Published in final edited form as:
J Pharm Health Serv Res. 2013 June ; 4(2): 89–94. doi:10.1111/jphs.12016.

Factors Affecting Sustained Medication Adherence and Its Impact on Health Care Utilization in Patients with Diabetes

Deborah Taira Juarez, Sc.D.[1], **Candace Tan, Pharm. D.**[1], **James Davis, Ph.D.**[2], and **Marjorie Mau, M.D.**

[1]University of Hawaii at Hilo, College of Pharmacy

[2]Biostatistics Core, John A. Burns School of Medication, University of Hawaii

[3]Department of Native Hawaiian Health, John A. Burns School of Medication, University of Hawaii

Abstract

Objective—To identify factors associated with years of medication adherence and to examine the relationship between years of adherence and health care utilization.

Methods—This retrospective analysis used administrative data from adult patients with diabetes enrolled in health plan in Hawaii for four years (n= 23,450 patients). Ordered logistic regression was used to examine factors related to years of medication adherence for three types of medications (anti-diabetic, antihypertensive, lipid-lowering). Multivariable logistic regression and negative binomial regression were used to examine relationship between years of adherence and health care utilization (hospitalizations and emergency department visits).

Key Findings—Adherence to any of the medications for all four years was significantly associated with lower odds of a hospitalization or emergency department visit in the third year. The magnitude of reduction in utilization was greater for adherence to anti-diabetic and lipid-lowering medications, at 31% compared to 22% for antihypertensives. The 9% of patients who were adherent to all three types of medications for all four years showed a reduction of 53%.

Conclusions—Improvement is needed in medication adherence across all three types of medication. Interventions may need to target younger adults, women, patients with congestive heart failure, Filipinos and Native Hawaiians.

Keywords

Medication adherence; health care utilization; health disparities

INTRODUCTION

Poor adherence to treatment regimens increases morbidity and mortality in patients with chronic disease and has been estimated to result in over $100 billion annually in avoidable health care costs.[1] In patients with diabetes, effective and comprehensive medical therapy requires treatment of not only hyperglycemia but also of hypertension and dyslipidemia to reduce the risk of cardiovascular disease. Although adherence to treatment regimens in patients with diabetes has been shown to be significantly related to glycemic control and improved outcomes,[2-4] rates of nonadherence in diabetes are high, with estimates varying between 36-93% .[5-7]

Corresponding Author: Deborah Taira Juarez, Sc.D. Associate Professor University of Hawaii at Hilo, College of Pharmacy 677 Ala Moana Boulevard, Suite 1025 Honolulu, HI 96813 dtjuarez@hawaii.edu.

Although the issue of poor medication adherence has been discussed for decades,[8] most studies have focused on adherence to one type of medication, such as oral diabetic medications, during a short time frame. There is an increasing realization, however, of the value of adherence to multiple medications over an extended period of time. Diabetes regimens typically include at least two to three medications; this pill burden is often compounded by an additional two to three antihypertensives and at least one lipid-lowering agent, making adherence particularly difficult for those with comorbid dyslipidemia and hypertension.[9-12]

The goals of our study were to identify factors associated with years of medication adherence for three types of medications (anti-diabetic, lipid lowering, and antihypertensive) and to examine the relationship between years of adherence and health care utilization, including hospitalizations and emergency department visits in an insured population of patients with diabetes in Hawaii.

METHODS

Study population

We conducted a retrospective analysis using administrative data from adult patients with diabetes who were enrolled in a large health plan in Hawaii for four years between 2007 and 2010 (n= 23,450 unique patients). Diabetes was identified using a disease management algorithm as either having 2 or more claims for type 2 diabetes in medical claims [*ICD-9-CM* codes 250.xx] on different dates or had at least 1 prescription for an oral hypoglycemic agent and/or insulin. Patients were only included in the study if they had at least one prescription for an oral diabetes medication. Duration of diabetes was calculated as years from initial identification by the disease management algorithm until year of adherence measurement.

Patient information including age, gender, history of cardiovascular disease, and morbidity level was obtained from administrative data. Patient morbidity level was determined by using *ICD-9-CM* codes according to the Johns Hopkins Adjusted Clinical Group methodology; levels of 4 or 5 on the 5-point scale were considered high morbidity.[13]

Data on ethnicity were available for 44 percent of patients from annual membership surveys. Members were asked to check all ethnicities that applied. Patients who selected more than one category were considered “mixed race (n=775) and combined with Other Race in analyses.” The one exception was Native Hawaiians. In keeping with the approach used by the Hawai‘i State Department of Health, we categorized as Hawaiian anyone who checked Hawaiian even if they checked more than one other ethnicity.[14] In analyses, we compared the four largest ethnic groups, Native Hawaiian, Filipino, Japanese and Chinese, to Whites.

