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Differences in cardiovascular disease risk when antihypertensive medication adherence is assessed by pharmacy fill versus self-report:

The Cohort Study of Medication Adherence among Older Adults (CoSMO)

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Permission for use of MMAS-8 is required. Licensure agreement is available from Dr. Donald E. Morisky, Department of Community Health Sciences, University of California, Los Angeles, Fielding School of Public Health.

Author Contributions:

All authors listed on the manuscript meet the criteria for authorship stated in the Uniform Requirements for Manuscripts Submitted to Biomedical Journals. Contributions are as follows: Marie Krousel-Wood: study design and oversight, acquisition of study subjects and data, interpretation of data and preparation of article; Elizabeth Holt: analysis and interpretation of data and preparation of article; Cara Joyce, Adriana Dornelles, Rachael Ruiz: analysis and interpretation of data and review of article; Larry Webber: study design, data interpretation, article review; Edward D Frohlich and Richard N Re: adjudication of cardiovascular outcomes, interpretation of data, and article review; Donald Morisky, Jiang He and Paul K Whelton: interpretation of data and article review; Paul Muntner: study design, data interpretation, article preparation and review. Dr. Krousel-Wood had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Abstract

Background—Pharmacy refill adherence assesses medication-filling behaviors whereas self-report adherence assesses medication-taking behaviors. We contrasted the association of pharmacy refill and self-reported antihypertensive medication adherence with cardiovascular disease (CVD) incidence.

Methods and Results—Adults (n=2075) from the prospective Cohort Study of Medication Adherence among Older Adults (CoSMO) recruited between August 2006 and September 2007 were included. Antihypertensive medication adherence was determined using a pharmacy refill measure, Medication Possession Ratio-MPR (low, medium, high MPR: <0.5, 0.5 to <0.8, ≥0.8, respectively) and a self-reported measure, 8-item Morisky Medication Adherence Scale-MMAS-8 (low, medium, high MMAS-8: <6, 6 to <8, and 8, respectively). Incident CVD events (stroke, myocardial infarction, congestive heart failure, or CVD death) through February 2011 were identified and adjudicated. The prevalence of low, medium and high adherence was 4.5 %, 23.7%, and 71.8% for MPR and 14.0%, 34.3%, and 51.8% for MMAS-8. During a median 3.8 years follow-up, 240 (11.5%) people had a CVD event. After multivariable adjustment and compared to those with high MPR, the hazard ratios (HR) for CVD associated with medium and low MPR were 1.17 (95% confidence interval [CI] 0.87, 1.56) and 1.87 (95% CI: 1.06, 3.30), respectively. Compared to those with high MMAS-8, the HRs (95% CI) for MMAS-8 for medium and low MMAS-8 were 1.04 (0.79–1.38) and 0.89 (0.58–1.35), respectively.

Conclusions—Pharmacy refill but not self-report antihypertensive medication adherence was associated with incident CVD. The differences in these associations may be due to distinctions in what each adherence measure assesses.

Keywords

hypertension; cardiovascular disease; medication adherence; Medication Possession Ratio; MMAS-8

INTRODUCTION

Hypertension is a common risk factor for cardiovascular disease (CVD) morbidity and mortality [1]. Effective medical therapies exist to lower BP and reduce the risk for CVD; yet, suboptimal adherence persists as a major public health challenge with approximately 50% of patients not taking chronic medications as prescribed [2, 3]. Poor adherence to antihypertensive therapy has been associated with worse BP control, increased hospitalization rates, higher health care costs and lower survival [3–9].

To address this public health challenge, it is important to consider that adherence to prescribed medications includes 2 key patient behaviors: 1) filling medications and 2) taking medications as prescribed after they are filled. Although these behaviors are related, they may reflect distinct activities which may differ among individual patients[11–13]. Pharmacy refill adherence assesses whether patients fill their medications over specified time intervals whereas self-reported adherence assesses whether patients take their medications after they are filled. Prior studies have demonstrated poor adherence measured by pharmacy refill in hypertensive patients to be associated with an increased risk for CVD[4–8, 14]. Few studies

have reported on the association of low adherence, assessed by a self-reported antihypertensive medication adherence scale, on increased risk for CVD events[10]. To our knowledge no large study has examined differences in the association between antihypertensive medication adherence and CVD events using both validated objective and multi-item self-reported adherence measures.

In this study, we sought to determine the prospective association of pharmacy refill and, separately, self-reported antihypertensive medication adherence, with CVD events in older adults. We used a well-established objective measure of pharmacy refill adherence, the Medication Possession Ratio (MPR) and a validated multi-item self-report measure widely used in national and international research settings[3, 15, 16], the Morisky Medication Adherence Scale 8-item (MMAS-8).

