Longitudinal Study of New and Prevalent Use of Self-Monitoring of Blood Glucose

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OBJECTIVE — We sought to assess longitudinal association between self-monitoring of blood glucose (SMBG) and glycemic control in diabetic patients from an integrated health plan (Kaiser Permanente Northern California).

RESEARCH DESIGN AND METHODS — Longitudinal analyses of glycemic control among *1*) 16,091 patients initiating SMBG (new-user cohort) and *2*) 15,347 ongoing users of SMBG (prevalent-user cohort). SMBG frequency was based on pharmacy use (number of blood glucose test strips dispensed), and glycemic control was based on HbA_{1c} (A1C). In the new-user cohort, ANCOVA models (pre- and posttest design) were used to assess the effect of initiating SMBG. In the prevalent-user cohort, repeated-measure, mixed-effects models with random-intercept and time-dependent covariates were used to assess changes in SMBG and A1C. All models were stratified by therapy (no medications, oral agents only, or insulin) and adjusted for baseline A1C, sociodemographics, insulin injection frequency, comorbidity index, medication adherence, smoking status, health care use, and provider specialty.

RESULTS — Greater SMBG practice frequency among new users was associated with a graded decrease in A1C (relative to nonusers) regardless of diabetes therapy ($P < 0.0001$). Changes in SMBG frequency among prevalent users were associated with an inverse graded change in A1C only among pharmacologically treated patients ($P < 0.0001$).

CONCLUSIONS — These observational findings are consistent with short-term benefits of initiating SMBG practice for all patients but continuing benefits only for pharmacologically treated patients. Differences in effectiveness between new versus prevalent users of SMBG have implications for guideline development and interpretation of observational outcomes data.

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Findings from the Diabetes Control and Complications Trial (1) and the U.K. Prospective Diabetes Study (2) and dissemination of the Self-Monitoring of Blood Glucose Consensus Conference (1986) have contributed to an increased attention to tight glycemic control in patients with diabetes and a concomitant promotion of self-monitoring of blood glucose (SMBG). However, SMBG is costly for patients and health insurers, and the clinical value of this practice for patients who are not treated by insulin remains controversial. Because of inconsistent evidence, current recommendations vary widely and are typically vague (3). For example, an American Diabetes Association's 2005 position statement states, "The optimal frequency and timing of SMBG for patients with type 2 diabetes on oral agent therapy is not known but should be sufficient to facilitate reaching glucose goals" (4). The high cost of test strips in an era of evidence-based medicine has created a demand for rigorous evaluation of the effectiveness of SMBG.

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Abbreviations: OHA, oral hypoglycemic agent; SMBG, self-monitoring of blood glucose.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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No studies, either experimental or observational, have addressed the long-term impact of various SMBG testing frequencies on glycemic control. In this article, we present results of the first longitudinal study of the association between SMBG frequency and glycemic control in diabetic members of a prepaid, integrated health plan. Additionally, special attention is directed at the distinct effects of newly initiating SMBG versus ongoing monitoring on glycemic control.

RESEARCH DESIGN AND METHODS

— We assessed the association between changes in SMBG frequency and glycemic control in two large cohorts during a 4-year observation window. The first cohort included 16,091 "new users," i.e., subjects who were not practicing SMBG before baseline. The new-user design reduces the chronology bias and case mix confounding associated with other observational study designs that pool new versus ongoing users (5). Among new users, we evaluated longitudinal changes in HbA_{1c} (A1C) after removing expected age-associated changes in glycemic control derived from the reference group: patients who did not initiate SMBG ("persistent nonusers"). In the second cohort of 15,347 "prevalent users" (diabetic members who practiced SMBG during the year before baseline), we evaluated how individual changes in frequency of SMBG during a 3-year follow-up were associated with changes in glycemic control.

