Journal of Diabetes Science and Technology
Volume 6, Issue 3, May 2012

ORIGINAL ARTICLE

Association between Sitagliptin Adherence and Self-Monitoring of Blood Glucose

Somesh Nigam, Ph.D.,[1] Naunihal S. Virdi, M.D.,[2] Mehmet Daskiran, Ph.D.,[1] Chris M. Kozma, Ph.D.,[3] Andrew Paris, M.B.A.,[3] and William M. Dickson, Ph.D.[3]

Abstract

Background:

We evaluated the association between self-monitoring of blood glucose (SMBG) use and sitagliptin or sitagliptin/metformin (SSMT) adherence. SSMT was chosen as these medications have little risk of hypoglycemia and are believed to not require SMBG data for titration.

Methods:

This was an observational study using data extracted from a large United States insurance claims database (i3 InVision™ Data Mart, Ingenix, Inc.). Data were extracted on noninsulin-using patients initiating SSMT for each 12-month period pre- and post-SSMT initiation. Logistic regression was used to assess the relationship between SMBG use and the likelihood of being medication adherent (defined as a medication possession ratio of ≥75%) while controlling for covariates.

Results:

This analysis included 7,306 patients (57.6% male; mean age 54.2 years). Mean pre-SSMT hemoglobin A1c (HbA1c) was 8.0%. In the post-SSMT initiation period, 58% of patients were adherent with SSMT. Older age, male gender, prior use of oral diabetes medication, and lower HbA1c were associated with improved SSMT adherence. SMBG use was associated with improved adherence [odds ratio (OR) ranged from 1.198 to 1.338; $p < .05$] compared with patients with no SMBG use pre- or post-SSMT initiation. For patients who began SMBG after starting SSMT, greater SMBG use was associated with better adherence (OR 1.449 for higher vs 1.246 for lower strip use; $p < .05$).

Conclusions:

This study demonstrated that SMBG is associated with improved SSMT adherence. This relationship is strengthened with greater SMBG use.

J Diabetes Sci Technol 2012;6(3):555-562

Author Affiliations: [1]Johnson & Johnson, New Brunswick, New Jersey; [2]LifeScan, Inc., Milpitas, California; and [3]CK Consulting, Saint Helena Island, South Carolina

Abbreviations: (CI) confidence interval, (HbA1c) hemoglobin A1c, (HCP) health care provider, (MPR) medication possession ratio, (OR) odds ratio, (SE) standard error, (SMBG) self-monitoring of blood glucose, (SD) standard deviation, (SSMT) sitagliptin or sitagliptin/metformin, (T2DM) type 2 diabetes mellitus

Keywords: diabetes mellitus, medication adherence, self-monitoring of blood glucose, sitagliptin, type 2 diabetes mellitus

Corresponding Author: Naunihal S. Virdi, M.D., LifeScan, Inc., 1000 Gibraltar Drive, Milpitas, CA 95035; email address nvirdi@its.jnj.com

Introduction

Glycemic control is an important aspect of disease management for patients with type 2 diabetes mellitus (T2DM). Studies have shown that better glycemic control is associated with lower rates of morbidity from microvascular complications.[1–3]

Numerous factors contribute to better glycemic control, including behavioral factors such as diet, exercise, and medication compliance. For patients with T2DM taking sulfonylurea or metformin, medication-adherent patients achieved a hemoglobin A1c (HbA1c) of ≤7% more often than nonadherent patients (82% vs 72% for sulfonylurea and 77% vs 62% for metformin; $p < .001$).[4] Sokol and colleagues[5] demonstrated that medication adherence (≥80% vs 60–79% medication supply over 12 months) was associated with a significantly lower disease-related risk of hospitalization (13% vs 20%, respectively; $p < .05$) and overall health care costs ($4570 vs $6291, respectively; p value not provided) in diabetes patients over the first 12 months of the study. Given the health and economic benefits associated with medication adherence, payers may be interested in strategies that promote medication adherence among persons with diabetes.

