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# Improving HbA<sub>1c</sub> with Glucose Self-Monitoring in Diabetic Patients with EpxDiabetes, a Phone Call and Text Message-Based Telemedicine Platform: A Randomized Controlled Trial

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## Abstract

**Background:** We conducted a randomized controlled trial of EpxDiabetes, a novel digital health intervention as an adjunct therapy to reduce HbA<sub>1c</sub> and fasting blood glucose (FBG) among patients with type 2 diabetes mellitus (T2DM). In addition, we examined the effect of social determinants of health on our system.

**Methods:** Sixty-five (n=65) patients were randomized at a primary care clinic. Self-reported FBG data were collected by EpxDiabetes automated phone calls or text messages. Only intervention group responses were shared with providers, facilitating follow-up and bidirectional communication.  $\Delta$ HbA<sub>1c</sub> and  $\Delta$ FBG were analyzed after 6 months.

**Results:** There was an absolute HbA<sub>1c</sub> reduction of 0.69% in the intervention group (95% confidence interval [CI], -1.41 to 0.02) and an absolute reduction of 0.03% in the control group (95% CI, -0.88 to 0.82). For those with baseline HbA<sub>1c</sub> >8%, HbA<sub>1c</sub> decreased significantly by 1.17% in the intervention group (95% CI, -1.90 to -0.44), and decreased by 0.02% in the control group (95% CI, -0.99 to 0.94). FBG decreased in the intervention group by 21.6 mg/dL (95% CI, -37.56 to -5.639), and increased 13.0 mg/dL in the control group (95% CI, -47.67 to 73.69). Engagement (proportion responding to  $\geq$ 25% of texts or calls over 4 weeks) was 58% for the intervention group (95% CI, 0.373-0.627) and 48% for the control group (95% CI, 0.296-0.621). Smoking, number of comorbidities, and response rate were significant predictors of  $\Delta$ HbA<sub>1c</sub>.

**Conclusions:** EpxDiabetes helps to reduce HbA<sub>1c</sub> in patients with uncontrolled T2DM and fosters patient-provider com-

munication; it has definite merit as an adjunct therapy in diabetes management. Future work will focus on improving the acceptability of the system and implementation on a larger scale trial.

**Keywords:** telemedicine, diabetes, glycemic control, self-monitoring, digital health, e-health

## Introduction

Diabetes is estimated to affect 30.3 million people (9.4% of the population) in the United States.<sup>1</sup> Long-term glycemic control can decrease the incidence of organ damage from microvascular and macrovascular complications.<sup>2</sup> The 2010 National Health and Nutrition Examination Survey estimates that 30% of adults with diabetes have not met target HbA<sub>1c</sub> levels.<sup>3</sup> In addition, 63.9% of adults with type 2 diabetes mellitus (T2DM) do not meet American Diabetes Association (ADA) recommended self-monitoring frequencies.<sup>4</sup> Generating new methods to promote self-blood glucose measurements and facilitate patient-provider assessment has the potential to positively impact blood glucose control in large populations.

Previous studies indicate that telemedicine interventions can improve patient outcomes by facilitating remote glycemic monitoring, patient-provider communication, and glycemic control.<sup>5-9</sup> However, multiple factors can influence the success of telemedicine interventions. The use of specialized telemedicine devices shows high attrition rates due to user frustration and high device costs.<sup>10,11</sup> Advancing age, low socioeconomic status, and low health literacy impair the ability to use new technology effectively, resulting in overall lower usage.<sup>12-18</sup> Telemedicine modalities using short messaging service (SMS) and phone calls are particularly appealing due to their ubiquity and standard integration into cellular phones, with findings that 92% of those making less than \$30,000 own a cellular phone.<sup>10</sup>

EpxDiabetes is a SMS and phone call-based intervention that allows for bidirectional patient-provider communication. This closed-loop communication is important for achieving glycemic control since many patients do not take action in

response to high or low readings<sup>19</sup> and may experience anxiety from uncontrolled blood glucose readings and infrequent physician feedback.<sup>20</sup> Barriers faced by other telemedicine interventions include response burden for patients and effort burden for physicians to provide real-time feedback.<sup>21</sup> EpxDiabetes reduces these particular barriers by utilizing a simple, widely used system, and triaging patient data to prioritize physician action. Upon detecting a dysglycemic event or trend from self-reported fasting blood glucose (FBG), EpxDiabetes prompts the patient's provider to follow-up with the patient, allowing for concerted provider detection and early intervention.

We previously demonstrated the real-world effectiveness of EpxDiabetes in lowering FBG and HbA<sub>1c</sub> in a community health care system implementation.<sup>5</sup> We have now conducted a randomized controlled trial (RCT) to assess the efficacy of EpxDiabetes in lowering FBG and HbA<sub>1c</sub> in patients with poor glycemic control (HbA<sub>1c</sub> > 7%), comparing the intervention group to our practice standard of care. In addition, we assessed the impact of social determinants of health on the efficacy of our system.