Study subjects were identified from the diabetes registry (n = ~180,000) maintained by Kaiser Permanente Northern California Medical Care Program (9–12) with the approval of the institutional review board at the Kaiser Foundation Research Institute. Kaiser Permanente Northern California is a not-for-profit, prepaid, integrated health care–delivery system, providing comprehensive medical services to >3,000,000 members (~35% of the catchment population) through 15 hospitals and 23 outpatient clinics. Eligibility for the study was restricted to registry members with continuous membership and full pharmacy benefits during the observation windows to avoid underascertainment of utiliza-

tion of blood glucose test strips ("test strips").

Cohort definitions

For the new-user cohort, we identified subjects who initiated SMBG during the 3.5-year period, 1 March 1999 through 31 August 2002, with a reference group of members who had no strip utilization recorded during the entire observation window. New users had no strip utilization in the 24 months before their first dispensing of test strips and had at least one refill in a separate month within the 12 months following the initial dispensing. Baseline was defined as the date of the first test strip dispensing for new users and was arbitrarily set to 1 January 2001 for the reference group. Subjects lacking sufficient A1C data were excluded. For the prevalent-user cohort, we identified health plan members who met the continuous membership and pharmacy benefit criteria and were test strip users in 1999. To avoid the confounding effects due to the strong association between therapy changes and both SMBG frequency and glycemic control, we excluded, from both cohorts, members who modified their diabetes pharmacy regimen (discontinued, switched, or added a therapeutic class) anytime during follow-up; however, we were not able to identify changes in dose during follow-up. Two percent ($n = 365$) of the new-user cohort had long enough follow-up postinitiation to also be included in the prevalent-user cohort. We also excluded members with end-stage renal disease or substantially elevated serum creatinine, since impaired renal function can lower A1C levels (6).

Data collection methods

The outcome of interest, glycemic control, was measured by A1C and captured from Kaiser's central laboratory database. All assays were conducted using high-performance liquid chromatography. For the new-user cohort, the most recent A1C measured before the baseline date was used as the prebaseline measure. Postbaseline data were sought between 3 and 12 months postbaseline, using the last value if multiple tests were recorded. For the prevalent-user cohort, we collected the last A1C recorded in each of the 4 calendar years during the observation window and controlled for timing of the data collection.

The exposure of interest, average daily SMBG testing frequency, was based on test strip use data in pharmacy prescription and refill records. This estimation procedure has been shown to be a valid measure for patients with a prescription benefit (7). For the new-user cohort, average daily SMBG testing frequency was calculated from number of strips dispensed divided by the number of days from the date of initiation to the date of the first strip refill subsequent to the postbaseline A1C test. In the prevalent-user cohort, average daily SMBG testing frequency was calculated from the number of strips dispensed per calendar year for each of the 4 years (1999–2002) during the study period.

Pharmacy records were used to classify patients into mutually exclusive treatment strata: "no medication" (e.g., medical nutrition therapy alone or diet controlled), "OHA" (oral hypoglycemic agents only), and "insulin" (use of insulin or any regimen that includes insulin). We excluded patients who switched between these treatment strata during follow-up to minimize the impact of changing therapy modalities on changes in SMBG and A1C. Pharmacy records were also used to calculate an index of medication adherence (percentage of time without adequate supply or "continuous, multiple-interval measure of medication gaps" [8]), as well as the frequency of daily insulin injections (based on recorded syringe utilization). Electronic administrative records were used to assess inpatient and outpatient utilization, the proportion of outpatient appointments that were neither attended nor cancelled ("no shows") (9), primary care provider specialty, smoking status, and a validated comorbidity score (10) based on inpatient, outpatient, and pharmacy utilization. Neighborhood-level socioeconomic status was characterized by geocoding each member's address to its 2000 census block group and creating variables for median household income in 1999, residence in a poorly educated neighborhood (defined as ≥25% of block group with less than a high school degree), and residence in a predominantly working-class neighborhood (defined as ≥66% of block group employed in a working-class occupation).

