THE MONITOR TRIAL

FINAL RESEARCH REPORT

Effect of Glucose Monitoring on Patient and Provider Outcomes in Non–Insulin Treated Diabetes

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ABSTRACT

For the nearly 75% of patients living with type 2 diabetes mellitus (T2DM) who do not use insulin, decisions regarding self-monitoring of blood glucose (SMBG) can be especially problematic. While in theory SMBG holds great promise for sparking favorable behavior change, it is a resource-intensive activity without firmly established patient benefits.

OBJECTIVES

The overarching goal was to assess the impact of 3 different SMBG testing approaches on patient-centered outcomes in patients with non–insulin treated T2DM within the real-world clinic setting.

Objective 1: Assess SMBG effectiveness on 2 primary patient-centered outcomes, glycemic control (A1c) and health-related quality of life (HRQOL), over 1 year in 450 participants with non–insulin treated diabetes mellitus (DM) in the following 3 groups: (1) no SMBG testing, (2) once-daily SMBG testing with standard patient feedback consisting of glucose values immediately reported to the patient through the glucometer, and (3) once-daily SMBG testing with enhanced patient feedback consisting of glucose values immediately reported to the patient plus automated, tailored messaging also delivered via the glucometer.

***Objective 2*:** Evaluate the impact of SMBG on secondary patient-centered outcomes including (1) DM-related quality of life, (2) DM self-care, (3) DM treatment satisfaction, (4) DM self-efficacy, (5) patient–provider communication, (6) hypoglycemia frequency, and (7) health care utilization.

***Objective 3*:** Conduct qualitative assessments of the patient participant and provider experience for all 3 intervention groups. This objective supports efficient translation of study findings to real-world clinic settings by exploring such issues as patient–provider communications, use of the glucometer and accompanying reports, utility of the treatment algorithm given to providers, and practice burden.

METHODS

Using a stakeholder engagement approach, we developed and implemented a pragmatic trial. We randomly assigned 450 patients with non–insulin treated T2DM in 15 North Carolina primary care practices to 3 arms without masking of treatment assignment: (1) no SMBG, (2) once-daily testing with standard feedback consisting of glucose values being immediately reported to the patient through the glucometer, and (3) once-daily SMBG with enhanced patient feedback consisting of glucose values being immediately reported to the patient plus automated, tailored feedback messaging delivered to the patient through the glucometer following each testing. Coprimary outcomes included glycemic control (A1c) and HRQOL at 52 weeks.

RESULTS

A total of 450 patients were randomized and 92.9% completed the final visit. There were no significant differences in glycemic control across all 3 groups (p = 0.74; estimated adjusted mean A1c difference: SMBG with messaging versus no SMBG –0.09%; 95% confidence interval [–0.31%, 0.14%]; SMBG versus No SMBG –0.05% [–0.27%, 0.17%]). There were also no significant differences found in HRQOL. There were no notable differences in key adverse events, including hypoglycemia frequency, health care utilization, or insulin initiation.

CONCLUSIONS

In patients with non–insulin treated type 2 diabetes, at 1 year we observed no clinically or statistically significant differences in glycemic control or HRQOL between patients who performed SMBG compared with those who did not perform SMBG. The addition of tailored feedback provided through messaging via a meter did not provide any advantage in glycemic control.

BACKGROUND

Impact of the Condition on the Health of Individuals and Populations

Diabetes mellitus (DM) is a metabolic disorder resulting from a defect in insulin secretion, insulin action, or generally both.[1] At least 387 million people worldwide have DM.[2] The estimated costs of the condition in the United States alone top $176 billion annually.[3] Now described as an epidemic, the global incidence of DM is expected to rise over the next 2 decades, reaching 642 million cases by 2040.[4] Type 2 diabetes mellitus (T2DM), closely linked to obesity, makes up about 90% of cases, with the remaining 10% being type 1 and gestational. Recent Centers for Disease Control and Prevention (CDC) reporting shows alarming increases in T2DM in the United States.[5] Complications from T2DM include heart disease, stroke, diabetic retinopathy leading to visual impairment or blindness, kidney failure requiring dialysis, and limb amputation. Other associations include higher risk of cognitive dysfunction, dementia, cancer, sexual dysfunction, and infection,[1,6] plus increased rates of hospitalization and a shorter life expectancy.[2] In the United States, DM is the leading cause of kidney failure, nontraumatic lower limb amputations, and new onset blindness, and the seventh leading cause of death.[4]

Given the devastating effects of DM, improving treatment for persons with DM is of obvious importance. DM is a chronic condition that can be controlled with major lifestyle changes. A main goal of DM management is to control blood glucose, which is evaluated primarily through blood levels of hemoglobin A1c (A1c). A1c relates closely to the average plasma glucose levels a patient experiences over ~3 months. An A1c of 6.5% or above is a criterion for diagnosis.[7] In addition to pharmaceuticals, self-monitoring of blood glucose (SMBG) through the use of strips and glucometers is a recommended method for maintaining better glucose regulation.[7] The process entails using a lancing device to obtain a sample of capillary blood, which is then placed on a testing strip and read by a small handheld device. After several seconds, the current plasma glucose concentration is reported on the device. For patients with DM who are treated with insulin, SMBG is an accepted procedure for daily monitoring effects of insulin therapy. However, the majority of T2DM patients do not use insulin.

According to the CDC, 26% of people with DM use insulin, while the remainder use oral medications only (58%) or no medications (16%).[5] While control of A1c is equally important for persons with DM who are non–insulin treated (NIT), the value of SMBG testing for these patients is debatable.[7-13] Proponents postulate that testing promotes better awareness of glucose levels, leading to improvements in diet and lifestyle. When test results are shared with health care providers, it is argued, there is also potential for more timely treatment modifications. Competing arguments point to the costs of SMBG, both in terms

of supplies (test strips and meters) and time, as well as discomfort and potentially quality of life. As a result no clear consensus exists regarding SMBG monitoring in non–insulin treated patients with T2DM.

Research on Testing by Persons With NIT DM

Scientific examinations of SMBG in NIT DM have provided mixed results. An early epidemiological evaluation of the issue using a retrospective, longitudinal analysis showed that nonfatal micro- and macrovascular event rates along with fatal event rates were lower in individuals performing SMBG routinely as compared with those who were not.[14] A multitude of clinical trials followed. These trials had mixed results: SMBG testing on improving glycemic control in some trials[15-18] but not in others.[9,19-22] In some studies routine SMBG in patients with NIT DM was associated with higher rates of depression and higher cost without accompanying benefits.[23,24]

Given these mixed results, a series of metaanalyses and systematic reviews were conducted to investigate the benefit or lack thereof of SMBG on glycemic lowering in patients with NIT DM.[8-13] While metaanalyses can be a useful way to assess the clinical effectiveness of an intervention, they are limited by the quality and comparability of the clinical trials included in the analyses. Sample size, duration/details of the intervention, and patient characteristics (e.g., newly diagnosed versus longer duration of disease; baseline A1c level) varied considerably across the available studies. Given these critical differences, it is not surprising that the results of the metaanalyses have also shown conflicting results. However, the overall conclusion has been that SMBG is likely not cost effective for this population of patients.[8,9,11]

Perhaps most important to understanding these mixed results is the fact that the question addressed by the studies is itself not consistent, falling generally into 2 camps: “simple” SMBG and “enhanced” SMBG. In studies testing simple SMBG, patients conducting SMBG were compared with patients who were not. In evaluations of enhanced SMBG, intervention group patients and/or providers were given education or feedback such that they were better able to interpret SMBG results and use them in a meaningful way regarding lifestyle changes and treatment modification. Among tests of simple SMBG, A1c levels were reduced on average by 0.2%, an amount that was statistically significant in these studies but of doubtful clinical significance.[11,12] Studies of enhanced SMBG found A1c reductions closer to 0.5%.[18,25,26] As additional enhanced intervention SMBG studies were added to the literature,[25,27] more recent reviews and metaanalyses have drawn conclusions more in favor of testing.[28] This pattern suggests that, for SMBG to be an effective self-management tool in NIT DM, the patient and the health care provider must both actively engage in performing, interpreting, and acting on the SMBG values.

Patient-centered Outcomes and SMBG: Quality of Life

The effect of SMBG could impact patient quality of life (QOL) both positively and/or negatively. Testing itself is a burden and could act as a constant reminder of one's less-than-ideal health status.[20,29] On the other hand, testing may provide a sense of agency, improving a patient's sense of self-efficacy and hope for maximizing health and independence into the future.[29] A recent Cochrane Review identified only a handful of studies that had examined health-related quality of life (HRQOL), well-being, or patient satisfaction.[8] While these studies did not find clinically relevant differences in HRQOL for those who do or do not test, the review called for additional research about the effect of SMBG on HRQOL.[8]

Enhanced SMBG interventions have not always been designed in an optimal way. In 1 study, for example, HRQOL initially decreased, but follow-up qualitative interviews showed that patients in the testing groups experienced an increased awareness of illness.[20] While both simple and enhanced versions of SMBG were evaluated, the enhanced version included only training in the meaning of the results and encouragement to explore how lifestyle and dietary choices affect test values. Without more hands-on use of results (e.g., reports provided to the care provider), patients might have felt more overwhelmed than empowered by the experience of testing. Future studies of HRQOL and other patient-centered outcomes must examine SMBG within the context of patients having actionable knowledge and improved opportunities for provider–patient collaboration.

Unclear Medical Guidelines Regarding SMBG for Non–insulin Treated Type 2 Diabetes

The lack of consensus regarding the benefits of employing SMBG for persons with NIT DM has led to virtually no standardization in SMBG recommendations worldwide.[30] Guidelines range from clear recommendations for regular testing, to general statements about ensuring that testing is an available option to patients, to not recommending testing except in specific cases.[31] The American Diabetes Association (ADA) suggests SMBG may be useful to guide other therapies.[7] Mirroring the lack of research in this area, very few guidelines on diabetes care and management even touch on quality of life issues.[31] Without medical consensus, it is not surprising that there is little consistency in either insurance reimbursement for or routine use of SMBG in patients with NIT DM.

Current Rates of SMBG Testing

While researchers and medical organizations debate the overall issue of the value of SMBG testing in NIT DM, patients face this choice daily and without adequate information as to its clinical or psychological outcomes. For some patients, their decision on testing will mirror that of their care provider. Yet more and more, patients play an active role in managing their own health. To some degree this is a necessary trend, because providers simply do not have sufficient time to provide intensive ongoing and

comprehensive education and decision making about diabetes self-management. Providers are looking for additional guidance on this question, including how to present options to patients and incorporate test results into care.[32]The fact that patients are taking a greater role in their health care is generally positive, because those who do so also improve their outcomes.[33,34] Diabetes self-management, however, encompasses an increasingly complex set of services and supports, including glucose monitoring; medication management; nutrition counseling; physical activity promotion; social support networking; and, when needed, psychotherapy.

While current SMBG testing rates have not been well documented, it is likely that patients' practices vary greatly. In a recent study of more than 500 patients with NIT DM, 14.1% reported never testing, 22.8% tested once a week or less, 22.3% tested once a day, and 54.7% tested more than twice a day.[35] In preparation for this grant application, we conducted a survey of SMBG habits and attitudes among patients with NIT DM who are part of the UNC Diabetes Care Center Patient Registry, a group that has provided prior consent for participation in research projects. Among the 62 patients who had NIT DM, only one-third said that they test 1 or more times daily, while 15% tested never or less than once a month. The remainder tested several times per week (38%), several times per month (20%), or less than once per month (5%).

