Published in final edited form as:
Hypertension. 2012 August ; 60(2): 303–309. doi:10.1161/HYPERTENSIONAHA.112.192096.

The Association between Medication Adherence and Treatment Intensification with Blood Pressure Control in Resistant Hypertension

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Abstract

Patients with resistant hypertension are at risk for poor outcomes. Medication adherence and intensification improve blood pressure control; however, little is known about these processes or their association with outcomes in resistant hypertension. This retrospective study included patients from 2002-2006 with incident hypertension from two health systems who developed resistant hypertension, or uncontrolled blood pressure despite adherence to ≥3 antihypertensive medications. Patterns of hypertension treatment, medication adherence (percentage of days covered) and treatment intensification (increase in medication class or dose) were described in the year after resistant hypertension identification. Then, the association between medication adherence and intensification with 1-year blood pressure control was assessed controlling for patient characteristics. Of the 3,550 patients with resistant hypertension, 49% were male and mean age 60. One year after resistance hypertension determination, fewer patients were taking diuretics (77.7% vs. 92.2%, p<0.01), beta blockers (71.2% vs. 79.4%, p<0.01) and ACE/ARB (64.8% vs. 70.1%, p<0.01) compared to baseline. Rates of blood pressure control improved over 1-year (22% vs. 55%, p=<0.01). During this year, adherence was not associated with 1-year blood pressure control (adjusted OR 1.18, 0.94-1.47). Treatment was intensified in 21.6% of visits with elevated blood pressure. Increasing treatment intensity was associated with 1-year blood pressure control (adjusted OR 1.64; 95% CI 1.58-1.71). In this cohort of patients with resistant hypertension, treatment intensification but not medication adherence was significantly associated with 1-year blood pressure control. These findings highlight the need to investigate why patients with uncontrolled blood pressure do not receive treatment intensification.

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DISCLOSURES

All authors report no conflicts on interest in regards to this manuscript.

Keywords

Hypertension; Resistant; Adherence; Intensification

INTRODUCTION

Hypertension is the most common cardiovascular risk factor worldwide and uncontrolled blood pressure is associated with worse cardiovascular outcomes.[1-4] Patients with resistant hypertension represent a subset of hypertensive patients whose blood pressure remains uncontrolled despite the optimal use of 3 or more medications.[5] It is generally believed that resistant hypertension patients are at even greater risks for poor outcomes compared to the general hypertension population.[5, 6] Therefore, BP control is even more important to achieve among patients with resistant hypertension, however, the factors associated with BP control have not been well described in this patient population.

Medication adherence and therapy intensification have been identified as important factors in achieving blood pressure control in general hypertension populations.[7-12] However, little is known regarding either therapy adherence or intensification among patients identified as having truly resistant hypertension based on the AHA scientific statement.[13, 14] Patients with resistant hypertension are prescribed multiple antihypertensive medications increasing their risk for poor adherence.[15] In addition, by definition, patients with resistant hypertension are already taking multiple medication classes and providers may be less likely to intensify therapy given limited therapeutic options. Further, some studies have suggested that evidence-based and guideline recommended antihypertensive classes such as diuretics may be underused among patients with resistant hypertension.[5, 16, 17] Describing patterns of medication class use, medication adherence and therapy intensification in a population of resistant hypertension patients is important for targeting future interventions aimed at improving hypertension outcomes.

Accordingly, among a cohort of patients with resistant hypertension treated within two large integrated health care delivery systems, we sought to describe their medication class use, medication adherence and treatment intensification in the year following identification of resistant hypertension. Next, we assessed the relationship between treatment adherence and therapy intensification with subsequent blood pressure control adjusting for patient and clinical characteristics. Understanding the relationship between these factors and hypertension control will inform interventions aimed at improving blood pressure outcomes among patients with resistant hypertension.