## Methods

### PARTICIPANT SELECTION, RECRUITMENT, AND ENROLLMENT

The IRB-approved 6-month RCT was conducted at a primary care clinic in St. Louis, Missouri. Standard of care consists of quarterly clinic visits and monthly provider calls from pharmacists to assess and modify patients' diabetes management plan.

We queried the clinic's electronic medical record (EMR) using ICD-9 and ICD-10 codes (250.x) and medication lists for patients with noninsulin-dependent T2DM seen within 18 months before the trial start date. Eligible patients were older than the age of 18 years and had a most recent HbA<sub>1c</sub> value of >7%. Patients were excluded from the trial if they did not have access to a mobile phone or landline, participated in previous implementations of EpxDiabetes, or were not currently monitored by the pharmacists.

Subjects meeting selection criteria were consented and recruited via phone from March to June 2016 on a rolling basis by independent research staff. Three hundred twenty-five (325) out of 346 eligible patients met enrollment criteria, 203 were successfully contacted, and 65 consented. Participants were allocated in a 1:1 ratio to intervention and control arms using simple randomization via the integrated function within the epx.wustl.edu platform. For each patient, a random IEEE754 float point value in the interval of [0, 1] was generated via the "Math.random" function from JavaScript. If the

value was >0.5, then the patient was added to the control group; otherwise, the patient was added to the intervention group. Simple randomization assigned 33 subjects to the intervention group, and 32 subjects to the control group (Fig. 1).

### STUDY DESIGN AND INTERVENTION

EpxDiabetes is based on an existing telemedicine platform, Epharmix, and customized for diabetes care as outlined in Peters et al.<sup>5</sup> by allowing for collection of FBG. Being mindful of limited health literacy requiring interventions with simple, easy-to-read instructions, all EpxDiabetes messages are designed at a fourth grade level as determined by the Flesch-Kincaid Grade Level formula and calculated on the Readable.io website. Text messages and phone calls were provided free of charge (excluding standard messaging rates) to patients on any network to further promote accessibility among low socioeconomic populations.

Patients self-report FBG values by responding to automated phone calls or SMS messages (Fig. 2). FBG values >400 or <70 mg/dL trigger an automated alert via text or phone call to the provider for a possible acute event, and the platform issues an automated instruction directly to patients to contact their providers and/or call 911 in an emergency. The algorithm recognizes hyperglycemic trends and notifies providers if bi-monthly average FBG exceeds 160 mg/dL. The Smart Scheduler modifies message frequency based on FBG to minimize message fatigue; patients reporting euglycemia receive messages less frequently.

The intervention group received messages an average of three times per week (twice a week to three times a day), depending on FBG stability. The control group received messages three times during the first week to establish a FBG baseline and once weekly thereafter without modifications from the Smart Scheduler. The control group did not receive any provider-initiated follow-up based on the self-reported FBG data, however, they were instructed to call their provider or 911 if severely dysglycemic and continue to receive standard of care.

### DATA GATHERING AND ANALYSIS

Demographic data were obtained from patients at the time of enrollment. Group differences were evaluated with a two-tailed *t*-test ( $\alpha=0.05$ ).

Pretrial, our primary outcomes were change in HbA<sub>1c</sub> and change in FBG. Secondary outcomes were response rate and engagement rate. Details on how each of these were calculated can be found below.

We included only those patients who had obtained a baseline HbA<sub>1c</sub> (within 3 months before enrolment into the