In addition to highlighting variability in testing rates, both a study by Wang et al and our pilot survey point to difficulties these patients encounter with regard to testing and using test results. Wang et al found that close to half (44.7%) reported missing or skipping blood sugar checks.[35] In our UNC sample, despite the low testing rates, a full 87% felt SMBG is an important part of diabetes self-care, and 79% said it was important to their provider. Indeed, 43% admitted that they test less often than suggested by their provider. At the same time, a small but important minority reported that their provider never instructed them on how often to test. Finally, even within the sample of patients for whom more than 75% test at least daily, most patients did not take appropriate problem-solving steps in response to high (hyperglycemia) or low (hypoglycemia) blood sugar levels.[35]

Modern Diabetes Self-management Technologies

Increasingly, patients are turning to the Internet and other new means of electronic communication for information, connections, and guidance.[36,37] In a study of mobile health applications for SMBG that included English-language interfaces, more than 900 were available for review.[37] But of the 137 applications that were comprehensive enough to meet basic review criteria, only 7% included a module providing personalized education or feedback. This study highlights both the demand for and current unmet need among patients considering or currently participating in SMBG. Recognizing this, some are

calling for greater use and development of such patient-centered medical options.[36] Kaufman and Woodley refer to these technologies as "a solution whose time has long since arrived" but argue that, to be most effective, they must be "clinically linked"; that is, occurring within the context of a trusted therapeutic relationship and an effective medical care system.[36] They note Internet and cell phone use is now so widespread and inexpensive that it is erasing geographic, economic, and demographic barriers to obtaining health information and support. Thus, the medical system should take advantage of these facts to further incorporate information technology into patient care and support.

Testing Approaches

In order to make informed patient choices, patients and their providers need accurate, generalizable, and meaningful information about the merits or demerits of SMBG testing for persons with NIT DM. Because the existing research, though relatively extensive, has not yet met this important need, more research must be conducted on this issue. The Consensus Report of the Diabetes Technology Society provides a list of recommendations for future research relating to SMBG in NIT DM. In regard to an ideal intervention, the society recommends that research (1) be linked to a structured program designed to facilitate behavior change; (2) have A1c as a primary endpoint but include patient-centered endpoints; (3) include encouragement and support, preferably in the form of personalized, automated feedback to patients in real time; (4) take advantage of telemedicine opportunities; and (5) incorporate best practices guidelines and standards for physicians.[28] Many of these recommendations overlap with others.[11,29,30,38] In addition to these critical features, future research should be designed with a pragmatic eye, adhering as closely as possible to the real-world setting in which SMBG would be carried out by patients and utilized by patients and health care providers collaboratively. *To date, no large-scale, pragmatic randomized controlled trial has evaluated the impact of SMBG testing in patients with NIT DM in which a multidimensional approach to SMBG value management has occurred.* Performing another randomized clinical trial of efficacy would not help clarify this hotly debated topic. Also missing from current research is an examination of SMBG testing for selected patient groups.[11] Racial and ethnic differences in A1c have been observed.[3,39-41] Compared with non-Hispanic white adults, the risk of diagnosed DM is 66% higher among Hispanics/Latinos and 77% higher among non-Hispanic blacks.[3] Persons from different racial or ethnic backgrounds might also respond differently to SMBG testing, as there may be differences in how individuals interact with providers or the ease with which they are able to use and make use of a wireless glucometer.

While SMBG may or may not be worthwhile, effective SMBG, if it exists for NIT DM, appears to require that it be embedded within the context of patient education about the use and interpretation of

glucose readings, provider awareness of the results of repeated testing, and collaborative use of this information at medical visits.[30] We would also argue for offering to providers treatment algorithms that are based on standard and accepted guidelines (such as the ADA guidelines) linked to SMBG report results.[42] This step facilitates the physician's use of glucometer result reports and can be used by health care providers during clinic visits to better illustrate their concerns when talking to patients. Finally, we feel it is important to evaluate objectively and in a real-world setting the possible additional benefits of personalized feedback for patients in the form of messages delivered via the glucometer based on patients' current and recent SMBG patterns. By pointing out troubling patterns and rewarding results that are at goal, this aspect of the approach, which we call "enhanced feedback," is akin to "mini consultations" with a provider between routine clinic visits, which are generally 3 to 6 months apart. Patients are curious about these enhanced approaches, as evidenced by 80% of our survey respondents reporting that they would perform SMBG as directed by their health care provider if they received instantaneous feedback on their glucose readings.

Given these unanswered questions regarding the impact of SMBG on patient quality of life and other patient-reported outcomes, there is a growing interest by patients and other stakeholders who are looking for data that will help them make better, informed decisions about their self-care when no standard of care exists and help providers make recommendations based on patients' experience and preferences. Our overarching goal was to answer the following question: Is SMBG testing effective for people with non–insulin treated T2DM in terms of either A1c or HRQOL? We also explored the potential for differential treatment effects across key subgroups of patients defined by 8 baseline characteristics that were prespecified in the study protocol. Our primary outcomes included change in glycemic control over 52 weeks and change in QOL over 52 weeks.

METHODS

Trial Design

We performed this pragmatic trial across 15 primary care practices in central North Carolina. Participating practices were community-based primary care practices, affiliated with 1 large health system, and distributed across central North Carolina. The trial included stakeholder input during grant design, implementation, and dissemination. The trial protocol was reviewed and approved by the UNC Institutional Review Board. All patients provided written informed consent before participation. We randomly assigned patients with non–insulin treated T2DM to 1 of 3 arms: (1) no SMBG; (2) standard once-daily SMBG consisting of glucose values immediately reported to the patient through the meter;

and (3) enhanced once-daily SMBG consisting of glucose values immediately reported to the patient plus automated, tailored messaging delivered to the patient through a Telcare (Concord, MA) meter. See Table 1 for examples of the content of the tailored messages. Following randomization, primary care providers guided participants' routine diabetes management. Providers received summaries of the SMBG data and potential treatment options based on American Diabetes Association Standards of Care[43] through the electronic health record for patients in both testing arms. The recommendations were not prescriptive and providers were encouraged to utilize them based on the clinical situation. The study team assessed participants a second time at 52 weeks $\pm$ 6 weeks following randomization.

Table 1. Sample Tailored Meter Messages
Sample Messages for Blood Glucose Values at Goal
• You are right on target. Remember to check your blood sugar tomorrow morning. • Keep up the good work. • Outstanding! • Way to go. Keep checking every morning before breakfast! • Your blood glucose goal is between 70 and 130 in the morning before you eat. You are doing marvelously.
Sample Messages for Blood Glucose Values That Are Mildly Elevated
• Keeping track of the foods you are eating and the physical activity you are doing may help you pinpoint reasons why your blood sugars are running high. • This number is a bit off target. Remember to check again tomorrow morning before eating. • Your target in the morning before eating is 70 to 130. • Staying on track with your diabetes can be tough at times. You can do this! Aim for a target fasting blood glucose value in the morning between 70 and 130.
Sample Messages for Blood Glucose Values That Are Very Elevated
• Please contact your health care provider to talk about ways to get your blood sugars down to a more healthy range. • Please consider making an appointment with your doctor. Your blood sugars have been too high lately. Your target before breakfast is 70 to 130. • Time to check in with your primary care provider about these blood sugar numbers. They have been running too high.

Patients

Eligibility criteria included (1) a diagnosis of T2DM, (2) >= 30 years old, (3) established with a primary care provider at a participating practice, (4) 6.5% $\leq$ A1c < 9.5% within the 6 months preceding screening, and (5) willing to be randomly assigned to a study group. Patients were excluded if they planned to see an endocrinologist in the upcoming year; currently used or planned to use insulin during the study period; planned to become pregnant or relocate in the next year; or had other conditions that would put them at risk in following the study protocol, such as a history of severe hypoglycemia.

Baseline Procedures

After the study field staff obtained written informed consent, patients completed an interview that included demographic, health history, and patient-reported measures. Patients also had their blood drawn for an A1c test and had height and weight recorded. The field coordinator then opened a numbered, opaque randomization envelope containing group assignment. Randomization was stratified by practice and used randomly permuted blocks of sizes 15 and 18 generated by a graduate research assistant not otherwise involved in the study. Patients who were previously testing were advised to completely stop testing their blood glucose values. The field coordinator taught patients randomized to the testing groups how to use the meter. All patients received educational brochures describing blood glucose number goals and symptoms of hypo- and hyperglycemia.

Outcomes

The 2 primary outcomes of the study were change in A1c and change in HRQOL. A1c was measured at baseline and 52 weeks $\pm$ 6 weeks after the baseline visit. Intermediate A1c values were captured passively from the electronic health record. We considered clinically significant changes in A1c to be more than 0.5%, which is what the U.S. Food and Drug Administration (FDA) uses to base approval of drugs for clinical efficacy. We assessed HRQOL using the physical and mental component scores of the Short Form 36 (SF-36).[44] In patients with diabetes, a change of 1 point is considered clinically significant and linked to worse clinical outcomes.[45] Secondary outcomes included assessment of diabetes-specific HRQOL and self-efficacy using the Problem Areas in Diabetes scale,[46] Diabetes Symptoms Checklist,[47] and Diabetes Empowerment Scale.[48] We examined diabetes self-care through the Summary of Diabetes Self-Care Activities.[49] We assessed treatment satisfaction and provider–patient communication through the Diabetes Treatment Satisfaction Questionnaire[50] and the Communication Assessment Tool.[51] There are no accepted values for clinically meaningful changes with these scales.

Preidentified potential study-related adverse events were finger stick infections and severe hypoglycemia. Emergency department and hospitalizations alerts from the electronic health record

allowed review of intrastudy events, which were adjudicated by committee. At follow-up, we also asked participants to describe any urgent care, emergency department visit, hospitalization, finger stick infection, or hypoglycemic episode over the past 52 weeks.

Qualitative Assessment

To gain a deeper understanding of patients' and health care providers' experiences with each of the SMBG testing approaches, including facilitators and barriers to dissemination, we conducted telephone interviews and focus group discussions at the UNC Physicians Network practices. Patients were also asked about their experiences with their health care providers during this study as well as preferences and suggestions about strategies for communicating with patients with diabetes.

Qualitative Assessment of Patient Outcomes

A total of 65 individual telephone interviews were conducted with patients from September 2015 to August 2016. Each interview lasted approximately 30 minutes, and participants received a $25 gift card for completing the interview. All interviews were digitally recorded. Trained research members conducted the interviews and completed debriefed post interview summary sheets with key findings, impressions, and considerations after each interview. Then a coinvestigator reviewed each digital recording and compared them with the relevant summary notes. All debrief post interview summary sheets were imported into ATLAS.ti 7.5.17 (Scientific Software Development GmbH), a qualitative software program, to facilitate analysis. Interview questions guided codebook development and interviews were coded using a directed content analysis approach until thematic saturation occurred.

Qualitative Assessment of Health Care Provider Outcomes

We conducted 8 focus group discussions with providers and practice staff from November 2015 to May 2016. The focus group discussions lasted approximately 45 minutes and were digitally recorded. Trained research members facilitated the discussions. After each focus group, participants completed a debrief post interview summary sheet with key findings, impressions, and considerations. A coinvestigator reviewed each digital recording and compared them with the relevant summary notes. All debrief postinterview summary sheets were imported into ATLAS.ti 7.5.17 to facilitate analysis. We purposefully selected 8 practices based on provider and study patient involvement to participate in the focus groups. The discussion analysis was descriptive and focused on capturing all relevant information provided by participants, allowing for both emergent and anticipated themes.

STATISTICAL ANALYSIS

We calculated power for the 2 degree of freedom overall tests comparing our primary outcomes across all 3 groups. Assuming a common standard deviation for change in A1c of 0.8% and a no more than 10% loss to follow-up, randomizing 150 patients per group would provide at least 90% power to detect a mean difference of –0.325% between the testing groups and the no SMBG group at the 0.05 significance level. Assuming an HRQOL standard deviation of 10 points, this sample size would provide at least 80% power to detect an overall difference between groups if the mean difference between the highest and lowest groups was at least 4 points on either component of the HRQOL scale at the 0.025 level (Bonferroni-corrected for 2 components).