METHODS

Study Population and Study Design

The Cohort Study of Medication Adherence in Older Adults (CoSMO) is a prospective cohort study of factors associated with antihypertensive medication adherence and CVD outcomes in elderly adults with established hypertension. The study design, response rates, and baseline characteristics have been published previously [3]. In brief, women and men aged 65 years or older with essential hypertension were randomly selected from the roster of a large managed care organization in southeastern Louisiana. From August 21, 2006 to September 30, 2007, 2,194 participants were recruited and completed the baseline survey [3]. The participants were followed through February 2011 to identify CVD events and mortality. The current analyses were limited to participants who had no hospitalizations for stroke, myocardial infarction (MI), or congestive heart failure (CHF) in the year prior to the administration of the baseline survey (N=2,075). CoSMO was approved by the Ochsner Clinic Foundation's Institutional Review Board and the privacy board of the managed care organization [3].

Data Collection Overview

Using an established conceptual framework of risk factors associated with antihypertensive medication adherence and clinical outcomes, we obtained data through participant surveys, medical records, administrative databases of the managed care organization, and vital records[17] (details below). Surveys were administered via telephone by trained interviewers.

Primary Exposures—The primary exposure was antihypertensive medication adherence [3, 17]. Medication adherence was measured objectively using pharmacy refill data to calculate the Medication Possession Ratio (MPR). For the main analyses, data were extracted for the year prior to the baseline survey from pharmacy utilization databases and included all antihypertensive prescriptions filled, date filled, drug class, and number of pills dispensed used to calculate days' supply. The MPR is the sum of the days' supply obtained between the first pharmacy fill and the last refill, with the supply obtained in the last refill excluded, divided by the total number of days in this time period [18]. In this population of patients with treated established hypertension, two pharmacy refills in a drug class in the one

year time period were required. MPR was calculated for each antihypertensive medication class and averaged across all classes to assign a single MPR to each participant for the year[19]; MPR values > 1 were truncated at 1.0. Low, medium and high MPR adherence were defined as <0.5, 0.5 to <0.8 and ≥0.8, respectively [20, 21].

Self-reported medication adherence was assessed using the eight-item Morisky Medication Adherence Scale (MMAS-8) [19, 22]; MMAS-8 was captured at baseline and during annual follow up surveys. For the main analyses, MMAS-8 collected during the baseline survey was used. This adherence measure was designed to facilitate the identification of barriers to, and behaviors associated with, adherence to chronic medications. In prior studies, the scale has been determined to be reliable [22], significantly associated with blood pressure control [3, 22], and modestly associated with pharmacy refill [19]. Overall, 99.4% of participants completed all 8 items of the scale in the baseline survey. The remaining 0.6% (n=12) of participants completed 6 or 7 of the 8 items on the MMAS-8 and the missing items were generated using the CoSMO sample median score for the item. Using previously published cut points, low, medium, and high MMAS-8 adherence were defined as scores of <6, 6 to <8, and 8, respectively [22].

Outcome variables

Composite CVD Outcome—The primary outcome was the composite CVD endpoint of stroke, MI, CHF or CVD death. All outcomes were ascertained through February 28, 2011. Data were collected on hospitalizations for CVD events and mortality. Hospitalizations for CVD events were determined by a combination of review of administrative records, medical record review and physician adjudication. A comprehensive search of primary and secondary International Classification of Diseases, Ninth Revision (ICD9) codes from administrative claims databases was used to identify hospitalizations for MI: codes 410.xx (except 410.x2); CHF: codes 402.x1, 428.xx, and stroke: codes 430.xx, 431.xx, 432.xx, 433.xx, 434.xx that occurred over the follow-up period. Deaths occurring over the follow-up period were first identified via searches of the Social Security Death Index and cross-checked against administrative claims databases and obituaries. For each identified death, death certificates were obtained from the respective health departments and cause of death (CVD or non-CVD) was recorded. When possible, supplemental data were abstracted from medical records to confirm cause of death. Then, trained research nurses abstracted information from medical records and death certificates for each CVD event onto standardized forms[23]. For hospitalizations occurring outside of the system, a patient release was obtained prior to requesting and reviewing the medical record. Medical information for each abstracted event was reviewed independently by two physician adjudicators (EDF, RNR) who were blinded to participant adherence status. If both adjudicators agreed on the outcome classification, it was binding. If there was a disagreement, they conferred, reconsidered their classification and could request consultation from a third independent and blinded adjudicator. In all cases, conflicting opinions among the adjudicators were resolved after conferment.

