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The Influence of Baseline Hemoglobin A1c on Digital Health Coaching Outcomes in Adults With Type 2 Diabetes: Real-World Retrospective Cohort Study

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Abstract

Background: Digital health coaching is an increasingly common diabetes self-management support strategy for individuals with type 2 diabetes and has been linked to positive mental and physical health outcomes. However, the relationship between baseline risk and outcomes is yet to be evaluated in a real-world setting.

Objective: The purpose of this real-world study was to evaluate trends in digital health coaching outcomes by baseline hemoglobin A_{1c} (HbA_{1c}) to better understand which populations may experience the greatest clinical and psychosocial benefit.

Methods: A retrospective cohort study design was used to evaluate program effect in a convenience sample of participants in a 12-week digital health coaching program administered by Pack Health. Participants were referred through their health care provider, payer, or employer. The program included patient-centered lifestyle counseling and psychosocial support delivered via telephone, text, and/or email. Self-reported HbA_{1c} and weight were collected at baseline and completion. Physical and mental health were assessed using the Patient-Reported Outcomes Measurement Information System (PROMIS) Global Health Short Form and the Diabetes Distress Scale-2. Changes in HbA_{1c}, weight, BMI, and physical and mental health were analyzed within three participant cohorts stratified by baseline HbA_{1c} level.

Results: Participants with complete HbA_{1c} data sets (n=226) were included in the analysis. The sample population was 71.7% (162/226) female, with 61.5% (139/226) identifying as white and 34.1% (77/226) as black. Most participants (184/226, 81.4%) reported a baseline HbA_{1c} ≥7%, and 20.3% (46/226) were classified as high risk (HbA_{1c} >9%). Across HbA_{1c} cohorts, the mean baseline BMI was 35.83 (SD 7.79), and the moderate-risk cohort (7% ≤ HbA_{1c} ≤ 9%) reported the highest mean value (36.6, SD 7.79). At 12 weeks, patients reported a significant decrease in HbAlc, and high-risk participants reduced their levels by the greatest margin (2.28 points; P<.001). Across cohorts, BMI improved by 0.82 (P<.001), with the moderate-risk cohort showing the greatest reduction (−0.88; P<.001). Overall, participants reported significant improvements for PROMIS scores, with the greatest change occurring in the high-risk cohort for whom physical health improved 3.84 points (P<.001) and mental health improved 3.3 points (P<.001). However, the lowest-risk cohort showed the greatest improvements in diabetes distress (−0.76; P=.005).

Conclusions: Acknowledging the limitations in this real-world study design, the results reported here suggest that adults with type 2 diabetes with a high baseline HbA_{1c} or high BMI may benefit the most from patient-centered digital health coaching programs when compared to their lower risk counterparts. While all participants improved in physical and mental health categories, participants with high HbA_{1c} experienced the greatest HbA_{1c} reduction and individuals with the highest baseline BMI lost the most weight. These results may be used to inform referrals for patients who are more likely to benefit from digital health coaching.

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KEYWORDS

type 2 diabetes; mobile health; digital health coaching; digital therapy; diabetes support program; hemoglobin A1c; body mass index; diabetes distress

Introduction

Background

Diabetes is a significant health concern in the United States, with an estimated 34.2 million Americans or 10.5% of the US population diagnosed with this condition [1]. More than 90% of those cases represent individuals with type 2 diabetes mellitus (T2DM), who face an increased risk of vascular health complications [2] in addition to substantial mental health burden [3-6]. Active diabetes self-management, healthy lifestyle behaviors, and improved psychosocial wellness have been associated with positive outcomes and a reduced risk of complications [7-10]. However, it is difficult for patients to learn about and sustain recommended changes given commonly faced barriers, including complex diabetes treatment plans [11], limited time during provider visits [12], and disparate access to education and community support resources [13-15]. Patient-centered strategies that address these barriers and provide sustained support are needed to drive positive behavioral, psychosocial, and clinical impacts [16-18].

Digital diabetes health coaching aligns with this need by complementing clinical care and education through individualized and ongoing support, which is delivered in an easily accessible format such as telephone, text, and email [19-24]. Randomized controlled trials have shown that digital diabetes health coaching programs have a positive impact on hemoglobin A_{1c} (HbA_{1c}), weight, BMI, and mental health [25-29]. However, the degree and significance of the impact is variable. For example, a recent systematic review of digital diabetes interventions reported HbA_{1c} reductions, resulting from mobile coaching, ranging from 0.40% to 1.9% [30]. The highest impact intervention targeted patients with a baseline HbA_{1c} >9.0% and provided participants with a mobile app, web portal, and physician report [26], while the lowest impact intervention targeted individuals with an average HbA_{1c} of 6.86% and offered a mobile app, a web portal, and electronic health record integration [31]. Similarly, a 2013 study of a phone-based peer coaching program (N=299) showed variance in outcomes by baseline psychosocial and behavioral patient characteristics [32]. Specifically, the study reported a larger effect on lowering HbA_{1c} in patients with low levels of medication adherence and self-management support when compared to patients with higher levels of adherence and support [32].

While these studies have demonstrated the impact of digital diabetes health coaching under controlled research settings, it is not clear how these findings translate to real-world practice, which can be influenced by patient experience and utilization [33,34]. Real-world observations become particularly important in the consideration of digital health coaching, which often aims to drive psychosocial and behavioral change beyond the clinical and research settings. Moreover, digital health coaching programs are rapidly scaling across the United States, making the understanding of their real-world application increasingly important.

To optimize the scaling of digital health coaching for patients with diabetes and allocate care in the most equitable and efficient way, it is important to understand which patients may benefit the most. While HbA_{1c} is widely accepted as the benchmark for assessing glycemic control and risk [35-37], it is currently unclear how baseline HbA_{1c} modifies trends in digital health coaching outcomes. By understanding the impact of baseline HbA_{1c} on real-world digital health coaching outcomes, providers can make more informed referrals for patient participation in such programs.

Objective

To build on the existing evidence base, this retrospective analysis examined real-world patient-reported data to evaluate the impact of a 12-week patient-centered digital diabetes health coaching program on glycemic control, BMI, weight, diabetes distress, and overall physical and mental health. Trends in outcomes were stratified by baseline glycemic risk, as assessed by HbA_{1c}. We hypothesized that individuals with the highest baseline glycemic risk would experience the greatest improvements in mental and physical health outcomes.

Methods

Intervention Overview

The diabetes intervention under investigation was a multichannel diabetes support program, developed and delivered by Pack Health. The program, which is currently listed on the American Diabetes Association (ADA) peer-reviewed *Diabetes Support Directory* [38], is designed to meet the ADA support programming criteria and align with the *Standards of Medical Care in Diabetes* [18]. It aligns with the *Standards* in multiple ways including, but not limited to, the provision of individualized psychosocial support and evidence-based behavioral modification strategies (eg, goal setting, motivational interviewing, problem solving) [18,39-42]. In accordance with ADA guidance for support programming [38], it aims to complement clinical care and education in an easily accessible format. To facilitate participant accessibility, Pack Health combines one-to-one phone-based health coaching with digital education and prompts via SMS text messaging and/or email, which can be accessed anywhere and at any time.

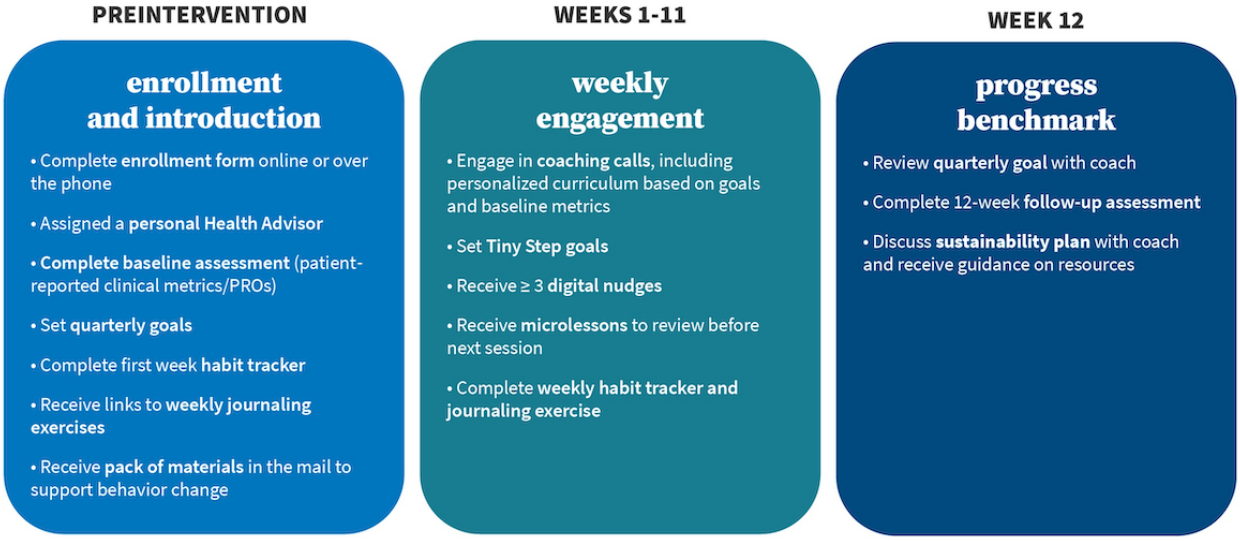
Coaches are allied health care professionals who complete a range of certification programs including, but not limited to, the American Association of Diabetes Care & Education Specialists (ADCES) Career Path Certificate Program [43], Centers for Disease Control and Prevention (CDC) Lifestyle Coach Training [44], and National Board for Health & Wellness Coaching (NBHWC) program [45]. Coaches also receive ongoing professional training on care escalation, health literacy, financial health, and cultural sensitivity. A multidisciplinary

advisory team of physicians, pharmacists, and nurses provide programmatic oversight and quality assurance.

Intervention Process

The digital health coaching intervention represented in this study was carried out over 12 weeks. During that time, all participants were exposed to the same core intervention process and modular diabetes curriculum, as outlined in Figures 1 and 2. Minor customizations of supplemental content, such as links to medication discount services and referrals to community resources, were provided by coaches in accordance with a defined framework to address individual concerns or health goals of the participants.

Figure 1. Program process: preprogram through week 12. PRO: patient-reported outcome.



At enrollment, potential participants were assigned a personal health coach, who remained their coach every week to promote a trusting interpersonal relationship. A preintervention introductory phone call was used to provide a detailed program overview and establish the participant's communication preference (ie, phone calls and SMS text messaging or phone calls and email). Once enrolled, participants were asked to complete an online preintervention survey assessment to collect baseline patient-reported outcome metrics, set an overarching health goal for their 12-week experience, and complete a habit tracker to assess their weekly progress. Participants then received a standard "pack" of materials in the mail designed to facilitate ongoing self-management. The pack included an exercise stretch band, a goal magnet, and a journal for tracking symptoms and personal goals.

Between weeks 1 and 11, participants received a standard diabetes curriculum in addition to targeted supplementary coaching related to their goals. Before each weekly session, participants were asked to review video-based micro-lessons and supplemental educational resources. During the weekly call, health coaches answered questions, addressed areas of need, and helped participants identify an achievable daily goal to be tracked between calls (eg, exercise for 30 minutes). These daily goals, referred to as "tiny steps," were used to reinforce desired behavioral and psychosocial changes and were reflected in 3 to 5 scheduled weekly SMS text messaging or email nudges. SMS text messaging and email nudges included reminders to prioritize goals and supplemental resources to help support goal attainment (eg, educational videos, recipes, worksheets, and articles). This process was repeated weekly as participants completed the curriculum. At week 12, coaches and participants reviewed goal progress and discussed strategies for sustainability. Throughout the 12-week process, coaches followed detailed call guidelines, which provide structure but not scripting, to deliver a modular diabetes curriculum that was provided to all participants. The standard curriculum covers symptom management, complication/comorbidity prevention, medication management, healthy eating, physical activity, patient-provider communication, gap elimination in care, psychosocial wellness (stress, sleep, and social support), and budgeting for health and sustainability (Figure 2).

Figure 2. Diabetes curriculum.

Participant Enrollment

Participation was voluntary, and individuals could withdraw from the program at any time with no risks or penalties. Participants were recruited between July 2016 and March 2020 from a variety of channels, including employer benefit programs, health plans, nonprofit partners, and provider referrals. Enrollment methods varied by channel. Customized emails and webpages were used to recruit participants through employer benefit programs, health plans, and nonprofit partners, while printable flyers were used by referring providers.

All potential participants were given the option to enroll in the intervention online or by phone. Individuals who opted for electronic enrollment completed an online interest form to determine eligibility, which has been defined below. Eligible individuals were emailed a program information sheet and a unique link to an electronic informed consent form, including a comprehensive description of rights, obligations, and risks. Telephone enrollment followed a similar process carried out by a program coordinator. The coordinator provided an oral description of the program, verified eligibility, and read the consent form over the phone. Eligible participants consented verbally.

The eligibility criteria for program participation included confirmed T2DM diagnosis, age 18 years or older, and ability to read, speak, and consent in English. Program participants were included in the study cohort if they were considered active at 12 weeks and completed all baseline and follow-up metrics included in the study (Table 1) [46,47]. Participants were defined as active if they completed at least one communication, including phone calls, SMS text messaging replies, and survey responses, in the previous 14 days.

Health coaching was provided at no cost to participants, with expenses covered by respective referral partners or through an external research grant. Data collected throughout the enrollment and coaching processes were anonymized, aggregated, and stored in a Health Insurance Portability and Accountability Act–compliant platform for future use in system and program optimization. Subsequently, no institutional review board approval was sought for this retrospective real-world analysis.

Table 1. Study measures and instruments.

Outcome and measurement	Instrument	Description	Scale or threshold
Clinical outcome			
HbA_{1c}[a]	Self-reported HbA_{1c}	Average blood sugar level (%) over the past 2-3 months	HbA_{1c} < 7%: low risk 7% ≤ HbA_{1c} ≤ 9%: moderate risk HbA_{1c} >9%: high risk
Weight	Self-reported weight in lbs	N/A[b]	N/A
BMI	Self-reported weight and height	BMI = 703 × weight (lbs)/height $(in)^2$	BMI ≤18.5: underweight 18.5 < BMI ≤ 24.9: healthy 25 < BMI ≤ 29.9: overweight BMI ≥30: obese
Patient-reported outcome			
GPH[c]	PROMIS[d] Global Health Short-Form v1.2 [46]	Physical health score is determined using Q3, Q6, Q7, and Q8	US average = 50 (SD 10) A higher value means better health
GMH[e]	PROMIS Global Health Short-Form v1.2 [46]	Mental health score is determined using Q2, Q4, Q5, and Q10	US average = 50 (SD 10) A higher value means better health
DDS-2[f]	Diabetes Distress Scale-2 [47]	Total DDS-2 score is determined by averaging scores across two items	DDS-2 score <2.0: little or no distress 2.0 ≤ DDS-2 score ≤ 3.0: moderate distress DDS-2 score >3.0: high distress

[a]HbA_{1c}: hemoglobin A_{1c}.

[b]N/A: not applicable.

[c]GPH: Global Physical Health.

[d]PROMIS: Patient-Reported Outcomes Measurement Information System.

[e]GMH: Global Mental Health.

[f]DDS-2: Diabetes Distress Scale-2.

Participant Characteristics and Process Measures

Demographic data, including participant gender, race, age, and state of residence, were collected during enrollment. Participant engagement was quantified by measuring the number and duration of completed weekly coaching calls and the number of opened digital nudges including micro-lessons and supplemental educational resources.

Outcome Measures

To assess change from preintervention to postintervention, survey data were collected electronically via participant self-report at enrollment (baseline) and completion (12 weeks). Surveys were voluntary and no incentives were provided. All surveys, totaling six pages, were delivered on the same schedule for all participants via the preferred communication method established by the patient, typically through email or SMS text messaging. At the time of survey delivery, participants received a unique link tied to their individual identifier. The link expired once the survey was complete, therefore eliminating the chance of duplication.

A summary of study measures and instruments is found in Table 1. Self-reported HbA_{1c} was used to estimate changes in blood glucose levels. While not as reliable as lab-based measurements, self-reported HbA_{1c} values are commonly used in real-world practice and have been shown to be reliable within half of a percentage point and reflect lab-based values over 75% of the time [48]. BMI, an indicator of weight status, was calculated using self-reported weight and height measurements [49]. HbA_{1c}, weight, and BMI calculations were tested across multiple test patients prior to implementation. Two validated web-based surveys were used to measure program impact on physical and mental health.

Overall physical and mental health were assessed using the 10-item Patient-Reported Outcomes Measurement Information System (PROMIS) Global Health Short-Form questionnaire version 1.2 [46], and diabetes-related distress was measured using the Diabetes Distress Scale-2 (DDS-2) [47]. The PROMIS Global Health short form measures health-related quality of life across the physical and mental domains, which are relevant to a variety of chronic conditions [46]. A Global Physical Health (GPH) score was determined using results from questions 3, 6, 7, and 8 pertaining to perceived physical health, physical ability, fatigue, and pain. A Global Mental Health (GMH) score was determined using results from questions 2, 4, 5, and 10 pertaining to overall mental health, including perceived quality of life, mood, satisfaction, and emotional problems. The GPH and GMH were normalized to a score of 50 (±10 for one standard deviation) to represent the average score for a person in the United States, with higher scores reflecting better physical and mental health. DDS-2 is a two-item instrument designed to assess emotional burden related to diabetes and diabetes regimen

distress in a clinical setting. Sources are reflected in two subscales, and an overall DDS-2 score is determined by averaging scores across subscales, with higher scores (>3.0) reflecting high distress [47].

Statistical Analysis

We conducted a retrospective cohort analysis to examine the impact of the digital health coaching program in a convenience sample of adults with T2DM stratified by baseline HbA_{1c}. Glycemic risk categories were defined using baseline HbA_{1c} values and were designed to align with participant risk for vascular complications and all-cause mortality. In accordance with the ADA *Standards of Care* [37] and Cavero-Rendondo et al [50], an HbA_{1c} value less than 7% was considered low risk and an HbA_{1c} value greater than 9% was considered high risk. For the purpose of this study, an HbA_{1c} value between 7% and 9% was considered moderate risk.

All statistical analyses, descriptive and correlational, were conducted using STATA 16 statistical software (StataCorp). Descriptive statistics were performed for all primary variables to measure baseline sample characteristics, participant engagement, and change across outcome metrics. Means and standard deviations were calculated for continuous variables, while frequencies and percentages were determined for categorical variables.

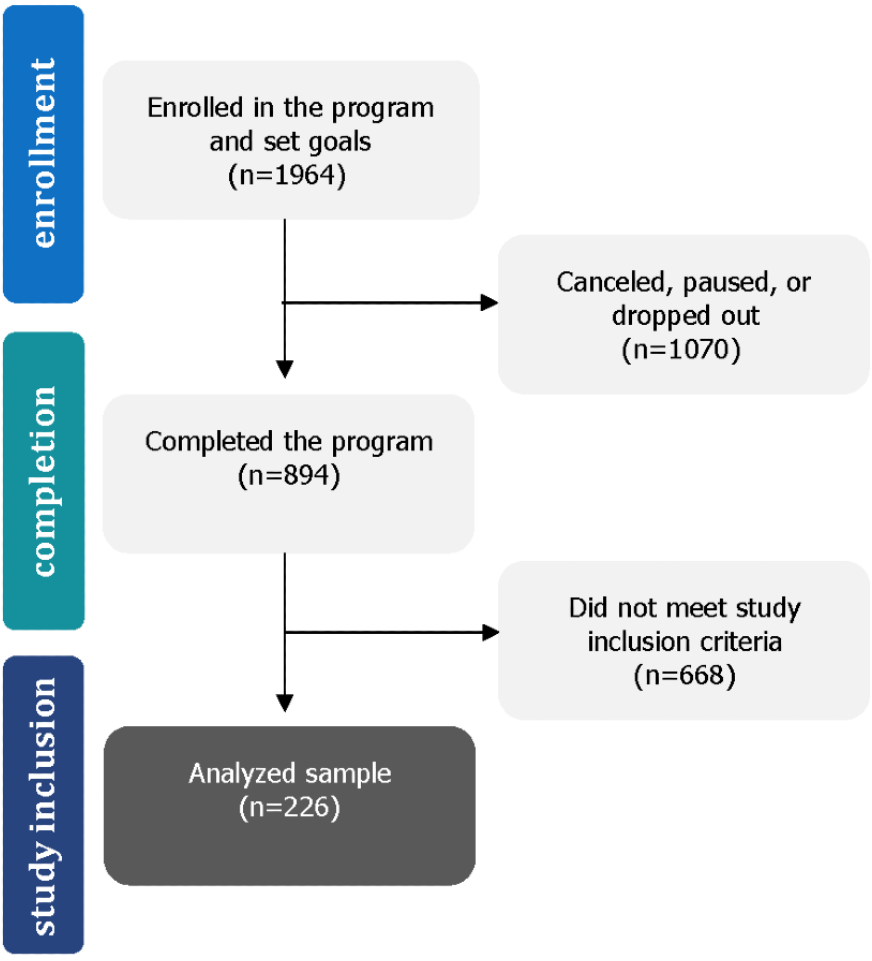
The absolute difference in each outcome metric (HbA_{1c}, BMI, GPH, GMH, and DDS-2) was calculated using preintervention to postintervention values for each cohort and for the overall sample population. One-sample paired *t* tests were performed to evaluate the significance of this difference, with the null hypothesis being no change in HbA_{1c}, BMI, or PROMIS scores. All tests were conducted at the significance level of α=.05. No weighting or matching methods were performed to adjust for a nonrepresentative sample. Incomplete surveys were excluded from the analysis.

Results

Participant Characteristics and Process Measures

Of the 1964 participants who enrolled in the program, 1070 (54.5%) did not meet our definition for active participation at 12 weeks. This is consistent with attrition rates for other digital diabetes interventions reflected in published observational studies [51]. Of those participants remaining in the sample, 668 (34.0%) failed to complete the surveys defined in the inclusion criteria for this study, which were optional for completing the program. Attrition includes individuals who enrolled in the program but did not complete a first call or who discontinued participation prior to the completion of the 12-week program. Of the 894 participants who completed the program, 226 (25.3%) had complete HbA_{1c} data sets at baseline and follow-up, and were subsequently included in the study (Figure 3).

Figure 3. Study flow chart.



Descriptive statistics for the study sample (n=226) are reported in Table 2. The sample population was 71.7% (162/226) female, and the majority of participants were white (139/226, 61.5%) or black (77/226, 34.1%). The mean age of participants at enrollment was 59.1 years (SD 9.23). The most common referral sources were providers (73/226, 32.3%), health-sponsored plans (54/226, 23.9%), and employers (43/226, 19.0%), drawing participants from 26 states within the continental United States.

Most patients were considered overweight or obese, with a mean BMI of 35.8 (SD 7.79) at enrollment [49]. Baseline HbA_{1c} levels ranged from 6.5% to 17.6%, with a mean self-reported baseline HbA_{1c} of 8.17% (SD 1.55%). For the purpose of glycemic risk stratification and subgroup analysis, 18.6% (42/226) of participants were considered low risk (HbA_{1c} <7.0%), 61.1% (138/226) were considered moderate risk (7% ≤ HbA_{1c} ≤ 9%), and 20.3% (46/226) were considered high risk (HbA_{1c} >9.0%).

Table 2. Patient and clinical demographics at enrollment (N=226).

Demographic	Value, n (%)
Gender	
Female	162 (71.7%)
Male	64 (28.3%)
Race	
White	139 (61.5%)
Black	77 (34.1%)
Other/multiracial	10 (4.4%)
Enrollment type	
Provider	73 (32.3%)
Payer	54 (23.9%)
Employer	43 (19.0%)
Pharmaceutical	31 (13.7%)
Self-enrollment	25 (11.1%)
HbA_{1c}[a] status at baseline	
Low risk (HbA_{1c} <7%)	42 (18.6%)
Moderate risk (7% < HbA_{1c} < 9%)	138 (61.1%)
High risk (HbA_{1c} >9%)	46 (20.3%)

[a]HbA_{1c}: hemoglobin A_{1c}.

On average, participants received 5.75 multichannel communications per week from their coaches over the course of the 12-week engagement. Weekly calls with personal health coaches lasted an average of 14.53 minutes per call, and participants received an average of 3.75 digital nudges and one digital educational resource via SMS text messaging or email per week.

Outcome Measures

Across the total sample, the mean HbA_{1c} decreased from 8.17% (SD 1.55%) to 7.44% (SD 1.33%), resulting in a clinically relevant reduction of 0.73 percentage points (P<.001) (Table 3, Figure 4A). Reductions in blood glucose levels were observed in all glycemic risk groups, though a greater reduction was observed in groups with higher baseline HbA_{1c} levels (Table 3, Figure 4A). High-risk participants with an HbA_{1c} ≥9% reported the largest improvements. Their HbA_{1c} levels decreased by 2.28 percentage points or 21% compared with baseline (P<.001). Moderate-risk participants reported a 0.37 percentage point decrease or a 5% reduction from baseline (P<.001). Low-risk participants maintained glycemic control with no significant change in HbA_{1c} from baseline to follow-up.

Table 3. Primary study outcomes.

