Evidence of a Strong Association Between Frequency of Self-Monitoring of Blood Glucose and Hemoglobin A_{1c} Levels in T1D Exchange Clinic Registry Participants

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OBJECTIVE—Despite substantial evidence of the benefit of frequent self-monitoring of blood glucose (SMBG) in type 1 diabetes, certain insurers limit the number of test strips that they will provide. The large database of the T1D Exchange clinic registry provided an opportunity to evaluate the relationship between the number of SMBG measurements per day and HbA_{1c} levels across a wide age range of children and adults.

RESEARCH DESIGN AND METHODS—The analysis included 20,555 participants in the T1D Exchange clinic registry with type 1 diabetes ≥1 year and not using a continuous glucose monitor (11,641 younger than age 18 years and 8,914 18 years old or older). General linear models were used to assess the association between the number of SMBG measurements and HbA_{1c} levels after adjusting for potential confounding variables.

RESULTS—A higher number of SMBG measurements per day were associated with non-Hispanic white race, insurance coverage, higher household income, and use of an insulin pump for insulin delivery ($P < 0.001$ for each factor). After adjusting for these factors, a higher number of SMBG measurements per day was strongly associated with a lower HbA_{1c} level (adjusted $P < 0.001$), with the association being present in all age-groups and in both insulin pump and injection users.

CONCLUSIONS—There is a strong association between higher SMBG frequency and lower HbA_{1c} levels. It is important for insurers to consider that reducing restrictions on the number of test strips provided per month may lead to improved glycemic control for some patients with type 1 diabetes.

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The advent in the 1980s of meters for self-monitoring of blood glucose (SMBG) has had a substantial impact on the management of type 1 diabetes (1). Several studies have demonstrated a strong correlation between frequency of SMBG and glycemic control (2–5). However, acceptance of the value of frequent SMBG has not been universal and many insurers limit the number of test strips that they will provide to four to six strips per day. In the past year, the Washington State Healthcare Authority questioned whether sufficient evidence is available to justify unlimited coverage of SMBG test strips for patients with type 1 diabetes (6).

The large database of the T1D Exchange clinic registry provided an opportunity to evaluate the relationship between the number of SMBG measurements per day and HbA_{1c} across a wide age range of children and adults, and to evaluate factors associated with the number of SMBG measurements per day.

RESEARCH DESIGN AND METHODS

The T1D Exchange Clinic Network includes 67 pediatric and adult endocrinology practices based in the United States. A registry of individuals with type 1 diabetes commenced enrollment in September 2010 (7). Each clinic received approval from an Institutional Review Board. Informed consent was obtained according to Institutional Review Board requirements from adult participants and parents/guardians of minors; assent from minors was obtained as required. Data were collected for the registry's central database from the participant's medical record and by having the participant or parent complete a comprehensive questionnaire, as previously described (7).

This report includes data of 20,555 participants enrolled through 1 August 2012 who met the following criteria: type 1 diabetes for at least 1 year; not pregnant; not using real-time continuous glucose monitoring; and availability of an HbA_{1c} measurement between 6 months before and 1 month after enrollment.

Information on SMBG measurements per day was obtained on a questionnaire completed by participants 18 years old or older, parent or guardian of participants

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younger than 13 years old, and by either the participant or the parent/guardian for participants 13 years old to younger than 18 years old, with the following question: Approximately how many times per day are you (is your child) checking your (his/her) blood glucose with a blood glucose meter? For a subset of the participants, the number of SMBG measurements per day was available from a meter download located in the clinic chart. HbA_{1c} levels, mainly measured with point-of-care devices (74% DCA, 4% from another point-of-care device, 19% from a laboratory, 3% by an unrecorded method), were obtained from the clinic chart. When more than one HbA_{1c} value was available between 6 months before and 1 month after enrollment, the value obtained closest to the enrollment date was used.

Statistical methods

Frequency of SMBG measurements per day was categorized for illustration purposes into five groupings: 0–2 times per day; 3–4 times per day; 5–6 times per day; 7–9 times per day; and ≥10 times per day. Analyses stratified by age used the following age-groups: 1 to younger than 6 years old; 6 to younger than 13 years old; 13 to younger than 18 years old; 18 to younger than 26 years old; 26 to younger than 50 years old; 50 to younger than 65 years old; and 65 years or older.