METHODS

Study Population

The study sample was identified from two health plans within the Cardiovascular Research Network (CVRN) hypertension registry from 2002-2006. The development of the CVRN hypertension registry has been described in detail elsewhere.[18, 19] In brief, patients with hypertension at Kaiser Permanente Colorado and Kaiser Permanente Northern California were identified using a published algorithm consisting of ICD-9 diagnosis codes, blood pressure (BP) measurements (from non-urgent visits), and pharmacy data.[20] The current analysis only includes patients with incident hypertension being started on anti-hypertensive medication who were subsequently identified as having resistant hypertension based on the American Heart Association scientific statement.[5] As described previously by our group in detail, incident hypertension was defined as being a member of the health plan for at least 1 year prior to meeting criteria for the registry without any prior diagnosis of hypertension and

without any prior pharmacy dispensing for anti-hypertensive medications.[21] Patients were then determined to have resistant hypertension based on their number of medications filled, blood pressure measurements, and medication adherence data over the year following initiation of treatment. Those patients who continued to have uncontrolled blood pressure despite 3 or more medications (or controlled on 4 or more medications) who were adherent to medications were deemed to have resistant hypertension. Patients who disenrolled from the health plan (n=17), died (n=53) within 12 months, or did not have at least 6 months of follow up (n=340) after the date resistance hypertension was determined were excluded. For this analysis, we followed patients for one year following the date that they were determined to have resistant hypertension to assess medication adherence, treatment intensification and their association with 1-year blood pressure control. (See Figure S1)

Medication use and blood pressure information

Medication dosing and class information was obtained from pharmacy dispensing databases. Medication classes studied included beta blockers, angiotensinogen converting enzyme inhibitors (ACE) or angiotensin receptor blockers (ARB), diuretics (thiazide, K-sparing, loop and CAI), alpha adrenergic blockers and peripheral vasodilators. For each medication, dosing was further characterized as the percentage of recommended maximum daily dose based on Micromedex® 2.0 dosing information for the treatment of hypertension.

Blood pressure values were obtained from each patient's electronic medical record. To avoid spuriously high values, we excluded all measurements that occurred in an inpatient setting on the day of a procedure (where BP medications may have been temporarily held) or during an emergency department visit (where pain or other emergent conditions may cause temporary elevations in BP). For this analysis, only systolic blood pressures (SBP) were used because resistant hypertension is most often due to uncontrolled SBP and SBP has a stronger association with outcomes than diastolic BP.[5, 22]

Medication Adherence

Medication adherence was calculated as the proportion of days covered (PDC), based on the number of days of BP medication supply divided by the numbers of days in the observation interval. For patients receiving multiple BP medications, an average PDC was calculated across all medications. Patients with a summary adherence measure of greater than 80% were considered adherent.[23] We were unable to calculate a PDC on 2 patients who had insufficient medication supply and they were therefore excluded from this analysis.

Treatment Intensification

Treatment intensification (TI) was calculated using a standard-based method score, as characterized by Rose et al.[24] The TI score assesses the number of times that treatment intensification appropriately occurs. The TI score is calculated by taking the number of observed treatment intensifications minus the number of expected TI divided by the number of clinic visits with SBP measurements over the observation period. For this analysis, we only included SBP measurements that occurred in specific departments (Family practice, Internal Medicine, OB/GYN, Cardiology or Nephrology) to avoid values measured in departments for which blood pressure management is not a routine part of clinical practice. Observed TI was the number of times a previously prescribed antihypertensive medication dose was increased or an antihypertensive medication class was added in the 4 weeks after the occurrence of an elevated SBP. We allowed a grace period of 4 weeks after the measurement of an elevated SBP to allow for the clinical scenario when providers may be waiting for any prior treatment intensification to take effect before taking further clinical action or for a new medication dispensing to be required if patients are told to increase the dose of a previously dispensed medication.[10] Expected TI was the number of visits when the

measured SBP was elevated above the target goal. Accordingly, the TI score could range from -1.0 to +1.0, with -1 indicating no treatment intensification at any visit where the SBP was elevated, 0 indicating treatment intensification at every visit where the SBP was elevated, and 1 indicating treatment intensification at every visit regardless of the SBP level. Patients with missing follow-up blood pressure information (n=762, 21%) were excluded from this analysis.

For all TI analyses, we assessed for treatment intensification only when the measured SBP was 5 mm Hg or more above the JNC VII goal (i.e. 135 mm Hg or more for patients with DM or renal disease, 145 mm Hg or more for all others) to account for potential clinical ambiguity in intensifying therapy when the SBP is only a few mm Hg above the target goal.[10]

Outcome

The outcome of interest was SBP control based on the blood pressure occurring closest to 1-year after meeting resistant hypertension criteria. In the primary analysis, elevated SBP was defined according to JNC7 thresholds of systolic blood pressure (SBP) ≥140 mm Hg with lower cut-offs of SBP ≥130 mm Hg for those with diabetes mellitus or chronic kidney disease.[22] In secondary analysis, we increased the cutoffs of SBP to define the outcome of blood pressure control by 5 mm Hg (SBP <145 mm Hg or SBP <135 mm Hg for those with DM or CKD).

