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Refill Adherence to Oral Hypoglycemic Agents and Glycemic Control in Veterans

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Abstract

BACKGROUND—Although medication nonadherence may contribute to inadequate diabetes control, adherence is not routinely measured. Persistence, the continuous refill of medications, is one metric that could be integrated into clinical care if associated with glycemic control.

OBJECTIVE—To characterize the association of persistence levels (non-, good, overpersistence) with hemoglobin A_{1c} (A1C) over 1 year in newly medicated diabetics in the Veterans Administration.

METHODS—Eligible veterans were ≥18 years and first filled a prescription for oral hypoglycemic agents (OHA) between January 1, 2000, and December 31, 2002. The date the OHA was first dispensed was defined as the baseline date. Subjects must have filled at least 1 prescription for any drug, but no diabetes medications, during the 12 months preceding the baseline date. Persistence was measured in days supply of medication over 365 days and defined as non- (<0.80), good (≥0.8–1.10), and over- (>1.10) persistence. The main outcome measure was achieving goal A1C (≤7.0%) after 1 year.

RESULTS—A total of 56,181 veterans were included. Veterans were male (97%) and white (67%) with comorbid hypertension (58%) and hyperlipidemia (40%). Median age was 63 years, while median baseline A1C was 7.7%. Fifty-two percent of patients had good persistence; 25% were overpersistent. Good persistence was associated with achieving goal A1C (RR 1.07; 95% CI 1.06 to 1.09). The association of overpersistence with the same outcome (RR 0.95; 95% CI 0.94 to 0.97) was lower than good persistence, but higher than nonpersistence (RR 0.93; 95% CI 0.92 to 0.94).

CONCLUSIONS—Good persistence was associated with glycemic control. Over-persistent patients were common and more likely than nonpersistent patients, but less likely than good persisters to attain goal A1C. Estimating these different strata of persistence may be useful in identifying patients at risk of poor glycemic control.

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Keywords

adherence; medication; pharmacy claims; refill

Adherence to oral hypoglycemic agents used in the management of diabetes is suboptimal, yet adherence is not routinely measured in clinical practice, in part because no gold standard measurement exists.^{1,2} Persistence, a measure of refill adherence, holds promise as a practical measure in systems of care where long-term pharmacy claims data are available, such as in the Veterans Administration (VA). In the VA system, calculating a persistence measurement imposes minimal burden to the provider or patient because the refill data are integrated with the electronic medical record (EMR).

Persistence, however, is a proxy for adherence, and filling large prescriptions (≥ 90 -day supplies) has been associated with oversupplies.³ Existing literature on oversupplies, which we refer to as overpersistence, is limited and has not been examined in the context of diabetes. Prior studies using persistence capture overpersistence as good persistence defined as filling $\geq 80\%$ of medications.⁴ Little is known, therefore, about the association of overpersistence with relevant clinical outcomes. The primary aim of this study was to characterize the association of different levels of persistence, including overpersistence, with attainment of goal hemoglobin A_{1c} (A1C), a measure of glycemic control. The secondary aim was to examine the association of persistence levels with A1C improvement.

Methods

SETTING

We conducted a retrospective cohort study examining persistence to diabetic pharmacotherapy after the initial receipt of any oral hypoglycemic prescription including metformin, sulfonylureas, thiazolidinediones, and other agents in the VA. The VA provides comprehensive services to over 4.6 million veterans and 2 million additional health-care beneficiaries through 163 medical centers.⁵ It boasts a fully integrated EMR system containing pharmacy data, health-care utilization information, ICD -9 codes, demographic and clinical information, as well as laboratory data.⁶ In addition, most patients who used the VA for pharmaceutical services from January 1, 2000, through December 31, 2002, paid only \$2.00–7.00 per prescription, decreasing the likelihood that patients would fill their prescriptions elsewhere.⁷

Study data were obtained from the national VA Pharmacy Benefits Management (PBM) database. Accuracy of medication data is verified and updated on a monthly basis. The PBM database includes every patient with activity at any VA facility or pharmacy. The data also contain dosing instructions for each prescription and medications filled at the Consolidated Mail Outpatient Pharmacy. Laboratory results and outpatient clinical variables were obtained through the VA Decision Support System (DSS). The VA DSS is a longitudinal secondary relational database combining selected financial and clinical records in the VA.