Analytical methods

All models were run with PROC MIXED in SAS version 8.2. Model specifications differed for the new- and prevalent-user cohort designs (see below). In both models, continuous measures of A1C were regressed on test strip use to provide an estimate of dose-responsive change in A1C as a function of changes in SMBG frequency (average daily SMBG testing). We assumed that these effects could differ by therapeutic modality and thus specified separate models for each diabetes therapy. In the new-user design, we estimated the effect of initiating different frequencies of SMBG on glycemic control above and beyond expected changes attributable to aging and secular trends. We used an ANCOVA model ("differences-in-difference" method) to estimate the change in A1C pre- and post-SMBG initiation after accounting for expected changes in A1C observed during the same time window among subjects who never initiated SMBG (reference group). We also controlled for prebaseline A1C, as well as for sex; age; inpatient comorbidity score; prebaseline measures of daily insulin injections frequency (for the insulin model only); diabetes medication refill adherence; diabetes therapies (therapeutic class); appointment "no show" rate; performance of annual ophthalmology exams; prebaseline rates of hospital, emergency room, primary care, and specialty visits; primary care provider type; smoking status; neighborhood level; median family income; residence in a poorly educated neighborhood; residence in a predominantly working-class neighborhood; and the length of time between pre- and post-A1C tests.

For the prevalent-user design, we assessed longitudinal changes in A1C as a function of changing frequency of SMBG practice (on an individual level) using repeated-measure, hierarchical linear models. We specified a random intercept and adjusted for baseline A1C to control for regression to the mean. Models were adjusted for the same covariates listed above; however, for these models, we specified the following as time-dependent covariates: SMBG, daily insulin injection frequency, appointment "no show" rate, inpatient comorbidity score, and inpatient and outpatient utilization.

RESULTS

— Patient characteristics varied by treatment strata and by whether patients were new users, persistent nonusers, or prevalent users of SMBG (Table 1). Compared with nonusers and prevalent users, new users had markedly higher A1C levels. A1C levels were lowest among patients not treated with medication, intermediate among OHA only, and highest among insulin users. New users also had the highest rate of out- and inpatient utilization among pharmacologically treated

Table 1—*Baseline characteristics of 16,091 subjects who newly initiated SMBG practice (new users) and 15,347 subjects who were ongoing users of SMBG (prevalent users)*

Characteristics	New-user cohort						Prevalent-user cohort		
	No medication		OHA only		Insulin users		No medication	OHA only	Insulin users
	Future new users	Persistent nonusers	Future new users	Persistent nonusers	Future new users	Persistent nonusers			
n	5,441	3,823	3,167	2,700	720	240	1,622	7,409	6,316
Average daily strip utilization after initiation	0.97 ± 0.7*	None	0.90 ± 0.7*	None	1.32 ± 1.2*	None	0.63 ± 0.5*	0.74 ± 0.6	1.94 ± 1.5
A1C (%)	8.2 ± 2.0*	6.6 ± 1.0	8.6 ± 2.0*	7.3 ± 1.4	9.3 ± 2.1*	8.2 ± 1.7	6.4 ± 0.8*	7.6 ± 1.4	8.1 ± 1.5
Age (years)	59.1 ± 12.8*	67.3 ± 11.9	62.8 ± 11.8*	66.5 ± 12.1	58.3 ± 14.3†	61.7 ± 13.6	61.2 ± 12.2*	60.5 ± 11.2	53.2 ± 18.4
Female	47.3	47.4	42.5	41.9	47.1	43.3	45.1*	45.4	50.3
Diabetes oral agent therapy refill adherence (proportion of time with insufficient pill supply)	—	—	0.12 ± 0.2	0.10 ± 0.2	0.16 ± 0.2	0.14 ± 0.2	—	0.14 ± 0.2	0.14 ± 0.2
Insulin injections per day									
<1/day	—	—	—	—	41.2	38.1	—	—	29.2
1–2/day	—	—	—	—	42.0	41.4	—	—	34.3
>2/day	—	—	—	—	16.8	20.5	—	—	36.5
Outpatient clinic appointment "no show" rate	0.12 ± 0.1*	0.10 ± 0.1	0.13 ± 0.1*	0.12 ± 0.2	0.15 ± 0.2	0.15 ± 0.2	0.09 ± 0.1*	0.11 ± 0.2	0.13 ± 0.2
Annual eye exam attendance	45.8	44.4	54.6‡	51.5	63.6	58.3	41.6*	48.3	57.2
Hospitalization during prebaseline year	9.7*	14.1	16.8*	11.5	24.2	17.9	9.1*	10.1	15.0
Emergency room visit during prebaseline year	16.8*	22.4	26.5*	20.1	37.6†	28.3	18.6*	19.7	27.8
Smoking status (yes)	20.6*	17.8	20.7	19.7	25.3	20.0	17.3*	18.6	20.7
Provider type									
Primary care	86.3†	86.0	84.5	84.2	82.9	84.2	84.3*	84.3	77.9
Specialist	8.7	12.2	11.8	14.1	13.9	13.8	10.1	11.4	17.2
None	4.9	1.8	3.7	1.7	3.2	2.1	5.6	4.3	4.8
Comorbidity score > median value	32.4*	58.4	49.1*	61.8	65.8‡	72.9	43.2*	42.2	61.7
2000 census block group median income for 1999 ($)	61,964 (24,244)	62,950 (25,370)	60,738 (23,634)	61,608 (25,993)	57,370 (24,189)	59,425 (24,391)	61,657 (24,274)	59,802 (23,473)	60,371 (24,452)
Residence in poorly educated neighborhoods§	22.4	21.7	25.9	26.5	30.0	34.3	18.9	24.3	22.3
Residence in predominantly working-class neighborhoods‖	29.4	29.2	31.5	29.9	36.7	34.3	27.1	32.4	30.2