Statistical Analysis

Baseline characteristics of all patients with resistant hypertension were described using frequencies, means and medians. Medication class use at baseline and follow up were compared using chi-squared tests. Finally, for each patient, the averaged percentage of recommended maximal daily dosing for their antihypertensive medications was compared at baseline and follow up using the paired T test.

In the primary outcome analysis, multivariable logistic regression models assessed the association between adherence and treatment intensification with subsequent blood pressure control 1-year after resistant hypertension identification adjusting for patient demographics, coexisting conditions, year of cohort entry, study site, blood pressure at time of resistance status determination and number of blood pressures over follow-up. Patients without a blood pressure measurement within 455 days of resistance status determination (n=762, 21%) were excluded from the outcomes analysis.

In additional analysis, based on prior literature suggesting variations in BP control in certain groups, we investigated whether SBP control varied significantly among the prespecified subgroups of gender, race, diabetes, chronic kidney disease, and medication class.[1, 25-29]

All analyses were performed using the SAS statistical package version 9.2 (SAS Institute, Cary, NC). The study was approved by the institutional review board of both health plans.

RESULTS

Of the 3,550 patients with resistant hypertension, 49% were men, 61% were white, and the median age was 60 (25^{th} quartile =51, 75^{th} quartile =70). The most common co-morbidity was diabetes (17%) followed by depression (9%) and asthma (9%). (Table 1) Compared with their antihypertensive regimen at the time of being classified as having resistant hypertension, one year later fewer patients were taking diuretics (77.7% vs. 92.2%, p<0.01), beta blockers (71.2% vs. 79.4%, p<0.01), ACE/ARB (64.8% vs. 70.1%, p<0.01) and adrenergic blockers (12.5% vs. 13.4%, p = 0.02) compared to baseline. The use of calcium

channel blockers (35.2% vs. 35.4%, p=0.85) and peripheral vasodilators (3.0% vs. 2.9%, p=0.91) did not significantly change from baseline to follow-up. On average, at baseline patients were taking 38.4% (95% CI 37.8-39.0%) of maximal recommended daily dosing compared to 43.2% of maximal recommended daily dosing (95% CI 42.4-43.9%) for hypertension 1-year later (p<0.0001 for comparison).

Medication Adherence

Over the year following resistance status determination, median medication adherence rates were 84.7% (25^{th} quartile 68.5%, 75^{th} quartile 94.9%) among the 3,548 patients with medication refill information. Over half of patients (57.6%) met our criteria for medication adherence by achieving a summary adherence measure of greater than 80%.

Treatment Intensification

Among the 2,788 patients with resistant hypertension who had follow-up blood pressure information, there were 13,653 visits (median visits per patient = 4) in which blood pressure was measured in the year following resistant hypertension identification. Almost all (99.5%) of these visits were in primary care (Family Practice, Internal Medicine or OB/GYN) with the remaining visits occurring in Cardiology. The majority (84.6%) of patients had at least one visit with an elevated blood pressure over the follow-up period (median number of visits with an elevated blood pressure per patient = 2). Treatment intensification (class addition or dosage increase) occurred in only 21.6% of visits with an elevated blood pressure. Of the 2,788 patients in the analysis, 10% of patients had a class addition and 32% had a dose increase. The median treatment intensification (TI) score was –0.43 (25^{th} quartile –0.67, 75^{th} quartile -0.13) indicating that most visits with an elevated BP were not associated with subsequent treatment intensification.

Outcomes

Among patients included in the primary outcomes analysis (n=2788), blood pressure control improved from the time of resistant hypertension identification to 1 year of follow-up (22% vs. 55%, p<0.01). In the unadjusted analysis, medication adherence was marginally associated with blood pressure control (OR 1.21, 95% CI 1.00-1.47, p=0.05). In the fully adjusted model, the association between medication adherence and blood pressure control was no longer significant (adjusted OR = 1.18, 95% CI 0.94-1.47, p=0.15).

In unadjusted analysis, increasing BP treatment intensity was significantly associated with better BP control. For each 0.1 increase in the TI score (indicating more intensive BP treatment), the odds of having controlled blood pressure at one year increased by 60% (OR = 1.60, 95% CI 1.54- 1.66, p<0.01). This relationship persisted in the multivariable models (OR= 1.64, 95% CI 1.58-1.71, p<0.01). In secondary analysis using a higher BP cutoff to define control (<135 mm Hg for DM and CKD, <145 mm Hg for all others), increasing treatment intensification remained significantly associated with blood pressure control (OR 1.66, 95% CI 1.59-1.73, p<0.01).

