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RESEARCH ARTICLE

Effect of Mobile-Based Application Usage on Time in Range and Time above Range in Patients with Diabetes Mellitus: A Pilot Cohort Retrospective Study

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ABSTRACT:
Achieving recommended glucose targets is challenging for many people with diabetes. An application that assists in self-management through continuous glucose monitoring may help reduce glycemic variability and help people with diabetes reach glucose targets. We aimed to evaluate how a digital collection of meal photos and postprandial continuous glucose monitoring data may impact glycemic stability. We assessed people with type 1 or type 2 diabetes and a time in range of <70%. Glucose parameters were measured at the beginning of application usage and after 14 days. To exclude time in range improvement due to continuous glucose monitoring use, the preceding glucose data of each user were collected in a control cohort. The intervention was via a photo-based food diary combined with continuous glucose monitoring data history. Users (n=21) demonstrated significant improvements in time in range (11.0%±5.0, P=.001) and time above range (-12.0%±5.0, P=.001). Combining continuous glucose monitoring data with meal photos in a mobile application could help improve time in range and time above range. A photo-based diabetes management application with visualized continuous glucose monitoring data and connection to specific meals allows better understanding of different meal-related decisions among individuals, thus decreasing fluctuations in glucose levels. Further research is needed to evaluate time in range and time above range changes caused by the regular use of the digital food diary combined with continuous glucose monitoring data.

Keywords: continuous glucose monitoring; diabetes; food diary; mobile apps; self-management; time in range

Introduction

Diabetes is one of the most challenging health problems worldwide.[1] People with diabetes require continuous treatment, including dietary guidelines; however, this is not always sufficient to stabilize their blood glucose levels. A high degree of variability in blood glucose levels, along with hyper- and hypoglycemic events, pose significant health risks.[2] It is essential to manage these factors as it may help prevent or delay the microvascular and macrovascular complications associated with diabetes [3-7] Blood glucose stability leads to fewer hospitalizations and, therefore, substantial reductions in diabetes management costs, while increased glycemic variability is associated with increased healthcare expenses.[8-10]

Regular measurement of blood glucose levels became commonplace in the second half of the 20th century. The first glucose meters for home use were marketed in 1981 and began to actively replace urine and in-office glucose checks, which were neither accurate nor prompt.[11,12] Frequent blood glucose level checks provide patients with the knowledge to optimize insulin dosing. Over the years, counting carbohydrates before meals and glucose meter usage have become the standard methods of diabetes self-care.[3,12] However, blood glucose monitoring and carbohydrate counting have serious limitations.[3,12-15] These approaches have two major disadvantages: patients are unable to accurately count carbohydrates in the food consumed [16,17]; and blood glucose meters provide information on blood glucose levels at only that particular point of time and do not indicate the direction or rate of change in blood glucose levels.[18,19] These can lead to erroneous conclusions, poor diabetes management, decreased self-care capacity, and, ultimately, diabetes distress and burnout.[12,20]

Furthermore, carbohydrate counting and multiple finger-stick blood check measurements throughout the day are not always accurate to predict glycemic variability.[21] Identical meals can cause variability in postprandial glucose levels in different people.[22] Protein and fat content also affect postprandial glucose levels. However, since the impact differs from person to person, there is no standardized approach to measure fat and protein content.[23] Therefore, patients need to evaluate how their bodies react to different meals.

The development and use of continuous glucose monitoring (CGM) partially solves the problems associated with glucose meters.[24,25] The development and use of CGM partially solves the problems associated with glucose meters.[19] These CGM readings are wirelessly sent to the user's smartphone and then aggregated in a data storage. Apple Health application, Dexcom cloud, and Nightscout cloud are examples of such storage applications. Apple Health is a health data storage system pre-installed on iPhones. It gathers data on blood pressure measurements, glucose levels, and physical activity. The Dexcom cloud service aggregates data from produced sensors. Nightscout is an open-source web application that accumulates diabetes management data from all connected devices, including CGM sensors.