Data are percent or means ± SD unless otherwise indicated. New-user cohort: prebaseline characteristics of 16,091 subjects who do not practice SMBG (nonusers) at baseline. These are stratifed into two groups: the 9,328 patients who initiate SMBG in the future (future "new users") and 6,763 who continued not practicing ("persistent nonusers"). Prevalent-user cohort: prebaseline characteristics of 15,347 subjects included in the prevalent-user cohort, consisting of patients who practice SMBG at baseline ("prevalent users"). *P* value reported from the Mantel-Haenszel χ^2 test for categorical variables and Spearman's correlation coefficient for continuous variables. *$P < 0.001$; †$P < 0.01$; ‡$P < 0.05$. §≥25% block group with less than high school degree; ‖≥66% block group employed in working-class occupations.

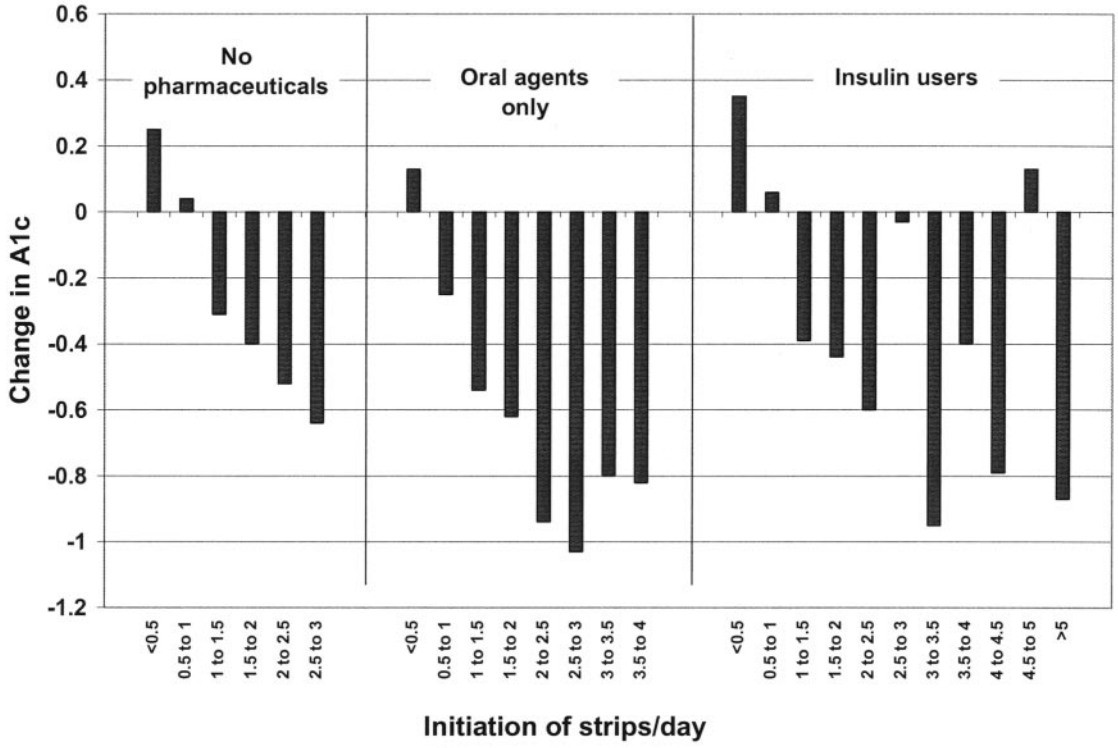

Figure 1—*Adjusted dose-responsive change in A1C associated with SMBG initiation among patients not previously using SMBG and not treated pharmacologically* (n = *7,872*)*, treated with an oral agent only* (n = *5,546*)*, and patients treated with insulin* (n = *840*)*. Patients-switching-therapy changes were excluded. Therapy changes were excluded. Models adjusted for age, sex, insulin injection frequency (insulin model only), comorbidity index, oral medication refill adherence (OHA model only), appointment keeping, inpatient and outpatient utilization, smoking status, type of primary care provider, socioeconomic status indicators, timing of A1C test, and baseline A1C.*

patients and were more likely to be smokers. Persistent nonusers were older than new or prevalent users and had higher comorbidity scores than new or prevalent users. Among insulin-treated patients, prevalent SMBG users were most likely to be treated with multiple daily insulin injections.

New-user cohort

In the new-user cohort, there was a marked improvement in A1C after initiation of SMBG practice in all three therapy groups. Initiating once-daily monitoring resulted in an ~0.35-, 0.42-, and 0.23-point lowering of A1C among no medication, OHA, and insulin-treated patients, respectively ($P < 0.0001$). Moreover, this benefit showed a dose-responsive relationship with frequency of testing in each