Medication adherence

Data on filled medications including medication names, fills, and days of supply were obtained from pharmacy claims databases. Medication adherence was assessed for three types of medications: 1) anti-diabetic, 2) lipid-lowering 3) anti-hypertensives. To estimate medication adherence for each type of medication, we calculated the Proportion of Days Covered (PDC), which equals:

$$\frac{\text{Number of days in period ‘‘covered”by medication}}{\text{Number of days of drug enrollment}}$$

PDC is a well-validated and widely-used measure of medication adherence.[15,16] We determined the patient's measurement period as the index prescription date to the end of the calendar year or disenrollment. Within the measurement period, we counted the days the patient was covered by at least one drug for each type of medication based on the prescription fill date and days of supply. The number of covered days was divided by the number of days of drug coverage and multiplied this number by 100 to obtain the PDC (as a percentage) for each patient. Medication adherence was defined using the standard threshold of PCD greater than 80%. Adherence was determined each year and summed to calculate years of adherence during the study time frame. For the purposes of these analyses, years of adherence did not need to be consecutive. A patient adherent in years 1 and 3 would have two years of adherence as would a patient adherent in years 1 and 2.

Classes of medication included: 1) Anti-diabetic (Sulfonylureas, Biguanides, Thiazolidinediones, Alpha-glucosidase inhibitors, Meglitinides, Dipeptidyl peptidase IV (DPP-IV) inhibitors); 2) Lipid-lowering (Statins, Fibrates); 3) antihypertensives (Diuretics, Beta adrenergic blockers, Calcium channel blockers, Angiotensin converting enzyme inhibitors, Angiotensin receptor blockers, Sympatholytics and adrenergic blockers, Direct arterial vasodilators).

Data analysis

Initial analyses included tabulating frequencies of the study variables. Subsequent analyses identified factors related to years of medication adherence (0 - 4 years) for each of the three types of medications (anti-diabetic, anti-hypertensive, lipid-lowering) using ordered logistic regression models. Next, we estimated a multivariable logistic regression model to examine the relationship between years of adherence and likelihood of a hospitalization or emergency department visit in year four. We also estimated a negative binomial regression model with number of hospitalizations or emergency department visits as the dependent variable. All models adjusted for age, gender, morbidity level, and ethnicity, comorbidities, and duration of diabetes. The University of Hawaii Committee on Human Studies approved this study as exempt. All analyses were conducted using Stata statistical software, Version 11.[17]

RESULTS

Patient characteristics

The mean age of the study population was 60.0 years SD(13.0) and the average duration of diabetes was 5.0 years SD(3.6). Approximately 48% were female, 29% had high morbidity, 21% had a history of coronary artery disease and 9% had congestive heart failure (Table 1). The study population was ethnically diverse with 41% Japanese, 10% White, 7% Chinese, 18% Filipino, 18% Hawaiian, 5% other race or ethnicity and 3.0% mixed race. Approximately 79% of patients with diabetes filled at least one prescription for an antihypertensive medication and 75% filled a prescription for a lipid-lowering medication. Approximately 64% filled at least one prescription for all three types of medication.

Annual medication adherence rates averaged 55% for anti-diabetic medications, 64% for antihypertensive medications, and 49% for lipid-lowering medications.

Factors related to medication adherence

The range of all dependent adherence variables was 0 to 4 years. Mean years of adherence was 2.41 years for diabetes medications, 2.17 years for antihypertensive medications, and 1.64 years for dyslipidemia medications. Relative to patients aged 50 to 64, being younger was significantly associated with fewer years of medication adherence in all three categories [anti-diabetic, lipid-lowering, and antihypertensive], while being older was significantly

associated with greater adherence (Table 2). Being female was significantly associated with fewer years of adherence for all three types of medication.

A history of either coronary artery disease or congestive heart failure was significantly associated with more years of adherence to antihypertensive medications, but having congestive heart failure was also negatively associated with years of adherence to diabetes and dyslipidemia medications and having coronary artery disease was associated with reduced years of adherence to anti-diabetic medications (Table 2).

