The Effect of a Smartphone-Based, Patient-Centered Diabetes Care System in Patients With Type 2 Diabetes: A Randomized, Controlled Trial for 24 Weeks

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OBJECTIVE

This study evaluated the efficacy of a smartphone-based, patient-centered diabetes care system (mDiabetes) for type 2 diabetes that contains comprehensive modules for glucose monitoring, diet, physical activity, and a clinical decision support system.

RESEARCH DESIGN AND METHODS

We conducted a 24-week, multicenter, randomized controlled trial with adult patients with inadequately controlled type 2 diabetes. The patients were randomly assigned to the mDiabetes group or the paper logbook (pLogbook) group. The primary end point was the difference of the change in HbA_{1c} from baseline between the two groups.

RESULTS

HbA_{1c} reduction from baseline was greater in the mDiabetes group (−0.40 ± 0.09%, *n* = 90) than in the pLogbook group (−0.06 ± 0.10%, *n* = 82). The difference of adjusted mean changes was 0.35% (95% CI 0.14–0.55, *P* = 0.001). The proportion of patients whose HbA_{1c} fell below 7.0% (53 mmol/mol) was 41.1% for the mDiabetes group and 20.7% for the pLogbook group (odds ratio [OR] 2.01, 95% CI 1.24–3.25, *P* = 0.003). The percentage of patients who attained HbA_{1c} levels below 7.0% (53 mmol/mol) without hypoglycemia was 31.1% in the mDiabetes group and 17.1% in the pLogbook group (OR 1.82, 95% CI 1.03–3.21, *P* = 0.024). There was no difference in the event numbers of severe hyperglycemia and hypoglycemia between the two groups.

CONCLUSIONS

The implementation of the mDiabetes for patients with inadequately controlled type 2 diabetes resulted in a significant reduction in HbA_{1c} levels, with tolerable safety profiles.

Diabetes is a chronic disease requiring lifelong management with lifestyle modification, medication, or both; therefore, diabetes self-management education and adherence to the treatment plans are considered key components in the management of diabetes (1). As information technology (IT) advances, medical services using IT devices, such as mobile health care (mHealth) systems, have been developed to aid chronic disease management. Currently, ~259,000 mHealth applications are

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available from major application stores (2). Among various chronic diseases, an IT-based intervention has most frequently been applied to diabetes (3). Although there was considerable heterogeneity among different applications and patient characteristics, a recent systematic review and meta-analysis of the mHealth application for diabetes self-management (which included 13 randomized controlled studies with 1,022 patients with type 2 diabetes) showed that the overall HbA_{1c} reduction was −0.40% (95% CI −0.69 to −0.11%) (4). However, smartphone applications for the management of type 2 diabetes that deal with diet, physical activity, glucose monitoring, insulin titration, and social networking service altogether are not common (5,6). In addition, although there are numerous commercial smartphone applications for diabetes management, only a few small-scale, randomized controlled trials have examined their glucose-lowering efficacy (7,8).

We also developed a smartphone-based, patient-centered diabetes care system (mDiabetes) featuring an individualized diabetes management algorithm, automatic input of daily glucose levels and physical activity, guidance for basal insulin dosage, and a range of interactive components, including a social networking service. In the 12-week, single-arm, noncontrolled pilot study, HbA_{1c} decreased by 0.6% from baseline and was accompanied by significantly improved diabetes self-management in areas including diet, exercise, and blood glucose monitoring (9). In the current study, we upgraded the mDiabetes system and conducted a 24-week, multicenter, randomized controlled trial to evaluate its efficacy and safety.

RESEARCH DESIGN AND METHODS

Study Participants

Patients aged 19–80 years who were diagnosed with type 2 diabetes with HbA_{1c} levels between 7.0% (53 mmol/mol) and 10.0% (86 mmol/mol) were recruited from three teaching hospitals. Inclusion criteria were stable control of diabetes with lifestyle modification, no change in oral antidiabetic agent prescription for at least 3 months, and less than 10% variation in total daily insulin doses over the previous 3 months. Insulin users were required to take basal insulin once a day or premixed insulin twice a day. Participants had to have their own Android-based smartphone and be able to use smartphone applications, and they agreed to check the 7-point glucose profile at the start and end of the study. Exclusion criteria are available in the Supplementary Data.

