VIA MEDICA
RESEARCH PAPER
ISSN 2450–7458
E-ISSN 2450–8187

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Use of a Diabetes Self-Management Application in Combination with a 4 mm Pen Needle and Its Impact on Glycemic Variability and Patient-Reported Outcomes in People with Type 2 Diabetes Using Basal-Bolus Insulin Therapy

ABSTRACT

Background: Studies of mobile diabetes applications (apps) have demonstrated improvements in glycemia, and patient-reported outcomes (PROs). In addition, shift to shorter pen needles (PN) and guidance on proper injection techniques have shown the potential for reduced glycemic variability. The purpose is to determine the impact of using a diabetes mobile app plus a novel 4 mm PN on PROs and glycemic outcomes in type 2 diabetes mellitus (T2DM) for multiple daily injection (MDI) insulin users.

Materials and methods: In this 8-week prospective, parallel-group, randomized controlled trial, subjects either received (1:1) intervention (BD Diabetes Care [DC] App + BD Nano ™ 2nd Gen PN) or control therapy. Controls used their current PN and did not use diabetes apps.

Results: Fifty-eight subjects were randomized. Fifty-seven completed the study (intervention n = 27, control n = 30). At study end, there were no significant differences in PROs between groups, except improved medication adherence (ARMS-D) in controls. From flash glucose monitoring (fGM) data, there were no significant differences in most glycemic measures between groups except for a trend for improved glycemic variability [mean amplitude of the glycemic excursions (MAGE)] in the Intervention (p = 0.06). Controls had significantly reduced time spent in hypoglycemia but had 2 to 3-fold higher incidence at baseline. In general, Intervention subjects reported satisfaction with both the app and PN.

Conclusions: This is the first BD DC App study, in combination with BD Nano ™ 2nd Gen PN, to assess glycemic outcomes. This combination intervention shows promising results for reduced glycemic variability and the potential to positively impact self-management. (Clin Diabetol 2022, 11; 3: 156–164)

ClinicalTrials.gov Identifier: NCT04090242

Keywords: diabetes self-management, mobile applications, injection technique, pen needles, insulin use, type 2 diabetes

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Clinical Diabetology 2022, 11; 3: 156–164
DOI: 10.5603/DK.a2022.0012
Received: 5.08.2021 Accepted: 24.10.2021

Introduction

Large multinational injection technique recommendations like those of FITTER [1] and organizations like

Table 1. Subject Inclusion/Exclusion Criteria

Inclusion criteria:
1. ≥ 22 years old with a diagnosis of type 2 diabetes mellitus (T2DM)
2. On MDI insulin therapy, ≥2 injections per day of basal/mealtime insulin or ≥ 2 injections mixed insulin per day
3. On MDI > 6 months prior to enrollment
4. HbA1c of 8.0–11.0% either at screening or from a documented HbA1c value on file that was drawn within 3 months of enrollment
5. Currently using an Apple iPhone with iOS Version 13.1 or greater or a Samsung phone with Android OS Version 8 or later
Exclusion Criteria:
1. Pregnant or breastfeeding (self-reported)
2. On basal insulin only
3. Currently using BD Nano ™ 2nd Gen PN
4. If currently using CGM or flash glucose monitor (ie. Freestyle Libre, fGM) and duration of use is < 6 months
5. Not on stable doses of diabetes medications
6. Actively using the DC App or a similar diabetes app and not willing to stop using it during the study

CGM — continuous glucose monitoring; DC App — Diabetes Care application; fGM — flash glucose monitoring; HbA1c — glycated glucose; MDI — multiple daily injection; PN — pen needle

the American Diabetes Association recommend a shift to shorter needles (e.g. 4 mm) to avoid intramuscular injections, which can alter insulin absorption and cause hypoglycemia [2–4]. These recommendations have demonstrated the importance of proper injection technique and site rotation to avoid negative consequences like lipohypertrophy (LH), which can increase glycemic variability when one injects into these areas [5].

