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Measuring Persistence to Oral Hypoglycemic Agents in Type 2 Diabetic Veterans

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Abstract

Background—Medication adherence is essential for diabetes control but difficult to measure. Persistence, the continuous refill of medications, is one measurement that could be integrated into practice, but concordance among definitions of persistence is unclear.

Objective—To compare persistence patterns in the use of oral hypoglycemic agents by diabetic veterans in the first year of treatment, using 2 separate refill metrics.

Methods—Eligible veterans were 18 years or older and had filled at least one prescription for any nondiabetes drug during the 6 months preceding study entry. Study entry was the date that patients first filled a prescription for oral hypoglycemic agents between January 1, 2000, and December 31, 2002. Persistence was defined as (1) total days (days' supply/study period) and (2) continuous fill (days' supply/refill interval).

Results—Inclusion criteria were met by 110,554 veterans. They had a median age of 63 years, 97% were male, and most had multiple comorbidities. Most patients received only one oral hypoglycemic agent. When total days was used, median persistence at 1 year was 83%, with 45% of subjects demonstrating poor persistence (<80%). When continuous fill was used, median persistence was 0.99, and 24% had poor persistence. Both metrics decreased over time. Continuous fill produced higher persistence estimates and a substantial proportion of overpersistence (>24% of patients). The 2 measures had a kappa agreement statistic of 0.56 (95% CI 0.55 to 0.57).

Conclusions—Although both metrics showed similar trajectories over time, more conservative estimates, ease of calculation, and transparency favor total days over continuous fill. Continuous fill revealed substantial overpersistence, which should be considered separately from good

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persistence. Explicit definitions of persistence are necessary to enhance comparisons among refill studies and provide context for clinical applications.

Poor adherence to medications contributes to inadequate glycemic control in patients with diabetes mellitus.¹ However, adherence is difficult to measure objectively in routine clinical practice. Persistence, the continuous refill of medications based on pharmacy data, could be integrated into clinical care because of the availability of refill data in many healthcare systems. Persistence can be conceptualized as a precursor to adherence. Without the refilling of prescriptions, no drugs are available to be consumed. Persistence assumes that patients begin taking the medication the day the prescription is filled and the way in which it was prescribed. In that way, persistence is the best possible adherence achieved by a patient and is necessary, though not sufficient, for adherence to occur. Despite its increasing use, definitions of persistence vary across studies.²⁻⁵

There is no gold standard for the calculation of any refill metric of adherence, and up to 8 different refill metrics and nomenclatures have been noted in the literature.⁴ The most commonly used persistence measure is called the medication possession ratio; however, this term has been applied to 2 distinct definitions.³ One is calculated using the total days' supply of medication divided by a prespecified observation period (total days).³⁻⁶ This measure of persistence provides a uniform study period but gives little information about the timeliness of filling. Another is defined as the days' supply of medication divided by the number of days between the refill interval (continuous fill).^{3,7} This measure provides insight into the continuity of fill or clinically important gaps of time in medication filling but does not provide a uniform observation period for study subjects. Yet, little is known about the concordance of these measures. The primary aim of this study was to compare persistence patterns in the use of oral hypoglycemic agents by veterans new to diabetic pharmacotherapy using total days and continuous fill.

Methods

SETTING

The Veterans Administration (VA) is among the largest integrated healthcare systems in the US, providing comprehensive services to more than 4.6 million veterans and 2 million additional healthcare beneficiaries through 163 medical centers.⁸ The VA has the largest electronic medical records system in the world, containing pharmacy data, healthcare utilization information, ICD-9 codes, and demographic and clinical information, as well as laboratory data.⁹

The study data were obtained from the Pharmacy Benefits Management (PBM) database for nationwide VA medication data. Accuracy of medication data is verified and updated on a monthly basis. The PBM data include information for every prescription filled at any VA facility, any pharmacy, or by mail. Laboratory results and outpatient clinical variables were obtained through the VA Decision Support System (DSS), a longitudinal secondary relational database combining selected data from financial and clinical records in the VA. The DSS data are audited as part of a monthly processing cycle.

PATIENTS

We conducted a retrospective cohort study looking at persistence to diabetic pharmacotherapy after the initial receipt of a prescription for any oral hypoglycemic in the VA. The observation period for each patient was 12 months, beginning from the date of the first prescription fill for an oral hypoglycemic (baseline date). To limit the analysis to adults with diagnosed type 2 diabetes, patients meeting eligibility criteria were 18 years of age or

older and had filled a prescription for any oral hypoglycemic for the first time between January 1, 2000, and December 31, 2002.