Participants were classified into four groups, based on antidiabetic treatment. Patients controlling their glucose by lifestyle modification only were assigned to group A. Patients on oral antidiabetic medication with a low risk of hypoglycemia (metformin, α-glucosidase inhibitors, thiazolidinediones, and dipeptidyl peptidase 4 inhibitors) were assigned to group B, and those on oral antidiabetic medication with a risk of hypoglycemia (sulfonylurea and meglitinide) were assigned to group C. Insulin users were assigned to group D. Glucagon-like peptide 1 receptor agonist users were not included in the study.

The study was conducted according to the guidelines of the Declaration of Helsinki. The study protocol was reviewed and approved by the Seoul National University Hospital Institutional Review Board (IRB No. H-1410-143-622) and the Ministry of Food and Drug Safety of the Republic of Korea (Approval No. 675). We obtained written informed consent from all participants before any study-related procedure was performed. This study was registered at ClinicalTrials.gov (NCT02451631).

mDiabetes

We upgraded the user interface and insulin dose adjustment algorithm and modified some clinical decision support systems of the previous mDiabetes system, which was used in the pilot study (9) (Supplementary Fig. 1). The measured blood glucose level by the Bluetooth glucometer (MyHealthPoint; Infopia Co., Ltd., Anyang, Korea) was automatically transferred to the mDiabetes application. Alternatively, the patient entered the data manually. When the blood glucose level was entered, an immediate feedback message appeared according to the glycemic control algorithm. Any patient whose prebreakfast self-measured glucose exceeded 17.8 mmol/L was instructed to visit the study center to confirm the indication for rescue therapy. Other criteria for rescue therapy are provided in Supplementary Table 1. When the measured glucose level was compatible with hypoglycemia, an immediate action algorithm was initiated.

For insulin users, an appropriate insulin dose was recommended based on the measured glucose level, using the insulin dose adjustment algorithm (Supplementary Table 2). The dose of insulin was determined by the median glucose level over the previous 3 days and the intensity category of insulin therapy (intensive, less intensive, and least intensive). A designated insulin titration specialist (E.K.K.) was responsible for the adjustment of the intensity category of insulin therapy and the reset of baseline insulin dose in indicated cases (Supplementary Table 3). Detailed information on the diet, physical activity, and social networking service was previously described (9) and is briefly shown in Supplementary Fig. 2.

Study Design

This study was a 24-week, multicenter, randomized, controlled, open-label clinical trial. At visit 1, informed consent was obtained before screening tests. We provided a glucometer with test strips and a logbook to record glucose levels. Participants were notified of their eligibility by phone call (visit 2). Noninsulin users and patients who used basal insulin were instructed to check glucose at least once a day. Patients who used premixed insulin were instructed to check glucose at least twice a day (prebreakfast and predinner). During a 2-week run-in period, the participants recorded blood glucose levels with a logbook every day as instructed. At the end of the run-in period, the patients performed the 7-point self-monitoring of blood glucose (SMBG) for 1 day. Patients with a compliance rate exceeding 80% were enrolled in the study. They were randomly assigned to the mDiabetes or the paper logbook (pLogbook) group by a stratified 1:1 block randomization by the study site and the group of antidiabetic treatment (e.g., A, B, C, and D) (visit 3). On visit 3, vital signs and anthropometric data were measured, and laboratory tests were performed. Body composition was measured by the bioelectrical impedance analysis method (InBody; InBody Co. Ltd., Seoul, Korea). Scores of the Summary of Diabetes Self-Care Activities (SDSCA) (10) and the

World Health Organization Quality of Life Scale Abbreviated Version (WHOQOL-BREF) (11) were recorded. The study application was installed for the mDiabetes group; a logbook for recording glucose levels and a printed education booklet were provided to the pLogbook group. A Bluetooth glucometer was given to both mDiabetes and pLogbook groups. An activity tracker was provided as a component of the mDiabetes package. Participants in the mDiabetes group were instructed on how to use the application and connect with the glucometer and the activity tracker. The patients in the pLogbook group were instructed to record measured glucose levels with the same frequency as the mDiabetes group and encouraged to report if they experienced severe hyperglycemia or hypoglycemia as adverse events to the study staff. The criteria for the rescue therapy were same for both groups.