Use of medical technologies may help patients achieve better adherence. Some studies indicating that self-monitoring of blood glucose (SMBG) is associated with improved HbA1c observed that patients using SMBG exhibited better behaviors, including achievement of nutritional and exercise goals and better medication adherence.[6–9] Similarly, in patients with hypertension, high-intensity intervention that includes self-monitoring of blood pressure is reported to improve medication adherence (61.3% at baseline vs 87.7% at final visit; $p = .004$).[10]

In order to further explore the relationship between SMBG and medication adherence, this study evaluated the association between SMBG use and sitagliptin or sitagliptin/metformin (SSMT) adherence during the first 12 months after initiation. These medications have little risk of hypoglycemia[11] and are believed to not require SMBG data for titration; thus, they were chosen to minimize factors that could confound the relationship between SMBG use and medication adherence. Additionally, this study focused only on patients who had recently (within 12 months) initiated SSMT to ensure greater within-group homogeneity.

Methods

Data Sources and Patient Inclusion Criteria

Data on patients who began their first SSMT prescription between October 1, 2006, and September 30, 2008, were extracted from a large (approximately 27 million commercially insured persons) United States administrative claims database (i3 InVision™ Data Mart, Ingenix, Inc., Eden Prairie, MN). The database provided information that supported the requirements of this analysis, including enrollment dates; patient demographics (age, gender, geographic location); medical claims (place of service, diagnosis, procedures); and pharmacy claims (quantity, strength, number of days' supply of drug). No identifiable health information was extracted from the database during this study, so according to the Health Insurance Portability and Accountability Act of 1996, no institutional review board approval or waiver of authorization was required.[12]

The date of the first prescription fill was considered the index date. Patients were included if they had at least two SSMT prescriptions on different dates in the postindex period; had continuous eligibility for 12 months before and after the index date; had no insulin prescription during the 12-month pre- and postindex periods; and had at least one HbA1c laboratory value reported in the 12-month preindex period. Identification of patients with T2DM was based on prescription claims; because no patients included in the analysis were treated with insulin, they were all considered to have T2DM.

Study Design

A medication possession ratio (MPR) based on SSMT use in the postindex period was calculated for each patient as the sum of days' supply for each SSMT prescription claim in the postindex period expressed as a percentage of 365 days. Patients were considered medication adherent if they achieved an MPR of ≥75%. While an MPR of ≥80% is often used, the MPR threshold of ≥75% was chosen for this analysis as it divides the patient population roughly in half.[13,14]

Patients were divided into four groups based on the presence of SMBG in the pre- and postindex period: no test strip claims in the pre- or postindex period (PRE/NO, POST/NO); no test strip claims in the preindex period but test strip claims in the postindex period (PRE/NO,

POST/YES); test strip claims in the preindex period but no test strip claims in the postindex period (PRE/YES, POST/NO); and test strip claims in the pre-and postindex period (PRE/YES, POST/YES). The group PRE/NO, POST/YES was further subdivided as below or above mean usage (based on mean testing frequency for all patients) based on the average number of test strips dispensed to this group. The mean for all patients was chosen as it divided the population in the group PRE/NO, POST/YES roughly in half.

Covariates included in the analysis were patient demographics (age and gender), presence or absence of another oral diabetes medication in the preindex period, and mean HbA1c for all values reported in the preindex period.

Analysis

Logistic regression was used to evaluate the relationship between an MPR of ≥75% (MPR75) and the four groups based on SMBG presence. The model tested the hypothesis that SMBG presence or absence in the pre- and/or postindex period influences MPR75. A nondirectional hypothesis permitted the identification of statistical differences in any direction.

Simulations

Using the parameter estimates obtained in the logistic regression analysis described earlier, simulations were performed to obtain the predicted proportion of patients achieving an MPR of ≥75% given the conditions for each of the scenarios based on SMBG use. The scenarios are as follows: (a) no patients used SMBG in the pre- or postindex period; (b) all patients were non-SMBG users in the preindex period and became SMBG users in the postindex period; (c) all patients used SMBG in the pre- and postindex period; (d) all patients used SMBG in the preindex period and discontinued using SSMT in the postindex period; and (e) all patients who did not use SMBG in the preindex period began using SMBG in the postindex period. In all scenarios, patient age, gender, presence or absence of another diabetes medication, and prior HbA1c were distributed as they existed in the data.

Results

Patients

The study population included 7,306 patients (**Table 1**). Patients had a mean age of 54.2 years and 57.6% were male. Most patients had received prior oral diabetes medication (89.6%). A slightly higher percentage of patients had claims for test strips in the pre- and postindex periods (37.8%) compared with patients who had no claims for test strips (31.9%). The overall mean preindex HbA1c was 8.0%. In this population, 58.0% of patients were considered adherent to sitagliptin therapy in the postindex year (**Table 1**). The mean number of test strips available for all patients was 195.8 test strips [standard deviation (SD) 306.1] or 0.54 strips per day. For patients who used SMBG postindex, the mean availability postindex was 351.8 test strips (SD 336.8) or 0.96 strips per day. The average test strip availability for patients using SMBG only postindex was 240.4 strips (SD 240.4), and for patients using SMBG both pre- and postindex, the average was 404.4 strips (SD 362.0).

