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Adherence to Guidelines for Screening and Medication Use: Mortality and Onset of Major Macrovascular Complications in Elderly Persons With Diabetes Mellitus

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Abstract

Objective—The objective of this study is to investigate relationships between adherence to recommended screening and medication use and severe macrovascular complications and all-cause mortality among persons aged above 68 years with diabetes mellitus (DM).

Method—Data came from a 5% Medicare claims sample of beneficiaries initially diagnosed with DM during 2006–2008; follow-up was up to 7 years.

Results—Adherence to screening guidelines led to reduced mortality—hazard ratio (HR) = 0.57, 95% confidence interval [CI] = [0.56, 0.58]; congestive heart failure [CHF], HR = 0.89, CI = [0.87, 0.91]; acute myocardial infarction [AMI], HR = 0.90, CI = [0.85, 0.95]; and stroke/transient ischemic attack [Stroke/TIA], HR = 0.92, CI = [0.87, 0.97]—during follow-up. Recommended medication use led to lower mortality: HR = 0.72, CI = [0.70, 0.73]; CHF, HR = 0.67, CI = [0.66, 0.69]; AMI, HR = 0.68, CI = [0.65, 0.71]; and Stroke/TIA, HR = 0.79, CI = [0.76, 0.83].

Discussion—Elderly persons newly diagnosed with diabetes who adhered to recommended care experienced reduced risk of mortality and severe macrovascular complications.

Keywords

diabetes mellitus; adherence; congestive heart failure; acute myocardial infarction; stroke

Introduction

Type 2 diabetes mellitus (DM) is a serious chronic condition highly prevalent in the United States and other countries (Engelgau et al., 2004; NCD Risk Factor Collaboration, 2016). This condition is linked to increased mortality and complication rates in multiple organ systems. Prevalence rates of DM have been rising and continue to grow (Shaw, Sicree, & Zimmet, 2010; Wild, Roglic, Green, Sicree, & King, 2004; Zimmet, Alberti, & Shaw, 2001).

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Authors' Note

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Declaration of Conflicting Interests

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Even though there has been a slight decrease in diabetes-related severe cardiovascular and cerebrovascular outcomes among U.S. elderly persons diagnosed with the condition (Yashkin, Picone, & Sloan, 2015), macrovascular complications of DM remain the major causes of disability and premature death (Engelgau et al., 2004; NCD Risk Factor Collaboration, 2016).

Macrovascular complications of DM are highly prevalent among elderly persons diagnosed with DM (Sloan, Bethel, Ruiz, Shea, & Feinglos, 2008) and require use of medications and other treatment modalities. Antidiabetic, diuretic, and other hypertensive agents are among the most frequently used medications by Medicare beneficiaries irrespective of whether or not they are diagnosed with DM (Gurwitz et al., 2003). A study of lifetime direct medical costs of treating type 2 DM and its complications calculated that macrovascular complications accounted for 48% to 64% of lifetime medical costs of DM. Of the medical cost of such complications, 57% was spent on treating stroke and coronary heart disease, both being important macrovascular complications of DM (Zhuo, Zhang, & Hoerger, 2013). Several studies have documented differential rates of macrovascular complications among women as compared with men (Barrett-Connor, Cohn, Wingard, & Edelstein, 1991; Baviera et al., 2014; Guzder, Gatling, Mullee, & Byrne, 2007; Huxley, Barzi, & Woodward, 2006; Lyon, Jackson, Kalyani, Vaidya, & Kim, 2015; Peters, Huxley, & Woodward, 2014; Zhao et al., 2014)

Adherence to physician practice guidelines published by the American Diabetes Association (ADA; 2016) provides evidence-based care standards. The ADA specifies and updates recommended guidelines designed to provide a consistent approach to the management of DM (ADA, 2016). Important elements of these guidelines include annual hemoglobin A1c, urine and cholesterol testing, annual physical and eye examinations, and, in the presence of suspected or documented complications, consultations with cardiologists, nephrologists, endocrinologists, and podiatrists depending on the complication.