At week 12 (visit 5), both mDiabetes and pLogbook groups, respectively, received advice based on the data on the web and logbook at the study clinic. At week 6 (visit 4) and week 18 (visit 6), compliance and adverse events were checked by telephone call. At week 12 (visit 5) and week 24 (visit 7), follow-up anthropometric measurements and laboratory tests were performed. At week 24, the 7-point SMBG was checked for 1 day.

Participants were not allowed to change their oral antidiabetic medication and dose unless they required rescue therapy. The patients in the mDiabetes group were instructed to follow the recommendation of the insulin dosing algorithm of the mDiabetes system. In contrast, the patients in the pLogbook group were instructed to keep their usual way of insulin dose adjustment as had been previously recommended by their physician and diabetes nurses. At week 12 (visit 5), the study physicians advised on insulin dose titration for the insulin users in both groups. During the study period, use of medication affecting blood glucose levels other than previously prescribed antidiabetic medication was not allowed, and neither were medications for the treatment of obesity (Supplementary Data).

End Points and Post Hoc Analysis

The primary end point was the change in HbA_{1c} levels after 24 weeks compared with baseline. Secondary end points were the change in HbA_{1c} levels after 12 weeks compared with baseline and the changes in the following parameters: the percentage of participants achieving HbA_{1c} $<$7.0% ($<$53 mmol/mol) and $\leq$6.5% ($\leq$48 mmol/mol) after 24 weeks; fasting blood glucose levels, lipid profile, body composition, and blood pressure after 12 and 24 weeks; and compliance of the mDiabetes group with the glucose monitoring module. Safety end points were the number of adverse events, abnormal vital signs, abnormal laboratory findings, and episodes of severe hypoglycemia. The definition of severe hyperglycemia was 17.8 mmol/L or higher regardless of fasting and that of hypoglycemia was lower than 3.9 mmol/L. The definition of severe hypoglycemia was an event requiring the help of another person for resuscitation (carbohydrate or glucagon administration).

Statistical Analysis

The sample size was calculated assuming the difference of HbA_{1c} between the two groups as 0.51% with a SD of 1.06 based on previous studies (12,13). Considering a 20% dropout rate, 92 participants per group were required for 90% power at a one-sided significance level of 0.025. The efficacy was analyzed in the full analysis set and the per protocol set; the safety was analyzed in the safety analysis set. Statistical significance was assumed at $P < 0.05$. Detailed statistical methods are described in Supplementary Data.

RESULTS

From April 2015 to October 2015, 214 patients were screened. Among them, 191 were randomly assigned to the mDiabetes group (n = 97) or the pLogbook group (n = 94). The full analysis set included 172 patients, and 151 patients completed the 24-week study (Supplementary Fig. 3).

Although we performed stratified 1:1 block randomization, the mean age of the mDiabetes group (60.0 $\pm$ 8.4 years) was older than that of the pLogbook group (56.7 $\pm$ 9.1 years, P = 0.027). The respective number of participants in subgroups A, B, C, and D was 6, 20, 46, and 18 for the mDiabetes group and 4, 17, 44, and 17 for the pLogbook group. Other baseline characteristics and distribution of treatment groups were not significantly different between the two groups (Table 1). Patients in the pLogbook group checked fasting glucose more often

Table 1—Baseline characteristics of participants

	mDiabetes (n = 90)	pLogbook (n = 82)	P value
Age (years)	60.0 $\pm$ 8.4	56.7 $\pm$ 9.1	0.027*
Male sex	50 (55.6)	39 (47.6)	0.295†
Body weight (kg)	67.7 $\pm$ 11.8	68.4 $\pm$ 13.0	0.708*
BMI (kg/m^2)	25.5 $\pm$ 3.2	25.8 $\pm$ 4.1	0.889‡
Diabetes duration (years)	13.2 $\pm$ 8.0	12.5 $\pm$ 7.3	0.854‡
Group distribution			0.951†
A	6	4	
B	20	17	
C	46	44	
D	18	17	
SBP (mmHg)	126.3 $\pm$ 12.0	126.4 $\pm$ 11.9	0.957‡
DBP (mmHg)	78.7 $\pm$ 9.5	79.6 $\pm$ 9.0	0.520‡
FPG (mmol/L)	7.8 $\pm$ 2.1	7.3 $\pm$ 1.8	0.114‡
HbA_{1c} (%)	7.7 $\pm$ 0.7	7.8 $\pm$ 0.7	0.344‡
Total cholesterol (mmol/L)	4.0 $\pm$ 0.7	3.8 $\pm$ 0.7	0.170‡
Triglyceride (mmol/L)	1.5 $\pm$ 0.8	1.4 $\pm$ 0.7	0.333‡
LDL cholesterol (mmol/L)	2.3 $\pm$ 0.6	2.1 $\pm$ 0.6	0.162‡
HDL cholesterol (mmol/L)	1.2 $\pm$ 0.3	1.3 $\pm$ 0.3	0.418‡
Lipid-lowering agent	65 (72.2)	59 (72.0)	0.968‡
Antihypertensive medication	52 (57.8)	30 (36.6)	0.006†