Table 1.
Patient Characteristics (N = 7306)[a]

Parameter	Study population
Age (years)	
Mean ± SE[b]	54.2 ± 0.10
Median (range)	55.0 (12.0–85.0)
Sex	
Female	3101 (42.4)
Male	4205 (57.6)
Prior oral diabetes medication	
Yes	6546 (89.6)
No	760 (10.4)
Strip use	
PRE/NO, POST/NO	2333 (31.9)
PRE/NO, POST/YES	1305 (17.9)
PRE/YES, POST/NO	906 (12.4)
PRE/YES, POST/YES	2762 (37.8)
≥75% adherent	
Yes	4241 (58.0)
No	3065 (42.0)
HbA1c preindex period value	
Mean ± SE	8.0 ± 0.02
Median (range)	7.5 (4.4–17.9)

[a] Values are number (percentage) unless otherwise indicated.
[b] SE = standard error.

When patients were grouped based on SMBG use in the pre- and postindex periods, there were significant differences in age, prior oral diabetes medication, medication adherence, and preindex HbA1c between groups (**Table 2**). Patients with SMBG available in the preindex period were more likely to have prior oral diabetes medication (SMBG preindex period only 94.4% and SMBG pre- and postindex period 94.2% vs SMBG postindex period only 87.1% and SMBG never 81.0%). Patients with SMBG available in the postindex period had higher medication adherence (SMBG pre- and postindex period 60.3% and SMBG postindex period only 61.3% vs SMBG preindex period only 51.4% and SMBG

Table 2.
Patient Characteristics by SMBG Group[a,b]

Parameter	SMBG group			
	PRE/NO, POST/NO (*n* = 2333)	PRE/NO, POST/YES (*n* = 1305)	PRE/YES, POST/NO (*n* = 906)	PRE/YES, POST/YES (*n* = 2762)
Age (years)				
Mean ± SE	54.3 ± 0.17[c]	54.0 ± 0.24[c]	52.8 ± 0.30[d,e,f]	54.5 ± 0.17[c]
Median (range)	55.0 (15.0–84.0)	55.0 (25.0–81.0)	55.0 (17.0–74.0)	56.0 (12.0–85.0)
Sex				
Female	896 (38.4)[f]	538 (41.2)[f]	377 (41.6)[f]	1290 (46.7)[c,d,e]
Male	1437 (61.6)	767 (58.8)	529 (58.4)	1472 (53.3)
Prior oral diabetes medication				
Yes	2031 (87.1)[c,e,f]	1057 (81.0)[c,d,f]	855 (94.4)[d,e]	2603 (94.2)[d,e]
No	302 (12.9)	248 (19.0)	51 (5.6)	159 (5.8)
≥75% adherent				
Yes	1311 (56.2)[c,e,f]	800 (61.3)[c,d]	466 (51.4)[d,e,f]	1664 (60.3)[c,d]
No	1022 (43.8)	505 (38.7)	440 (48.6)	1098 (39.7)
HbA1c preindex period value[g]				
Mean ± SE	7.4 ± 0.03[c,e]	8.1 ± 0.05[d,f]	8.0 ± 0.06[d,f]	7.4 ± 0.03[c,e]
Median (range)	7.4 (4.4–16.1)	7.6 (5.0–16.0)	7.6 (5.0–14.6)	7.4 (5.1–17.9)

[a] Values are number (percentage) unless otherwise indicated.
[b] Continuous variables were tested in an analysis of variance with follow-up *t* test. Categorical variables were tested with pair-wise chi-square tests.
[c] $p < .05$ vs PRE/YES, POST/NO.
[d] $p < .05$ vs PRE/NO, POST/NO.
[e] $p < .05$ vs PRE/NO, POST/YES.
[f] $p < .05$ vs PRE/YES, POST/YES.
[g] Comparison between the groups may not be appropriate given that HbA1c values were taken at various times during the 1-year preindex period.

never 56.2%). Patients for whom SMBG use changed between the pre- and postindex periods (PRE/NO, POST/YES and PRE/YES, POST/NO) had higher preindex HbA1c levels than patients with no change in SMBG use (PRE/NO, POST/NO and PRE/YES, POST/YES) (8.0–8.1 vs 7.4%).