Proper adherence to prescribed medications is another important element of chronic disease management (Balkrishnan, 2005; Sokol, McGuigan, Verbrugge, & Epstein, 2005). However, studies incorporating multiple aspects of adherence, in particular medication adherence, have been rare due to lack of large nationally representative longitudinal datasets. Until recently, national longitudinal data on elderly persons' medication utilization at the individual level have not been available on a public use basis.

This study investigated the relationship between adherence to screening guidelines and use of prescription medication on four outcomes using a sample of Medicare beneficiaries initially diagnosed with type 2 DM at ages 68 years and above. Outcomes were all-cause mortality and the following macrovascular complications of DM: diagnoses of congestive heart failure (CHF), and hospitalizations for acute myocardial infarction (AMI) and transient ischemic attack/stroke (Stroke/TIA). Beneficiaries were followed up to 7 years after the initial DM diagnosis.

Our empirical analysis focused on the relationship between adherence to guidelines and use of medications among elderly persons newly diagnosed with type 2 diabetes. Our study

makes several contributions to the literature. First, we analyzed data from a large nationally representative of elderly persons. Previous studies have focused on younger populations using small samples (e.g., Gaede, Lund-Andersen, Parving, & Pedersen, 2008) or a single private insurer (Simpson, Lin, & Eurich, 2016) or single practice (An & Nichol, 2013). As summarized by Asche, LaFleur, and Conner (2011) and Doggrell and Warot (2014), the vast majority of previous studies of adherence to guidelines for DM have used glycemic control rather than DM complication endpoints. One reason for using intermediate endpoints is that complications of DM may take years to develop and researchers are constrained by having a lack of a sufficient follow-up period. There are exceptions. An and Nichol (2013) analyzed the link between multiple medication adherence in a population of persons diagnosed with DM and hypertension and microvascular and macrovascular complication endpoints, but with data from a single large group practice in Korea and on a minority of sample persons above age 65 years. Using a large U.S. integrated insurance claim and laboratory database with a follow-up of up to 6 years, Simpson et al. (2016) assessed the relationship between medication adherence and risk of new microvascular and macrovascular complications of DM. But the majority of observations were from persons below age 65 years.

Second, we could follow newly diagnosed beneficiaries for up to 7 years, which is a long follow-up period relative to the vast majority of previous studies. Third, studies of long-term health outcomes and adherence to recommended care for DM, especially medication adherence, have been rare, mainly because of a paucity of data nationally representative of U.S. elderly population. To our knowledge, this is the first study to use Medicare Part D claims data to study the link between medication use and new diagnoses of macrovascular complications of DM. The availability of public use data from Medicare Part D claims has made national analysis of medication use by elderly persons possible. Particularly important is the ability to monitor medication use over time and on a regular basis. Finally, many previous studies have measured adherence from information provided by survey respondent self-report. By contrast, our study based our adherence measure on Medicare claims data.

Method

Data

Data came from public use files provided by the U.S. Centers for Medicare & Medicaid Services (CMS) on a nationally representative 5% sample of claims for provision of services to Medicare beneficiaries enrolled in Parts A, B, and D spanning calendar years 2003–2012. Enrollment data giving basic demographic characteristics of the beneficiary, type of Medicare programs in which the beneficiary was enrolled with associated enrollment dates, place of residence, and date of death (when applicable) were linked to claims data. Claims data for 2003–2005 were only used to (a) ascertain that there were no claims with a DM diagnosis during this period and (b) identify comorbid conditions prior to the first claim during 2006–2008 containing a diagnosis of DM, which identified the date of the initial DM diagnosis. Claims data from the initial DM diagnosis date through 2012 were exclusively used for monitoring study events during follow-up. Medicare Part A and B claims provided information on diagnoses (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM]), procedures performed (ICD9-CM procedure codes and/or

Current Procedural Terminology, Version 4 [CPT-4] codes), hospitalizations, and the specialty of the beneficiary's physician (CMS specialty codes). Medicare Part D claims data, available since Part D's introduction in 2006, provided information on prescription drugs obtained by beneficiaries (Table 1).