Becton Dickinson has expanded on its pen needle (PN) innovation with the development of the BD Nano ™ 2nd Gen 32 G × 4 mm PN with a redesigned contoured hub and a 5-bevel needle tip. The contoured needle hub was designed to distribute injection force evenly over a greater surface area resulting in improved injection depth consistency, thereby reducing the potential for intramuscular injection [6]. When compared to PNs of similar gauge and length, BD Nano ™ 2nd Gen PN, was rated as being overall preferred, more comfortable, less painful, and easier to use [7]. BD Nano ™ 2nd Gen PN was also associated with less participant-reported injection pain when compared with four thinner gauge PNs [8].

Becton Dickinson's Diabetes Care (DC) App is focused on diabetes self-management education and support (DSME/S), with a focus on insulin use and proper injection technique. In addition, the DC App contains logging features for blood glucose, medications, and physical activity, as well as a 'Reminders' feature which can be set to prompt patients to check blood glucose and administer medication. The DC App educational content and additional features may offer value to patients by clarifying or reinforcing DSME concepts and providing support between office visits.

This study was designed to include the combination of the DC App and BD Nano ™ 2nd Gen PN for three reasons: 1) patients who receive the DC App may improve adherence to therapy and lifestyle choices, leading to better glycemic control and patient-reported outcomes (PROs) (i.e. greater empowerment and less diabetes distress); 2) patients receiving the DC App will obtain knowledge on proper injection technique leading to reduced glycemic variability; and 3) the shift to 4mm PN should reduce the risk of intramuscular injections, leading to reduced glycemic variability. To our knowledge, no prior studies have used continuous glucose monitoring (CGM) to assess the impact of diabetes apps. The addition of CGM may be considered a novel aspect of this diabetes app study.

We proposed that having access to the DC App for DSME/S in combination with the BD Nano ™ 2nd Gen PN would lead to improvements in PROs, as well as improved glycemic control/variability. The purpose of the current study was to assess whether the combination of using the app for education and switching to a novel 4mm PN would result in improved metrics of diabetes control and PRO questionnaires.

Methods

Study population

Subjects were recruited at four clinical sites within the US located in Honolulu, HI, Austin, TX, San Mateo, CA, and West Palm Beach, FL. Ethics approval was received from a central IRB in the US before any study procedures were started and the study was conducted according to the principles laid out in the protection of human subjects in the Declaration of Helsinki.

Inclusion and exclusion criteria are listed in Table 1.

Study design

This was a multi-center, open-label, parallel-group, randomized controlled trial (RCT) in subjects with T2DM

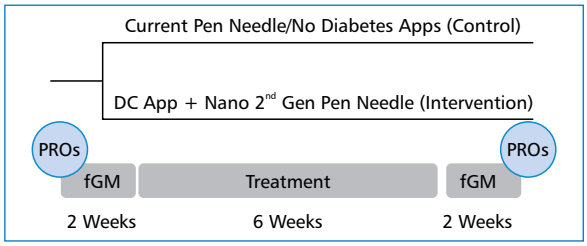

Figure 1. Study Design
DC App — Diabetes Care Application; fGM — flash glucose monitoring; PROs — patient reported outcomes

using multiple daily injection (MDI) insulin therapy. Subjects were randomized to either the DC App to be used in combination with BD's Nano ™ 2nd Gen 4mm PN (Intervention) or continue with the ongoing standard of care utilizing the subject's currently prescribed PN and diabetes management plan (Controls). Figure 1 shows study design.

The BD Diabetes Care (DC) App is a mobile application that focuses on DSME/S, with a focus on insulin administration and proper insulin injection techniques. A 'locked down' version of DC App version 1.15 was used for this clinical study, which was not updated for the duration of the trial.

The study consisted of four in-clinic visits and two phone calls over 10 weeks. Site staff were trained by qualified personnel familiar with the operation and use of the DC App.

At the initial visit (Visit 1), site staff screened and enrolled qualified subjects. Those that qualified received a blood glucose meter (BGM) (Accu-Chek Guide, Roche), and a 14-day intermittently scanned glucose sensor (Libre Freestyle Pro, Abbott) was applied to their arm. Subjects were blinded to their fGM data for the duration of wear. Subjects provided baseline medical information and answered four PRO questionnaires, including the Diabetes Empowerment Scale (DES), Diabetes Distress Scale (DDS), Insulin Delivery System Rating Questionnaire (IDSRQ), and Adherence to Refills and Medicines Scale for Diabetes (ARMS-D).