We included only patients who had filled at least one prescription, but no prescriptions for diabetes, during the 6 months preceding their baseline date. This approach ensured that patients used the VA pharmacy system but did not fill prescriptions for oral hypoglycemics, suggesting that our baseline date was the first time that a prescription for diabetic medication had been filled. We excluded patients whose index medication was insulin, as measuring adherence to insulin is difficult when only pharmacy data are used. Patients included in the study had to be alive 12 months after the index date.

OUTCOME

Our primary outcome was persistence, defined as the continuous refill of medications. Two methods of measuring persistence were used because each gives different insights into filling behavior. The first measure, total days, was calculated as:

$$\frac{\text{Total days' supply of any oral hypoglycemic agent} \times 100}{365 \text{ days}}$$

This general method has been used before and has the advantage of including subjects with only one prescription fill.¹⁰ In our study, it can be considered the most generous estimate of adherence since it captures days' supply of any oral hypoglycemic filled over the year rather than just index medication. In this manner, it provides a summary of refill behavior over a uniform period (365 days) regardless of any change from one oral hypoglycemic class to another. Because it is calculated in a manner that queries whether a drug is available on a specific day with a dichotomous answer (yes or no), total days is bounded from 0 to 100%. Total days does not provide information on continuity of refill or gaps in medication supply.

The second measure, continuous fill, was based on Steiner's medication possession ratio. It was defined as:

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

It requires at least 2 fills for calculation and therefore excludes those who fill a prescription only once. This method provides information on the continuity of refilling behavior but does not provide a uniform denominator of time. Due to variations in days' supply, values greater than 1.00 are possible.

All persistence values were evaluated in 2 ways: dichotomized and ordinalized. When dichotomized, poor persistence was defined as total days less than 80% or a continuous fill of less than 0.80; good persistence was total days of 80% or greater or a continuous fill of 0.80 or greater.^{2,3,5} When ordinalized, poor persistence was defined as total days less than 80% or a continuous fill of less than 0.80; good persistence was defined as total days of greater than or equal to 80–100% or continuous fill greater than or equal to 0.80–1.10. Overpersistence was a continuous fill greater than 1.10.⁷ Because total days was bounded from 0 to 100%, overpersistence was not possible with this measure. Specific examples of calculations from both methods can be seen in Figure 1.

For total days, analyses were performed quarterly, reflecting a common period for the refill of drugs by mail. The calculation examines drug availability from 0 to 90 days, 91 to 180 days, 181 to 270 days, and 271 to 365 days. It allows for the identification of persistence

changes over time. A summary measure of an individual's persistence over 12 months represented the final definitive overall measure of total days and was used in comparisons with continuous fill at 12 months.

Interval analyses for continuous fill were conducted at 3, 6, 9, and 12 months. Unlike the quarterly measures for total days, continuous fill intervals are cumulative and represent fill/refill behavior over the designated periods (from 0 to 90 days, 0 to 180 days, 0 to 270 days, 0 to 365 days). Subjects who filled at time 0 but did not refill until 110 days after time 0 would not have a 3-month calculation, but they would have a 6-month calculation. Adjustments were made for any time the patient was hospitalized for both persistence measures. For both metrics, 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).

ASSESSMENTS

To better characterize our study population, we assessed comorbidity based on ICD-9 codes collected from the VA's Austin Automation Center (Austin, TX) and recorded any time from 12 months prior to or 6 months after the index date. We required 2 separate outpatient codes or one inpatient code for the condition to be considered present. 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.^{9,11} We measured the prevalence of 8 comorbid conditions based on their known association with adherence or their clinical association with diabetes or self-management skills. The conditions we examined included hypertension, hyperlipidemia, coronary artery disease, cerebrovascular disease, psychiatric illnesses, depression, alcohol abuse/dependence, and drug abuse. ICD-9 code groupings are available on request.

The baseline hemoglobin A_{1c} (A1C) value was defined as that value closest to the index date ± 3 months. This reflects the clinical judgment that A1C is a reflection of glucose control over 3 months. Endocrinology and primary care encounters were determined using the corresponding DSS stop codes 306 and 323, respectively. The DSS stop codes are identifiers that indicate the clinic where treatment was given within the VA. Patient age was calculated at the date of the index fill. The number of oral hypoglycemics represented a sum of discrete oral hypoglycemics filled over the study period. The medications studied included metformin, sulfonylureas (glipizide, glyburide), thiazolidinediones (pioglitazone, rosiglitazone, troglitazone), and other drugs (chlorpropamide, repaglinide, nateglinide, acarbose, miglitol, tolazamide, tolbutamide). The combination class of drug represents taking more than one pill simultaneously, while the metformin + glyburide class is a single pill combining these 2 medications.