Sample Selection

Beneficiaries enrolled in Medicare Parts A, B, and D newly diagnosed with DM in 2006, 2007, and 2008 were the subjects of this study. To establish an initial diagnosis, two claims with a diagnosis of DM within a 180-day period during 2006–2008 and no diagnosis of DM during the 3-year look-back period were required to confirm an initial DM diagnosis. Beneficiaries were followed until occurrence of a study event corresponding to one of the study's adverse health outcomes, exits from the dataset, or December 31, 2012, whichever came first. The follow-up period was up to 7 years. Our initial sample consisted of 163,536 beneficiaries (Table 2).

Medicare does not collect claims data on beneficiaries who enroll in Medicare Advantage (MA), a private alternative to traditional Medicare. Moreover, Medicare does not cover care for beneficiaries residing outside of the geographical borders of the United States. Thus, beneficiaries who resided outside the United States or enrolled in an MA plan prior to the initial DM diagnosis were excluded (n = 23,889). A 3-year look-back period from the date of the baseline diagnosis of DM was used to identify comorbidities. Therefore, individuals less than 68 at the baseline DM diagnosis date were excluded (n = 65,503). Claims data do not contain indicators of severity of DM other than for DM complications. We eliminated some heterogeneity in DM severity by focusing on persons newly diagnosed with DM during 2006–2008. Finally, 2,611 beneficiaries who did not receive any medications paid for by Part D during the year of the initial DM diagnosis were excluded (Kozma, Dickson, Phillips, & Meletiche, 2013). The rationale for this exclusion was to drop persons who may not have enrolled in Part D. This yielded a net sample of 71,533 for the analysis of all-cause mortality.

For the analysis of time to the first diagnosis of CHF or first hospitalizations for AMI or Stroke/TIA, we imposed the additional sample restriction that the beneficiary did not have a diagnosis (CHF) or a hospitalization with the diagnosis (AMI or Stroke/TIA) specific to the dependent variable during the look-back period, yielding somewhat smaller analysis samples for CHF, AMI, and Stroke/TIA than for all-cause mortality. We imposed these exclusions to eliminate persons from the analysis who experienced these adverse outcomes before they were first diagnosed with DM.

Empirical Specification

We included seven variables to create an index of adherence to ADA screening guidelines. Information on whether a beneficiary had a blood pressure, urine, hemoglobin A1c, or lipid test was obtained by querying the claims data for the appropriate CPT-4 codes (Table 1). Visits to a general physician, eye care specialist, or other specialist physician were identified from the CMS physician specialty code assigned to the Medicare claim. Eye care specialists were treated as a separate category as ADA guidelines recommend annual eye exams,

independent of whether the patient with DM experiences visual impairment. Factor analysis (varimax rotation) was conducted to convert seven measures of health services use into a single index for screening adherence (Table 3).

Using Medicare Part D claims data, which allowed us to monitor medication refills, we calculated fixed denominator medication possession ratios (MPRs) for each of the study medications for the year of the initial DM diagnosis (Table 1; Steiner, Koepsell, Fihn, & Inui, 1988; Steiner & Prochazka, 1997). The numerator of the associated MPR was the number of units prescribed for a day's use. The denominator was fixed at 365 days. If, for example, a beneficiary only filled one prescription for a 30-day supply in a year, the MPR was 0.082 (30/365). If the beneficiary filled 12 prescriptions, the MPR was 1.0. We adjusted calculations of total day's supply for rollover (e.g., a prescription of 30-day's supply filled on December 31 would roll over 29 days to the next year). We used these rules to fill in missing information for individuals who did not have a prescription for any given drug on record: (a) Individuals with a prescription for at least one drug in the diabetes or cardiac categories who filled this prescription on a regular basis were assumed to be fully adherent (MPR = 1.0) for all other diabetes or cardiac medication regimens; (b) if no cardiac drugs were obtained by a beneficiary, but there was a diagnosis on a Part A or B claim for a cardiovascular condition, the beneficiary was assumed to be nonadherent (MPR = 0.0).

The resulting 11 drug-specific MPRs were then converted into a single index using factor analysis. For both factor-based measures, we selected the first factor as it was the only factor with an eigenvalue above 1.0 (Table 3). Loadings on the first factor were positive for all MPRs.