Subjects were sent home and asked to keep their medication regimen the same unless adjusted by their healthcare professional (HCP). Any change to diabetes medication was documented. While at home, subjects were asked to test BG concentrations using the provided BGM and continue with their usual insulin dosing regimen before returning to the clinic for the second visit. There was no direct recommendation for a specific number of BG measurements per day and patients were instructed to follow guidance from their HCP.

Subjects were asked to return to the clinic after 14 days (Visit 2) and had their fGM sensor removed, where they were randomized 1:1 into Intervention or Control therapy. The Intervention group was also trained on the use of DC App and switched to the BD Nano ™ 2nd Gen PN. For weeks 3–8, subjects in both groups continued with their usual insulin routine. While the Control group followed their usual practice of managing their diabetes, the Intervention group utilized the DC App for relevant educational content, in addition to using BD Nano ™ 2nd Gen PN for all insulin injections. At week 8, subjects returned to the clinic (Visit 3) to have a second fGM sensor placed for the final 2 weeks. During the final visit (Visit 4), subjects had the fGM sensor removed and their data downloaded. Subjects completed the same 4 PROs as they did at baseline. During this visit only, all subjects completed a non-validated Injection Technique Questionnaire. The Intervention group also responded to a non-validated survey on satisfaction with the DC App and BD Nano ™ 2nd Gen PN.

Outcome measures

The primary endpoint was the change in the DES, which was used to compare changes from baseline (Visit 1) to study end (Visit 4), both within and between groups.

Secondary outcomes included DDS, IDSRQ, and ARMS-D.

There were also three secondary outcome measures of glycemia from fGM data, including:

1) 24-hour (24 h) average glucose
2) Time in and out of glycemic range, which included percent of time spent at 70-180 mg/dL, < 70 mg/dL, < 54 mg/dL, > 180 mg/dL, and > 250 mg/dL
3) Glycemic variability measures, including the mean amplitude of the glycemic excursions (MAGE), standard deviation (SD), coefficient of variation (CV), mean of daily differences (MODD).

Glycemic data was collected at baseline and study end with fGM. Changes were assessed from baseline to study end within and between groups.

Four exploratory measures included:

1) A non-validated questionnaire, which was administered only at study end in the Intervention group to assess satisfaction with the DC App and PN.
2) A non-validated Injection Technique Questionnaire (ITQ) which was administered only at study end, in both groups.
3) Patient engagement with the DC App (Intervention group only), which was a measure of time spent within the app, frequency of opening the app, types of modules accessed, the time spent in each, and data types logged.