Socio-demographics, Clinical and Behavioral Variables—Based on an established conceptual model[17], information was collected from participants' surveys, the medical

record, and claims databases of the managed care organization. Sociodemographic and clinical characteristics obtained from the participant survey included marital status, age, sex, race, educational attainment, height and weight, depressive symptoms, and duration of hypertension. Body mass index was calculated as weight (kg)/height $(m)^2$. Depressive symptoms were assessed using the 20-item Center for Epidemiologic Studies Depression Scale [24]. Self-reported healthy lifestyle behaviors included nonsmoking status, less than 2 alcoholic drinks per week, and use of lifestyle modifications (exercise, salt reduction, fruit and vegetable consumption)[25] to lower blood pressure. Claims data were used to calculate the Charlson Comorbidity Index [26, 27] and to determine the number of classes of antihypertensive medication filled by each participant.

Blood Pressure (BP)—Using standardized forms, trained research staff (blinded to participant adherence category) recorded seated systolic and diastolic BP measurements from medical records for clinic visits occurring during the year before the baseline survey and after the baseline survey through February 2011 or a CVD event (follow-up), whichever came first. BP levels were averaged for visits when more than one measurement was taken. Then, the average BP level across all visits during baseline and, separately, during follow up was calculated [3]. Uncontrolled BP was defined as mean systolic BP ≥140 mm Hg or diastolic BP ≥ 90 mm Hg[28].

Statistical Analysis

Participant characteristics were calculated overall and by level of adherence on each measure (MPR and MMAS-8, separately). The statistical significance of trends across adherence levels was determined using Cochran-Armitage trend tests. The association of adherence (MPR and MMAS-8, separately) with uncontrolled BP during follow-up was determined using logistic regression models. Cumulative incidence of CVD events was calculated by level of adherence using the Kaplan-Meier method. Cox proportional hazards models were used to estimate hazard ratios (HR) and 95% confidence intervals (CI) of CVD associated with low and medium versus high adherence. Separate models were used for MPR and MMAS-8. Initial models were adjusted for age, sex, race, marital status, and education, and subsequent models were further adjusted using the Charlson Comorbidity Index, number of classes of antihypertensive medication, body mass index, depressive symptoms, and healthy lifestyle behaviors. Differences in the association between antihypertensive medication adherence and the composite CVD outcome across subgroups defined by race and sex were evaluated by including an interaction term in final multivariable regression models (e.g. MPR * race). Analyses were performed using SAS version 9.2 (SAS Institute, Cary NC).

Sensitivity Analyses

In sensitivity analyses, the HRs for CVD associated with MMAS-8 and MPR each modeled using a single cut-point (MMAS-8 <8 versus 8 and MPR <0.8 versus ≥ 8) were calculated. Also, the HRs for CVD associated with MMAS-8 and MPR modeled as continuous variable (log transformed) were calculated. To investigate whether differences in CVD risk by adherence measure could be explained by differing definitions of low MMAS-8 adherence, we used alternate cut-points to define low, medium, and high MMAS-8 (<4.5, 4.5 to <7, and

≥7 to 8, respectively). This strategy resulted in a similar percentage of participants with low adherence by MMAS-8 and MPR. We also assessed the association with CVD incidence of two measures of MMAS-8 averaged over 1 year. For this analysis, we restricted the sample to participants who completed baseline and first follow up MMAS-8, had pharmacy refill data in the year prior to the first follow up survey, and did not have a CVD event in the time between the two surveys(n=1,690).

Lastly, prescription-based proportion of days covered (PDC) was calculated as an alternate measure of pharmacy refill[29]. For each antihypertensive medication class, we calculated PDC as the number of days with medication available divided by the number of days between the first and last pharmacy refill in the one year time period. An overall PDC for each participant was calculated as the average of the class-specific PDC.

Results

Of the 2,194 participants in the CoSMO cohort, 57 were hospitalized for a CVD event in the year prior to baseline and were not eligible for these analyses. There were 62 participants excluded from analyses because of missing pharmacy refill data (Figure 1). There were no differences in age, sex, race, education or duration of hypertension ($p>0.05$ for all comparisons) between those missing versus not missing pharmacy refill data. The mean age of the 2,075 participants included in the analyses was 75 years (standard deviation, 5.6), 30.4% were black, 59.8% were women, and 57.0% were married. Also, 62.9% had been diagnosed with hypertension for 10 or more years, 48.3% had 2 or more comorbid conditions, and 34.1% had uncontrolled hypertension (Table 1). Over a median follow-up of 3.8 years (maximum 4.8 years), 240 (11.6%) individuals had a CVD event (i.e., MI, stroke, CHF, or CVD death). Overall, 2.3% of the participants had a stroke event, 4.1% had a MI event, 6.2% had a CHF event, and 3.5% had a CVD death.