group (Fig. 1), although with diminishing returns after approximately three strips per day for OHA-only and insulin-treated patients. The dose-responsive relationship continued up to three strips per day for patients not treated pharmacologically; however, there were insufficient numbers testing at higher frequencies to make inferences. Note that because most insulin-treated patients already use SMBG, the cohort available for this analysis (previous nonusers) was small, explaining the less stable response pattern relative to the other groups; nonetheless, the dose-response curve was significant ($P < 0.0001$). In addition to glycemic benefits, new users of SMBG treated with oral agents had statistically significant ($P = 0.04$) improvements in medication adherence relative to persistent nonusers. However, this improvement (~1%) was not large enough to be clinically relevant.

Prevalent-user cohort

Among the prevalent users, during the 3 years of follow-up, the individual level changes in the frequency of SMBG practice were lowest for those not treated pharmacologically, intermediate for OHA only, and greatest for insulin treated. The mean (±SD) of the absolute change in frequency (greatest average daily frequency minus lowest average daily frequency of SMBG for each individual) was 0.4 ± 0.4, 0.5 ± 0.5, and 1.1 ± 0.9 strip changes in daily monitoring frequency for the no medication, OHA-only, and insulin-treated groups, respectively. Longitudinal changes in SMBG frequency were related to significant changes in glycemic control in pharmacologically treated subjects only. Among subjects on no medications, changes in SMBG were not associated with significant changes in glycemic control. For OHA-only and insulin-treated patients already practicing SMBG, subsequent changes in SMBG frequency by one strip daily resulted in a 0.16- and 0.12-point inverse change in A1C, respectively ($P < 0.0001$). As with new users, the relationship between changes in SMBG testing frequency and changes in A1C were dose responsive with diminishing returns, with changes larger than approximately two or three strips per day having minimal further effect on A1C changes for OHA and insulin-treated patients, respectively (data not shown).