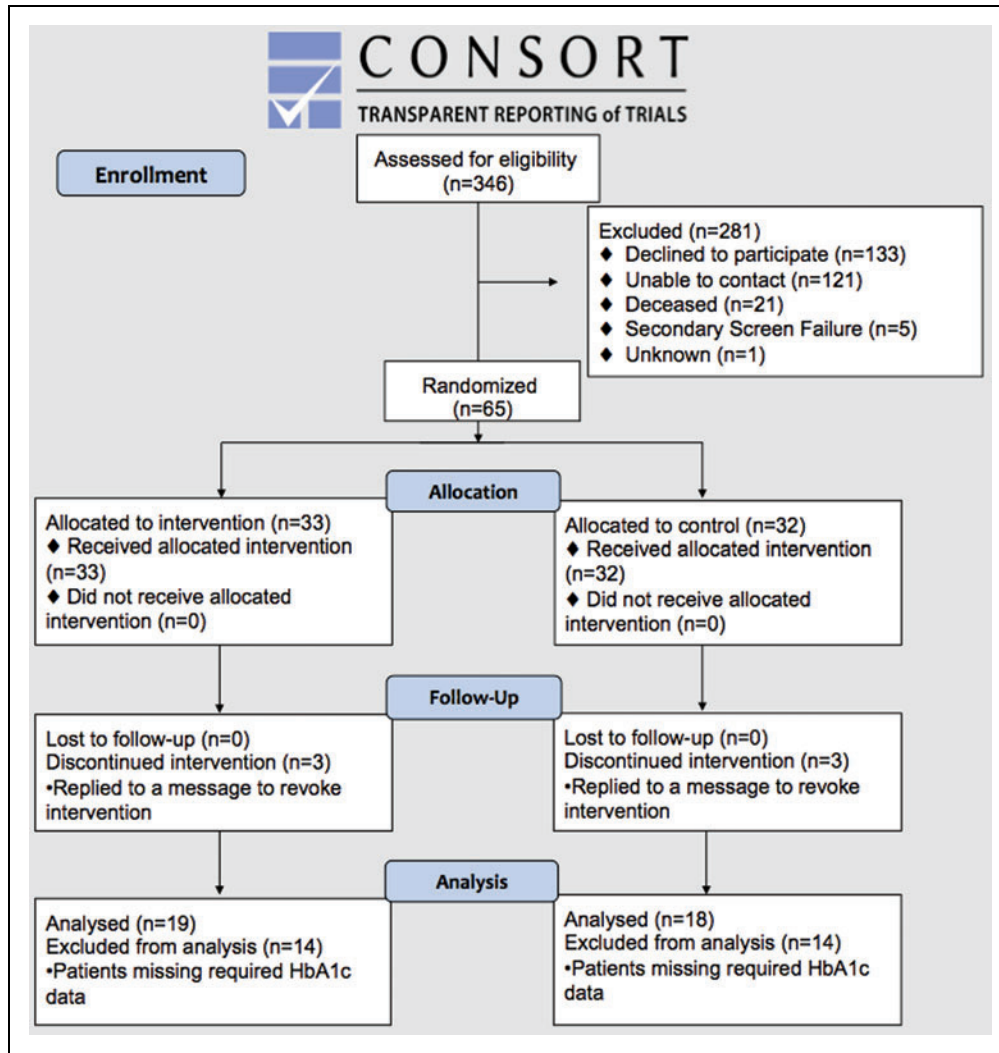


Fig. 1. CONSORT diagram. Color images are available online.

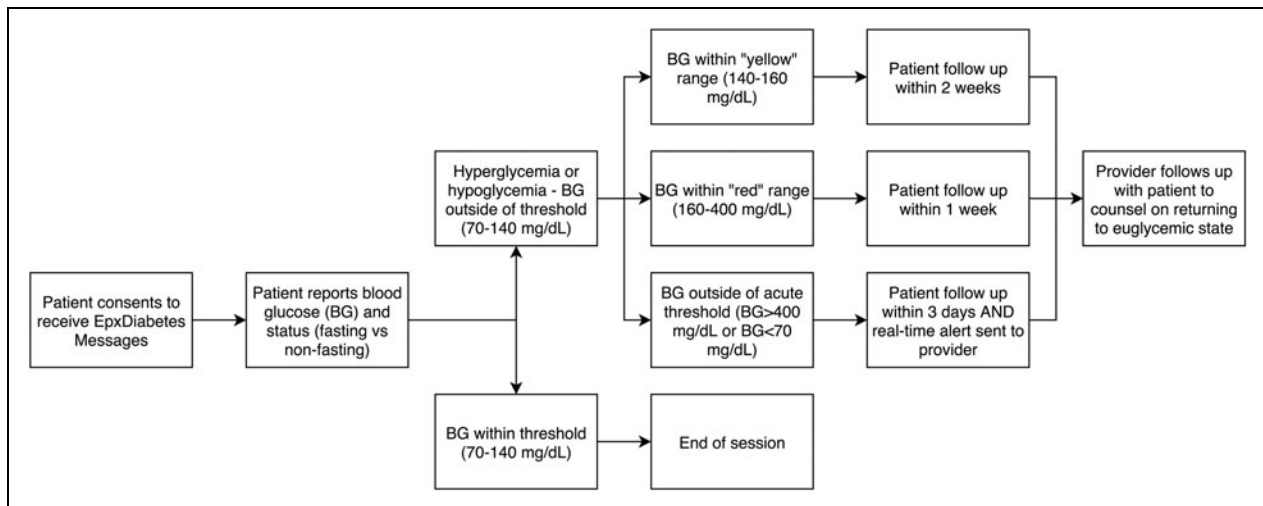


Fig. 2. EpxDiabetes intervention design and Alert protocol. Adapted from Peters et al.,<sup>5</sup> a concomitant quality improvement trial using EpxDiabetes.

trial) and a posttrial HbA<sub>1c</sub> (within 4–8 months after enrolment into the trial) in our analysis for HbA<sub>1c</sub> to evaluate a direct glycemic effects of SMS intervention. HbA<sub>1c</sub> values were extracted from the EMR 6 months after trial start date for each patient. ΔHbA<sub>1c</sub> from baseline to posttrial was calculated. An intention to treat analysis was performed for patients who did not respond through 6 months, but who did have HbA<sub>1c</sub> measurements. A subgroup analysis was performed for patients with baseline HbA<sub>1c</sub> >8%.