Demographic and clinical factors associated with the number of SMBG measurements per day were assessed in linear regression models adjusted for age-group. Factors with a significance level ≤0.05 from individual factor models adjusted for age were included in the initial multivariate linear regression model and were removed from the final model if adjusted $P \geq 0.01$. General linear models were used to assess the association between the number of SMBG measurements per day and HbA_{1c} in each age-group after adjusting for potential confounding variables. Additional analyses assessing the association between frequency of SMBG per day and HbA_{1c} <7.0% were performed using logistic regression. Covariates adjusted for in the multivariate models included the following: sex; race/ethnicity; insulin delivery method; insurance status (private, other, none); and household income (participants who were living alone but still supported by parents were asked to estimate their family income). The effect of the

Table 1—*Descriptive characteristics of the cohort*

Characteristics	Total *N* = 20,555
Age (years)	
1 to <6	819 (4)
6 to <13	5,445 (26)
13 to <18	5,377 (26)
18 to <26	3,307 (16)
26 to <50	3,351 (16)
50 to <65	1,646 (8)
≥65	610 (3)
Female*	10,266 (50)
Race/ethnicity	
White non-Hispanic	16,919 (82)
Black non-Hispanic	1,043 (5)
Hispanic or Latino	1,673 (8)
Asian	243 (1)
More than one race	567 (3)
Other	110 (<1)
Diabetes duration (years)	
1 to <5	6,853 (33)
5 to <10	5,553 (27)
10 to <20	4,614 (22)
20 to <30	1,632 (8)
30 to <40	1,060 (5)
40 to <50	631 (3)
≥50	212 (1)
Annual household income†	
<$25,000	1,857 (12)
$25,000 to <$35,000	1,278 (8)
$35,000 to <$50,000	1,759 (12)
$50,000 to <$75,000	2,674 (18)
$75,000 to <$100,000	2,648 (17)
≥$100,000	4,988 (33)
Education level†‡	
Less than a high school diploma	867 (4)
High school diploma/GED	7,278 (37)
Associate's degree	2,134 (11)
Bachelor's degree	5,426 (28)
Master's degree	2,826 (14)
Professional or doctorate degree	1,147 (6)
Insurance status†	
Private	13,957 (74)
Other	4,563 (24)
No insurance	236 (1)
Family history of type 1 diabetes§	3,294 (16)
Pump use	10,783 (52)
HbA_{1c}¶ (mean ± SD)	8.3 ± 1.5
Group	
<6.5%	1,383 (7)
6.5 to <7.5%	4,864 (24)
7.5 to <8.5%	6,661 (32)
8.5 to <9.5%	4,095 (20)
9.5 to <10.5%	1,821 (9)
≥10.5%	1,731 (8)

Data are presented as *n* (%) unless otherwise stated. *Total of 3 transgender individuals in cohort. †877 participants are missing education level; 5,351 participants are missing household income; 1,799 participants are missing insurance status. ‡For participants younger than 18 years of age, education reported is highest parent education. §Indicates those with a first-degree family member with type 1 diabetes including parent, sibling, half-sibling, or child. ¶Most recent HbA_{1c} recorded, within six months prior or 30 days after enrollment visit.

interaction between SMBG and household income on HbA_{1c} levels was evaluated. Separate analyses for pump and injection users also were performed. The Van der Waerden normal scores of the frequency of SMBG per day were used in the models as a result of the skewed distribution of the data.

Self-reported SMBG measurements per day were used in the analyses. Analytic results were similar when data from clinic meter downloads were used from the subset of participants for whom downloaded data were available (data not shown). Analyses were conducted using SAS software version 9.3 (SAS Institute, Cary, NC). All *P* values are two-sided. In view of the large sample size and multiple comparisons, only $P < 0.01$ was considered statistically significant.

RESULTS—The cohort included 20,555 participants: 11,641 younger than 18 years old and 8,914 who were 18 years old or older. Characteristics of the cohort are shown in Table 1. Mean number of SMBG measurements per day was lower among participants 13 to younger than 26 years old (4.9 ± 2.2) than among younger (6.7 ± 2.3) and older participants (5.3 ± 2.5; $P < 0.001$; Table 2). Among 10,384 participants for whom a meter download was available, self-reported SMBG measurements averaged 5.7 ± 2.5 per day compared with the clinic assessment from meter downloads of 4.8 ± 2.8 per day (Pearson correlation = 0.65).