Pharmacy Refill Adherence

The prevalence of low, medium and high antihypertensive medication adherence was 4.5%, 23.7%, and 71.8%, respectively, for MPR. Participant characteristics by MPR are shown in the left panel of Table 1. Participants with worse medication adherence by MPR were more likely to be black and have fewer than 2 alcoholic drinks per week, depressive symptoms, and uncontrolled blood pressure at baseline. They were less likely to be married, have at least a high school education, be taking 3 or more classes of antihypertensive medications, have Charlson comorbidity ≥ 2, and have hypertension ≥ 10 years. Lower adherence by MPR at baseline was associated with higher odds ratio of uncontrolled blood pressure during follow-up: 1.55 (95% CI 1.23, 1.96) for medium versus high MPR and 2.06 (95% CI 1.26, 3.36) for low versus high MPR.

The proportion of the sample with a CVD event was 16.1%, 13.4% and 10.7% among those with low, medium and high MPR (Figure 2a and Table 2). After multivariable adjustment and compared to those with high MPR, the HR (95% CI) for the composite CVD outcome associated with medium and low MPR were 1.17 (0.87, 1.56) and 1.87 (1.06, 3.30), respectively (Table 2). The associations between adherence by MPR and the composite

CVD outcome for MPR were consistent across race and sex groups (Supplemental Table 1; P-interaction for race = 0.801, for sex = 0.339).

Self-Reported Adherence-MMAS-8

The prevalence of low, medium and high antihypertensive medication adherence was 14.0%, 34.3%, and 51.8% for MMAS-8. Participant characteristics by category of MMAS-8 are shown in the right panel of Table 1. Participants with worse medication adherence by MMAS-8 were more likely to be black, and have a BMI ≥ 30 kg/m^2, depressive symptoms, and uncontrolled blood pressure at baseline; they were less likely to be ≥ 75 years old and report reducing salt to control their blood pressure. Lower adherence by MMAS-8 at baseline was associated with uncontrolled blood pressure during follow-up with odds ratios (95% CI) of 1.15 (0.92, 1.45) for medium versus high MMAS-8, and 1.58 (1.17, 2.12) for low versus high MMAS-8.

In unadjusted analyses, there was no association between MMAS categories and CVD events (Figure 2b and Table 2). After multivariable adjustment and compared to those with high MMAS-8, the HRs (95% CI) for the composite CVD outcome associated with medium and low MMAS were 1.04 (0.79, 1.38) and 0.89 (0.58, 1.35), respectively. These results were consistent across race and sex subgroups (Supplemental Table 1; P-interaction for race = 0.093, for sex = 0.663).

Sensitivity Analyses

When adherence by MPR and MMAS-8 were separately evaluated for association with CVD events using a single cut-point, the results were qualitatively similar (adjusted HRs (95% CI) of 1.00 (0.78, 1.30) for MMAS-8 < 8 versus 8 and 1.32 (0.99, 1.75) for MPR <0.8 versus ≥0.8. When MPR was modeled as a log-transformed continuous variable, a 25% decrease in MPR was associated with a HR (95% CI) for CVD events of 1.04 (1.00–1.09; p value = 0.073). When MMAS-8 was modeled as a log-transformed continuous variable, a 25% decrease in MMAS-8 was associated with a HR (95% CI) of 1.21 (0.57-2.58; p value = 0.623) for CVD events.

When alternate cut-points were used to define low, medium and high adherence on the MMAS-8 (<4.5, 4.5 to <7, and ≥7 to 8, respectively), no association was present between MMAS-8 and CVD events (adjusted HRs (95% CI) 1.04 (0.78, 1.38) for 4.5 to ≥7 versus >7 and 1.57 (0.64, 3.86) for <4.5 versus >7). Averaging the two measures of MMAS-8 collected at baseline and first follow-up, no association was present between MMAS-8 and subsequent CVD. The adjusted HRs (95% CI) for those with medium and low compared to high MMAS-8 were 0.90 (0.65, 1.37) and 0.98 (0.56, 1.73), respectively.

When PDC was used as the measure of pharmacy refill adherence to assess the association with CVD outcome, the results were qualitatively similar to MPR (Supplemental Table 2).

Discussion

In the current study conducted in a real world setting of older insured patients with established hypertension, low adherence to antihypertensive medications identified using a

pharmacy refill measure and self-report was significantly associated with uncontrolled blood pressure at baseline and during follow-up for both measures. Compared to their counterparts with high adherence, those with low adherence to antihypertensive medication, defined as an MPR <0.5, had a nearly 2-fold higher risk of a CVD event over a median follow up of 3.8 years. In contrast, there was no association between adherence measured by MMAS-8 and CVD. The results were consistent in sensitivity analyses. For pharmacy refill adherence, these findings are similar to prior studies revealing that pharmacy refill adherence is associated with lower risk of long-term adverse clinical outcomes in patients treated for hypertension [4–8, 14]. However, fewer studies have contrasted pharmacy refill versus self-reported antihypertensive medication adherence on CVD outcomes.