Other covariates were male gender, Black race, beneficiary age at DM diagnosis, the calendar year in which the initial DM diagnosis occurred (2006, 2007, or 2008), the Charlson index (Charlson, Pompei, Ales, & Mackenzie, 1987), and binary variables for insulin dependence and cerebrovascular and cardiovascular comorbidities that were diagnosed during the 3-year look-back period *before* the initial DM diagnosis date. The Charlson index, also based on diagnoses in the look-back period, was modified to exclude diagnoses included separately as covariates. Insulin dependence, measured as a binary variable, was defined at the time of the initial DM diagnosis. The calendar year of the initial DM diagnosis was included as an explanatory variable to account for national changes in technology and practice patterns.

Software for the factor analysis and the Cox proportional hazard analysis came from Stata 11 (StataCorp, 2009).

Results

The analysis sample consisted of 75% females (Table 4). Females were on average more likely to adhere to screening guidelines but less likely to be adherent in medication use. Females were 3 or more years older than males on average. The proportion of Blacks was higher, and the mean value of the Charlson index was lower for women. Smaller fractions of

females had cardiovascular and cerebrovascular comorbidities during the 3-year look-back period.

Screening adherence was protective of all-cause mortality—hazard ratio (HR) = 0.57, 95% confidence interval (CI) = [0.56, 0.58]; first diagnosis of CHF, HR = 0.89, 95% CI = [0.87, 0.91]; first hospitalizations for AMI, HR = 0.90, 95% CI = [0.85, 0.95]; and Stroke/TIA, HR = 0.92, 95% CI = [0.87, 0.97]—all following the initial DM diagnosis (Table 5). Adherence to recommended medication was also protective for all study outcomes: all-cause mortality, HR = 0.72, 95% CI = [0.70, 0.73]; CHF, HR = 0.67, 95% CI = [0.66, 0.69]; AMI, HR = 0.68, 95% CI = [0.65, 0.71], and Stroke/TIA, HR = 0.79, 95% CI = [0.76, 0.83].

Being male, older, in poorer overall health as indicated by higher values of the Charlson index, insulin dependent, and having cerebrovascular comorbidities identified during the look-back period increased the risk of all-cause mortality. Being Black, older, in poorer overall health, insulin dependent, and having prior cardiovascular diagnoses during the look-back period led to an increased probability of a first diagnosis of CHF during follow-up. Holding other factors constant, male gender and a later initial DM diagnosis year were associated with a decreased probability of a first diagnosis of CHF. The result for DM diagnosis year could reflect a shorter follow-up period for persons first diagnosed with DM in a later year.

Patterns were similar for first hospitalization for an AMI during follow-up except, unlike CHF, men were more likely to experience a heart attack. A first hospitalization for TIA or stroke was more likely for persons who were Black, older, in poorer overall health, and with a cerebrovascular comorbidity documented during the look-back period. The patterns for year of the initial DM diagnosis were similar to first hospitalization for AMI.

Table 6 presents results stratified by gender. There was only one statistical difference in the relationship between screening and medication adherence between men and women—screening adherence for CHF, which was more important for men than for women. The HR for screening adherence was significantly below 1.0 for men in the Stroke/TIA analysis, implying that being adherent improves such outcomes for men. But for women, the corresponding result was statistically insignificant. The difference in HRs between men and women in the Stroke/TIA analysis was almost statistically significant at the .05 level. HRs for mediation adherence were consistently below 1.0 and statistically significant for both genders.

Discussion

In a nationally representative sample of persons aged 68 years and above at the time of initial diagnosis of type 2 DM, adherence to ADA guidelines for screening and medication use led to reduced rates of occurrence of new severe macrovascular DM complications and all-cause death during an up to 7-year period following an initial type 2 DM diagnosis.

The results add to evidence on the importance of regular screening and consistent use of prescribed medications for achieving glycemic control (Asche et al., 2011; Doggrell & Warot, 2014), in preventing complications of diabetes (An & Nichol, 2013; Simpson et al.,

2016), in reducing direct medical cost, and in increasing longevity and quality of life. One study of persons below the age of 65 years documented savings over a 1-year period in spending on personal health services other than for drugs for persons diagnosed with DM that more than offset the additional costs of drugs (Sokol et al., 2005). A systematic review of the literature on costs of medication adherence in patients diagnosed with DM concluded low MPRs were generally associated with higher total health care costs, but there was some variation in results among studies the authors reviewed, based in part on differences in underlying methodologies (Salas, Hughes, Zuluaga, Vardeva, & Lebmeier, 2009).