ANALYSES

All analyses were conducted in accordance with an analysis plan developed before the study. The total days and continuous fill measures were calculated for the entire study sample, as were age, sex, index drug class, comorbidity, and care characteristics, using SAS v 9.1.1 (SAS Institute, Cary NC). Additionally, agreement statistics were computed to assess the concordance of both persistence measures. The kappa statistic is an index of agreement adjusted for chance and was performed for dichotomous categories, while a weighted kappa statistic was used for ordinal categories of persistence. Approval was obtained from the Human Investigation Committee at the Yale School of Medicine and the VA Connecticut Human Subjects Subcommittee.

Results

The median age of the incident diabetes cohort was 63 years (Table 1). The majority of the cohort was male and white. Hypertension, hyperlipidemia, and coronary artery disease were the most common comorbidities. The patients had a median of 4 visits to their primary care physician, and 26% were seen by an endocrinologist during the study period.

Ninety-four percent started on a single pill. The most common single agents were sulfonylureas and metformin. Patients were on a median of one diabetes medication during the study period and had a median baseline A1C of 7.6%.

In general, persistence, measured by both metrics, declined over the year, with the steepest drop occurring between 3 and 6 months, as seen in Figure 2. Although both metrics revealed the same trajectory of filling, continuous fill (days' supply/refill interval) consistently demonstrated more drug available than did total days (days' supply/365 days). At the end of the 1-year study period, the median total days for all oral hypoglycemics was 303 days (83%), with 45% of patients having less than 80% adherence. The median continuous fill was 0.99, with 24% of patients having poor persistence (<0.80).

When dichotomized, both metrics demonstrated that the proportion of patients with good persistence declined over time (Figure 3). Continuous fill consistently categorized more patients as persistent compared with total days and also revealed a substantial amount of oversupplies or overpersistence (Table 2). The kappa agreement statistic between the 2 measures was 0.56 (95% CI 0.55 to 0.57) for dichotomous categories. The weighted kappa for ordinal categories of persistence was poor at 0.37 (95% CI 0.36 to 0.37).

Discussion

This study of a large national sample of diabetic veterans evaluates utilization patterns of inexpensive oral hypoglycemic medications in the patient's first year of therapy. Our filling estimates of 83% (total days) and 0.99 (continuous fill) are somewhat higher than those from other studies, where filling varied from 48% to 80% in incident diabetics in insured and Medicaid populations as measured by total days.^{12,13} However, the proportion of patients in our study who were persistent at a level of 80% or more was low (55%) when we used total days and consistent with other studies, which reported that 54% of patients achieved this level of persistence at year's end (using a similar calculation).¹⁰ When we used continuous fill, however, the proportion of patients with persistence of 0.80 or more (good and overpersistent) was much higher (76%), underscoring the need for explicit definitions of persistence in the literature.

Our higher persistence estimates may be explained by the older age of our patients (median 63 y) and by their increased contact with providers. According to the National Health and Nutrition Examination Survey (NHANES) 1999–2000, the mean age at diagnosis for patients with type 2 diabetes was 46 years.¹⁴ In prior studies, older age has been associated with improved refill adherence among patients with diabetes^{15–18}; in the Diabetes Prevention Program, older patients (>60 y) were more likely to report no barriers to taking medications compared with a middle-aged group (45–59 y).¹⁹ Our patients also had frequent contact with their primary care providers, consistent with the American Diabetes Association recommendation of 2–4 visits within a year, or more often when starting a new drug.²⁰ It is possible that this degree of contact could have boosted medication persistence.

The mechanism by which veterans both activate refills and receive their medications may also have contributed to our higher observed refill rates. In the VA, veterans can activate refill prescriptions in 1 of 4 ways: (1) by phone, using the Prescription Refill line (24 h/day,

7 days/wk); (2) by mail, using the mailing label enclosed with the last received prescription; (3) online, through MyHealtheVet, a personalized health record that has been available to patients electronically since August 31, 2005; and (4) in person.²¹ The VA also fills prescriptions either in person or by using automated pharmacy dispensing through the Consolidated Mail Outpatient Pharmacy (CMOP) system. In 2002, the VA filled 105 million prescriptions with great accuracy, using 90-day fills through the CMOP system.²² Estimates from 2001 suggest that the CMOP system accounted for approximately 67% of the total prescription workload of the VA.²³ These diverse strategies enable patients to activate prescription orders and receive medications quickly, without having to leave home, optimizing fill rates from a systems perspective.