Logistic Regression Results

Results from the primary logistic regression analysis are presented in **Figure 1**. The Hosmer–Lemeshow statistic indicates an acceptable model fit ($p = .7900$). Older age, male gender, prior use of oral diabetes medication, and lower preindex (mean) HbA1c were associated with improved SSMT adherence. Compared with patients who had no claims for SMBG, having SMBG test strips available was associated with improved adherence [odds ratio (OR) 1.198, 95% confidence interval (CI) 1.068–1.344 for patients continuing to use SMBG (PRE/YES, POST/YES), and 1.338 (95% CI 1.161–1.543) for patients who did not use SMBG in the preindex period (PRE/NO, POST/YES)]. All variables in the model were significant ($p < .05$).

Among patients initiating SMBG after SSMT, greater than average SMBG use was associated with higher odds of being adherent compared with less than average use. The odds ratio for SSMT adherence was 1.449 (95% CI 1.202–1.747) for strip use above the mean of 195.8 strips per year ($n = 629$, mean 398.3 strips per year, SD 266.5) versus 1.246 (95% CI 1.042–1.489) for strip use below the mean ($n = 627$, mean 93.5 strips per year, SD 25.7) ($p < .05$).

Simulations

Simulations were performed using the analysis results shown earlier. As reported earlier, the frequency of

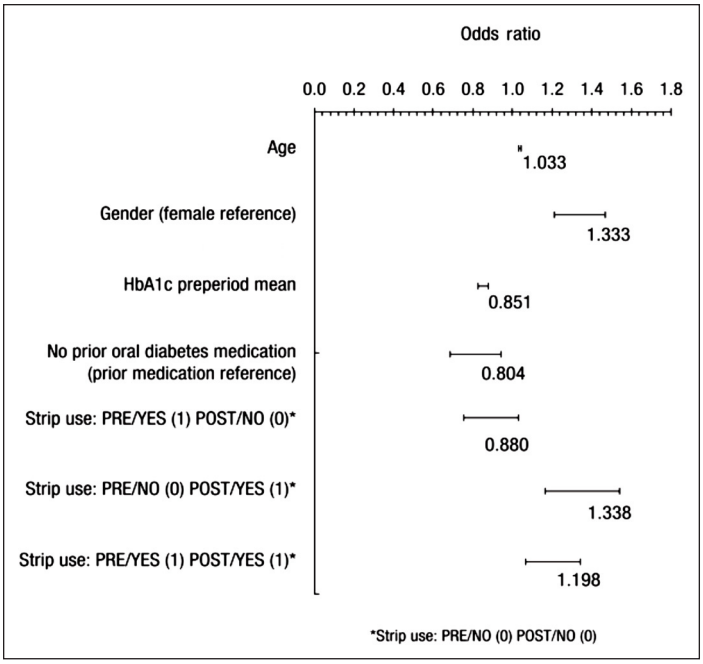

Figure 1. Logistic model results: ORs with 95% CIs are shown. Probabilities modeled were MPR <75% and MPR ≥75%. Overall model test was likelihood ratio of <.0001.

adherence to SSMT in the 1-year postindex period was 58%. The simulations indicated the probability that a patient would be ≥75% adherent ranged from 52.63% (PRE/YES, POST/NO) to 62.38% (PRE/NO, POST/YES). **Figure 2** summarizes the probability of being ≥75% adherent under various assumptions.

Discussion

This study demonstrated that noninsulin-using diabetes patients beginning SSMT therapy who performed SMBG were more likely to be medication adherent than those who did not perform SMBG. This association was strengthened by more frequent SMBG use. Other factors that influenced adherence included older age, male gender, prior use of oral diabetes medication, and lower HbA1c prior to SSMT initiation.