An alternative source of medication utilization information on an individual patient basis to the administrative data used in this study is survey data, such as from the Health and Retirement Study (HRS). The HRS does not routinely collect drug utilization data, but it has done this periodically (2003, 2005, and 2007) for small subsets of the HRS sample. Two recent longitudinal studies used biannual HRS data supplemented by a special 2003 survey of respondents diagnosed with DM to assess how adherence to recommended care for diabetes relates to health and longevity outcomes.

Han, Blaum, Ferris, Min, and Lee (2015) based their measure of adherence on a composite of five self-reported DM care process measures divided into two groups—three to five processes followed versus zero to two processes followed. Holding other factors constant, those respondents adhering to three to five processes experienced a 24% lower risk of dying during the 9-year follow-up period than did those who adhered to zero to two care processes.

Chen, Sloan, and Yashkin (2015) also used HRS biennial interview data and the 2003 special HRS survey of respondents diagnosed with DM merged with Medicare claims data. Using patient self-reports from the 2003 survey, they defined indexes for screening, physical activity (not possible to measure with claims data), and medication adherence. The Medicare claims data were used to measure nonmortality health outcomes with a 5-year follow-up period. They found that adherence to screening recommendations decreased the risk of developing CHF, stroke, and death by 14%. The effect size is not directly comparable with our result because the scale of the screening adherence measures in the two studies differs. Chen et al.’s results for medication adherence were far weaker than in the present study. Similar to Han et al. (2015), this is likely due to the limited statistical power of the dataset and reliance on self-reported adherence to medication use measured at one point in time.

Our study has several important strengths. The Medicare 5% sample of claims and enrollment data of Medicare beneficiaries diagnosed with DM is large, nationally representative of persons enrolled in traditional Medicare, who represent the vast majority of Medicare beneficiaries, and is longitudinal. Although use of data from randomized controlled trials is the gold standard, observational data such as those used in this study have the advantage of allowing researchers to observe care practices off protocol and for longer follow-up periods. Availability of Medicare Part D claims since the program’s inception in 2006 made it possible for us to assess the relationship between medication use and new diagnoses of macrovascular complications and death during follow-up. The index of adherence to screening guidelines reflected use of common laboratory tests and regular receipt of office visits by both general physicians and physicians specialized in the care of

persons diagnosed with diabetes rather than patient self-report. The ADA guidelines encompass recommendations for control of cardiovascular, cerebrovascular, and other chronic conditions. By contrast, many other guidelines do not account for care of persons with multiple chronic conditions (Boyd et al., 2005).

We also acknowledge some study limitations. Medicare claims are designed for billing rather than for clinical purposes, although the diagnoses and procedures reported should reflect information in medical records. The validity of Medicare data use for the conduct of clinical research has been demonstrated (Baron, Lu-Yao, Barrett, McLerran, & Fisher, 1994; Hennessy et al., 2010; Sloan, Brown, Carlisle, Ostermann, & Lee, 2003). However, in contrast to medical records, specific values of test results are lacking in claims data. We assumed that adherence is exogenous to outcomes at follow-up and did not study determinants of adherence to DM guidelines, which has been investigated in several previous studies (Brundisini, Vanstone, Hulan, DeJean, & Giacomini, 2015; Cramer, 2004; Farmer et al., 2015; Slade, 2012; Sloan, Padron, & Platt, 2009). The administrative data used in our study lack information on important potential determinants of adherence, such as socioeconomic status and living arrangements. The CMS does not provide data on cause-specific mortality that can be linked with public use Medicare claims data. Thus, we used all-cause mortality as one of our dependent variables.