STUDY SAMPLE

Our baseline date was the date the first diabetic medication was filled within the VA. The observation period for each patient was 12 months, beginning from the baseline date. To limit the analysis to adults with newly medicated type 2 diabetes, we included only patients who filled at least 1 prescription starting at the baseline date and no prescriptions for diabetes during the 12 months preceding their baseline date. This approach attempted to ensure that patients used the VA pharmacy system but had not previously filled an oral hypoglycemic prescription.

Patients meeting eligibility criteria were ≥ 18 years of age, filled at least 2 prescriptions for any oral hypoglycemic for the first time between January 1, 2000, and December 31, 2002, were alive 12 months after the index date, and had a follow-up A1C determined within 3 months of the end of the observation period (365 days), as seen in Figure 1. We excluded patients whose index medication was insulin, as measuring persistence to injectable agents such as insulin is difficult using only pharmacy refill data. Those who started insulin during the observation period were retained in all analyses.

PRIMARY PREDICTOR VARIABLE: PERSISTENCE

Our primary predictor variable was persistence, defined as:

$$\frac{\text{Total days supply of index oral hypoglycemic}}{\text{Days between (first date of first fill) – (first date of last fill)}}$$

It requires at least 2 fills for calculation and therefore excludes individuals who fill a prescription only once (Appendix I). This method provides information on the continuity of refilling behavior, but does not provide a uniform denominator of time. It typically ranges from 0 to 1.00, in which higher values indicate higher medication persistence. Due to variations in days supply, values >1.00 are possible. We defined nonpersistence as <0.80 , good persistence as ≥ 0.80 – 1.10 , and overpersistence as >1.10 .⁸ Adjustments were made for any time the patient was hospitalized. The quantity of medication dispensed to cover the number of hospitalized days was subtracted from the numerator and the denominator (number of days supplied by each refill).

PRIMARY OUTCOME VARIABLE: GLYCEMIC CONTROL

We assessed 2 metabolic outcomes: goal A1C and improved A1C. The 2 outcomes were dichotomous and defined, respectively, as last A1C $\leq 7.0\%$ versus last A1C $>7.0\%$ and last A1C less than baseline A1C versus last A1C greater than baseline A1C. We included subjects with no change in A1C from baseline to the end of the observation period and defined them as “not improved.”

OTHER ASSESSMENTS

Comorbidity was assessed based on ICD-9 codes collected from the Austin Automation Center (Austin, TX) recorded anytime from 12 months before to 6 months after the index date. For comorbidity to be considered present, we required 2 separate outpatient codes or 1 inpatient code. This method of defining comorbidities has been used in other work and has been shown to improve the validity between ICD-9 codes and other sources.^{6,9} We measured the prevalence of 8 comorbid conditions based on their known association with adherence or clinical association with diabetes or self-management skills. The prevalence of the following conditions was examined: hypertension, hyperlipidemia, coronary artery disease, stroke, psychiatric illnesses (other than depression), depression, alcohol dependence and/or abuse, and illicit substance dependence and/or abuse. Depression, alcohol use, and drug use were retained as single items because each has been described as a determinant of adherence.¹⁰⁻¹²

The baseline A1C value was defined as that value closest to the index date ± 3 months. The last A1C was defined as that value closest to the (index date + 365 days) ± 3 months. This reflects the clinical judgment that A1C represents glucose control over 3 months. Endocrinology and primary care encounters were determined using the corresponding DSS stop codes (306 and 323, respectively), which are identifiers that indicate the clinic within the VA where treatment was given. Patient age was calculated at the date of the index fill.