Prior investigations exploring associations between self-reported adherence and CVD outcomes in older adults have yielded inconsistent results [30, 31]. In outpatients treated for stable coronary artery disease, a single self-reported medication adherence question was associated with a greater than 2-fold increase in CVD events [30]. In the Second Australian National Blood Pressure Study trial, participants reporting good adherence using a 4-item scale were marginally less likely to experience some types of cardiovascular events[10]. In contrast, Wu and colleagues found that self-report adherence using a similar single item was not associated with outcomes in patients treated for heart failure[31], and discussed issues regarding reliability[32, 33] and the potential for recall and social desirability biases[34] with self-reported measures. Previous research has demonstrated reliability and validity of the MMAS-8 in its association with blood pressure [22, 35] and modest association between pharmacy refill and MMAS-8 [19]. An explanation for the differences in association between adherence and long-term outcomes using the 2 measures may reflect that MPR and MMAS-8 measure different aspects of adherence behavior which may vary within the same patient and differentially impact associations with long-term outcomes. MPR assesses medication filling behavior whereas MMAS-8 assesses medication-taking behavior (presumably after medications are obtained via pharmacy refill or via office samples) and provides information on reasons why patients may not be taking their medications. Thus, MMAS-8 reflects medication-taking determinants further down the chain of linked adherence behaviors (linked behaviors such as going to the doctor’s office for diagnosis and prescription, then filling prescriptions, and then taking the medications) [12, 36]. In addition, although blacks and those with depressive symptoms were identified as low adherers by both measures, low adherers by MPR in this study were less likely to be married, to have higher education and to be taking three or more medications. These differences may be markers of poor health outcomes and contribute to CVD events. For example, marital status has been shown to confer health advantages in the general population and in those undergoing CVD procedures[37]. Differences in what each measure assesses and the characteristics of those identified as low adherers may have important implications when determining associations with long-term outcomes. Finally, our prior work revealed low incidence of declining adherence using MMAS-8 in older patients with established hypertension over 2 years of follow up (4.3% annual rate of decline in adherence)[35]. Pharmacy refill is calculated using monthly data points over twelve months and may be more reflective of adherence behavior over time.

Healthcare providers may benefit from having information on both self-report and pharmacy refill adherence behavior. During medical encounters, MMAS-8 is a quick way to identify which patients are adhering to prescribed therapies, to obtain important information on barriers to adherence that can be targeted for interventions to improve medication adherence and blood pressure control in the short-term, and to monitor change in adherence[35]. MPR can be used to identify those not filling prescriptions over time and assess risk of adverse outcomes in the long-term. Unlike MMAS-8, MPR does not provide information on barriers to adherence. Together, the objective and self-reported adherence measures provide complementary information that can guide appropriate engagement of patients and providers in the management of high blood pressure and other chronic conditions. Pharmacy refill measures may be particularly important for research studies and population management projects given the association between this measure and CVD events.

Study Limitations and Strengths

The current study was limited to English-speaking adults 65 years of age and older with health insurance in one region of the US and relatively high adherence rates, and thus, may not be generalizable to all persons with hypertension. Higher adherence in older versus younger adults have been reported[15, 38–41]. We report a similar prevalence of high adherence rates as a recent meta-analysis including 11 studies of patients taking antihypertensive medications (good adherence rates were 59% (95% CI 42% – 77%)[14]. Neither pharmacy refill nor self- reported adherence measures provide evidence that medications are actually taken correctly by patients, and primary nonadherence was not assessed. There is no gold standard for measuring medication adherence, and each method has strengths and limitations [42, 43]. Although pharmacy refill data are becoming increasingly available, a low proportion of adults receive care in settings where pharmacy refill data are readily available [44]. All pharmacy claims captured through the managed care organization were included in the analyses; however, it is possible that some participants filled prescriptions outside of the system and these claims were not included. Furthermore, the diverse nature of the MMAS-8 questions – while an important feature for identification of the varied barriers to adherence –may impede the scale's ability to predict future events. Self-report tools are subject to recall and social desirability biases resulting in misclassification of participants and overestimation of adherence behavior. Although one prior study found no social desirability in responses provided on the MMAS-8, future investigation is warranted[22]. Although we confirmed CVD events against medical records to increase reporting accuracy, use of ICD-9 codes to identify CVD events may be subject to misclassification bias. The potential misclassification, however, is unlikely to be differential among the adherence groups.