Glycemic stability increases with continuous and intermittent CGM use.[26] However, the exact causes of glycemic fluctuations may remain vague for individuals with diabetes.[18,19,27] With CGM, patients can observe fluctuations in glucose levels as a result of their lifestyle decisions. To determine the exact causes of fluctuation in blood glucose levels, people with diabetes must recollect data pertaining to their meals, exercise, insulin injection, and other lifestyle factors such as stress levels or sleep duration; this can prove to be a challenging task.[12]

In addition to CGM technology developments, time in range (TIR) has been introduced as a new and important clinical metric for diabetes management and is used to monitor glucose variability.[5,28-31] The International Consensus defines TIR as blood glucose levels of 70–180 mg/dL (3.9–10 mmol/L), with a goal of 70% of readings in a day within the target range for most people with type 1 or type 2 diabetes, and 50% for those at a higher risk of hypoglycemia.[19,28,31] TIR is a clinical tool that, alongside A1C, is included in the American Diabetes Association's guidelines and allows clinicians to monitor patients' glucose level variability throughout the day.[3] Regular TIR monitoring and correlated lifestyle adjustments lead to a reduction in diabetes complication risks and mortality.[3-5,32,33]

In addition to TIR, time below range (TBR) and time above range (TAR) can be calculated from CGM data. These metrics characterize hyperglycemic and hypoglycemic episodes, respectively.[19] An increase in TIR and a concomitant decrease in TBR can be considered as evidence of effective and safe glucose management.[29]

CGM-based applications can be used to track time within the target range.[34,35] These software tools allow TIR analysis in addition to keeping a food diary, thereby enabling people with diabetes to evaluate their responses to the food they consume and make better decisions about their future meals and insulin timing or doses. There is growing evidence of improvement in patient engagement, self-management, and glycemic

stability among individuals with diabetes using mobile applications.[36-41]

We hypothesized that an application that enables the patient to analyze the effects of routine events, such as meals, physical activity, and insulin dosing, on glucose levels with CGM, would reduce glycemic variability; this may lead to an increase in TIR together with a decrease in TBR and TAR more considerably than a CGM-only approach. To test this hypothesis, we assessed the impact of such application usage in individuals with type 1 and type 2 diabetes mellitus.

Materials and methods

Study design and selection criteria

The 'Undermyfork' application was chosen for this investigation. This free application is distributed via the Apple App Store and Google Play. It combines meal photos and insulin data with glucose readings from CGM. It allows users to comprehend which meal-related decisions drive them out of the target glucose range and which ones allow them to remain within the target range. As a result of using the application, a library of events such as meals and corresponding bolus insulin dosing data are created. By automatically connecting this library to glucose data, individuals with diabetes can see the relationship between logged events and changes in glucose values. The application receives CGM readings automatically from the Apple Health, Nightscout, and Dexcom clouds.

With the application, people with diabetes take photos of each meal and optionally adds keywords (tags) with the meal description and the meal context data (for example, time of the day or preceding physical activity). The Insights section of the app allows users to review meal photos classified by two-hours postprandial TIR, analyze how different lifestyle strategies (e.g., meal choices, insulin dosing, and timing) affect postprandial TIR after similar foods, and identify meals associated with high and low glycemic variability. Based on this section, people with diabetes can evaluate their responses to the food choices and make more informed decisions about future meals, insulin timing, and dosing.

For the retrospective cohort study, data were collected from the application's cloud database. The database contains records of individual glucose levels, photos of meals, and insulin dose information. Informed consent was obtained when study participants signed up to use the application for the first time. The user data were anonymized, and each user was under a depersonalized ID number.