The number of oral hypoglycemics represents a sum of discrete oral hypoglycemics filled over the observation period. The sulfonylureas include glipizide, glyburide, chlorpropamide, tolazamide, and tolbutamide; the thiazolidinediones include pioglitazone, rosiglitazone, and troglitazone; and the “other” category includes repaglinide, nateglinide, acarbose, and miglitol. The combination class of drugs represents taking more than 1 pill simultaneously, and the metformin and glyburide class is a single pill combining these 2 medications. Insulin started during the year was recorded as a binary variable.

ANALYSES

All analyses were conducted in accordance with an analysis plan developed before the study. Persistence was calculated for the entire study sample, as were age, sex, index drug class, comorbidity, and clinical characteristics, using SAS version 9.1.1 (Cary, NC). The association of diabetic metabolic control with patient demographic, clinical, and persistence characteristics was modeled using bivariate and multivariable statistical methods. Approval was obtained from the Human Investigation Committee at the Yale School of Medicine and the VA Connecticut Human Subjects Subcommittee.

Because the prevalence rates of our outcomes of glycemic control were not small, we estimated risk ratios directly using SAS PROC GENMOD rather than odds ratios.^{13,14} We analyzed both dichotomous and ordinal persistence groupings because of their non-normal distribution. We dichotomized persistence using the accepted threshold of <0.80 (nonpersistence) or ≥ 0.80 (good persistence). In a separate analysis, persistence was also considered an ordinal variable (<0.80 , ≥ 0.80 – 1.10 , >1.10) with persistence ≥ 0.80 – 1.10 as the referent.

Indicator terms were created for age, race, number of oral hypoglycemics, class of diabetes medication, and comorbidity with the following respective referents: age <50 years, white race/ethnicity, 1 oral hypoglycemic (metformin), and zero comorbid conditions. The final model was adjusted for all variables seen in Tables 2 and 3. These variables were statistically significant in bivariate analysis at the $p < 0.05$ level. The convergence criteria for all logistic models were satisfied.

Results

The median age of the subjects was 63 years, 67% were white, and 97% were male (Table 1). Subjects filled a median of 1 oral hypoglycemic prescription during the entire observation period and had a median of 4 (interquartile range 3–6) visits to primary care providers. Twenty-seven percent saw an endocrinologist during the year. Median baseline A1C was 7.7% with a median change of -0.8% . Seventy-three percent of patients lowered their A1C by the end of the year, 24% showed a worse A1C, and 3% had no change in their A1C from baseline to study end. Sixty-five percent of patients achieved $A1C \leq 7.0\%$. Fewer than 4% of patients filled any prescription for insulin during the observation period. Seventy-seven percent of patients had good persistence (≥ 0.80). When we ordinalized persistence, only 52% of subjects achieved good persistence, with 25% categorized as overpersistent.

PERSISTENCE AND GLYCEMIC CONTROL

Good persistence was independently associated with goal A1C (RR 1.07; 95% CI 1.06 to 1.09) when compared to nonpersistence (Table 2). Good persistence was also associated with improved A1C (RR 1.06; 95% CI 1.05 to 1.07) when compared to nonpersistence. Baseline A1C demonstrated a robust influence on A1C achieved, while insulin use showed a

strong inverse association with achieving goal A1C (RR 0.67; 95% CI 0.63 to 0.71) and improved A1C (RR 0.88; 95% CI 0.85 to 0.90) at 1 year.

Older subjects were more likely to achieve goal A1C of $\leq 7.0\%$ with a monotonic increase as age increased by decades, and those of nonwhite race were less likely to reach goal A1C. Both endocrinologist care (RR 1.04; 95% CI 1.03 to 1.05) and 1 or 2 comorbid conditions (RR 1.04; 95% CI 1.03 to 1.05) were associated with achieving goal A1C compared to no endocrinologist care and no comorbidity. Markers of diabetes severity, such as filling prescriptions for ≥ 2 different oral hypoglycemics in the year, were associated with lower likelihood of achieving goal A1C than was filling prescriptions for only 1 oral hypoglycemic. Similarly, not starting on metformin or using ≥ 2 index oral hypoglycemics was inversely associated with achieving goal A1C than was starting on metformin. Depression, alcohol dependence and/or abuse, and illicit substance dependence and/or abuse demonstrated no significant association with achieving goal A1C. Results were similar when considering the outcome of improved A1C.

