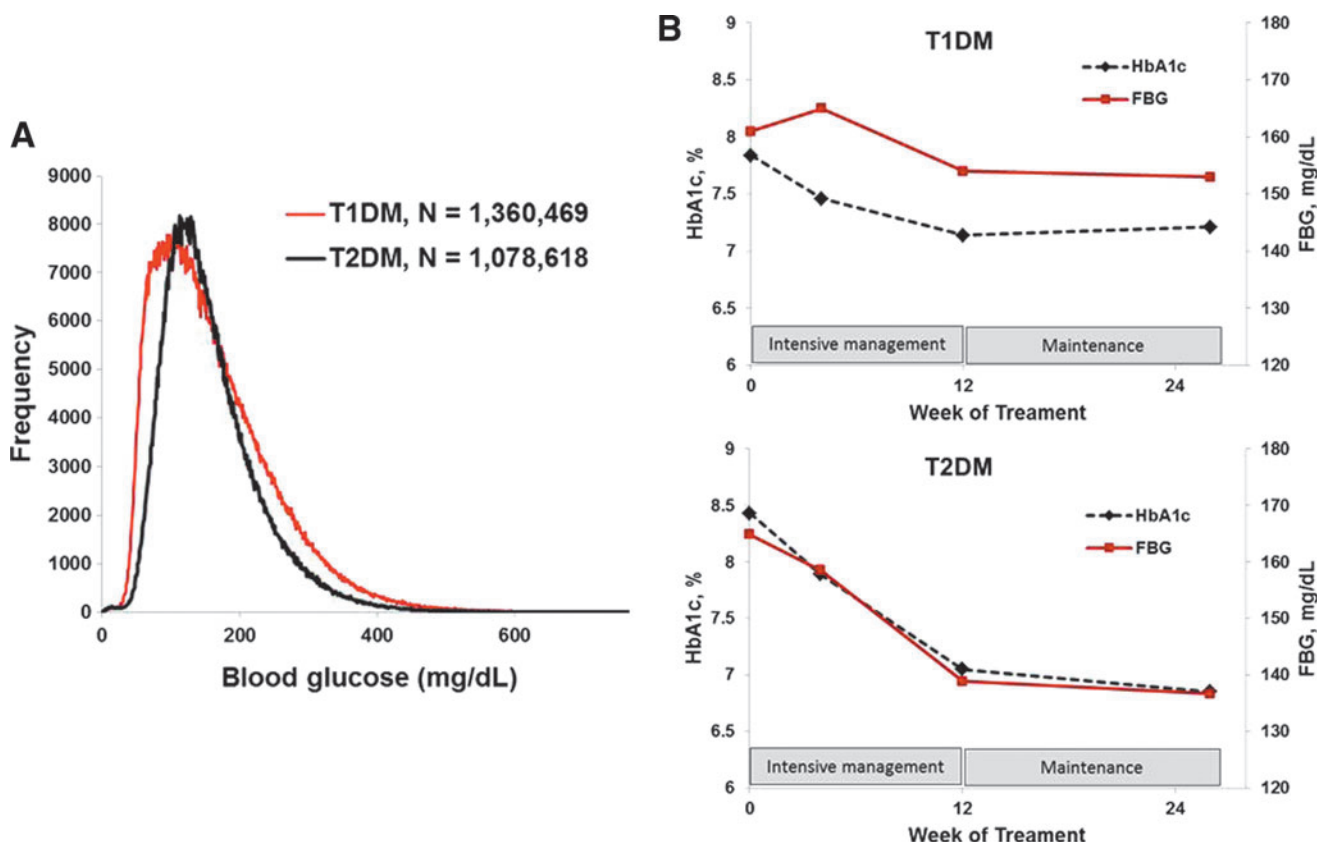
FIG. 2. Frequency histograms of blood glucose values and mean hemoglobin A1c (HbA1c) and fasting blood glucose (FBG) values during the study: (A) frequency distribution of all BG values collected via the e-diaries during the 28-week period from both study arms, by type of diabetes, and (B) outcome data by type of diabetes for all patients in both treatment arms. At each time point shown, the patients visited the sites and had blood drawn for HbA1c determination. The concurrent FBG number was calculated for each patient as the mean of pre-breakfast SMBG measurements on the previous 7 days. Each data point represents the mean of all patients at that time point for HbA1c or FBG. T1DM, n = 1,534 and 1,522 at baseline for HbA1c and FBG, respectively. For type 2 diabetes mellitus (T2DM) patients, n = 1,356 and 1,343 at baseline for HbA1c and FBG, respectively. T1DM, type 1 diabetes mellitus.