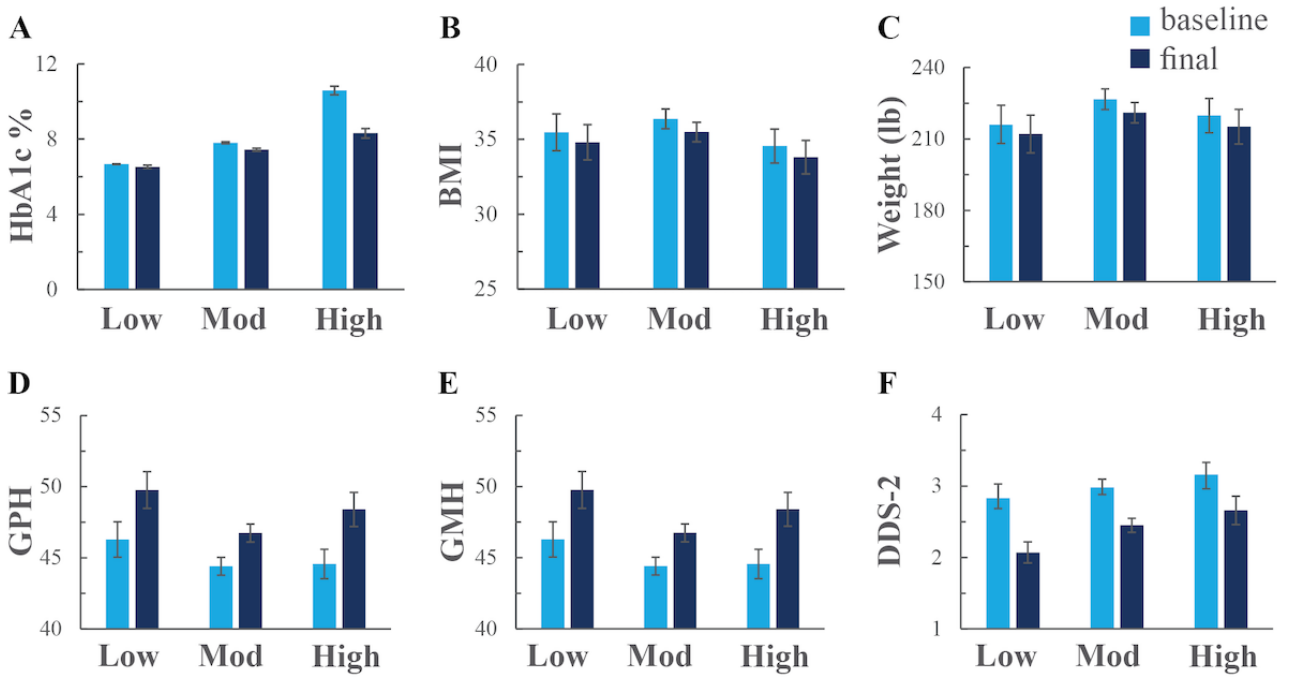
Measurement[a]	Baseline value, mean (SD)	Final value, mean (SD)	Difference, Δ (%)	*P* value[b]
HbA_{1c}[c] (%)				
Low risk	6.67 (0.13)	6.52 (0.56)	−0.15 (−2.25)	.09
Moderate risk	7.81 (0.59)	7.44 (0.93)	−0.37 (−4.74)	<.001
High risk	10.59 (1.57)	8.31 (1.74)	−2.28 (−21.43)	<.001
Overall	8.17 (1.55)	7.44 (1.23)	−0.73 (−8.94)	<.001
Weight (lbs)				
Low risk	216.05 (52.31)	212.13 (51.58)	−3.92 (−1.81)	.003
Moderate risk	226.70 (51.54)	221.09 (50.48)	−5.61 (−2.47)	<.001
High risk	219.83 (49.25)	215.19 (49.23)	−4.64 (−2.11)	.002
Overall	223.21 (51.19)	218.23 (50.35)	−5.09 (−2.28)	<.001
BMI				
Low risk	35.47 (7.95)	34.80 (7.62)	−0.67 (−1.89)	.002
Moderate risk	36.36 (7.77)	35.48 (7.69)	−0.88 (−2.42)	<.001
High risk	34.55 (7.68)	33.81 (7.58)	−0.74 (−2.14)	.001
Overall	35.83 (7.79)	35.01 (7.66)	−0.82 (−2.29)	<.001
Global Physical Health score				
Low risk	46.28 (8.06)	49.76 (8.36)	3.48 (7.52)	.007
Moderate risk	44.40 (7.28)	46.74 (7.44)	2.34 (5.27)	<.001
High risk	44.56 (6.98)	48.40 (8.10)	3.84 (8.62)	.001
Overall	44.78 (7.34)	47.64 (7.81)	2.86 (6.39)	<.001
Global Mental Health score				
Low risk	48.85 (7.15)	52.02 (8.86)	3.17 (6.49)	.01
Moderate risk	48.19 (7.27)	50.02 (7.91)	1.83 (3.80)	.006
High risk	46.11 (7.84)	49.41 (7.86)	3.3 (7.16)	.001
Overall	47.88 (7.39)	50.27 (8.09)	2.39 (4.99)	<.001
Diabetes Distress Scale-2 score				
Low risk	2.83 (1.29)	2.07 (0.95)	−0.76 (−26.86)	.005
Moderate risk	2.98 (1.37)	2.45 (1.15)	−0.53 (−17.78)	<.001
High risk	3.16 (1.17)	2.66 (1.35)	−0.5 (−15.82)	.05
Overall	2.99 (1.31)	2.42 (1.17)	−0.57 (−19.06)	<.001

[a]Categorized by baseline HbA_{1c} as follows: low risk, HbA_{1c} <7%; moderate risk, 7% ≤ HbA_{1c} ≤9%; high risk, HbA_{1c} >9%.

[b]*P* value calculated using the chi-square test with comparison of the relative value to baseline.

[c]HbA_{1c}: hemoglobin A_{1c}.

Figure 4. Clinical and patient-reported outcomes before and after digital health coaching across glycemic risk groups including (A) blood glucose levels according to hemoglobin A_{1c} (HbA_{1c}), (B) weight status according to BMI, (C) weight in pounds, (D) physical health according to Patient-Reported Outcomes Measurement Information System (PROMIS) Global Physical Health (GPH), (E) mental health status according to PROMIS Global Mental Health (GMH), and (F) distress according to the Diabetes Distress Scale-2 (DDS). Self-reported measures were collected at enrollment (baseline) and upon completion of the 12-week program (final) for participants with low, moderate, and high baseline HbA_{1c} levels, reported as mean ± standard error of the mean for each cohort. Mod: moderate.



Overall, participants who completed the program lost weight, thereby reducing their BMI. The weight decreased by an average of 5.09 pounds (P<.001), and BMI decreased by an average of 0.82 points (P<.001). The trend observed for reductions in weight and BMI within glycemic risk groups was different from the trend observed for reductions in HbA_{1c} levels (Table 3, Figure 4B-C). In this case, the moderate-risk cohort saw the greatest change in BMI with a 0.88 point reduction (P<.001), followed by the high-risk cohort with a 0.74 point reduction (P<.001) and the low-risk cohort with a 0.67 point reduction (P=.002).

Improvements in physical and mental health, as measured by PROMIS scores, were also significant across all groups (Table 3, Figure 4D-E). Across cohorts, the GPH score significantly increased by 6.4% to a final score of 47.64 (SD 7.81; P<.001), and the GMH score increased by 5% to a final score of 50.27 (SD 8.09; P<.001). Participants with high glycemic risk showed the greatest improvement in physical and mental health scores, with increases of 3.84 points (P<.001) for GPH and 3.3 points (P=.001) for GMH.

Improvements in diabetes distress were also significant across all groups (Table 3), where the average DDS-2 score improved by 0.57 (from 2.99 [SD 1.31] to 2.42 [SD 1.17]). For this metric, trends by glycemic risk did not align with the other patient-reported outcomes; the greatest improvement was observed for the low-risk cohort. An improvement of 0.76 (P=.005) (from 2.99 to 2.42) was observed for the low-risk cohort compared with an improvement of 0.5 (P=.053) (from 3.16 to 2.66) for the high-risk cohort.

Discussion

Principal Findings

This retrospective study of real-world data indicated that participants with T2DM who completed the multichannel digital health coaching program and provided complete HbA_{1c} data sets achieved improved glycemic control and body weight, in addition to positive changes in their physical and mental health status. Cohort analysis revealed that individuals with the highest glycemic risk (HbA_{1c} >9% at enrollment) achieved the greatest level of change in all clinical and patient-reported outcomes, except for weight loss (BMI). The findings reported here are consistent with the study hypothesis and align with emerging evidence on digital health coaching intervention outcomes [20-32].

Prior randomized controlled trials and observational studies have established the efficacy of digital health coaching to improve glycemic control and encourage weight loss among individuals with T2DM [25-27]. The average weight loss and HbA_{1c} reduction in the overall cohort was consistent with values reported in response to similar digital interventions. However, comparatively few studies reported specific outcomes for individuals with a high glycemic risk [25,26]. To our knowledge, this is the first study to evaluate the differential impact of digital health coaching for cohorts stratified based on baseline glycemic risk.

This study showed that patients with elevated blood glucose (HbA_{1c} >9%) reduced their HbA_{1c} levels by 2.28 points (P<.001). This degree of HbA_{1c} reduction is greater than many

values reported in existing literature on the impact of similar digital health coaching interventions [25,26,52]. While some studies have shown comparable improvements for high-risk participants, these interventions have typically relied upon clinicians for management and/or education [30]. This result observed in real-world self-reported HbA_{1c} levels is promising, though it should be confirmed with laboratory measurements of HbA_{1c} in a larger randomized efficacy trial. If verified, these results could imply that digital health coaching for this high-risk population can have a significant impact on diabetes outcomes beyond glycemic control alone. For every 0.9% decrease in HbA_{1c}, patients benefit from a 10% decrease in diabetes-related mortality, a 25% reduction in microvascular complications, and a 6% reduction in overall mortality [53].

In this study, we also noted an average weight loss of 5.09 pounds and an average reduction in BMI of 0.82 points (2.29%; $P<.001$) across all cohorts. Weight loss is associated with substantial health benefits for obese patients, where losing 5% to 10% of body weight reduces the risk of cardiovascular comorbidities [54]. However, even modest weight loss in the range of 2% to 5% can provide clinically meaningful reductions in fasting blood glucose for obese patients with diabetes [54]. In contrast to the trend observed in HbA_{1c} level reduction, the moderate-risk cohort lost more weight and reduced BMI more than the high-risk cohort. Importantly, this may be explained by differences in average cohort weight at enrollment. The moderate-risk cohort reported the highest baseline BMI (36.36) at enrollment, which may indicate that baseline BMI is a stronger predictor of weight loss than baseline HbA_{1c}. These findings are important to consider in future digital health coaching research given the role of weight loss in improved cardiometabolic outcomes for individual with T2DM [54,55].

Moreover, findings from this study suggest that individuals at high baseline glycemic risk may experience the greatest benefit in overall physical and mental health in response to digital health coaching. Trends in PROMIS GPH for high-risk participants showed the most notable impact when compared to individuals with lower baseline HbA_{1c}. At the 12-week follow-up, the high-risk group's GPH score improved by 3.84 points ($P=.001$) compared with 2.86 points ($P<.001$) for the overall population. Similar trends were observed for PROMIS GMH scores.

At baseline, the average patient-reported GMH score was 47.89, which is below the national average of 50.00 [46]. For high-risk patients, that average was 46.11, indicating more room for improvement. After the intervention, the average score across cohorts was 50.27 or slightly above the national average. High-risk participants reported an improvement of 3.3 points ($P<.001$). If sustained, the positive shift for this cohort could drive improvements to physical health given the relationship between mental health and glycemic control [5,6].

Change in distress from preintervention to postintervention was significant across all cohorts ($P<.001$). The high-risk group demonstrated the greatest need for change, with a baseline score of 3.16, indicating high distress, compared with a baseline score of 2.83 for the low-risk group, indicating moderate distress. High distress scores are associated with negative diabetes outcomes, including high HbA_{1c}, low self-efficacy, and poor diet [56]. The reductions in diabetes-related distress reported here are larger than those reported after a 12-month mobile diabetes intervention, which may be explained by differences in distress levels at baseline [29]. Interestingly, the trend observed in overall mental health status did not translate to diabetes distress levels, and instead, those individuals with the lowest baseline glycemic risk showed the greatest improvement, reducing their distress levels to low or nearly no distress. This indicates that even those groups with well-controlled HbA_{1c} at baseline can benefit from the program.

Overall, these findings indicate that higher glycemic risk patients may have a greater need for mental and physical health monitoring and, with the exception of reducing distress, may also have the greatest potential for experiencing a positive impact from multichannel digital diabetes health coaching.

Limitations of the Study

Although this study provides valuable insights into the real-world application of digital diabetes health coaching and specifically who may benefit most, the reported findings are limited by the real-world cohort study design. Most notably, no control group was available to compare interventions to standard of care practices. As a result, we cannot rule out that the observed improvements were due to factors unrelated to the digital health coaching program. Furthermore, patients were not incentivized using the same tools typical of a research trial (eg, financial incentives, trust in clinicians, and access to better health care), which can impact attrition rates and data collection [57]. While these issues are well documented in diabetes supportive care programs [58], they resulted in incomplete data sets and a subsequently limited cohort size. Finally, self-reported HbA_{1c} and BMI were not confirmed by laboratory data. As a result, while our findings are consistent with results presented in other studies, there were too many uncertainties to make definitive conclusions. However, we believe these results and observations can be leveraged to inform the design of future prospective efficacy studies investigating baseline HbA_{1c} and BMI as possible mediators of the impact of digital health coaching.

Conclusions

This real-world analysis provides valuable insights on the impact of digital health coaching on T2DM control for participant glycemic risk. While program completion was associated with improved patient-reported outcomes for the average participant, participants with a high HbA_{1c} level at baseline saw the greatest improvement in glycemic control and overall physical and mental health. Further research is warranted to fully understand the differential impact of multichannel digital health coaching support for patients with increasing HbA_{1c}.

Perspectives and Implications

To our knowledge, this is the first real-world study to examine the clinical predictors of program outcomes for diabetes patients who participate in digital health coaching. These findings are relevant to many stakeholders, including clinicians, health systems, employers, and payers, who must decide which patients

to refer to such a program. As this type of low-cost and accessible intervention continues to scale nationally, informed referral strategies will become increasingly important.

Conflicts of Interest

MM, JP, MA, BBO, and DP are employed by Pack Health.

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Abbreviations

ADA: American Diabetes Association
DDS-2: Diabetes Distress Scale-2
GMH: Global Mental Health
GPH: Global Physical Health
HbA_{1c}: hemoglobin A_{1c}
PROMIS: Patient-Reported Outcomes Measurement Information System
T2DM: type 2 diabetes mellitus

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Original Paper

Improved Low-Glucose Predictive Alerts Based on Sustained Hypoglycemia: Model Development and Validation Study

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Abstract

Background: Predictive alerts for impending hypoglycemic events enable persons with type 1 diabetes to take preventive actions and avoid serious consequences.

Objective: This study aimed to develop a prediction model for hypoglycemic events with a low false alert rate, high sensitivity and specificity, and good generalizability to new patients and time periods.

Methods: Performance improvement by focusing on sustained hypoglycemic events, defined as glucose values less than 70 mg/dL for at least 15 minutes, was explored. Two different modeling approaches were considered: (1) a classification-based method to directly predict sustained hypoglycemic events, and (2) a regression-based prediction of glucose at multiple time points in the prediction horizon and subsequent inference of sustained hypoglycemia. To address the generalizability and robustness of the model, two different validation mechanisms were considered: (1) patient-based validation (model performance was evaluated on new patients), and (2) time-based validation (model performance was evaluated on new time periods).

Results: This study utilized data from 110 patients over 30-90 days comprising 1.6 million continuous glucose monitoring values under normal living conditions. The model accurately predicted sustained events with >97% sensitivity and specificity for both 30- and 60-minute prediction horizons. The false alert rate was kept to <25%. The results were consistent across patient- and time-based validation strategies.

Conclusions: Providing alerts focused on sustained events instead of all hypoglycemic events reduces the false alert rate and improves sensitivity and specificity. It also results in models that have better generalizability to new patients and time periods.

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KEYWORDS

machine learning; quantile regression forests; sustained hypoglycemia; continuous glucose monitoring; false alert rate; model generalizability; diabetes; glucose monitoring; hypoglycemia

Introduction

Glucose measurements are critical for effective diabetes management. Real-time continuous glucose monitoring (CGM) devices allow for frequent, automated glucose readings from interstitial fluid in the subcutaneous tissue space. CGM has been shown to improve glycemic control and reduce glycemic excursions—decreasing both hypoglycemia and hyperglycemia [1]. An important feature of CGM devices is their ability to provide real-time auditory alerts for trending glucose excursions

above or below customized threshold levels. The CGM data can also be used to develop models to predict future hypoglycemia [1,2].

Since the first attempt at predicting future glucose values based on CGM data in 1999 [3], numerous studies have been performed to provide alerts for hypoglycemia based on predictive models. Some of the initial works relied on classical time-series based forecasting methods such as autoregressive integrated moving average (ARIMA)–ARIMAX [4-9] and state-space models [10-19]. Later, different machine learning methods were explored to predict future glucose values [20-25]. More recently, deep learning techniques have been proposed toward solving the problem [26-33]. Some works have also explored incorporating contextual data such as meal information, insulin levels, heart rate, and physical activity as features in the predictive model [34-40]. However, currently integrated information on the data sources is not readily available for real-time predictions.

Predictive hypoglycemia alerts have the potential to be extremely helpful in reducing hypoglycemia risk; however, false alerts have been a major hindrance to the acceptance of predictive hypoglycemia alerts among users [41-43]. In our earlier work, we developed a machine learning–based hypoglycemia predictive model with a sensitivity and specificity of >95%, comparable with the best predictive models in the literature [44]. Typically, the number of hypoglycemic events is very small compared with that of nonhypoglycemic events. For example, only 2.13% (35,075/1,644,875) of readings in the data set used in this study were in the hypoglycemic range (ie, <70 mg/dL). The high-class imbalance resulted in a false alert rate (FAR) of around 85% (40,502/47,683), even with an impressive specificity of 95%. Improvement in specificity in such highly imbalanced class cases will reduce the FAR and therefore improve user experience and trust in the alerts, facilitating persuasive adoption of alerts.

Previous studies have found that hypoglycemia prediction model performance is reduced when applied to new patients and different time periods [45]. Improvement in model generalizability to new patients and time periods will facilitate ease of deployment and retention of performance postdeployment.

Thus, despite the many advances made in terms of hypoglycemia prediction models, the shortcoming of a high FAR makes the alerts ill-suited for real-world application [42,46,47]. These results indicate a need for the development of approaches to reduce the FAR, maintain high sensitivity, and improve the generalizability of the prediction model.

Methods

Data Description

The CGM data sets were obtained from 110 pediatric patients with type 1 diabetes over 30 to 90 days. The data comprised over 1.6 million CGM values under normal living conditions. Dexcom G6 CGM devices were used to collect the CGM readings. The cohort-level profile of patients in this study can be found in Table 1. Summary statistics of a patient hypoglycemia profile and a patient pump profile are presented in Multimedia Appendices 1 and 2, respectively. Of note, data were obtained from a mix of patients using multiple daily injections, sensor-augmented pump therapy without automated basal rate modulation, and sensor-augmented pump therapy with a predictive low-glucose suspend feature (ie, t:slim X2 insulin pump with Basal-IQ technology; Tandem Diabetes Care, Inc [48]). The t:slim X2 insulin pump uses a simple linear regression algorithm to predict glucose levels 30 minutes ahead and suspend basal insulin in the pump if glucose values are predicted to drop below 80 mg/dL in the next 30 minutes or if a CGM value falls below 70 mg/dL. Insulin delivery can remain suspended for a minimum of 5 minutes to a maximum of 2 hours and will then resume as soon as glucose values begin to rise.

Table 1. Demographic and diabetes profile of patients enrolled in the study.

Characteristic	Mean (SD)	Minimum	Maximum
Baseline demographics			
Age (years)	12.67 (4.84)	1	21
Glycated hemoglobin A_{1c} (%)	7.70 (1.63)	5.00	12.50
Duration of diabetes (years)	4.93 (4.09)	0.25	19.18
Continuous glucose monitoring metrics			
Number of hypoglycemic values per day per patient	6.20 (5.98)	0.10	23.73
Percentage of hypoglycemic values below 70 mg/dL	2.13 (2.10)	0.50	12.20

Hypoglycemic Events

A glucose threshold of 70 mg/dL is used to identify the hypoglycemic range [49,50]. Of the 1.6 million CGM readings in the study data, approximately 35,000 values representing 6010 events were in the hypoglycemic range. The period of time between a first CGM reading below the threshold and the point where the CGM value rises to ≥70 mg/dL is considered a single “hypoglycemic event.”

Table 2 shows the frequency distribution of the duration of the hypoglycemic events. The hypoglycemic events in this analysis were further classified as transient (lasting less than 15 minutes; 77.24% [4642/6010] of the hypoglycemic events) or sustained (lasting 15 minutes or longer; 22.76% [1368/6010] of the events) based on the recommendations in previous studies [51,52]. Nonhypoglycemic events are CGM observations of ≥70 mg/dL. Detailed information regarding the distribution of hypoglycemic

events and a breakdown of sustained events by day and night are presented in Multimedia Appendices 3-5.

Table 2. Frequency distribution of the duration of hypoglycemic events (n=6010).

Hypoglycemic events	Duration of consecutive CGM values falling below 70 mg/dL (minutes)									
	5	10	15	20	25	30	35	40	45	>45
Frequency, n (%)	572 (9.51)	796 (13.24)	885 (14.73)	842 (14.01)	676 (11.25)	562 (9.35)	391 (6.51)	283 (4.71)	209 (3.48)	794 (13.21)

Evaluation Metrics

We define the following metrics for evaluating model performance: sensitivity, specificity, and FAR.

Sensitivity measures the proportion of true positives that are correctly identified. It is also known as the true-positive rate.

where TP are the true positives and FN are the false negatives.

Specificity measures the proportion of true negatives that are correctly identified. It is also known as the true-negative rate.

where TN are the true negatives and FP are the false positives.

FAR was defined based on the definition provided by Mosquera-Lopez et al [53] and measures the proportion of alerts that are not truly indicative of predicted hypoglycemic events.

Machine Learning Methodologies

Random Forest

Random forest (RF) is a nonparametric approach that builds on an ensemble prediction of a "forest" of regression trees grown via bootstrap sampling. Model predictions are obtained from the mean of the predictions of the individual trees. RF performs well when dealing with nonlinear relationships among variables and makes no assumptions about data distributions. Owing to these characteristics, utilizing RF-based machine learning modeling resulted in good performance in our previous work [44] compared with other machine learning methods for hypoglycemia prediction. In this study, an RF-based model was used to classify events as sustained hypoglycemic events (positive class) or transient and nonhypoglycemic events (negative class).

Quantile Regression Forest

For the multistep prediction approach, future CGM values were predicted using quantile regression forests (QRFs). The concept of quantile regression was introduced by Koenker and Hallock [54] and is advantageous when quantile functions are of interest. Quantile functions provide information about the spread of the response variable beyond the conditional mean by estimating the full conditional distribution. This is particularly useful for predicting values other than the mean (eg, median or 90th quantile). QRFs are a generalization of RFs and provides an accurate way of estimating the conditional quantiles [55]. Since it is more important to accurately predict CGM values near the hypoglycemic range rather than within the euglycemic or hyperglycemic range, QRFs were used to predict future CGM values using the regression approach.

QRFs were used as a multistep forecasting method to predict the glucose values for every 5-minute interval in the prediction horizon (PH). This resulted in 6 predictions for the 30-minute PH and 12 predictions for the 60-minute PH. Based on these predictions, a sustained hypoglycemic event was detected if 3 or more consecutive predicted CGM values were <70 mg/dL.

Validation Mechanism

An appropriate validation mechanism is critical to assess the performance of a machine learning model [56,57]. This validation strategy helps to ascertain the generalizability of the model and ensures that the model performs well in real-world scenarios. This can be performed by sampling a subset of the data for model development and sampling a different sample of data for model validation [58]. Two validation strategies—patient-based and time-based—were used to evaluate model performance.

Patient-Based Approach

In this approach, the prediction model was developed on a subset of patients and validated on a different set of patients. Of the 110 patients, 70 patients (approximately 65% of the data) were randomly selected for training and the remaining 40 patients were used for performance evaluation. The final model performance reported is the mean of 5 replications of this procedure of 65%/35% split of training and validation data.

Time-Based Approach

In this approach, for each of the 110 patients, the first 70% of the data was used for model training and the last 30% of the data was used for validation. The average performance using validation data on all 110 patients was reported.

Features Extracted for the Prediction

A rich combination of demographic, dynamic, snowball, interaction, and contextual features were extracted from the data. An optimal set of features for hypoglycemia prediction was identified in our previous work [44] and these features were used for the model development in this study (Multimedia Appendix 6). Records associated with missing data were eliminated from the analysis; that is, if a feature was dependent on a missing CGM value, that record—as well as all dependent time-lagged records—were eliminated from the analysis.

Results

Model Performance

Table 3 summarizes the performance of the model based on patient-based and time-based validation strategies. The total number of false alerts when considering transient and nonhypoglycemic events as false alerts and when considering nonhypoglycemic events as false alerts are provided along with sensitivity and specificity metrics.

In the patient-based validation approach, for both 30-minute and 60-minute PHs, the QRF method provided a significant advantage over the RF method with high sensitivity, high specificity, and low FAR. The patient-based validation approach indicated that the sustained hypoglycemic model developed using QRFs is generic and can be applied to new patients without performance degradation.

In a time-based validation setting, the RF method performed well for both 30-minute and 60-minute predictions with high sensitivity, high specificity, and low FAR, but the QRF method still outperformed it. The time-based validation methodology indicated that both models retain performance when applied to new time periods and in postdeployment.

Table 3. Comparison of model performance based on sensitivity, specificity, and false alerts with patient-based and time-based validation for 30-minute and 60-minute prediction horizons (PHs).

Metrics	Patient-based validation				Time-based validation			
	30-minute PH		60-minute PH		30-minute PH		60-minute PH	
	Method 1: RF[a]	Method 2: QRF[b]	Method 1: RF	Method 2: QRF	Method 1: RF	Method 2: QRF	Method 1: RF	Method 2: QRF
Sensitivity, % (SD)	39.11 (2.25)	99.09 (0.16)	49.27 (3.03)	97.61 (0.41)	96.17	98.94	95.34	97.91
Specificity, % (SD)	98.65 (0.09)	98.19 (0.10)	98.63 (0.12)	98.09 (0.11)	98.3	98.29	97.95	98.20
False alerts, n (SD)								
Considering transient and nonhypoglycemic events as false	6936 (356)	9339 (459)	7043 (317)	9672 (431)	6476	8211	7346	8465
Considering only nonhypoglycemic events as false	3907 (200)	5368 (162)	4109 (156)	5677 (201)	3324	4531	4334	4799
False alert rate, % (SD)	26.32 (2.56)	26.50 (2.41)	26.44 (2.37)	26.36 (2.57)	22.79	23.86	26.41	23.79

[a]RF: random forest.

[b]QRF: quantile regression forest.

Comparison of Sustained Versus All Hypoglycemic Events Prediction Models

Table 4 provides a comparison of model performance between sustained hypoglycemia and all-hypoglycemia prediction models. Even though the all-hypoglycemia model had high sensitivity, a specificity of 93% on a large number of nonhypoglycemic events resulted in an FAR of 85%. Focusing the alerts on sustained hypoglycemic events resulted in an increase in specificity to 98% and reduced the FAR to approximately 20% to 30%. Also, the performance of the all hypoglycemic events prediction model was adversely affected when evaluated on new patients and new time periods (drop in sensitivity of 5%). On the other hand, prediction models based on sustained hypoglycemic events retained their performance for new patients and new time periods, indicating better generalizability of the sustained hypoglycemic events model.

Table 4. Comparison of model performance based on sensitivity, specificity, and false alert rate with different characterizations of hypoglycemic events and different validation strategies (patient-based and time-based) for giving predictive alerts.

Model	30-minute prediction horizon			60-minute prediction horizon		
	Sensitivity (%)	Specificity (%)	False alert rate (%)	Sensitivity (%)	Specificity (%)	False alert rate (%)
All hypoglycemic events prediction (5-fold validation)	93.61	93.50	84.94	91.01	89.82	77.20
All hypoglycemic events prediction (new time periods)	87.10	92.66	85.16	73.87	87.29	79.81
All hypoglycemic events prediction (new patients)	87.60	92.47	75.20	73.79	87.06	71.50
Sustained hypoglycemic events prediction (QRF[a]—new patients)	99.08	97.79	30.00	98.13	97.58	30.19
Sustained hypoglycemic events prediction (QRF—new time periods)	98.54	98.57	22.36	97.72	98.49	22.44

[a]QRF: quantile regression forest.