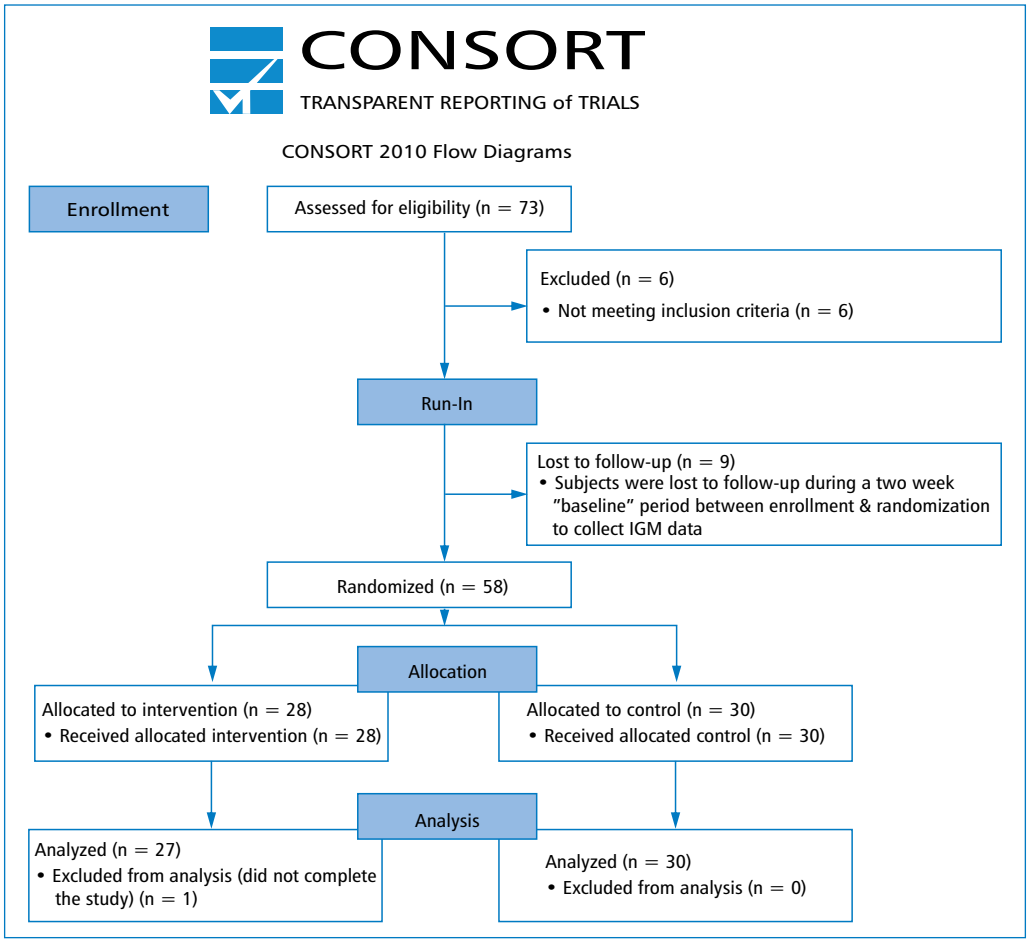

Figure 2. Consort Diagram for Subject Recruitment, Enrollment, and Study Completion

4) The incidence and rate of hypoglycemic events (< 70 mg/dL and < 54 mg/dL) as measured by BGM. Blood glucose values indicating hypoglycemia were counted as separate events if data points were >30 min apart.

Statistical analyses

The sample size calculation was based on showing a significant difference between the two study arms for patient-reported outcomes for the DES at end of study. We assumed: 1) the baseline DES was similar for the two arms, 2) the difference between control and test arms at end of study was 0.4 (about 10% of baseline), 3) the standard deviations for pre- and post-intervention DES were 0.8 and 0.6, respectively, and 4) the correlation coefficients between pre- and post-measurement pairs for both arms was 0.6. Therefore, we calculated that a sample size of 43 per arm (86 subjects in total) has > 80% power to detect a significant difference between the two arms at end of study. All continuous outcomes were summarized with a mean (SD) or median (range) as appropriate, and count and percentage were used to describe categorical and count outcomes.

An analysis of DES, DDS, IDSRQ, ARMS-D scores, and glycemic variability was performed using a linear mixed-effect model to evaluate the intervention effect on the response. Logistic mixed-effect models were used for the incidence of hypoglycemia, and negative binomial mixed-effect models were used for the rate of hypoglycemia.

All statistical tests were two-sided with a significance level of 5%, and adjustments were made for multiple comparisons when appropriate. Analyses were carried out using the R language for statistical computing (version 3.5.1; https://www.r-project.org/).

Results

Figure 2 shows the trial profile for subject recruitment, enrollment, and study completion.

The initial sample size planned for this study was n = 86. With COVID-19 occurring in 2020 near the end of our trial, we allowed subjects who were currently enrolled to complete the study if they chose to and