Results from the simulation, which was performed to help illustrate the benefits of SMBG use in the real world, indicate that the greatest benefit of SMBG in terms of medication adherence is observed soon after

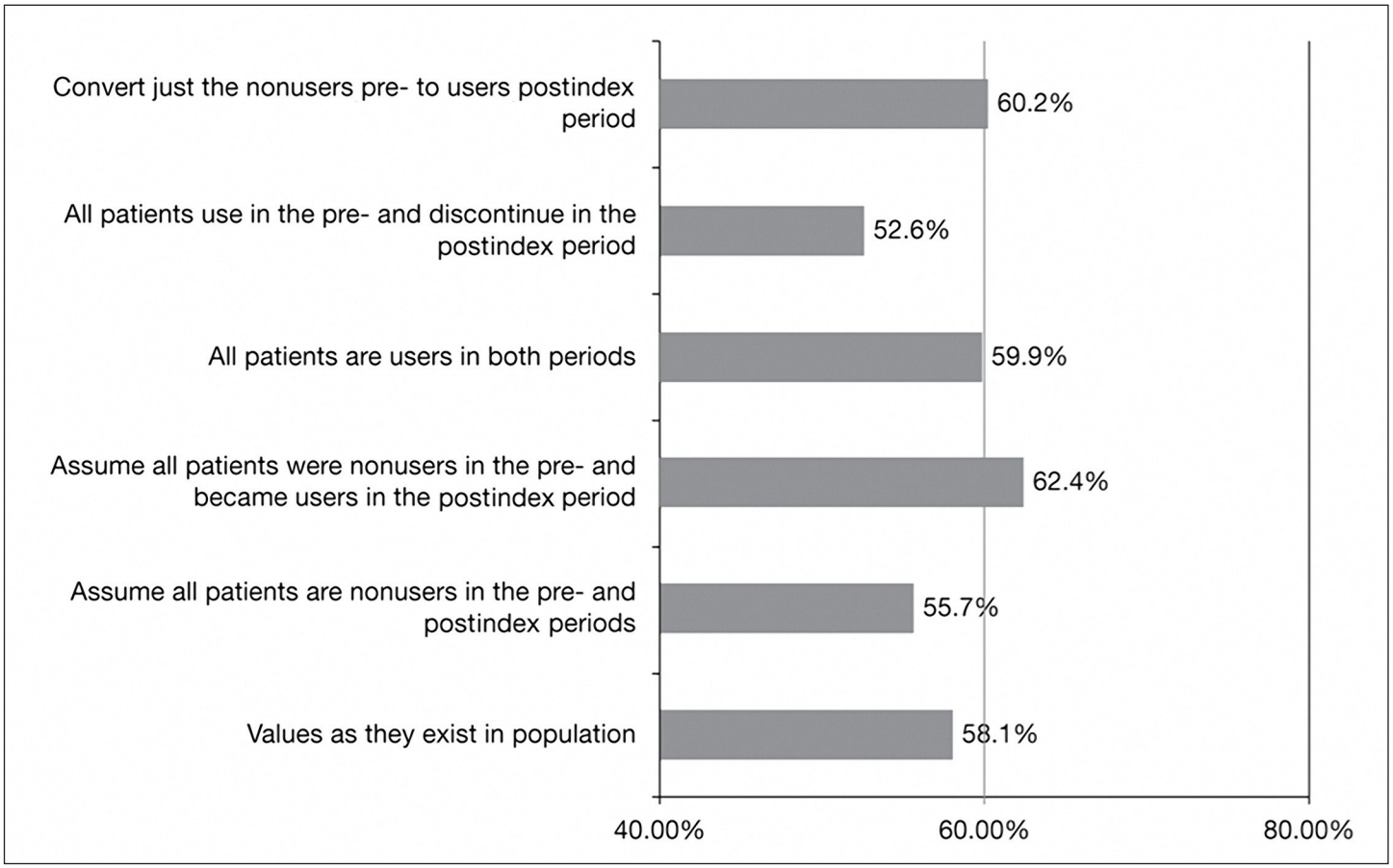

Figure 2. Probability of being ≥75% compliant under various assumptions (original model). Probabilities were derived by applying model weights to the original sample and varying their responses under various assumptions. Note: Pair-wise comparison between scenarios "All patients are users in both periods" and "Convert just the nonusers pre- to users postindex period" was significant at $p = .0458$. All other pair-wise comparisons between the probabilities were significantly different at $p < .0001$.

initiation (62% in patients who convert to SMBG use) and remains beneficial with continued use (60% in patients who continue SMBG use vs 53–56% in patients who discontinue or never use SMBG).

As SMBG is not a therapeutic intervention, patients and health care providers (HCPs) must use the information it provides to guide management decisions in order for SMBG to have a clinical impact. As management of diabetes includes multiple factors (e.g., nutrition, exercise), medication adherence would be expected to be only one part of an overall strategy for managing diabetes that might be affected by SMBG use.