A graphical comparison between the classifiers at different threshold values using receiver operating characteristic (ROC) curves can be found in Multimedia Appendix 7. The ROC plots show that the QRF model outperformed the RF models over the entire range of sensitivity and specificity levels. Table 5 shows the QRF model's performance metrics at different threshold levels. The table also presents the average time required to predict a hypoglycemic event at different threshold levels.

Table 5. Performance of the quantile regression forest model at different thresholds and the average time to predict a hypoglycemic event.

Metric	30-minute prediction horizon			60-minute prediction horizon		
	Threshold 1	Threshold 2	Threshold 3	Threshold 1	Threshold 2	Threshold 3
Sensitivity (%)	98.54	99.27	99.51	97.72	98.29	98.99
Specificity (%)	98.57	97.56	96.68	98.49	97.06	95.53
False alerts (n)	6932	11,960	16,049	7215	14,027	21,297
False alerts with transient events as positives (n)	3736	8149	12,007	3974	9956	16,775
False alert rate (%)	22.36	35.36	43.34	22.44	37.19	46.96
Average time to predict an event (minutes)	18.78	22.95	26.51	25.24	35.08	48.35

Discussion

Principal Findings

We present a robust prediction model for providing high-quality alerts for sustained hypoglycemic risk in patients with type 1 diabetes. The final model (QRF model) was demonstrated to be robust to different validation approaches that best represent real-world application scenarios (new patients and new time periods). The primary research contributions of this work are (1) the development of a prediction model that focused on sustained hypoglycemic events and resulted in high sensitivity, high specificity, and a low FAR; and (2) improved generalizability of the model to new patients and new time periods. The model makes use of only CGM data in the past 4 hours and contextual information about the current hour of the day and day of the week to make predictions. A methodology contribution is the use of glucose predictions at multiple time points to facilitate inference of sustained hypoglycemia. The model was built using data collected from 110 patients over a range of 30 to 90 days under normal living conditions, ensuring validity of the results. The QRF model proposed in this work had sensitivity and specificity >97% for both 30- and 60-minute PHs. The FAR was also kept low at 22% and 29% for 30-minute and 60-minute PHs, respectively, which will lead to improved user trust in and adoption of CGM-based alerts.

Comparison with the Literature

A comparative analysis of different hypoglycemia prediction methodologies can be found in the literature [11,20,59,60]. A straightforward comparison between different hypoglycemia prediction studies is complicated due to differences in CGM sensors used, sampling intervals, and data collection (synthetically generated, controlled study, free-living conditions). In addition, different studies have used different definitions of hypoglycemia, which makes their findings difficult to compare [21,61-63]. When using a regression approach, the majority of the works present an overall root-mean-square error (RMSE) value, but accuracy pertaining to the observations in the hypoglycemic range might be more relevant. Thus, providing an overall RMSE for the entire data set could misrepresent the model's performance. On the classification side, sensitivity and specificity provide accurate information on the TPs and FPs, respectively. However, due to high-class imbalance, even a

moderately high specificity can lead to a high FAR. It becomes important to consider the FAR, in addition to sensitivity and specificity, in such class-imbalanced applications.

In machine learning, a standard approach to validate prediction models is to split the data into a training set (to train the model) and a validation set (to evaluate model performance) [64]. This random partitioning of the data into training and validation subsets and repeating the process across multiple folds is called cross-validation. Studies across the literature have used different validation strategies such as random sampling [20,65-67], time-based splitting [4,5,67-69], patient-specific splitting [6,32,53,70,71], or a combination of these methods to estimate predictive model performance. Simple random sampling–based cross-validation [72,73] may not fully address the generalizability aspect of the model to new patients and new time periods. Some studies [6] using a patient-based validation strategy used a part of their test data for tuning model parameters, which affected the validity of the performance estimation. The model presented in this paper had high performance in both patient- and time-based validation methods.

Mosquera-Lopez et al [28] used a patient-specific validation approach in which patient data in the test set were exclusive from the training data. Performance was reported on metrics such as sensitivity, RMSE, and FARs. However, leveraging some of the preprocessing and postprediction error-correction steps to improve performance made it difficult to achieve similar results in a real-world setting. Also, the test performance was evaluated on a small sample size of 10 patients (in a 4-week study). This might affect the generalizability of the presented results.

Dave et al [44] recently showed good results with respect to sensitivity and specificity using a random sampling–based validation approach and a threshold of 70 mg/dL for hypoglycemia. However, it was observed that performance of this model was reduced when applied to new patients and new time periods (Table 3). In addition, even with sensitivity and specificity of >95%, the model resulted in an FAR of 80% due to a large number of nonhypoglycemic events relative to the number of hypoglycemic events. From a user experience perspective, this will lead to false alert fatigue. The model presented in this paper reduced the FAR to 22%.

Having an accurate and actionable hypoglycemia prediction model with low FARs is essential to the durability of CGM in diabetes management. Furthermore, a patient-facing hypoglycemia prediction algorithm may give patients the confidence to aim for in-range glucose values without fear of hypoglycemia, potentially leading to lower glycated hemoglobin A_{1c} (HbA_{1c}) values and increased time in range. Of note, 22.3% of patients analyzed were using sensor-augmented pump therapy with a predictive low-glucose suspend feature (ie, Basal-IQ technology). Patients using this system are still at risk for hypoglycemia because of insulin on board, exercise, overdosing on carbohydrates, and/or hyperglycemia, so a notification for predicted hypoglycemia using advanced machine learning models with good performance could still be clinically useful.

Limitations

A limitation of our approach is that transient hypoglycemic events were ignored in generating alerts. Ignoring the transient events helped the machine learning model better learn the more stable patterns of sustained events. Even though the alerts were focused on detecting sustained events, 61% of the transient events were still classified as FPs. This resulted in just 39% of the transient events (representing 13% of the total hypoglycemic events) not being detected. This trade-off was justified because transient events are not as serious as sustained hypoglycemic events. Transient events may occur because of random variations in glycemic levels (ie, noise) or temporal lag in the effect of an intervention taken by the patient (eg, consuming fast-acting carbohydrates). In either case, ignoring transient events will help in learning the stable patterns of sustained hypoglycemia. The improved FAR, sensitivity, specificity, and generalizability of the sustained hypoglycemia model presented in this paper justify this trade-off.

This study was based on patients with pediatric type 1 diabetes in the age range of 0 to 20 years using Dexcom G6 CGM devices. As such, the results are directly applicable to this population. The model may need to be recalibrated to other CGM devices such as the Guardian (Medtronic) or FreeStyle Libre (Abbott Laboratories Co.); however, the performance measures should be generalizable to other platforms provided the accuracy and frequency of incoming glucose readings remain the same. Similarly, while no specific activity profile of pediatric patients was explicitly used in the model development, the model may need to be calibrated to an adult cohort by retraining on adult CGM data [74-76]. Pediatric patients were selected as the focus of the study because of our collaboration in the United States Food and Drug Administration (FDA)–funded Southwest National Pediatric Device Innovation Consortium [77]. Additionally, there is a need for a paradigm shift in diabetes management in pediatrics to avoid risk of hypoglycemia to ameliorate parental and patient fear and move toward optimizing time in range and lowering HbA_{1c}.

Conclusions

Providing predictive alerts for hypoglycemia focused on sustained events instead of all hypoglycemic events reduces FARs and improves sensitivity and specificity. It also results in models that have better generalizability to new patients and time periods. This has important implications for sustaining CGM use and optimizing glycemic control with fewer hypoglycemic events, improved confidence, and potentially lower HbA_{1c}. To that end, the predictive model presented in this paper will be implemented in a smartphone app in an upcoming clinical pilot study at Texas Children's Hospital.

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This study involves the use of secondary analysis of deidentified data that were not collected specifically for this project and is not human subject research (Texas A&M IRB number 2019-0710).

Authors' Contributions

DDave, ME, and ML conceived the idea for the study. DDave implemented the model and analyzed the data. DDave and ME wrote the manuscript. All authors provided input and helped in revising the manuscript.

Conflicts of Interest

DDeSalvo serves as an independent consultant for Dexcom.

Multimedia Appendix 1
Patient hypoglycemia profile.
[PDF File (Adobe PDF File), 57 KB - diabetes_v6i2e26909_app1.pdf]

Multimedia Appendix 2
Patient pump profile.
[PDF File (Adobe PDF File), 68 KB - diabetes_v6i2e26909_app2.pdf]

Multimedia Appendix 3
Breakdown of sustained events by daytime and nighttime.
[PDF File (Adobe PDF File), 858 KB - diabetes_v6i2e26909_app3.pdf]

Multimedia Appendix 4
Breakdown of sustained and transient events.
[PDF File (Adobe PDF File), 46 KB - diabetes_v6i2e26909_app4.pdf]

Multimedia Appendix 5
Breakdown of sustained events.
[PDF File (Adobe PDF File), 48 KB - diabetes_v6i2e26909_app5.pdf]

Multimedia Appendix 6
Features extracted for prediction.
[PDF File (Adobe PDF File), 59 KB - diabetes_v6i2e26909_app6.pdf]

Multimedia Appendix 7
Receiver operating characteristic plot showing a comparison between different classifiers for giving out predictive alerts for 30-minute (top) and 60-minute (bottom) prediction horizons.
[PDF File (Adobe PDF File), 782 KB - diabetes_v6i2e26909_app7.pdf]

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Abbreviations

ARIMA: autoregressive integrated moving average
CGM: continuous glucose monitoring
FAR: false alert rate
FDA: Food and Drug Administration
FN: false negatives
FP: false positives
HbA1c: glycated hemoglobin A1c
PH: prediction horizon
QRF: quantile regression forest
RF: random forest
RMSE: root-mean-square error
ROC: receiver operating characteristic
TN: true negatives
TP: true positives

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Viewpoint

Technological Ecological Momentary Assessment Tools to Study Type 1 Diabetes in Youth: Viewpoint of Methodologies

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Abstract

Type 1 diabetes (T1D) is one of the most common chronic childhood diseases, and its prevalence is rapidly increasing. The management of glucose in T1D is challenging, as youth must consider a myriad of factors when making diabetes care decisions. This task often leads to significant hyperglycemia, hypoglycemia, and glucose variability throughout the day, which have been associated with short- and long-term medical complications. At present, most of what is known about each of these complications and the health behaviors that may lead to them have been uncovered in the clinical setting or in laboratory-based research. However, the tools often used in these settings are limited in their ability to capture the dynamic behaviors, feelings, and physiological changes associated with T1D that fluctuate from moment to moment throughout the day. A better understanding of T1D in daily life could potentially aid in the development of interventions to improve diabetes care and mitigate the negative medical consequences associated with it. Therefore, there is a need to measure repeated, real-time, and real-world features of this disease in youth. This approach is known as ecological momentary assessment (EMA), and it has considerable advantages to in-lab research. Thus, this viewpoint aims to describe EMA tools that have been used to collect data in the daily lives of youth with T1D and discuss studies that explored the nuances of T1D in daily life using these methods. This viewpoint focuses on the following EMA methods: continuous glucose monitoring, actigraphy, ambulatory blood pressure monitoring, personal digital assistants, smartphones, and phone-based systems. The viewpoint also discusses the benefits of using EMA methods to collect important data that might not otherwise be collected in the laboratory and the limitations of each tool, future directions of the field, and possible clinical implications for their use.

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KEYWORDS

ecological momentary assessment; continuous glucose monitoring; actigraphy; accelerometer; ambulatory blood pressure monitoring; personal digital assistant; mobile phone; smartphone; mHealth

General Introduction

Type 1 diabetes (T1D) is one of the most common chronic childhood diseases with a rapidly rising incidence and prevalence [1,2]. It is an autoimmune disease characterized by the loss of insulin-producing β cells of the pancreas, leading to an inability to use glucose as fuel, thus requiring life-saving exogenous insulin administration [3]. The management of glucose is challenging because patients must consider a myriad of factors when making diabetes care decisions (eg, insulin administration and glucose checks), such as the amount of carbohydrates consumed, insulin administered, physical activity, stress, illness, hormonal changes that cause natural spikes in glucose (eg, *dawn phenomenon*), and access to diabetes treatment technologies (eg, continuous glucose monitoring [CGM] and insulin pump) [4-6]. This complex web of factors and subsequent management decisions can lead to a significant amount of glucose variability throughout the day, with frequent

fluctuations between normal (euglycemia), high (hyperglycemia), and low (hypoglycemia) glucose levels [4]. In fact, research has shown that young children with T1D are in a hyperglycemic state approximately 50% of the time [7] and experience thousands of hypoglycemic events in their lifetime [8]. These types of glycemic states have been shown to be associated with short- and long-term complications, including, but not limited to, hypoglycemia (sometimes severe), diabetic ketoacidosis (DKA), heart disease, retinopathy, nephropathy, neuropathy, sleep disturbances, and cognitive impairments [9-11].

At present, most of what is known about each of these complications and the health behaviors that may lead to them have been uncovered in the clinical setting or laboratory-based research using medical record data extraction, retrospective interviews asking participants to recall information from past events, and tests that measure health over extended periods (eg, hemoglobin A_{1c} [HbA_{1c}]). However, there are known limitations with measurements of this type, given their inability to capture the dynamic behaviors, feelings, and physiological changes associated with T1D that fluctuate from moment to moment throughout the day. Importantly, these measurements can also be confounded by recall bias [12], thus limiting our capacity to characterize and understand T1D. A better understanding of T1D in daily life could potentially aid in the development of behavioral and pharmaceutical interventions to improve diabetes care and mitigate the negative medical complications often associated with T1D. Therefore, there is a need to measure repeated, real-time, real-world features of T1D in daily life. This approach, known as ecological momentary assessment (EMA), can include a variety of methods, such as handheld computers, diaries, phones, smartphones, activity trackers, and physiological monitors (eg, CGM and ambulatory blood pressure monitoring [ABPM]) [12]. These methods can provide more valid ecological representations of patients' experiences, behaviors, and physiological measures with in-the-moment collection of information [12]. Fortunately, the widespread use of EMA is becoming more feasible because of the lower cost, greater familiarity, and usefulness of ambulatory technological devices such as smartphones and activity trackers (eg, Fitbit), especially in youth [13-15]. As a result, the use of wearable devices to collect real-world data is becoming increasingly popular across a variety of scientific fields to better understand disease states in a person's natural environment [16].

The use of EMA to understand factors related to T1D in daily life may be particularly important in youth, as they typically have more challenges with glycemic control than other age groups with diabetes [17] and are reaching developmental milestones that could impact their daily glucose management behaviors. For example, youth may behave differently with their T1D care if they are in a group of peers they feel the need to fit in with, or act differently, as they begin to seek independence from their parents [18]. Furthermore, it has been suggested that youth may not have yet developed the full cognitive abilities needed to integrate the information and skills needed to make appropriate management decisions [19]. This limitation could be even more concerning in patients with T1D, as a rich body of the literature has shown that acute complications (eg, severe hypoglycemia and DKA) and chronic hyperglycemia measured in the laboratory are associated with lower cognitive scores [11]. Furthermore, youth may still be unburdened by medical complications that often accompany T1D later in life. EMAs could potentially provide a more sensitive tool for early tracking of T1D complications that may not yet be detected in a clinical setting. Taken together, EMA methods could provide insight into important daily factors that influence T1D care behaviors and track physiological changes that may be predictive of complications in this particularly vulnerable population.

This viewpoint aims to describe EMA tools that have been used to collect data in the daily lives of youth with T1D and discuss studies that explored the nuances of T1D in daily life. This viewpoint focuses on several methods used to assess behavioral and physiological measures, including CGM, actigraphy, ABPM, personal digital assistants (PDAs), smartphones, and phone-based systems. The viewpoint also includes a discussion of the benefits of using EMA methods to collect important data that might not otherwise be collected in the laboratory and the limitations of each tool, future directions of the field, and possible clinical implications of using these tools.

Overview of Methods Used to Identify and Assess EMA Tools

The following keywords were searched using the PubMed database between January and September 2020: ("type 1 diabetes" and "ecological momentary assessment"), ("type 1 diabetes" and "EMA"), ("type 1 diabetes" and "actigraphy"), ("type 1 diabetes" and "field study"), ("type 1 diabetes" and "smartphone app"), ("type 1 diabetes" and "smartphone"), ("type 1 diabetes" and "phone"), ("type 1 diabetes" and "personal digital assistant"), ("type 1 diabetes" and "PDA"), ("type 1 diabetes" and "mHealth"), ("type 1 diabetes" and "mobile health"), ("type 1 diabetes" and "wearable"), ("type 1 diabetes" and "electronic health"), ("type 1 diabetes" and "eHealth"), ("type 1 diabetes" and "sleep"), ("type 1 diabetes" and "ambulatory"), ("type 1 diabetes" and "accelerometer"), ("type 1 diabetes" and "CGM"). Each pair of search terms was combined with "youth," "adolescent," and "children." Articles were reviewed starting in 2005, given the rapid development of technology, particularly real-time CGM, around this year.

To narrow the focus of the viewpoint, articles for the *literature review* portion of each section were not typically included in our synthesis of the literature if youth with T1D were not the primary study population (eg, articles combining all youth and adult data and articles focused on the caregivers of youth with T1D); the article was a review, case report, book chapter, editorial, conference abstract, study protocol, or comment; the article was written in a language other than English; the study was conducted in an animal model; the article did not directly seek to obtain EMA measures multiple times per day on a technological device; the study was conducted entirely in an in-lab setting; physical activity was the primary focus of an actigraphy study; or the article focused on flash glucose monitoring versus CGM. This viewpoint was intended to provide an overview of popular EMA tools to collect data in youth with

T1D and provide a generally comprehensive but not exhaustive discussion of the articles that have used each tool.

Viewpoint of Methodologies

Continuous Glucose Monitoring

Introduction

It is becoming increasingly clear that HbA_{1c} has many limitations and is not the only important factor for measuring glycemic control and predicting the risk of medical complications in T1D [20]. Although glucose variability remains poorly understood, it has recently been highlighted as a potential risk factor for developing disease complications [21]. Understanding the importance of glucose variability is becoming much more feasible with the use of CGM technology, perhaps the most well-known EMA method used in T1D. Real-time CGMs typically measure interstitial glucose every 1-5 minutes via a sensor embedded under the skin, and information is then transmitted to a tracking device such as a smartphone app, receiver, or insulin pump [22-24]. Most current CGMs usually measure glucose every 5 minutes, with 288 measurements per day [24] compared with self-monitored blood glucose (SMBG), which is often only measured to test for hypoglycemia or in situations such as with meals, exercise, bedtime, or certain tasks (eg, driving). This can vary among participants but typically requires SMBG measurements 6-10 times per day [25]. Thus, the frequent testing of glucose with CGM provides a more comprehensive view of glucose patterns and variability over time compared with glucose snapshots provided by SMBG or HbA_{1c}. Data collected via CGM can provide information on glucose trends, the amount of time a person is in a specified glucose range (eg, euglycemia: 70-180 mg/dL), asymptomatic glycemic events, the amount of glycemic variability, the mean glucose over discrete periods (eg, 14 days), overnight glucose patterns—not typically captured with SMBG—and postprandial glucose peaks [22,25-29].

This more encompassing view of glucose patterns can aid health care providers in the development of optimized goals and plans aimed at improving glucose levels and mitigating negative medical complications [20]. CGM has also been shown to be *empowering* for youth with T1D, as it allows them to easily access data such that they can have more control over their glucose, provides motivation for dietary intake changes, and helps them manage hyper- and hypoglycemia [30]. As a result of these benefits, the use of CGM is increasing rapidly, especially in young children [31-33]. For example, CGM use in youth in a large diabetes registry increased from 4% to 31% between 2013 and 2017 [33].

Literature Review

Using CGM to Identify Relationships Between Daily Factors and T1D Symptoms and Behaviors

CGM data have been used to better help understand the relationship between daily activities, behaviors, and glucose control including diets and eating patterns [34-39], exercise or activities [40-50], sleep [51-53], amount of time spent at home (eg, before and during the COVID-19 lockdown) [54], and externalizing behaviors [55].

Using CGM to Measure Outcomes

Data collected with CGM have also provided an important tool for testing the feasibility and effectiveness of insulin delivery systems, insulin treatments, adjunctive diabetes medications, T1D screening, new glucose monitoring systems, algorithms for the promotion of improved glycemic control, sensor-augmented therapy algorithms, and closed-loop systems [56-91]; diabetes alert dogs [92]; education programs aimed at improving impaired hypoglycemia unawareness, daily therapy decisions, and cardiovascular health [93-95]; and use of glucose sharing data with others [96]. This technology has also been used to assess the relationship between continuous glucose measures and other diabetes-related outcomes, including long-term glycemic control, dysglycemia [97,98], future T1D diagnosis or dysglycemia in preclinical youth [99-101], HbA_{1c} [102-105], C-peptide [102], insulin sensitivity [106], severe hypoglycemia [107], time in target range [108-110], glucose variability [109-113], detection of hypo- or hyperglycemia [108-110,114-116], glycated albumin [104], fructosamine [104], and 1,5-anhydroglucitrol [104]. Furthermore, CGM has been used to determine the relationship between continuous glucose measures and other medical outcomes, including body composition [117], markers of inflammation [118], cardiovascular health [119], and brain health (eg, white matter integrity) [120].

Using CGM to Improve T1D

Thus far, there is substantial evidence to suggest that CGM use is associated with improved glycemic control, including lower or improved HbA_{1c}, reaching target HbA_{1c} [121-146], decreased hyper- or hypoglycemic events or time in a hyper- or hypoglycemic state [137,138,145-148], reduced SD or mean glucose [134,146], reduced glucose variability [134,137,148], and increased time in the target glucose range [127,137,146]. CGM use has also been shown to be related to improved treatment and outcomes, including more advanced and optimized treatment recommendations by physicians to improve glycemic outcomes [149,150], increased satisfaction with diabetes treatment [123,151], improved perceived awareness of or hormonal responses to hypoglycemia [123,152], reduced fear of hypoglycemia [153,154], reduced patient distress [139], and altered amount of insulin used per day (eg, both decreased and increased insulin use per day) [140,154]. Outside of direct diabetes outcomes, CGM use has been shown to be associated with a higher quality of life (when a new algorithm was used to help guide insulin administration) [155], improved school attendance [151], and increased comfort with diabetes management in the school setting [156].

Furthermore, studies have shown significant benefits of using CGM sensor-augmented pump therapy systems that can initiate automatic functions for suspending insulin in the event of current or predicted low-glucose and closed-loop systems. For example, predictive low-glucose suspension or hyperglycemia and hypoglycemia minimization functions have been shown to be related to improvements in HbA_{1c} [89], greater time in range [74], reduced mean glucose levels in the morning [74], reduced

area under the curve for hypoglycemia and hyperglycemia (eg, >240 mg/dL), and hypoglycemia [67,69,70]. Closed-loop systems have also been shown to improve T1D, including lower mean glucose [60,75,76,80,86], reduced frequency of hypoglycemia intervention [60,80], lower proportion of time or less time in hypoglycemia [68,72,80], and increased time in range or time in tight range of control (80-140 mg/dL) [68,75,76,85,86]. Furthermore, youth have expressed positive experiences with closed-loop systems, including self-reported positive impact on sleep, their routines, and safety [157]. Interestingly, a study evaluated the ability of a heart rate monitor to inform closed-loop system decisions with exercise and found that the incorporation of heart rate data into the closed-loop system improved time below a glucose level of 70 mg/dL even though it did not reduce the number of hypoglycemic events [48]. When comparing the 2 types of systems, studies have shown significant benefits for closed-loop systems versus sensor-augmented therapies with glucose suspend functions. For example, youth with closed-loop systems or control-to-range algorithms have been shown to have less time below the target range [71], reduced symptomatic hypoglycemia at night [71], increased time in range [75], and lower mean glucose [75].

Although there is a significant amount of evidence showing the benefits of CGM in improving T1D, it is important to note that not all studies have found statistically significant improvements in all measures between CGM users and CGM nonusers or with the initiation of CGM use across different time points and age groups [126,129,138,140,148,153,154,158-166]. The lack of evidence for the benefits of CGM could potentially be the result of the amount of time spent using the tool. For example, more and consistent use versus intermittent use, full compliance with the research protocol, age, baseline glycemic control, and self-efficacy with CGM use have all been suggested to be important factors for clinical improvements with CGM [56,122,124,131,132,134,140,148,159,161,167-169].

Limitations of CGM

It is clear that CGM has many advantages; however, there are limitations to its use. There is still the potential for measurement error, false alarms (eg, alert for hypoglycemia when the patient is euglycemic), alarms that do not awake patients at night [24,170-173], signaling loss-driven gaps in data, and data interpretation challenges [174]. The sensors can also be uncomfortable or painful or fall out, which is of significant concern given the high cost of the technology and difficulties with insurance coverage [24,171,173-179]. There can also be an annoyance or *alarm fatigue* with frequent alerts about glucose and sensor status, potentially causing patients to feel overwhelmed or embarrassed, especially in public environments [28,171,172,177,180-182]. Furthermore, the abundance of information provided by CGMs may cause anxiety, frustration, and self-thoughts of failure or that they have *bad* blood glucose patterns, especially if they have difficulty interpreting the substantial amount of data provided by CGM [24,28,174]. In the same vein, youth may fear chastisement from others (eg, parents and physicians) if they have frequent hypo- or hyperglycemic events that would not otherwise be observed with SMBG [24]. All these factors could significantly affect the adherence to CGM use. However, programs are being developed to help better teach youth how to overcome the challenges associated with CGM [183].

CGM Conclusions

Overall, frequent, repeated glucose measurements with CGM can provide great benefits over one-time snapshots of glucose. In addition to a significant enrichment of glucose information, CGMs could further enhance our knowledge of T1D when paired with other EMA methods to determine how in-the-moment behaviors are associated with subsequent glucose patterns and how glucose patterns relate to daily health (eg, sleep). CGM is growing in popularity among youth with T1D and has significant advantages over in-lab glucose measures or SMBG, as it provides a wealth of knowledge that can be used to better understand glucose fluctuations. However, there are still limitations to its use, such as inaccurate readings and discomfort, that need to be addressed in future technological development.

Actigraphy

Introduction

Actigraphy is a noninvasive, motion-sensing tool often worn on the wrist for extended periods to collect information about measures such as physical activity or sleep [184]. Sleep is of particular concern for youth with T1D, as research has shown consistent sleep disturbances compared with their peers without T1D [10], with an average of approximately 26 minutes less sleep per night [185]. Actigraphy provides numerous advantages over in-lab methods of collecting sleep data, as it is inexpensive and can be used to examine sleep patterns over multiple days [186-188]. Furthermore, it is relatively suitable for correctly identifying sleep periods in youth and can assess numerous facets of sleep (eg, sleep onset, sleep onset latency, frequency of nocturnal waking, duration of nocturnal waking, wake after onset, the midpoint of sleep, nap duration, total sleep period, wake time, total sleep time, sleep efficiency, fragmentation of sleep, and longest continuous sleep episodes) by repeatedly measuring movement and heart rate (with some, but not all trackers) [188]. Taken together, actigraphy offers an affordable and convenient method of measuring sleep at home, providing a unique means of collecting more information about how sleep is affected in the daily lives of youth with T1D.