Table 2. Baseline Characteristics

	Control (n = 30)	Intervention (n = 28)	Overall (n = 58)
Age [years]	59.4 (10.8)	57.0 (9.8)	58.3 (10.3)
Gender, n (%)			
Male	18 (60%)	9 (32.1%)	27 (46.6%)
Female	12 (40.0%)	19 (67.9%)	31 (53.4%)
Race, n (%)			
White/Caucasian	16 (53.3%)	17 (60.7%)	33 (56.9%)
Asian	6 (20.0%)	6 (21.4%)	12 (20.7%)
African American	5 (16.7%)	3 (10.7%)	8 (13.8%)
Hawaiian Islander or Other Pacific Islander	1 (3.3%)	0 (0.0%)	1 (1.7%)
Other	2 (6.7%)	2 (7.1%)	4 (6.9%)
Ethnicity			
Hispanic or Latino	4 (13.3%)	7 (25.0%)	11 (19.0%)
Duration of diabetes [years]	17.2 (7.5)	18.5 (9.3)	17.8 (8.4)
Duration of insulin therapy [years]	9.0 (4.8)	10.1 (8.5)	9.5 (6.8)
Pen needle length, n (%)			
4 mm	17 (56.7%)	13 (46.4%)	30 (51.7%)
5 mm	6 (20.0%)	4 (14.3%)	10 (17.2%)
6 mm	2 (6.7%)	6 (21.4%)	8 (13.8%)
8 mm	5 (16.7%)	4 (14.3%)	9 (15.5%)
Other	0 (0.0%)	1 (3.6%)	1 (1.8%)
Currently use a diabetes app, n (%)			
No	29 (96.7%)	26 (92.9%)	55 (94.8%)
Yes	1 (3.3%)	2 (7.1%)	3 (5.2%
Subject currently on CGM device, n (%)	11 (19.0%)	12 (20.7)	23 (39.7%)
Mean basal insulin total daily dose [units] (n = 50)	59 U (30)	57 U (28)	58 (28)
Mean bolus insulin total daily dose [units] (n = 50)	83 U (76.0)	83 U (125)	83 U (102)

CGM — continuous glucose monitoring

terminated further enrollment. This resulted in only n = 57 completers (n = 30 controls, n = 27 intervention), reducing the sample size and making the study underpowered. Data for glucose measurements from fGM and all PROs were for n = 57 subjects, whereas hypoglycemia data from BGM measurements were only from n = 54. Three of the 57 subjects had no BG values that were taken with their BGM device during the trial.

Subject baseline characteristics are listed in Table 2 below as mean ± (SD) unless otherwise noted.

Subjects were taking a mean of 1.2 ± 0.4 (mean ± SD) daily injections of basal insulin and a mean of 2.9 ± 0.5 daily injections of mealtime insulin. Subjects taking mixed insulin (n = 8) were taking a mean of 2.0 ± 0.0 injections per day with an average daily dose of 69 ± 23 U.

PRO data

Table 3 shows PRO data at baseline and study end for both groups. There were no significant differences for DES, DDS, or IDRQS between groups at study end. It is important to note that empowerment was rather high (> score of 4) at baseline and diabetes distress was fairly low (< score of 3), leaving little room for improvement in this study population. There was no significant change in self-reported medication adherence (ARMS-D) from baseline to study end in the Intervention group, but contrary to the initial hypothesis, there was an improvement in self-reported medication adherence in controls (p = 0.03), leading to significant differences in ARMS-D scores between groups (p = 0.04). A similar finding was observed in controls for the ARMS-D Medication Refill subscale leading to a significant difference between groups (p = 0.05), showing significant improvement in controls.

Glycemic data

Table 4 shows data for glycemic measures derived from fGM at baseline and study end for both groups. There were no significant differences between groups at study end for mean glucose, % time-in-range (70–180 mg/dL), % time > 180 mg/dL, or % time > 250 mg/dL). It is important to note that within groups

Table 3. Patient-Reported Outcomes (PROs)

PRO	Group	Baseline	Study end	P (change from baseline)	P (difference in change between groups)
Diabetes Empowerment Survey (DES)	Control	4.09 (0.66)	4.26 (0.52)	0.19	0.39
	Intervention	4.16 (0.55)	4.17 (0.84)	0.95	
Diabetes Distress Scale (DDS)	Control	2.03 (0.92)	2.10 (1.0)	0.54	0.75
— **total score**	Intervention	1.81 (0.66)	1.83 (0.61)	0.89	
Insulin Delivery System Rating	Control	X	X	All subscales	All subscales
Questionnaire (IDSRQ) **(7-subscales)**	Intervention	X	X	$p > 0.05$	$p > 0.05$
				All subscales	
				$p > 0.05$	
Adherence to Refills and Medicines Scale	Control	16.57 (4.08)	15.43 (3.07)	0.03*	0.04*
for Diabetes (ARMS-D) — **total score**	Intervention	15.67 (3.46)	16.07 (3.65)	0.46	
ARMS-D medication refill **subscale**	Control	6.07 (2.07)	5.30 (1.37)	0.01*	0.05*
	Intervention	5.30 (1.51)	5.37 (1.50)	0.81	

*represents values that are statistically significant at $p \leq 0.05$ level; X — data not shown for each of the 7 subscales for IDSRQ; all p-values not significant

for measures of 24-hr mean glucose, time-in-range, and time ≥ 180 mg/dL, the data showed non-significant improvements in the intervention group and decrements in the control group over time.