The data are presented as mean $\pm$ SD values or n (%). DBP, diastolic blood pressure; FPG, fasting plasma glucose; SBP, systolic blood pressure. *Two-sample t test. †Pearson χ^2 test. ‡Wilcoxon rank sum test.

(149.7 ± 23.2 times) than those in the mDiabetes group (140.3 ± 33.0 times, $P = 0.024$) (Supplementary Table 4). Total numbers of glucose measurement were not different between the mDiabetes group (180.3 ± 67.3) and the pLogbook group (167.6 ± 51.8, $P = 0.151$) (Supplementary Table 4).

After 24 weeks, HbA_{1c} level reduction from baseline was greater in the mDiabetes group (−0.40 ± 0.09%) than in the pLogbook group (−0.06 ± 0.10%) (Fig. 1*A*). The difference of the adjusted mean changes was 0.35% (95% CI 0.14–0.55, $P = 0.001$). In the per protocol analysis, the change in HbA_{1c} level was −0.40 ± 0.09% in the mDiabetes group and 0.00 ± 0.10% in the pLogbook group (Fig. 1*B*). The difference of the adjusted mean changes was 0.40% (95% CI 0.19–0.60, $P = 0.0002$). The reduction in HbA_{1c} levels was more evident among patients with a baseline HbA_{1c} of 8.0% (64 mmol/mol) or higher (−0.87 ± 0.16% vs. −0.30 ± 0.17%, $P = 0.016$) and among insulin users (−0.74 ± 0.16% vs. −0.15 ± 0.16%, $P = 0.014$) (Fig. 1*C* and *D*). When we compared groups A+B and groups C+D, there was a significant reduction in HbA_{1c} levels among patients in groups C+D (Fig. 1*E*). The proportion of patients with HbA_{1c} levels <7.0% (<53 mmol/mol) was 41.1% for the mDiabetes group and 20.7% for the pLogbook group (odds ratio [OR] 2.01, 95% CI 1.24–3.25, $P = 0.003$) (Fig. 2), and the proportion of patients in these groups with HbA_{1c} ≤6.5% (≤48 mmol/mol) was 14.4% and 2.4%, respectively (OR 5.78, 95% CI 1.40–23.86, $P = 0.004$). The proportion of patients achieving HbA_{1c} <7.0% (<53 mmol/mol) without hypoglycemia (<3.9 mmol/L) was 31.1% in the mDiabetes group and 17.1% in the pLogbook group (OR 1.82, 95% CI 1.03–3.21, $P = 0.024$). The proportion of patients with HbA_{1c} ≤6.5% (≤48 mmol/mol) without hypoglycemia was 11.1% in the mDiabetes group and 2.4% in the pLogbook group (OR 4.56, 95% CI 1.03–20.18, $P = 0.050$).