For primary analyses, we analyzed all randomized patients according to their randomized group regardless of the extent to which they performed SMBG (intention-to-treat, or ITT). The statistician (MW) remained blinded to true treatment groups until after finalization of programming for the primary comparisons. We ignored missing 52-week outcome data for the primary analyses (i.e., a complete case analysis). We compared change in A1c from baseline through 52 weeks across the 3 randomization groups using an analysis of covariance (ANCOVA) conducted at the 0.05 significance level. This model controlled for site, baseline A1c, use of SMBG at baseline, duration of diabetes, baseline use of antihyperglycemic treatment, age, race/ethnicity, health literacy, and number of baseline comorbidities. We planned to compare each SMBG group against the no testing group separately using the Dunnett-Tamhane Step-Up procedure.[52] We also conducted a contrast test comparing the average of the 2 SMBG groups to the no testing group at the 0.05 level. We used similar ANCOVA models to compare the groups for the change in the HRQOL component scores as well as the listed secondary outcomes; besides the covariates listed above, each of these models also controlled for the corresponding baseline scale score. Additionally, we explored the potential for effect modification by each of the baseline variables included in the models by adding appropriate interaction terms to the ANCOVA model 1 at a time; these tests were all exploratory (i.e., not specifically hypothesis driven, although some were suggested by prior literature), but they were all prespecified in the study protocol and statistical analysis plan, including the thresholds for defining the subgroups. For each of the 3 primary outcomes, we conducted 8 tests of interaction (use of SMBG at baseline, duration of diabetes [≤ 1 year versus > 1 year], baseline use of antihyperglycemic treatment, age [< 65 years versus ≥ 65 years], race/ethnicity, health literacy, and number of baseline comorbidities [≤ median versus greater]), with no adjustment for multiple comparisons since these were intended as exploratory analyses.

We conducted 3 prespecified sensitivity analyses for the A1c comparison. First, we repeated the ITT analysis using a per protocol population that excluded participants who initiated insulin use during the

study or who were not sufficiently compliant with their assigned treatment. In the testing arms, we excluded participants who uploaded a meter reading on fewer than 80% of their days in the study. In the no testing arm we excluded participants who admitted to ever testing with any regularity during the study. Second, we repeated the ANCOVA model using linear mixed models that included all intermediate A1c values captured from the electronic health record, excluding any following initiation of insulin use. This model included fixed effects for linear and quadratic time trends and time-by-treatment group interactions, as well as random intercepts and slopes for each patient. As a final sensitivity analysis, we used last observation carried forward to impute the 52-week A1c value for any patient who was lost to follow-up or who initiated insulin during the study.

PCORI'S METHODOLOGY STANDARDS

Methodology Standards to Address	**Report How These Methodology Standards Are Being Met**
Upon Study Protocol Completion	
Data Integrity and Rigorous Analysis (IR-1, IR-2 IR-3, IR-4)	IR-1 does not seem to be directly relevant regarding confounding variables because this is a randomized trial. However, we will adjust analyses for prespecified covariates, all of which were collected at baseline. IR-2 is not applicable to this trial. IR-3 – We developed and submitted a detailed Statistical Analysis Plan before the first participant was enrolled in the trial. IR4 – We document all scales, with references and selected psychometric properties, in the study protocol.
Missing Data (MD-1, MD-2, MD-3, MD-4)	MD-1 – This trial has only 2 participant contacts, once at baseline and at 1-year follow-up. The only potential for missing data is due to failure to provide data at 1 year. In the protocol, we anticipated up to 10% loss, but our current retention rate is at least 92%.We have a retention plan for contacting participants at 12 months that has been working well thus far. We contact participants 2 to 3 weeks in advance of their completion date to schedule the follow-up clinic visit. If we are unable to reach a participant by phone or e-mail, we send a letter to the participant asking him or her to contact us. We also check the electronic health record for updated contact information. In the rare case that a participant has moved, we conduct the interview by phone and arrange for the participant to go to a LabCorp facility for his or her blood draw (if he or she is willing and if there is a lab nearby). (This is a rare occurrence.) If we are unable to arrange for a LabCorp blood draw and the participant has had an A1c in his or her participating clinic within 6 weeks of the completion date, we use the clinic A1c value. If the blood sample is not processed by LabCorp, we note that in our database and will assess the potential for differential results by lab in sensitivity analyses. MD-2 – In our Statistical Analysis Plan, we prespecify that missing 52-week outcome data will be ignored (ie, treated as missing completely at random) for the primary analysis. However, we have proposed sensitivity analyses to assess this assumption. MD-3 – As mentioned for MD-2, for the primary analysis of this trial we do not intend to impute any missing outcome data. However, we have prespecified sensitivity analyses that use other approaches. MD-4 – We are collecting reasons for dropout, when possible, and we are attempting to collect outcome data for all randomized participants, to the extent possible. Per our protocol, once randomized, participants will not be discontinued from the study for any reason except participant request or withdrawal of consent.
Heterogeneity of Treatment Effects (HT-1, HT-2)	HT-1 – We have prespecified the plans and rationale for testing for potential heterogeneity of treatment effects in our study protocol and Statistical Analysis Plan. Although these tests have been prespecified, we will not account for multiple testing, so in that sense they will be exploratory.

	HT-2 – All HTE analyses have been prespecified in the protocol and Statistical Analysis Plan. The study protocol provides nonspecific hypotheses and references for most of the planned analyses.
Causal Inference (CI-1, CT-2, CT-3, CT-4, CT-5, CT-6)	CI-1 through CI-6 are not applicable as this is a randomized trial.
Data Registries (DR-1, DR-2, DR-3)	DR-1 through DR-3 are not applicable.
During Each Interim Progress Report	
Data Integrity and Rigorous Analysis (IR-1, IR-2 IR-3, IR-4)	IR-1 does not seem to be directly relevant regarding confounding variables because this is a randomized trial. However, we will adjust analyses for prespecified covariates, all collected at baseline. IR-2 is not applicable to this trial. IR-3 – We developed and submitted a detailed Statistical Analysis Plan before the first participant was enrolled in the trial. IR4 – We describe below and document in the study protocol all scales, with references and selected psychometric properties and MCID. A1c – Clinically significant changes in A1c over time are typically considered to be more than 0.5%. This is what the FDA uses to base approval of drugs for clinical efficacy. This is a well-established standard and is also the basis of our sample size. SF-36 – The Short Form 36 (SF-36) is a well-accepted tool to assess overall quality of life. It has been widely used and validated in medical studies generally and diabetes studies in particular.[45,53-55] The SF-36 encompasses physical functioning, role limitations due to physical health problems, bodily pain, general health perceptions, vitality, social functioning, role limitations due to emotional problems, and mental health. Subscale scores range from 0 to 100, with high scores representing better HRQOL. We will use the physical component score and the mental component score, with scores standardized to a normal distribution (mean = 50 and standard deviation = 10).[56] In patients with diabetes, a change of 1 point is considered to be clinically significant and linked to worse clinical outcomes.[45] Problem Areas in Diabetes – Developed at the Joslin Diabetes Center, this scale is the most widely utilized tool to assess psychological and social stress associated with diabetes. This self-report measure contains 20 items with scores ranging from 0 (no distress) to 100 (high distress). It has been shown to have high internal reliability (Cronbach's alpha = 0.90), sensitivity to change (*r* = 0.83), and clinical utility.[45,57-58] There is no widely accepted value for clinically meaningful change for this scale. Diabetes Symptom Checklist (DSC) – The DSC is a 34-item self-report measure of diabetes-related symptom frequency and perceived severity during the prior month covering 6 symptom categories: hyperglycemic, hypoglycemic, cardiac, neuropathic, psychological, and vision related.[46] Patients respond on a 5-point scale (1 = symptom has not occurred or was not troublesome, to 5 = symptom was extremely troublesome). The DSC is valid, reliable, and responsive to change. Higher scores are associated with poorer glycemic control and depression.[59,60] There is no widely accepted value for clinically meaningful change for this scale. Diabetes Self-Care – To assess compliance with diabetes self-care, we will use the Summary of Diabetes Self-Care Activities (SDCA) survey. This is a widely used, multidimensional measure of diabetes self-management activities with high internal and test–retest reliability.[48] The SDCA assesses diet, exercise, blood glucose testing, foot care, and smoking status. Determining clinical significance with this score is easier than with others as the score is represented as number of days in a week. No standard for clinical significance exists for this scale and it is very subjective. Diabetes Treatment Satisfaction – Treatment satisfaction is an inherently patient-centered outcome. We will utilize the Diabetes Treatment Satisfaction Questionnaire standard version to assess this variable at baseline. This 8-item survey has been widely used to assess patient satisfaction with current treatment.[61] There is no widely accepted value for clinically meaningful change for this scale. Diabetes-Specific Self-Efficacy – Diabetes-specific self-efficacy focuses on beliefs about one's ability to adhere to diet, exercise, SMBG, and medication regimens and is only moderately related to general self-efficacy.[62] Higher diabetes-related self-efficacy is related to enhanced adherence to self-care activities.[63,64] Study participants will complete the 8-item Diabetes Empowerment Scale Short Form (DES-SF). The DES-SF is highly reliable (Cronbach $\alpha = 0.85$) and is responsive to change over time.[47] There is no widely accepted value for clinically meaningful change for this scale.

	Patient–Provider Communication – Patients' perceived connection with their health care provider significantly influences their sense of satisfaction and degree of concern about their health.[65] Good patient–provider communication also predicts better diabetes self-care, improved adherence to treatment, and fewer diabetes-related morbidities.[66-68] In general, patients prefer interactions that involve shared decision making. By providing shared and timely SMBG values, the new technology implemented in this study has the potential to strengthen the patient–provider relationship. Communication Assessment Tool (CAT) – The CAT is a 15-item survey that asks patients to rate different dimensions of the communication and interpersonal skills of their health care provider using a 5-point scale (1 = poor, 2 = fair, 3 = good, 4 = very good, 5 = excellent).[69] Overall scale reliability is high (Cronbach's alpha = 0.96). There is no widely accepted value for clinically meaningful change for this scale.
Adaptive Trials (AT-1, AT-2, AT-3, AT-4, AT-5)	AT-1 through AT-5 are not applicable.
Missing Data (MD-1, MD-2, MD-3, MD-4)	MD-1 – This trial has only 2 participant contacts, once at baseline and at 1-year follow-up. Thus, the only potential for missing data is due to failure to provide data at 1 year. In the protocol, we anticipated up to 10% loss, but our current retention rate is at least 92%. We have a retention plan for contacting participants at 12 months that has been working well thus far. We contact participants 2 to 3 weeks in advance of their completion date to schedule the follow-up clinic visit. If we are unable to reach a participant by phone or e-mail, we send a letter to the participant asking him or her to contact us. We also check the electronic health record for updated contact information. In the rare case that a participant has moved, we conduct the interview by phone and arrange for the participant to go to a LabCorp facility for his or her blood draw (if he or she is willing). (This is a rare occurrence.) If we are unable to arrange for a LabCorp blood draw and the participant has had an A1c in his or her participating clinic within 6 weeks of the completion date, we use the clinic A1c value. If the blood sample is not processed by LabCorp, we note that in our database and will assess the potential for differential results by lab in sensitivity analyses. MD-2 – In our Statistical Analysis Plan, we prespecify that missing 52-week outcome data will be ignored (ie, treated as missing completely at random) for the primary analysis. However, we have proposed sensitivity analyses to assess this assumption. MD-3 – As mentioned for MD-2, for the primary analysis of this trial we do not intend to impute any missing outcome data. However, we have prespecified sensitivity analyses that use other approaches. MD-4 – We are collecting reasons for dropout, when possible, and we are attempting to collect outcome data for all randomized participants, to the extent possible. Per our protocol, once randomized, participants will not be discontinued from the study for any reason except participant request or withdrawal of consent.