An unexpected finding was that the control group had significantly reduced time spent in levels 1 and 2 hypoglycemia (< 70 and < 54 mg/dL, respectively) from baseline to study end (p's = 0.02 and 0.03, respectively) and there were strong trends for statistical differences between groups at study end, favoring controls. However, baseline values of fGM data for hypoglycemia were nearly 2 to 3-fold higher in Controls as compared to Intervention and may help explain the reduction observed in hypoglycemia.

For glycemic variability, which included MAGE, CV, and MODD, there were no significant changes in groups from baseline or between groups at study end. However, there was a strong trend for a difference in MAGE in the Intervention over time (p = 0.07) and between groups (p = 0.06).

Injection Technique Questionnaire (ITQ)

Responses were similar between groups for most questions on the survey.

Engagement with DC App

Engagement with DC app over 8 weeks is listed in Table 5. Data is shown in 'number of times accessed' unless otherwise noted. The large standard deviations show the large variability in app usage by subjects.

Patient satisfaction with app and PN

At study end, Intervention subjects answered a 16-question survey related to their satisfaction with the DC App and BD Nano™ 2nd Gen PN. Higher scores indicated higher satisfaction and are shown in Table 6. In general, patients reported satisfaction with both the app and PN.

Incidence of hypoglycemia from BGM data

Data for incidence and rate of hypoglycemia < 70 mg/dL from the BGM data are shown in Figure 3. For both groups, there was no significant change in incidence or rate of hypoglycemia < 70 mg/dL during weeks 9–10 compared to weeks 1–2. However, there was a non-significant trend for a reduced incidence (p = 0.097) and rate (p = 0.13) of hypoglycemia < 70 mg/dL in the Intervention group. There were no significant differences between the two groups at study end, likely because of the limited amount of data points. This finding (< 70 mg/dL) contrasted directly with the findings for hypoglycemia from the fGM-generated glucose data, with the Intervention showing a trend for reduced hypoglycemia over time with BGM data and the control group showing a significant reduction in hypoglycemia over time with fGM data.

Analysis of the incidence and rate of hypoglycemia < 54 mg/dL was not performed because of the extremely limited amount of BGM values below this level.

Adverse events

Twenty-three mild/moderate adverse events (AE) were reported during the study, along with 2 categorized as 'severe' (and one of them was a Serious AE). However, neither of these severe AEs was considered related to the devices or study procedures. There was 1 mild AE that was likely related to the BD Nano ™ 2nd Gen PN. All AEs resolved before study end, except

Table 4. Glycemic Measures

	Group	Baseline	Study End	P (change from baseline)	P (difference in change between groups) *all differences between groups were not statistically significant
% Time-in-range	Control	58.8 (18.6)	57.2 (23.4)	0.64	0.40
(70–180 mg/dL) (SD)	Intervention	48.5 (19.2)	51.9 (23.2)	0.47	
24-h mean glucose, mg/dL (SD)	Control	161.8 (37.9)	173.1 (45.3)	0.12	0.20
	Intervention	187.0 (39.7)	184.9 (55.7)	0.78	
% Time >180 mg/dL (SD)	Control	34.9 (22.0)	39.4 (24.8)	0.22	0.14
	Intervention	48.1 (20.2)	44.8 (24.8)	0.39	
% Time > 250 mg/dL (SD)	Control	11.3 (11.1)	15.5 (18.5)	0.12	0.32
	Intervention	18.9 (17.7)	19.3 (21.1)	0.90	
% Time < 54 mg/dL (SD)	Control	2.7 (5.1)	1.1 (1.3)	0.02*	0.08
	Intervention	0.7 (1.1)	0.8 (1.1)	0.89	
% Time < 70 mg/dL (SD)	Control	6.4 (9.3)	3.5 (3.5)	0.03*	0.052
	Intervention	2.5 (3.2)	3.3 (3.5)	0.57	
MAGE, mg/dL (SD)	Control	121.7 (20.0)	124.2 (19.1)	0.43	0.06
	Intervention	133.6 (26.4)	127.6 (25.0)	0.07	
CV, mg/dL (SD)	Control	0.36 (0.07)	0.34 (0.06)	0.09	0.50
	Intervention	0.35 (0.06)	0.34 (0.08)	0.49	
MODD, mg/dL (SD)	Control	56.8 (17.6)	55.6 (13.8)	0.56	0.56
	Intervention	59.8 (17.3)	56.9 (16.7)	0.18	