OVERPERSISTENCE AND GLYCEMIC CONTROL

In this cohort, 25% of patients had persistence > 1.10 . In multivariable analysis, overpersistent patients were less likely to achieve goal A1C (RR 0.95; 95% CI 0.94 to 0.97) compared to patients with good persistence (≥ 0.80 – 1.10), but were more likely to achieve goal A1C than were those with nonpersistence (RR 0.93; 95% CI 0.92 to 0.94) after adjustment for demographics, comorbidity, care, and regimen characteristics (Table 3). The same was true when examining the outcome of improved A1C. Overpersisters were less likely to improve (RR 0.98; 95% CI 0.98 to 0.99) compared with good persisters, but were more likely to improve than were nonpersisters (RR 0.94; 95% CI 0.93 to 0.95) after adjustment for the characteristics listed in Table 3.

Discussion

Persistence demonstrated a strong and consistent positive association with both measures of glycemic control in our sample of diabetic veterans new to oral hypoglycemic therapy. Controlling for patient and clinical factors did not diminish the association of persistence and glycemic control. Other studies using claims data have shown similar results. A retrospective study of 1668 diabetes management program patients demonstrated a strong association with A1C goal attainment and refill adherence to sulfonylureas or metformin determined with the same measure of persistence as ours over a 9-month period.¹⁵ Schectman et al. also found an association between persistence and A1C improvement in 810 adults receiving diabetes care at a single university-based internal medicine clinic.¹⁶ Pladevall et al. demonstrated an association between adherence to oral hypoglycemic agents measured using claims data and A1C improvement among 677 adults with diabetes, hyperlipidemia, and hypertension participating in a health maintenance organization.¹⁷ In all studies, the subjects had prevalent diabetes at baseline. Our main finding confirms prior work, but uses a much larger national sample and an incident diabetic population, highlighting the value of early persistence surveillance.

By the end of the study year, 77% of veterans achieved the threshold of 80% refill, which is generally recognized as good persistence. The significant associations between persistence and A1C outcomes confirm assumptions that adherence is important for glycemic control, thus making the measure relevant for monitoring and intervention. Good persistence demonstrated the strongest association with both outcomes of metabolic control after baseline A1C, insulin use, ≥ 3 hypoglycemics filled in the year (all possible markers for diabetes severity), and age (Table 2). Thus, persistence is an important modifiable determinant of glycemic control and deserves more clinical attention.

Younger subjects and those who were not white were less likely to achieve goal A1C, as has been shown in previous studies.^{17,18} Insulin use was also inversely associated with both glycemic outcomes. One explanation is that patients who fill insulin prescriptions may have higher A1C than those who do not take insulin, although both baseline A1C and insulin use were included in the multivariable model and each still demonstrated a strong negative association with glycemic control. It may also be that insulin is more difficult for patients to administer than simply taking a pill. Lastly, it may take more trial and error to titrate insulin to the correct dose to control glucose, so patients may have worse glycemic control until a stable insulin regimen is established.

Conversely, having seen an endocrinologist was positively associated with both measures of glycemic control. This may be related to the finding that specialists are more likely to intensify therapy in diabetes.¹⁹ Given the time and effort the VA places on process measures of diabetes in the primary care clinics, this finding was a bit surprising. Future work should explore the extent to which endocrinology and primary care diabetes visits differ and adapt the best practices from endocrinology to the primary care setting.

When persistence was ordinalized, overpersistence demonstrated intermediate associations with both goal A1C and improving A1C when compared to nonpersistence and good persistence. Our findings are consistent with Steiner et al.'s finding that overpersistent patients with epilepsy had lower phenytoin concentrations than persistent patients.⁸ We chose 1.10 as the upper boundary of good persistence because it allows for a 10% grace period of overfilling medications to reflect the real-world practice of obtaining refills before the total drug on hand is used. Rather than represent pill hoarding, this likely represents a desirable practice to minimize any gaps in medication taking. Persistence >1.10, or oversupplies, however, may not represent careful pill-taking behavior, despite the fact that patients have medication on hand; this merits study in future work.