CONCLUSIONS — This is the first study to assess the effects of changing SMBG practice on glycemic control over a longer period and to separately evaluate new and ongoing SMBG users. We observed a significantly different effect between new and ongoing users, suggesting

that pooling may have biased previous analysis. Among new users, initiating SMBG was associated with a graded improvement in glycemic control, even among those not treated pharmacologically. Among prevalent users, there was a significant association between change in SMBG and A1C only in those receiving pharmacologic therapy; decreases in SMBG frequency were significantly associated with a modest worsening in glycemic control, whereas increases in SMBG were associated with modest improvements in control. All of the above associations were significant and graded but with diminishing returns.

Among new users, the biological feedback associated with SMBG may help patients understand how behaviors (e.g., exercise and diet) and clinical states (e.g., different insulin doses or timing) impact their glycemic control. Among prevalent users not receiving pharmacologic therapy, changes in SMBG had no substantive impact on A1C; perhaps this constant feedback maintains value only if used in real time to guide behavioral and therapeutic modifications or recorded to inform their provider about glycemic patterns.

In prevalent users, the impact on control of changing average testing frequency by one test per day was somewhat smaller in insulin-treated than in OHA-only users (0.12- vs. 0.16-point decrease in A1C for a one strip per day increase in monitoring frequency; $P < 0.0001$), perhaps because insulin-treated patients typically require multiple tests throughout the day to adjust insulin, whereas OHA-only patients rely on less frequent testing. It has been demonstrated that well-informed insulin-treated patients readily modify insulin dose and timing in response to SMBG readings and that improved insulin administration effectively improves glycemic levels (11). Patients treated by OHAs only are rarely instructed to change or titrate dose themselves in response to home glucose readings; however, they may change timing of oral medications. Our findings differ from a study concluded by the Veterans Administration (12). These authors reported no significant worsening in A1C after modest reductions in SMBG frequency (reduction of 0.4 and 0.6 strips/day on average) among stable, diet-controlled type 2 diabetic and oral agent–treated patients, respectively, all of whom were prevalent SMBG users at baseline. It is important to note that after the reduction, both groups were still testing quite regularly (~0.7 strips/day). It is unclear as to whether SMBG lacked effect or, alternatively, whether their patient population was overutilizing SMBG prior to their study, and the reduction in SMBG frequency was small enough to cross a threshold after which further reductions in utilization would have caused harm.

Several potential limitations and strengths of this study deserve comment. Causal interpretation of these findings is limited by the lack of randomization. However, randomized controlled trials also have limitations for the study of SMBG. Blinding is not possible in studies of SMBG, and thus such studies are potentially biased when patient preferences are not incorporated (16). For such interventions that are not amenable to blinding, a strong patient preference and randomization to the nonpreferred intervention can reduce the internal validity of an randomized controlled trial by biasing the estimate of effect (16). Randomized controlled trials may be biased when behavioral improvements are stimulated by the subjects' knowledge that their outcomes will be observed (Hawthorne effect) (13). Furthermore, most current SMBG practice guidelines make it unethical to include an unexposed arm. Thus, we suggest that these observational findings are an important complement to those derived from experimental studies.

Observational studies of SMBG are susceptible to well-described biases, which require analytic attention. Reverse causality (endogeneity) is one potential source of bias in observational studies if not analyzed correctly. This would occur if changes in the study outcome (glycemic control) actually led to subsequent changes in the exposure (SMBG), instead of the other way around. We found some evidence of such a pattern. We evaluated glycemic control among subjects not using SMBG (i.e., before initiation of SMBG in the new-user cohort) and found that initiators of SMBG had substantially poorer control versus nonusers who did not initiate SMBG during the follow-up (A1C 9.3 vs. 8.2% in insulin-treated, 8.6 vs. 7.3% in OHA-only, and 8.2 vs. 6.6% in diet-controlled patients).