TABLE 3. INSULIN DOSES AND ADJUSTMENTS

	T1DM (n=1,569)	T2DM (n=1,369)
Patient-generated data		
Insulin doses recorded (n)	1,071,544	892,933
Per patient per day (mean)	3.5	3.3
Basal insulin [n (% of total)]	240,870 (22.5)	201,327 (22.5)
Bolus insulin [n (% of total)]	830,674 (77.5)	691,606 (77.5)
Premeal bolus insulin doses (n)[a]	564,993	550,188
Use of bolus dosing feature (n)[b]	86,165	84,983
Premeal bolus doses recorded, by plan		
Carbohydrate counting plan		
Patients [n (% of total number)	791 (50.4)	197 (14.4)
Doses recorded [n (% of total)]	269,433 (47.7)	75,430 (13.7)
Preprandial action plan		
Patients [n (% of total number)]	285 (18.2)	339 (24.8)
Doses recorded [n (% of total)]	106,860 (18.9)	136,819 (24.9)
Pattern adjustment action		
Patients [n (% of total number)]	493 (31.4)	833 (60.8)
Doses recorded [n (% of total)]	188,700 (33.4)	337,939 (61.4)
Investigator-generated data		
Investigator assessments, total	100,570	98,930
Basal insulin [n (% of total)]	14,734 (14.7)	13,864 (14.0)
Bolus insulin [n (% of total)]	85,836 (85.3)	85,066 (86.0)
Investigator dose adjustments, total	75,571	73,757
Basal insulin [n (% of total)]	8,687 (11.5)	9,559 (13.0)
Bolus insulin [n (% of total)]	66,884 (88.5)	64,198 (87.0)
Insulin adjustments per patient-year (mean)		
Basal insulin	11.6	14.6
Bolus insulin	86.9	97.9

[a]Categorized by patient as morning meal, midday meal, evening meal, or other.
[b]The use of the optional bolus dosing feature as prescribed by the investigator on the electronic diary.
T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus.

TABLE 4. INVESTIGATOR AND PATIENT DOSING ADHERENCE MEASURES

	T1DM		T2DM	
	0–12 weeks[a]	12–26 weeks[b]	0–12 weeks[a]	12–26 weeks[b]
Patients (n)	1,564	1,426	1,368	1,275
Investigator use of protocol algorithms when prescribing basal insulin				
Insulin prescriptions (n)	10,590	3,741	10,456	3,337
Prescriptions following algorithm [n (% of total)]	5,456 (51.5)	1,885 (50.4)	5,825 (55.7)	1,656 (49.6)
Investigator reason for deviation (% of all reasons)				
Investigator decision	74.2	64.3	79.6	78.6
Patient decision	6.3	10.6	2.3	3.2
Hyperglycemia fear	2.1	2.0	2.2	1.5
Hypoglycemia fear	12.0	18.0	10.3	13.4
Other	5.5	5.1	5.6	3.3
Patient adherence to investigator prescription for basal insulin				
Injections recorded (n)	101,260	102,474	86,637	90,655
Adherent injections [n (% of recorded)]	92,846 (91.7)	96,862 (94.5)	78,612 (90.7)	86,260 (95.2)
Patient reason for deviation (% of all reasons)				
Diet change	2.9	3.3	5.3	6.1
Exercise change	2.9	3.8	1.6	2.4
Hyperglycemia fear	11.3	10.9	4.3	3.6
Hypoglycemia fear	16.4	27.5	6.5	14.3
Other	66.5	54.4	82.4	73.6

[a]Weeks 0–12 of treatment was the period of intensive insulin adjustment.
[b]Weeks 12–26 of treatment was the maintenance period.
T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus.

Discussion

The introduction of innovative technology into a clinical trial setting that is not currently used in clinical care has inherent risks, including lack of acceptance or use of the system by investigators and patients as well as possible interference with patient care. With the data collected during a 28-week period of use in three global clinical trials across multiple geographies, cultures, and languages, we demonstrated that comprehensive data capture is not only possible, but it can be accomplished in large, diverse T1DM and T2DM patient populations.

Patient usage of the e-diary was reflected in the average number of SMBG values transmitted per day (more than four per patient), which met protocol and clinical diabetes care requirements. In addition, 96% of SMBG values were transferred within the protocol-specified 72-h response window, demonstrating the ongoing integration of the glucose meter and e-diary into the patient's daily diabetes self-management. Each SMBG value was accompanied by a date and time stamp directly transferred from the glucose meter, such that investigators were provided with a detailed account of patient metabolic control in real time, facilitating intensive insulin management. The patient's categorization of the SMBG values and recording of insulin doses administered by meal enhanced the value of the data captured.