This study has many strengths, including its prospective design, relatively large sample size, broad range of data collected (survey, administrative, and clinical data), availability of both pharmacy refill and self-reported adherence data, diversity of the sample with respect to sociodemographic characteristics and the presence of risk factors, and ability to perform sensitivity analyses. Because the CoSMO study is limited to community-dwelling older adults in a managed care organization, confounding by access to care and health insurance is reduced. Finally, because hypertension is a prevalent disease in older adults, the results of

this study may be useful in the evaluation and management of a substantial segment of the population.

Conclusion

Poor antihypertensive medication adherence assessed using pharmacy refill data was associated with uncontrolled BP and increased risk for CVD events in community-dwelling patients with established hypertension. In contrast, while associated with BP control, self-report antihypertensive medication adherence using MMAS-8 was not associated with CVD incidence. The differences in the association of pharmacy refill versus self-report with CVD may be due to traits in the behaviors each adherence measure assesses. Self-report tools may provide important information to clinicians regarding barriers to adherence that can be targeted for intervention; pharmacy refill measures may provide medication filling patterns and enable assessment of barriers to refilling medications and of adverse event risk in clinical, population-based, and research settings. Identification of patients with poor medication adherence in outpatient settings may be important in facilitating patients achieving controlled blood pressure and ultimately improved cardiovascular health.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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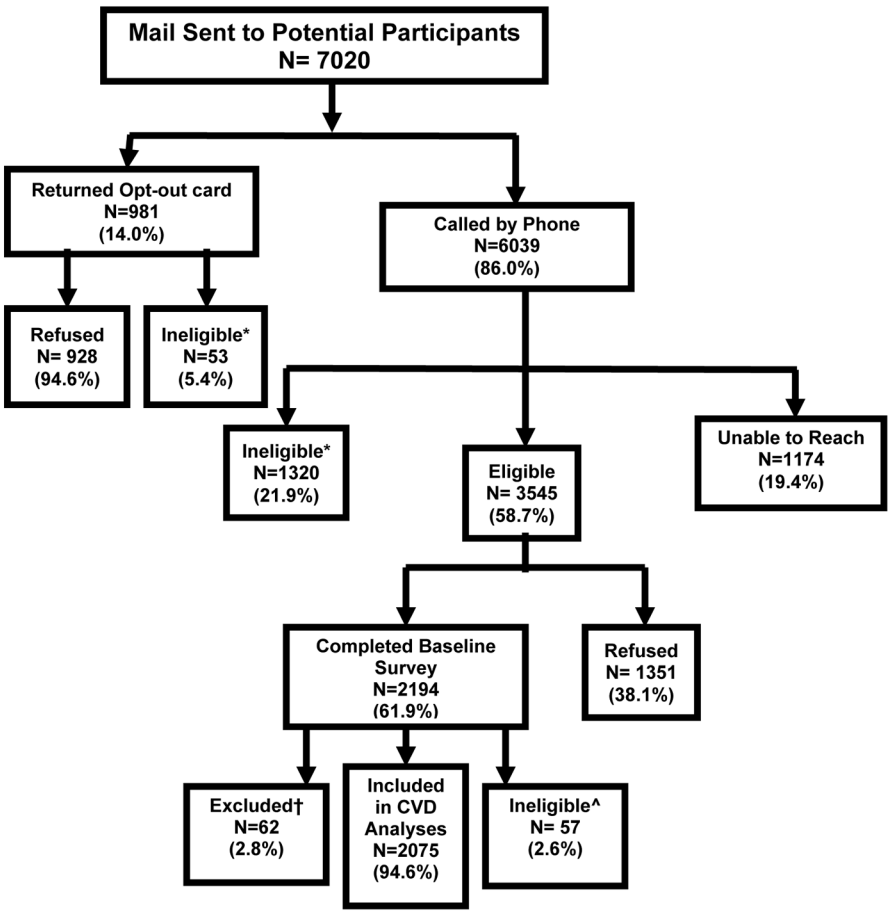

Figure 1. Recruitment and Follow up Flowchart for the Cohort Study of Medication Adherence among Older Adults (CoSMO)

Adapted from Krousel-Wood et al. *Med Clin N Am* 93:753–769, 2009

*Ineligible during the recruitment phase due to no confirmed diagnosis of hypertension (22.9%), hard of hearing (16.4%), too ill to complete survey (12.6%), deceased (11.5%), cognitive screen failure (11.1%), not currently prescribed antihypertensive medication (8.4%), no longer enrolled in managed care organization (6.9%), non-English speaker (5.8%), confined to a nursing home (1.9%), moved out of state (1.1%), current treatment for cancer (1%), or miscellaneous reason (<1%).