Baseline FBG for each patient was calculated by averaging the first three patient-reported FBG values. To account for the variable weekly message frequency, monthly FBG was determined for each patient by averaging four consecutive weekly FBG averages. The group average monthly ΔFBG was calculated for the two groups.

Deidentified patient engagement data and response rates were obtained from the Epharmix database. Patient monthly engagement rate was defined as the proportion of patients responding to at least 25% of texts or calls over 4 weeks. Average group monthly engagement was calculated. Patient response rate was the proportion of sent SMS messages or phone calls responded to.

Multiple linear regressions predicting ΔHbA<sub>1c</sub> and ΔFBG after 6 months was found using backward elimination and interpreted using adjusted R<sup>2</sup>. Data analysis was performed using Microsoft Excel 2016 (2016; Microsoft, Redmond, WA), PRISM (2016; GraphPad Software, La Jolla, CA), and SPSS (2016; IBM Corp, Armonk, NY).

**Results**

**BASELINE PATIENT CHARACTERISTICS**

African Americans represent the majority in both groups. The median income was \$14,440 for the intervention group and \$12,600 for the control group. The demographic differences between intervention and control groups were nonsignificant (*p* > 0.05) (Table 1). There were no significant differences in the distribution of specific comorbidities, other than lung disease, nor in number of comorbidities between the intervention group and control group (Table 1).

**HbA<sub>1c</sub> AND FBG ANALYSIS**

Pretrial and posttrial HbA<sub>1c</sub> were available for 19 patients in the intervention group and 18 patients in the control group due to missing the appointment within 4–8 months after enrollment into the trial; 29 out of 37 patients had a baseline HbA<sub>1c</sub> >8%. On average, patients obtained their posttrial HbA<sub>1c</sub> values 6 months after start of messages (181 days for intervention, 186 days for control). Patients were enrolled with an indefinite endpoint, outcomes were assessed at 6 months after enrolment.

Table 1. Patient Demographics		
	INTERVENTION GROUP	CONTROL GROUP
	33	32
Sex		
Male	12 (37.5%)	8 (25%)
Female	20 (62.5%)	24 (75%)
Age		
Average ± SEM	54.6 ± 1.82	55.34 ± 1.94
Race		
Caucasian	6 (18%)	2 (7%)
African American	27 (82%)	29 (93%)
Disability status		
Disabled <sup>a</sup>	19 (58%)	20 (63%)
Nondisabled	14 (42%)	12 (37%)
Education		
No formal education	0 (0%)	0 (0%)
Grade school	1 (3%)	1 (3%)
Some high school	4 (12%)	10 (31%)
High school graduate	11 (33%)	10 (31%)
Some college	13 (39%)	7 (22%)
College graduate or beyond	4 (12%)	4 (13%)
Income		
Mean ± SEM	\$18,993 ± 3,843	\$16,525 ± 2,125
Median	\$14,440	\$12,600
Comorbidities		
Hypertension	26 (79%)	25 (78%)
Lung disease <sup>b</sup>	6 (18%)	14 (44%)
Heart disease	2 (6%)	6 (19%)
Thyroid disease	2 (6%)	5 (16%)
Neurological disease	1 (3%)	3 (9%)
Cancer	3 (9%)	2 (6%)
Other	9 (27%)	10 (31%)
No. of comorbidities		
0	5 (15%)	4 (13%)
1	15 (45%)	11 (34%)
2	5 (15%)	7 (21%)
3	6 (19%)	4 (13%)
4	1 (3%)	4 (13%)
5+	1 (3%)	2 (6%)

<sup>a</sup>Receiving disability pay.  
<sup>b</sup>*p* < 0.05 between groups.  
SEM, standard error of the mean.

Average HbA<sub>1c</sub> in the intervention group was 9.80% (standard error of the mean [SEM]=0.45%, *n* = 19) at baseline and decreased to 9.11% ( $\Delta$ HbA<sub>1c</sub> = -0.69%, SEM=0.34%, *p* = 0.055) posttrial. Average HbA<sub>1c</sub> in the control group was 9.23% (SEM=0.32, *n* = 18) at baseline and barely decreased posttrial to 9.20% ( $\Delta$ HbA<sub>1c</sub> = -0.03%, SEM=0.40, *p* = 0.946). Baseline HbA<sub>1c</sub> was not significantly different between groups (*p* = 0.31).