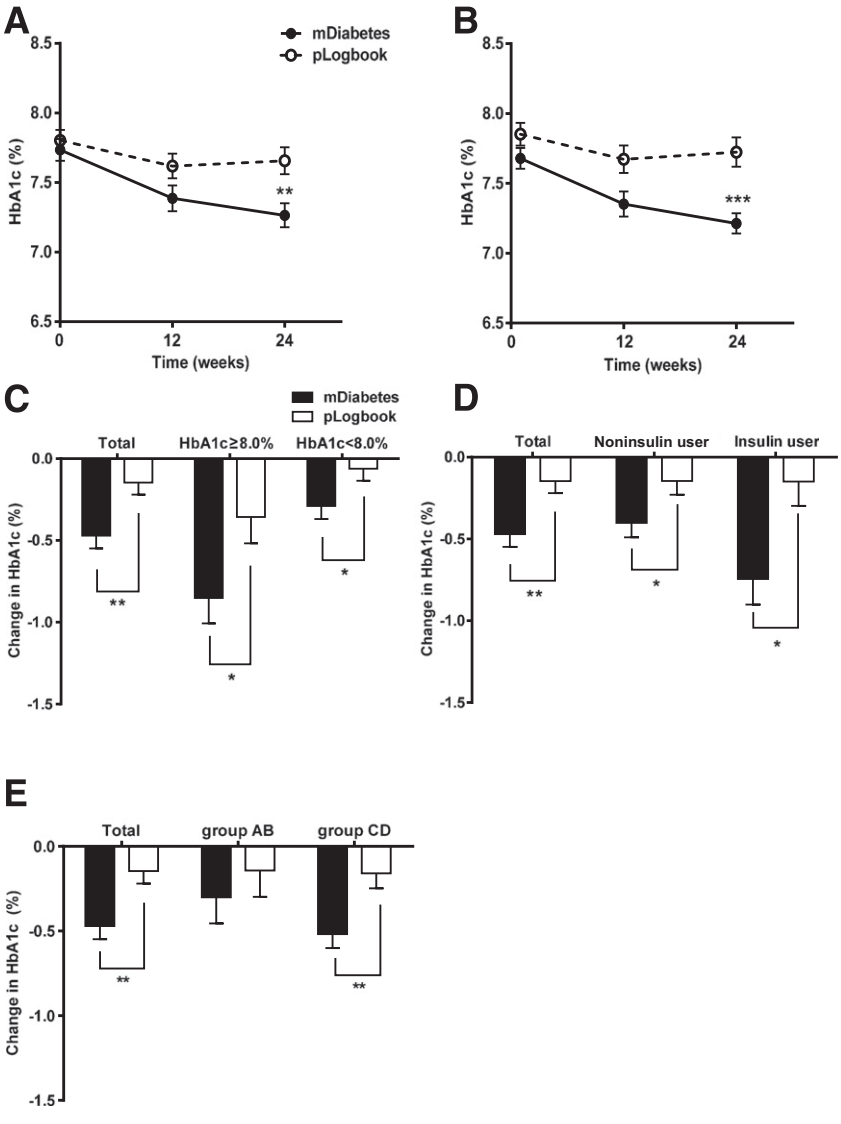

Figure 1—Changes in HbA_{1c} levels after intervention. *A*: After 24 weeks, HbA_{1c} levels were significantly decreased in the mDiabetes group compared with the pLogbook group. *B*: Per protocol analysis showed a more remarkable difference in the change of HbA_{1c} between the two groups. *C* and *D*: There was a more remarkable reduction in HbA_{1c} levels among the patients with baseline HbA_{1c} levels ≥8.0% (≥64 mmol/mol) and insulin users. *E*: The reduction in HbA_{1c} was significant among patients in groups C+D but not in groups A+B. The data were analyzed by ANCOVA (*A* and *B*) or Wilcoxon rank sum test (*C–E*). *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$.

A total of 136 patients (68 patients in each group) completed the 7-point SMBG with no missing entries. There was no difference between the mDiabetes group and the pLogbook group at baseline (Supplementary Fig. 4*A*). After 24 weeks, the glucose levels of the mDiabetes group at the prebreakfast, prelunch, and postdinner times were lower compared with those of the pLogbook group (Supplementary Fig. 4*B*).

Other secondary outcomes, including blood pressure, body composition, fasting plasma glucose, and lipid profile are provided in Supplementary Table 5. Body weight modestly decreased in the mDiabetes group from 67.7 ± 11.8 to 67.1 ± 11.6 kg ($P = 0.005$) and in the pLogbook group from 68.4 ± 13.0 to 68.0 ± 12.7 kg ($P = 0.041$), which, however, were not different between the two groups ($P = 0.531$). At week 24, the mDiabetes group showed a greater reduction in the percentage of body fat than the pLogbook group did (−0.93 ± 0.29% vs. −0.25 ± 0.31%, $P = 0.038$). Fasting plasma glucose in the mDiabetes group decreased from 7.8 ± 2.1 mmol/L to 7.7 ± 2.2 mmol/L, whereas that in the pLogbook group increased from 7.3 ± 1.8 mmol/L to 8.0 ± 1.6 mmol/L. The mean changes of fasting glucose between the groups were statistically significant ($P = 0.026$). Blood pressure and lipid profile were not significantly changed after 24 weeks of intervention compared with baseline in both groups.