Despite the importance of therapeutic adherence in chronic disease management, medication compliance is generally relatively poor. An earlier study used claims data (Thomson Reuters MarketScan® Research) from 700,000 patients from 2001 to 2004 to determine medication adherence rates during the first year of therapy for three common chronic conditions.[15] The proportion achieving ≥80% adherence was 72.3%, 65.4%, and 54.6% for hypertension, T2DM, and hypercholesterolemia medications, respectively. Consistent with the current study, increasing age, male gender, and previous experience with taking drugs were associated with higher levels of adherence for T2DM medications. In the current study, SMBG presence was also associated with improved medication adherence. Investigators in the ROSSO study (Retrolective Study Self-Monitoring of Blood Glucose and Outcome in Patients with Type 2 Diabetes) observed similar medication behaviors associated with SMBG use: a higher proportion of SMBG users received medication, there were more changes to diabetes therapy among SMBG users, and SMBG users were more likely to begin insulin therapy.[8]

Several studies have reported that numerous factors can influence medication adherence, including drug cost, age, demographics, additional comorbidities, dosing schedule, depression, alcohol abuse, medication side-effect profiles, and patient–physician relationship.[15–21] The complexity of a regimen can also influence adherence. For example, in elderly patients with T2DM, adherence to sulfonylureas (measured by electronic monitoring) is 94% for once-daily regimens and 57% for two- or three-times-daily regimens.[22]

Earlier studies have demonstrated associations between medication adherence with diabetes therapy and improved outcomes. Lawrence and colleagues[4] observed a correlation between average MPR and HbA1c for sulfonylureas and metformin. A retrospective review of the Kaiser Permanente of Colorado Diabetes Registry found that patients who were nonadherent to medications (MPR <80%) had higher rates of all-cause hospitalization (OR 1.58) and all-cause mortality (OR 1.81).[23] Poor adherence to diabetes therapy, if unrecognized, may be mistaken for therapeutic ineffectiveness and result in unnecessary medication intensification (increased dosage only or additional medications), which can lead to adverse consequences such as hypoglycemia.

Studies evaluating the impact of SMBG use on glycemic outcomes in noninsulin-treated patients with T2DM have been mixed. Studies, which could not demonstrate value in SMBG, generally treated SMBG as an intervention rather than a tool to adjust treatment. SMBG use has been linked to improved HbA1c, particularly when used in conjunction with education and structured testing to help patients and HCP utilize glucose data to manage therapy.[6,7,24–29]

Although this analysis cannot determine causation, it may provide insight as to how SMBG use can influence outcomes. By reviewing SMBG data, patients may better understand how diet, exercise, and medications influence their blood glucose. Patients who perform SMBG may see improvement in their blood glucose results, confirming that the medication has the intended effect. Conversely, if these patients miss medication doses, they may notice their blood glucose rise.

This study has several limitations. First, a lower MPR could indicate that patients had SSMT available but later stopped using the medication (per HCP recommendation) or switched medications; this analysis did not distinguish between the two. Additionally, MPR only measured the proportion of days covered by medication availability as a surrogate measure for medication adherence.

Secondly, other variables that could potentially affect the relationship between adherence and SMBG behavior (e.g., comorbidities, use of health care services, diet, and exercise) were not evaluated. The logistic regression model had a relatively low R^2, which reflects the numerous factors that can influence medication adherence. Many of these variables such as diet, exercise, weight, and stress are not available in administrative databases. Also, the preindex HbA1c values were obtained at any time in the 12-month preindex period, so the actual HbA1c prior to SSMT initiation may have changed. A low R^2 was observed in other studies of medication adherence that utilize claims databases.[30–32]

Finally, because this was an analysis of association, the relationship between SMBG use and drug adherence is not necessarily causal. This is a general limitation of observational studies.

Conclusions

This study demonstrated that SMBG use was associated with improved SSMT adherence and that this relationship was strengthened with greater SMBG use. Therefore, use of SMBG in noninsulin-treated T2DM should be considered because it might be an important tool to improve adherence.

Funding:

This study was funded by LifeScan, Inc. and Johnson & Johnson.

Disclosures:

Somesh Nigam and Mehmet Daskiran are employees of Johnson & Johnson. Naunihal Virdi is an employee of LifeScan, Inc. Chris Kozma, William Dickson, and Andrew Paris are employees of CK Consulting, which received payment from LifeScan, Inc. and Johnson & Johnson for conducting the analyses.

Acknowledgments:

The authors would like to thank Excerpta Medica for assistance in preparation of this paper.