In a multivariate model adjusted for age-group, participants who reported a higher number of SMBG measurements per day were more likely to be non-Hispanic white, have private insurance, have higher household income, and use an insulin pump for insulin delivery (Supplementary Table 1; $P < 0.001$ for each factor).

A higher number of SMBG measurements per day was strongly associated with a lower HbA_{1c} in all age-groups (Fig. 1*A* adjusted means and Table 3 unadjusted means; $P = 0.002$ for 1 to younger than 6 years and $P < 0.001$ for all other age-groups adjusted for potential demographic and socioeconomic confounders) despite the differences in HbA_{1c} between age-groups. The association was present in both insulin pump and injection users (Fig. 1*B* and *C* adjusted means; $P < 0.001$) and across annual household income categories (Supplementary Table 2). There was no significant interaction between SMBG and household income on HbA_{1c} levels for any age-group. The association between SMBG and HbA_{1c} levels appeared to level-off at approximately 10 SMBG measurements per day, with adjusted mean HbA_{1c} being similar in participants testing 10–12 times as in those testing ≥13 times per day, 7.8 and 7.7%, respectively. Results were similar when evaluating the association between SMBG measurements per day and HbA_{1c} <7.0% (Table 3).

CONCLUSIONS—SMBG is the cornerstone of modern-day therapy for people with type 1 diabetes. Early studies clearly demonstrated that capillary glucose information was valuable for making appropriate decisions regarding insulin dosing and therefore for improvement of diabetes control (1). The intensive therapy group in the Diabetes Control and Complications Trial (DCCT) was asked, as part of their therapy, to perform SMBG before meals and at bedtime as well as overnight once per week (8). Whereas this was not a randomized trial for SMBG, it is, to our knowledge, the last study comparing a treatment regimen including glucose testing four times daily against little to no testing (9). Today, it would be impossible to perform a randomized trial in type 1 diabetes comparing SMBG with no SMBG given our understanding of the importance of glucose control in preventing the complications of type 1 diabetes (10). The best alternative is to use a large database, such as the T1D Exchange clinic registry, to analyze associations between frequency of SMBG and HbA_{1c} and to provide the evidence desired by payers, such as the State of Washington, to support the cost-effectiveness of providing coverage for test strips.

Consistent with other smaller studies in the United States and the large Germany and Austria DPV registry (2–5), we clearly show that for all ages and with both major forms of insulin delivery (pump and multiple injections), increased frequency of SMBG is associated with lower mean HbA_{1c}. This is true even after adjusting for demographic and socioeconomic confounders. Our study observed a similar association between SMBG and HbA_{1c} across levels of household income, which has not been previously reported. Nevertheless, because diabetes management in those with more frequent SMBG likely differs from those with less frequent SMBG, frequent SMBG by itself is not the sole explanation for the association with lower HbA_{1c}, but it almost certainly is an important contributor. Of course, for frequent SMBG to influence HbA_{1c}, the blood glucose information must be

Table 2—*SMBG by age-group*

	Total	1 to <6 years old	6 to <13 years old	13 to <18 years old	18 to <26 years old	26 to <50 years old	50 to <65 years old	≥65 years old
Self-reported SMBG	*N* = 20,555	*n* = 819	*n* = 5,445	*n* = 5,377	*n* = 3,307	*n* = 3,351	*n* = 1,646	*n* = 610
Mean ± SD	5.5 ± 2.5	7.1 ± 2.7	6.6 ± 2.2	5.2 ± 2.1	4.4 ± 2.3	5.2 ± 2.6	5.5 ± 2.5	5.6 ± 2.2
Group (%)								
0 times/day*	<1	0	<1	<1	2	1	<1	<1
1–2 times/day	6	<1	<1	5	15	11	7	3
3–4 times/day	31	15	15	38	45	36	34	33
5–6 times/day	34	34	40	36	24	29	32	36
7–9 times/day	20	32	32	15	10	16	20	22
≥10 times/day	8	18	13	5	4	8	8	6

*A total of 127 (<1%) participants reported 0 SMBG checks per day.