RESULTS

Overview of Trial Conduct

A total of 450 patients underwent randomization from January 2014 to July 2015 (Figure 1). A total of 92.9% of patients completed the final visit and provided data on both outcomes (A1c and HRQOL). The demographic and clinical characteristics were similar among the groups (Table 2). The mean age was 61 years old, patients had diabetes an average of 8 years, 75% were performing SMBG at baseline, and 38% had low health literacy (less than 4 on the Newest Vital Sign).[70] Patient testing preference at baseline was similar among the groups, with 22% preferring no SMBG and 40% preferring to test. The majority were taking metformin (80%), followed by sulphonylurea (35%).

Figure 1. The Monitor Trial CONSORT Flow Diagram

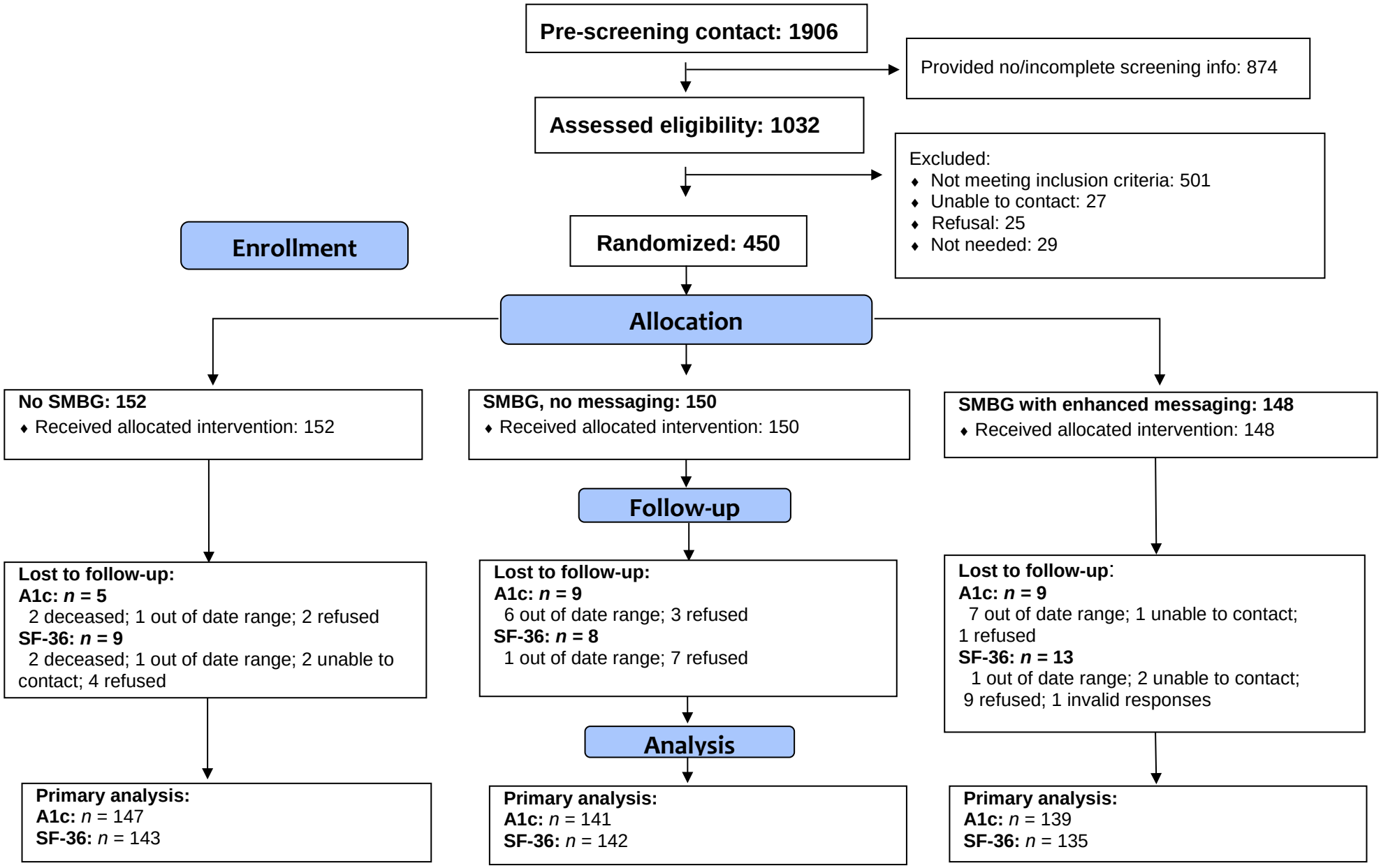


Table 2. Baseline Characteristics

	Randomization Group			
	No SMBG (*N* = 152)	**SMBG, no Messaging (*N* = 150)**	**SMBG With Messaging (*N* = 148)**	**Total (*N* = 450)**
Age in years, median (range)	61 (31-89)	63 (32-82)	61 (35-92)	61 (31-92)
Sex, male, %	48.7	44.7	44.6	46.0
Race, % Black	27.6	36.7	34.5	32.9
White	68.4	59.3	58.1	62.0
Other	3.9	4.0	7.4	5.1
Ethnicity, Hispanic, %	2.6	1.3	1.4	1.8
Education, % < High school	4.0	6.7	6.1	5.6
High school/some college	62.9	58.0	60.1	60.4
College or higher	33.1	35.3	33.8	34.1
BMI, median (range)	33 (22-58)	33 (21-62)	34 (21-75)	33 (21-75)
Low health literacy, %*	40.8	36.5	37.2	38.2
Years with diabetes, median (range)	6 (0-45)	6 (0-44)	6 (0-50)	6 (0-50)
Diabetes 1 year or less, %	16.4	18.0	9.5	14.7
Number comorbidities, median (range)	3 (0-9)	3 (0-10)	3 (0-8)	3 (0-10)
Current use of SMBG, %^	75.0	72.0	78.4	75.1
Ever used SMBG, %	90.8	90.0	96.6	92.4
Testing preference, %				
Any SMBG	41.4	37.3	39.9	39.6
No SMBG	20.4	22.7	21.6	21.6
Uncertain	1.3	0.7	0.7	0.9
No preference	36.8	39.3	37.8	38.0
Diabetes medications, %⁺				
Metformin	80.9	76.7	81.1	79.6
Sulfonylurea or Glinide	33.6	33.3	40.5	35.8
Thiazolidinedione	5.3	2.0	6.8	4.7
GLP-1 agonist	3.3	1.3	6.8	3.8
DPP-4 inhibitor	7.9	7.3	11.5	8.9

* Scoring < 4 on Newest Vital Sign

⁺ Other diabetes medications were < 5% ^ SMBG = self-monitoring of blood glucose

BMI = Boss Mass Index

Primary Outcomes

At 1 year, we found no evidence that SMBG led to improved glycemic control (estimated adjusted mean A1c difference: SMBG with messaging versus no SMBG –0.09%; 95% confidence interval [–0.31%, 0.14%]; SMBG versus no SMBG –0.05% [–0.27%, 0.17%]; average over SMBG arms versus no SMBG –0.07% [–0.26%, 0.12%]) (Table 3). There were also no significant differences found in HRQOL (estimated adjusted mean difference for SF-36 physical score: SMBG with messaging versus no SMBG –0.83 points [–2.33, 0.67]; SMBG versus no SMBG –0.05 points [–1.54, 1.44]; average over SMBG arms versus no SMBG –0.44 points [–1.73, 0.85]; estimated adjusted mean difference for SF-36 mental score: SMBG with messaging versus no SMBG –0.19 points [–1.82,1.44]; SMBG versus no SMBG 0.19 points [–1.43,1.81]; average over SMBG arms versus no SMBG 0 points [–1.40, 1.40]).

Secondary Outcomes

We did not find significant differences in patient-reported outcomes by the Problem Areas in Diabetes scale, Diabetes Symptom Checklist, Diabetes Empowerment Scale, Diabetes Treatment Satisfaction Questionnaire, and Communication Assessment Tool (Table 4). There were significant differences in the Summary of Diabetes Self-Care Activities (mean change 0.01 points, 0.51 points, 0.45 points, in no SMBG, SMBG, and SMBG with messaging, respectively; overall $P < 0.001$). However, this was due to the influence of the intervention of SMBG (blood sugar testing subscale mean change –1.46 points, 2.94 points, 2.81 points in no SMBG, SMBG, and SMBG with messaging, respectively; overall $P < 0.001$). Among the arms, there were no significant differences in insulin initiation (8.6%, 4%, 5.4% in no SMBG, SMBG, and SMBG with messaging, respectively; overall $P = 0.23$). The proportion who initiated insulin in both SMBG groups taken together was 4.7% versus 8.6% in the no SMBG group ($p = 0.14$).

Sensitivity Analyses

The proportion of patients testing decreased over time (Figure 2b). In the per protocol and last observation carried forward analyses, results were not notably different from those in the primary analyses (data not shown). We did find evidence that mean A1c values differed across groups over time. At 3 months, the estimated mean A1c difference between the testing arms and the no testing arm was –0.23% (95% CI: –0.41%, –0.05%; $p = 0.014$). At 6 months, the estimated mean A1c difference between the testing arms and the no testing arm was –0.33% (95% CI: –0.54%, –0.12%; $p = 0.002$). At 9 months, the estimated mean A1c difference between the testing arms and the no testing arm was –0.29% (95% CI: –0.53%, –0.07%; $p = 0.011$). By 12 months, however, the mean differences between groups were similar to the primary analysis and did not show a significant difference (–0.08%; 95% CI: –0.29%, 0.14%; $p = 0.47$) (Figure 2a).

Table 3. Summary of Primary Outcomes by Randomization Group

	Randomization Group							
	No SMBG		**SMBG, No Messaging**		**SMBG With Messaging**			
	N	**Mean (SD)**	***N***	**Mean (SD)**	***N***	**Mean (SD)**	**Overall *p*-Value[1]**	**Contrast *p*-Value[2]**
Hemoglobin A1c								
Baseline	152	7.52 (1.12)	150	7.55 (1.10)	148	7.61 (0.97)		
Follow-up	147	7.55 (1.24)	141	7.49 (1.12)	139	7.51 (1.13)		
Change	147	0.04 (1.12)	141	–0.05 (1.00)	139	–0.10 (1.14)	0.74	0.48
Health-related quality of life, SF-36								
Physical score								
Baseline	152	48.72 (8.00)	150	47.27 (8.40)	148	46.22 (10.13)		
Follow-up	143	48.47 (7.21)	142	47.42 (9.03)	135	46.44 (9.68)		
Change	143	–0.43 (6.86)	142	0.07 (6.77)	135	–0.35 (6.95)	0.48	0.50
Mental score								
Baseline	152	53.52 (9.29)	150	52.94 (8.77)	148	53.43 (9.58)		
Follow-up	143	53.39 (10.55)	142	52.04 (9.57)	135	52.57 (10.39)		
Change	143	–0.94 (7.46)	142	–0.71 (7.72)	135	–1.39 (6.85)	0.90	1.00

[1] Test comparing all 3 groups from ANCOVA model controlling for site, baseline A1c, prior use of SMBG, duration of T2DM, baseline antihyperglycemic treatment, age, race/ethnicity, health literacy, and number of baseline comorbidities; for health-related quality of life scores, we also controlled for baseline score.
[2] Contrast test from same ANCOVA model comparing average of SMBG groups with no SMBG group. SMBG = self-monitoring of blood glucose.