To our knowledge, this study is among the first to explore the issue of overpersistence in diabetes. One explanation for our finding that overpersistent patients may be less likely to achieve goal A1C or improve A1C is the fact that they are sicker than other patients, as evidenced by their higher baseline A1C and higher prevalence of comorbidities and hospitalizations. Another explanation could be that pharmacy records may not accurately reflect instructions for medication taking. It is not uncommon for a physician to increase the dose of an existing drug without issuing a new prescription to the patient, potentially resulting in misclassification of some patients in our data set. These same patients may have more aggressive disease and require more experimentation in the first year of therapy to achieve the proper diabetes regimen. This increased medication turbulence strengthens the argument that overpersistent patients may benefit from adherence monitoring and possibly intervention, rather than lumping them with patients who demonstrate good persistence.

Existing literature on overpersistence is limited and conflicting. One study in the VA found that populations receiving large supplies (≥ 90 days) at one time obtained a mean of 129% of all maintenance drugs given in large supplies compared to prescriptions <90 days.³ In contrast, a study of antihypertensive medications by Christensen found that prescriptions of <60 days demonstrated "overcompliance" nearly 40% of the time compared with prescriptions of 61–120 days.²⁰ In our data, days supplied by each prescription was a median of 60 days for patients with good persistence. Taken together, these data suggest that overpersistence cannot simply be considered an artifact of prescription size. Finally, the clinical implications of overpersistence will vary across disease conditions. For diabetes, patients in this intermediate category were less likely to achieve goal A1C. For other diseases, such as HIV, persons in the intermediate category had a higher risk for developing resistance to antiretroviral drugs.²¹ Researchers and clinicians alike should be cautious when

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Figure 1.
Flow diagram of patient inclusion.

Table 1

Patient Characteristics by Persistence Category

Pts., N = 56,181	Nonpersistence		Good Persistence		Overpersistence	
	n (12,903)	%	n (29,242)	%	n (14,036)	%
Age, y (median, IQ range)	63 (54–72)		64 (55–72)		62 (53–71)	
Male	12,468	96.6	28,478	97.4	13,568	96.7
Race/ethnicity						
Hispanic	935	7.3	1,465	5.0	651	4.5
black	2,179	16.9	3,304	11.3	1,733	12.4
white	7,891	61.2	19,812	67.8	9,963	71.0
other	1,898	14.7	4,661	15.9	1,689	12.0
Comorbid conditions						
hypertension	7,060	54.7	17,009	58.2	8,555	61.0
hyperlipidemia	4,630	35.9	11,746	40.2	6,061	43.2
coronary artery disease	2,133	16.5	5,640	19.3	3,120	22.2
stroke	406	3.2	1,027	3.5	608	4.3
depression	1,137	8.8	2,626	9.0	1,754	12.5
drug use	217	1.7	287	1.0	249	1.8
alcohol use	467	3.6	787	2.7	596	4.3
other psychiatric conditions	458	3.6	1,051	3.6	866	6.2
Endocrinologist visit	3,241	25.1	7,723	26.4	4,460	31.8
Primary care visits (median, IQ range)	4 (2–5)		4 (3–5)		4 (3–6)	
Hospitalized	1,435	11.1	2,950	10.1	2,572	18.3
Median persistence (IQ range)	0.62 (0.49–0.74)		0.99 (0.91–1.04)		1.24 (1.15–1.38)	
Oral hypoglycemics (median, IQ range)	1 (1–1)		1 (1–1)		1 (1–2)	
Prescriptions (median, IQ range)	4 (3–7)		5 (4–9)		6 (5–9)	
Days supply (median, IQ range)	30 (30–90)		60 (30–90)		90 (30–90)	
Index medication						
sulfonyleureas ^a	6,358	49.3	15,273	52.2	8,551	60.9
metformin	5,811	45.0	12,422	42.5	4,979	35.5
thiazolidinediones ^b	284	2.2	633	2.2	182	1.3