^ Ineligible in the follow up phase due to hospitalization for CVD outcome in the year prior to the baseline survey

†Reason for exclusion: missing Medication Possession Ratio (MPR) data in the year prior to the baseline survey

CVD-cardiovascular disease

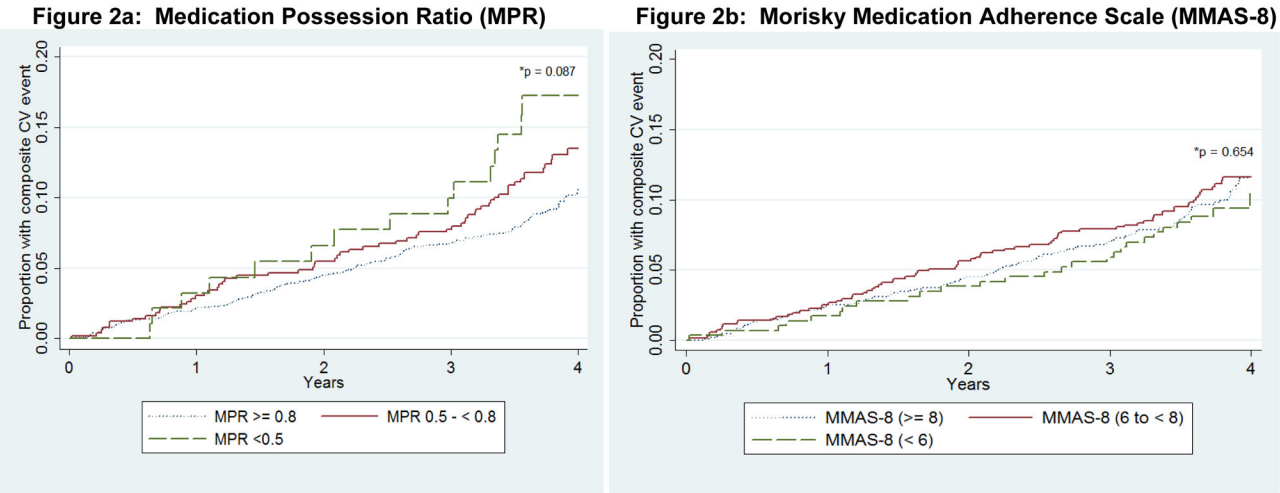

Figure 2. Cumulative incidence of Cardiovascular Disease Outcome by Level of Antihypertensive Medication Adherence at Baseline

Figure 2a: Medication Possession Ratio (MPR)

Figure 2b: Morisky Medication Adherence Scale (MMAS-8)

*P-value for Log-Rank test

CVD-Cardiovascular Disease

MPR—Medication Possession Ratio

MMAS-8—Morisky Medication Adherence Scale 8-item

Composite CVD outcome-myocardial infarction, congestive heart failure, stroke, or cardiovascular death

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Table 1

Baseline Characteristics of the Study Participants according to Antihypertensive Medication Adherence Category

		Pharmacy Refill Adherence				Self-Reported Adherence			
	Overall	**MPR <0.5**	**MPR 0.5-<0.8**	**MPR ≥0.8**	**P-value***	**MMAS-8 <6**	**MMAS-8 6 to <8**	**MMAS-8 =8**	**P-value†**
Total Number	2,075	93	492	1490		290	711	1074	
Age ≥75 years, n(%)	1012 (48.8)	46(49.5)	238(48.4)	728(48.9)	0.958	118(40.7)	361(50.8)	533(49.6)	0.047
Female, n(%)	1241 (59.8)	60(64.5)	298(60.6)	883(59.3)	0.314	188(64.8)	408(57.4)	645(60.1)	0.458
Black race, n(%)	631 (30.4)	47(50.5)	200(40.7)	384(25.8)	<0.001	114(39.3)	231(32.5)	286(26.3)	<0.001
Married, n(%)	1182 (57.0)	48(51.6)	261(53.1)	873(58.6)	0.020	163(56.2)	412(58.0)	607(56.5)	0.873
High school education or greater, n(%)	1652 (79.6)	67(72.0)	369(75.0)	1216(81.7)	<0.001	232(80.0)	559(78.6)	861(80.2)	0.686
Hypertension duration ≥ 10 Years, n(%)	1301 (62.9)	48(52.2)	302(61.8)	951(64.0)	0.036	171(59.2)	451(63.6)	679(63.5)	0.279
Charlson Comorbidity Index score ≥ 2 n (%)‡	1003 (48.3)	43(46.2)	278(56.5)	682(45.8)	0.004	145(50.0)	357(50.2)	501(46.7)	0.160
Body mass index: ≥ 30 kg/m^2, n(%)	1592 (76.8)	75(80.7)	387(78.8)	1130(75.9)	0.110	244(84.4)	552(77.6)	796(74.2)	<0.001
3+ classes of antihypertensive medication, n(%)‡	901 (43.4)	14(15.1)	225(45.7)	662(44.4)	0.001	124(42.8)	316(44.4)	461(42.9)	0.833
Depressive symptoms, n(%)	267 (12.9)	18(19.4)	88(17.9)	161(10.8)	<0.001	62(21.4)	99(13.9)	106(9.9)	<0.001
Never a smoker, n(%)	1024 (49.7)	51(55.4)	242(49.8)	731(49.4)	0.392	136(47.1)	337(48.0)	551(51.6)	0.091
<2 alcoholic drinks per week, n(%)	1627 (78.7)	81(88.0)	393(80.4)	1153(77.6)	0.015	223(77.7)	563(79.3)	841(78.6)	0.910
Increasing fruits and vegetables, n(%)	1412 (68.1)	65(69.9)	344(69.9)	1003(67.3)	0.285	189(65.2)	487(68.5)	736(68.5)	0.376
Exercising more, n(%)	912 (44.0)	38(40.9)	212(43.1)	662(44.4)	0.427	115(39.7)	317(44.6)	480(44.7)	0.208
Reducing salt, n(%)	1660 (80.0)	72(77.4)	396(80.5)	1192(80.0)	0.813	220(75.9)	565(79.5)	875(81.5)	0.033
Uncontrolled blood pressure, n(%)	662 (34.1)	36(41.9)	181(38.7)	445(32.0)	0.003	115(42.4)	241(36.4)	306(30.3)	<0.001