*represents values within groups from start to end of the study that are statistically significant at $p \leq 0.05$ level; CV — coefficient of variation; MAGE — mean amplitude of glycemic excursions; MODD — mean of daily differences; SD — standard deviation

Table 5. App Data Analytics

DC app category	Additional information	App usage (mean ± SD)
Hours using app		7.2 ± 20.1
# of times app launched		148.8 ± 141.2
App launches per day		3.4 ± 1.9
# of logged glucose		63.0 ± 87.3
# of logged insulin		127.7 ± 151.1
# times dashboard was viewed	Shows graphical displays of glucose, insulin, and physical activity data.	101.6 ± 79.8
# of time reminders used	Set reminders for BG checks and taking medication	6.4 ± 5.5
# of times learn content was accessed	Contains a combination of 200+ articles, videos, and tutorials	8.5 ± 7.1
# of times 'Briight' chatbot was used	Enables search for content, recipes, and access to Calorie King database	5.4 ± 5.1

BG — blood glucose; SD — standard daviation

for one event that persisted and was documented as 'worsening hyperlipidemia'.

Discussion

To our knowledge, this is the first RCT assessing outcomes from using an intervention consisting of a combination of a diabetes app and a novel PN. In addition, to our knowledge, no prior studies have used CGM to assess the impact of diabetes apps (not counting apps designed for presenting CGM data) and the use of CGM for this purpose may be considered another novel aspect of this study. We hypothesized

Table 6. Patient Satisfaction

Survey subscale	Highest possible score	Patient rating
DC App	30	22.0 ± 6.7
Nano ™ 2nd Gen PN	30	25.3 ± 6.4
Combination App and PN	20	16.3 ± 4.4

DC App — Diabetes Care Application; PN — pen needle

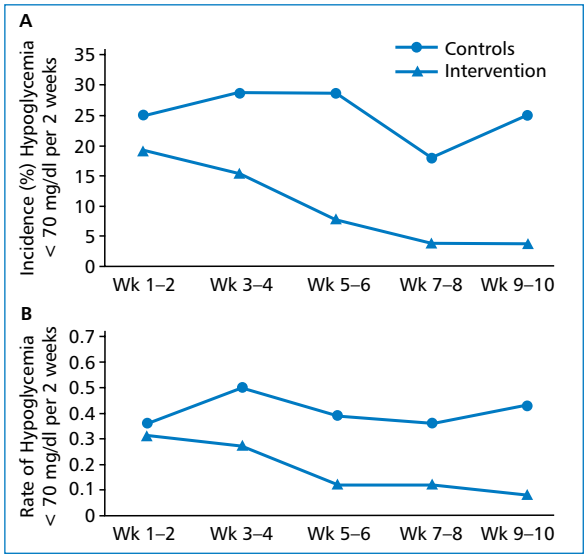

Figure 3. Incidence and Rate of Hypoglycemia < 70 mg/dL from BGM Data for Controls and Intervention Groups from Weeks 1 through 10

that the use of the DC App would support patients with education on insulin therapy and proper injection technique, help with tracking of health data, and prompt patients to make better lifestyle choices. This assistance, in combination with a shorter 4mm PN would reduce the risk of intramuscular injection and the likelihood of increased glycemic variability and hypoglycemia. The findings of less painful injections with BD Nano ™ 2nd Gen PN[7-8] may also lead to improvements in adherence to insulin therapy.

Use of the DC App and BD Nano ™ 2nd Gen PN for 8 weeks did not lead to significant improvements in any PROs, except for control subjects who showed greater self-reported improvement in medication adherence (from ARMS-D). Contrary to our initial hypothesis, controls spent significantly less time in hypoglycemia from fGM data but had a 2–3-fold higher incidence at baseline compared to Intervention subjects. There were no other significant differences for glycemic outcomes between groups, possibly because of small sample sizes. However, there was a strong trend for improvements in the Intervention group for MAGE, with weaker trends for improvements for time-in-range, 24 h mean glucose, and time above 180 mg/dL (see table 4).