The administrative data used in this study did not allow inclusion of behavioral aspects of DM management such as smoking, physical exercise, and diet. To ascertain whether our results on adherence were sensitive to exclusion of health behaviors, we used data from biannual HRS interviews linked to the HRS 2003 Diabetes Study (HRS-DS) and the HRS 2005 and 2007 Prescription Drug Study (HRS-DRUG). The HRS-DS and HRS-DRUG were conducted as supplements to the main HRS but were limited to persons who self-reported a diagnosis of DM as of 2002. These data provided information on exercise, smoking, a binary variable for a body mass index of 30 or higher, income, educational attainment, and marital status. Data on the use of oral agents for DM and self-reported adherence to the prescribed medications primarily came from the HRS-DS rather than from Medicare claims as in the present study because the data included a period before Medicare Part D was implemented. HRS-linked Medicare claims data were used to construct the measure of screening adherence and health outcomes—all-cause mortality, and a first hospitalization stroke and first diagnosis of CHF. The follow-up period was 5 years. Whether or not the covariates for the health behaviors and for income educational attainment and marital status were included, adherence to screening recommendations was associated with a reduced probability of these adverse health outcomes. Although the results were not much affected by this change in specification, adherence to recommended medications did not have a statistically significant relationship to health outcomes in any specification, which we attribute to not having as accurate measure of medication adherence as in the present study. Results on screening adherence were robust to whether or not the health behaviors and socioeconomic covariates were included.

Conclusion

The personal and social burden of DM and its complications is high and continues to grow. A striking example is a near 90% chance of the occurrence of an adverse outcome over a 5-year period following initial diagnosis (Sloan et al., 2008). However, elderly persons newly diagnosed with DM who adhere to recommended care for screening and medications can expect reductions in the risk of death and such macrovascular complications as CHF, AMI, and TIA or stroke during up to 7 years following their initial DM diagnosis.

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Table 1.

List of Study Codes

Condition/utilization		Administrative code[a]
Study inclusion requirements		
Diabetes mellitus	ICD-9:	250.xx
Study outcomes		
Congestive heart failure	ICD-9:	428.xx 398.91 402.01 402.11 402.91 404.11 404.91
Acute myocardial infarction[b]	ICD-9:	410.xx
Stroke/transient ischemic attack[b]	ICD-9:	431.xx 435.xx 436.xx 434.01 434.91 434.11
Insulin dependence	ICD-9:	250.1× 250.3× 250.01 259.03
Cardiovascular complication		
Angina	ICD-9:	413.xx
Ischemic heart disease	ICD-9:	411.xx 414.xx
Cerebrovascular complication		
Carotid bruit	ICD-9:	785.9
Occlusion or stenosis	ICD-9:	433.xx 434.xx
Elements of adherence to diabetes treatment guidelines		
General physician visit	CMS:	01 08 11 70 50 97
Specialist physician visit	CMS:	46 39 06 48
Eye specialist visit	CMS:	18 41
Blood pressure test	CPT-4:	90201 90205 99211–99215 99241–99245 99301–99303 99311–99313 99321–99323 99341–99349 99350 99387 99397 99401–99404 99411 99412 9942× 99331–99333
Urine test	CPT-4:	81001–81005 82040 82042 82043 82044 84155
HB1AC test	CPT-4:	82985 83036
Lipid test	CPT-4:	80061 82465 83715–83719 83721 84478
Elements of adherence to prescribed medications[c]		
Diabetes		Metformin, sulfonylureas, meglitinides, thiazolidinediones
Cardiac		Diuretics, sympatholytics, ACE inhibitors, calcium channel blockers, angiotensin 2 antagonists, vasodilators, anticoagulants

Note. ICD-9 = International Classification of Diseases, Ninth Revision; CMS = U.S. Centers for Medicare & Medicaid Services; CPT-4 = Current Procedural Terminology, Version 4; ACE inhibitors = Angiotensin-converting-enzyme inhibitors.

[a] Codes are drawn from International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9 for condition, ICD-9(P) for procedure), CPT-4 and CMS specialty codes. Codes are supplemented by questionnaire data where available.

[b] Includes Part A inpatient claims only.

[c] Includes all brand and generic names in drug group.

Table 2.

