



Utilization of angiotensin converting enzyme inhibitors (ACEI) and angiotensin receptor blockers (ARB) in patients diagnosed with diabetes: Analysis from the National Ambulatory Medical Care Survey

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ABSTRACT

Objective. The objective of this study was to determine if a difference exists in the proportion of visits for the prescribing of angiotensin converting enzyme inhibitors (ACEI), or angiotensin receptor blockers (ARBs) in diabetic patients during 2007–2010.

Methods. This retrospective, cross-sectional, observational study included adults diagnosed with diabetes mellitus from the National Ambulatory Medical Care Survey (NAMCS) during 2007–2010. Weighted chi-square tests and a multivariable logistic regression model were used to analyze associations between ACEI/ARB prescriptions and predictors of interest. Odds ratios and 95% confidence intervals were reported.

Results. An unweighted total of 13,590 outpatient ambulatory care visits were identified for adult patients with diabetes without contraindications to ACEIs or ARBs in the NAMCS for the years studied. No statistically significant increase in the proportion of visits with an ACEI/ARB prescription was identified for years 2007–2010 (28.1% in 2007 to 32.2% in 2010). Females (OR 0.78, 95% CI 0.69–0.89), patients 18–39 years old (OR 0.56, 95% CI 0.43–0.75), and Medicare users (OR 0.81, 95% CI 0.70–0.94) were significantly less likely to receive an ACEI/ARB prescription. Patients with hypertension (OR 2.80, 95% CI 2.39–3.29), hyperlipidemia (OR 1.42, 95% CI 1.22–1.65), and ischemic heart disease (OR 1.36, 95% CI 1.10–1.70) were significantly more likely to receive an ACEI/ARB prescription.

Conclusions. Despite extensive evidence showing the benefits of ACEI/ARB medications in diabetic patients, disparities of treatment remain evident.

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Introduction

Diabetes is a chronic disease that increasingly affects a growing percentage of the American population. Currently, it is the seventh leading cause of death in the United States, with 9.3% of the US population having a diagnosis (Centers for Disease Control and Prevention, 2014). Diabetes care is complex and requires an expansive range of interventions for improved disease outcomes. Concurrent disease states such as hypertension, hyperlipidemia, and ischemic heart disease (IHD) add to this complexity. The Standards of Medical Care in Diabetes, compiled annually by the American Diabetes Association (ADA), recommend that the first line treatment for patients with diabetes and

hypertension should be an angiotensin-converting enzyme inhibitor (ACEI) or an angiotensin receptor blocker (ARB) (American Diabetes Association, 2010). ACE inhibitors are also recommended in patients with diabetes and known cardiovascular disease to reduce the risk of cardiovascular-related events and mortality (American Diabetes Association, 2010). Data from several clinical trials support these recommendations and provide insight for the treatment of diabetes complications in various subsets of the diabetic population (Eurich et al., 2004; Yusuf et al., 2000; Lindholm et al., 2002). More specifically, these medications have shown benefit beyond blood pressure optimization and have nephroprotective and cardioprotective properties (Fioretto and Solini, 2005; Parving et al., 2001; Viberti et al., 2002). Despite these recommendations and guidelines, previous research indicates that a large proportion of diabetes patients are not receiving these medications as indicated (Rosen, 2006). The Rosen study used data from the National Health and Nutrition Examination Survey and found national estimates of ACEI/ARB use in the elderly diabetic population to be no higher than 53%, despite risk factors indicating that the majority of all of these patients should be prescribed an ACEI/ARB. Additional data regarding national trends for ACEI/ARB

Abbreviations: ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; NAMCS, National Ambulatory Medical Care Survey; ADA, American Diabetes Association; OR, odds ratio; CI, confidence interval; NCHS, National Center for Health Statistics.

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prescriptions in the diabetic population is lacking. The objective of the study was to determine if there was an association between the proportion of visits with a prescription for ACEI/ARB medications and the year of visit in adult diabetic patients who participated in the National Ambulatory Medical Care Survey (NAMCS) between the years 2007–2010. Additionally, several demographic and comorbidity variables were analyzed to determine their effect on receipt of medication.