Prior work suggests that patients new to therapy have worse adherence than do those who have been on oral hypoglycemics for longer periods.²⁰ When starting a new medication it is plausible that patients may fill the prescription once or twice and then intentionally discontinue the drug for a variety of reasons, including adverse effects.²⁴ In our study, continuous fill revealed high estimates of persistence in diabetics new to therapy because it creates a bias in favor of those who stop filling early. A person who stops filling after one timely refill will have a higher continuous fill than one who, although occasionally late on refills, remains on therapy for 1 year.²

This upward bias of continuous fill was also noted by Karve et al.,⁴ who found that a measure of total days had better predictive validity for hospitalization than did a measure of continuous fill among Medicaid-eligible diabetics in Arkansas. In addition to providing more conservative estimates of adherence reflective of our clinical experience, total days offers several research advantages over continuous fill: transparency; uniform denominator of time, values bounded between 0% and 100%, and the inclusion of single-fillers. This is aligned with prior work by Hess et al.,²⁵ who found that their Medication Refill Adherence (MRA), defined in the same manner as our total days, was the easiest of 11 different refill metrics to calculate.

Finally, the upward bias of continuous fill is supported by our finding that 24% of subjects were overpersistent. This is consistent with Steiner et al.'s⁷ finding that 33% of hypertensive patients had a continuous fill greater than 1.10. Because this metric, by definition, heavily weights the timeliness of prescription filling rather than medication availability over time, it is much more likely to result in patients with overpersistence than is total days' supply. The implications of overpersistence, however, are unknown, and Steiner et al.⁷ found that as overpersistence became more extreme, hypertension worsened. The association of overpersistence with clinical outcomes is particularly germane to the VA because large prescriptions (≥ 90 -day supplies) are commonly filled and have been associated with oversupplies.²⁶

Our decision to evaluate overpersistent individuals separately was based on the clinical observation that patients who take more medication than prescribed are infrequently encountered in routine practice. 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 refilling medications before the total drug on hand is used. Rather than representing pill hoarding, this likely represents a desirable practice to minimize any gaps in medication taking. Persistence greater than 1.10, or oversupplies, however, may not represent careful pill-taking behavior, despite the fact that patients have medication on hand. Given the large proportion of subjects found to be overpersistent and the suggestion that overpersistence does not have the same association with clinical endpoints as good persistence, we do not support the common truncation of all values of continuous fill to 1.00.^{2,3}

Because this is a secondary analysis of existing pharmacy records of veterans, the study was inherently limited by the type of data available. Our sample was predominantly male and white, so it is unclear how our findings would generalize to women and nonwhite populations, who are disproportionately affected by diabetes. Additionally, our sample was older than the national average age of those with diabetes, so applicability of our results beyond the VA sample is uncertain. We also excluded undiagnosed diabetic individuals, as well as diabetics who did not obtain oral hypoglycemics as a primary form of treatment. Our dataset, however, represents the largest nationally representative VA sample to examine issues of adherence measured by refill of oral hypoglycemics. In addition, most patients who used the VA for pharmaceutical services during the study period paid only \$2.00–7.00 per prescription, decreasing the likelihood that patients would fill their prescriptions elsewhere and nearly eliminating economics as a determinant of nonadherence.²⁷ Lastly, because our refill information relies on computer records and not on surveys, it is unlikely that patient behavior was influenced by our study.

Although both total days and continuous fill showed similar trajectories over time, total days is preferable because of its more conservative estimates, ease of calculation, and transparency. If continuous fill is used, investigators should consider analyzing overpersistence separately from good persistence. Because of the lack of standardized nomenclature in the refill adherence literature, explicit definitions of persistence are necessary to enhance comparisons among refill studies and provide context for clinical applications. Unlike other behaviors, such as diet, exercise, and smoking, adherence can be measured objectively at a population level via persistence metrics without added burden to the patient or provider. Integrating these refill metrics into routine practice is a natural locus of intervention to enhance provider awareness of adherence and, ultimately, clinical outcomes.