Sample Selection Summary

	Observations
Initial *n*	163,536
Left the United States or entered 9 Medicare Advantage plan prior to baseline	−23,889
Younger than 68 at baseline	−65,503
Had no Part D record for any of the study drugs	−2,611
Final sample size	71,533
Additional outcome specific restrictions	
Initial *n*	71,533
Had congestive heart failure prior to baseline	−17,086
Had acute myocardial infarction prior to baseline	−1,594
Had Stroke/TIA prior to baseline	−2,460
Final congestive heart failure sample size	54,447
Final acute myocardial infarction sample size	69,939
Final Stroke/TIA sample size	69,073

Note. Stroke/TIA = stroke/transient ischemic attack.

J Aging Health. Author manuscript; available in PMC 2019 July 26.

Table 3.

Factor Analysis for Measures of Adherence.

Factor components	Factor loadings
ADA screening guidelines	
General physician visit	0.30
Specialist physician visit	0.22
Eye care specialist visit	0.29
Urine test	0.42
HB1AC test	0.53
Lipid test	0.56
Blood pressure test	0.35
Factor eigenvalue[a]	1.12
Prescription drug use (MPR)	
Metformin	0.40
Sulfonylureas	0.41
Meglitinides	0.08
Thiazolidinediones	0.29
Diuretics	0.47
Sympatholytics	0.44
ACE inhibitors	0.42
Calcium channel blockers	0.37
Angiotensin 2 antagonists	0.30
Vasodilators	0.19
Anticoagulants	0.15
Factor eigenvalue[a]	1.30

Note. Varimax rotation was used. ADA = American Diabetes Association; MPR = medication possession ratio; ACE inhibitors = Angiotensin-converting-enzyme inhibitors.

[a]Satisfies Kaiser criterion for retaining the factor.

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Table 4.

Summary Statistics.

Variables	Males	Females	Total
Screening adherence	0.14 (0.63)	0.17 (0.60)	0.17 (0.61)
Rx adherence	0.02 (0.66)	−0.04 (0.68)	−0.02 (0.68)
Black	0.08	0.11	0.11
Age	75.83 (6.29)	79.07 (7.10)	78.27 (7.05)
Baseline year	2,006.99 (0.83)	2,006.64 (0.82)	2,006.73 (0.83)
Charlson index	1.64 (2.06)	1.47 (1.83)	1.51 (1.89)
Insulin dependence	0.03	0.04	0.04
Cardiovascular comorbidity	0.50	0.31	0.36
Cerebrovascular comorbidity	0.37	0.25	0.29
Sample size (*n*)	17,678	53,855	71,533
Dead	0.30	0.36	0.35
Congestive heart failure	0.50	0.55	0.54
Acute myocardial infarction	0.08	0.07	0.07
Stroke/transient ischemic attack	0.11	0.10	0.10

Note. Numbers presented are sample means. For continuous variables, the standard deviations are provided in parentheses. Rx = prescription drug use.

Table 5.

Cox Proportional Hazard Results for Pooled Model.

	All-cause death	Congestive heart failure	Acute myocardial infarction	Stroke/TIA
Explanatory Variable	**HR [95% CI]**[a]	**HR [95% CI]**[a]	**HR [95% CI]**[a]	**HR [95% CI]**[a]
Screening adherence	0.57** [0.56, 0.58]	0.89** [0.87, 0.91]	0.90** [0.85, 0.95]	0.92** [0.87, 0.97]
Rx adherence	0.72** [0.70, 0.73]	0.67** [0.66, 0.69]	0.68** [0.65, 0.71]	0.79** [0.76, 0.83]
Male	1.12** [1.09, 1.16]	0.89** [0.85, 0.92]	1.12* [1.03, 1.22]	0.92* [0.85, 0.99]
Black	0.99 [0.95, 1.03]	1.14** [1.09, 1.19]	0.97 [0.86, 1.08]	1.24** [1.14, 1.36]
Age	1.08** [1.08, 1.08]	1.05** [1.05, 1.05]	1.04** [1.03, 1.04]	1.04** [1.04, 1.05]
Baseline year	1.00 [0.99, 1.02]	0.87** [0.86, 0.89]	0.73** [0.69, 0.76]	0.80** [0.77, 0.83]
Charlson index	1.20** [1.19, 1.20]	1.12** [1.11, 1.13]	1.08** [1.06, 1.10]	1.15** [1.13, 1.16]
Insulin dependence	1.27** [1.20, 1.35]	1.25** [1.17, 1.34]	1.14 [0.95, 1.35]	1.05 [0.90, 1.22]
Cardiovascular comorbidity	1.01 [0.98, 1.04]	1.20** [1.16, 1.24]	1.23** [1.14, 1.32]	
Cerebrovascular comorbidity	1.07** [1.04, 1.10]			1.30** [1.21, 1.38]
n	71,533	54,447	69,939	69,073