Methods

Data Source

This study was a retrospective, cross-sectional, observational analysis of data collected in the NAMCS. The NAMCS is an annual, national probability sample of visits made to the offices of non-federally employed physicians classified by the American Medical Association or the American Osteopathic Association as “office-based, patient care”. Physicians in the specialties of anesthesiology, pathology and radiology are excluded. Further details on the types of contact excluded can be found at (http://www.cdc.gov/nchs/ahcd/ahcd_scope.htm#namcs_scope). The survey has been conducted annually from 1973 to 1981, in 1985, and annually from 1989 to present. The multi-staged sample design is composed of 3 stages that involves probability samples of primary sampling units (PSUs), physician practices within PSUs, and patient visits within practices. Details of the sampling procedure can be found at (http://www.cdc.gov/nchs/ahcd/ahcd_scope.htm#namcs_scope).

The data collected included information on patient demographics, reasons for visit, vital signs, continuity of care, diagnosis for the visit, diagnostic screening services, health education, non-medication treatment, medications and immunizations, provider type, visit disposition, and time spent with provider. On average, for the years 2007–2010, approximately 68% of physicians sampled met the criteria required for database eligibility. The eligibility criteria include office based physicians who are principally engaged in patient care activities that are non-federally employed and are not in specialties of anesthesiology, pathology, or radiology. Of the eligible (in-scope) physicians, the average unweighted response rate was approximately 60% (McCaig and Burt, 2012).

NAMCS datasets from 2007 to 2010 were included in this study. Patients that were 18 years of age or older with an International Classification of Diseases, Ninth Revision (ICD-9) code for diagnosis of diabetes (249.00–250.93) in any of the diagnoses fields (DIAG1-DIAG3) or a ‘Yes’ response to the DIABETES variable were included in the final analysis dataset. Pregnant patients (ICD-9 code v22.2) or those diagnosed with angioedema (ICD-9 code 995.1) were excluded. Across the four years included in this study, a total of 13,590 raw patient visit records met the inclusion/exclusion criteria.

The survey data were analyzed using the sampled visit weight that is the product of the corresponding sampling fractions at each stage in the sample design. The sampling weights have been adjusted by NCHS for survey nonresponse as appropriate within each database, yielding an unbiased national estimate of visit occurrences, percentages, and characteristics (McCaig and Burt, 2012).

Because of the complex sample design, sampling errors were determined using the SAS SURVEYFREQ and SURVEYLOGISTIC procedures which take into account the clustered nature of the sample (Centers for Disease Control and Prevention, 2014). The appropriate SAS procedure options (NOMCAR and DOMAIN) to address missing data and to utilize domains to determine accurate variance estimates were implemented in the analyses as recommended by the NCHS.

This data was previously collected, de-identified and cleaned by the CDC and is available to the public at ftp://ftp.cdc.gov/pub/Health_Statistics/NCHS/Datasets/NAMCS/. The study was submitted to the Campbell University Institutional Review Board (IRB) and received an exemption.

Outcome Variable

The outcome variable of interest was ACEI/ARB prescription (Yes versus No), where the denominator was the number of cases meeting the inclusion/exclusion criteria. ACEI/ARB prescription was defined by a code of ‘042’ or ‘056’ for any of the level 2 Multum database drug category variables (<http://www.multum.com> 2013).

Independent Variables

The choice of independent variables was made based on factors determined to be relevant to ACEI/ARB prescription in diabetics but was limited by the data available in the NAMCS surveys. The selected variables and information on their coding is located in Table 1. Note that tobacco use was excluded from all analyses due the high percentage (>30%) of missing data.

Statistical analysis

A series of weighted odds ratios (ORs) and corresponding 95% confidence intervals (CIs) were analyzed and reported to determine whether there was any association between ACEI/ARB prescription (Yes vs. No) and each of the independent variables shown in Table 1 in adult patients with diabetes. The term ‘weighted’ refers to the NCHS determined survey design weights that allow extrapolation of the raw data to national estimates.