Literature Review

Using Actigraphy to Identify Relationships Between Daily Factors and T1D Symptoms and Behaviors

Actigraphy has uncovered important relationships between sleep and diabetes care behaviors in daily life. For example, both average sleep duration and sleep variability have been shown to be associated with diabetes care behaviors (eg, less average sleep duration related to decreased SMBG or more sleep variability related to decreased SMBG) [189,190]. Furthermore, actigraphy-derived data have shown a relationship between HbA_{1c} and altered sleep (eg, more total sleep time related to lower HbA_{1c}) [51,189], found a relationship between sleep in children and sleep in their parents [191], and showed that youth with T1D who have obesity may have different sleep patterns compared with patients with T1D without obesity [192].

Importantly, actigraphy has uncovered relationships between specific patterns of glucose control (eg, greater glucose variability, more time in hypoglycemia, and suboptimal HbA_{1c}) and disrupted or variable sleep [53,193-195]. For example, Monzon et al [193] found that measures of sleep (eg, sleep onset latency and nighttime awakenings) predicted more variability in glucose on weekend days, highlighting the potential importance of maintaining consistent sleep routines throughout the week.

It is important to note that most of these studies were correlational and therefore could not determine the directionality of the relationship between sleep and glycemic control [51,53,189,190,195]. It has been suggested that there is bidirectionality in the relationship (eg, more glycemia outside of the recommended range increases the likelihood of hypoglycemia and hyperglycemia at night, which can then impair sleep [190]). Monzon et al [193] found a bidirectional association between glucose variability and awakenings on weekend nights, suggesting that youth with more weekend awakenings may have more glycemic variability in the following days and that youth may have more awakenings after weekend days where they have more glucose variability. They also suggest that future research considers how both physiology (eg, physiological changes in glucose) and behavior (eg, waking to check glucose at night) could explain the bidirectional relationship between glucose control and sleep [193].

Using Actigraphy to Measure Outcomes

Given that youth with T1D often have sleep impairments or do not meet current sleep recommendations [51,189,190,193-196], interventional strategies are needed to help improve sleep in this population; 2 recent studies found that smartphone app–based interventions improved sleep measured via actigraphy in youth with T1D. Jaser et al [197] found that their intervention improved sleep efficiency and increased total sleep time by approximately 48 minutes. Similarly, Perfect et al [198] found that their sleep intervention protocol increased actigraphy-measured sleep by approximately 29 minutes. These studies highlight the promise of mobile health (mHealth) interventions (ie, medical care supported by a mobile device) [199] to treat sleep in this vulnerable population. Furthermore, not only is actigraphy being used to assess whether these mHealth interventions can improve sleep, but it is also being used to determine whether new diabetes management systems (eg, hybrid closed-loop systems) can improve sleep among youth with T1D and their parents [200].

Limitations of Actigraphy

It is important to note that although actigraphy has been shown to be relatively sensitive in measuring sleep, not all studies have shown comparative results between actigraphy and the gold standard of sleep measurement—polysomnography—and it has been shown that actigraphy has low specificity for certain measures such as detection of wake after sleep onset [188]. It has been suggested that actigraphy may be a better tool for collecting typical sleep data and may be less reliable in adequately measuring disturbed sleep [186]. Furthermore, studies have used a wide range of tracking devices (eg, Fitbits and Actigraphs), which could potentially create discrepancies between results [188]. More tool development and validation testing are needed to measure sleep adequately, especially disrupted sleep.

Actigraphy Conclusions

Actigraphy is increasingly being used to assess sleep in youth with T1D. The EMA tool provides an inexpensive way to objectively measure sleep in the daily lives of youth in their natural environments. Studies have shown more sleep disturbances in youth with T1D, and these disturbances have also been shown to be related to important T1D self-care behaviors and glycemic control. Promising preliminary studies have shown the potential use of app-based interventions to improve sleep; however, more trials are needed. Furthermore, more validation testing and consistent tracker use should be considered in future studies.

Ambulatory Blood Pressure Monitoring

Introduction

Cardiovascular disease is a significant concern in patients with T1D. Unfortunately, in-office blood pressure measurements only capture a snapshot of blood pressure, which changes continuously throughout the day [201]. In-office monitoring is also influenced by masked hypertension (patients can have normal in-office blood pressure but elevated when measured 24 hours per day out of the office) and the white-coat phenomenon (patients have elevated blood pressure when measured in the office but have normal blood pressure in daily life) [202]. Specific to youth with T1D, 9.5% have been shown to have masked high blood pressure, whereas 32% have been shown to have white-coat hypertension [203]. To mitigate these phenomena and better assess the impact of circadian rhythms on blood pressure, researchers and clinicians have turned to ABPM as a tool to collect EMA data on heart function [202,204,205]. Importantly, a more accurate determination of heart function using the EMA tool could lead to a more appropriate use of blood pressure medications [206]. ABPM is typically measured via an ambulatory blood pressure cuff every 15-20 minutes during the day and every 20-30 minutes at night (varying by study), providing a large amount of information on blood pressure and heart rate variability in varying contexts [201].

Literature Review

Using ABPM to Measure Outcomes

A large number of studies have used ABPM to measure cardiovascular function outcomes in youth with T1D and found that patients often have high blood pressure measures (eg, high systolic or diastolic pressure at different times of day), prehypertension, or higher blood pressure than their peers who do not have T1D [203,207-225], with higher blood pressure–measured with ABPM being predictive of future hypertension [220]. Many factors have been found to be associated with measures of high blood pressure in this population, including higher HbA_{1c} [208,209,215,226], age [209], sex [208,209], diabetes duration [208,209,214,225,226], unstable glycemic control [225], insulin dose [209,215,225], BMI [209,215,226], genetics [227,228], triglycerides [214],

high salt intake [226], and selectins involved in inflammation (eg, E-selectin) [214,229].

People without T1D typically have a dip in nocturnal systolic and diastolic blood pressure by approximately 10%-20% from daytime blood pressure [201]. However, research using ABPM has consistently shown that patients with T1D often do not have this normal *dip* or have less dipping than youth without T1D [207,209,218,221,222,224,230-234]. This abnormal dipping has been shown to be related to age, sex (ie, being female associated with more abnormal dipping) [209], HbA_{1c} [209,226], higher ambulatory arterial stiffness—a potential marker of arterial stiffness to predict heart mortality [232], reduced 24-hour heart rate [233,234], reduced mean daytime heart rate [233,234], prolonged QT interval (interval from the Q to the T electrical wave), greater left ventricular end-diastolic and end-systolic diameters [233,234], greater left ventricular mass index [234], and specific heart oscillation patterns [235]. In addition, not only does high blood pressure present a problem in itself, but it is also associated with other negative medical complications. In fact, several studies have found a relationship between high blood pressure measures obtained with ABPM and markers of kidney damage or disease in youth with T1D [211,215,220,222,236-239].

Although there is substantial evidence for increased blood pressure in youth with T1D, not all studies have found robust, statistically significant relationships between diabetes and high blood pressure across contexts [240,241]. For example, Raes et al [240] found no significant difference in blood pressure between youth with T1D and those without T1D when participants were at rest but observed significantly higher blood pressure in patients with T1D while they were participating in exercise. Furthermore, not all studies have found a relationship between blood pressure and markers of kidney damage [218,242]. For example, Soltysiak et al [242] found no relationship between blood pressure and increases in neutrophil gelatinase-associated lipocalin, an early marker of kidney damage.

Limitations of ABPM

ABPM use in research is limited by the potential interference it presents with a patient's activities in daily life and inaccurate readings if the cuff is placed incorrectly during measurement [243]. Therefore, more research is needed to develop less intrusive and more valid devices or protocols. Furthermore, the nocturnal dipping status may not be consistently reproducible. Thus, it has been suggested that the focus of research is on 24-hour systolic blood pressure versus dipping status [206].

ABPM Conclusions

ABPM provides an excellent tool for measuring real-world heart function while avoiding potentially confounding variables, such as the white-coat phenomenon and masked hypertension, which might otherwise conceal heart function complications when measured in a laboratory setting. The use of this EMA method has uncovered important heart function complications in youth with T1D. Overall, blood pressure measurements obtained from ABPM have consistently been shown to be elevated in youth with T1D, and this increased blood pressure has been associated with markers of kidney damage. Thus, real-world testing could highlight the need to conduct earlier tracking of heart function and interventions in youth with T1D.

Personal Digital Assistant

Introduction

All of the EMA tools discussed so far have passively collected repeated, real-time data such that the patients did not consciously and purposefully have to interact with the device. To collect more information about a patient's conscious behavior or perceived experiences, more active EMA methods are needed, such as PDAs. PDAs are often referred to as handheld computers, as they can connect to the internet, be used to organize information, and communicate via email or a personal computer [244]. Although PDAs can function similarly to more recent technological developments (eg, smartphones), supplying PDAs to participants could help reduce limitations related to patients not having their own devices or owning devices that are not compatible with the study software.

Literature Review

Using PDAs to Identify Relationships Between Daily Factors and T1D Symptoms and Behaviors

Several studies have been conducted using PDAs to determine how environmental factors impact patient experiences and diabetes care behaviors in youth with T1D in real-world settings. For example, Helgeson et al [18] had patients complete periodic measures of interpersonal interactions (eg, had the participant had a social interaction? Was the interaction positive or negative?) and mood on a PDA throughout the day and found that less enjoyment and being upset from a social interaction predicted depressed mood and anxiety. PDA devices also found that patients were more likely to check their glucose when they reported a strong desire to blend in with their companions and less likely to check glucose when they wanted to impress people [245]. Taken together, the results suggest that peer relationships in daily life are associated with self-care behavior and psychological well-being in youth with T1D.

As described in the *General Introduction*, lower cognitive scores have been shown to be associated with severe hypoglycemic events, DKA, and chronic hyperglycemia when measured in a laboratory setting [11]; thus, it is important to understand how momentary cognitive function is related to T1D in daily life. Gonder-Fredrick et al [246] had patients use a PDA device to determine the relationship between SMBG and cognitive function (ie, mental math and reaction time task) in a real-world setting. Performance was worse during periods of hypoglycemia (<54 mg/dL) and hyperglycemia (>400 mg/dL) compared with euglycemia (although not statistically different for hyperglycemia and the reaction time task). Thus, mental efficiency is altered by hypo- and hyperglycemia in the daily lives of youths with T1D [246]. Importantly, it is possible that cognitive impairment is not only affected by glucose levels but may also affect subsequent glucose levels through poor T1D care decisions. More research is needed to better understand the complex relationship between glucose levels, cognitive impairment, and T1D care decisions.

Using PDAs to Measure Outcomes

PDA devices have also provided important information on T1D outcomes in daily life. Gonder-Fredrick et al [247] assessed real-world glucose symptoms in which youths were asked to estimate their current blood sugar and rate symptoms on a PDA (with the help of a parent) immediately before measuring SMBG. The youths struggled to correctly estimate glucose, making clinically accurate estimates less than one-third of the time and did not detect >40% of hypoglycemic episodes. Children less accurate in detecting low glucose levels also had more severe low blood sugar levels in the subsequent 6-month period. This inability to recognize hypoglycemia is problematic and suggests that more education may be needed to improve the detection of low glucose levels in this population [247].

Limitations of PDA

As with most EMA methods that require self-report, there can be uncertainty about the validity of the data, given that they are collected without researcher or clinician supervision [248]. Therefore, it is possible that someone other than the participant is completing the measure or that the patient is not fully dedicated to the task at hand. With the technological nature of PDAs, there is always the risk of software and hardware issues [12] (eg, poor connection to the system transmitting the data). Furthermore, as with most EMA studies, there is a significant concern with testing compliance [12] and dropping out when asked to use these devices in everyday life. Finally, PDAs may now be less available as they have been replaced with smartphones.

PDA Conclusions

PDAs have captured complex relationships and nuances that could significantly impact a patient's daily life, which might otherwise be lost if measured only in a clinical or laboratory setting. Several psychosocial and contextual factors have been found to be associated with T1D self-care behavior and psychological well-being, such as wanting to fit in and wanting to impress others. Research has also revealed information about T1D symptoms in the real world, including undetected hypoglycemia and impaired cognitive function. Information collected via PDAs could potentially help provide an avenue for directly addressing these factors to improve T1D management and treatment.

Smartphone Apps and Phone-Based Systems

Introduction

The use of phones to collect EMA data is becoming more feasible as their ownership in childhood and adolescence continues to increase. In those aged 8-12 years, phone ownership increased from 24% to 41% between 2015 and 2019, and in those aged 13-18 years, ownership increased from 67% to 84% [14]. Phone ownership has been shown to be even more common in youth with T1D, with a study reporting that over 92% of patients aged ≥12 years (n=279) carry a phone in their daily lives [249]. The increased feasibility provides an ideal window for the development of new assessment platforms using these tools. As with PDAs, phones can collect data in a variety of ways. For example, they can prompt participants with a notification to enter information at fixed or random intervals throughout the day, or patients could be instructed to upload diabetes information when applicable (eg, when they miss an insulin dose, they tell an app what was happening in their lives at the moment that led to the missed dose).

Literature Review

Using Smartphone Apps and Phone-Based Systems to Identify Relationships Between Daily Factors and T1D Symptoms and Behaviors

Researchers have developed several smartphone apps to collect EMAs in pursuit of assessing environmental factors related to T1D care behaviors. For example, the *MyDay* smartphone app developed by Mulvaney et al [250] was used to identify psychosocial and contextual factors that impact self-care behaviors (eg, SMBG and insulin administration) in youth with T1D and found that patients reported significant social and contextual barriers to T1D management, including being with family, friends, and alone, fatigue, hunger, having fun, and being in a rush. Importantly, some of the barriers were shown to be significantly associated with self-care behaviors (eg, fatigue was associated with more missed insulin administration) [250], highlighting the potential for tailored treatments to address specific environmental barriers.

Several apps and systems have also been developed that synchronize cellphones to glucometers, allowing patients to upload glucose readings to their phones (eg, SMBG and CGM readings) or synchronize their glucose to their parents' phones. These apps and systems have also been designed to include features that allow a patient to manually log blood glucose, carbohydrate intake, meals, exercise, medications, insulin pump basal and bolus settings, glucose trends, illness, or life events (eg, vacation), often providing users with an integrated view of the myriad of daily factors that could affect glycemic control. Several of the apps include chat rooms for youth with T1D to communicate with one another, functions that allow patients to contact health care providers, reminders for patients to participate in T1D self-care behaviors, insulin and carbohydrate calculators, tips for diabetes treatment, information about T1D, and gamification incentives for participating in diabetes self-care behaviors [19,251-266].

For example, the *DiaMob* app was partly developed to help patients understand carbohydrate counting and insulin dosing. Participants were asked to provide information about physical activity around mealtimes and the amount of insulin needed to account for carbohydrate intake and capture a photograph of their food. Glucose data could also be integrated to provide an all-inclusive app interface with information about glucose levels, activity, insulin dosage, and meal composition. The results revealed that patients consumed more carbohydrates than they expected and, in the beginning, miscalculated the insulin dosage required to account for carbohydrate intake. Patients found the app supportive for diabetes management, feeling that observing their food made them more mindful of their eating habits and helped them calculate carbohydrates more accurately [19]. A previous study using the app found that participants thought the pictures, physical activity information, integration of pre- and postprandial glucose measurements, and insulin dosages helped

them develop a better understanding of how those factors impact glucose measurements [251].

Text message– and phone call–based systems have also been used to collect EMA [252,267-269]. For example, Warnick et al [269] recently tested the accuracy of self-reported SMBG and identified in-the-moment factors that create barriers and motivation for SMBG checks via text surveys. They found that only 39.6% of self-reported SMBG values were accurate, with health being a motivator for SMBG checks, whereas forgetting, not having their devices, and ignoring diabetes tasks were reported as barriers [269]. Furthermore, phone call–based systems have been developed to determine what real-life dietary factors (eg, carbohydrate intake, fiber intake, and physical activity) impact glucose fluctuations and diabetes self-care behaviors (eg, SMBG checks and insulin administration) [270,271]. For example, Mulvaney et al [271] used an automated, interactive touch-tone telephone response system to determine the environmental factors influencing SMBG checks and insulin administration. Overall, participants reported missing more glucose checks in the morning (59.4%) than in the afternoon (27.5%) or evening (13.2%). Participants also reported missing more insulin doses in the morning (74.1%) than in the afternoon (17.9%) or evening (8.0%) [271], suggesting that mornings may be particularly challenging for youth with T1D. This information, which may otherwise have been missed if collected in a laboratory setting, could potentially provide a unique target for more tailored interventions addressing challenges with morning routines.

Using Smartphone Apps and Phone-Based Systems to Improve T1D

The apps and phone-based programs often include educational components (eg, teaching T1D-related information, promoting problem-solving skills, reminders to participate in diabetes care behaviors, positive psychology interventions, and cognitive behavioral treatments) with the goal of improving T1D self-care and glycemic control [272-284]. These app and phone-based mHealth programs have been shown to be related to improved glycemic control (eg, lower HbA_{1c}, mean blood glucose, mean fasting glucose, and postprandial glucose levels), increased frequency of SMBG testing, reduced frequency of hypoglycemia, improved quality of life, decreased disengagement coping, reduced parental intrusions in diabetes care for youth who checked glucose regularly, reduced urgent diabetes-related calls by school nurses, decreased hospitalizations, reduced emergency department visits, increased feelings of safety, increased confidence, decreased worry over hypoglycemia, and increased T1D self-care compliance [13,254,255,257,258,262,263,272,273,276-278,280,285,286]. For example, the SuperEgo system was designed to provide patients with individually tailored texts on topics such as stigma, burnout, stress, and sports and exercise with regard to T1D. They found that the intervention group maintained their HbA_{1c} level, whereas the control group had an increased HbA_{1c} level [272]. These tools can also be integrative such that participants receive momentary feedback about their T1D treatment based on the information they log in the app or phone system. For example, Bin-Abbas et al [276] found that youth in an intervention where patients sent glucose readings to their T1D management team and received feedback (eg, how to adjust insulin dosage to avoid dysglycemia) had improved T1D control.

Importantly, these studies have revealed that certain patient characteristics may make a child with T1D more likely to respond to phone-based systems. For example, Herbert et al [268] found that girls and patients who said they sent a large amount of personal texts in their daily lives were more likely to respond to a text message–based intervention. Furthermore, Bergner et al [275] found that youths with T1D found a text-based system for a positive psychology intervention more acceptable than phone call–based systems. However, although some studies have found that app- and phone-based program usage can improve T1D not all found statistically significant differences [282,287], and some found increased patient burden. For example, studies have shown increased conflict in families with app usage, including an increased perception of conflict about logging blood sugars, a sense of increased *nagging* from parents if the youths checked their glucose irregularly, decreased caring behaviors from parents, and increased unsupportive behaviors from parents [263,281].

Social app platforms have also been considered for better understanding and treating T1D in youths in their daily lives. For example, a study found that participants wanted to incorporate a social platform in a diabetes decision tool app [288], whereas another study used the Instagram social platform as a tool to collect data about what T1D looks like in daily life [289]. However, it is important to note that youth with T1D could also potentially feel pressured or discouraged by social media if they observe others posting about *perfect* blood glucose levels if they do not obtain similar readings. This is concerning as research has shown a relationship between comparison in social media and poor mental health [290]. Furthermore, there can be misleading information on social media about diabetes and health [291], which could potentially be harmful to self-care in youth.

Limitations of Smartphone Apps and Phone-Based Systems

The limitations associated with smartphone apps and phone-based systems are similar to those described for PDA. However, there are additional limitations. If a study uses a *bring-your-own-device* protocol, there may still be a sizable number of participants who do not own a device, resulting in selection bias if only individuals in higher economic groups have access to their own device. A *bring-your-own-device* platform might also require the development of different smartphone app versions (eg, iOS and Android) as participants may have a variety of phone types (eg, iPhone vs Android) that may not be compatible with the same app version. Finally, there may be concerns about damage to a participant's own device or a study-provided device, such as cracked screens, that may interfere with data collection. On the other hand, if the study needs to provide a device for all participants, there could be study cost challenges.

Smartphone Apps and Phone-Based Systems Conclusions

Overall, smartphone apps and phone-based systems can provide a platform for collecting information that helps paint a more detailed picture of the daily experiences and challenges youth with T1D face that may not be otherwise captured reliably if assessed retrospectively in a laboratory or clinical setting. Thus far, numerous psychosocial and contextual factors have been found to be associated with T1D self-care behavior, such as fatigue, time of day, inaccessible devices, forgetfulness, and ignoring diabetes tasks. Taken together, this knowledge could potentially promote more defined interventional targets for improved glycemic control in youth with T1D (eg, developing different morning routines to promote self-care) that could potentially be delivered via an mHealth platform.

Discussion

Principal Findings

Overall, EMA has been used to better understand T1D in the daily lives of youth. EMA collection methods can provide significant advantages over in-lab testing, which may be confounded by phenomena such as recall bias and changes in behavior that result from the mere fact of being observed (eg, white-coat phenomenon) [12,202]. These methods also have the benefit of producing a much richer data set to better describe patterns of physiological and behavioral responses in T1D versus one-time snapshots.

EMA tools have already provided important information on care behaviors, physiological fluctuations, and complications of T1D that youth can experience in everyday life. CGMs have provided a great deal of information on glucose patterns, actigraphy has highlighted daily sleep challenges, and ABPM has shown the prominence of abnormalities in blood pressure and heart function in young people with T1D that can lead to other complications such as kidney disease. PDAs, smartphone apps, and phone-based systems have also uncovered numerous psychosocial and contextual environmental factors associated with T1D self-care (eg, wanting to fit into a group or time of day) and the negative consequences of glucose outside the recommended range (eg, cognitive impairment) [18,246,250]. Preliminary studies have also shown that smartphone apps and phone-based systems provide a potential platform for mHealth interventions for T1D and other conditions, such as impaired sleep [197,198].

Given the significant benefits of EMA, there is a great need for its expansion to study T1D-related factors in the daily lives of youth. Larger and more diverse study samples are of the utmost importance. Including individuals with newly diagnosed T1D could provide the opportunity for clinicians to intervene with behaviors that can lead to medical complications early before they are established versus trying to eliminate them later in the course of the disease. EMA methods may also provide an opportunity to reach populations currently underrepresented in research, such as those with lower socioeconomic status, racial or ethnic minority status, or those living in rural areas that may have less access to clinics and research facilities [292,293]. This is especially important because some of these populations have consistently been shown to have worse T1D-related outcomes [294]. Furthermore, EMA methods are less dependent on physical laboratory space, which may be an advantage in circumstances when there are barriers to access, such as during the COVID-19 pandemic or for patients who have barriers to travel to the laboratory.

Future research should also expand the use of combined EMA method systems. An area in which this combination could be particularly helpful is measuring the relationship between glucose patterns and T1D complications in daily life, such as cognitive impairment (eg, glucose measured via CGM or cognitive function measured via testing on a smartphone app). Given that acute T1D complications and chronic hyperglycemia have been associated with acute and long-lasting cognitive differences when measured in the laboratory [11] and the relationship between SMBG and cognitive impairment in Gonder-Fredrick's EMA study [246], it is essential to better understand the relationship between daily glucose patterns measured via CGM and cognitive function in the real world, especially considering that youths spend about 25% of their time participating in school activities during the academic year [295,296], which requires substantial, ongoing cognitive effort using cognitive functions that can fluctuate throughout the day [297-301].

There may also be other fluctuating short-term complications associated with daily glycemic changes to be explored, such as vision. In-lab research has shown that short-term fluctuations in glucose can significantly alter nerve function and morphology in the eye [302]. Given that youths can have significant glucose variability [7], it is possible that they may experience daily vision changes. Research studies using EMA methods could be conducted to determine how frequently patients experience vision changes throughout the day and whether regular disruptions predict long-term complications such as retinopathy.

Furthermore, psychiatric conditions are more common in individuals with T1D than in those without T1D [303]. EMA methods can be used to gain better insight into the patterns of psychiatric symptoms in daily life. For example, one could collect repeated information about anxiety to determine whether its origin is T1D related, given that symptoms of glucose variability and feelings of anxiety can overlap (eg, shakiness and sweatiness because of hypoglycemia or because of nerves over a school exam). The timing of symptoms could also be evaluated to determine if there is a relationship between these symptoms and glucose fluctuations (eg, anxiety is higher with frequent swings in glucose). This information could potentially be used to aid therapists and medical care teams in tailoring behavioral interventions to help ameliorate symptoms when they are most severe.

More sophisticated analytical systems could also be used to better integrate data from different EMA modalities (eg, machine learning) for a more fully developed model of factors that predict T1D self-care behaviors or disease complications. The rapid development of new T1D care systems, such as the closed-loop system, makes this a unique time to conduct such combination EMA studies. EMA data collection could also be combined

with mHealth interventional platforms to make treatment adjustments in real time, as youths appear to enjoy technology platforms. Furthermore, these technology-based interventions may provide motivation, self-efficacy, and adherence benefits [304]. The implementation of mHealth interventions while simultaneously collecting in-the-moment data could potentially help individualize treatment by providing a type of precision-based medicine.

General Conclusions

In conclusion, as shown in the textboxes (Textboxes 1 and 2), EMA methods such as CGM, actigraphy, ABPM, PDAs, smartphone apps, and phone-based systems have unique strengths that can help the field better understand T1D in the daily lives of youth. Such an understanding could potentially lead to tailored interventions to improve quality of life and reduce the risk of short- and long-term complications of T1D. However, the field is still in its infancy and should be expanded in future research to address the limitations of each tool.

Textbox 1. Strengths of popular technological ecological momentary assessment tools to measure type 1 diabetes in the daily lives of youth, including continuous glucose monitoring, actigraphy, ambulatory blood pressure monitoring, personal digital assistants, and phone app, call, and text-based systems.

Continuous glucose monitoring

- Increased amount of glucose data
- More comprehensive glucose patterns
- Improved diabetes management and outcomes
- Provides a sense of empowerment for youth

Actigraphy

- Inexpensive
- Noninvasive
- Objective; more valid than self-report
- More comprehensive view of sleep patterns
- Records numerous measures of sleep
- Captures sleep in the natural environment

Ambulatory blood pressure monitoring

- Provides large amounts of data
- Measures heart function across daily contexts
- Avoids confounding in-lab factors (eg, white-coat phenomenon)

Personal digital assistant

- Captures complex relationships between diabetes-related variables in real life
- Connects to the internet for data upload
- Organizes information

App, call, text

- Captures complex relationships between diabetes-related variables in real life
- Typically with a participant in real time
- Potential platform for treatment intervention

Textbox 2. Limitations of popular technological ecological momentary assessment tools to measure type 1 diabetes in the daily lives of youth, including continuous glucose monitoring, actigraphy, ambulatory blood pressure monitoring, personal digital assistants, and phone app, call, and text-based systems.