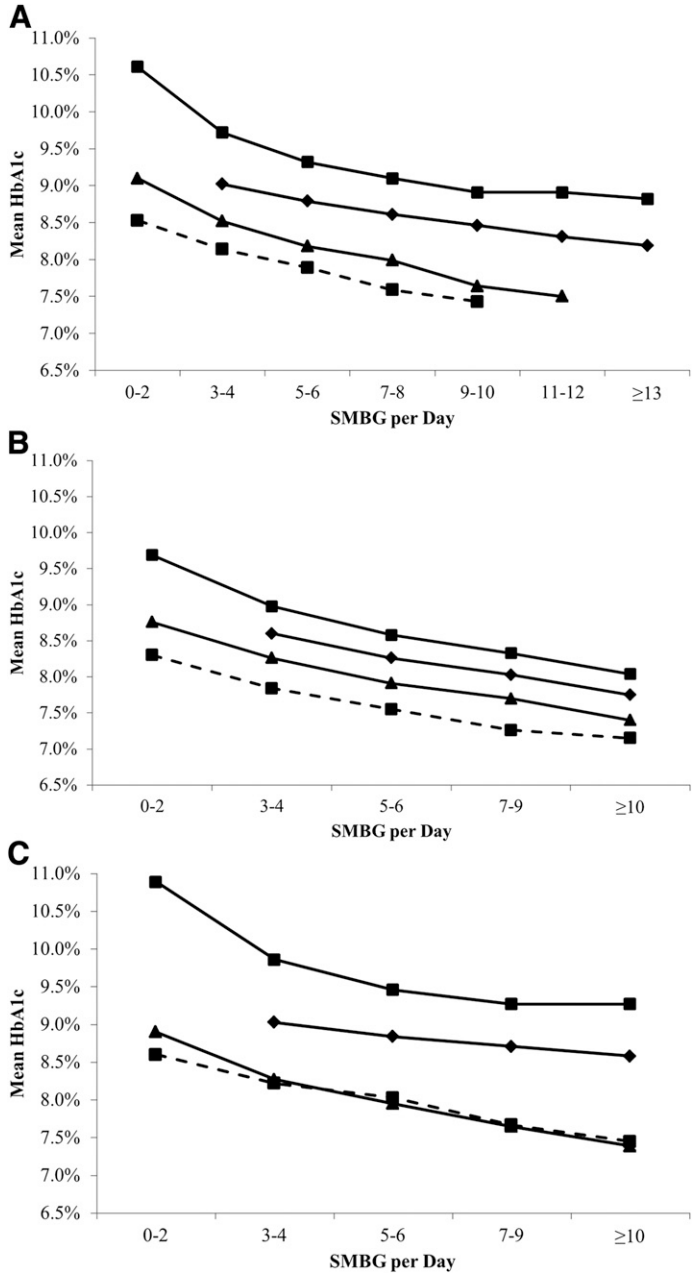

Figure 1—A: *Association between frequency of SMBG per day and HbA$_{1c}$. Solid black line and diamonds represent those 1 to younger than 13 years old. Solid black line and squares represent those 13 to younger than 26 years old. Solid black line and triangle represent those 26 to younger than 50 years old. Dotted black line and squares represent those 50 years old and older. HbA$_{1c}$ means with numbers <30 are not included here. Means are adjusted for insulin delivery method, sex, race/ethnicity, insurance status, and household income (treated as ordinal variables with a missing indicator).* B: *Association between frequency of SMBG per day and HbA$_{1c}$ among insulin pump users. Solid black line and diamonds indicate those 1 to younger than 13 years old. Solid black line and squares indicate those 13 to younger than 26 years old. Solid black line and triangle indicate those 26 to younger than 50 years old. Dotted black line and squares indicate those 50 years old or older. HbA$_{1c}$ means with numbers <30 are not included here. Means are adjusted for sex, race/ethnicity, insurance status, and household income (treated as ordinal variables with a missing indicator).* C: *Association between frequency of SMBG per day and HbA$_{1c}$ among injection users. Solid black line and diamonds represent those 1 to younger than 13 years old. Solid black line and squares represent those 13 to younger than 26 years old. Solid black line and triangle represent those 26 to younger than 50 years old. Dotted black line and squares represent those 50 years old and older. HbA$_{1c}$ means with numbers <30 are not included here. Means are adjusted for sex, race/ethnicity, insurance status, and household income (treated as ordinal variables with a missing indicator).*

used effectively in diabetes management including insulin dosing and meal and snack composition; the act of performing SMBG alone is not directly related to improvements in HbA$_{1c}$. Thus, frequent SMBG is a behavior associated with good glycemic control but in itself does not have a direct causal relationship with glycemic control.