Table 4. Secondary Outcomes by Randomization Group—DM Patient-Reported Outcomes

	Randomization Group							
	No SMBG		SMBG, No Messaging		SMBG With Messaging			
	N	Mean (SD)	*N*	Mean (SD)	*N*	Mean (SD)	Overall *p*-Value[1]	Contrast *p*-Value[2]
Summary of Diabetes Self-care Activities (total score)								
Baseline	152	3.42 (1.32)	150	3.64 (1.42)	148	3.46 (1.34)		
Follow-up	143	3.39 (1.23)	142	4.12 (1.30)	135	3.87 (1.32)		
Change	143	0.01 (1.00)	142	0.51 (1.14)	135	0.45 (1.16)	< 0.001	< 0.001
Summary of Diabetes Self-care Activities (blood sugar testing subscale)								
Baseline	152	2.54 (2.62)	149	2.65 (2.77)	148	2.64 (2.87)		
Follow-up	143	0.95 (2.00)	142	5.60 (2.29)	135	5.39 (2.30)		
Change	143	–1.46 (2.83)	141	2.94 (3.23)	135	2.81 (3.30)	< 0.001	< 0.001

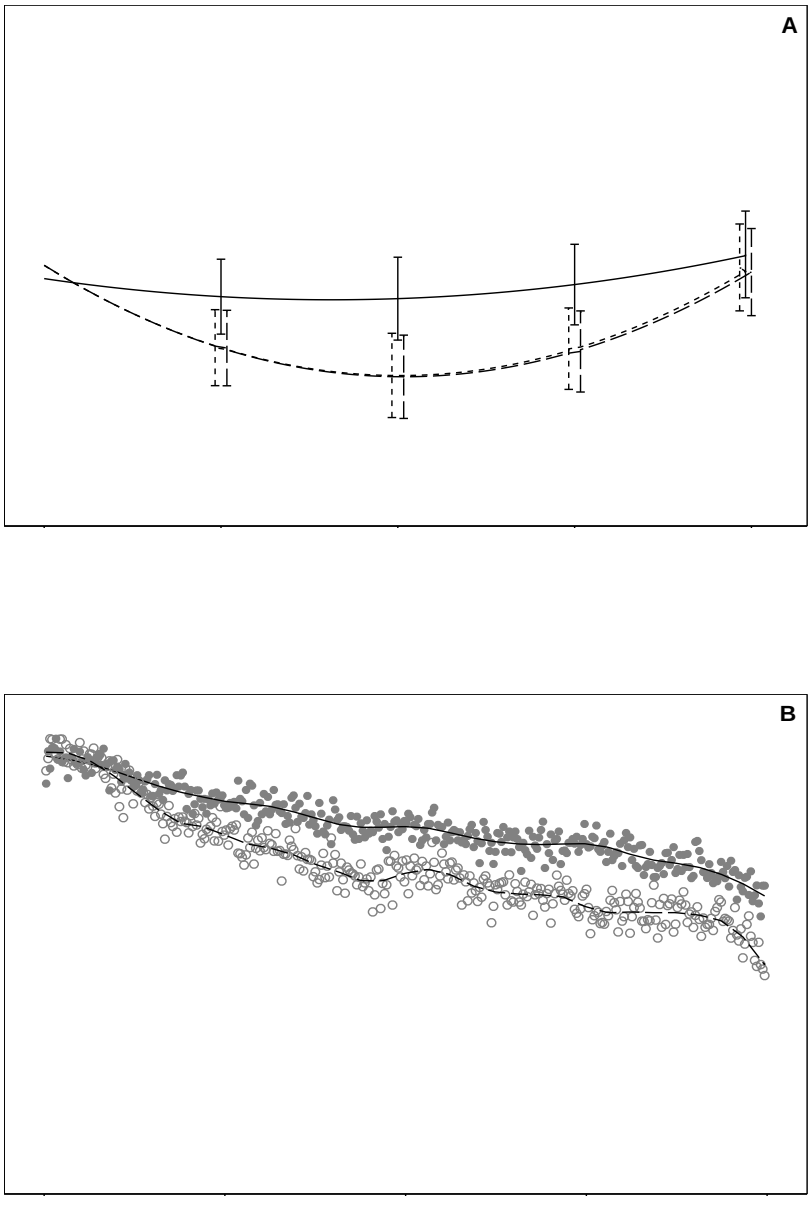
[1] Test comparing all 3 groups from ANCOVA model controlling for site, baseline scale score, baseline A1c, prior use of SMBG, duration of T2DM, baseline antihyperglycemic treatment, age, race/ethnicity, health literacy, and number of baseline comorbidities.
[2] Contrast test from same ANCOVA model comparing average of testing groups with no testing group.
SMBG = self-monitoring of blood glucose.

Table 4. Secondary Outcomes by Randomization Group—DM Patient Reported Outcomes, Continued

	Randomization Group							
	No SMBG		SMBG, No Messaging		SMBG With Messaging			
	N	**Mean (SD)**	***N***	**Mean (SD)**	***N***	**Mean (SD)**	**Overall *p*-Value[1]**	**Contrast *p*-Value[2]**
Diabetes Treatment Satisfaction Questionnaire								
Baseline	149	31.74 (5.52)	147	31.71 (4.92)	148	31.89 (4.96)		
Follow-up	135	31.66 (6.27)	141	32.21 (4.89)	135	31.74 (5.90)		
Change	133	–0.16 (6.26)	138	0.67 (4.95)	135	–0.28 (5.84)	0.48	0.48
Communication Assessment Tool								
Baseline	152	4.53 (0.69)	150	4.53 (0.70)	148	4.49 (0.76)		
Follow-up	141	4.57 (0.68)	142	4.52 (0.74)	134	4.53 (0.71)		
Change	141	0.03 (0.68)	142	–0.02 (0.65)	134	0.01 (0.75)	0.68	0.45

[1] Test comparing all 3 groups from ANCOVA model controlling for site, baseline scale score, baseline A1c, prior use of SMBG, duration of T2DM, baseline antihyperglycemic treatment, age, race/ethnicity, health literacy, and number of baseline comorbidities.
[2] Contrast test from same ANCOVA model comparing average of testing groups with no testing group.
SMBG = self-monitoring of blood glucose.

Figure 2. (A) Model-estimated mean A1c values obtained by fitting a quadratic polynomial regression with linear mixed models using all observed A1c values, including those at interim visits, but excluding any following insulin use. The model included 1,875 total A1c measurements from 450 patients; only 10 patients contributed no interim A1c measurements and the median number was 4. The intervals represent pointwise 95% confidence intervals for each group. (B) Daily proportions of patients in the SMBG groups uploading a result with the meter on each study day. Lines represent locally weighted smoothing using local quadratic polynomials across the observed proportions. SMBG = self-monitoring of blood glucose.



Effect Modification

In analyses examining the potential for effect modification of prespecified subgroups (prior experience using SMBG, duration of T2DM, baseline glycemic control, baseline use of insulin secretagogues, age, race, ethnicity, health literacy, and number of baseline comorbidities), there were no significant interactions for glycemic control (A1c). For the HRQOL physical component score, we identified a significant interaction by race (P = 0.016); African Americans in the SMBG with messaging group scored significantly lower on the HRQOL physical component than the no testing group, but the same was not true for the SMBG without messaging group (estimated adjusted mean differences of SF-36 physical component score: SMBG with messaging versus no SMBG –2.91 points [–5.69, –0.13]; SMBG versus no SMBG 0.78 points [–1.91, 3.47]) (Figures 3-5).

Testing Compliance

Compliance dropped consistently in both testing groups, with a larger initial decrease after 1 month in the SMBG with messaging arm (Figure 2b). In the no SMBG arm, 23.7% (36) reported that they tested a few times a month or more during the study. Compliance-adjusted analyses suggest that differences in change in A1c were related to the extent of compliance at 6 to 9 months postrandomization but any benefit obtained by participants in the SMBG groups was greatly diminished, on average, by the conclusion of the study, even for those participants who were consistently the highest compliers (see Appendix).

Safety and Adverse Events

The following adverse events occurred during the study: 0 finger stick infections, 1 severe hypoglycemia (secondary to urosepsis, recurrent bladder neoplasm, and acute kidney injury), 61 hospitalizations (no difference by arm), and 2 deaths (1 during cardiac surgery and 1 due to Amyotrophic lateral sclerosis). None of the adverse events were adjudicated to be study related. Results tables reported to clinical trials.gov are currently under review. Table 5 presents the number and type of adverse events by study arm.

Qualitative Results

From the patient interviews and focus group discussions with providers and practice staff, 3 themes (and multiple subthemes) emerged: (1) the experience of participating in the Monitor Trial, (2) enhance patient-focused tools for providers, (3) the patient–provider interaction, and (4) strategies for communication and long-term engagement. The themes were derived inductively or arose directly from discussion questions. Overall thematic content was generally distributed equally among the patient interviews and practice focus groups.

Figure 3. Forest Plot of Prespecified Subgroups and A1c

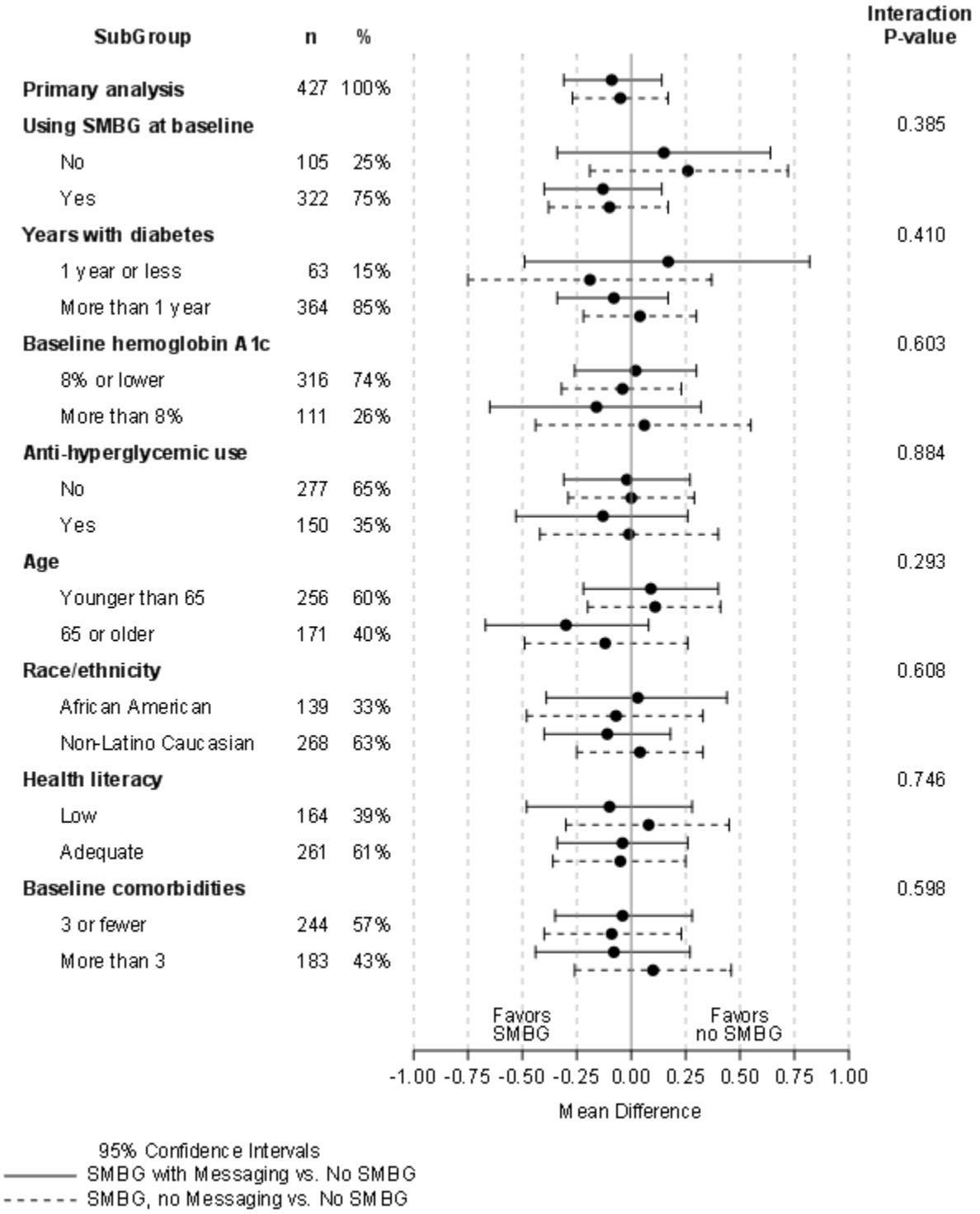


Figure 4. Forest Plot of Prespecified Subgroups and Health-related Quality of Life, SF-36 Physical Component Score