Continuous glucose monitoring

- Expense and insurance difficulties
- Sensor discomfort
- Alarm fatigue
- Psychological toil (eg, anxiety)
- Measurement errors

Actigraphy

- Low specificity
- Imperfect measure of atypical sleep
- Not always comparable with polysomnography
- Variable device use across studies

Ambulatory blood pressure monitoring

- Potential obstacle in daily life
- Inaccurate readings

Personal digital assistant

- Validity concerns
- Testing compliance difficulties

App, call, and text

- Validity concerns
- Expensive equipment
- Hardware and software issues
- *Bring your own device* can lead to selection bias (eg, only recruiting those able to afford devices)
- *Bring your own device* can lead to data collection difficulties (eg, cracked screens)
- Testing compliance difficulties

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Authors' Contributions

MKR wrote the first draft of this manuscript. All authors (MKR, AM, MRS, JN, and TH) developed the review design, critically reviewed the manuscript, and edited the manuscript.

Conflicts of Interest

MRS has family reporting stock in Pfizer. Other authors declared no conflict of interest.

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Abbreviations

ABPM: ambulatory blood pressure monitoring
CGM: continuous glucose monitoring
DKA: diabetic ketoacidosis
EMA: ecological momentary assessment
HbA_{1c}: hemoglobin A_{1c}
mHealth: mobile health
PDA: personal digital assistant
SMBG: self-monitored blood glucose
T1D: type 1 diabetes
WUSTL: Washington University in St. Louis

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Original Paper

Improving Management of Type 2 Diabetes Using Home-Based Telemonitoring: Cohort Study

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Abstract

Background: Diabetes is present in 10.5% of the US population and accounts for 14.3% of all office-based physician visits made by adults. Despite this established office-based approach, the disease and its adverse outcomes including glycemic control and clinical events tend to worsen over time. Available home technology now provides accurate, reliable data that can be transmitted directly to the electronic medical record.

Objective: This study aims to evaluate the impact of a virtual, home-based diabetes management program on clinical measures of diabetes control compared to usual care.

Methods: We evaluated glycemic control and other diabetes-related measures after 1 year in 763 patients with type 2 diabetes enrolled into a home-based digital medicine diabetes program and compared them to 794 patients matched for age, sex, race, BMI, hemoglobin A_{1c} (HbA_{1c}), creatinine, estimated glomerular filtration rate, and insulin use in a usual care group after 1 year. Digital medicine patients completed questionnaires online, received medication management and lifestyle recommendations from a clinical pharmacist or advanced practice provider and a health coach, and were asked to submit blood glucose readings using a commercially available Bluetooth-enabled glucose meter that transmitted data directly to the electronic medical record.

Results: After 1 year, usual care patients demonstrated no significant changes in HbA_{1c} (mean 7.3, SE 1.7 to mean 7.3, SE 1.6; P=.41) or changes in the proportion of patients with HbA_{1c}≥9.0 (n=117, 15% to n=113, 14%; P=.51). Digital medicine patients demonstrated improvements in HbA_{1c} (mean 7.3, SE 1.5 to mean 6.9, SE 1.2; P<.001) and significant changes in the proportion of patients with HbA_{1c}≥9.0 (n=107, 14% to n=49, 6%; P<.001), diabetes distress (n=198, 26% to n=122, 16%; P<.001), and hypoglycemic episodes (n=313, 41.1% to n=91, 11.9%; P<.001).

Conclusions: A digital diabetes program is associated with significant improvement in glycemic control and other diabetes measures. The use of a virtual health intervention using connected devices was widely accepted across a broad range of ethnic diversity, ages, and levels of health literacy.

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KEYWORDS

diabetes; digital health; ehealth; digital medicine; connected devices

Introduction

The confluence of population trends, poor health outcomes, and rising costs of care make diabetes management a high global priority for health care [1]. In 2019, nearly half a billion people (9.3% of adults aged 20-79 years) were living with diabetes worldwide, representing a 62% increase from 10 years ago [2]. According to the US Centers for Disease Control and Prevention and the 2016 National Ambulatory Medical Care Survey, diabetes is the seventh leading cause of death, present in 10.5% of the US population, and accounts for 14.3% of all office-based physician visits made by adults [3,4]. Diabetes ranks the highest among all disease categories in health care spending, with expenditures per capita approximately 2.3 times higher than people without diabetes [3,5,6]. Moreover, 40% of the cost of diabetes is associated with the cohort whose hemoglobin A_{1c} (HbA_{1c}) values are 9.0% or greater [7].

Although progress has been made to improve risk factors for microvascular and macrovascular disease in diabetes, approximately half of individuals with diabetes do not meet individualized targets for HbA_{1c}, and less than 15% meet all three targets of glycemic control, blood pressure, and low-density lipoprotein (LDL) cholesterol [8-10]. Moreover, outcomes such as emergency department visits, lower extremity amputations, hospitalizations for hyperglycemic crisis, and deaths due to diabetes have worsened over the past decade [10,11].

Several factors account for these poor outcomes, including the use of suboptimal numbers or doses of medications, therapeutic inertia, lack of patient engagement, and limited resources and time to educate and provide lifestyle recommendations [12,13]. Although many types of interventions have been tested, recent reviews conclude that what is needed is a reorganization of clinical practice using care teams that empower nonphysician clinicians to adjust diabetes therapy from algorithms developed in collaboration with other team members [14-16].

Home blood glucose monitoring with direct transmission of data to the medical record addresses several limitations of traditional office-based care, including a larger sample of biologic data and an ability to take more timely action including therapy modifications [17-19]. Current technology including Bluetooth-enabled digital glucometers is accurate and easy to use, and automatically transmitted home-based glucose measurements have the capacity to better identify hypoglycemic events.

We sought to evaluate the effectiveness of a remote, home-based telemonitoring program in a clinical setting using commercially available technologies on glycemic control in adults with type 2 diabetes (T2D).

Methods

As part of a quality improvement initiative, adult patients with the diagnosis of T2D at the Ochsner Health System (a large integrated delivery network based in New Orleans, LA) were offered enrollment into a digital diabetes program by their physician during an office encounter or through an offer letter. Patients were required to possess a smartphone, purchase a Bluetooth connected glucose meter (iHealth Smart) that had direct access to the electronic medical record (EMR; Epic Systems), and have an active account in the patient portal (MyChart). If patients did not have an active patient portal account, they were given the opportunity and online assistance to sign up for one. Program details, questionnaires, and electronic consent to participate took place online through MyChart. Questionnaires assessed factors related to diabetes and chronic disease management, including diet, physical activity, depression, medication adherence, patient activation, health literacy, and social circumstances (eg, medication affordability and number of people living in home). Diabetes-related emotional distress was assessed using the Diabetes Distress Scale [20,21]. Health literacy was measured using the single item literacy screener [22]. Additional clinical data was obtained from the EMR, including serum glucose, HbA_{1c}, lipid levels, creatinine, estimated glomerular filtration rate (eGFR), thyroid function tests, urine protein, and BMI as well as completion of a retinal examination. This data was used to create a patient phenotype that assisted in the design of the intervention process. As an example, a poorly controlled individual with low health literacy and financial stress would be differentiated from an individual with high patient activation and reduced physical activity. Digital glucose meters were obtained, and initial training and setup was provided at the Ochsner O Bar, a patient-facing service that provides information, training, and tech support for patients interested in apps, wearables, and connected home devices [17]. All blood glucoses obtained via the patient's home glucometer were automatically transmitted via Bluetooth to the MyChart phone app and thus were available to the management team within the medical record. Hypoglycemia was defined as a blood glucose measurement less than 70 mg/dl, level 1 hypoglycemia as 54 to 70 mg/dl, level 2 as 40 to 54 mg/dl, and level 3 as less than 40 mg/dl.

A second control group of patients who met all eligibility criteria but whose physician was either not participating in the program or did not choose to enroll patients were followed. Of these, 794 patients were propensity matched to the digital medicine group according to age, sex, race, BMI, HbA_{1c}, creatinine, eGFR, and insulin use, and were followed as a usual care group over time.

Doctoral pharmacists, advanced practice providers (APPs) including nurse practitioners and physician assistants, and health coaches participated in the intervention that included education, lifestyle recommendations (medical nutrition therapy and appropriately prescribed physical activity), and medication management as per diabetes guidelines [16,23]. Each health coach had a background in a lifestyle intervention field (eg, nutrition and exercise specialist) or in public health.

Each doctoral pharmacist, APP, and health coach received training in diabetes management and education as well as use of the custom tools within the EMR created to facilitate optimal management [17,19]. Doctoral pharmacists, APPs, and health coaches were also educated regarding the importance of patient

activation and methods used to enhance engagement and lifestyle change [24-26].

Pharmacists and APPs contacted patients by phone and discussed screening results and treatment options for achieving glycemic control. Patients were encouraged to actively participate in their diabetes management and collaborated with the doctoral pharmacist or APP to cocreate the treatment plan by choosing among various lifestyle and medication recommendations [27]. Current American Diabetes Association guidelines were used by the pharmacy team for medication management [28]. Patients were also directed to a dedicated diabetes education website that offered further educational and lifestyle materials including custom videos and downloadable handouts.

Patients with medication affordability issues were, as much as possible, switched to generics or less expensive combination agents and, when appropriate and feasible, enrolled in medication assistance programs. Those with medication adherence issues were provided educational materials, pill reminder apps and resources, and a simplified medication regimen when possible.

Patients received monthly reports by mail and electronically detailing their progress, including HbA_{1c} and upcoming health maintenance metrics as well as lifestyle tips based on their screening phenotype. Physicians also received monthly reports on their patient's progress including blood glucose control and health maintenance metrics. Incoming glucose data was analyzed via internally developed algorithms as to its validity and directional change, and alerts were established to highlight which patients needed what intervention and when. Individualized targets for HbA_{1c} were created based on current guideline recommendations [16].

The primary outcome was the proportion of patients achieving their glycemic control. Secondary outcomes included incidence of hypoglycemia and achievement of health maintenance measures (HbA_{1c} measurements, retinal imaging for retinopathy, and screening for diabetic kidney disease).

To assess association between the digital medicine program for diabetes and patient outcomes, general linear models were used [29]. Distributions of outcomes were assessed, and all were approximately normally distributed. For each outcome, an unadjusted model containing only a main effect for digital medicine (vs usual care) and a multivariable model incorporating covariates were constructed. The multivariable model included covariates for patient age, sex, and race. Additional covariates for baseline fasting glucose and baseline eGFR were included in the model for HbA_{1c}. The response variable in each model was the change in the outcome from baseline to 12 months. Results are presented as means and SEs of the changes within each group (digital medicine and usual care), differences in group means, 95% CIs, and *P* values. To evaluate changes in medications from baseline to 12 months, a logistic model for repeated measures was constructed [30]. The model included main effects for digital medicine (vs usual care) and time and the digital medicine × time interaction. No covariates were considered. The multivariate binary response indicated medication status (yes or no) at baseline and 12 months. A compound symmetric covariance structure was used to model within-patient correlation. Results are presented as odds ratios of medication (12 months vs baseline) within each group, ratios of the group odds ratios, 95% CIs, and *P* values. Because no patients in the digital medicine program were treated with alpha glucosidase inhibitors, this medication class was not included in the analysis. A significance level of .05 was used for all statistical tests. Analyses of outcomes were carried out using SAS version 9.4 for Windows (SAS Institute).

Results

We evaluated all patients at baseline and again following 1 year. Prior to enrollment in the digital diabetes program, patients were under the care of their primary care clinician for their diabetes for an average of 5.2 years, averaging 2.8 visits per year. Of the 763 patients at baseline, 328 (43%) patients had not achieved their goal HbA_{1c} target, while 107 patients (14%) had HbA_{1c} values greater than or equal to 9.0% (range 9.0-13.9).

The baseline characteristics of the digital diabetes (n=763) and the propensity matched usual care groups (n=794) are outlined in Table 1. There were no significant differences in age, sex, BMI, HbA_{1c}, creatinine, eGFR, and use of insulin. There were, however, lower levels of total and high-density lipoprotein (HDL) cholesterol as well as higher systolic and diastolic blood pressure in digital medicine patients. It is noteworthy that digital medicine patients' age ranged from 31 to 98 years, with 28% (n=215) of enrollees 70 years or older.

Table 1. Baseline comparison of digital medicine (n=763) and usual care (n=794).

Metric	Digital medicine	Usual care	Standard difference	*P* value
Age (years), mean (SE)	63 (11)	63 (12)	0.031	.54
Male, n (%)	373 (49)	357 (45)	0.068	.11
Black, n (%)	299 (39)	310 (39)	0.013	.99
White, n (%)	447 (59)	468 (59)	0.002	.99
Fasting glucose (mg/dl), mean (SE)	155 (67)	151 (64)	0.065	.20
HbA_{1c}[a] (%), mean (SE)	7.3 (1.5)	7.3 (1.7)	0.020	.70
Creatinine (mg/dl), mean (SE)	1.06 (0.4)	1.03 (0.04)	0.057	.76
Estimated glomerular filtrate rate (ml/min), mean (SE)	58.5 (9.5)	58.6 (9.1)	0.012	.44
Total cholesterol (mg/dl), mean (SE)	161 (38)	165 (44)	0.107	.04
HDL[b] cholesterol (mg/dl), mean (SE)	45 (12)	46 (13)	0.109	.04
LDL[c] cholesterol (mg/dl), mean (SE)	92 (49)	95 (50)	0.050	.34
Triglycerides (mg/dl), mean (SE)	146 (95)	149 (150)	0.021	.69
BMI (kg/m^2), mean (SE)	34.7 (7.3)	35.0 (8.3)	0.034	.51
Systolic blood pressure (mmHg), mean (SE)	132 (13)	130 (14)	0.101	.05
Diastolic blood pressure (mmHg), mean (SE)	78 (8)	76 (8)	0.196	<.001

[a]HbA_{1c}: hemoglobin A_{1c}.

[b]HDL: high-density lipoprotein.

[c]LDL: low-density lipoprotein.

Additional characteristics were uniquely obtained in digital medicine patients. At entry, 168 of the 763 (22%) patients exhibited symptoms of depression, 160 (21%) patients described financial difficulty in paying for medication, and 122 (16%) patients had low levels of health literacy. Basic technology skills were assessed at entry, of which 69 (9%) patients scored as deficient [31,32]. Moderate to high levels of diabetes distress was reported in 198 (26%) patients at entry, which improved to 122 (16%) patients at 1 year (*P*<.001). Finally, a net promotor score (likelihood to recommend the program to a friend or colleague) survey was collected yielding 385 responses (50% response rate), generating a score of 83 (range –100 to 100).

Tables 2 and 3 describe the impact of digital medicine and usual care on key metrics. Usual care patients demonstrated no improvements in HbA_{1c}, fasting glucose, or blood pressure but did show improvements in total cholesterol and BMI.

Table 2. Impact of digital medicine management at 12 months.

Metric	Baseline, mean (SE)	12 months, mean (SE)	Change (%)	*P* value
Fasting glucose (mg/dl)	155 (67)	137 (47)	–12	<.001
HbA_{1c}[a] (%)	7.3 (1.5)	6.9 (1.2)	–7	<.001
Total cholesterol (mg/dl)	161 (38)	154 (37)	–4	<.001
HDL[b] cholesterol (mg/dl)	45 (12)	46 (13)	5	<.001
LDL[c] cholesterol (mg/dl)	92 (49)	86 (52)	–6	.02
Triglycerides (mg/dl)	146 (95)	140 (87)	–7	.04
BMI (kg/m^2)	34.7 (7.3)	34.4 (7.1)	–1	<.001
Systolic blood pressure (mmHg)	132 (13)	131 (10)	–1	.31
Diastolic blood pressure (mmHg)	78 (8)	77 (7)	–1	<.001

[a]HbA_{1c}: hemoglobin A_{1c}.

[b]HDL: high-density lipoprotein.

[c]LDL: low-density lipoprotein.

Table 3. Impact of usual care at 12 months.

Metric	Baseline, mean (SE)	12-months, mean (SE)	Change (%)	*P* value
Fasting glucose (mg/dl)	151 (64)	151 (66)	0	.61
HbA_{1c}[a] (%)	7.3 (1.7)	7.3 (1.6)	0	.41
Total cholesterol (mg/dl)	165 (44)	160 (40)	–3	.02
HDL[b] cholesterol (mg/dl)	43 (13)	46 (14)	7	.25
LDL[c] cholesterol (mg/dl)	95 (50)	96 (64)	1	.33
Triglycerides (mg/dl)	149 (150)	152 (139)	2	.46
BMI (kg/m^2)	35.0 (8.3)	34.6 (8.2)	–1	<.001
Systolic blood pressure (mmHg)	130 (14)	131 (12)	0.8	.21
Diastolic blood pressure (mmHg)	76 (8)	76 (7)	0	.68

[a]HbA_{1c}: hemoglobin A_{1c}.

[b]HDL: high-density lipoprotein.

[c]LDL: low-density lipoprotein.

Digital medicine patients achieved significant improvements in HbA_{1c}, lipids, BMI, and diastolic blood pressure, which took place without changes in lipid or antihypertensive therapy. Digital medicine management yielded a 57% reduction in the percent of patients whose HbA_{1c}≥9.0% (14% to 6%; *P*<.001), whereas no statistically significant change was observed in usual care patients (15% to 14%; *P*=.51; Table 4).

Digital medicine patients were significantly more likely to complete annual health maintenance measures (Table 5) than those in usual care.

Tables 6 and 7 describe medication use and changes in both digital diabetes and usual care groups.

Medication changes were similar in both groups except for a greater reduction in sulfonylurea use in the digital medicine group (Table 8).

Table 4. Proportion of patients in digital medicine (n=763) and usual care (n=794) whose hemoglobin A_{1c}≥9.0%.

Group	Baseline	12 months	Change (%)	*P* value
Digital medicine, n (%)	107 (14)	49 (6)	–54	<.001
Usual care, n (%)	117 (15)	113 (14)	–3	.51

Table 5. Proportion of patients completing annual health maintenance in the digital medicine (n=763) and usual care (n=794) groups.

Annual health maintenance metric	Digital medicine	Usual care	*P* value
HbA_{1c}[a], n (%)	684 (90)	584 (74)	<.001
Retinopathy exam, n (%)	649 (85)	554 (70)	<.001
Urine protein, n (%)	746 (98)	751 (95)	.001

[a]HbA_{1c}: hemoglobin A_{1c}.

Table 6. Changes in diabetes medications over 12 months of digital medicine management.

Medication class	Baseline	12 months	Change (%)	*P* value
Insulin (%)	27	24	–13	.10
Biguanide (%)	70	56	–20	<.001
Sulfonylureas (%)	27	15	–43	<.001
GLP-1[a] agonists (%)	25	33	30	.001
DPP-4[b] inhibitors (%)	14	8	–43	<.001
SGLT-2[c] inhibitors (%)	11	18	67	<.001
Alpha glucosidase inhibitors (%)	0	0	0	>.99
Thiazolidinedione (%)	4	3	–18	.48

[a]GLP-1: glucagon-like peptide 1.

[b]DPP-4: dipeptidyl peptidase 4.

[c]SGLT-2: sodium-glucose cotransporter 2.

Table 7. Changes in diabetes medications over 12 months in usual care.

Medication class	Baseline	12 months	Change (%)	*P* value
Insulin (%)	25	23	–12	.41
Biguanide (%)	64	49	–23	<.001
Sulfonylureas (%)	23	16	–31	<.001
GLP-1[a] agonists (%)	16	20	27	.03
DPP-4[b] inhibitors (%)	13	8	–39	.001
SGLT-2[c] inhibitors (%)	9	12	38	.03
Alpha glucosidase inhibitors (%)	0.3	0.1	–50	.56
Thiazolidinedione (%)	4	3	–30	.17

[a]GLP-1: glucagon-like peptide 1.

[b]DPP-4: dipeptidyl peptidase 4.

[c]SGLT-2: sodium-glucose cotransporter 2.

Table 8. ORs of medication use at 12 months by group.

Outcome	Digital medicine, OR[a,b] (95% CI)	Usual care, OR (95% CI)	Ratio[c] (95% CI)	*P* value
Insulin	0.82 (0.74-0.92)	0.91 (0.81-1.01)	0.91 (0.78-1.06)	.22
Biguanide	0.54 (0.47-0.63)	0.54 (0.47-0.62)	1.00 (0.82-1.22)	>.99
Sulfonylureas	0.49 (0.42-0.57)	0.63 (0.54-0.74)	0.78 (0.62-0.97)	.02
GLP-1[d] agonists	1.45 (1.26-1.66)	1.34 (1.14-1.57)	1.08 (0.87-1.34)	.47
DPP-4[e] inhibitors	0.53 (0.42-0.66)	0.58 (0.46-0.72)	0.92 (0.67-1.26)	.60
SGLT-2[f] inhibitors	1.83 (1.51-2.21)	1.43 (1.16-1.78)	1.27 (0.95-1.70)	.10
Alpha glucosidase inhibitors	—[g]	—	—	—
Thiazolidinedione	0.82 (0.61-1.10)	0.69 (0.52-0.92)	1.18 (0.78-1.78)	.44

[a]OR: odds ratio.

[b]ORs for groups are odds of using the medication at 12 months divided by odds of using the medication at baseline.

[c]Ratio (95% CI) is the OR for the digital medicine divided by the OR for the usual care group along with the 95% CI.

[d]GLP-1: glucagon-like peptide 1.

[e]DPP-4: dipeptidyl peptidase 4.

[f]SGLT-2: sodium-glucose cotransporter 2.

[g]Not available.

Baseline and 1-year hypoglycemic episodes were recorded in digital medicine patients (Table 9). A total of 313 (41%) patients experienced at least 1 hypoglycemic event per month, averaging 0.84 episodes per month per patient enrolled, of which 6% were level 3 hypoglycemic events. At 1 year, there was a 74% reduction (*P*<.001) in total hypoglycemic episodes with a commensurate 82% reduction in frequency to 0.15 episodes per patient per month (*P*<.001).

The average change in these metrics per patient are described in Table 10, and Table 11 adjusts these changes based on patient age, sex, and race. Following adjustment, there were statistically greater improvements observed in fasting glucose, HbA_{1c}, HDL and LDL cholesterol, and diastolic blood pressure in the digital medicine managed patients compared to usual care.

Table 9. Changes in hypoglycemic events over 1 year in digital medicine patients (n=763).

Monthly hypoglycemia	Baseline	12 months	Change (%)	*P* value
Patients with any hypoglycemic episode, n (%)	314 (41.1)	91 (11.9)	–74	<.001
Patients with level 1 episodes	175 (22.9)	63 (8.3)	–64	<.001
Patients with level 2 episodes	93 (12.2)	16 (2.1)	–83	<.001
Patients with level 3 episodes	46 (6.0)	11 (1.5)	–75	<.001
Frequency of hypoglycemic episodes per month, mean	0.84	0.15	–82	<.001

Table 10. Unadjusted mean within-patient change in outcomes by group.

Outcome	Digital medicine, mean (SE)	Usual care, mean (SE)	Difference (95% CI)	*P* value
Fasting glucose	–17.7 (2.7)	1.3 (2.5)	–19.0 (–26.2 to –11.7)	<.001
HbA_{1c}[a]	–0.40 (0.05)	0.04 (0.05)	–0.44 (–0.58 to –0.30)	<.001
Total cholesterol	–5.9 (1.2)	–3.7 (1.6)	–2.2 (–6.1 to 1.7)	.27
HDL[b] cholesterol	1.6 (0.3)	0.4 (0.3)	1.2 (0.4 to 2.1)	.003
LDL[c] cholesterol	–5.1 (2.2)	2.7 (2.8)	–7.8 (–14.8 to –0.8)	.03
Triglycerides	–6.5 (3.2)	4.9 (6.6)	–11.4 (–25.8 to 3.0)	.12
BMI	–0.25 (0.06)	–0.30 (0.08)	0.05 (–0.14 to 0.24)	.62
Systolic BP[d]	–0.38 (0.38)	0.52 (0.41)	–0.90 (–2.00 to 0.20)	.11
Diastolic BP	–0.87 (0.22)	–0.09 (0.23)	–0.77 (–1.39 to –0.15)	.01

[a]HbA_{1c}: hemoglobin A_{1c}.

[b]HDL: high-density lipoprotein.

[c]LDL: low-density lipoprotein.

[d]BP: blood pressure.

Table 11. Covariate-adjusted mean within-patient change in outcomes by group.

Outcome	Digital medicine[a], mean (SE)	Usual care, mean (SE)	Difference (95% CI)	*P* value
Fasting glucose	–17.4 (2.7)	1.1 (2.5)	–18.5 (–25.7 to –11.2)	<.001
HbA_{1c}[b,c]	–0.38 (0.05)	0.03 (0.05)	–0.41 (–0.54 to –0.27)	<.001
Total cholesterol	–5.8 (1.2)	–3.8 (1.6)	–2.0 (–6.0 to 1.9)	.31
HDL[d] cholesterol	1.6 (0.3)	0.3 (0.3)	1.3 (0.5 to 2.1)	.002
LDL[e] cholesterol	–4.9 (2.2)	2.5 (2.7)	–7.5 (–14.4 to –0.5)	.04
Triglycerides	–6.7 (3.2)	5.1 (6.6)	–11.8 (–26.4 to 2.7)	.11
BMI	–0.25 (0.06)	–0.30 (0.08)	0.05 (–0.14 to 0.25)	.59
Systolic BP[f]	–0.40 (0.38)	0.53 (0.41)	–0.93 (–2.03 to 0.17)	.10
Diastolic BP	–0.86 (0.22)	–0.10 (0.23)	–0.76 (–1.38 to –0.14)	.02

[a]All models incorporate covariates for patient age, sex, and race.

[b]HbA_{1c}: hemoglobin A_{1c}.

[c]Model for HbA_{1c} incorporated additional covariates for baseline fasting glucose and baseline estimated glomerular filtration rate.

[d]HDL: high-density lipoprotein.

[e]LDL: low-density lipoprotein.

[f]BP: blood pressure.

Discussion

There are several important findings from this investigation. First, the digital health monitoring and intervention program significantly improved HbA_{1c} levels, attainment of goal HbA_{1c}, lipid levels, diabetes distress, and annual health maintenance adherence compared to usual care. Second, hypoglycemia is frequently present and is often unrecognized in individuals with diabetes managed in clinical practice; the severity and frequency of hypoglycemic events can be markedly reduced with timely knowledge and intervention through real-time capture of home self-monitoring of blood glucose [33,34]. Finally, a successful digital managed diabetes program need not be limited to a younger, more technology-advanced population, and can fully embrace a wide range of racial diversity, age, and health literacy levels with high levels of patient satisfaction.

The standard management of diabetes in clinical practice has significant system and process limitations including limited episodic interactions with patients, access to a small fraction of glucose data, a reduced ability to evaluate patient comprehension and needs, and a brief amount of time to educate and reinforce essential health-promoting behaviors [12,33-36]. Physicians report that they are less satisfied providing care to people with chronic conditions such as diabetes than to patients in general, which may result from difficulty in care coordination, inadequate clinical training, and poor reimbursement for the time necessary

[37,38]. As a result, over the past decade, the United States has experienced worsening of clinical outcomes in diabetes, including an increase in emergency department visits, lower extremity amputations, hospitalizations for hyperglycemic crisis, and deaths due to diabetes [10,11].