We defined the start point of application use as the day when the first meal photo was added. The eligibility criteria were type 1 or type 2 diabetes diagnoses. Data from 155 patients who used the application while wearing CGM devices were investigated. All these 155 patients, taken from a cohort of 1,365 users with type 1 and type 2 diabetes, met the following selection criteria. They had to have at least 70% complete CGM data in three 14-day periods: 1) 14 days prior to the use of the mobile application (before period); 2) 14 days after the first use of the mobile application (after period); 3) 14 days prior to the before period (control period). All CGM readings were placed into a single framework, with the average glucose level during the five-minute periods as the basic data point. Missing data in CGM readings were filled via interpolation if the missed period was less than 60 minutes.[42]

The TIR, TAR, and TBR were calculated for each user and each period. TIR was defined as the quotient of the division of the number of CGM readings in the 70–180 mg/dL (or 3.9–10 mmol/L) range to the total number of readings. TAR and TBR were defined as the quotient of the division of the number of CGM readings more than 180 mg/dL (or 10 mmol/L) and less than 70 mg/dL (or 3.9 mmol/L), respectively, to the total number of readings. A TIR of over 70% approximates an A1C of less than 7%, which is associated with a significant reduction in long-term complications of diabetes [3,30,33] We selected users with a TIR of less than 70% in the *before* period to investigate changes in this parameter only for the users at risk of delayed complications.

Active use of the application was defined as at least five days (35%) with meal uploads for 14 days with a start point on the first day of application usage. Thus, specific selection criteria were as follows: 1) diagnosis of type 1 or 2 diabetes mellitus; 2) 70% CGM readings in each of the periods under review; 3) at least five days with photos uploaded to the application at the *after* period; and 4) TIR in *before* period less than 70%. The overall number of selected users was 21 (Figure 1). The resulting TIR, TAR, and TBR for each eligible user in the cohorts are presented in Table 1 and Figure 2.

Figure 1. Study flow diagram. Participants with type 1 diabetes or type 2 diabetes, 70% continuous glucose monitoring readings in each period, at least five days with photos uploaded at the after period, and time in range (TIR) in the before period less than 70% were enrolled. CGM, continuous glucose monitoring

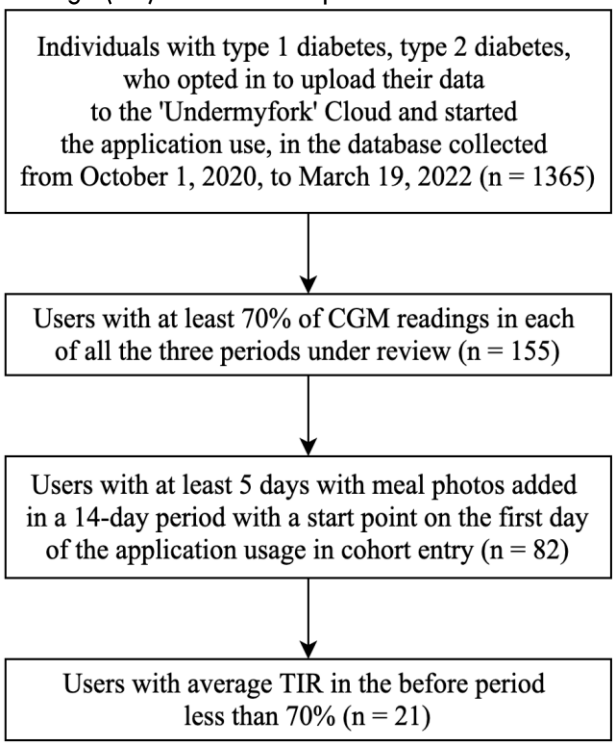

Figure 2. Resulting blood glucose level parameters of each participant. TIR, time in range; TAR, time above range; TBR, time below range