References

1. Koro CE, Bowlin SJ, Bourgeois N, et al. Glycemic control from 1988 to 2000 among US adults diagnosed with type 2 diabetes: a preliminary report. *Diabetes Care*. 2004; 27:17–20. [PubMed: 14693960]
2. Sikka R, Xia F, Aubert RE. Estimating medication persistency using administrative claims data. *Am J Manag Care*. 2005; 11:449–57. [PubMed: 16044982]
3. Andrade SE, Kahler KH, Frech F, Chan KA. Methods for evaluation of medication adherence and persistence using automated databases. *Pharmacoepidemiol Drug Saf*. 2006; 15:565–74. [PubMed: 16514590]
4. Karve S, Cleves MA, Helm M, et al. An empirical basis for standardizing adherence measures derived from administrative claims data among diabetic patients. *Med Care*. 2008; 46:1125–33. [PubMed: 18953222]
5. Briesacher BA, Andrade SE, Fouayzi H, Chan KA. Comparison of drug adherence rates among patients with seven different medical conditions. *Pharmacotherapy*. 2008; 28:437–43. [PubMed: 18363527]
6. Cantrell CR, Eaddy MT, Shah MB, et al. Methods for evaluating patient adherence to antidepressant therapy. *Med Care*. 2006; 44:300–3. [PubMed: 16565629]
7. Steiner JF, Koepsell TD, Fihn SD, et al. A general method of compliance assessment using centralized pharmacy records. *Med Care*. 1988; 26:814–23. [PubMed: 3398608]
8. Pogach LM, Brietzke SA, Cowan CL, et al. Development of evidence-based clinical practice guidelines for diabetes. *Diabetes Care*. 2004; 27:B82–9. [PubMed: 15113788]
9. Justice AC, Lasky E, McGinnis KA, et al. Medical disease and alcohol use among veterans with human immunodeficiency infection. *Med Care*. 2006; 44:S52–60. [PubMed: 16849969]

10. Hertz RP, Unger AN, Lustik MB. Adherence with pharmacotherapy for type 2 diabetes: a retrospective cohort study of adults with employer-sponsored health insurance. *Clin Ther.* 2005; 27:1064–73. [PubMed: 16154485]
11. Goulet JL, Fultz SL, Rimland D, et al. Aging and infectious diseases: do patterns of comorbidity vary by HIV status, age, and HIV severity? *Clin Infect Dis.* 2007; 45:1593–601. [PubMed: 18190322]
12. Dailey G, Kim MS, Lian JF. Patient compliance and persistence with antihyperglycemic drug regimens: evaluation of a Medicaid patient population with type 2 diabetes mellitus. *Clin Ther.* 2001; 23:1311–20. [PubMed: 11558867]
13. Boccuzzi SJ, Wogen J, Fox J, et al. Utilization of oral hypoglycemic agents in a drug-insured US population. *Diabetes Care.* 2001; 24:1411–5. [PubMed: 11473078]
14. Koopman RJ, Mainous AG, Diaz VA, et al. Changes in age at diagnosis of type 2 diabetes mellitus in the United States, 1988–2000. *Ann Fam Med.* 2005; 3:60–3. [PubMed: 15671192]
15. Lee R, Taira DA. Adherence to oral hypoglycemic agents in Hawaii. *Prev Chronic Dis.* 2005; 2:1–7.
16. Sclar DA, Robison LM, Skaer TL, et al. Sulfonylurea pharmacotherapy regimen adherence in a Medicaid population: influence of age, gender, and race. *Diabetes Educ.* 1999; 25:531–8. [PubMed: 10614258]
17. Schectman JM, Bovbjerg VE, Voss JD. Predictors of medication-refill adherence in an indigent rural population. *Med Care.* 2002; 40:1294–300. [PubMed: 12458310]
18. Venturini F, Nichol MB, Sung JC, Bailey KL, Cody M, McCombs JS. Compliance with sulfonylureas in a health maintenance organization: a pharmacy record-based study. *Ann Pharmacother.* 1999; 33:281–8. 10.1345/aph.18198 [PubMed: 10200850]
19. Walker EA, Molitch M, Kramer MK, et al. Adherence to preventive medications. Predictors and outcomes in the Diabetes Prevention Program. *Diabetes Care.* 2006; 29:1997–2002. [PubMed: 16936143]
20. American Diabetes Association. [accessed 2008 Mar 11] www.diabetes.org/diabetes-statistics.jsp
21. United States Department of Veterans Affairs. [accessed 2008 May 19] www.maryland.va.gov
22. Center for Health Transformation. [accessed 2009 Jul 20] www.healthtransformation.net/cs/veterans_administration_hospital_consolidated_mail_out_patient_pharmacy_cmops
23. Department of Veterans Affairs Office of Inspector General. [accessed 2008 May 19] Audit of VA Consolidated Mail Outpatient Pharmacy Inventory Management. Report No. 00-01088-97. May 17. 2002 www.va.gov/oig/52/reports/2002/00-01088-97.pdf
24. Barber N, Parsons J, Clifford S, et al. Patients' problems with new medication for chronic conditions. *Qual Saf Health Care.* 2004; 13:172–5. [PubMed: 15175485]
25. Hess LM, Raebel MA, Conner DA, Malone DC. Measurement of adherence in pharmacy administrative databases: a proposal for standard definitions and preferred measures. *Ann Pharmacother.* 2006; 40:1280–8. Epub 25 Jul 2006. 10.1345/aph.1H018 [PubMed: 16868217]
26. Steiner JF, Robbins LJ, Roth SC, et al. The effect of prescription size on acquisition of maintenance medications. *J Gen Intern Med.* 1993; 8:306–10. [PubMed: 8320574]
27. Kopjar B, Sales AE, Pineros SL, et al. Adherence with statin therapy in secondary prevention of coronary heart disease in Veterans Administration male population. *Am J Cardiol.* 2003; 92:1106–8. [PubMed: 14583366]