We have demonstrated that redesigning care delivery using a digital health program can substantially improve multiple metrics important in caring for patients with T2D, namely, achievement of HbA_{1c} targets, reduction of hypoglycemia, reducing diabetes distress, and completing necessary health maintenance. These improvements are in contrast to outcomes that often occur when people with diabetes are seen only 2 to 3 times a year, resulting in persistence of hyperglycemia or hypoglycemia over prolonged periods of time [33,34]. This was evidenced in the usual care group where the percentage of patients with the highest levels of HbA_{1c} remained unchanged after 1 year. Moreover, after an average of 5 years under the care of their primary care physician, 41% (n=314) of patients were discovered to have hypoglycemic events each month, of which 6% (n=46) were level 3. Finally, the digital intervention was provided to a diabetes population with a broad range of ages (range 31-98 years), races, and health literacy, and it overcame many potential barriers to care, including access.

There are several factors worth describing in our care delivery redesign. First, the clinical team of doctoral pharmacists and APPs prescribed medications based on current guideline recommendations, which contrasts the high rate of care variation observed in routine practice [39-42]. Second, adjustments to guideline-recommended medication used glucose values received directly from home, providing the clinical team with just-in-time actionable data. This improved the ability to recognize and reduce both hypoglycemia and hyperglycemia. Third, each patient benefited from a dedicated health coach proficient in lifestyle intervention and skills to improve health literacy; patient activation; and, when possible, financial strain related to the cost of medications [12,31]. Fourth, patients received monthly reports outlining their status regarding diabetes control and additional tips and reminders needed for optimal outcomes. Finally, most interactions took place during openings in the patient's schedule rather than openings in the care team's schedule, making receiving care highly convenient and desirable [18].

It is noteworthy that costs of care were not assessed, and future studies will be needed to determine the financial impact of this digital intervention.

There are, however, several limitations to this study. First, this was a single-center study with a 1-year follow-up occurring in an integrated health care delivery system and involved a relatively modest number of individuals whose average glycemic, blood pressure, and lipid control were not markedly abnormal. Despite the advantages of Bluetooth-enabled glucose meters, it is likely that the use of continuous glucose monitoring (CGM) would have identified a greater number of hypoglycemic events. With recent improvements in CGM performance and availability, it is likely this technology will be offered to appropriate participants in the future. Second, patients were not prospectively randomized into intervention and usual care groups. Finally, only patients who possessed a smartphone were eligible to enroll, which raises issues about education, socioeconomic, and motivational biases. However, the mean age of our population was 63 years, and on screening, 9% (n=69) lacked common technology skills, suggesting that our cohort was not biased toward a younger, more technically competent population.

In summary, a team-based digital health program that incorporates a higher frequency of real-time glucose data and touchpoints with the clinical team is an effective modality for delivering diabetes management, outperforming traditional office-based care. Although the bulk of our results were obtained prior to the COVID-19 pandemic, this mode of care provides unique value in this setting.

Conflicts of Interest

PC is on the speaker bureau for Janssen Pharmaceuticals and Novo Nordisk Pharmaceuticals.

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Abbreviations

APP: advanced practice provider
CGM: continuous glucose monitoring
eGFR: estimated glomerular filtration rate
EMR: electronic medical record
HbA1c: hemoglobin A1c
HDL: high-density lipoprotein
LDL: low-density lipoprotein
T2D: type 2 diabetes

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Original Paper

Stigma as a Barrier to Participant Recruitment of Minority Populations in Diabetes Research: Development of a Community-Centered Recruitment Approach

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Abstract

Background: The development of evidence-based care geared towards Black and Latina women living with uncontrolled type 2 diabetes is contingent upon their active recruitment into clinical interventions. Well-documented impediments to recruitment include a historical mistrust of the research community and socioeconomic factors that limit awareness and access to research studies. Although sociocultural and socioeconomic factors deter minorities from participating in clinical research, it is equally important to consider the role of stigma in chronic disease intervention studies.

Objective: We aim to share our discovery of diabetes-related stigma as an underrecognized impediment to recruitment for the Women in Control 2.0 virtual diabetes self-management education study.

Methods: Our initial recruitment plan used traditional strategies to recruit minority women with uncontrolled type 2 diabetes, which included letters and phone calls to targeted patients, referrals from clinicians, and posted flyers. After engaging a patient advisory group and consulting with experts in community advocacy, diabetes-related stigma emerged as a prominent barrier to recruitment. The study team reviewed and revised recruitment scripts and outreach material in order to better align with the lived experience and needs of potential enrollees.

Results: Using a more nuanced, community-centered recruitment approach, we achieved our target recruitment goal, enrolling 309 participants into the study, exceeding our target of 212.

Conclusions: There is a need for updated recruitment methods that can increase research participation of patients who experience internalized diabetes stigma. To address disparities in minority health, further research is needed to better understand diabetes-related stigma and devise strategies to avert or address it.

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KEYWORDS

diabetes; stigma; research; recruitment; minority health; disparities; virtual health; virtual management

Introduction

Type 2 diabetes mellitus (T2DM) disproportionately impacts racial and ethnic minority communities in the United States [1]. Although there is a need for research in delivering evidence-based care tailored to a diversity of patients living with diabetes, minority persons represented only 36.1% of individuals enrolled in clinical trials sponsored by the National

Institutes of Health in 2018 [2]. Well-documented impediments to recruitment of minorities for research trials are linked to socioeconomic factors and mistrust of the research community stemming from structural racism [3-9]. Included in this viewpoint is the experience of diabetes-related stigma among minority populations as a barrier to recruitment. Diabetes-related stigma is defined as "the experiences of negative feelings such as exclusion, rejection, or blame due to the perceived stigmatization of having diabetes" [10].

Our research team encountered these challenges in the recruitment of Black and Latina women for Women in Control 2.0 (WIC2), a randomized controlled trial (NCT02726425) studying the comparative effectiveness of online diabetes self-management (DSM) medical group visit (MGV) education with in-person DSM MGV education. However, it was the participants' experience of diabetes-related stigma, a persistent and underrecognized barrier to recruitment, that proved to be our greatest challenge in reaching our enrollment target of 212 study participants completing 6 out of 8 group visits. Herein, we share our lessons learned from our encounter with the issue of diabetes-related stigma while recruiting minority women with T2DM in clinical research.

WIC2 is a 2-arm randomized controlled trial (National Institute of Diabetes and Digestive and Kidney Diseases; grant no. R01DK106531) comparing the effectiveness of DSM MGV education delivered in a virtual social-gaming platform (intervention) or a face-to-face setting (control) [11]. We aimed to enroll 212 English- and Spanish-speaking Black and Latina women with uncontrolled diabetes (baseline hemoglobin A_{1c} [HbA_{1c}] ≥ 8.0% or 64 mmol/mol) from the Boston Medical Center Health System over the course of a 4-year period. Participants were assigned into 13 cohorts (8-10 participants each) of virtual and face-to face MGVs. The 2 primary outcomes are mean changes in pre-to-post DSM MGV physical activity and glucose control between baseline and 6-month follow-up. Prior to randomization, we obtained written informed consent from all participants. During the 8-week MGVs, participants engaged in facilitated discussions adapted from the Power to Prevent curriculum created by the Center for Disease Control and Prevention's National Diabetes Education Program, which emphasizes lifestyle changes including healthy eating and physical activity [12]. Participants also received a brief individual clinical consultation at each session to discuss medical treatments, gaps in care, and ensure safety.

Methods

Initial Recruitment Protocol (November 2016 to August 2017)

Prior to the start of the clinical trial, we engaged a patient advisory group (PAG) comprising 10 Black women with T2DM from the community to review and inform our recruitment strategy and study materials. The PAG met for 10 sessions and provided feedback on our outreach protocol and scripts. In addition, to prepare for recruitment, we established channels for clinician referrals at Boston Medical Center and protocols for direct outreach by study staff. To encourage referrals from allied health providers, the WIC2 principal investigator (SM) announced the study opportunity at local community health centers and during hospital grand rounds. Outreach coordinators distributed study flyers at affiliated clinics and community health centers to raise awareness about the study. The team also identified eligible potential participants by using electronic medical record (EMR) query; these patients received a study recruitment letter followed by a telephone call by a trained research assistant.

Challenges Encountered

Despite initial success with recruitment for the first 3 study cohorts, after enrolling 46 participants, we were unable to reach our enrollment milestones. Between August 2017 and October 2017, we were unable to enroll the required 16 participants to conduct the fourth cohort of study implementation. Careful assessment of our recruitment channels and procedures revealed key deficits in our strategy. First, we were not successful with clinician referrals to the study. Feedback from primary care colleagues revealed that many providers were too busy to explain the study opportunity to patients, while others raised concerns that study clinicians would alter patients' medication regimens without consulting the primary providers. Despite our attempts to reassure clinicians, referrals from clinics were low. As an alternative means of recruiting participants, we attempted to foster community partnerships using strategies from community-based participatory research, such as outreach to local churches and businesses, including beauty salons, grocery stores, and laundromats in target communities [13]. However, similar to challenges encountered by other researchers, our efforts to establish and build sustainable community partnerships were stymied by time and resource constraints set by our study timeline and budget [14,15]. We found that potential community partners were themselves strapped for resources, and generating interest in our research effort was difficult.

Re-evaluation of the Recruitment Protocol (August 2017 to December 2017)

We investigated the failure modes in our recruitment approach by consulting with community health advocacy experts experienced in working with vulnerable populations, re-engaging our PAG, and observing study staff conversations with potentially eligible participants to identify reasons for declination. We first conducted interviews with local public health activists with extensive experience working with the Black and Latino Boston-area communities to explore reasons for participation resistance. They advised us to consider the role of diabetes-related stigma: the sense of shame associated with being responsible for developing or failing to manage a disease or illness [16].

In order to broaden our understanding of potential barriers to participation, we reconvened the WIC2 PAG to review additional recruitment materials, outreach scripts used by study staff, and elements of the study website. It was evident during the reunion that our recruitment materials did not fundamentally address experiences of isolation and disempowerment. It became apparent after observing recruitment outreach calls that our recruitment script underemphasized the study as an opportunity to participate in a relationship-centered intervention and instead

focused on the transactional, compensatory components of the study.

Revised Recruitment Protocol (December 2017 to October 2019)

Starting December 2017, we hired culturally concordant staff with previous outreach experience from the local Boston community to deliver a relationship-centered message during recruitment. By drawing upon a growing understanding of the existence and implications of stigma, we implemented four key strategies to revise our recruitment approach: (1) communicate study relevance to the community, (2) promote the idea of personal empowerment with message mapping, (3) cultivate connections between participants prior to the start of the DSM MGVs, and (4) encourage enrollees to recruit others via snowball sampling. Each of these strategies helped us engage women who may have otherwise been unwilling to participate in clinical research due to diabetes-related stigma.

Study Relevance to the Community

When introducing the WIC2, we emphasized our mission for health equity and educated potential participants about how the DSM MGVs could potentially reduce disparities in diabetes care. To lessen the sense of isolation often associated with stigmatizing illnesses, we shared facts regarding high rates of diabetes among communities of color. Relaying information in a way that reminded potential participants that their involvement mattered beyond the study-specific aims was crucial. We also highlighted the fact that their active engagement embodied the power of a community to effect change. We emphasized the potential of giving back to the community in order to create a lasting dialogue around diabetes care management and prevention for families at risk.

Personal Empowerment With Message Mapping

Informed by valuable insights gained from our PAG collaborators, flyers were redesigned to capture three key messages of the study: taking control of diabetes, experiencing personal transformation, and finding a community. We also recorded testimonial videos featuring PAG participants who shared their experience working with the study team and the WIC2 intervention. These testimonials, which were posted on the newly designed WIC2 website, framed the study as an opportunity for self-empowerment through engagement in a strengths-based DSM education intervention.

Cultivating Connections Among Current Participants

Potential participants were invited to attend enrollment sessions in groups of 6 to 10 to mirror the upcoming group-based format during the intervention. The purpose of these informal sessions was to foster a sense of connection and familiarity among participants before the official start of the study; they were encouraged to introduce themselves and share their lived experience with T2DM. In addition, reminder calls and appointment cards were issued a few days prior to enrollment to maintain interest and excitement about future participation in the study.

Involving Former Participants in Recruitment

We found that women who had themselves participated in the study were excellent advocates for study participation. Because of their goodwill toward WIC, we implemented a Refer-a-Friend program, whereby we offered current and past participants US $20 for every friend referred who ultimately enrolled in the study and attended at least one group visit. By the end of the study period, 58 participants were recruited by word of mouth or participant referral. The referral program also increased participants' sense of giving back by contributing to the WIC2 recruitment mission.

Results

A total of 1960 patients were identified as potentially eligible for the WIC2 study from a variety of sources including EMR query, flyers, word of mouth, and referrals. After completing the 17th study cohort in December 2019, 1349 potential participants were screened, 349 were eligible, and 309 were enrolled (Figure 1).

Of the 1449 potentially eligible English-language patients, 88.47% (1282/1449) were recruited by EMR query, 5.45% (79/1449) by flyers, 4.00% (58/1449) by word of mouth or participant referral, 1.38% (20/1449) by primary care provider referral, and 0.69% (10/1449) by other sources. All 511 Spanish-speaking participants were identified and recruited via EMR query. Despite the low rate of eligibility, of the participants who were deemed eligible, 88.5% (309/349) enrolled, 90.9 % (281/309) completed baseline HbA_{1c} and/or physical activity data collection, and 73.1% (207/281) attended at least 6 out of 8 group visits. Participants who completed baseline requirements had a mean age of 55 years (SD 10), a mean baseline HbA_{1c} of 9.9% (SD 1.8), and 69.7% reported Medicaid or Medicare as their primary insurance provider. The characteristics of participants who completed baseline activities (N=281) are displayed in Table 1.

Common reasons for ineligibility included unavailability to attend MGVs at scheduled times, current HbA_{1c}<8.0%, outdated HbA_{1c} (outside of the 90-day window prior to the start of the first MGV), and lack of interest in participating.

Qualitative analysis of transcripts from 3 focus groups (n=22) that were conducted postintervention elucidated feelings of shame and responsibility for lack of "control" of their T2DM. Participants describe a sense of shame that diabetes progression is self-caused, which translated to diabetes-related stigma.

> *[Women in Control] has helped me elevate my self-esteem and to walk because before I wanted to be locked away in my home without doing anything, a strong depression...in my house, I am alone with my husband, like that for me it's harder. But...Women in control…activated me.* [Virtual World participant]
>
> *And I tell you, my children offer me because of course they are not sick. They tell me, "mama, eat," and I say, "no, son, you guys eat and know how to eat because if one day you are sick, do not blame me because a lot of people say it's hereditary." But that's*

a lie, we give it to ourselves because of our carelessness. [Background laughter] Because I'm going to tell you something, my mom, my dad and my brothers never had sugar and only I have it. So that was because of my carelessness. [face-to-face participant]

This qualitative data supports the insights gleaned from the PAG and public health activists between December 2017 and October 2019.

Figure 1. Women in Control 2.0 Consolidated Standards of Reporting Trials (CONSORT) diagram. CHF: congestive heart failure; COPD: chronic obstructive pulmonary disease; DKA: diabetic ketoacidosis; dx: diagnosed with; T2DM: type 2 diabetes mellitus.

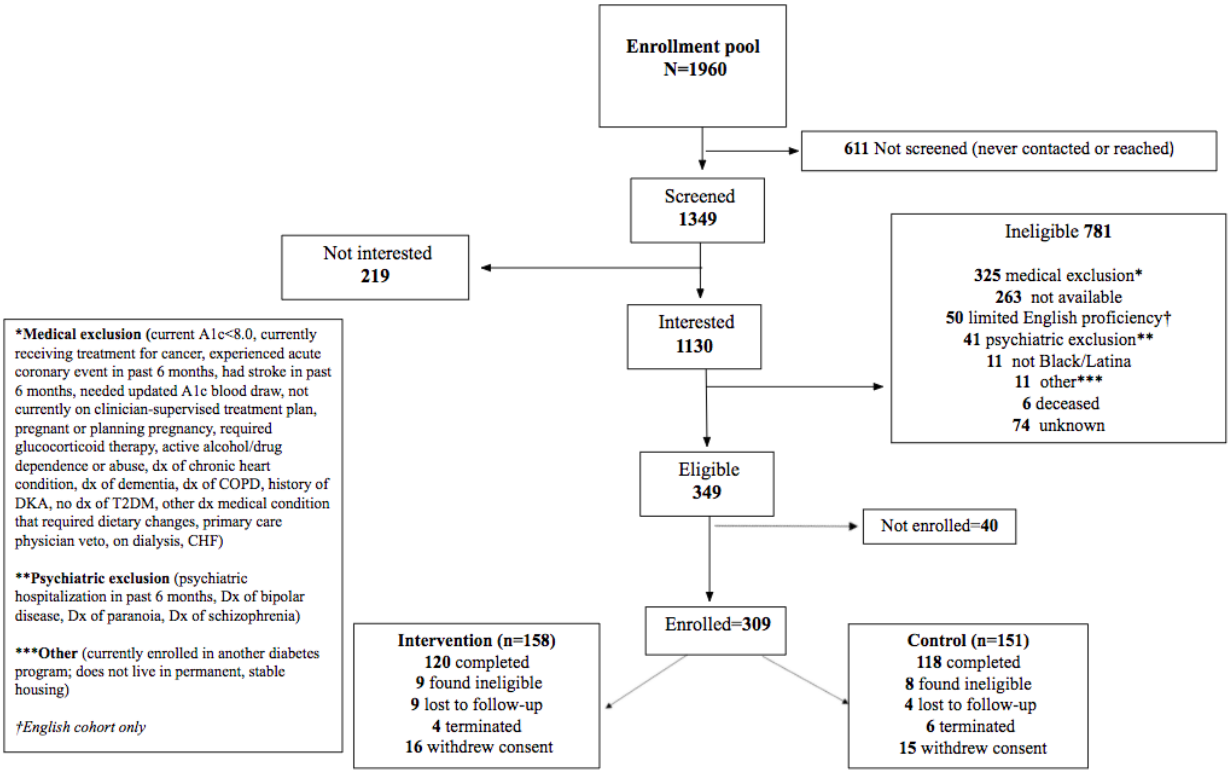

Table 1. Baseline sample characteristics (N=281).

Characteristic	Total (N=281, 100%)	Control (n=137, 49%)[a]	Intervention (n=144, 51%)[a]
Age (years), mean (SD)	56 (10)	55 (10)	56 (11)
Ethnicity, n (%)			
Hispanic/Latina	98 (34.9)	46 (33.6)	52 (36.1)
White	25 (8.9)	13 (9.5)	12 (8.3)
Race, n (%)			
Black	185 (65.8)	92 (67.2)	93 (64.6)
Other	60 (21.4)	27 (19.7)	33 (22.9)
Refused to answer/unknown	1 (0.4)	0 (0.0)	1 (0.7)
More than one race	6 (2.1)	2 (1.5)	4 (2.8)
Spanish speaking, n (%)	53 (18.9)	26 (19.0)	27 (18.6)
Insurance, n (%)			
Medicaid (MassHealth)	129 (45.9)	64 (47.4)	65 (44.4)
Medicare	31 (11.0)	17 (12.4)	14 (9.7)
Medicaid + Medicare	46 (16.4)	21 (15.3)	25 (17.4)
Commercial	64 (22.8)	29 (21.2)	35 (24.3)
Don’t know or prefer not to answer	7 (2.5)	3 (2.2)	4 (2.8)
Has children, n (%)	249 (88.6)	121 (88.3)	128 (89.9)
Work status, n (%)			
Full-time	69 (24.6)	33 (24.1)	36 (25.0)
Retired	26 (9.3)	13 (9.5)	13 (9.0)
Disabled	61 (21.7)	29 (21.2)	32 (22.2)
Part-time	39 (13.9)	22 (16.1)	17 (11.8)
Unemployed	34 (12.1)	16 (11.7)	18 (12.5)
Other	12 (4.3)	6 (4.4)	6 (4.2)
Refused to answer/unknown	13 (4.6)	5 (3.6)	8 (5.6)
Education history, n (%)			
Less than high school (grade 0-8)	52 (18.5)	25 (18.4)	27 (18.6)
Some high school (grade 9-<12)	36 (12.8)	21 (15.3)	15 (10.4)
GED[b] + high school graduate	53 (18.8)	23	30
Post high school	139 (49.5)	68 (49.6)	71 (49.3)
Refused to answer/unknown	1 (0.4)	0 (0.0)	1 (0.7)
Attended at least 6 group visits, n (%)	207 (73.7)	99 (72.3)	108 (75.0)
Hemoglobin A_{1c} (%), mean (SD)	10.0 (2.0)	10.0 (2.0)	10.0 (2.0)

[a]Percentages below this heading are based on the total for this column only (column %).

[b]GED: General Educational Development Test.

Discussion

Although sociocultural and socioeconomic factors deter minority persons from enrolling in clinical research studies, we also encountered diabetes-related stigma as an unseen barrier to recruitment. Similar findings regarding the impact of disease-related stigma on research efforts are reported in other research fields including HIV and mental health research [17-19]. Despite diabetes-related stigma being potentially underrecognized among researchers, it is a common shared experience among those living with diabetes [20]. The WIC2 study participants in our postintervention focus groups indicated that, in their communities, people with T2DM are often depicted with negative traits, such as “laziness” and a lack of self-control, resulting in a desire not to disclose the fact that one is living with diabetes. Myriad testimonies from individuals living with

diabetes reveal a shared sense of personal shame related to feeling "responsible" for acquiring diabetes [15]. Stigmatization of T2DM as a lifestyle disease contributes to a sense of "hopelessness and fear of discussing diabetes complications" and bars patients from seeking clinical care [21]. As a result, many patients have poor diabetes control and health outcomes [16,22,23]. We redesigned our recruitment strategy to focus on relationship-centered communication, which addressed unseen diabetes-related stigma in a research context [23]. To accomplish this goal, we hired culturally concordant research staff who communicated the study's relevance to the community, emphasized personal empowerment with message mapping, fostered connections among participants prior to the start of the DSM MGVs, and encouraged current and former participants to recruit others via snowball sampling. Collectively, these efforts helped us successfully avert the risk posed by diabetes-related stigma to our study implementation. Most importantly, we exercised cultural humility in the face of this unforeseen obstacle, allowing ourselves to be educated and navigated by our participant community and our colleagues toward a successful solution.

To effectively address disparities in health outcomes and healthcare, we must design and conduct health services research involving those most at risk for poor health outcomes. These efforts require a diverse pool of participants from underserved and underrepresented communities. Through WIC2, we identified diabetes-related stigma as an unseen impediment to participation in diabetes research. Although stigma has been noted in other diseases like HIV, there is limited research specifically about diabetes-associated stigma, especially its role as a barrier to recruitment in clinical trials. Further work is needed to better understand diabetes-related stigma and devise evidence-based strategies to avert or address it.

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Conflicts of Interest

SM is a consultant on health communication and relationship centered care and has provided workshops and lectures on this topic funded by pharmaceutical and other industry sponsors. No product endorsement is permitted during these programs. SM also holds equity in See Yourself Health LLC, a digital health service provider.

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Abbreviations

DSM: diabetes self-management
EMR: electronic medical record
HbA_{1c}: hemoglobin A_{1c}
MGV: medical group visit
PAG: patient advisory group
T2DM: type 2 diabetes mellitus
WIC2: Women in Control 2.0

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Original Paper

Improved Glycemic Control With a Digital Health Intervention in Adults With Type 2 Diabetes: Retrospective Study

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Abstract

Background: Traditional lifestyle interventions have shown limited success in improving diabetes-related outcomes. Digital interventions with continuously available support and personalized educational content may offer unique advantages for self-management and glycemic control.

Objective: In this study, we evaluated changes in glycemic control among participants with type 2 diabetes who enrolled in a digital diabetes management program.

Methods: The study employed a single-arm, retrospective design. A total of 950 participants with a hemoglobin A_{1c} (HbA_{1c}) baseline value of at least 7.0% enrolled in the Vida Health Diabetes Management Program. The intervention included one-to-one remote sessions with a Vida provider and structured lessons and tools related to diabetes management. HbA_{1c} was the primary outcome measure. Of the 950 participants, 258 (27.2%) had a follow-up HbA_{1c} completed at least 90 days from program start. Paired *t* tests were used to evaluate changes in HbA_{1c} between baseline and follow-up. Additionally, a cluster-robust multiple regression analysis was employed to evaluate the relationship between high and low program usage and HbA_{1c} change. A repeated measures analysis of variance was used to evaluate the difference in HbA_{1c} as a function of the measurement period (ie, pre-Vida enrollment, baseline, and postenrollment follow-up).

Results: We observed a significant reduction in HbA_{1c} of –0.81 points between baseline (mean 8.68, SD 1.7) and follow-up (mean 7.88, SD 1.46; t_{257}=7.71; *P*<.001). Among participants considered high risk (baseline HbA_{1c}≥8), there was an average reduction of –1.44 points between baseline (mean 9.73, SD 1.68) and follow-up (mean 8.29, SD 1.64; t_{139}=9.14; *P*<.001). Additionally, average follow-up HbA_{1c} (mean 7.82, SD 1.41) was significantly lower than pre-enrollment HbA_{1c} (mean 8.12, SD 1.46; $F_{2, 210}$=22.90; *P*<.001) There was also significant effect of program usage on HbA_{1c} change (β=–.60; *P*<.001) such that high usage was associated with a greater decrease in HbA_{1c} (mean –1.02, SD 1.60) compared to low usage (mean –.61, SD 1.72).

Conclusions: The present study revealed clinically meaningful improvements in glycemic control among participants enrolled in a digital diabetes management intervention. Higher program usage was associated with greater improvements in HbA_{1c}. The findings of the present study suggest that a digital health intervention may represent an accessible, scalable, and effective solution to diabetes management and improved HbA_{1c}. The study was limited by a nonrandomized, observational design and limited postenrollment follow-up data.

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KEYWORDS

type 2 diabetes; digital health; diabetes intervention; diabetes; mobile health; mHealth; app-based; health coaching; HbA1c; glycemic improvements

Introduction

Diabetes continues to plague the United States and the rest of the globe [1]. An estimated 34.1 million adults, 13% of the US adult population, have diabetes, with just under 80% diagnosed [2]. Amid the seemingly inexorable rise, it can be easy to forget what a truly modern phenomenon this is. In *The Principles and Practice of Medicine* of 1892, William Osler estimated a diabetes prevalence of just 2.8 per 100,000 in the United Sates, which, in his day, lumped together both types 1 and 2 [3]. This modernity would seem to suggest the tide can be rolled back if only its causes were understood, but, alas, the disease marches on [4].

Among those with diabetes, disease control is clearly a major challenge. Although clinical guidelines broadly agree on hemoglobin A_{1c} (HbA_{1c}) targets of 7.0% or less for most people with diabetes, some 50% of those diagnosed are, by this standard, not on target, and thus at elevated risk of macrovascular and microvascular complications [2,5,6]. This serves only to highlight the challenges people with diabetes face. It is a disease that requires daily attention to and navigation of myriad decisions—choosing foods, taking medication, monitoring blood glucose, and accessing preventive and acute care [7]. Although diabetes self-care behaviors have been found to be positively correlated with improved glycemic control and quality of life, clearly many people with diabetes struggle to adopt such behaviors [8].