Another limitation is that patient receipt of education or instruction on SMBG practice is unknown to us. Kaiser Permanente offers diabetes health education classes that include training on the use of SMBG when diabetes is initially diagnosed and further on in the natural history of diabetes; Kaiser Permanente SMBG guidelines are in line with the American Diabetes Association clinical recommendations for SMBG. In accord with those guidelines, provider recommendations are flexible and will likely vary over time, depending on changes in type of therapy, disease severity, patient motivation, etc. We do not know how well health educators or care providers follow guidelines, to what extent provider recommendations change over time, how providers instruct the patients to use the SMBG data, or how well patients understand or incorporate these instructions.

Poor glycemic control likely motivates health care providers to urge their patient to initiate or intensify SMBG practice or may motivate the patient to initiate on his/her own. A simple cross-sectional anlysis of this new-user cohort would have resulted in distorted (and counterintuitive) findings, suggesting that SMBG initiators had 1- to 2-point–poorer glycemic control, i.e., the opposite direction of effect observed in our longitudinal analysis of new users. This may account for some of the negative findings in previous observational studies that did not separate new and prevalent users. Another possible source of endogeneity would be that providers could simultaneously intensify diabetes therapy because of poor control and recommend increasing SMBG. Thus, the improvement in A1C could be due to therapy intensification, SMBG, or both. Since our intention was to evaluate the SMBG effect, we therefore excluded any subjects that initiated new therapies during follow-up subsequent to the baseline A1C measurement. However, our study is limited by the lack of data on change in medication dose. Thus, the limits of our data also preclude us from separating the impact of SMBG results influencing providers to modify the patient's therapy dose from the impact of SMBG on self-care. However, we see both pathways as potentially important benefits of SMBG, and the benefit likely differs on an individual basis; therefore, quantifying the importance of each pathway may be of secondary importance from a public health point of view.

We further addressed these concerns of endogeneity by specifying an augmented regression (17) to test the null hypothesis that SMBG is exogenous (predetermined) in the A1C regression. This method is widely used in the econometrics literature where observational data analyses are the norm. In brief, the augmented regression is equivalent to

putting the predicted values of the potentially endogenous regressor (i.e., change in SMBG) into the second-stage model for the outcome (change in A1C), along with the residuals from the first-stage prediction model. The prediction model includes an "instrumental variable;" in this case, an exogenous policy change that altered the copayment for test strips but should not have had an impact on A1C independent of its effect mediated through SMBG. Failure to reject the null hypothesis that the residuals have any effect implies that changes in SMBG utilization are exogenous and that the single-equation estimates are consistent, i.e., two-stage instrumental variable modeling is unnecessary. Intuitively, the effect of the predicted regressor is the instrumental variables estimate of the unbiased "causal" effect of that regressor. Therefore, if the residuals from the prediction model for SMBG demonstrate independent explanatory power in the A1C regression, it must be because the error terms in the SMBG and A1C equations are correlated, i.e., SMBG is endogenous to A1C. As this was not the case with our data, we present only the single-equation estimates. It is worth noting that the most likely form of endogeneity (poorer glycemic control leading to increased monitoring) would have biased findings toward the null, and thus, if anything, our findings should be conservative. Omitted-variable bias is another limitation of observational study design. For example, SMBG frequency may simply be a marker for better, more intensive disease management, which more directly influences health outcomes. Because this study was conducted in a single health maintenance organization, the quality of diabetes care was probably more uniform than in a community sample. However, differences in disease management approach across providers and over time could confound our findings. Therefore, we assessed the sensitivity of our regression results by simulating how strong an unmeasured (residual) confounder would have to be to make our findings attenuate to nonsignificance (18). This analysis showed that only a very potent residual confounder would negate our conclusions. Such an unmeasured confounder would have to confer an effect comparable to initiating a pharmacological agent (e.g., 1% lowering of A1C) and be highly prevalent in those who practice SMBG and not prevalent in those who do not practice. While theoretically possible, we think it is unlikely such a strong confounder (associated with SMBG and control) would have gone unnoticed.