A multivariable logistic regression model was also constructed for ACEI/ARB prescription in order to evaluate the predictive value of each independent variable, adjusting for covariates of interest. As a primary

Table 1
Demographics/Patient Characteristics of Diabetic Patients in the NAMCS, 2007–2010^a.

| Variable | Number of Patient Visits (%) |
|------------------------|------------------------------|
| Race | |
| Other | 15,380,788 (4.7) |
| Black | 49,212,081 (14.9) |
| White | 265,913,006 (80.5) |
| Sex | |
| Female | 240,904,506 (53.5) |
| Male | 209,517,989 (46.5) |
| Ethnicity | |
| Hispanic/Latino | 41,692,227 (12.8) |
| Not Hispanic/Latino | 284,077,272 (87.2) |
| Age Group | |
| 18–39 | 31,603,090 (7.0) |
| 40–54 | 97,941,690 (21.7) |
| 55 + | 320,877,715 (71.2) |
| Payment Type | |
| Other ^b | 23,173,473 (5.3) |
| Medicaid | 36,537,103 (8.3) |
| Medicare | 201,495,671 (45.9) |
| Private | 178,194,033 (40.6) |
| Region | |
| Midwest | 99,830,986 (22.2) |
| Northeast | 79,311,364 (17.6) |
| West | 85,928,435 (19.1) |
| South | 185,351,710 (41.2) |
| Hypertension | |
| Yes | 288,771,724 (64.1) |
| No | 161,650,771 (35.9) |
| Ischemic Heart Disease | |
| Yes | 48,481,513 (10.8) |
| No | 401,940,982 (89.2) |
| Hyperlipidemia | |
| Yes | 185,793,309 (41.2) |
| No | 264,629,186 (58.8) |
| Chronic Renal Failure | |
| Yes | 25,925,596 (5.8) |
| No | 424,496,899 (94.2) |

^a Weighted data. Reference groups are listed last for each variable.

^b Other insurance type includes worker’s compensation, self-payment, and no charge.

model filter, only variables with an overall chi-square test p-value <0.2 were included in the multivariable model. Weighted, adjusted ORs with corresponding 95% CIs for each level of each variable included in the model (in comparison to each variable's reference group) were reported. The term 'adjusted' refers to the effect of the covariates in the model on the other variables. All analyses were conducted with SAS version 9.3 (Copyright © 2012 SAS Institute Inc.) Per NCHS recommendations, any variable i) missing more than 30% of its data ii) with a survey estimate based on less than 30 records or iii) with a relative standard error (RSE) of more than 30% was excluded from the analyses due to potential unreliability. As this was a retrospective, hypothesis generating study, no adjustments for multiple comparisons were made.

Results

An unweighted total of 13,590 visits were identified for adult patients with diabetes without contraindications to ACEIs or ARBs in the NAMCS between the years of 2007 and 2010 (Table 1). Accounting for the weighting, the majority of patients were white (80.5%), female (53.5%), 55 or older (71.2%) and not Hispanic/Latino (87.2%). Approximately 64.1% of the study population had hypertension, 41.2% had hyperlipidemia, 10.8% had IHD and 5.8% had chronic renal failure (CRF).

While the proportion of visits with ACEI/ARB prescriptions in adult diabetic patients who participated in the NAMCS in 2007–2010 was increasing (28.1% in 2007 to 32.2% in 2010), all of the confidence intervals for the odds ratios of each year compared to 2007 contained unity, suggesting no significant difference in the proportion across survey years (Table 2).

Based on individual weighted ORs and their associated CIs, several of the predictor variables of interest were found to be significantly associated with the proportion of visits with an ACEI/ARB prescription (Table 3). Females (OR 0.76, 95% CI 0.69–0.84), patients 40–54 (vs 55+) (OR 0.84, 95% CI 0.73–0.97), patients 18–39 (vs 55+) (OR 0.37, 95% CI 0.29–0.48), Medicaid/SCHIP users (vs private payers) (OR 0.78, 95% CI 0.62–0.97) and those with "Other" form of payment (vs private payers) (OR 0.76, 95% CI 0.60–0.96) were all significantly less likely to be prescribed an ACEI/ARB. Conversely, patients visiting physician offices in the Northeast (OR 1.29, 95% CI 1.02–1.62) and the West (OR 1.23, 95% CI 1.01–1.49) were significantly more likely to be prescribed an ACEI/ARB than those in the South. In addition, hypertensive patients (OR 3.33, 95% CI 2.93–3.80), hyperlipidemic patients (OR 1.84, 95% CI 1.63–2.07) and patients with IHD (OR 1.67, 95% CI 1.38–2.01) were significantly more likely than those without each respective condition to be prescribed an ACEI/ARB.