With great prevalence and barriers to control comes great cost. In 2017, total estimated costs of diabetes in the United States were US $327 billion, of which US $237 billion came from direct medical costs [9]. A safe, effective, efficient, and scalable intervention would be welcome. Many drug trials have shown disappointing results notably with no improvement in macrovascular outcomes in the UK Prospective Diabetes Study (UKPDS) 33 trial and increased mortality despite lower HbA_{1c} achieved in the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial [10,11]. Lifestyle interventions have similarly seen prominent disappointments in the Look AHEAD and MOVE! projects [12,13]. Some interventions, such as the Diabetes Remission Clinical Trial (DiRECT), have shown promise, but it remains unclear whether strategies that include such intensive interventions as meal replacement can be scaled up to the millions of people living with diabetes in highly varied social, economic, and cultural settings [14-16].

Digital health may offer some solutions. Traditional outpatient interventions, however extensive, are limited by their sporadic nature and thus leave a substantial burden on the patient to internalize behaviors. A digital solution has the potential to deliver guidance and support anywhere and anytime it may be needed. Preliminary efforts to this effect have shown promise to the point that diabetes care standards already recognize the potential benefits of “connected care” [17-21].

Benefits may include increased access to care and health improvements. In addition to removing traditional barriers to face-to-face interactions, such as transportation and daytime office hours, digital platforms are linked to mental and metabolic outcomes. Small randomized controlled trials of these programs have found improvements in diabetes self-care behaviors and self-efficacy along with glycemic and mental health measures [22,23]. A common theme in qualitative analyses of these interventions is the perception of feeling connected at all times to a human who cares [23].

Operationalizing the effect of a “human who cares” via a digital platform does come with challenges. As Markert et al [24] note in a literature review of telehealth coaching for seniors, it can be challenging and time consuming to foster a therapeutic relationship and tailor the intervention to the individual.

Furthermore, there is little standardization of digital intervention components in both the literature and products in the market. Greenwood et al [25] conducted a systematic review of technology-enabled diabetes management interventions. Of these interventions, 18 reported significant reductions in HbA_{1c} albeit with heterogeneity in intervention components and methodologies. They did identify 4 key intervention elements present with HbA_{1c} reduction: two-way communication, patient-generated health data tracking or analysis, education, and feedback. These elements are cornerstones of the Vida Health program.

Vida Health is an app-based digital health platform for chronic disease prevention and management. Vida Health is available as an employee benefit through select health plans and direct to consumers across the United States. Type 2 diabetes management is one of the core offerings on the Vida Health platform. Vida’s platform combines mobile technology and human-centered digital coaching to foster shared decision-making, goal setting, and accountability between provider and patient in daily diabetes self-care. App content covers a wide spectrum of lifestyle priorities including nutrition, blood glucose self-monitoring, and medication management. From a standard initial sequence, content is rapidly tailored to patient needs using both machine-learning recommendation algorithms and provider input. Our hypothesis was that this continuously available, highly personalized combination of provider guidance and content would drive improvements in diabetes control as assessed by changes in HbA_{1c}. We further hypothesized that app-based usage would be positively correlated with HbA_{1c} improvements.

Methods

Design and Measures

A single-arm, retrospective design was used to investigate the impact on HbA_{1c} in adults whose baseline value reflected suboptimal type 2 diabetes control and who enrolled in Vida Health’s app-based digital health intervention. The study was approved by an independent institutional review board (Western Institutional Review Board, Inc), which waived informed consent because the study was identified as having minimal risk and because the data were fully anonymized before use in the analysis.

Study Sample and Recruitment

The study included adults (18 years or older) from 2 major insurance carriers that were clients of Vida Health, and so participants received the Vida Health Program free of charge. HbA_{1c} data were obtained directly from these insurance carriers via their data sharing arrangements with outpatient laboratory networks. Participants were eligible for the study if they had a baseline HbA_{1c} value of at least 7.0% (as described in Statistical Analysis). All participants in the study were enrolled in the Vida Health Diabetes Management Program (henceforth "Program"), had smartphone or web-based access, and were fluent in spoken and written English or Spanish. Vida has made the Program available in both English and Spanish through professional translation and employs bilingual providers.

Eligible participants were recruited through a combination of brochures, outbound calling campaigns, and email announcements with general information provided about the Program and how to enroll. They were directed to download the Vida Health app from the Apple App Store (Apple Inc) or Google Play Store (Google) and to enter an invitation code to confirm insurance coverage.

After installing the app and prior to enrolling in the Vida Health Program, participants were presented with a series of brief in-app intake forms through which they provided contact information, basic demographic information (self-reported weight, height, age, and gender), and existing health conditions. Informed consent for digital nutrition therapy was a standard part of the initial app content. Exclusion criteria were type 1 diabetes, chronic kidney disease stages 4 or 5, congestive heart failure classes III or IV, pregnancy, and breastfeeding.

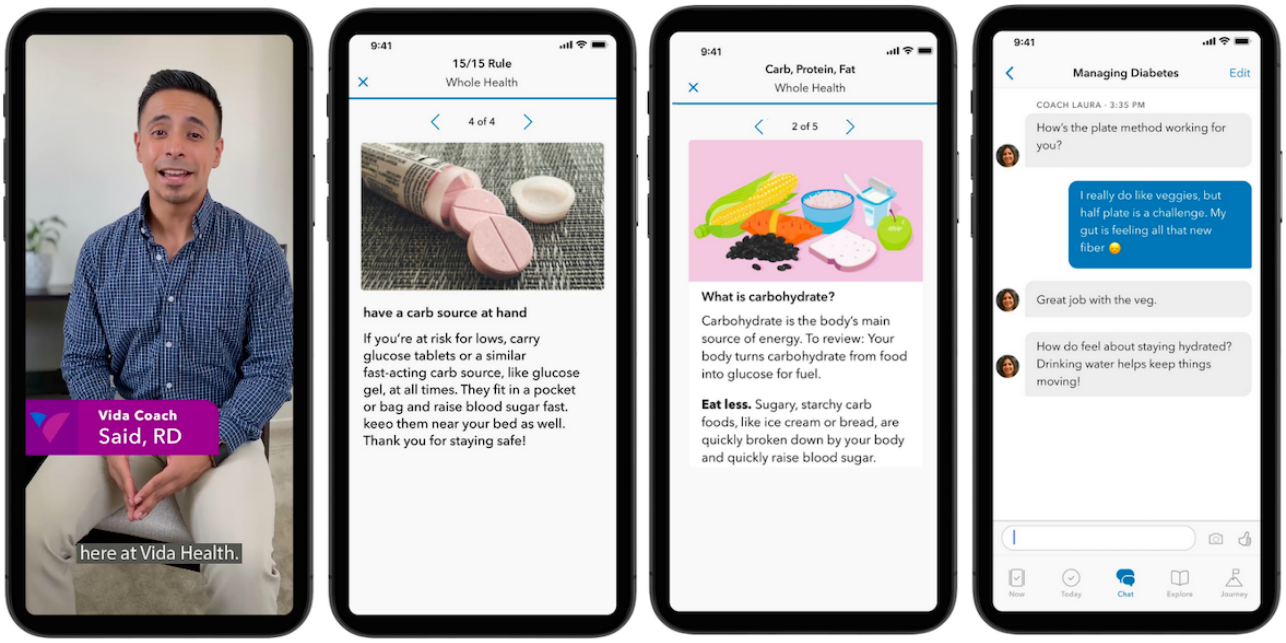
Therapeutic Approach and Intervention

The Program is a digital diabetes intervention program with remote coaching sessions encouraged up to weekly for the first 12 weeks and monthly thereafter. Participants are paired with a Vida provider—certified health coach, registered dietitian, or certified diabetes care and education specialist—who specializes in diabetes self-management. Vida providers receive intensive evidence-based training on motivational interviewing techniques that promote self-efficacy and autonomy for behavior change [26].

The Program combined one-to-one support, educational content, biomarker tracking, and data analysis to address self-care behaviors. Provider support was delivered through live in-app audio-video sessions (audio-only also available) and text messaging. The initial encounter included a detailed health assessment. The Vida provider used motivational interviewing to guide the participant in defining the initial area of focus for lifestyle change and identifying any associated barriers. Subsequent sessions followed up on these goals and worked to resolve ambivalence to change. Each session concluded with an individualized wellness plan including specific goals. Between counseling sessions, participants were encouraged to text message their Vida provider for further support. The Vida provider used text messaging to offer feedback on data tracking and motivational interviewing to overcome barriers to change.

App content was the primary emphasis to support scalability. It included structured lessons and multimedia content (see Figure 1) with evidence-based approaches to health behavior change, such as blood glucose self-monitoring, medication adherence, and nutrition [27]. Participants could review and interact with the lessons by responding to question prompts therein. The Vida provider reviewed completed lessons to help members apply their learnings to their goals and diabetes self-management behaviors.

Figure 1. Vida Health educational content screens.



For those participants who reported having been recommended self-monitoring of blood glucose, logging was encouraged. The Vida app supports connections to a variety of commercially available cellular connected blood glucose meters and also allows for manual logging of data. Structured logging capabilities for food intake and physical activity are also available.

Statistical Analysis

The primary outcome measure for this study was HbA_{1c}. HbA_{1c} was measured in clinical laboratories and the data made available by Vida Health's payer clients. Baseline HbA_{1c} was defined as the laboratory test closest to Program start, measured between 6 months before to within 21 days after enrollment. For 7 participants, HbA_{1c} laboratory data results were >14. In these instances, we confirmed the Logical Observation Identifiers Names and Codes (LOINC) test description as HbA_{1c} and the result unit of measurement as % of total hemoglobin and used a conservative approach to assign a HbA_{1c} value of 14.0.

The follow-up measure was defined as a HbA_{1c} test completed a minimum of 90 days post Program start. In order to evaluate possible systematic baseline differences between participants with a valid follow-up measure and those with no follow-up, we performed a 2-tailed chi-square test to assess gender-based differences. Additionally, a set of 2-tailed *t* tests were employed to evaluate differences between groups based on age and baseline HbA_{1c}.

A paired *t* test was used to assess change in HbA_{1c} from baseline. A repeated measures analysis of variance (ANOVA) with the measurement period as a within-subject factor was used to analyze changes in HbA_{1c} from the pre-enrollment measure to baseline and from baseline to follow-up. Pre-enrollment was defined as a HbA_{1c} measure obtained at least 90 days prior to the baseline. A Mauchly test was used to confirm that assumptions of sphericity had not been violated. We conducted a series of post hoc pairwise comparisons of means to evaluate HbA_{1c} changes between each measurement window.

Program usage was a secondary focus of this study. Although conceptually related to user engagement, program usage or adherence comprises objective measures of a user's interaction with the digital interface over time (eg, number of log-ins, counseling sessions, lessons and tools completed). User engagement, on the other hand, includes the subjective experience of the digital intervention with a focus on the quality of the experience [28,29]. Although the behavioral aspect of engagement (usage) and the subjective or experiential aspect (eg, satisfaction, interest, perceived relevance) can no doubt influence one another, their independent or interactive effect on clinical outcomes in the context of digital health remains unclear [29]. Measures of the experiential dimension of engagement were not assessed in this study. Program usage was conceptualized using 3 in-app behaviors. First, we computed a cumulative sum for each of the following factors: number of counseling sessions, number of messages sent to the provider by the participant, and the number of lessons completed within the first 6 weeks of Program start. We then created a binary program usage variable where high usage was defined as participants with greater-than-or-equal-to-median coach interaction and greater-than-or-equal-to-median content interaction. A cluster-robust multiple regression analysis was used to evaluate the association between the extent of usage and HbA_{1c} change. Data preparation and analyses were performed using Python Version 3.7.7 and Stata/IC 16.0 (StataCorp).

Data Availability

The data sets analyzed for this study are available from the corresponding author upon request.

Results

Member Characteristics

In all, 950 participants enrolled in the Vida Health Diabetes Management Program. A total of 692 participants (72.8%) had no postenrollment follow-up HbA_{1c} value, which was defined as a HbA_{1c} test completed at least 90 days from Program start. A schematic of participant flow is presented in Figure 2. Of the 692 participants with no follow-up, 248 (35.5%) did have a follow-up HbA_{1c} laboratory measure available; however, the measure was completed within 90 days of program start. Because our a priori definition of follow-up, based on the physiological characteristics of the HbA_{1c} test, was a laboratory test obtained a minimum of 90 days after Program start, participants with a postenrollment test obtained before 90 days were excluded from the outcome analyses and were considered to be missing a 3-month follow-up measure [30]. Basic demographics of the study cohort are presented in Table 1.

A 2-tailed *t* test revealed no significant group-level differences in baseline HbA_{1c} levels between follow-up HbA_{1c} availability status (t_{948}=1.27; P=.21). Participants with a valid follow-up HbA_{1c} appeared to be younger (mean 56.79, SD 9.52) than those without a follow-up available (mean 60.22, SD 11.8; t_{948}=4.18; P<.001). Additionally, a 2-tailed chi-squared test showed no significant gender-based differences between the groups (X^2=0.46; P=.79). Average baseline HbA_{1c} for the study cohort was 8.79 (SD 1.62).

Figure 2. Schematic of participant flow. HbA_{1c}: hemoglobin A_{1c}.

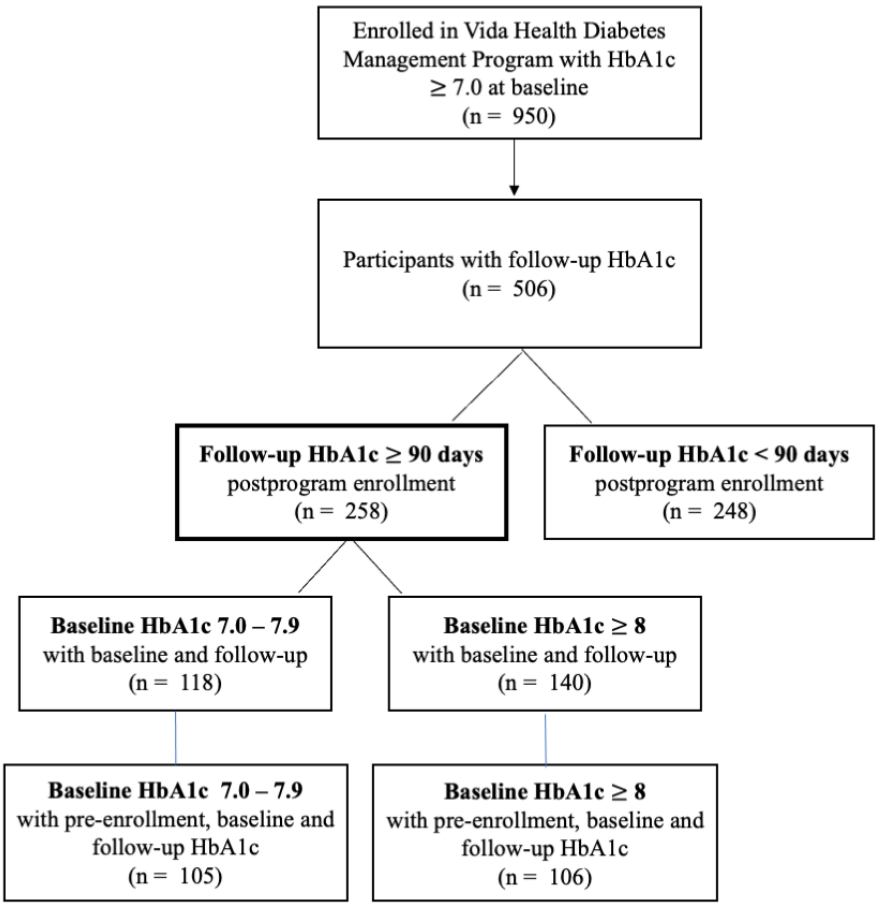


Table 1. Demographic characteristics of the study cohort (N=950).

Group	Count (n)	Proportion (%)	Age (years), mean (SD)	Baseline HbA_{1c}[a], mean (SD)
No post-90 day HbA_{1c} follow-up available (n=692)	692	72.8	60.22 (11.80)	8.83 (1.59)
Female	405	42.6	59.72 (10.98)	8.83 (1.66)
Male, n (%)	286	30.1	60.91 (12.87)	8.84 (1.48)
Unspecified	1	0.1	63.00[b]	7.10[b]
Post-90 day HbA_{1c} follow-up available (n=258)	258	27.2	56.79 (9.52)	8.68 (1.70)
Female	154	16.2	55.85 (9.38)	8.74 (1.76)
Male	104	11.0	58.19 (9.60)	8.60 (1.62)
Overall	950	100	59.29 (11.32)	8.79 (1.62)

[a]HbA_{1c}: hemoglobin A_{1c}.

[b]SD value is not applicable.

Primary Outcome

Follow-up HbA_{1c} measurements were completed on average 132.68 days (SD 31.46) from Program start. As shown in Figure 3, a paired *t* test revealed a significant reduction in HbA_{1c} of –0.81 points between baseline (mean 8.68, SD 1.7) and follow-up (mean 7.88, SD 1.46; t_{257}=7.71; *P*<.001). Among high-risk participants with a baseline HbA_{1c} ≥8, we observed an average reduction of –1.44 points between baseline (mean 9.73, SD 1.68) and follow-up (mean 8.29, SD 1.64; t_{139}=9.14; *P*<.001; see Figure 4).

Figure 3. A boxplot of HbA_{1c} at baseline and a minimum 90-day follow-up (N=258). HbA_{1c}: hemoglobin A_{1c}.

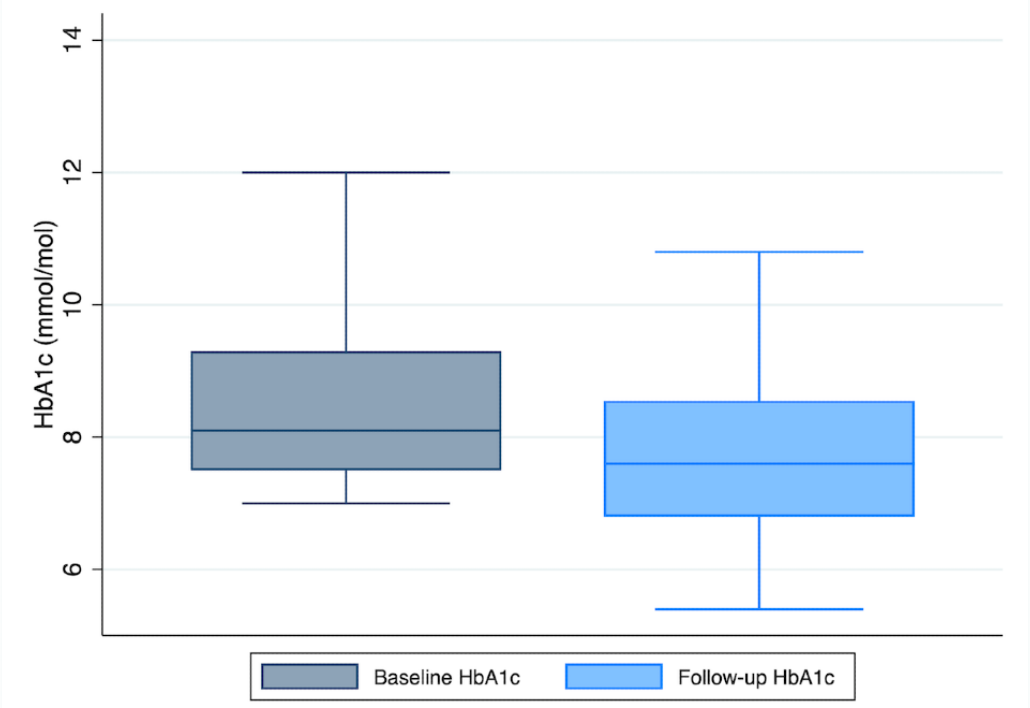
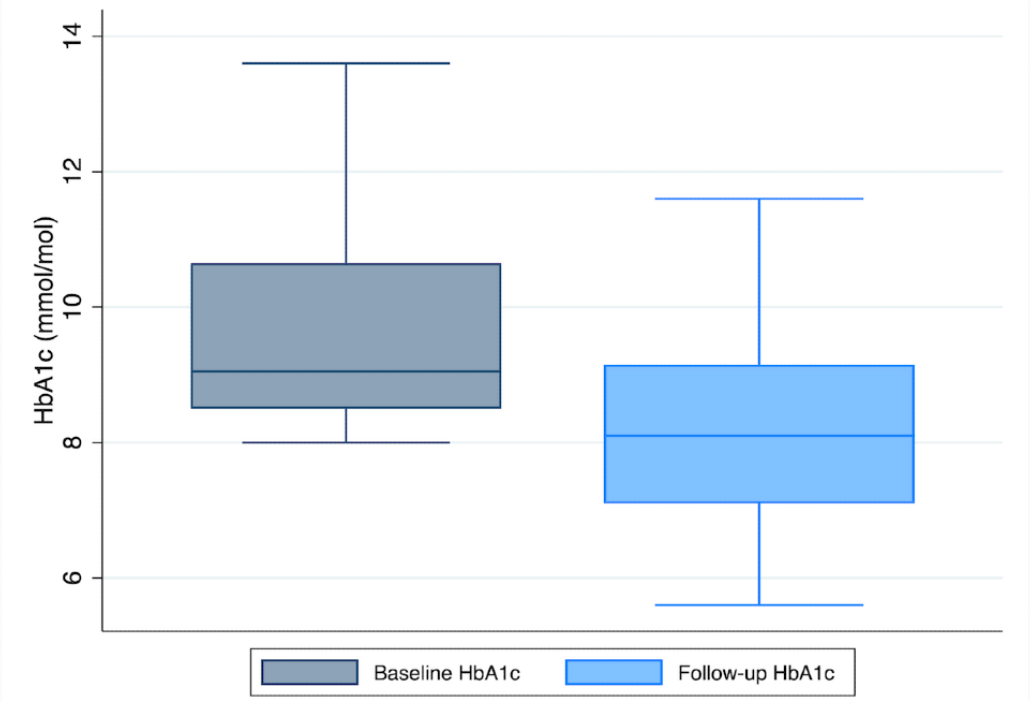


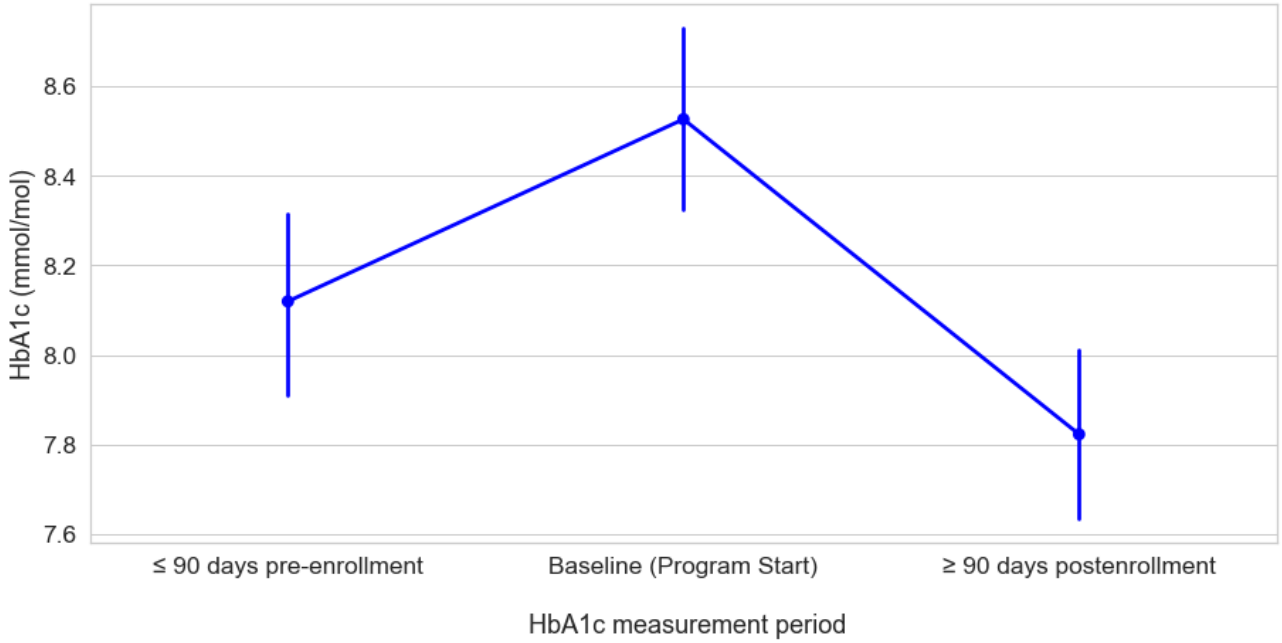
Figure 4. A boxplot of change in HbA_{1c} from baseline to follow-up among high-risk participants with a baseline $HbA_{1c} \geq 8$ (N=140). HbA_{1c}: hemoglobin A_{1c}.



In terms of provider interaction, a majority (167/258, 64.7%) had completed at least one provider session within the first 6 weeks of the program. Although both groups did have a significant decrease in HbA_{1c} relative to follow-up, change in HbA_{1c} varied as a function of consultation status (t=2.63; P<.001) such that participants who had completed at least one counseling session with a provider had a greater decrease in HbA_{1c} (mean –1.00, SD 1.66) compared to those who had never completed a session (mean –0.44, SD 1.65). A similar pattern emerged for the high-risk cohort (baseline $HbA_{1c} \geq 8$). Among participants with baseline $HbA_{1c} \geq 8$, the majority (93/140, 66.4%) had completed at least one counseling session within the first 6 weeks of program start. A Welch t test revealed a significant difference in HbA_{1c} change as a function of session status, (t=2.34; P=.02). Participants who had completed at least one session had an average reduction of –1.71 points (SD 1.70) compared to participants who had yet to complete a session (mean –0.90, SD 2.04).