In additional analysis evaluating factors associated with BP control among resistant hypertension patients, gender (p=0.59), race (p=0.46), diabetes mellitus (p=0.71) and CKD (p=0.25) were not associated with BP control. In regards to medications class use 1-year after resistance status determination, use of an ACE/ARB, calcium channel blocker or adrenergic blocker was associated with less BP control (OR 0.74, 95% CI 0.59- 0.94; OR 0.79, 95% CI 0.64-0.97; OR 0.70, 95% CI 0.52-0.94, respectively); while the use of any diuretic was significantly associated with blood pressure control (OR 1.64, 95% CI 1.27-2.12). (Table 2)

DISCUSSION

Among this cohort of patients with resistant hypertension followed in 2 large integrated healthcare systems, only 55% achieved blood pressure control one year later. The use of many antihypertensive medication classes declined over one year, including diuretics. The majority of resistant hypertension patients were adherent to their antihypertensive medications and on average, they received less than expected treatment intensification over the 1-year of follow-up. Treatment intensification, but not therapy adherence, was significantly associated with 1-year blood pressure control.

Despite recognition of the importance of resistant hypertension by the AHA and others, this group of patients has been relatively poorly described.[5, 6, 14, 30-32] Our study expands the current literature by studying a large population of resistant hypertension patients identified within both general and subspecialty clinics using current clinical guidelines.[5] Further strengths of this study include our ability to longitudinally follow patients using detailed medication and clinical information allowing a description of medication adherence and therapy intensification and their association with blood pressure control.

In the current study, we have shown that the use of many classes of antihypertensive medications decreases one year after resistant hypertension identification. Importantly, one of the largest declines was in diuretic use; over 90% of the patients were prescribed any diuretic at baseline but only 78% remained on a diuretic one year later ($p<0.01$). Patients with resistant hypertension are thought to have inappropriate volume expansion and therefore, the AHA criteria for resistant hypertension state that these patients should ideally be on a diuretic.[5, 33] In fact, studies have shown that optimizing diuretic therapy was the most common means of improving blood pressure control in patients with resistant hypertension.[14] Similarly, in additional analysis, we have demonstrated that diuretic use tended to be associated with improved blood pressure control (OR1.64, 95% CI 1.27-2.12). Taken together, these studies support the importance of treating patients with resistant hypertension with diuretics and future work should investigate why some patients were no longer filling this important class of medications.

Another important finding of this study is the persistently low rates of blood pressure control seen among resistant hypertensive patients. Only 55% of patients had their blood pressure controlled one year after resistant hypertension identification. In another cohort (n=141) of patients referred to a hypertension subspecialty clinic, Garg et al. similarly reported that 53% of patients identified as having resistant hypertension subsequently had their blood pressure controlled.[14] Identifying low rates of hypertension control among a resistant hypertension population is significant as poor blood pressure control is associated with worse cardiovascular outcomes.[1-4] Understanding potential contributors to poor blood pressure control among this population is a crucial first step to potentially improve their outcomes.

Our study is one of the first to investigate both medication adherence and treatment intensification and their relationships with blood pressure control in a broad population of patients with resistant hypertension. Overall, the majority of our patients with resistant hypertension were adherent (median adherence 85%) to their antihypertensive medications over one year of follow-up. In accordance with the AHA definition of resistant hypertension, we purposely selected a population of patients with “true” resistant hypertension excluding patients who were deemed to have “pseudoresistant” hypertension, or uncontrolled blood pressure due to poor medication adherence in the year prior to entry.[21] Importantly, one year later, 42% of patients in our study cohort no longer met criteria for high adherence (>80% PDC) suggesting significant drops in adherence occurred in a previously adherent group.

These findings highlight the importance of continued monitoring of adherence and suggest that as regimens become more complex, patient adherence may decline. Overall, we found no significant association between patient medication adherence and eventual blood pressure control. Another study of 44 patients with "true" resistant hypertension found high rates of medication adherence (94%) over follow up and no significant association between medication adherence and subsequent blood pressure control.[13] Together, these findings suggest that poor blood pressure control in "true" resistant hypertension patients is not largely due to their failure to take medications.