Baseline scores of all SDSCA domains taken after 2 weeks of the run-in period and the glucose monitoring scores were similar between the mDiabetes group (6.4 ± 1.5) and the pLogbook group

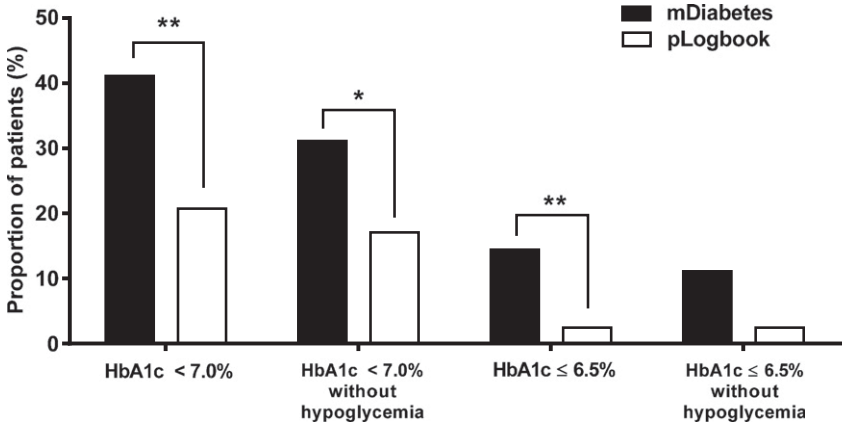

Figure 2—Patients reaching target HbA_{1c} after 24 weeks of intervention. The proportions of subjects with HbA_{1c} <7.0% (<53 mmol/mol) or with HbA_{1c} ≤6.5% (≤48 mmol/mol) in the mDiabetes group were significantly higher than those in the pLogbook group. The proportion of subjects achieving HbA_{1c} levels <7.0% (<53 mmol/mol) without hypoglycemia was also significantly higher in the mDiabetes group. The data were analyzed by the Cochran-Mantel-Haenszel test. *$P < 0.05$, **$P < 0.01$.

(6.7 ± 0.9). The SDSCA scores did not change significantly at week 24 in either group compared with week 0 (Supplementary Fig. 5*A* and *B*). Among WHOQOL-BREF components, the quality of health in the mDiabetes group at week 24 increased significantly compared with week 0 (44.0 ± 21.9 to 50.6 ± 21.2, P = 0.0008) (Supplementary Fig. 5*C* and *D*).

A total of 231 adverse events occurred in 65.6% of patients in the mDiabetes group, and 316 events occurred in 65.2% of patients in the pLogbook group (Table 2). The most frequent adverse event was severe hyperglycemia, mostly in the nonfasting state, in both groups. The proportion of patients who experienced severe hyperglycemia was not different between the mDiabetes group and the pLogbook group (32.3% vs. 33.7%, P = 0.948). Hypoglycemia occurred in 28.0% of patients in the mDiabetes group and in 29.3% of patients in the pLogbook group, which was not statistically different between the groups (P = 0.857). No severe hypoglycemic events occurred in either group. Serious adverse events occurred in four subjects, all of whom required hospitalization, but they were not related to the intervention (ureter stone, unacceptable hyperglycemia, finger fracture, and breast cancer). Adverse events associated with the use of mDiabetes did not occur.

Table 2—Adverse events

	mDiabetes (n = 93)		pLogbook (n = 92)	
	Patients (%)	Events (n)	Patients (%)	Events (n)
Total AEs	65.6	231	65.2	316
Serious AEs*	2.2	2	2.2	2
Severe hypoglycemia	0.0	0	0.0	0
AEs related to mDiabetes	0.0	0	–	–
AEs occurring in ≥5% of patients				
Severe hyperglycemia	32.3	94	33.7	155
Hypoglycemia**	28.0	91	29.3	117
Nasopharyngitis	3.2	3	5.4	6

The definition of severe hyperglycemia was 17.8 mmol/L or higher, and the definition of hypoglycemia was lower than 3.9 mmol/L. AE, adverse events. *Serious AEs were related to hospital admissions only. **There were no severe hypoglycemic events.