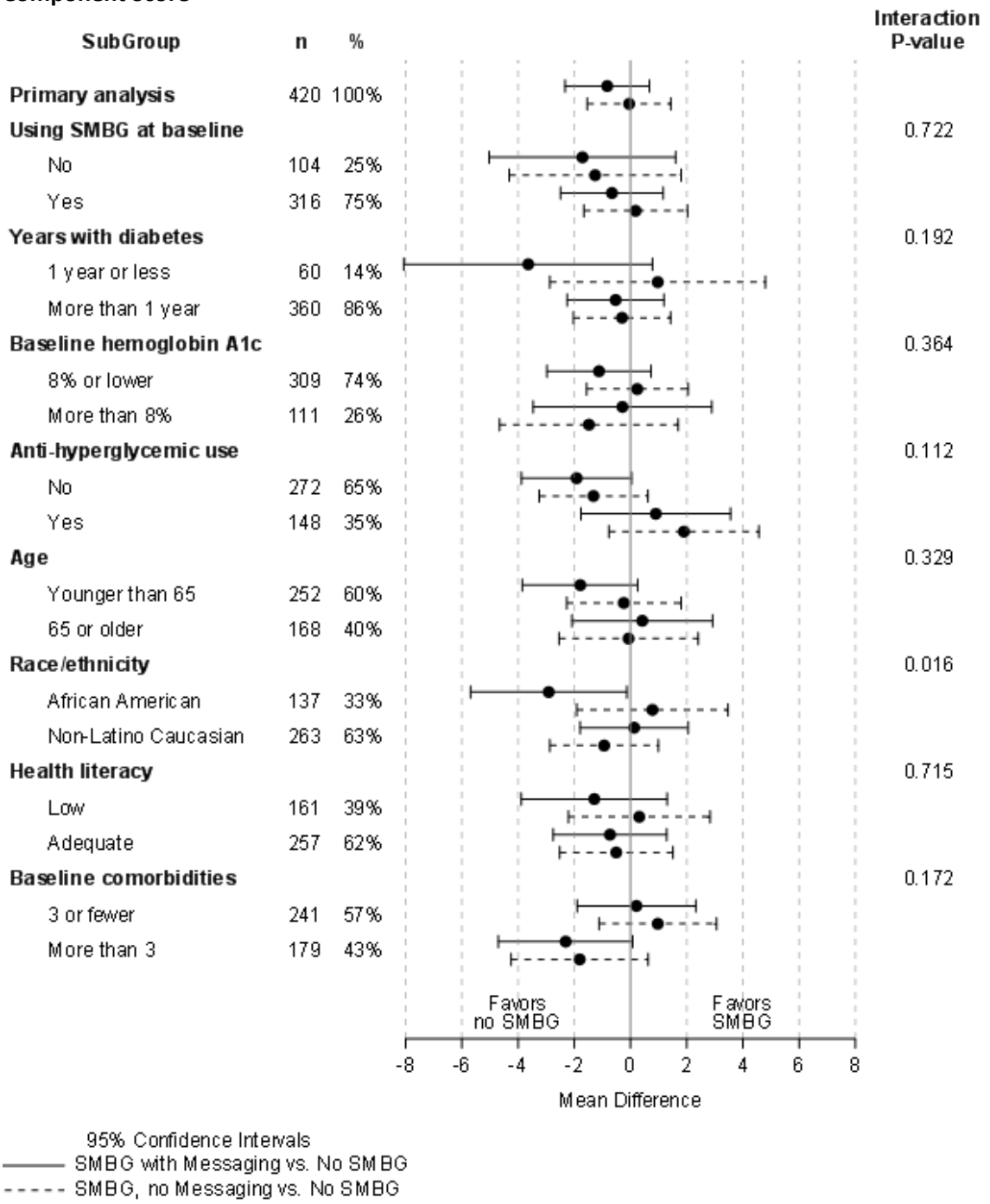


Figure 5. Forest Plot of Prespecified Subgroups and Health-related Quality of Life, SF-36 Mental Component Score

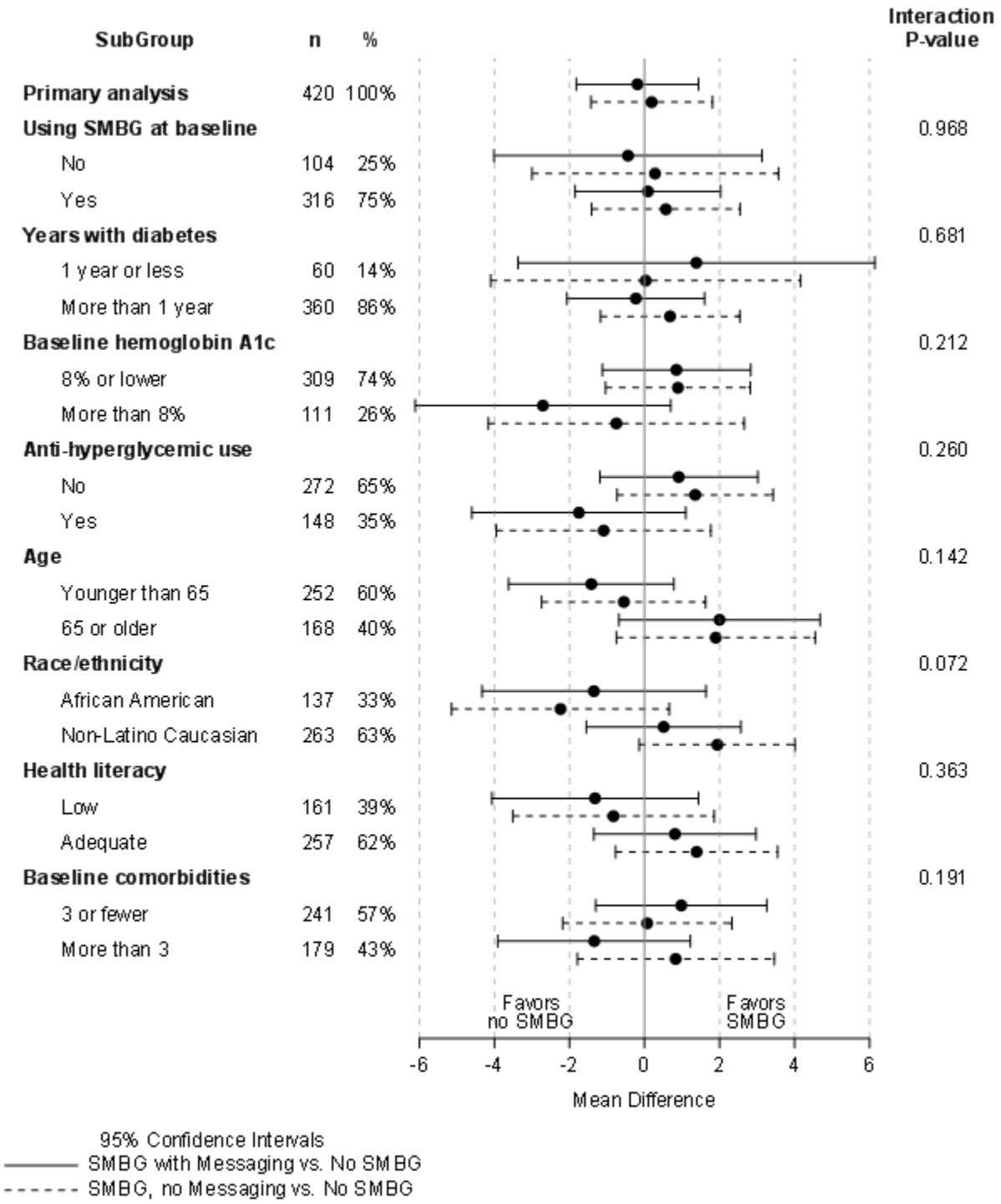


Table 5. Adverse Effects by Arm

Arm	Total Events	Infection at Finger Stick Site	Severe Hypoglycemia	Hospitalization	Death
A	22	0	0	20	2
B	20	0	0	20	0
C	22	0	1	21	0

Theme 1: The Experience of Participating in the Monitor Trial

Personal benefit, behavior changes, and study incentives were themes linked with the experience of participating in the Monitor Trial. These issues influenced why patients, providers, and practice staff liked the trial and why patients were engaged in the self-monitoring study activities.

Direct Patient Benefit. Overall, patients reported positive comments about their experiences with the trial. A main theme that emerged from the interviews was the desire to gain more information. For patients randomized to the testing intervention arms, receiving daily numbers and accompanying messages was well received. Patients wanted more diabetes-specific information and felt they would have additional tools and resources by taking part in a research study. They also felt the trial could teach them new ways to better manage and monitor their diabetes.

Patient education and information was also considered a benefit for providers and practice staff. Providers explained that their patients with diabetes always seek more information about their diabetes and care. According to these focus group participants, the trial helped them provide additional educational materials and resources to their patients. It also gave providers different tools to use in their diabetes discussions and counseling.

Behavior Changes. Behavior changes as a result of a patient's participation in the trial were viewed as being both a positive and a negative aspect of the trial. Many of the patients were open to the study knowing they would be required to test routinely. Some said they enjoyed having to test each day, felt encouraged by their health care team, and really liked the idea of being more in control of managing their diabetes. They found this study expectation to be a positive result of the trial. In contrast, a key challenge for some of the patients randomized to the no testing arm was the change in behaviors. Patients talked about feeling "nervous" about changing their behaviors from testing daily to not being

able to test for a year. They also shared their worries about their blood sugar levels getting out of control and not being able to do anything about it.

Providers and practice staff also commented that the trial's changes in patients' diabetes behaviors caused concern with some patients. They explained some patients were initially confused about not being able to check their blood glucose levels regularly and concerned about "not knowing their numbers." This resulted in some providers having to spend more time during clinic to reassure their patients. Other providers mentioned that the behavior changes had a positive impact on patients. Some felt their patients were more proactive with their care, even checking their blood pressure more frequently.

Study Incentives. Patients across all 3 intervention arms mentioned a variety of reasons, including free testing equipment and financial incentives, that motivated their participation in the study. They liked receiving a personal machine to use and keep after the study and found the free testing strips to be a benefit.

Providers and practice staff said that patients were more likely to come in for nutrition and counseling visits because of the study incentives. They indicated that patients seemed to appreciate the self-monitoring supplies and educational materials. Collectively, the incentives had a positive impact on patients' participation and adherence to the trial.

Theme 2: Enhance Patient-focused Tools for Providers

Providers and practice staff talked about the usefulness of the summary reports and treatment algorithms and suggested different ways to make them relevant for use in practice settings.

Accessibility and Ease of Use. Providers and practice staff described the summary reports as "very helpful" and "simple." They viewed the reports as another tool to help educate patients. For example, some participants said that their patients liked the information in the reports and brought it to their clinic visits as a discussion point with their diabetes educators. However, many providers and practice staff said that these reports were often overlooked and not used. They explained that issues of accessibility and time made it difficult to incorporate them into a clinic visit. Providers found the time required to log in to access the study information or find it within the correct tab of a patient's chart to be burdensome and a hindrance. We have grouped the suggestions for modifying the patient summary reports into 3 main categories (Table 6).