One of the most important findings of our study is an investigation of appropriate therapy intensification among resistant hypertensive patients. Over one year of follow–up, the average patient with resistant hypertension received less than expected intensification of either their medication class or dose despite having opportunities for intensification (blood pressure visits) and documentation of elevated blood pressures. Garg et al. similarly found that a suboptimal medication regimen was common, accounting for 57% of those referred to their subspecialty clinic for resistant hypertension.[14] In this same study, the largest improvement in hypertension control was seen among those whose blood pressure medications were optimized over follow-up. Similarly, we have shown a significant relationship between increasing degrees of treatment intensification and subsequent blood pressure control further supporting the importance of medication intensification for achieving blood pressure control in this population. Based on the literature from general hypertension populations, potential reasons for less than expected treatment intensification in our study may include clinical inertia and competing demands of co-morbid conditions.[34-38] Another potential reason for less than expected treatment intensification may be blood pressure levels felt to be "close enough" to control levels. In secondary analysis, we allowed higher cut off values of SBP to define BP control and found similarly lower than expected degrees of treatment intensification. Failure to intensify therapy may also be related to a lack of evidence to support the efficacy of adding additional agents to those already on 3 or more antihypertensive classes.[5] This lack of evidence may in part contribute to therapeutic nihilism, or skepticism about the benefit of efforts to intensify therapy in patients who are already taking multiple antihypertensives. However, we also demonstrated that, on average, patients were taking <50% of the recommended maximal daily doses of their antihypertensive medications at follow-up suggesting room for dosage increases that do not require a class addition. Our findings highlight the importance of therapy intensification to improve BP control in patients with resistant hypertension and should encourage provides to attempt to optimize therapy in this population at high risk for poor cardiovascular outcomes.[21]

Certain limitations should be considered in the interpretation of the study results. First, this study relies on blood pressure measurements from an electronic medical record. However, we have shown that the algorithms used to identify hypertensive patients were valid and the analytic data accurately reflect the data in the charts.[19] Further, office based blood pressure measurements reflect current practice and are used routinely in the management of hypertension. Second, our medication adherence and treatment intensification estimations rely on pharmacy refill information. Similar to other studies using pharmacy dispensing data, we assumed that dispensed medications were consumed if the prescription was refilled, but could not determine whether prescribed medications were filled or if medications orders were discontinued.[39] However, pharmacy refill data is correlated with a broad range of clinical outcomes.[8, 9, 40] In addition, the act of refilling a medication is the necessary first step towards taking a medication and reflects the patients' active decision to continue with therapy.[39] Finally, the findings in these integrated healthcare systems may not apply to other healthcare settings. However, these 2 systems care for almost 4 million patients in geographically distinct areas and our population was drawn from an ambulatory population

of hypertension patients seen in both primary care and subspecialty clinics whereas most prior studies have primarily studied resistant hypertension in subspecialty clinic populations.

PERSPECTIVES

In this cohort of patients with resistant hypertension, treatment intensification but not medication adherence was significantly associated with 1-year BP control. Overall, the findings of this study have several clinical and research implications. First, rates of blood pressure control for patients with resistant hypertension were low; approximately 1 in 2 patients with resistant hypertension met blood pressure targets one year after identification. Given their higher risk for poor outcomes, efforts to improve control rates among this high risk population are important for preventing cardiovascular disease. Second, patients with resistant hypertension appear to have at least average medication adherence and unlike other hypertension populations, poor adherence does not appear to contribute to low rates of blood pressure control. Third, lower than expected treatment intensification was significantly associated with poor blood pressure control. Therefore, system changes directed at improving blood pressure control among patients with resistant hypertension should devote attention to understanding and improving appropriate treatment intensification.

Acknowledgments

None

FUNDING SOURCES

The Cardiovascular Research Network is supported by a grant from the National Heart Lung and Blood Institute (NHLBI) of the NIH (U19HL91179-01). Dr. Daugherty is supported by Award Number K08HL103776 from the National Heart, Lung and Blood Institute. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NHBLI or NIH. Dr. Daugherty and J. David Powers had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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Novelty and Significance: 1) What Is New, 2) What Is Relevant?

1. What Is New?

   - This is one of the first studies to investigate the relationship between medication adherence and treatment intensification with blood pressure control among a large population of patients with resistant hypertension identified within both general and subspecialty clinics.

2. What Is Relevant?

   - Patients with resistant hypertension are at high risk for poor outcomes.

   - Understanding potential causes of uncontrolled blood pressure in these high risk patients will help direct future efforts to improve their outcomes.