Pts., N = 56,181	Nonpersistence		Good Persistence		Overpersistence	
	n (12,903)	%	n (29,242)	%	n (14,036)	%
metformin + glyburide (1 pill)	382	3.0	819	2.8	333	2.4
other ^c	68	0.5	88	0.3	1	<0.01
combination (>1 medication)	846	6.6	2,127	7.3	333	2.4
Insulin use during year	451	3.5	834	2.9	858	6.1
Baseline A1C, % (median, IQ range)	7.6 (6.7–9.0)		7.6 (6.7–8.9)		8.0 (7.0–9.8)	
Last A1C, % (median, IQ range)	6.7 (6.1–7.7)		6.5 (6.0–7.3)		6.7 (6.0–7.6)	

A1C = hemoglobin A1c; IQ = interquartile.

^a Sulfonylureas included glipizide, glyburide, chlorpropamide, tolazamide, tolbutamide.

^b Thiazolidinediones included pioglitazone, rosiglitazone, troglitazone.

^c Other drugs included repaglinide, nateglinide, acarbose, miglitol.

Table 2

Multivariable Associations with Goal and Improved A1C

Feature in Model	Last A1C $\leq 7.0\%$ N = 56,181			Last A1C Improved N = 56,181		
	Risk Ratio	95% CI	p Value	Risk Ratio	95% CI	p Value
Persistence (≥ 0.80)	1.07	1.06 to 1.09	<0.01	1.06	1.05 to 1.07	<0.01
Age (<50 y is referent)						
old (50 to <60)	1.04	1.02 to 1.07	<0.01	1.02	1.01 to 1.04	<0.01
older (60 to <70)	1.10	1.07 to 1.12	<0.01	1.04	1.03 to 1.06	<0.01
oldest (≥ 70)	1.12	1.10 to 1.15	<0.01	1.05	1.04 to 1.07	<0.01
Male (yes, no)	1.00	0.97 to 1.03	0.96	1.00	0.98 to 1.02	0.91
Race/ethnicity (white is referent)						
black	0.97	0.95 to 0.99	<0.01	0.99	0.98 to 1.00	0.12
Hispanic	0.92	0.90 to 0.95	<0.01	0.95	0.93 to 0.97	<0.01
other	0.98	0.97 to 0.99	<0.01	0.99	0.98 to 1.00	0.08
Primary care visits	1.00	0.97 to 1.03	0.97	1.02	1.00 to 1.04	0.10
Endocrinologist visit (yes, no)	1.04	1.03 to 1.05	<0.01	1.05	1.04 to 1.06	<0.01
Hospitalization (yes, no)	1.03	1.01 to 1.04	<0.01	1.01	1.00 to 1.02	0.12
Oral hypoglycemics, n (1 is referent)						
2	0.85	0.83 to 0.86	<0.01	0.97	0.96 to 0.98	<0.01
≥ 3	0.66	0.62 to 0.71	<0.01	0.93	0.90 to 0.96	<0.01
Oral hypoglycemic (metformin is referent)						
sulfonylurea	0.95	0.94 to 0.96	<0.01	0.98	0.97 to 0.99	<0.01
metformin/glyburide	0.95	0.92 to 0.99	<0.01	0.98	0.96 to 1.00	0.07
combination	0.91	0.88 to 0.95	<0.01	0.92	0.90 to 0.94	<0.01
other drug	0.86	0.77 to 0.96	<0.01	0.98	0.90 to 1.07	0.71
Insulin use (yes, no)	0.67	0.63 to 0.71	<0.01	0.88	0.85 to 0.90	<0.01
Depression (yes, no)	1.00	0.98 to 1.02	0.94	0.98	0.97 to 0.99	<0.01
Alcohol use (yes, no)	0.98	0.95 to 1.02	0.34	0.99	0.97 to 1.02	0.51
Illicit drug use (yes, no)	0.93	0.87 to 0.99	0.02	0.97	0.93 to 1.01	0.16
Comorbidities (zero is referent)						
1–2	1.04	1.03 to 1.05	<0.01	1.01	1.00 to 1.02	<0.01

Feature in Model	Last AIC ≤7.0% N = 56,181			Last AIC Improved N = 56,181		
	Risk Ratio	95% CI	p Value	Risk Ratio	95% CI	p Value
≥3	1.01	0.99 to 1.03	0.23	0.99	0.98 to 1.01	0.26
Baseline AIC ≤7.0% (yes, no)	1.42	1.40 to 1.44	<0.01	0.61	0.60 to 0.62	<0.01

AIC = hemoglobin A1c.