Theme 3: The Patient–Provider Interaction

Participants freely discussed the patient–provider interaction before and during the trial.

Patient Support. Overall, patients described their relationships with their providers as "very supportive," "excellent," "good," "trust," and "satisfying." Some patients had long-established relationships with their providers and others were going through transitions. However, patients generally reported strong relationships with their providers and felt comfortable addressing health issues, including diabetes. Patient support also came in the form of the extended health care team, through the nurses reviewing the study data reports with patients and the staff inquiring about how testing was going during the study.

Limited Engagement. Patients perceived their participation in the trial to have had a small impact on their relationships. Across all 3 intervention arms, patients described the role of their providers as supportive but mostly "hands off" during the trial. While a few indicated that their providers did mention and encourage them to participate in the study, most patients interviewed recalled very little discussion, if any, of the study reports or treatment algorithms by their providers. In these situations, patients took the initiative to discuss their diabetes and study data during their clinic visits.

Table 6. Strategies for Enhancing Patient Summary Reports Suggested by Focus Group Participants

Data Integration

- Create separate research section in patient records for study reports
- Improve access to the summary reports (i.e., one click or one button to be easy and quick)
- Develop multiple strategies to collect and record summary reports (electronic health record is a temporary record)

Data Presentation

- Provide flexibility with display of patient data (e.g., scatterplots, graphs)
- Provide graph trend data to show point of intervention and changes over time
- Personalize patient information in the reports to be specific and target patient's health

Data Dissemination

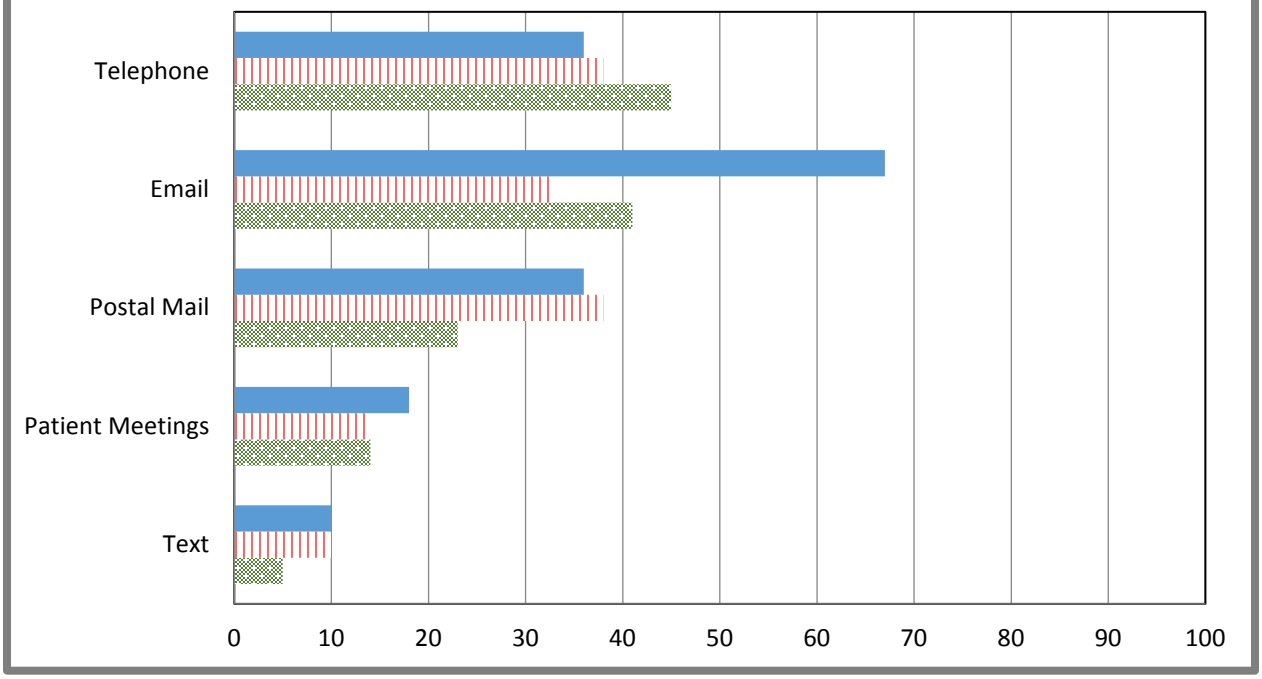
- Create a print/hardcopy option for providers to distribute to patients after clinical visit
- Allow patients access to reports after study activities

Providers and practice staff echoed the comments shared by their patients about how little their relationships changed during the trial. They talked about their appreciation of their roles in the trial being limited to encouragement and support. Additionally, many of the providers and practice staff said that the study's minimal requirement of them made it feasible to balance their support and patient engagement within the context of a clinical visit.

Theme 4: Strategies for Communication and Long-term Engagement

Patients, providers, and practice staff talked about their preferred methods of communication and had several suggestions for long-term engagement strategies.

Figure 6. Patients Preferred Communication Methods, by Intervention Arm



Balancing Active and Passive Communication Methods. We asked patients about their preferred methods of communication and how they would like information about this trial and other diabetes-related materials to be shared with them. Their preferences are presented in Figure 6. Patients advocated for multiple strategies, including e-mails that were "not intrusive" and "could be read or ignored" and more active strategies like in-person meetings that would allow patients to meet and support each other. For some, receiving phone calls was a higher priority than in-person meetings because of the ability to connect with a live person without the transportation issues to get to a central location. Receiving a letter or postcard in the mail was another preferred communication method because of the low burden for patients. They liked the ease of use, the accessibility, and having a

physical document sent to them. A few patients indicated that text messages were likely more useful for younger patients more involved with technology.

From the perspective of providers and practice staff, limited time was an obstacle in communicating with patients. Participants talked about incorporating communication strategies like e-mails (containing research summaries, results, and next steps) with options like a lunchtime wrap-up presentation because “food always works.” There was also a general sense that any practice staff with an active role in the trial, including providers, lead front office staff, nutritionists, educators, and phlebotomists, should be included in the communications.

More Dialogue and Social Media. Patients said they want more information and seek different ways to stay connected with their providers and other patients with diabetes. They said they would like to receive newsletters about information on any new discoveries about diabetes. Patients also wanted postcards that could direct them to specific websites discussing study research findings. Additionally, social media was mentioned as an effective way to communicate with patients. Some strategies discussed among patients included blogs that covered tips on healthy eating and exercise for diabetics and a social media page focused on helping patients with diabetes stay motivated by interacting with others and gaining access to resources.

Diabetes-focused Events. In addition to the online social opportunities, patients also talked about having in-person diabetes-focused events. They wanted to be a part of small-group discussions and seminars to connect with other patients with diabetes. Patients mentioned they were interested in health fairs or specific diabetes education sessions at practices or community locations. Last, patients talked about having more opportunities to participate in other diabetes-related research studies to facilitate long-term engagement.

Providing additional educational and research opportunities for patients was also a theme among providers and practice staff. They talked about ways to make patients see their practice as “a value-added place to get care.” One example suggested by participants was to hang signs or banners in the practices to highlight different partnerships with universities that could link patients to various diabetes information and research opportunities.

Provider Engagement in and Outside of the Practice. One of the key themes that emerged from the discussion was that providers were a trusted source of health- and diabetes-related care. Patients receive information from their providers; however, they want their providers to be engaged in their care beyond the clinic visit. Their suggestions for provider engagement ranged from strategies like providers

directly providing diabetes information and brochures to patients, to conducting periodic check-ins (by phone, mail, or e-mail) with patients between clinic visits to establish an ongoing relationship.

DISCUSSION

Context for Study Results

After 1 year, we identified no clinically or statistically significant differences in glycemic control or HRQOL in patients who performed once-daily SMBG compared with those who did not perform SMBG. The addition of instant tailored feedback messages via a meter did not improve glycemic control. This null result occurred despite training participants and primary care providers on the use and interpretation of the meter results.

Our findings align with earlier studies that demonstrated the limited utility of SMBG in patients with non–insulin treated T2DM.[9,19-22] Surprisingly, SMBG has remained a cornerstone in the clinical management of non–insulin treated T2DM, in part fueled by other studies showing that SMBG may positively impact glycemic control.[17,18,71,72] Our trial was pragmatic in nature, designed with less-intense intervention and monitoring than traditional clinical trials and intended to mirror real-world clinical practice. This less-intense approach may have affected the decline in adherence to SMBG over time. Our sensitivity analyses showed that over the first 6 months, glycemic control did improve for all patients engaging in SMBG regardless of messaging type. In addition, compliance with testing showed progressive attrition in both SMBG monitoring groups. Compliance-adjusted analyses suggest that differences in change in hemoglobin A1c were related to the extent of compliance at 6 to 9 months postrandomization, but any benefit obtained by participants in the SMBG groups was diminished by the conclusion of the study, even for those participants who were consistently the highest compliers. These findings have the potential to inform current clinical practice for patients and their providers by shining a spotlight on the perennial question, “To test or not to test?”

Generalizability of the Findings

The majority of patients had some experience with SMBG at baseline and all were willing to be randomized; this may not reflect the typical population of patients with T2DM. Because our population included patients with T2DM not using insulin, these results cannot be generalized to insulin users. SMBG has important efficacy and safety roles in insulin users for dose titration and hypoglycemia detection. Furthermore, participating primary care practices were affiliated with a single health care

system, though patients were typical of those found in primary care nationally regarding patient demographics including race, ethnicity, and education.[77]

Implementation of Study Results

Health care providers are typically divided on the issue of SMBG monitoring; most providers either do or do not recommend SMBG monitoring.[43,73] Additionally, patient preferences for testing are quite variable; in our study, patient testing preference at baseline was split. Prior work has also described that the nonuse of SMBG results occurs when patients put a low priority on diabetes care and physicians do not engage in shared decision making.[74] Based on our findings, we propose a more patient-centered approach in which patients and providers engage in a 2-way dialogue discussing the pros and cons of SMBG based on their clinical situation and then jointly determine if routine SMBG is indicated.

Furthermore, encouraging a shared decision-making approach between patient and provider is informed by the results of our secondary analyses. Proponents of routine SMBG in patients with non–insulin treated T2DM have cited evidence that this testing approach is useful for patients with newly diagnosed diabetes or patients with poor glycemic control[18]; however, our analyses do not support this recommendation. Disease duration, experience using SMBG, baseline glycemic control (A1c upper quartile distribution range 8.1 to 13), antihyperglycemic treatment, age, race, health literacy, and number of comorbidities made no difference in glycemic control at 52 weeks. Only race was significant by interaction testing for HRQOL physical component score; African Americans in the SMBG with messaging group had significantly lower scores. There were no significant differences by race for the HRQOL mental component score. Given multiple comparisons across groups, we suspect this significant finding may be spurious.

Incorporating technology into self-management activities has been touted as potentially transformative for patients with diabetes, and to date some smaller studies[75,76] support this notion. However, our findings dampen enthusiasm for the profusion of mHealth apps the focus on routine SMBG. It is possible that the enhancement of SMBG with 1-way messaging back to the patient does not adequately engage the patient. This notion is supported by the sensitivity analyses showing initial glycemic control improvement at 6 months and regression back to baseline afterward. A more interactive approach or the use of 2-way messaging between the patient and provider may improve the durability of this approach.