3. Summary

   - Treatment intensification but not medication adherence was significantly associated with improved blood pressure control.

   - Studies are needed to better understand and improve lower than expected treatment intensification among patients with resistant hypertension.

Table 1

Characteristics of cohort at the time of resistant hypertension identification.

Characteristic	N=3,550
Gender	
Male	49.4%
Race	
Black	8.1%
Missing	11.9%
Other	19.6%
White	60.5%
Age (Mean)	60.4 (60.0, 60.8)
Baseline Systolic BP (Mean)	140.2 (139.6, 140.7)
Baseline Diastolic BP (Mean)	77.7 (77.3, 78.0)
Body Mass Index (Mean)	30.8 (30.5, 31.1)
Current smoker	10.0%
Site	
Kaiser Northern California	94.4%
Kaiser Colorado	5.6%
Year of hypertension registry entry	
2000	2.7%
2001	16.2%
2002	38.6%
2003	20.3%
2004	12.1%
2005	7.1%
2006	3.0%
Baseline co-morbidities	
Albuminuria	0.7%
Alcohol abuse	3.5%
Angina	0.8%
Asthma	9.3%
Atrial fibrillation	2.8%
Bipolar	0.6%
Coronary Artery Bypass	0.7%
Congestive Heart Failure	1.8%
Chronic Kidney Disease	5.0%
Diabetes	17.4%
Depression	9.4%
Myocardial infarction	1.5%
Peripheral Vascular Disease	1.9%
Sleep apnea	2.0%
Stroke	2.5%

Characteristic	N=3,550
Hypertension Medications	
Beta Blockers	79.4%
ACE/ARB	70.1%
Diuretics	92.2%
Calcium Channel Blocker	35.4%
Alpha Adrenergic Blocker	13.4%
Peripheral Vasodilators	3.0%

Table 2

Predictors of one year blood pressure control among patients with resistant hypertension.

Effect	Adjusted OR (95% CI)	P-value
Treatment Intensification Score (per 0.1 unit)	1.64 (1.58, 1.71)	<0.01
Adherent vs. Non-adherent (≥80% PDC)	1.18 (0.94, 1.47)	0.15
Number of blood pressures over follow-up	0.99 (0.97, 1.01)	0.37
Medication classes at time of outcome BP status		
ACE/ARB	0.74 (0.59, 0.94)	0.01
Diuretic Thiazide, Loop, CAI or K-sparing	1.64 (1.27, 2.12)	<0.01
K-sparing diuretic only	0.81 (0.62, 1.08)	0.15
Beta blocker	0.88 (0.71, 1.10)	0.27
Calcium channel blocker	0.79 (0.64, 0.97)	0.03
Alpha 1 and 2 Adrenergic blocker	0.70 (0.52, 0.94)	0.02
Other (Peripheral Vasodilator and Reserpine)	0.75 (0.44, 1.27)	0.28
Demographics		
Gender - Male vs. Female	0.95 (0.77, 1.16)	0.59
Race		0.46
Black vs. White	1.16 (0.81, 1.66)	0.41
Missing vs. White	0.92 (0.64, 1.31)	0.63
Other vs. White	0.87 (0.68, 1.11)	0.25
Smoking status - current vs. not	0.99 (0.70, 1.38)	0.94
Age at index in years	1.00 (0.99, 1.01)	0.74
Hypertension registry entry year	1.10 (1.02, 1.19)	0.02
Baseline Co-morbidities		
Albuminuria	0.85 (0.29, 2.48)	0.76
Alcohol abuse	1.25 (0.73, 2.12)	0.42
Angina	2.01 (0.70, 5.79)	0.19
Asthma	1.03 (0.74, 1.42)	0.87
Atrial Fibrillation	1.17 (0.66, 2.05)	0.59
Bipolar	1.33 (0.38, 4.68)	0.66
Chronic Kidney Disease	0.78 (0.51, 1.20)	0.25
Diabetes Mellitus	0.96 (0.75, 1.22)	0.71
Depression	1.08 (0.77, 1.51)	0.65
Migraine	1.29 (0.66, 2.53)	0.46
Other Arrhythmias	0.93 (0.45, 1.91)	0.85
Peripheral Vascular Disease	1.34 (0.69, 2.60)	0.39
Schizophrenia	1.03 (0.18, 5.84)	0.98
Sleep Apnea	1.56 (0.74, 3.26)	0.24