Table 3

Multivariable Associations of Overpersistence with Goal and Improved A1C

Feature in Model	Last A1C $\leq 7.0\%$ N = 56,181			Last A1C Improved N = 56,181		
	Risk Ratio	95% CI	p Value	Risk Ratio	95% CI	p Value
Persistence (good persistence is referent)						
nonpersistence (<0.80)	0.93	0.92 to 0.94	<0.01	0.94	0.93 to 0.95	<0.01
overpersistence (>1.10)	0.95	0.94 to 0.97	<0.01	0.98	0.98 to 0.99	<0.01
Age (<50 y is referent)						
old (50 to <60)	1.03	1.01 to 1.05	<0.01	1.02	1.01 to 1.03	<0.01
older (60 to <70)	1.08	1.05 to 1.10	<0.01	1.04	1.03 to 1.06	<0.01
oldest (≥ 70)	1.10	1.08 to 1.12	<0.01	1.05	1.04 to 1.07	<0.01
Male (yes, no)	1.00	0.97 to 1.03	0.92	1.00	0.98 to 1.02	0.90
Race/ethnicity (white is referent)						
black	0.97	0.95 to 0.99	<0.01	0.99	0.98 to 1.00	0.11
Hispanic	0.93	0.91 to 0.96	<0.01	0.95	0.93 to 0.97	<0.01
other	0.98	0.97 to 0.99	<0.01	0.99	0.98 to 1.00	0.07
Primary care visits	1.01	0.98 to 1.03	0.67	1.02	1.00 to 1.04	0.09
Hospitalization (yes, no)	1.03	1.02 to 1.04	<0.01	1.01	1.00 to 1.02	0.10
Oral hypoglycemics, n (1 is referent)						
2	0.88	0.87 to 0.90	<0.01	0.97	0.96 to 0.98	<0.01
≥ 3	0.74	0.70 to 0.79	<0.01	0.93	0.90 to 0.96	<0.01
Oral hypoglycemic (metformin is referent)						
sulfonylurea	0.96	0.95 to 0.97	<0.01	0.98	0.98 to 0.99	<0.01
metformin/glyburide	0.96	0.94 to 0.99	0.01	0.98	0.96 to 1.00	0.07
combination	0.93	0.90 to 0.96	<0.01	0.92	0.90 to 0.94	<0.01
other	0.89	0.81 to 0.98	0.02	0.99	0.91 to 1.08	0.78
Insulin use (yes, no)	0.75	0.72 to 0.79	<0.01	0.88	0.86 to 0.90	<0.01
Depression (yes, no)	1.00	0.99 to 1.02	0.90	0.98	0.9 to 0.99	<0.01
Alcohol use (yes, no)	0.99	0.96 to 1.02	0.43	0.99	0.97 to 1.02	0.52
Drug use (yes, no)	0.95	0.90 to 1.00	0.06	0.97	0.93 to 1.01	0.17
Comorbidities (zero is referent)						

Feature in Model	Last AIC ≤7.0% N = 56,181			Last AIC Improved N = 56,181		
	Risk Ratio	95% CI	p Value	Risk Ratio	95% CI	p Value
1-2	1.04	1.02 to 1.05	<0.01	1.01	1.00 to 1.02	<0.01
≥3	1.01	1.00 to 1.03	0.12	0.99	0.98 to 1.00	0.35
Baseline AIC ≤7.0% (yes, no)	1.33	1.32 to 1.34	<0.01	0.61	0.60 to 0.62	<0.01

AIC = hemoglobin A1c.