Hypoglycemia events are a key outcome of clinical trials testing insulins and are an important determinant in insulin dosing adjustment. Ninety-six percent of hypoglycemia event records transmitted from patient e-diaries were accompanied by an SMBG value, and 95% included patient-reported outcomes. This supports the feasibility and comprehensiveness of electronic hypoglycemia event capture in clinical trials and the potential value for insulin dosing adjustment in clinical care. Together with the SMBG values and insulin doses recorded, hypoglycemia event data provided the investigators with crucial information for intensive insulin management, as well as an important outcome for the clinical trials.

The overall improvement in the HbA1c and FBG values during 26-week insulin treatment was comparable to that obtained in previous clinical trials that used intensive insulin therapy.[6,7] It is well known that implementation of intensive insulin therapy in a clinical trial setting will result in improved metabolic control.[8] The use of the e-diary system did not impede the expected clinical outcome.

Typically, SMBG values are captured only periodically during a clinical trial because of the burden of record keeping and data entry for the investigative site and the patient. Our database of protocol-directed SMBG measurements is one of the largest collections of BG values from a clinical trial setting to date. Because the SMBG values were wirelessly transmitted from the glucose meter to the e-diary to the central servers, not only were data entry error or collection bias precluded, but a reassuringly complete recording of metabolic data was possible. With the SMBG values, hypoglycemia event data and recorded insulin doses provide a more complete representation of the clinical trial outcomes. These data may allow the simulation of outcome measures (such as HbA1c) based on the glucose values generated in these studies, which could be useful in the design of future clinical trials.[9]

The frequency histograms of our SMBG measurements (Fig. 2) are right-skewed in contrast to the normal distribution, which is typical and consistent with BG distributions created from continuous glucose monitoring recorded data.[10] Continuous glucose monitoring–recorded data have been used to develop models to predict the probability of hypo- and hyperglycemia for both individuals and populations,[10] as well as to inform dosing such as in a closed-loop system.[11,12] Similar models could be developed to work with our large database of SMBG values and hypoglycemia events. Being able to better predict the probability of hypoglycemia could assist in the design of future studies to help patients minimize risk of hypoglycemia. These models could also be used, for example, to make insulin dosing suggestions for patients using SMBG and intermittent subcutaneous insulin administration instead of an insulin pump.

Electronic capture of both investigator-prescribed and patient-administered insulin doses, along with tracking records of the algorithm-recommended dosing, provided a unique opportunity to evaluate adherence and to better understand deviations from protocol-stipulated treatments. Overall, investigators followed the recommended doses generated by the protocol algorithms just over 50% of the time. Although most of the deviations were due to investigator discretion, the second most common factor was fear of hypoglycemia, which has been cited previously as an important factor in protocol dosing overrides.[13]

Lack of patient adherence to the prescribed insulin dose has been recognized as a major impediment to optimal patient outcomes as measured by metabolic control.[14,15] Our data demonstrated that overall patient adherence to the investigator-prescribed basal insulin dose was very high (93%), and the e-diary questions provided insights into the reasons for the occasional deviations from the prescribed dose, which may occur in clinical practice as well as in a clinical trial. A future enhancement may include wireless communication of the insulin dose from an insulin pen device.

The strength of our evaluation of the e-diary system for insulin clinical trials was the size and geographic scope of the studies. The e-diary system was implemented successfully in these trials in part because the insulin dosing approaches and protocol algorithms programmed into the system were the same or similar to those currently used by the patients and investigators who participated in the trials. A weakness of our evaluation was the lack of a side-by-side test of the e-diary system and paper-based data collection in the same study. Thus we were unable to make direct comparisons of clinical outcomes from the two methods for reporting, although the metabolic outcome from our study was comparable to those of intensive insulin studies in the literature.

Possible limitations of our evaluation

We did not prospectively capture patient or investigative site data regarding satisfaction with the e-diary or fatigue with using the e-diary over time and based our conclusions primarily on our analysis of the data collected for the 6-month period. Patient and investigator satisfaction measures could be added to a future study. Although the patient base was diverse in terms of demography and ethnicity, the race of the participants was primarily white. Coupled with the lack of a

formal assessment of technological aptitude, these may limit the generalizability of our results.

Conclusions

In three global studies of basal insulin peglispro encompassing diverse populations of patients with T1DM or T2DM, the e-diary system met the requirements of the study protocols and accomplished the goals of enhanced communication between patients and investigators and comprehensive data collection for insulin management. The effectiveness of the e-diary system supports its value for similar diabetes trials, and analysis of the large database collected may reveal new avenues for implementing and simulating intensive insulin therapy in future diabetes clinical trials.

Acknowledgments

Author Disclosure Statement

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