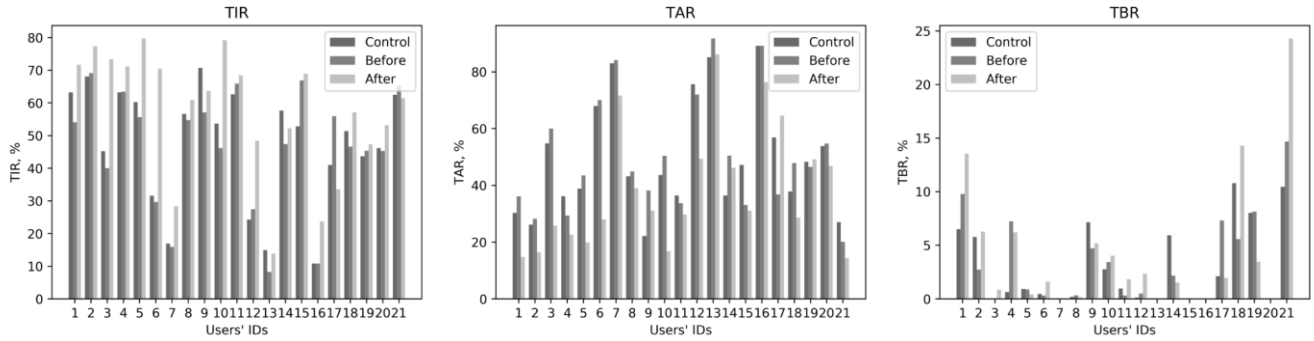

Table 1. Resulting blood glucose level parameters of each user with type 1 and 2 diabetes mellitus, at least five days with photos uploaded to the application at the *after* period, 70% CGM readings in each of the periods under review, and TIR in the *before* period less than 70% in cohorts

	Mean TIR			**Mean TAR**			**Mean TBR**		
	Control	**Before**	**After**	**Control**	**Before**	**After**	**Control**	**Before**	**After**
1	63.2	54.1	71.7	30.3	36.1	14.8	6.5	9.8	13.5
2	68.1	69.1	77.3	26.1	28.2	16.4	5.8	2.7	6.3
3	45.2	40.0	73.4	54.8	60.0	25.8	0.0	0.0	0.8
4	63.2	63.4	71.2	36.1	29.3	22.6	0.6	7.3	6.2
5	60.2	55.7	79.7	38.8	43.5	19.9	0.9	0.9	0.4
6	31.6	29.7	70.4	68.0	70.0	28.0	0.5	0.3	1.6
7	17.0	15.9	28.4	83.0	84.1	71.6	0.0	0.0	0.0
8	56.6	54.8	60.9	43.2	44.9	39.0	0.2	0.3	0.2
9	70.7	57.1	63.7	22.1	38.2	31.1	7.1	4.7	5.2
10	53.6	46.2	79.2	43.6	50.4	16.8	2.8	3.4	4.0
11	62.6	66.0	68.5	36.4	33.7	29.7	1.0	0.3	1.8
12	24.3	27.5	48.4	75.6	72.0	49.3	0.1	0.5	2.3
13	14.9	8.3	13.8	85.1	91.7	86.2	0.0	0.0	0.0
14	57.6	47.4	52.3	36.4	50.4	46.2	5.9	2.2	1.5
15	52.8	66.9	68.9	47.2	33.1	31.1	0.0	0.0	0.0
16	10.8	10.8	23.6	89.2	89.2	76.4	0.0	0.0	0.0
17	41.0	55.9	33.5	56.9	36.8	64.5	2.1	7.3	1.9
18	51.4	46.6	57.1	37.8	47.8	28.6	10.8	5.6	14.3
19	43.7	45.4	47.4	48.3	46.5	49.2	8.0	8.1	3.5
20	46.1	45.3	53.1	53.9	54.7	46.8	0.0	0.0	0.0
21	62.5	65.3	61.4	27.1	20.1	14.3	10.4	14.7	24.3

CGM: continuous glucose monitoring; TIR: time in range; TAR: time above range; TBR: time below range

Procedures

We chose three time-based cohorts. A 28-day period prior to the first meal photo added to the application was divided into two groups: 1) *before* cohort, two weeks preceding the start point (days from -14 to -1); 2) *control* cohort, two weeks preceding the *before* cohort (days from -28 to -15). An *after* cohort included glucose level data from the first to the 14th day of application use.

Data Analysis

The data were gathered for 16.5 months, from October 1, 2020, to March 19, 2022, and processed using Spyder (the Scientific Python Development Environment), a free and open-source distribution of the Python programming language.[43] We used the Pandas library for data analysis and

SciPy and scikit-posthocs packages to compute statistics.