According to the multivariable logistic regression analysis which adjusted for the covariates included in the model (Table 4), patients were significantly less likely to be prescribed an ACEI/ARB relative to the referent group if they were female (adjusted OR 0.78, 95% CI 0.69–0.88), aged 18–39 (adjusted OR 0.56, 95% CI 0.43–0.75) or on Medicare (adjusted OR 0.81, 95% CI 0.70–0.94). Conversely, based on the multivariable logistic regression model, patients were significantly more likely to be prescribed an ACEI/ARB relative to the referent group if they had hypertension (adjusted OR 2.81, 95% CI 2.40–3.29), hyperlipidemia

Table 2
Individual Chi-Square Results of ACEI/ARB Prescriptions by Year for Diabetic Patients in the NAMCS, 2007–2010^a.

| Variable | ACEI/ARB Prescription n (%) ^b | Overall p-value OR (95% CI) |
|----------|--|-----------------------------|
| | | 0.1789 |
| 2010 | 35,958,841 (32.2) | 1.22 (0.99, 1.50) |
| 2009 | 40,049,037 (30.4) | 1.12 (0.91, 1.38) |
| 2008 | 30,007,234 (28.3) | 1.01 (0.83, 1.24) |
| 2007 | 28,382,266 (28.1) | Referent |

^a Analyses appropriately weighted and clustered to reflect national estimates.

^b Percent in each stratum of variable.

Table 3
Individual Chi-Square Results for Predictors of ACEI/ARB Prescriptions for Diabetic Patients in the NAMCS, 2007–2010^a.

| Variable | ACEI/ARB Prescription n (%) ^b | Overall p-value OR (95% CI) |
|------------------------|--|-----------------------------|
| Race | | 0.7694 |
| Other | 5,040,051 (32.8) | 1.13 (0.82, 1.55) |
| Black | 14,916,110 (30.3) | 1.01 (0.83, 1.22) |
| White | 80,318,053 (30.2) | Referent |
| Sex | | <0.0001 |
| Female | 65,414,653 (27.2) | 0.76 (0.69, 0.84) |
| Male | 68,982,725 (32.9) | Referent |
| Ethnicity | | 0.1052 |
| Hispanic/Latino | 11,323,979 (27.2) | 0.84 (0.68, 1.04) |
| Not Hispanic/Latino | 87,418,363 (30.8) | Referent |
| Age Group | | <0.0001 |
| 18–39 | 4,669,615 (14.8) | 0.37 (0.29, 0.48) |
| 40–54 | 27,591,438 (28.2) | 0.84 (0.73, 0.97) |
| 55+ | 102,136,325 (31.8) | Referent |
| Payment Type | | 0.0231 |
| Other ^c | 5,791,478 (25.0) | 0.76 (0.60, 0.96) |
| Medicaid/SCHIP | 9,251,717 (25.3) | 0.78 (0.62, 0.97) |
| Medicare | 61,378,898 (30.5) | 1.00 (0.89, 1.13) |
| Private | 54,217,361 (30.4) | Referent |
| Region | | 0.0752 |
| Midwest | 30,980,923 (31.0) | 1.20 (0.98, 1.46) |
| Northeast | 25,817,965 (32.6) | 1.29 (1.02, 1.62) |
| West | 27,050,280 (31.5) | 1.23 (1.01, 1.49) |
| South | 50,548,210 (27.3) | Referent |
| Hypertension | | <0.0001 |
| Yes | 109,397,454 (37.9) | 3.33 (2.93, 3.80) |
| No | 24,999,924 (15.5) | Referent |
| Hyperlipidemia | | <0.0001 |
| Yes | 69,459,880 (37.4) | 1.84 (1.63, 2.07) |
| No | 64,937,498 (24.5) | Referent |
| Ischemic Heart Disease | | <0.0001 |
| Yes | 19,414,863 (40.0) | 1.67 (1.38, 2.01) |
| No | 114,982,515 (28.6) | Referent |
| Chronic Renal Failure | | 0.1863 |
| Yes | 8,701,625 (33.6) | 1.20 (0.91, 1.58) |
| No | 125,695,753 (29.6) | Referent |

^a Analyses appropriately weighted and clustered to reflect national estimates.