CONCLUSIONS

This study showed that the reduction in HbA_{1c} from the baseline was greater in the mDiabetes group than in the pLogbook group. The mDiabetes group exhibited a lower blood glucose level at prebreakfast, prelunch, and postdinner than the pLogbook group did. The HbA_{1c}-lowering efficacy of the mDiabetes coincided with the overall HbA_{1c} change that was reported in a recent systematic review and meta-analysis of the mHealth application for diabetes self-management (4). It was of note that the patients in the control group using the pLogbook were very compliant with the study protocol. The patients in the pLogbook group checked fasting blood glucose levels more frequently than those in the mDiabetes group, although total numbers of glucose measurement were not different between the two groups. Therefore, the mDiabetes might be more effective than simple SMBG. In this regard, it is noteworthy that studies of enhanced SMBG (14–17), when participants were educated to interpret SMBG values, showed lower HbA_{1c} values than studies of simple SMBG (14,18).

The mDiabetes was equipped with an insulin dose adjustment algorithm not only for the once-daily basal insulin but also for the twice-daily premixed insulin. The effect of the mDiabetes was relatively greater in the insulin users than in the noninsulin users. The mean baseline total daily dose of insulin was numerically higher in the pLogbook group than in the mDiabetes group (36.9 ± 21.9 units vs. 30.1 ± 13.9 units, P = 0.618) (Supplementary Table 6). Even though the change in insulin dose was very modest (1.8-unit increase in the mDiabetes group and 0.3-unit decrease in the pLogbook group) (Supplementary Table 6), the proportion of the patients who changed insulin doses was significantly higher in the mDiabetes group than in the pLogbook group (15 of 18 vs. 7 of 17, P = 0.005), which indicated that appropriate dose adjustment may be the key component for successful insulin therapy. In addition, the median and the range of the insulin dose increment in the patients with baseline HbA_{1c} ≥8.0% (≥64 mmol/mol) tended to be higher in the mDiabetes group (3.0 [−2.0 to 20.0] units, n = 11) compared with the pLogbook group (0.0 [−10.0 to 6.0] units, n = 9), although it was not statistically significant (P = 0.056). Several insulin titration applications are commercially available that have not yet been thoroughly investigated for efficacy and safety. A cloud-based diabetes management program for adjusting the basal insulin dose was tested in a 12-week randomized controlled study involving 40 patients with type 2 diabetes at the start of basal insulin (19), in which the intervention group showed a greater reduction in

HbA_{1c} than the control group (−3.2% vs. −2.0%, $P = 0.048$). Taken together, the mHealth-based insulin dosing algorithm may be helpful to guide insulin dose self-adjustment in patients with type 2 diabetes.

It is conceivable that the improved HbA_{1c} in the mDiabetes group might be the result of increased interaction between the participants and the research staff. The time spent for installation of the software and instructions on how to use the program, which took about 1 h, was inevitable for mHealth intervention. The number of unscheduled visits including telephone counseling was nominally higher in the mDiabetes group compared with the pLogbook group (39 vs. 31), which was not statistically significant ($P = 0.578$). However, additional time (~10–15 min for each case) was spent by health care professionals for the remote adjustment of the insulin titration algorithm in the mDiabetes group (22 incidents in total), which did not directly involve the patient.

The proportion of patients achieving HbA_{1c} <7.0% (<53 mmol/mol) in the mDiabetes group was 41.1% compared with 20.7% in the pLogbook group. These results corroborate those of a previous study, which showed that the number of patients who reached HbA_{1c} <7% (<53 mmol/mol) was 34% in the ubiquitous health care group and 20.4% in the control group (12). The proportion of patients achieving HbA_{1c} ≤6.5% (≤48 mmol/mol) in the mDiabetes group was also significantly higher than those in the pLogbook group. Furthermore, the proportion of patients achieving HbA_{1c} levels <7.0% (<53 mmol/mol) without hypoglycemia was significantly higher in the mDiabetes group than in the pLogbook group. These results indicate that with further improvement, the mDiabetes might be a useful tool to attain target HbA_{1c} without increasing the risk of hypoglycemia.