Patients in the intervention group with baseline HbA<sub>1c</sub> >8% (*n* = 13) had a statistically significant decrease in HbA<sub>1c</sub> from 10.92% at baseline to 9.75% posttrial ( $\Delta$ HbA<sub>1c</sub> = -1.17%, SEM=0.33, *p* = 0.004), while those in the control group with baseline HbA<sub>1c</sub> >8% (*n* = 16) had a nonsignificant decrease from 9.46% at baseline to 9.44% posttrial ( $\Delta$ HbA<sub>1c</sub> = -0.02%, SEM=0.46, *p* = 0.957) (Fig. 3).

Patient-reported FBG was retrieved from the Epharmix system and only patients who responded throughout 6 months were analyzed. Average FBG in the intervention group was 172.5 mg/dL (SEM = 12.3 mg/dL, *n* = 17) at baseline and decreased to 150.9 mg/dL ( $\Delta$ FBG -21.6 mg/dL, SEM = 7.5 mg/dL, *p* = 0.01) posttrial. Average FBG in the control group was 191.1 mg/dL (SEM = 17.1 mg/dL, *n* = 16) at baseline and increased posttrial to 204.1 mg/dL ( $\Delta$ FBG +13.0 mg/dL, SEM = 28.5 mg/dL, *p* = 0.65). Baseline FBG was not significantly different between groups (*p* = 0.38). These results are consistent with our HbA<sub>1c</sub> changes from baseline in the intervention group.

At baseline, all patients in the study had HbA<sub>1c</sub> >7%. Posttrial, 11% of patients in the intervention group had HbA<sub>1c</sub> <7%, while none did in the control group (Fig. 4). In the intervention group, 63% of patients had HbA<sub>1c</sub> >9%, which decreased to 47% posttrial (Fig. 4). Changes of this magnitude were not seen in the control group (50–44% with HbA<sub>1c</sub> >9%).

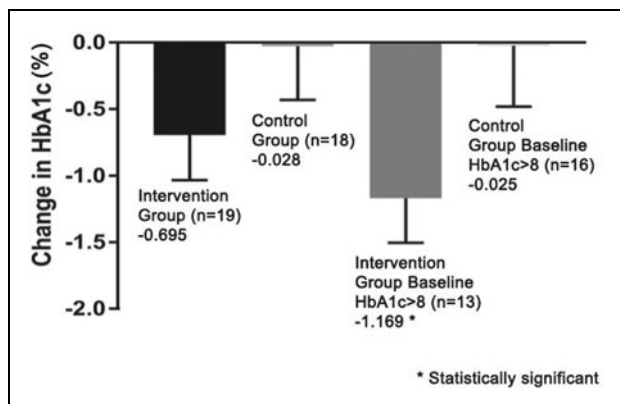


Fig. 3. Comparison of intervention and control group  $\Delta$ HbA<sub>1c</sub> after 6 months.

Correspondingly, at baseline, 63% of the intervention group had FBG above 150 mg/dL, which reduced to 32% posttrial (Fig. 4). The control group had 67% with FBG above 150 mg/dL at baseline, which decreased slightly to 56% posttrial (Fig. 4).

## RESPONSE RATE

Response rate was defined as the absolute proportion of total text messages or calls responded to. The overall average response rate for the entire duration of the trial was 64.9% for the control group and 63.6% for the intervention group (Fig. 5).