^b Percent in each stratum of variable.

^c Other insurance type includes worker's compensation, self-payment, and no charge.

(adjusted OR 1.42, 95% CI 1.22–1.64) or IHD (adjusted OR 1.36, 95% CI 1.10–1.70). Second order interaction terms were investigated, found to contribute nothing significant to the understanding of the overall results and were excluded from the final reported model.

Discussion

While no statistically significant difference was found in the prescribing rates of ACEI and ARBs in adult diabetic patients included in the NAMCS during the years 2007 to 2010, the prescribing rate did consistently increase from 28.1% in 2007 to 32.2% in 2010. However, across all four years, only 29.6% of the study population received a prescription. These results indicate that though adherence to the ADA guidelines as they pertain to ACEI/ARB prescribing appears to be improving, the guidelines are not being implemented as indicated for the diabetic population. These results, based on the most recently available data, are suggestive of a lower prescription rate of these medications as compared with previous studies which found 43% of the older diabetic population received appropriate therapy when indicated (Rosen, 2006). In addition the Rosen study found that only 53% of patients in the highest risk categories received ACEI/ARB therapy. These percentages are higher than those found in the present study, which found only an average of 29.6% of the study population to receive an ACEI/ARB prescription.

Cardiovascular disease risk factors, such as hypertension, are known to be widespread in diabetic patients (Goldberg, 2003). However, despite 64.1% of patients having hypertension, only 37.9% of these patients

Table 4
Multivariable Logistic Regression Model of ACEI/ARB Prescription for Diabetic Patients in the NAMCS, 2007–2010^a.

| Variable | Adjusted OR (95% Wald CI) |
|------------------------|---------------------------|
| Year | |
| 2010 | 1.17 (0.94, 1.47) |
| 2009 | 1.12 (0.87, 1.43) |
| 2008 | 0.98 (0.77, 1.26) |
| 2007 | Referent |
| Age | |
| 40–54 | 0.87 (0.72, 1.05) |
| 18–39 | 0.56 (0.43, 0.75) |
| 55 + | Referent |
| Payment Type | |
| Other ^b | 0.80 (0.62, 1.03) |
| Medicaid/SCHIP | 0.91 (0.71, 1.17) |
| Medicare | 0.81 (0.70, 0.94) |
| Private | Referent |
| Sex | |
| Female | 0.78 (0.69, 0.89) |
| Male | Referent |
| Region | |
| West | 1.23 (0.94, 1.60) |
| Midwest | 1.10 (0.88, 1.37) |
| Northeast | 1.19 (0.85, 1.67) |
| South | Referent |
| Hypertension | |
| Yes | 2.80 (2.39, 3.29) |
| No | Referent |
| Hyperlipidemia | |
| Yes | 1.42 (1.22, 1.65) |
| No | Referent |
| Ischemic Heart Disease | |
| Yes | 1.36 (1.10, 1.70) |
| No | Referent |
| Chronic Renal Failure | |
| Yes | 1.06 (0.77, 1.45) |
| No | Referent |

^a Analyses appropriately weighted and clustered to reflect national estimates.

^b Other insurance type includes worker's compensation, self-payment, and no charge.

received a prescription for an ACEI/ARB, which is the recommended first line therapy. This is alarming due to the fact that hypertension contributes to cardiovascular disease, which causes approximately 70% of deaths associated with diabetes. Thus, prevention in this subset of the diabetic population is critical in decreasing mortality (Basina and Kraemer, 2002). Conversely, 10.8% of patients had IHD yet 40.0% received an ACEI/ARB prescription. These results suggest that physicians are more likely to follow the ADA recommendations in patients with known cardiovascular disease but are not taking the appropriate preventive measures in the high risk population.