	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
A	<u>Fill 1: 60 days</u>		<u>Fill 2: 60 days</u>									
B	<u>Fill 1: 60 days</u>								<u>Fill 2: 60 days</u>			
C	<u>Fill 1: 60 days</u>		<u>Fill 2: 60 days</u>								<u>Fill 3: 60 days</u>	
D	<u>Fill 1: 60 days</u>											

For A: Total days = $\frac{120 \text{ days}}{365 \text{ days}} \times 100 = 32.9\%$

Continuous fill = $\frac{60 \text{ days}}{59 \text{ days (days between 1/1/00 and 3/1/00)}} = 1.02$

For B: Total days = $\frac{120 \text{ days}}{365 \text{ days}} \times 100 = 32.9\%$

Continuous fill = $\frac{60 \text{ days}}{243 \text{ days (days between 1/1/00 and 9/1/00)}} = 0.25$

For C: Total days = $\frac{180 \text{ days}}{365 \text{ days}} \times 100 = 49.3\%$

Continuous fill = $\frac{60 + 60 \text{ days}}{243 \text{ days (days between 1/1/00 and 9/1/00)}} = 0.49$

For D: Total days = $\frac{60 \text{ days}}{365 \text{ days}} \times 100 = 16.4\%$

Continuous fill not calculated because of single fill

Figure 1.
Examples of persistence calculations.

Figure 2.
Median persistence (drug available) overtime.

Figure 3.
Good persistence overtime.

Table 1Patient Characteristics^a

PARAMETER	n(%)
Age, y, median (interquartile range)	63 (54–72)
Male	107,081 (96.9)
Race/ethnicity	
Hispanic	5,692 (5.1)
black	15,753 (14.3)
white	70,408 (63.7)
other	18,701 (16.9)
Comorbid conditions	
hypertension	61,399 (55.5)
hyperlipidemia	40,023 (36.2)
coronary artery disease	20,765 (18.8)
cerebrovascular accident	4,150 (3.8)
depression	10,706 (9.7)
drug use	1,993 (1.8)
alcohol use	4,163 (3.8)
other psychiatric illness	4,839 (4.4)
Seen by endocrinologist	28,341 (25.6)
Primary care visits, n, median (interquartile range)	4 (2–5)
Hospitalized	14,317(13.0)
Oral hypoglycemics, n, median (interquartile range)	1 (1–1)
Index medication	
sulfonylurea	54,458 (49.3)
metformin	41,342 (37.4)
metformin + glyburide	2,816 (2.5)
combination	6,418 (5.8)
other	5,520 (5.0)
Insulin use during year	13,120 (11.9)

PARAMETER	n(%)
Baseline A1C, %, median (interquartile range)	7.6 (6.7–9.2)

A1C = hemoglobin A_{1c}.

^aN = 110,554.

Table 2

Patients Persistent at 12 Months

PERSISTENCE, %	TOTAL DAYS, % (n = 106,074)	CONTINUOUS FILL, % (n = 90,863)
<80	45	24
80–100	55	52
>100	0	24