## ENGAGEMENT RATE

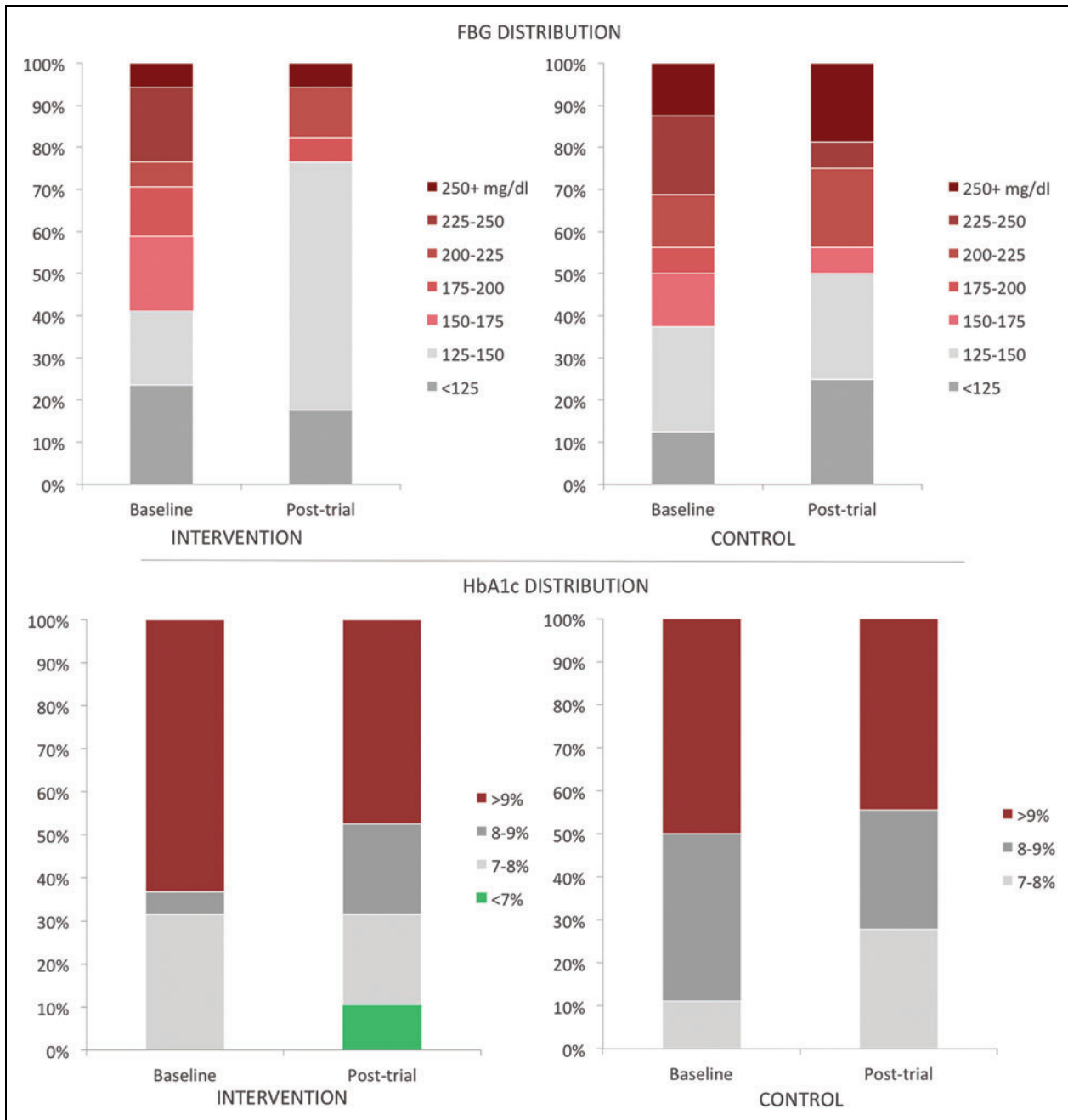
Engagement rate was defined as the proportion of participants who responded to at least 25% of SMS or phone calls over 4 weeks. The average engagement rate was 48% for the control group (95% confidence interval [CI], 0.296–0.621) and 58% for the intervention group (95% CI, 0.373–0.627) (Fig. 5).

## MULTIPLE LINEAR REGRESSION ANALYSIS: DEMOGRAPHIC FACTORS PREDICTING CHANGES IN $\Delta$ HbA<sub>1c</sub>

Multiple linear regressions were calculated to predict  $\Delta$ HbA<sub>1c</sub> at the end of the 6-month trial based on baseline  $\Delta$ HbA<sub>1c</sub>, education, smoking status, income, age, number of comorbidities, and response rate (Table 2). Significant predictors of intervention  $\Delta$ HbA<sub>1c</sub> were smoking status, number of comorbidities, and response rate. In contrast, the only significant predictor of control  $\Delta$ HbA<sub>1c</sub> was baseline HbA<sub>1c</sub>. Significant predictors of intervention  $\Delta$ FBG were baseline FBG and smoking status. There were no significant predictors of control  $\Delta$ FBG.

## Discussion

As the prevalence of diabetes continues to rise, it is essential to develop and implement cost-effective therapeutic strategies to achieve glycemic control. Current methods are less effective for the 30.9–33.4% of adults in the United States who are above target HbA<sub>1c</sub> levels.<sup>3,22</sup> Our study shows a statistically significant HbA<sub>1c</sub> reduction of 1.17% for patients in the intervention group with baseline HbA<sub>1c</sub> >8% by using SMS and phone-based interventions that allow for bidirectional patient-provider communication. This change in HbA<sub>1c</sub> was supported by a significant decrease in self-reported average FBG, half of patients with baseline FBG >150 mg/dL getting below 150 mg/dL posttrial, and a 11% increase in the amount of patients with well-controlled diabetes (HbA<sub>1c</sub> <7%) in the intervention group. This is clinically significant because