SMBG utilization may have been slightly underascertained if members purchased additional testing supplies in non–Kaiser Permanente pharmacies, although exclusion of the ~5% of patients lacking pharmacy benefits should have minimized this potential misclassification. The exclusion of individuals who change diabetes therapy reduces the generalizability of this study. However, we felt that this exclusion was necessary to avoid the observed change in A1C being more due to change in therapy than due to change in SMBG (i.e., a threat to internal validity). Exclusion of those individuals who, on the basis of SMBG, advanced their pharmacologic therapies may have caused us to underestimate the potential benefit of such an intervention.

A unique strength of this study is its longitudinal design and duration of follow-up (4 years). The longest study included in the most recent systematic review by Welschen et al. (13) was <1 year, while the remainder of the studies were concluded within 6 months. Another strength of this study is the distinct new-user and ongoing-user design, which carefully accounts for the timing of SMBG initiation. The comprehensive data included in the Kaiser Permanente Northern California Diabetes Registry make it possible to adjust for important potential confounders, including diabetes self-care practices, medication adherence, and lifestyle behaviors, each of which may be independently associated with monitoring frequency and glycemia. We have shown previously that self-care and health behaviors (e.g., better refill adherence and lower rates of smoking) and appropriate annual screenings were more common in patients who adhered to the American Diabetes Association SMBG guidelines (7). Thus, self-monitoring could simply be a marker for more intensive disease management or better self-care, which more directly impacts glycemia. However, our models suggest an independent effect even after adjustments for diabetes medication adherence: number of daily insulin injections, appointment "no show" rate, performance of annual ophthalmology exams, and markers of severity (a hospitalization or emergency room visit during the baseline year). In fact, adjustment for these potential confounders resulted in only minimal changes in the point estimates for the effect of SMBG, suggesting a robust relationship. Finally, the study population is large, ethnically diverse, and socioeconomically and demographically representative of the surrounding geographical region (19–21).

These observational findings are consistent with a short-term benefit of initiating SMBG practice for all patients but a maintained benefit only for pharmacologically treated patients. As with all observational research, bias poses a potential threat to the validity of these findings. However, concerns should be lessened given that the effect size and direction observed in this study closely match those reported by the two most recent and comprehensive meta-analyses (13,14) of randomized controlled trials of SMBG. This large observational study complements extant experimental studies. Additionally, it examines something not previously examined: the impact of SMBG in new users versus ongoing users.

Current SMBG guidelines generally encompass only ongoing practice and recommend minimal (if any) monitoring for patients not treated pharmacologically and thus may have missed an important teaching opportunity by failing to make special recommendations for those who initiate SMBG. The benefit of SMBG may be further increased by better integrating SMBG practice into an overall program of health education (promoting patient-level behavioral modifications in response to SMBG readings) and therapeutic decision making (22–26). Research is needed to develop specific clinical guidelines for patients regarding optimal timing and frequency of SMBG initiation and practice maintenance and to help clinicians better integrate patient's SMBG records into the therapeutic decision-making process.

Evidence-based practice recommendations are rarely based on observational study findings, relying instead almost exclusively on randomized trials. Unfortunately, authors of the existing meta-analytic studies reported that few of the reviewed randomized studies were of high quality (i.e., design flaws, underpowered, or inadequate follow-up). The controversy surrounding this costly practice will not likely be resolved until a large-scale, well-designed randomized trial of SMBG adequately informs us about its effectiveness and cost-effectiveness. In the meantime, the similar finding of effect in the meta-analyses of existing randomized trials and this observational study is compelling enough evidence to warrant support

of SMBG for motivated patients who are appropriately educated in its use.

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A.J.K. had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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