Study Limitations

Although designed with an eye toward the real-world clinical setting, 1 limitation is that our study team was not engaged with the patients beyond the baseline visit. Health care providers likewise had

minimal interaction with the study team. Our qualitative findings also noted that providers had some difficulty incorporating the time to login in and download the SMBG reports during the patient visit. This may have impacted persistence of SMBG testing by patients. More active engagement of both the patients and the health care providers during the study period may have improved patient outcomes, although this would have diminished the pragmatic nature of this study. Additionally, not all patients adhered to the group to which they were assigned; however, per protocol analyses were not notably different from the intent-to-treat analyses. Although underpowered to detect differences between subgroups, none of our analyses suggested clinically meaningful differences between the subgroups based on a large number of parameters examined. It is possible that the intervention was off-putting in some ways causing user fatigue or provided false reassurance; most of what is learned from SMBG is learned early by patients. Although not the primary outcomes of this study, we don't know HRQOL and diabetes specific self-care during this midpoint in the study. Perhaps more can be learned in a future study that collects HRQOL at the 6-month time point.

Future Research

Although our trial did not find any differences with SMBG in our population, there may be subpopulations that benefit from SMBG. Future research could examine the role of SMBG in subpopulations, including patients who are newly diagnosed or patients who undergo a diabetes treatment change. Additionally, this trial examined once-daily testing. Given the declining adherence with long-term testing, different formats may be of benefit (e.g., increased number of test times during the day but for shorter intervals).

CONCLUSIONS

In conclusion, in patients with non–insulin treated T2DM, there were no clinically or statistically significant differences at 1 year in glycemic control or HRQOL in patients who performed SMBG compared with those who did not perform SMBG. Although sensitivity analyses showed that over the first 6 months glycemic control did improve for all patients engaging in SMBG regardless of messaging type, improvements in glycemic control regressed back to baseline. It is our hope that these findings will inspire both patients and providers to routinely engage in collaborative conversations about the question, "To test or not to test?"

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Appendix: Compliance-Adjusted Exploratory Analyses

For any randomized controlled trial, it is important to acknowledge that any compliance-adjusted analyses could be highly susceptible to bias because the comparisons would no longer be randomized. This is the case because any participant's level of compliance is inherently self-selected, as was certainly the case in this study. Furthermore, in this study, we have only very rough, self-reported measurements of the frequency with which participants randomized to the "no SMBG" group might have self-tested during the study, and it is unknowable how often they might have tested had they been randomized to 1 of the SMBG groups. For these reasons, all exploratory, compliance-adjusted analyses included only participants randomized to 1 of the 2 SMBG groups, for whom we have objective measures of compliance; however, the results should be interpreted with caution.

A variety of exploratory compliance-adjusted analyses could be performed. We chose to use 3 different measures of compliance, all based on the relative frequency with which participants assigned to 1 of the SMBG groups used their assigned meters, which uploaded time- and date-stamped results automatically. The first measure was the most straightforward, albeit the crudest, in which participants were categorized as "high compliers" if they tested on at least 80% of their days enrolled in the trial, "moderate compliers" if they tested between 50% and 80% of their days, or "low compliers" otherwise. Therefore, in analyses using this measure, compliance was treated as a time-independent covariate and each participant would be assigned to a single compliance group. As our second measure, we used the cumulative proportion of days compliant up until each successive A1c measurement. As our final measure of compliance, we used the proportion of days compliant between each successive A1c measurement. For each of the latter 2 measures, compliance was categorized as for the first measure, and compliance was treated as a time-dependent covariate in the models; participants could shift from 1 compliance category to another between A1c measurements. For each compliance measure, we fit a quadratic polynomial model over time using a linear mixed model with change from baseline in A1c% as the outcome. We included random regression coefficients for each participant to account for correlation between repeated measurements. We controlled for the same covariates that we controlled for in the primary analysis of A1c, namely site, baseline A1c, use of SMBG at baseline, duration of diabetes, baseline use of antihyperglycemic treatment, age, race/ethnicity, health literacy, and number of baseline comorbidities. In addition, because the interim A1c values were obtained from the electronic health record and they could have been measured using any available test, we also controlled for type of A1c test (point-of-care or a rapid test versus a lab-based test). Furthermore, the interim A1c values were irregularly timed over any participant's enrollment in the study. For these analyses we chose to exclude any A1c measurements that occurred prior to 2.5 months in the study because the data were sparse in that region, particularly for the lowest-complying group. We included A1c values measured up to 13.5 months postrandomization, which aligns with the 6-week window used for the primary analysis.
The results of these analyses are presented in the 3 figures below. Figure A.1 presents results using the measure of compliance from over the entire study period, Figure A.2 presents results using cumulative compliance up until each successive A1c measure, and Figure A.3 presents

results using SMBG compliance between each successive A1c measure. The results in all 3 graphs are mostly similar.

Figure A.1. Compliance-adjusted Analyses With Compliance Measured Over All Days Enrolled in Study

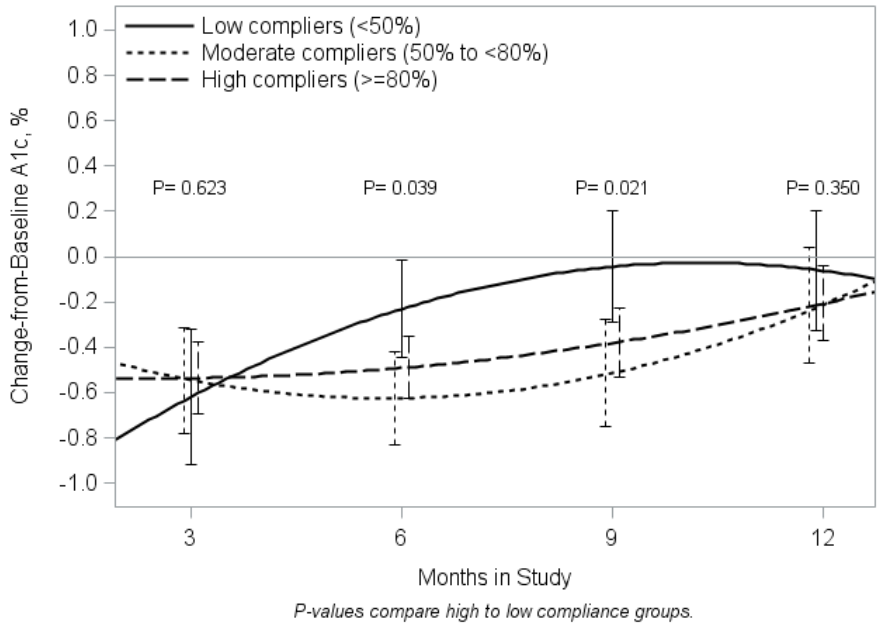


Figure A.2. Compliance-Adjusted Analyses Using Cumulative Compliance up to Each A1c Measurement

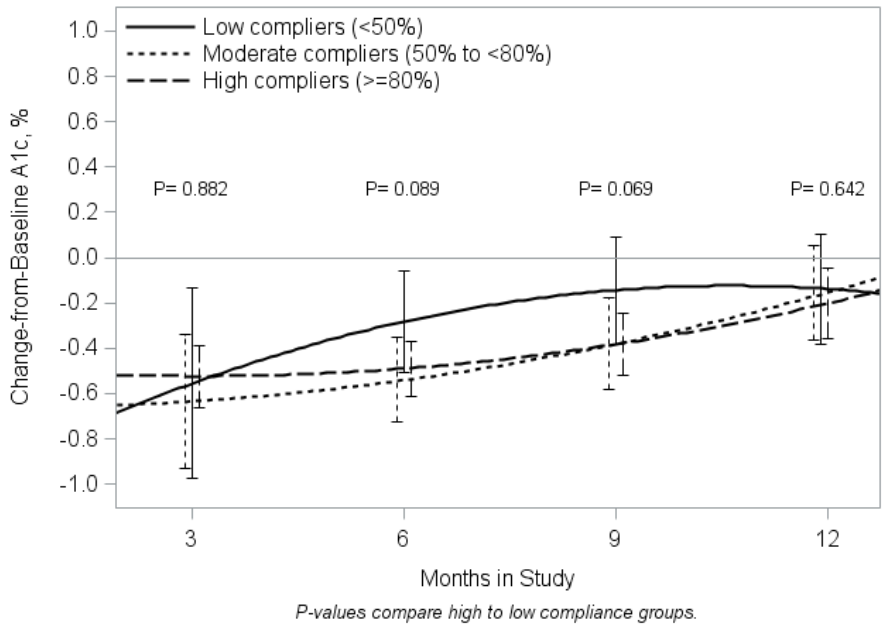
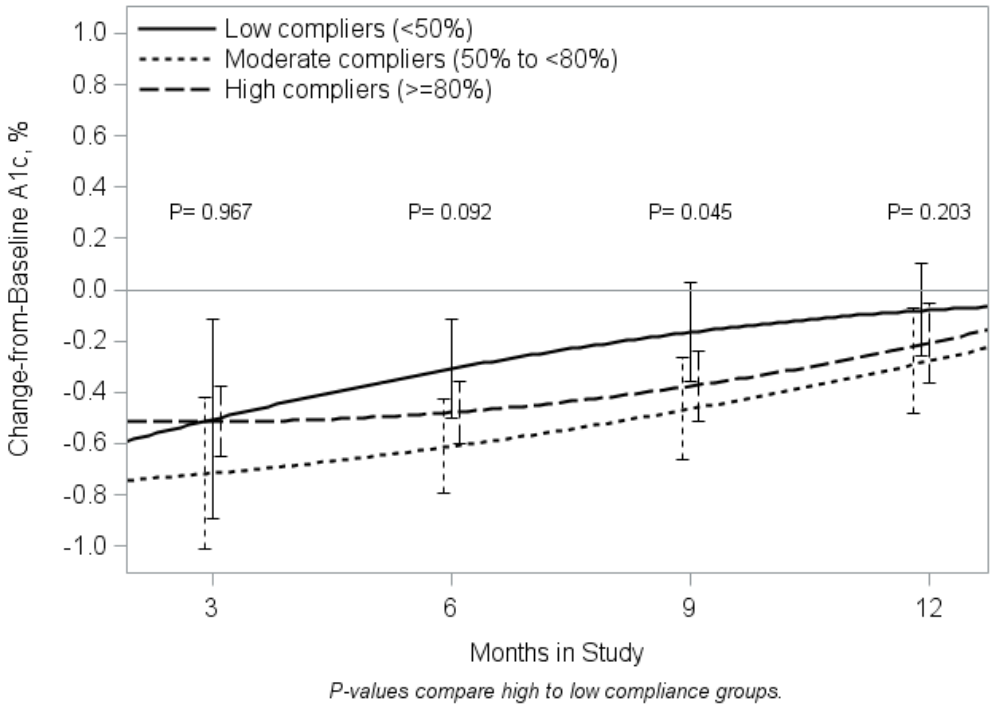


Figure A.3. Compliance-Adjusted Analyses Using Compliance Between Each A1c Measurement



Regardless of the measure of compliance used, our results do suggest that differences in change in A1c were related to the extent of compliance with daily SMBG, particularly at 6 to 9 months postrandomization. Given our results presented in Figure 2a in the main report, this observation should not have been unexpected. In the analyses summarized in Figure 2a, we found that participants in the 2 SMBG groups had significantly lower A1c values than the participants in the no SMBG group between 3 to 9 months postrandomization; however, any benefit that might have been obtained by being randomized to 1 of the SMBG arms must have been obtained by actually performing SMBG rather than simply having the meter available. An observation that is perhaps more interesting is that, regardless of the measure of compliance used, any benefit obtained by participants in the SMBG groups was greatly diminished, on average, by the conclusion of the study, even for those participants who were consistently the highest compliers (a group that includes about 55% of all participants randomized to 1 of the SMBG groups). This would seem to suggest, in agreement with our conclusion from our primary analysis, that daily SMBG by itself is insufficient to achieve a long-term reduction in A1c for the majority of patients within this study population.

Acknowledgement:
Research reported in this report was [partially] funded through a Patient-Centered Outcomes Research Institute® (PCORI®) Award (CE-12-11-4980).