In the pilot study with the mDiabetes, diabetes self-care activities, which were measured by SDSCA, were remarkably improved, especially for diet, exercise, and blood glucose testing (9). The improvement of diabetes self-care activities was associated with improved HbA_{1c} (9). In the current study, however, the mHealth exhibited no effect on diabetes self-care activity, which was also measured by SDSCA. Unlike the pilot study, baseline SDSCA scores in this current study were obtained after 2 weeks of a run-in period, which involved daily glucometer use (one of the components of SDSCA). Therefore, the scores of glucose monitoring were already high at baseline. In addition, baseline scores of all other domains of SDSCA were high in both the mDiabetes group and the pLogbook group. It is conceivable that performance of SMBG itself may help improve other diabetes self-care activities. Similar results were reported in a study with a smartphone-based diabetes management system, in which the participants were also instructed to use the application for 2 weeks before baseline measurement of SDSCA scores (8). Given that diabetes self-care activities were not different between the two groups, the difference in the HbA_{1c}-lowering effect could be ascribed to other factors such as timely insulin dose adjustment and perhaps a modest reduction in the percentage of body fat. Nonetheless, we need to explore which component(s) of the mDiabetes are responsible for the improved HbA_{1c}.

The most common adverse event was severe hyperglycemia, followed by hypoglycemia. The numbers of events of severe hyperglycemia and hypoglycemia were not statistically different between the mDiabetes and the pLogbook group. There were no cases of severe hypoglycemia. Adverse events associated with the use of mDiabetes did not occur. In terms of quality of life measured by WHOQOL-BREF scores, the patients in the mDiabetes group were more satisfied with their overall health after 24 weeks of intervention compared with the baseline. Therefore, mDiabetes was well tolerated and possibly increased the quality of life in some aspects.

There were limitations in this study. Although the overall HbA_{1c} reduction of −0.35% may be a modest improvement, some subgroups (e.g., patients with initial HbA_{1c} of 8.0% or higher, insulin users, and the C+D group) exhibited a more evident decrease of HbA_{1c}. However, the number of patients in each subgroup is relatively small; further studies are warranted to confirm the clinically meaningful improvement of HbA_{1c}. Furthermore, the insulin titration algorithm needs to be upgraded to include patients using basal plus rapid acting insulin. Some of the benefits found in the mDiabetes group might be due to the Hawthorne effect, but there was no difference in the number of total glucose measurements between the two groups. However, we are not sure whether the Hawthorne effect might have affected eating habits and physical activity in the mDiabetes group compared with the pLogbook group, which were measured only in the mDiabetes group.

The duration of the study was relatively short for examining the long-term sustainable efficacy and safety. Although we randomized our study participants, the mean age of the mDiabetes group was significantly older than that of the pLogbook group. However, despite older age, which might be a disadvantage to using IT devices, the mDiabetes group showed a significantly lower HbA_{1c} than the pLogbook group. We provided the pLogbook group with printed education materials, which were electronically provided for the mDiabetes group. If we had provided education classes for the pLogbook group, they would be a better control group in comparison with the sophisticated mDiabetes intervention. In addition, an activity tracker was not provided to the pLogbook group.

Last, we did not plan to analyze the access frequency to each module and the outcomes a priori. As a post hoc analysis, we examined the relationship between HbA_{1c} reduction and adherence parameters such as glucose measurement, diet input, and step count. Only the number of glucose measurements was correlated with the change in HbA_{1c} level ($r = -0.27$, $P = 0.011$) (Supplementary Fig. 6).

To summarize, a 24-week mDiabetes intervention in patients with inadequately controlled type 2 diabetes resulted in a significant reduction of HbA_{1c} levels and attained the target HbA_{1c} goal with less hypoglycemia, compared with pLogbook-based diabetes management. HbA_{1c} reduction with mDiabetes was more prominent in patients with higher HbA_{1c} or treated with insulin at baseline. Perceived overall quality of health was improved after 24 weeks in the mDiabetes group. Taken together, the newly developed mHealth-based comprehensive diabetes management is an efficacious and safe tool, which may improve daily management of type 2 diabetes.

Appendix

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Author Contributions. E.K.K., S.H.K., H.S.J., B.K.K., M.K.M., S.L., H.C.J., K.S.P., and Y.M.C. collected data. E.K.K., S.H.K., and Y.M.C. searched literature and designed the study. E.K.K., M.K.M., S.L., H.C.J., K.S.P., and Y.M.C. interpreted data. E.K.K. and Y.M.C. analyzed data. E.K.K. and Y.M.C. drafted the manuscript. S.H.K., H.S.J., M.K.M., S.L., H.C.J., and K.S.P. approved the final version of the manuscript. E.K.K. and Y.M.C. had final responsibility for the decision to submit for publication. E.K.K. and Y.M.C. are the guarantors of this work and, as such, had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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