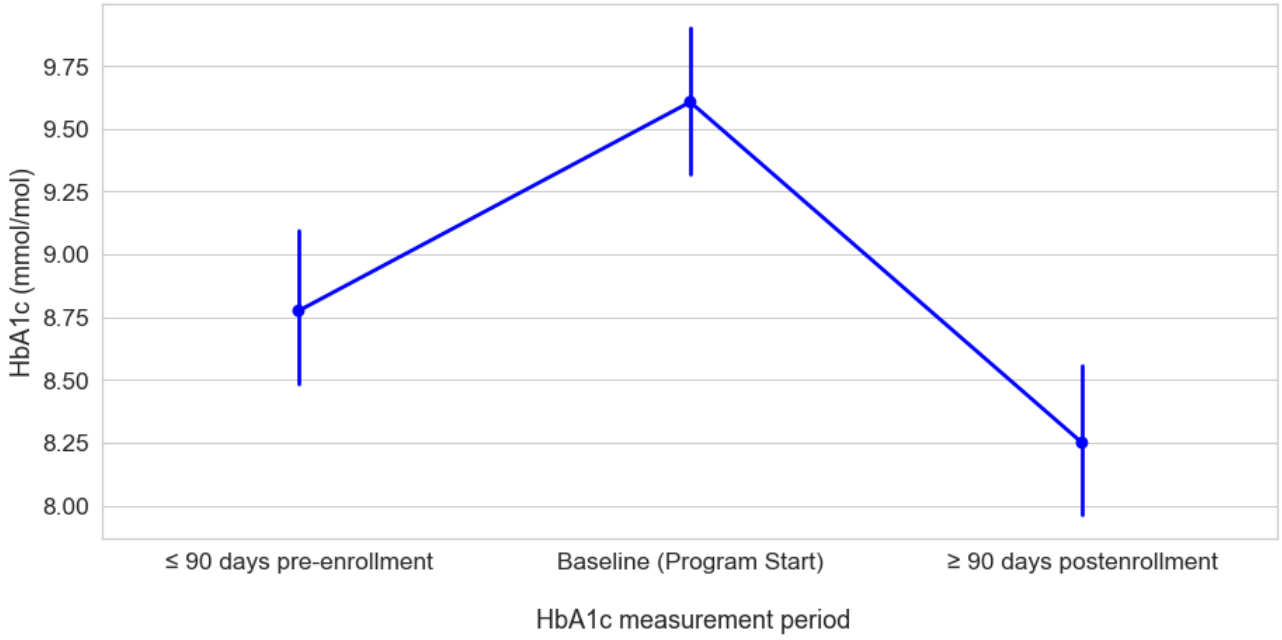
In order to evaluate the effects of no program intervention, we used a repeated measures approach. The model included HbA_{1c} measured at 3 time points (time 1: HbA_{1c} from at least 90 days up to 12 months prior to the baseline HbA_{1c} test; time 2: baseline HbA_{1c}; time 3: minimum 90-day postenrollment HbA_{1c} follow-up). The vast majority of participants (211/258, 81.7%) had data available for all 3 time points. A 1-way repeated measures ANOVA was conducted to assess the effect of measurement time point on HbA_{1c} prior to, at baseline, and at follow-up. A Mauchly test of sphericity confirmed that the assumption of sphericity had not been violated (X^2=5.91; P=.05). We observed a significant effect of measurement time on HbA_{1c}, ($F_{2,\ 210}$=22.90; P<.001). A post hoc pairwise comparison of marginal means between measurement time points showed a significant increase between pre-enrollment HbA_{1c} (mean 8.12, SD 1.46) and baseline (mean 8.53, SD 1.56; t_{210}=3.90; P<.001). As anticipated, we observed a significant decrease from baseline to 90-day postenrollment follow-up (mean 7.82, SD 1.41; t_{210}=–6.74; P<.001). Additionally, we noted that follow-up HbA_{1c} (mean 7.82, SD 1.41) was significantly lower than pre-enrollment HbA_{1c}, (mean 8.12, SD 1.46; t_{210}=–2.84; P=.005. In summary, we observed an increase in HbA_{1c} between pre-enrollment and baseline but a significant reduction between baseline and follow-up (see Figure 5).

Figure 5. Estimated marginal means of HbA_{1c} as a function of measurement period (N=211). HbA_{1c}: hemoglobin A_{1c}.



A similar pattern of results emerged among participants with a HbA_{1c} ≥8. In this high-risk cohort, 75.7% (106/140) of the participants had data available for the 3 measurement periods. As shown in Figure 6, there was a significant effect of measurement period HbA_{1c}, ($F_{2,105}$=31.6; P<.001). A post hoc pairwise comparison of marginal means revealed a significant increase between pre-enrollment HbA_{1c} (mean 8.78, SD 1.57) and baseline (mean 9.60, SD 1.56; t_{105}=0.83; P<.001). As expected, there was a significant decrease in HbA_{1c} from baseline to follow-up (mean 8.25, SD 1.61; t_{105}=–7.88; P<.001). Additionally, we noted the 90-day postenrollment HbA_{1c} (mean 8.25, SD 1.61) was significantly lower than the average pre-enrollment HbA_{1c} (mean 8.78, SD 1.57; t_{105}=–0.52; P=.003).

Figure 6. Changes in HbA_{1c} as a function of measurement period among high-risk participants with a baseline HbA_{1c} ≥8 (N=106).



Program Usage Outcomes

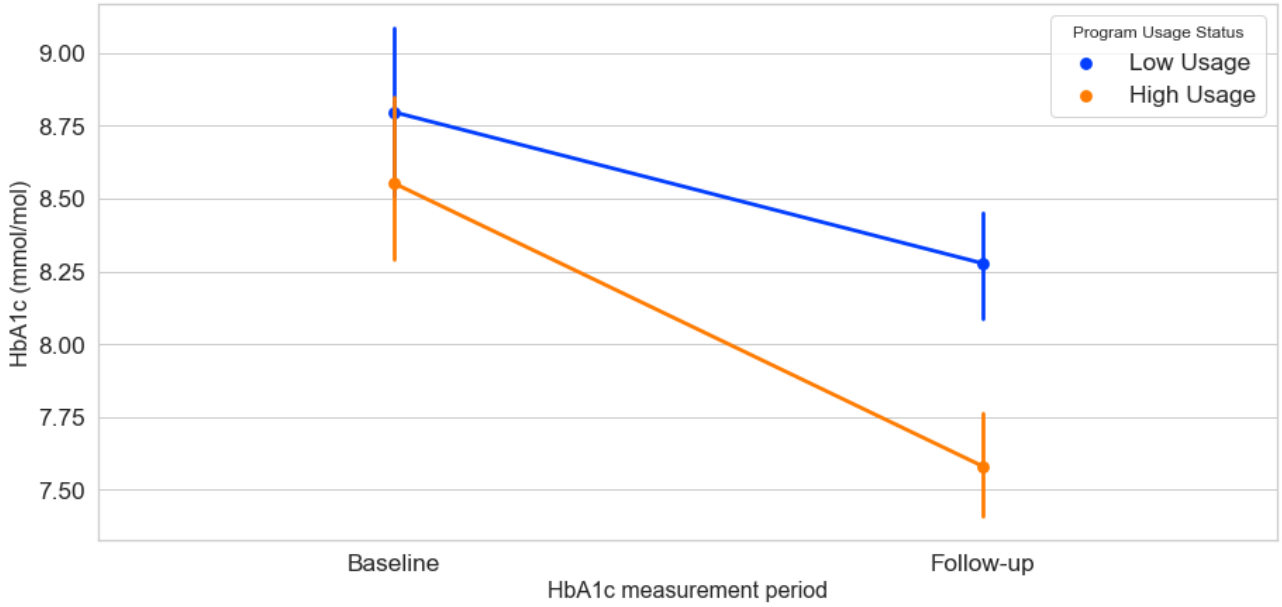
We hypothesized that program usage would be associated with improvements in HbA_{1c} reduction at follow-up. In order to test this hypothesis, we used a cluster-robust linear regression model that included all participants with postenrollment follow-up HbA_{1c} data, irrespective of days between baseline and follow-up. Active program usage was operationalized as a binary variable that was derived from 3 measures of program usage within the first 6 weeks of enrollment: number of sessions, number of messages sent to the provider, and number of lessons completed. These factors were left skewed, indicative of possible "super users" of the app (see Table 2). Therefore, we used the median to define cutoffs for high and low program usage. High usage was defined as participants having completed at least 2 sessions or having sent at least 7 messages to their provider and completed at least 4 lessons in the app within the first 6 weeks of the program. These cutoffs were determined using the median value for each of these factors. Greater relative usage of lessons and app content relative to provider sessions was expected given Program design. A 2-tailed *t* test revealed no significant difference in baseline HbA_{1c} between the high and low program usage groups (P=.25). Based on the above described cutoffs, 47.2% (122/258) of participants were considered to have high usage, and 52.7% (136/258) were considered to have low usage.

Table 2. Summary statistics for Program usage within the first 6 weeks of the Program (N=258).

Statistic	Number of sessions	Number of messages	Number of in-app lessons
Mean	2.8	17.30	8.17
SD	2.61	26.53	9.72
Median	2	7	3.5

Gender, age, time to follow-up, and the binary program usage variable were included as fixed factors and baseline HbA_{1c} as a covariate. We employed a cluster-robust multiple regression analysis to account for possible differences in provider effectiveness. Change in HbA_{1c} was defined as the outcome variable. As shown in Figure 7, we observed a significant main effect of usage on change in HbA_{1c}, (β=–.60; P<.001), such that high usage was associated with a greater decrease in HbA_{1c} at follow-up ($M_{high\text{-}usage}$=–1.02; $SD_{high\text{-}usage}$=1.60; $mean_{low\text{-}usage}$=–.61; $SD_{low\text{-}usage}$=1.72). A higher baseline HbA_{1c} was associated with greater improvement in HbA_{1c} (β=–.63; P<.001) such that participants with a higher baseline HbA_{1c} showed a greater decrease at follow-up. We observed no significant effect of time to follow-up (measured in days), age, or gender.

Figure 7. Estimated marginal means of HbA_{1c} at Program start (baseline) and at follow-up as a function of high and low program usage (N=258).



Discussion

Principal Findings

The objective of this study was to assess the effectiveness of Vida's digitally delivered continuous care platform on HbA_{1c} improvement. In this retrospective study of 258 participants with suboptimally controlled type 2 diabetes (baseline HbA_{1c} ≥7) who enrolled in an app-based digital health intervention paired with one-to-one remote health coaching, we observed an average reduction in HbA_{1c} of –0.81 at post-90 day follow-up relative to baseline. Among participants considered high-risk (baseline HbA_{1c} ≥8), we observed a stronger average reduction in HbA_{1c} (mean –1.44 points, SD 1.86) relative to baseline. We used a repeated measures approach in which participants serve as their own control to evaluate changes in HbA_{1c} pre- and postenrollment in the Vida Health Program. As detailed below, a substantial portion of the initial cohort has not yet obtained a follow-up HbA_{1c}. It is, however, notable that follow-up HbA_{1c} was significantly lower even than the average pre-enrollment HbA_{1c}.

The results also provide preliminary insight into the role of program usage as a possible moderator of glycemic control. The majority of the study cohort had completed at least one session with their provider within the first 6 weeks of the Program. Both groups showed a significant decrease in HbA_{1c}, while participants who had at least one session showed greater improvement in HbA_{1c} (mean –1.00, SD 1.66) than those who had yet to complete a session. A similar pattern emerged when we operationalized usage in the digital platform as a combination of provider-reliant actions (ie, video call sessions and asynchronous messaging) and app-based interactions (eg, reading lessons, viewing multimedia content). We observed a significant positive association between program usage and improved glycemic control. The analysis revealed a statistically significant and clinically meaningful reduction in HbA_{1c} from baseline to follow-up at least 3 months postenrollment. A growing body of evidence suggests digital interventions as an innovative way to deliver and engage people in their diabetes care. Yet, many open questions remain about the best combination of provider interaction and other components, such as educational content, interactive prompts, and data tracking, via a digital platform. The Vida hybrid model of digital diabetes management suggests an effective, scalable way to improve key diabetes-related health outcomes.

Although the Vida experience, including content and data tracking, can be navigated without provider contact and in a self-paced manner, we observed that the combination of human interaction and content app components is associated with improved HbA_{1c}. In a secondary outcome measures analysis, we observed a significant effect of usage, as defined by interaction with the provider and the digital platform. Higher program usage was associated with a more pronounced reduction of HbA_{1c}. This suggests Vida's hybrid model, which offers a combination of curated and self-paced app-based components and ongoing support from a human provider, may offer advantages over a hypothetical analogue without a human provider. Although the study design lacked a control group or matched comparison group, and so prevents causal inference, it suggests promising avenues for future research. A flexible, scalable solution to population-level diabetes management would certainly be welcome.

The provider interaction that shows correlation with outcomes here provides a vehicle for motivational interviewing throughout a participant's experience. Motivational interviewing has been shown to be effective in supporting diabetes self-care [26,31,32]. Vida providers receive extensive training and ongoing evaluation in behavioral counseling with motivational interviewing techniques being a core component. Further research is warranted to explore if this human interaction and motivational interviewing methodology explain these atypical improvements in HbA_{1c}.

Limitations

This study used a nonrandomized, observational design that does not allow for causal inferences about the intervention and its impact on the primary outcome measure, change in HbA_{1c}. Participants self-selected to enroll in Vida and so may be more motivated to change their behavior and improve their health than those who were eligible but did not enroll. Similarly, while eligible participants were not known by their insurance carrier to be engaged with a similar diabetes intervention, simultaneous efforts to explain the effect cannot be excluded. This may be a particular concern among those with lower usage. Furthermore, while the program was completely free at the point of care to participants, the participant sample included only individuals with health insurance and so does not well represent underserved populations.

Despite possible systematic baseline differences between groups based on age—HbA_{1c} at baseline and gender—no significant gender-based differences were observed. Age-based differences were observed only for the presence of valid HbA_{1c} follow-up data. Of the 950 participants who enrolled, a total of 692 participants (72.8%) did not have a postenrollment follow-up HbA_{1c} value, defined as a HbA_{1c} test completed at least 90 days from Program start. Of the 692 participants with no follow-up, 248 (35.5%) did have a follow-up HbA_{1c} laboratory measure available; however, the measure was completed within 90 days of Program start, and thus this cohort was not included in the outcomes analysis due to the clinical significance of these values being difficult to interpret. The lack of follow-up HbA_{1c} among these participants is likely multifactorial. Participants with valid HbA_{1c} follow-up data were younger than those without a follow-up. Given the fact that the majority of the participants were enrolled in this study during the COVID-19 pandemic, it is reasonable to assume that access to HbA_{1c} tests might have been impacted by stay-at-home orders, restrictions on nonemergent care, and public health communication about COVID-19 risks and that these might have particularly impacted older participants [33]. With these limitations related to participants, the findings are not generalizable to all adults with type 2 diabetes.

Limitations with the secondary outcome include the modest sample size and the related numbers of provider and content interactions that stratified program usage. It may be that with a different definition of program usage or engagement, we would see a different impact on HbA_{1c} outcomes. Acceptability of the intervention for participants cannot be assessed by the study or generalized to other people living with diabetes.

Finally, the analysis examined only the intensive, first 12-week portion of the Vida Program, which is offered to participants as a 1-year experience. No inferences are possible about the persistence of usage with the digital health intervention or of sustained HbA_{1c} improvements until further follow-up data become available.

Conclusions

In this study, adults with type 2 diabetes were enrolled in the Vida Health digital diabetes management program with rich educational content and one-to-one coaching grounded in motivational interviewing. The results of this study indicate statistically significant and clinically meaningful glycemic improvements post intervention. The nonrandomized observational design, modest sample size, and low number of participants who met the follow-up HbA_{1c} criteria were study limitations. Although further research will be welcome, evidence-based, digitally delivered interventions like Vida Health may already represent an accessible, scalable, and effective solution to diabetes management and improved HbA_{1c}.

Acknowledgments

We are grateful to the study participants and all people enrolled in Vida Health programs. We appreciate the health coaches, registered dietitians, diabetes care and education specialists, and therapists at Vida Health for their professional expertise, commitment, and ongoing support of people seeking to manage complex, polychronic conditions including type 2 diabetes. We note the key contributions of Ashritha Dhanak, RDN; and Camilla Hardin, RD; in content development; and Yara Mukaled in product management and program design.

Authors' Contributions

MS, GZ, AV, and KR developed the study concept and design. GZ and MS oversaw the study intervention. AV performed statistical analyses and interpretation of data. GZ, KR, AV, and MS drafted the manuscript. Program design and educational materials were developed by KR and GZ. Provider training was developed and delivered by GZ.

Conflicts of Interest

GZ is an employee of Vida Medical, PC; MS, AV, and KR are employees of Vida Health; and all receive compensation in the form of salary and equity.

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Abbreviations

ACCORD: Action to Control Cardiovascular Risk in Diabetes
ANOVA: analysis of variance
DiRECT: Diabetes Remission Clinical Trial
HbA_{1c}: hemoglobin A_{1c}
LOINC: Logical Observation Identifiers Names and Codes
UKPDS: UK Prospective Diabetes Study

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Original Paper

Change in Glycemic Control for Patients Enrolled in a Membership-Based Primary Care Program: Longitudinal Observational Study

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Abstract

Background: Both primary care practices based on the chronic care model (CCM) and digital therapeutics have been shown to improve the care of patients with diabetes.

Objective: The aim of this observational study was to examine the change in diabetes control for patients enrolled in a membership-based primary care service that is based on the CCM.

Methods: Using a diabetes registry, we analyzed the change in glycated hemoglobin (HbA_{1c}) for patients with uncontrolled diabetes mellitus (initial HbA_{1c}≥9%). All patients had access to a technology-enhanced primary care practice built on the CCM.

Results: The registry included 621 patients diagnosed with uncontrolled diabetes. All patients had at least two HbA_{1c} measurements, with the average time between the first and last measurement of 1.2 years (SD 0.4). The average starting value of HbA_{1c} was 10.7, which decreased to 8.7, corresponding to a reduction of 2.03 (P<.001). Secondary analyses showed statistically significant reductions in total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and triglycerides.

Conclusions: Patients with initially uncontrolled diabetes who undergo care in a technology-enhanced primary care practice based on the CCM have long-term clinically meaningful reductions in HbA_{1c}.

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KEYWORDS

diabetes mellitus; primary care; chronic care model; diabetes; self-management; patient; observational; digital health; decision support; decision-making; clinical information system

Introduction

Uncontrolled diabetes mellitus (DM) has serious complications, including increasing the risk for heart disease, peripheral vascular disease, and kidney disease [1]. Most patients with DM are treated in primary care [2]; yet, traditional models of primary care often do not have the adequate resources to manage this chronic disease.

The chronic care model (CCM) has been described as a way for primary care practices to control chronic diseases, including diabetes [3,4]. The CCM comprises 6 components that are hypothesized to affect functional and clinical outcomes associated with disease management: (1) health system—organization of health care, (2) self-management support, (3) decision support, (4) delivery system design, (5) clinical information systems, and (6) community resources and policies.

One Medical is a membership-based (US $199/year) primary care practice based in urban and suburban locations throughout the United States. The practice mostly serves an insured population. The practice is a Patient-Centered Medical Home, as it is built on the core attributes of primary care, along with enhanced access, a quality-improvement structure, and some

blended payments [5]. The aim of this observational study was to assess the change in diabetes control for patients receiving care in this nationwide practice. We hypothesized that patients engaging in our primary care model, built on the principles of the CCM, would have improved glycemic control.

Methods

This was a retrospective observational analysis of primary care patients. As members of One Medical, these patients have access to all of the components of the CCM. The key features of the One Medical model and how they correspond to the CCM are shown in Table 1. All patients in our practice, including those with diabetes, have enhanced access to in-office and remote care, longer appointments, and self-management tools (eg, tracking of lab results and blood pressure on a mobile app). A patient with diabetes will have an evaluation and a care plan developed and documented in our problem-based electronic health record. Between primary care provider visits, the patient has constant virtual access to a team of clinicians, care navigators, and health coaches, all of whom are employed by One Medical. Care issues such as hypoglycemia or questions about medications can be addressed when they arise in this team-based care model.

Table 1. Chronic care model components of the One Medical model.

Chronic care model component	Feature of One Medical
Health system	Enhanced access with same-day primary care appointments and 24/7 access through messaging and on-demand video chat
Self-management	Mobile app, which provides care reminders and allows self-tracking of diabetes lab results and blood pressure
Decision support	In-house–built electronic health record that gives providers disease management “tips” and lab order sets
Delivery system design	Care navigators and virtual care providers who can manage patient care between visits with their primary care providers
Clinical information systems	Population health and quality improvement infrastructure that allows tracking of process metrics and outcomes

We used an existing quality-improvement registry of One Medical members with prediabetes and diabetes (N=7805) who had at least two glycated hemoglobin (HbA_{1c}) lab measurements over a follow-up period of 180 days or longer as the source for our analysis. The registry is derived from our health system’s proprietary electronic health record, including all types of DM, with data collected from 2017 to 2020. The registry’s primary use is to improve the quality of care for patients with diabetes. From this registry, we selected a sample of patients whose first HbA_{1c} result in the practice showed their condition as uncontrolled (HbA_{1c}≥9%). We performed a retrospective analysis of changes in lab-measured HbA_{1c} for this sample of patients with uncontrolled diabetes.

We report the basic demographics, BMI, as well as the Charleston Comorbidity Index (CCI) of our patients. The CCI is a chronic disease scoring system that is correlated with 10-year risk of mortality [6]. The CCI generally gives 1-6 points for each chronic disease a patient has and 1 point for every decade over age 50. The predicted 10-year survival is 96% for patients with a score of 1, 90% for those with a score of 2, 77% for those with a score of 3, and so on.

We analyzed the change in HbA_{1c} between the initial and last available value using a paired *t* test. In secondary analyses, we also evaluated changes in total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, and triglycerides. Very few patients had missing data, and therefore we chose to not remove any patients due to missing data. We used STATA Version 14 for all analyses.

Results

The analysis included a dataset for 621 patients (8% of the registry of 7805 patients) who met our inclusion criteria as their diabetes was uncontrolled upon presentation. The average time between lab values was 1.2 years (SD 0.4). The characteristics of the patients at the time of data extraction from the registry are shown in Table 2. Patients had a median CCI of 2, indicating that the majority of patients had an additional chronic disease or were over the age of 50.

Table 3 shows the change in lab values. There was an overall decrease in the mean baseline and follow-up HbA_{1c}, total cholesterol, LDL cholesterol, and triglycerides, with an average increase in HDL cholesterol.

Table 2. Characteristics of patients (N=621).

Characteristic	Value
Age (years), mean (SD)	51.2 (12.0)
Female, n (%)	189 (30.4)
BMI (kg/m^2), median (IQR)[a]	31.5 (27.6-36.2)
CCI[b] score, median (IQR)	2 (2-4)
Major depressive disorder, n (%)	126 (20.3)
Generalized anxiety disorder, n (%)	26 (4.2)

[a]BMI data were missing for 76 (12%) patients.

[b]CCI: Charleston Comorbidity Index.

Table 3. Changes in glycated hemoglobin (HbA_{1c}) and cholesterol.

Variables	Patients, N	First value, mean (SD)	Latest value, mean (SD)	Mean difference (95% CI)	*P* value[a]
HbA_{1c} (%)	621	10.7 (1.44)	8.7 (2.16)	–2.03 (–1.85 to –2.20)	<.001
Total cholesterol (mg/dl)	599	192.9 (63.2)	172.7 (60.8)	–20.2 (–16.3 to –24.1)	<.001
LDL[b] cholesterol (mg/dl)	542	103.4 (40.1)	90.7 (38.9)	–12.6 (–9.86 to –15.4)	<.001
HDL[c] cholesterol (mg/dl)	596	43.3 (13.7)	44.5 (13.4)	+1.2 (0.60 to 1.8)	<.001
Triglycerides, mg/dl	597	263.1 (443.5)	206.0 (173.6)	–57.0 (–37.2 to –76.8)	<.001

[a]Based on a two-sided *t* test.

[b]LDL: low-density lipoprotein.

[c]HDL: high-density lipoprotein.

Discussion

Principal Results

This analysis shows that a technology-enhanced primary care practice based on the principles of the CCM can effectively control diabetes. As hypothesized, patients who had uncontrolled diabetes on initial presentation showed a marked reduction in HbA_{1c} after engaging in technology-enhanced primary care that utilizes the CCM.

Comparison With Prior Work

Other technology-enabled diabetes interventions outside of primary care settings have also shown promise. A program focusing on diets and virtual coaching showed a 1.3% reduction in HbA_{1c} over 1 year [7]. A similar program delivered via a mobile app showed a reduction of 1.1% over 12 weeks for patients who had an initial HbA_{1c} >7% [8]. A remote monitoring intervention for diabetes with an average starting HbA_{1c} of 8.5% showed a 1% decrease in HbA_{1c} over 12 weeks [9]. The same program showed a nonsignificant decrease of 0.66% HbA_{1c} at 1 year [10]. However, patients on insulin, who started with a higher HbA_{1c}, had a statistically significant 0.9% decrease in HbA_{1c}.

In comparison to the above studies, our population showed a reduction of 2% in HbA_{1c}. This improvement is clinically meaningful as each 1% reduction in mean HbA_{1c} is associated with relative risk reductions of 21% for deaths related to diabetes, 14% for myocardial infarction, and 37% for microvascular complications [11]. The likely reason we were able to show larger reductions was because our program combined two methods that have been shown to improve diabetes care: technology-delivered care and care based on the CCM. The above-cited studies used technology and remote care, but were not integrated in a primary care practice. Incorporating a diabetes management program with primary care practices enables accessing additional patient touch points and engagement.

A systematic review has shown that the CCM is being used across the United States to treat diabetes in primary care, with some large interventions showing improvement in diabetes control [4,12]. However, one study in the Netherlands using the CCM found reductions in cardiovascular risk factors, but not improvement in HbA_{1c} [13]. One study on chronic care clinics showed that the reduction of HbA_{1c} was dependent on the number of interactions with the patient [14]. Other research has shown that simply displaying reminders to providers in the electronic health record can improve process metrics, but not glycemic control [15,16]. Yet, increasing provider continuity—the basis of good primary care—does seem to improve disease control [17]. Further, adding specialty care to primary care does not seem to improve the control of diabetes [18]. Ease of access and the availability of a smartphone app for patient-provider communication may have contributed to effective diabetes control in our CCM-based care model. Our results provide further evidence that implementing the CCM for diabetes care in primary care can improve diabetes control.

Limitations

This study's design is the main limitation, as it was observational. It is possible that these patients would improve with any primary care model, even one that does not include the components of the CCM. Since we selected patients who had uncontrolled diabetes with a high baseline HbA_{1c}, regression to the mean may explain some of the reductions in HbA_{1c} we observed. However, if the underlying theory of the CCM is correct, then any practice that incorporates the key features of the CCM, such as ours, should improve care.

The anticipated reduction in future cardiovascular risk may be further enhanced by lowering of LDL cholesterol as noted in this analysis. Although we did not analyze medications in this study, it is likely that many of these patients were placed on a statin. The likely reason for continued elevations in triglycerides is that our practice's standard procedure is to test nonfasting cholesterol levels. Thus, the levels would be higher than observed in previous studies that found a correlation between triglycerides and elevated cardiovascular risk. Even if these levels confer an elevated cardiovascular risk, triglycerides have a very small independent effect on this risk [19].

Findings such as the higher variance in follow-up HbA_{1c} than in the initial measurement could not be further assessed due to the limited number of variables included in this dataset. This can be common in studies where some individuals respond to treatment and others do not. Future research should assess potential contributors to variance in similar cohorts.

Conclusions

We demonstrated that patients with uncontrolled diabetes who receive ongoing care in a technology-based primary care model can achieve marked improvements in glycemic control. With sustained improvements, these patients will have a reduced risk for the micro- and macrovascular complications of diabetes attributed to glycemic control. This study provides further evidence that primary care practices that adopt the CCM as a model of care can improve diabetes care.

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Authors' Contributions

LIL and RB both contributed to study design, data analysis, and manuscript writing.

Conflicts of Interest

Both authors are employees and hold equity in One Medical, the sponsor of the study.

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Abbreviations

CCI: Charleston Comorbidity Index
CCM: chronic care model
DM: diabetes mellitus
HbA_{1c}: glycated hemoglobin A1c
HDL: high-density lipoprotein
LDL: low-density lipoprotein

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