Compared to Whites, Japanese had more years of adherence to all three types of medications, while being Filipino or Native Hawaiian was negatively associated with adherence to all three types of medications (Table 2). Being Chinese or other/mixed race or ethnicity was not significantly associated with adherence to any of the medications. Patients with missing information on race had fewer years of adherence than Whites for all three types of medications.

Medication adherence was also positively associated with being on other types of medication. For instance, being on anti-hypertensive and lipid lowering medications increased adherence to anti-diabetic medications.

Demographic factors and health care utilization

Age was significantly associated with odds of a hospitalization or emergency department visit, with patients under age 35 and over age 65 more likely to experience these events than patients aged 50 to 64 (Table 3). Having high morbidity or a history of either coronary artery disease or congestive heart failure was also significantly associated with increased odds of a hospitalization or emergency department visit. Compared to patients who were diagnosed with diabetes for less than two years, patients with longer disease duration were less likely to have a hospitalization or emergency department visit. Race and ethnicity was not significantly associated with having a hospitalization or an emergency department visit in the logistic model.

Results from the negative binomial regression examining how these variables were related to the number of hospitalizations or emergency department visits were very similar, with the same variables, age, comorbidity, and duration of diabetes, being statistically significant, except that being Chinese or having race missing was significantly associated with fewer hospitalizations or emergency department visits (Table 3). The strongest predictors were having a high morbidity, coronary artery disease or congestive heart failure.

Medication adherence and health care utilization

Relative to patients who were not adherent, being adherent to any of the three types of medications (anti-diabetic, lipid-lowering, or antihypertensives) for all four years was significantly associated with a lower odds of a hospitalization or emergency department visit in the third year (Figure). The size of the reduction was greater for diabetes [OR=0.69, 95%CI(0.56, 0.83)] and lipid lowering [OR=0.67, 95%CI(0.54, 0.84)] medications than for antihypertensive [OR=0.78, 95%CI(0.63, 0.96)] medications.

Being adherent for three years to anti-diabetic medications was also associated with a reduced odds of hospitalization or emergency department visit [OR=0.83, 95%CI(0.69, 1.00)] but the magnitude of the reduction was not as great as for patients who were adherent for all four years (Figure). Being adherent for only one or two years to any of the medications did not significantly reduce the odds of a hospitalization or emergency department visit.

Approximately 9 percent of patients were adherent to all three types of medications for all four years. This level of adherence was significantly associated with reduced odds of a hospitalization or an emergency department visit [OR=0.46, 95%CI (0.36, 0.60)].

DISCUSSION

A World Health Organization report called the lack of adherence to prescribed medications a "worldwide problem of striking magnitude."[18] The Institute of Medicine included interventions to improve adherence as some of the top 100 priorities for comparative effectiveness research.[19] Patients with diabetes often have co-morbidities that increase the complexity of their treatment regimens. Although it is well known that anti-diabetic, antihypertensive, and lipid-lowering therapies significantly reduce the risk of ischemic events, adherence to these medications has been found to be poor.[20-23]

Our study of over 23,000 patients with diabetes enrolled in a health plan in Hawaii confirmed previous findings of low annual medication adherence rates in chronic disease, with adherence rates of 55 percent for anti-diabetic medications, 49 percent for lipid-lowering medications, and 64 percent for antihypertensive medications. Most prior studies that have examined the impact of medication utilization on outcomes have focused on a single type of medication over a single year. The strength of our study is its examination of the concurrent use of multiple types of medications [anti-diabetic, antihypertensive, and lipid-lowering] over a four year time frame. While adherence to any one type of medication reduces these odds of a hospitalization or emergency department visit, adherence to all three types of medications for all four years results in an even greater reduction in the odds of a hospitalization or emergency department visit of approximately 53 percent [OR=0.047, $p<0.001$; Figure].

There are several limitations to this study. First, all patients were enrolled in a large health plan in Hawaii so results may not be generalizable to other areas. Second, to be included in the study, patients had to have four years of enrollment. Hence, our estimates of adherence may be higher than those without this continuous health plan enrollment. Third, medication compliance was determined indirectly from pharmacy claims; the actual consumption of medication was not assessed and the provision of free drug samples [if any] would not be captured by the pharmacy claims system. The extent data is missing on these samples likely would result in underestimation of adherence to medications. Fourth, we do not have information on education or income level that might affect both adherence and health care utilization. Fifth, as we did not focus on new starts, patients may have had additional years of adherence or nonadherence prior to the start of the study that were not captured in these analyses. Finally, we did not assess reasons for nonadherence. This would require a qualitative component that was beyond the scope of this study but essential to developing effective and relevant interventions.