There were three paired periods; thus, the significance of the differences between the TIRs of each user during all three periods (continuous measures) was assessed using Friedman's two-way analysis of variance by ranks with pairwise comparison.[44] We conducted a pairwise comparison to examine the mean differences within the periods using the Nemenyi test. Statistical significance was accepted at an adjusted p-value $< .05$.

Results

The study population included 21 accounts. Ninety-one percent of patients (n = 19) had type 1 diabetes mellitus and 9% (n = 2) had type 2 diabetes mellitus. Table 2 presents the postprandial blood glucose level characteristics of the users in the cohorts.

Table 2. Postprandial blood glucose level parameters of the 'Undermyfork' application users with type 1 and 2 diabetes mellitus in cohorts

Parameter	Control period	Before period	After period
TIR, mean (SD)	47.5 (18.1)	46.3 (18.3)	57.3 (19.0)
TAR, mean (SD)	49.5 (20.1)	50.5 (20.5)	38.5 (21.3)
TBR, mean (SD)	3.0 (3.7)	3.2 (4.1)	4.2 (6.2)
%CGM data, mean (SD)	90.0 (6.8)	97.0 (2.3)	96.8 (3.9)

CGM: continuous glucose monitoring; TIR: time in range; TAR: time above range; TBR: time below range; SD: standard deviation

The mean ± standard deviation (SD) TIRs during *control*, *before*, and *after* periods were 47.5% ± 18.1, 46.2% ± 18.3, and 57.3% ± 19.0), respectively. The mean ± SD TARs during the same periods were 49.5% ± 20.1, 50.5% ± 20.5, and 38.5% ± 21.3, respectively. The corresponding mean ± SD TBRs were 3.0% ± 3.7, 3.2% ± 4.1, and 4.2% ± 6.2, respectively. The number of days with meal photo uploads had a mean of 10, and the mean ± SD of meal photos uploaded per day was 1.8 ± 1.0. The mean ± SD differences between the *before* and *after* cohort groups were 11.1% ± 14.0 in TIR and -12.0% ± 14.9 in TAR. The mean percentage of CGM data available *after* interpolation was 90.0% ± 6.8, 97.0% ± 2.3, and 96.8% ± 3.9 in the *control*, *before*, and *after* periods, respectively. The effects of mobile-based interventions on glycemic parameters are presented in Table 3.

Table 3. Effects of the mobile-based intervention on glycemic parameters in the three periods

Parameter	Friedman's test	Control vs. before period	Before vs. after period	Control vs. after period
TIR (p-value)	.0005 < .0500	.526 > .050	.001 < .05	.019 < .050
TAR (p-value)	.0004 < .0500	.348 > .050	.001 < .05	.029 < .050
TBR (p-value)	.3334 > .0500			

TIR: time in range; TAR: time above range; TBR: time below range

Time in range.

A significant difference between the three measurements was observed while comparing the change of the TIRs within each period (related-samples Friedman's test $\chi_r^2 = 15.4$, p-value = .0004). After performing the Nemenyi pairwise test

for multiple comparisons of mean rank sums, no significant difference was observed between the *control* and *before* periods (p-value = .526). On the contrary, when the *before* and control periods were compared with the *after* period, significant differences were observed in both comparisons (p-value = .001; p-value = .019, respectively).

Time above range.

The TAR evolution was also tested using Friedman's χ_r^2 criterion. A significant difference was found between the periods ($\chi_r^2 = 16.1$, $p = .0003$). The Nemenyi test did not reveal a significant difference between the *control* and *before* periods ($p = .348$). However, when comparing pairs *before* and *after* and *control* and *after* periods, significant differences were observed (p-value = .001; p-value = .029, respectively).

Time below range.

No statistical difference was observed within the groups in TBR evolution (Friedman's test $\chi_r^2 = 2.2$, $p = .333$).