We hypothesized that patients who have access to DSME/S through the DC App as well as access to BD Nano ™ 2nd Gen PN would have better adherence to insulin therapy. This prediction turned out to be in direct contrast with the actual outcome of this study, which was an improvement in medication adherence (self-reported) in the Control group. The reason for this was not clear but we postulate that site staff, which had to be unblinded to the intervention, may have given more support and time to patients in the Control group during office visits and phone calls because they were not receiving additional diabetes support from DC App. Although there was an improvement in self-reported medication adherence (ARMS-D) in controls, this did not translate to improvements in glycemic parameters. In fact, measurements like 24hr mean glucose and time above 180 mg/dL and 250 mg/dL worsened in this group over the study indicating that PRO data for medication adherence did not match clinical outcomes in this study.

An unexpected finding was that controls had significantly reduced time in hypoglycemia from baseline to study end, which led to trends for differences between groups. Although this was a randomized trial, it was not controlled for baseline hypoglycemia incidence between groups. Baseline values for hypoglycemia from fGM data were nearly 2–3-fold higher in controls. This disparity may help explain why there was a significant reduction in hypoglycemia in this group. It is important to note that at study end, both groups had nearly the same magnitude for hypoglycemia < 54 mg/dL and < 70 mg/dL. Using fGM to determine the frequency of hypoglycemia, defined as glucose below 70 mg/dL, the control group experienced a decrease during the course of the study which was statistically significant ($p = 0.02$). This outcome was in direct contrast to what we observed using BGM data to determine the frequency of hypoglycemia, where the Intervention group experienced a decrease in the same parameter during the course of the study, which was not statistically significant ($p = 0.097$). This difference in hypoglycemia responses for fGM (many data points) and BGM (few data points) in this study highlight the need for CGM data in studies.

For app engagement, the Intervention group spent on average 7.2 hours using the app over 8 weeks, and spent limited sessions reading educational content (i.e. Learn Content) in the app (each patient opened educational content a mean of 8.5 times over the 8-week study period). The use of the 'Briight' chatbot feature

to ask diabetes-related questions and access 'Calorie King' database was limited. The large standard deviations observed for app engagement in Table 5 (comparable in magnitude to the mean values themselves) shows the large variability in usage by subjects. Results for the Injection Technique Questionnaire responses between groups were similar with the exception that self-reported PN re-use was higher in Controls. These findings may be confounded by the fact that the sponsor supplied PNs only to the Intervention group during the trial. Regarding satisfaction with the app and PN, patients generally reported being satisfied with these devices.

There were several limitations in this study. First, the study occurred during the COVID19 pandemic, which may have impacted subjects' ratings of PROs and potentially their glycemic data. In addition, a smaller than anticipated sample size impacted statistical power, especially when trends existed. Second, participants used the DC App v1.15 which was outdated at the time of this publication (current version = v3.1). In addition, requiring subjects to be using newer Android or Apple smartphones may have limited the types of patients enrolled in this study. Finally, nearly 40% of this cohort was wearing a CGM at study start and this type of monitoring may limit generalizability to the overall T2DM population.

In conclusion, we studied an intervention intended for patients with T2DM consisting of a mobile app that encourages treatment adherence along with a novel PN to manage diabetes. This combination intervention showed some promise for reduced glycemic variability and the potential to positively impact self-management, however, no consistent outcomes in PROs or glycemic metrics were noted among those who were in the Intervention group compared to those in the Control group. We attribute this lack of consistent differences between groups to inadequate recruitment due to the COVID-19 pandemic. Repeat studies after the end of the COVID-19 pandemic, powered with larger numbers of subjects, will be useful to address whether our endpoints can be met with the currently developed intervention.

Conflict of interests

Becton Dickinson (BD) was the sponsor of the study and provided all funding for this study. Edward Mahoney, Stanislav Glezer, and Wen Yue are full-time employees of BD and are shareholders of BD stock. Jason Liebowitz is a full-time employee of BD. Leah Baccari and David Klonoff have no conflicts of interest to declare.

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