Conclusion

Our findings highlight the need to encourage sustained medication adherence across multiple types of therapy. Mean years of adherence was higher for anti-diabetic medications and antihypertensive medications at over 2 years compared to dyslipidemia medications, for which patients were adherent for less than half of the three year period [1.6 years]. This shorter duration of adherence to lipid-lowering medication regimens is particularly concerning given that we found the impact of medication adherence on health care utilization was as great for lipid-lowering medications as for anti-diabetic ones in this sample of patients with diabetes. Potential barriers to adherence to anti-diabetic and other medications include fear of hypoglycemia, fear of giving self-injection, weight gain, complexity of regimen, low health literacy, and medication cost.

Clearly, more needs to be done to improve medication adherence; however, the specific approaches that are most effective are still somewhat unclear. A Cochrane review of interventions to improve adherence by Haynes and colleagues found that most interventions produced little improvement in adherence rates.[24]

Our study provides additional evidence for the need to improve medication adherence across all three types of medication (anti-diabetic, antihypertensive, lipid-lowering) for patients with diabetes. Interventions may need to target younger adults, women, patients with congestive heart failure and coronary artery disease, Filipinos and Native Hawaiians.

Acknowledgments

This publication was made possible by Award Numbers P20MD000173 and S21MD999228 from the National Center on Minority Health and Health Disparities. Dr. Davis was partially supported by grants from the National Institute on Minority Health and Health Disparities U54MD007584 and G12MD007601 from the National Institutes of Health. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Center on Minority Health and Health Disparities or the National Institutes of Health.

REFERENCES

1. Ostenberg L. Adherence to medications. N Engl J Med. 2005; 353:487–97. [PubMed: 16079372]
2. Lawrence DB, et al. 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; 12:466–71. [PubMed: 16925454]
3. Ho PM, et al. Effect of medication nonadherence on hospitalization and mortality among patients with diabetes. Arch Intern Med. 2006; 166:1836–1841. [PubMed: 17000939]
4. Rhee MK, et al. Patient adherence improves glycemic control. Diabetes Educ. 2005; 31:240–250. [PubMed: 15797853]
5. Nair KV, et al. Prescription Co-pay Reduction Program for Diabetic Employees. Population Health Management. 2010; 13:235–45. [PubMed: 20879904]
6. Rozenfeld Y, et al. Oral antidiabetic medication adherence and glycemic control in managed care. Am J Manag Care. 2008; 14:71–5. [PubMed: 18269302]
7. Bailey CJ, Kodack M. Patient adherence to medication requirements for therapy of type 2 diabetes. Int J Clin Pract. 2011; 65:314–22. [PubMed: 21314869]
8. Gellad, WF., et al. A Review of Barriers to Medication Adherence: A Framework for Driving Policy Options. The Rand Corporation; 2009. Technical ReportAvailable from http://www.rand.org/pubs/technical_reports/TR765.html [Accessed 10 Oct 2012]
9. Bloomgarden Z. Five Ms of medication adherence. J Diabetes. 2011; 3:169–171. [PubMed: 21631902]
10. Briesacher BA, et al. Comparison of drug adherence rates among patients with seven different medical conditions. Pharmacotherapy. 2008; 28:437–43. [PubMed: 18363527]
11. Emslie-Simith A, et al. The problem of polypharmacy in type 2 diabetes. Br J Diabetes Vasc Dis. 2003; 3:54–56.
12. van Bruggen R, et al. Refill adherence and polypharmacy among patients with Type 2 diabetes in general practice. Pharmacoepidemiol Drug Saf. 2009; 18:983–91. [PubMed: 19623570]
13. Clark DO, et al. A chronic disease score with empirically derived weights. Med Care. 1995; 33:783–795. [PubMed: 7637401]
14. State of Hawaii Department of Health. [Accessed 10 Sept 2012] Hawai‘i Behavioral Risk Factor Surveillance System. Available from http://hawaii.gov/health/statistics/brfss/index.html
15. Choudhry NK, et al. Measuring Concurrent Adherence to Multiple Related Medications. Am J Manag Care. 2009; 15:457–464. [PubMed: 19589013]
16. Martin BC, et al. Contrasting Measures of Adherence with Simple Drug Use, Medication Switching, and Therapeutic Duplication. Ann Pharmacother. 2009; 43:36–44. [PubMed: 19126828]