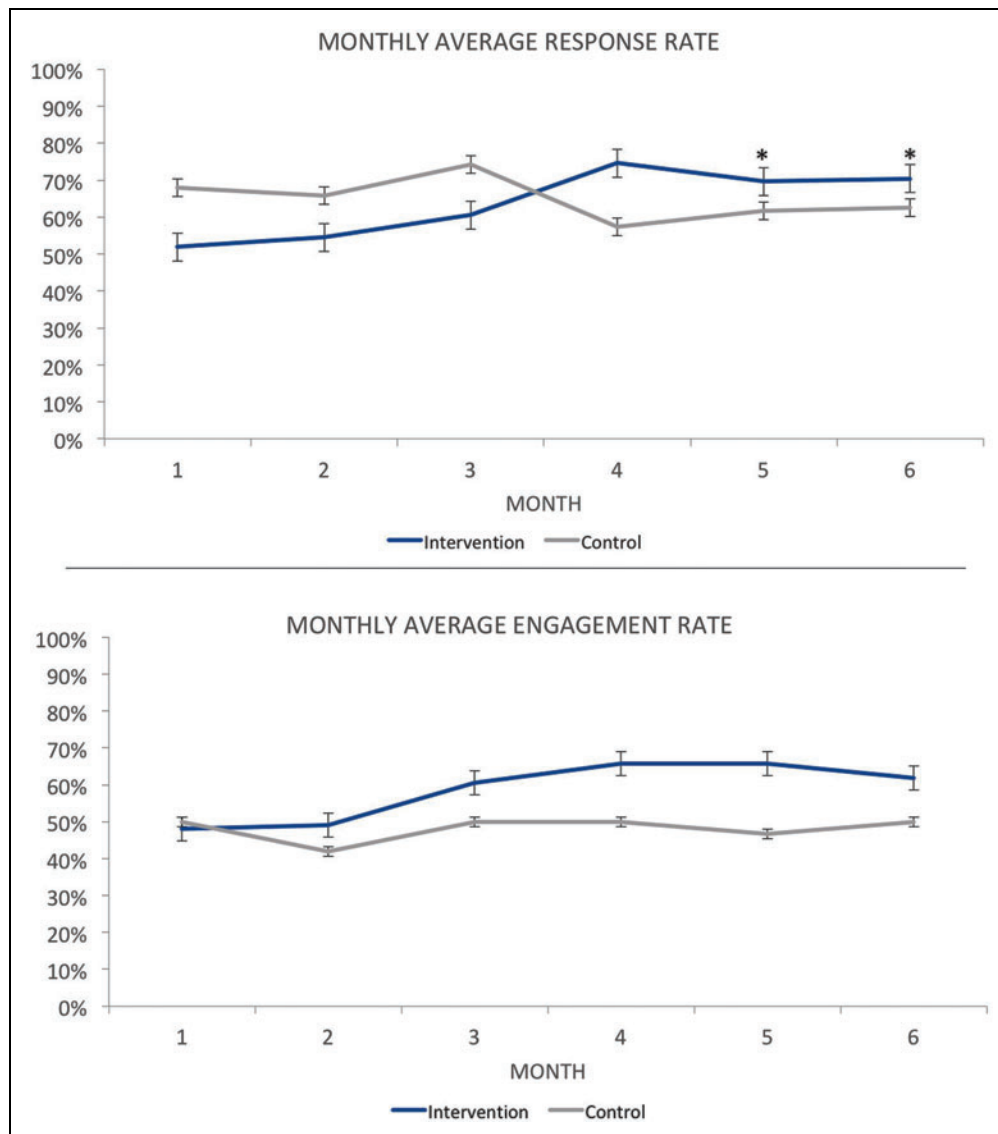
**Fig. 4.** Distribution of the intervention and control groups across HbA<sub>1c</sub> values and FBG values from baseline to post-trial. FBG, fasting blood glucose. Color images are available online.

standard therapies for T2DM, which include oral anti-hyperglycemic agents, are known to lower HbA<sub>1c</sub> by 0.5–1.25%.<sup>23</sup> Our nonpharmacologic, low-cost, and low-risk intervention complements standard pharmacologic therapies by further reducing HbA<sub>1c</sub> by a comparable amount. While it has been demonstrated that the lowest risk of complications is achieved when patients can lower their HbA<sub>1c</sub> to <6%, it is also

clear that any reduction from baseline HbA<sub>1c</sub> can be beneficial in risk reduction.<sup>24</sup>

Smoking status was a significant predictor of HbA<sub>1c</sub> and FBG changes. Those who never smoked saw greater decreases in HbA<sub>1c</sub> and FBG than former and current smokers. These findings correlate with previous studies demonstrating that smoking exacerbates insulin resistance and the micro- and





**Fig. 5.** The average response rates and average engagement rates for each month of intervention. Standard error bars are displayed. \*Response rates were significantly different during months 5 and 6. Color images are available online.

macrovascular complications of T2DM.<sup>25</sup> Response rate was a significant predictor of HbA<sub>1c</sub> in the intervention group, but not in the control group. This difference is likely due to the greater messaging frequency and the bidirectional communication between patients and providers experienced by the intervention group. Greater response rate to the intervention was associated with decreases in HbA<sub>1c</sub>.