There is an enormous economic burden associated with the extensive complications from diabetes. Although hyperlipidemia is not directly correlated with ACEI/ARB usage, it is correlated with the risk of developing cardiovascular disease; therefore it is also interesting to note that patients with hyperlipidemia were significantly more likely to receive a prescription. Effective preventive measures should be taken and proper medication management should be implemented to aid in the reduction of this fiscal burden (Sequist, 2014).

Not surprisingly, age also appears to have an important association with ACEI/ARB prescribing, as the 2007 ADA guidelines recommended that patients over the age of 55 with a cardiovascular risk factor such as hypertension, smoking, dyslipidemia or history of cardiovascular disease be given an ACEI/ARB in order to reduce the risk of a cardiovascular event (American Diabetes Association, 2007). In 2008 and 2009, this age cutoff was reduced to 40 (American Diabetes Association, 2008; American Diabetes Association, 2009). In our study, patients 55 or older received a higher percentage of ACEI/ARB prescriptions than either of the other age groupings, which is in line with the established recommendations. Payment type and gender were also determined to

have an association with ACEI/ARB prescriptions. The significant payment type associations suggest that disparities between prescribing rates of these medications still exist and parallels previous research highlighting differences in diabetic treatment based on payment type (Devoe et al., 2009). The differences in prescribing patterns between genders in this study highlight another disparity. Previous research indicates that female diabetic patients experience higher rates of all-cause mortality, with CVD mortality remaining higher in this subset than either gender without diabetes (Arnetz et al., 2014). Conversely, our study determined that females were less likely than males to receive medications that prevent these problems. Due to the gender differences identified in this study, as well as notable gender differences in the progression of CVD, future research that includes separate analyses based on gender may be warranted to determine if similar trends are identified in each gender separately.

Similar to Rosen et al. which looked at national prevalence trends using the Kaiser Permanente Northern California Diabetes Registry, no differences in prescriptions were found in race and ethnicity. Rosen et al. did identify disparities in black diabetic patients with albuminuria receiving significantly less ACEI/ARB prescriptions; however the current study did not examine this subset of individuals for comparison (Rosen et al., 2004).

Research performed in other health care settings have shown that ACEI/ARB usage can be as high as 74% in patients that have both diabetes and hypertension, demonstrating that compliance to guidelines can be achieved (Rosen et al., 2004). This study's findings indicate that there is still room for improvement in diabetes care and management when analyzing a national subset of ambulatory care patients in the US. Previous research suggests that guidelines and treatment algorithms be simplified to allow additional patients to receive effective diabetes treatment (Rosen, 2006). Additionally, Toth et al. suggests that treatment goals that are presented in guidelines may need to become more realistic and applicable in clinical practice (Toth et al., 2003). Diabetic patients often have multiple disease states that require the use of numerous medications in order to obtain control, which results in polypharmacy. Incorporating patient commitment and compliance into the development of treatment regimens is also important in the prevention of diabetic complications (Winocour, 2002). Using the most effective regimens that include the proper medications can ensure patients achieve optimal targets and outcomes.

Strengths and Limitations

Due to the nature of the NAMCS survey, it was not possible to assess compliance with the medication, only receipt of the prescription. Also, the survey limits the number of medications that can be reported which may not adequately capture every drug that a patient is prescribed. Despite these limitations, the study utilized data from the NAMCS, which is a nationally renowned database that weights and clusters data, allowing for findings to be extrapolated to the national population. Further, this study was also the first, to our knowledge, to examine the effectiveness of recent national guidelines as well as to assess disparities in receipt of these pharmacological treatments based on the most current publicly available data.

Conclusion

Although an increase in ACEI/ARB prescribing rates over the years was identified, there is still progress to be made in the utilization of these drug classes in diabetic patients in order to comply with current ADA guidelines. Despite an apparent increase in the proportion of prescriptions in recent years, there are still large percentages of diabetic patients with known indications who are not receiving appropriate treatment. This study highlights the need for additional research into the low ACEI/ARB prescription rates in the diabetic population, with particular emphasis on females and the younger aged population.

Conflict of interest statement

The authors declare that there are no conflicts of interest.

Transparency document

The [Transparency document](#) associated with this article can be found, in online version.

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