17. StataCorp. Stata Statistical Software. Release 11. College Station, TX; StataCorp LP: 2009.
18. World Health Organization. Adherence to Therapies: Evidence for Action. World Health Organization; Geneva: 2003.
19. Institute of Medicine. Initial national priorities for comparative effectiveness research. Institute of Medicine; Washington, DC: 2009.
20. Amarenco P, Labreuche J. Lipid management in the prevention of stroke: review and updated meta-analysis of statins for stroke prevention. Lancet Neurol. 2009; 8:453–463. [PubMed: 19375663]
21. Baigent C, et al. Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90,056 participants in 14 randomised trials of statins. Lancet. 2005; 366:1267–1278. [PubMed: 16214597]
22. Law MR, et al. Use of blood pressure lowering drugs in the prevention of cardiovascular disease: meta-analysis of 147 randomised trials in the context of expectations from prospective epidemiological studies. BMJ. 2009; 338:b1665. [PubMed: 19454737]
23. Glader EL, et al. Persistent use of secondary preventive drugs declines rapidly during the first 2 years after stroke. Stroke. 2010; 41:397–401. [PubMed: 20075360]
24. Haynes RB, et al. Interventions for enhancing medication adherence. Cochrane Database Syst Rev. 2008; 2:CD000011. [PubMed: 18425859]

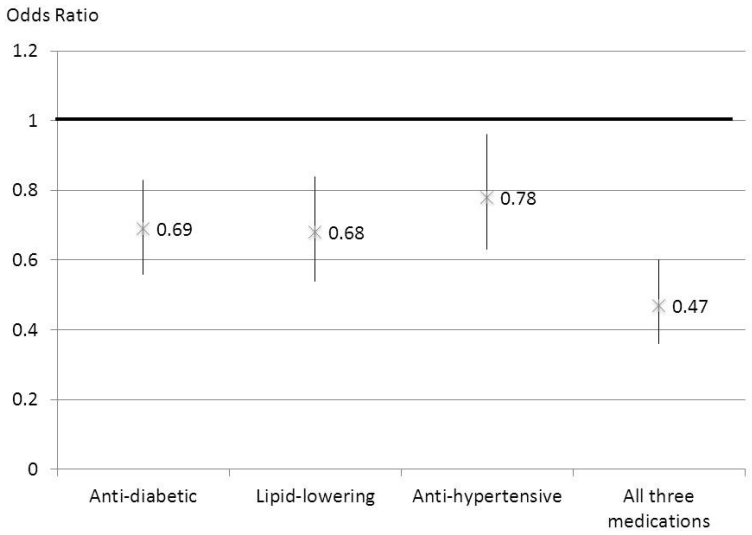

Figure.

Odds ratio of hospitalization or emergency department visit related to years of adherence, by type of medication, adjusted. Adjusted for age, gender, high morbidity, history of coronary artery disease or congestive heart failure, ethnicity, and duration of diabetes. All odds ratios are relative to zero years of medication adherence. DM=anti-diabetic medications; HTN=antihypertensives; LIP=dyslipidemia medications.

Table 1

Characteristics of the study population.

Category	Variable	N (Percent)
Age	Age <35	761 (3.2%)
	Age 35-49	4,017 (17.1%)
	Age 50-64	10,001 (42.6%)
	Age 65+	8,671 (37.0%)
Gender	Female	11,335 (48.3%)
Comorbidity	High morbidity	6, 719 (28.7%)
	Coronary Artery Disease	5,037 (21.4%)
	Congestive Heart Failure	2,224 (9.5%)
Ethnicity	Japanese	3,921 (41.2%)
	White	929 (9.8%)
	Chinese	688 (7.2%)
	Filipino	1,748 (18.4%)
	Native Hawaiian	1,724 (18.1%)
	Other Race	485 (4.8%)
	Mixed Race	775 (3.0%)
	Race missing	13,159 (56.0%)
Diabetes duration	Diabetes duration <2 years	6,976 (29.7%)
	Diabetes duration 2-4 years	4,744 (20.2%)
	Diabetes duration 5-8 years	6,185 (26.4%)
	Diabetes duration 9+ years	5,545 (23.6%)

Table 2

Factors related to years of medication adherence by type of medication.