The 2012 American Diabetes Association clinical guidelines recommend SMBG at least three times per day for patients using insulin pump therapy or multiple insulin injections (11). In this analysis of individuals with type 1 diabetes, participants testing 3–4 times per day had a mean HbA$_{1c}$ of 8.6% compared with an HbA$_{1c}$ of 7.6% among those testing ≥10 times per day. Because prospective trials testing how the frequency of SMBG impacting HbA$_{1c}$ are not likely, we are hopeful that future guidelines better-reflect our current understanding of the relationship of SMBG and HbA$_{1c}$.

Our data suggest a slight over-reporting of the frequency of SMBG compared with meter downloads, which could, in part, be explained by incomplete data for patients who use more than one meter and difficulty in interpreting downloaded meter data when the date of the meter is incorrect. However, these issues are not germane to our results, because the same association between frequency of SMBG and HbA$_{1c}$ is seen when the meter download glucose values were used in the analyses (data not shown).

In conclusion, there is a strong association between a higher SMBG frequency and lower HbA$_{1c}$ across the entire age range in our large population of patients with type 1 diabetes, with similar findings in pump users and injection users. The observational nature of the study precludes a definitive statement regarding causality. Nevertheless, it is important for insurers to consider that reducing restrictions on the number of test strips provided per month may lead to improved glycemic control for some patients with type 1 diabetes, resulting in a potential cost-savings from both short-term and long-term complications.

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The nonprofit employer of R.W.B. has received consultant payments on his behalf

Table 3—*Association between frequency of SMBG per day and HbA_{1c} according to age*

	SMBG 0–2‡ times per day		SMBG 3–4 times per day		SMBG 5–6 times per day		SMBG 7–9 times per day		SMBG ≥10 times per day		*P*
Mean HbA_{1c}*											
	n	HbA_{1c} Mean, %	*n*	HbA_{1c} Mean, %	*n*	HbA_{1c} Mean, %	*n*	HbA_{1c} Mean, %	*n*	HbA_{1c} Mean, %	
Age 1 to <6 years	3	–	124	8.5	281	8.4	260	8.1	151	7.8	0.002
Age 6 to <13 years	22	–	840	8.7	2,172	8.4	1,725	8.1	686	7.8	<0.001
Age 13 to <18 years	302	10.3	2,056	9.0	1,929	8.5	820	8.2	270	8.0	<0.001
Age 18 to <26 years	564	9.6	1,489	8.6	795	8.0	320	7.7	139	7.5	<0.001
Age 26 to <50 years	393	8.6	1,190	8.0	965	7.6	551	7.4	252	7.1	<0.001
Age 50 to <65 years	112	8.4	553	8.0	526	7.7	331	7.3	124	7.2	<0.001
Age ≥65 years	21	–	201	7.6	219	7.5	135	7.2	34	6.9	<0.001
HbA_{1c} < 7.0%†											
	n	% with HbA_{1c} <7.0%	*n*	% with HbA_{1c} <7.0%	*n*	% with HbA_{1c} <7.0%	*n*	% with HbA_{1c} <7.0%	*n*	% with HbA_{1c} <7.0%	
Age 1 to <6 years	3	–	124	6	281	6	260	11	151	17	0.06
Age 6 to <13 years	22	–	840	9	2,172	8	1,725	11	686	17	<0.001
Age 13 to <18 years	302	4	2,056	9	1,929	11	820	14	270	18	<0.001
Age 18 to <26 years	564	8	1,489	13	795	21	320	26	139	35	<0.001
Age 26 to < 50 years	393	13	1,190	21	965	30	551	39	252	50	<0.001
Age 50 to <65 years	112	15	553	17	526	25	331	34	124	44	<0.001
Age ≥65 years	21	–	201	31	219	27	135	46	34	53	0.01

*Means are unadjusted. *P* values are from general linear regression models adjusted for insulin delivery method, sex, race/ethnicity, insurance status, and household income (treated as ordinal variables with a missing indicator). †Percentages are unadjusted. *P* values are from logistic regression models adjusted for insulin delivery method, sex, race-ethnicity, insurance status, and household income (treated as ordinal variables with a missing indicator). ‡The median HbA_{1c} for the 127 participants who reported 0 SMBG checks per day was 9.6

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