References:

1. Ohkubo Y, Kishikawa H, Araki E, Miyata T, Isami S, Motoyoshi S, Kojima Y, Furuyoshi N, Shichiri M. Intensive insulin therapy prevents the progression of diabetic microvascular complications in Japanese patients with non-insulin-dependent diabetes mellitus: a randomized prospective 6-year study. Diabetes Res Clin Pract. 1995;28(2):103–17.
2. UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). Lancet. 1998;352(9131):837–53.
3. ADVANCE Collaborative Group, Patel A, MacMahon S, Chalmers J, Neal B, Billot L, Woodward M, Marre M, Cooper M, Glasziou P, Grobbee D, Hamet P, Harrap S, Heller S, Liu L, Mancia G, Mogensen CE, Pan C, Poulter N, Rodgers A, Williams B, Bompoint S, de Galan BE, Joshi R, Travert F. Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes. N Engl J Med. 2008;358(24):2560–72.
4. Lawrence DB, Ragucci KR, Long LB, Parris BS, Helfer LA. Relationship of oral antihyperglycemic (sulfonylurea or metformin) medication adherence and hemoglobin A1c goal attainment for HMO patients enrolled in a diabetes disease management program. J Manag Care Pharm. 2006;12(6):466–71.
5. Sokol MC, McGuigan KA, Verbrugge RR, Epstein RS. Impact of medication adherence on hospitalization risk and healthcare cost. Med Care. 2005;43(6):521–30.
6. Durán A, Martín P, Runkle I, Pérez N, Abad R, Fernández M, Del Valle L, Sanz MF, Calle-Pascual AL. Benefits of self-monitoring blood glucose in the management of new-onset type 2 diabetes mellitus: the St Carlos study, a prospective randomized clinic-based interventional study with parallel groups. J Diabetes. 2010;2(3):203–11.
7. Karter AJ, Parker MM, Moffet HH, Spence MM, Chan J, Ettner SL, Selby JV. Longitudinal study of new and prevalent use of self-monitoring of blood glucose. Diabetes Care. 2006;29(8):1757–63.
8. Kolb H, Schneider B, Heinemann L, Lodwig V, Scherbaum WA, Martin S. Altered disease course after initiation of self-monitoring of blood glucose in noninsulin-treated type 2 diabetes (ROSSO 3). J Diabetes Sci Technol. 2007;1(4):487–95.
9. Martin S, Schneider B, Heinemann L, Lodwig V, Kurth HJ, Kolb H, Scherbaum WA. Self-monitoring of blood glucose in type 2 diabetes and long-term outcome: an epidemiological cohort study. Diabetologia. 2006;49(2):271–8.
10. Zillich AJ, Sutherland JM, Kumbera PA, Carter BL. Hypertension outcomes through blood pressure monitoring and evaluation by pharmacists (HOME study). J Gen Intern Med. 2005;20(12):1091-6.
11. Miller S, St Onge EL. Sitagliptin: a dipeptidyl peptidase IV inhibitor for the treatment of type 2 diabetes. Ann Pharmacother. 2006;40(7–8):1336–43.
12. Centers for Medicare and Medicaid Services [Internet]. Health Insurance Portability and Accountability Act of 1996. Public Law 104-191, 104th Congress. Available from: http://www.cms.hhs.gov/HIPAAGenInfo/Downloads/HIPAALaw.pdf. Accessed August 4, 2011.
13. Karve S, Cleves MA, Helm M, Hudson TJ, West DS, Martin BC. Good and poor adherence: optimal cut-point for adherence measures using administrative claims data. Curr Med Res Opin. 2009;25(9):2303–10.
14. Cramer JA, Roy A, Burrell A, Fairchild CJ, Fuldeore MJ, Ollendorf DA, Wong PK. Medication compliance and persistence: terminology and definitions. Value Health. 2008;11(1):44–7.
15. Briesacher BA, Andrade SE, Fouayzi H, Chan KA. Comparison of drug adherence rates among patients with seven different medical conditions. Pharmacotherapy. 2008;28(4):437–43.

16. Schneeweiss S, Patrick AR, Maclure M, Dormuth CR, Glynn RJ. Adherence to statin therapy under drug cost sharing in patients with and without acute myocardial infarction: a population-based natural experiment. Circulation. 2007;115(16):2128–35.