*P-value for comparison of characteristics among low, medium, and high MPR groups

†P-value for comparison of characteristics among low, medium, and high MMAS-8 groups

‡- in the prior year

Characteristics with missing values:

High school education or greater, n=1(0.05%) missing

Hypertension duration ≥ 10 Years, n=8 (0.39%) missing

Charlson Comorbidity Index score ≥ 2, n=2 (0.10%) missing

Body mass index: ≥ 30 kg/m^2, n=2 (0.10%) missing

Never smoker, n=16 (0.77%) missing

<2 alcoholic drinks per week, n=8 (0.39%) missing

Uncontrolled blood pressure, n=131 (6.31%) missing

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Table 2

Unadjusted and Adjusted Hazard Ratios for the Cardiovascular Disease Outcome associated with Antihypertensive Medication Adherence

	n(%) with CVD outcome	Unadjusted HR (95% CI)	Model 1 HR (95% CI)	Model 2 HR (95% CI)	Model 3 HR (95% CI)
Overall	240(11.6)				
Pharmacy Refill					
Low (MPR <0.5)	15 (16.1)	1.58 (0.93,2.68)	1.70 (0.99,2.90)	2.06 (1.19,3.56)†	1.87 (1.06,3.30)*
Medium (MPR 0.5-<0.8)	66 (13.4)	1.29 (0.96,1.72)	1.31 (0.98,1.75)	1.16 (0.87,1.56)	1.17 (0.87,1.56)
High (MPR ≥0.8)	159 (10.7)	1(reference)	1(reference)	1(reference)	1(reference)
Self-Reported Adherence					
Low (MMAS-8 <6)	30 (10.3)	0.90 (0.60, 1.36)	0.99 (0.66,1.48)	0.91 (0.61,1.37)	0.89 (0.58,1.35)
Medium (MMAS-8 6 to <8)	88 (12.4)	1.09 (0.83,1.43)	1.08 (0.82,1.42)	1.03 (0.78,1.36)	1.04 (0.79,1.38)
High (MMAS-8 =8)	122 (11.4)	1(reference)	1(reference)	1(reference)	1(reference)

*p<0.05,

†p<0.01

HR-Hazards Ratio; 95% CI - 95% confidence interval

Composite CVD outcome-myocardial infarction, congestive heart failure, stroke, or cardiovascular death

CoSMO-Cohort Study of Medication Adherence among Older Adults

MPR-medication possession ratio

MMAS-8 – Morisky Medication Adherence Scale-8 item;

CVD-cardiovascular disease;

Model 1 adjusted for age, sex, race, marital status, and education.

Model 2 adjusted for age, sex, race, marital status, education, Charlson Comorbidity

Index, number of classes of antihypertensive medications, and depressive symptoms.

Model 3 adjusted for age, sex, race, marital status, education, Charlson Comorbidity Index, number of classes of antihypertensive medications, depressive symptoms, smoking status, body mass index, alcohol intake, and healthy lifestyles for blood pressure control (fruit and vegetable intake, exercise, and sodium reduction