*Note.*Dependent variables are shown in the headings; Stroke/TIA = stroke/transient ischemic attack; HR = hazard ratio; CI = confidence interval.

[a]Numbers presented are HRs with 95% CIs in brackets.

*$p < .05$.

**$p < .01$.

Table 6.

Cox Proportional Hazard Results for Stratified Model.

	All-cause death		Congestive heart failure		Acute myocardial infarction		Stroke/TIA	
	Males	Females	Males	Females	Males	Females	Males	Females
Explanatory Variable	**HR [95% CI]**[a]		**HR [95% CI]**[a]		**HR [95% CI]**[a]		**HR [95% CI]**[a]	
Screening adherence	0.55** [0.53, 0.58]	0.57** [0.56, 0.58]	0.82** [0.78, 0.87]	0.90** [0.88, 0.93]	0.80** [0.71, 0.91]	0.93* [0.87, 0.99]	0.82** [0.73, 0.91]	0.95 [0.89, 1.00]
Rx adherence	0.70** [0.67, 0.72]	0.72** [0.71, 0.74]	0.69** [0.66, 0.72]	0.67** [0.66, 0.69]	0.69** [0.63, 0.77]	0.68** [0.64, 0.71]	0.80** [0.73, 0.88]	0.79** [0.76, 0.83]
Black	1.08 [0.98, 1.18]	0.96 [0.92, 1.01]	1.27** [1.14, 1.41]	1.12** [1.07, 1.17]	1.11 [0.86, 1.44]	0.93 [0.82, 1.06]	1.26* [1.00, 1.58]	1.24** [1.12, 1.37]
Age	1.08** [1.08, 1.08]	1.08** [1.08, 1.09]	1.05** [1.05, 1.06]	1.05** [1.05, 1.05]	1.03** [1.01, 1.04]	1.04** [1.03, 1.05]	1.05** [1.04, 1.06]	1.04** [1.04, 1.05]
Baseline year	1.09** [1.05, 1.12]	0.98 [0.96, 1.00]	1.00 [0.96, 1.04]	0.84** [0.82, 0.86]	0.86** [0.78, 0.94]	0.68** [0.64, 0.72]	0.85** [0.78, 0.92]	0.78** [0.75, 0.82]
Charlson index	1.19** [1.18, 1.21]	1.20** [1.19, 1.21]	1.11** [1.09, 1.12]	1.13** [1.12, 1.13]	1.10** [1.06, 1.13]	1.07** [1.05, 1.10]	1.13** [1.09, 1.16]	1.15** [1.14, 1.17]
Insulin dependence	1.20** [1.05, 1.38]	1.29** [1.21, 1.38]	1.16 [0.98, 1.37]	1.26** [1.17, 1.36]	1.15 [0.78, 1.69]	1.13 [0.93, 1.37]	1.02 [0.70, 1.48]	1.06 [0.90, 1.25]
Cardiovascular comorbidity	1.05 [0.99, 1.12]	1.01 [0.97, 1.04]	1.25** [1.17, 1.33]	1.20** [1.16, 1.24]	1.32** [1.13, 1.53]	1.23** [1.13, 1.33]		
Cerebrovascular comorbidity	1.12** [1.05, 1.19]	1.06** [1.02, 1.09]					1.34** [1.16, 1.54]	1.29** [1.20, 1.39]
n	17,678	53,855	12,789	41,658	17,043	52,896	16,891	52,182

Note. Dependent variables are shown in the headings. Stroke/TIA = stroke/transient ischemic attack; HR = hazard ratio; CI = confidence interval; Rx = prescription drug use.

[a]Numbers presented are HRs with 95% CIs in brackets.

*p < .05.

**p < .01.