The engagement rate was high for both the intervention group (58%) and control group (48%). While definitions of engagement vary, in similar studies, the proportion of people ever using an intervention ranged from 28% to 53%.<sup>26,27</sup> Interestingly, the intervention group, which received more mes-

sages relative to the control group, showed higher response and engagement rates after 6 months of intervention. However, the response rate was a nonsignificant predictor of changes in FBG. Higher response rates were correlated with increases in FBG. This may seem to contradict the effectiveness of EpxDiabetes, but patients with FBG instability receive additional messages by platform design, and higher FBG may trigger increased engagement with the system due to concerns about glycemic control. Patients are more likely to enroll in and engage with telemedicine interventions when it is perceived to be beneficial.<sup>28-30</sup> Patients are less likely to consider an intervention beneficial when their blood glucose seems to be in control.<sup>30,31</sup>

**Table 2. Demographic and Socioeconomic Factors Predicting Changes in HbA1c**

INDEPENDENT VARIABLE	INTERVENTION ΔHbA <sub>1c</sub>	CONTROL ΔHbA <sub>1c</sub>	INTERVENTION FBG	CONTROL FBG
	COEFFICIENT	COEFFICIENT	COEFFICIENT	COEFFICIENT
Baseline HbA <sub>1c</sub>		-0.756 <sup>a</sup>	–	–
Baseline FBG	–	–	-0.265 <sup>a</sup>	-0.378
Education		-0.649		
Smoking status	-0.929 <sup>a</sup>		-28.920 <sup>a</sup>	
Income (thousands)	0.004	0.000	1.00	1.00
Age		-0.066		
No. of comorbidities	-0.635 <sup>a</sup>			
Response rate	-2.595 <sup>a</sup>		31.205	245.878
Constant	2.551	9.918	24.883	-113.875
R <sup>2</sup> <sub>adj</sub>	0.669	0.302	0.598	0.248
F-ratio	7.062 <sup>a</sup>	2.512	5.459 <sup>a</sup>	2.207
n	19	18	17	16

A higher value for smoking status indicates less smoking.

<sup>a</sup>p < 0.05.

FBG, fasting blood glucose.

At baseline, the intervention group had a lower response rate. This may reflect the heavier message burden before the Smart Scheduler reduced the frequency of messages based on FBG stability. We believe that the bidirectional patient-provider communication the intervention group received encourages greater response and engagement rates compared to the control group without physician feedback. Macdonald et al.<sup>12</sup> noted that diabetes telemedicine interventions allow for timely physician feedback, which increases patient perceptions of intervention usefulness, increasing usage, and engagement. Bidirectional communication can encourage engagement by increasing feelings of connectivity between patients and their health care providers.<sup>32,33</sup> The higher engagement rate of the intervention group demonstrates the ability of EpxDiabetes to facilitate high engagement over long periods of time.

This intervention is a scalable and effective way of managing large numbers of patients and optimizing response to patient needs. In a previous study, EpxDiabetes was implemented as a single-arm quality improvement project across community clinics in St. Louis, Missouri, and managed 314 patients.<sup>5</sup> EpxDiabetes gives actionable data to providers, enabling providers to follow-up and adjust treatment plans, and then to receive real-time feedback on those changes. We

believe that this RCT is an appropriate ancillary study to follow up implementation of EpxDiabetes in a community setting in a more rigorous research setting.

Limitations to this study relate to sample size and scheduling for follow-up. As a result of low sample size, the trial had low power to detect significant changes in the intervention arm. In addition, a larger, more diverse study sample is needed to better understand differences in intervention effectiveness. Our study population reflected the patient population of our city, so generalizability would improve with a larger national or global trial.

We did not track the antihyperglycemic therapies or lifestyle interventions that the patient groups were given since it was assumed that they were on optimal medical therapy and care plan. In addition, since there were no differences in characteristics between the intervention and control groups at baseline, we are reasonably confident that any changes in FBG or HbA<sub>1c</sub> as a result of lifestyle or medication adherence changes can be attributed to aspects of our intervention. However, we acknowledge that it is important to identify which, if any, standard medical therapies or lifestyle interventions, such as diet or exercise, may have better complementarity to telemedicine. This will enable us to further tailor and individualize EpxDiabetes to patients on particular therapy plans. We will

make every effort to include collection and analysis of these data in future studies.

Finally, not every patient was able to obtain HbA<sub>1c</sub> measurements that corresponded to an end-of-trial measurement, which results in a limitation to our sample size and a possible bias from self-selection of patients who prioritized management of their T2DM. We believe that this highlights the disparities in access to care and transportation barriers in our community, further emphasizing the need for a telemedicine tool in communities such as ours. In future studies, it will be beneficial to schedule both pretrial and posttrial measurements to ensure more patients meet the criteria for analysis. Finally, we recommend examining patient satisfaction to address barriers to engaging with the system.

## Conclusion

EpxDiabetes is an effective telemedicine intervention that facilitates glycemic control for patients with T2DM, especially with baseline HbA<sub>1c</sub> >8%. It is low-cost, accessible, and facilitates high engagement for patients of different ages, health literacy, and socioeconomic levels.

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## Disclosure Statement

No competing financial interests exist.

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