Discussion

This retrospective cohort study aimed to test the hypothesis of an association between photo-based food diary mobile application usage and an increase in TIR along with a corresponding decrease in TAR and TBR in patients with type 1 and type 2 diabetes mellitus. There was a statistically and clinically significant increase in time in range with a corresponding reduction in time above range. In addition, there was no statistical difference in glycemic parameters between the *control* and *before* periods. Thus, the effect discovered is suggested to be determined by the application usage, not by CGM-related improvement in blood glucose levels.

The mobile app provided users with a review of their postprandial blood glucose level excursions in response to different meals. With this information, they were able to grasp their personal reactions to the food consumed and, consequently, adjust their subsequent meal choices. These results show that an application that provides a better understanding of glucose level fluctuations after different meal-related decisions may help patients increase their TIR. Such comprehension in people living with diabetes may increase their involvement in the decision-making process, leading to positive behavioral changes, including development of lifelong healthy eating habits. These improvements result in a decrease in glycemic variability with the potential to reduce the risk of diabetes complications.

Previous studies have shown that fluctuations in blood glucose levels after the same meal may vary considerably from person to person.[22] Since there is no standardized way of eating for diabetes [9], self-education and decision-making skills are essential factors in reducing glycemic variability. Evidence suggests that the level of self-care is higher among diabetes application users.[41,45] Food diaries and CGM data trackers have been shown to be the most relevant features of these applications.[45,46] Such approaches provide individuals with diabetes with practical tools for nutrition self-care, which is an essential part of diabetes management.[47]

Recent studies have suggested that, in addition to overall average blood glucose levels, the duration of hyperglycemic episodes also affects the initiation and progression of diabetes complications.[48] A decrease in TAR is shown to reduce the risk of cardiovascular diseases and neuropathic complications.[47-49] Lifestyle changes associated with an increase in glycemic stability can improve the quality of life of people with diabetes.

There was no correlation between application use and the time the participants spent below the target blood glucose range, although the time below range was relatively low in all groups. This is also consistent with prior literature, which states that TIR has a strong correlation with TAR but is not correlated with TBR.[50,51]

It is important to note that this study had several limitations. First, since all the data were anonymized, we did not know the sex, age, race, duration of diabetes, or continuance of CGM use for the participants. Second, this study only included people with smartphones who are proficient in mobile applications and, simultaneously, were wearing CGMs. This indicates that the research participants may not be representative of people with diabetes in low-income socioeconomic groups. Third, there is no information on the long-term effects of the application usage. Finally, since this was a pilot study, another limitation was the small sample size which included mostly people with type 1 diabetes. We plan to conduct further research on the effects of this mobile application on TIR, TAR, and TBR in a broader population of people with type 1 and type 2 diabetes. An additional future research direction should be a collaboration with a healthcare team to review the user data and give feedback on lifestyle decisions and medication adjustments. It is important to test our hypothesis for a longer period of time, up to six months, with a possible follow-up in a year, to check the sustainability of changes in patients' outcomes. To further improve the quality of the investigation, an increase in sample size is required, along with an

independent control group of patients who have not received the intervention.

Looking ahead, as more and more digital therapeutics tools also in the field of diabetes become available on the market, the research aiming to reveal their synergies and effectiveness requires collaboration between healthcare professionals and the scientific community. More studies are needed to compare various applications between each other and in combination with other tools. The results of these studies will be recommendations that healthcare professionals can use to track their patients, make treatment decisions, and also improve the people with diabetes outcomes. Not only should time in range but also A1C be among the primary clinical endpoints for future research. Clinics that keep patients under observation regularly already collect data on A1C. The next step is to overlay this data with efficacy findings from different diabetes management applications to evaluate what is the best for the patient.

Conclusion

This study demonstrated how a mobile application that includes a digital collection of meal photos combined with postprandial continuous glucose monitoring data led to an increase in time in range and reduced time above range. This is likely related to changes in eating and insulin dosing in response to the insights from the data and corresponding report. These results are important as increased time in range is associated with reduction in microvascular complications of diabetes and improved quality of life. Further research is required to confirm the results of this study. The long-term outcomes of partial substitution of carbohydrate counting with the visualization of individual retrospective postprandial continuous glucose monitoring data should be the subject of additional research.

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