17. Soumerai SB, Pierre-Jacques M, Zang F, Ross-Degnan D, Adams AS, Gurwitz J, Adler G, Safran DG. Cost-related medication nonadherence among elderly and disabled Medicare beneficiaries: a national survey 1 year before the Medicare drug benefit. Arch Intern Med. 2006;166(17):1829–35.

18. Chapman RH, Benner JS, Petrilla AA, Tierce JC, Collins SR, Battleman DS, Schwartz JS. Predictors of adherence with anti-hypertensive and lipid-lowering therapy. Arch Intern Med. 2005;165(10):1147–52.

19. Ahmed AT, Karter AJ, Liu J. Alcohol consumption is inversely associated with adherence to diabetes self-care behaviours. Diabet Med. 2006;23(7):795–802.

20. Gonzalez JS, Peyrot M, McCarl LA, Collins EM, Serpa L, Mimiaga MJ, Safren SA. Depression and diabetes treatment nonadherence: a meta-analysis. Diabetes Care. 2008;31(12):2398–403.

21. Kressin NR, Wang F, Long J, Bokhour BG, Orner MB, Rothendler J, Clark C, Reddy S, Kozak W, Kroupa LP, Berlowitz DR. Hypertensive patients' race, health beliefs, process of care, and medication adherence. J Gen Intern Med. 2007;22(6):768–74.

22. Winkler A, Teuscher AU, Mueller B, Diem P. Monitoring adherence to prescribed medication in type 2 diabetic patients treated with sulfonylureas. Swiss Med Wkly. 2002;132(27–28):379–85.

23. Ho PM, Rumsfeld JS, Masoudi FA, McClure DL, Plomondon ME, Steiner JF, Magid DJ. Effect of medication nonadherence on hospitalization and mortality among patients with diabetes mellitus. Arch Intern Med. 2006;166(17):1836–41.

24. Franciosi M, Lucisano G, Pellegrini F, Cantarello A, Consoli A, Cucco L, Ghidelli R, Sartore G, Sciangula L, Nicolucci A; ROSES Study Group. ROSES: role of self-monitoring of blood glucose and intensive education in patients with type 2 diabetes not receiving insulin. A pilot randomized clinical trial. Diabet Med. 2011;28(7):789–96.

25. Polonsky WH, Fisher L, Schikman CH, Hinnen DA, Parkin CG, Jelsovsky Z, Petersen B, Schweitzer M, Wagner RS. Structured self-monitoring of blood glucose significantly reduces A1C levels in poorly controlled, noninsulin-treated type 2 diabetes: results from the Structured Testing Program study. Diabetes Care. 2011;34(2):262–7.

26. Farmer AJ, Wade AN, French DP, Simon J, Yudkin P, Gray A, Craven A, Goyder L, Holman RR, Mant D, Kinmonth AL, Neil HA; DiGEM Trial Group. Blood glucose self-monitoring in type 2 diabetes: a randomised controlled trial. Health Technol Assess. 2009;13(15):1–72.

27. Kleefstra N, Hortensius J, Logtenberg SJ, Slingerland RJ, Groenier KH, Houweling ST, Gans RO, van Ballegooie E, Bilo HJ. Self-monitoring of blood glucose in tablet-treated type 2 diabetic patients (ZODIAC). Neth J Med. 2010;68(1):311–6.

28. O'Kane MJ, Bunting B, Copeland M, Coates VE. Efficacy of self monitoring of blood glucose in patients with newly diagnosed type 2 diabetes (ESMON study): randomised controlled trial. BMJ. 2008;336(7654):1174–7.

29. Kempf K, Kruse J, Martin S. ROSSO-in-praxi: a self-monitoring of blood glucose-structured 12-week lifestyle intervention significantly improves glucometabolic control of patients with type 2 diabetes mellitus. Diabetes Technol Ther. 2010;12(7):547–53.

30. Dickson M, Plauschinat CA. Racial differences in medication compliance and healthcare utilization among hypertensive Medicaid recipients: fixed dose vs free-combination treatment. Ethn Dis. 2008;18(2):204–9.

31. Svarstad BL, Shireman TI, Sweeney JK. Using drug claims data to assess the relationship of medication adherence with hospitalization costs. Psychiatr Serv. 2001;52(6):805–11.

32. McCombs JS, Nichol MB, Stimmel GL, Sclar DA, Beasley CM Jr, Gross LS. The cost of antidepressant drug therapy failure: a study of antidepressant use patterns in a Medicaid population. J Clin Psychiatry. 1990;51(Suppl):60–9.