	Anti-diabetic (n= 23,450)		Lipid-Lowering (n= 17,634)		Anti-hypertensive (n= 18,647)	
	Odds Ratio[‡]	95%CI	Odds Ratio	95%CI	Odds Ratio	95% CI
Age <35	0.45	(0.39, 0.52)	0.24	(0.19, 0.31)	0.20	(0.16, 0.25)
Age 35-49	0.67	(0.62, 0.72)	0.56	(0.52, 0.61)	0.54	(0.49, 0.58)
Age 50-64	1		1		1	
Age 65+	1.09	(1.04, 1.16)	1.28	(1.20, 1.35)	1.33	(1.26, 1.42)
Female	0.87	(0.83, 0.91)	0.79	(0.75, 0.84)	0.94	(0.89, 0.99)
High morbidity	0.94	(0.89, 0.99)	1.01	(0.95, 1.07)	1.03	(0.97, 1.10)
Coronary Artery Disease	0.86	(0.81, 0.92)	1.02	(0.95, 1.09)	1.19	(1.11, 1.28)
Congestive Heart Failure	0.79	(0.73, 0.86)	0.86	(0.76, 0.94)	1.20	(1.09, 1.32)
White	1		1		1	
Japanese	1.22	(1.11, 1.34)	1.35	(1.22, 1.50)	1.34	(1.21, 1.48)
Chinese	1.01	(0.91, 1.12)	1.07	(0.80, 1.20)	1.04	(0.93, 1.17)
Filipino	0.84	(0.76, 0.92)	0.73	(0.65, 0.82)	0.90	(0.80, 1.00)
Native Hawaiian	0.79	(0.71, 0.88)	0.77	(0.68, 0.86)	0.88	(0.78, 0.99)
Missing race	0.80	(0.73, 0.87)	0.75	(0.68, 0.83)	0.81	(0.74, 0.90)
Mixed/Other Race	1.00	(0.89, 1.04)	0.93	(0.81, 1.07)	1.04	(0.91, 1.20)
Antihypertensive use	1.34	(1.26, 1.43)	1.38	(1.28, 1.49)		
Lipid-lowering use	1.45	(1.37, 1.53)			1.31	(1.23, 1.40)

[‡]Proportional odds ratio resulting from ordered logistic regression, with years of adherence (0, 1, 2, 3, or 4) as the dependent variable.

Table 3

Hospitalization and/or emergency department visits related to demographic variables, adjusted*. (n=23,405)

	Had hospitalization or emergency department visit in year 4		Number of hospitalizations or emergency department visits in year 4	
	Adjusted Odds Ratio	**95%CI**	**Incidence Rate Ratios**	**95%CI**
Age <35	1.52	(1.006, 2.29)	1.57	(1.18, 2.09)
Age 35-49	0.92	(0.73, 1.15)	0.91	(0.78, 1.06)
Age 50-64	1		1	
Age 65+	1.71	(1.49, 1.97)	1.64	(1.48, 1.81)
Female	1.07	(0.95, 1.20)	1.11	(1.01, 1.21)
High morbidity	1.88	(1.66, 2.13)	1.84	(1.67, 2.02)
Coronary Artery Disease	1.76	(1.52, 2.03)	1.81	(1.62, 2.02)
Congestive Heart Failure	3.18	(2.73, 3.69)	2.71	(2.37, 3.10)
Japanese	1.07	(0.79, 1.46)	0.96	(0.81, 1.13)
Chinese	1.08	(0.72, 1.62)	0.79	(0.65, 0.96)
Filipino	0.90	(0.64, 1.27)	0.84	(0.70, 1.01)
Native Hawaiian	0.91	(0.65, 1.28)	1.08	(0.89, 1.31)
Missing Race	0.92	(0.61, 1.38)	0.82	(0.70, 0.97)
Mixed/Other Race	1.11	(0.71, 1.72)	1.10	(0.88, 1.38)
Diabetes duration < 2 years	1		1	
Diabetes duration 2-4 years	0.76	(0.64, 0.89)	0.74	(0.66, 0.85)
Diabetes duration 5-8 years	0.70	(0.60, 0.83)	0.71	(0.62, 0.80)
Diabetes duration 9 plus years	0.76	(0.63, 0.91)	0.79	(0.69, 0.91)
Lipid-lowering drug use	0.95	(0.80, 1.12)	0.96	(0.84, 1.09)
Antihypertensive drug use	1.68	(1.33, 2.12)	1.60	(1.36, 1.88)

*Adjusted for years of medication adherence (results in Figure).