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Sex Differences in Barriers to Antihypertensive Medication Adherence: Findings From the Cohort Study of Medication Adherence Among Older Adults (CoSMO)

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Abstract

Objectives—We assessed whether socio-demographic, clinical, health care system, psychosocial, and behavioral factors are differentially associated with low antihypertensive medication adherence scores among older men and women.

Design / Setting—A cross-sectional analysis using baseline data from the Cohort Study of Medication Adherence in Older Adults (CoSMO, n=2,194).

Measurements—Low antihypertensive medication adherence was defined as a score <6 on the 8-item Morisky Medication Adherence Scale. Risk factors for low adherence were collected using telephone surveys and administrative databases.

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Conflicts of Interest:
Dr. Krousel-Wood receives grant money from the NIH to support Ochsner's participation in the SPRINT trial (blood pressure lowering trial). She is also a member of the NIH Center for Scientific Review Advisory Council.
Dr. Morisky is the developer/owner of the copyrighted MMAS-8 which is available free through a license agreement for publicly-funded researchers and students. 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.

Results—The prevalence of low medication adherence scores did not differ according to sex (15.0% in women and 13.1% in men p=0.208). In sex-specific multivariable models, having issues with medication cost and practicing fewer lifestyle modifications for blood pressure control were associated with low adherence scores among both men and women. Factors associated with low adherence scores in men but not women included reduced sexual functioning (OR = 2.03; 95% CI: 1.31, 3.16 for men and OR = 1.28; 95% CI: 0.90, 1.82 for women), and BMI ≥25 (OR = 3.23; 95% CI: 1.59, 6.59 for men and 1.23; 95% CI: 0.82, 1.85 for women). Factors associated with low adherence scores in women but not men included dissatisfaction with communication with their healthcare provider (OR = 1.75; 95% CI: 1.16, 2.65 for women and OR =1.16 95% CI: 0.57, 2.34 for men) and depressive symptoms (OR = 2.29; 95% CI: 1.55, 3.38 for women and OR = 0.93; 95% CI: 0.48, 1.80 for men).

Conclusion—Factors associated with low antihypertensive medication adherence scores differed according to sex. Interventions designed to improve adherence in older adults should be tailored to account for the sex of the target population.

Keywords

medication adherence; hypertension; older adults; gender differences

INTRODUCTION

Hypertension, an important risk factor for cardiovascular disease, is a highly prevalent condition among older populations (1;2). Persistent adherence to prescribed medications is an important cornerstone of blood pressure control (3). However, suboptimal medication adherence remains a challenge among older adults (4–9). Previous studies have identified patient, health care system, and provider factors associated with low medication adherence (10). Despite this, many of the interventions designed to improve medication adherence and blood pressure control have not been very effective (11). This may be because interventions which employ a “one size fits all” approach have failed to appropriately tailor strategies to address barriers specific to population subgroups.

Because barriers to medication adherence can vary substantially among individuals, many researchers have concluded that patient-specific barriers should be identified through individualized screening techniques, and interventions “tailored” to address the individual needs of each patient. However, initiatives to improve adherence may need to be balanced between highly individualized interventions and effective programs that can work for larger groups of patients (10). The identification of sex differences in barriers to antihypertensive medication adherence could assist providers and health care systems to tailor interventions on a population level. Yet, the extent to which barriers to achieving high adherence differ between men and women is not well described. Using data from the Cohort Study of Medication Adherence among Older Adults (CoSMO) we sought to determine whether socio-demographic, clinical, health care system, and psychosocial/behavioral factors are differentially associated with antihypertensive medication adherence in men and women.

METHODS

Study Population

Data for the current analysis come from the baseline survey of the CoSMO study (n=2,194). The primary goal of CoSMO is to investigate factors that influence adherence to antihypertensive medication in older adults; the study design, response rates, and baseline characteristics have been published previously (12). In brief, adults 65 years and older being treated for essential hypertension were randomly selected from the roster of a large managed

care organization in southeastern Louisiana, and study recruitment was conducted from 21 August 2006 to 30 September 2007. CoSMO was approved by the Ochsner Clinic Foundation's Institutional Review Board and the privacy board of the managed care organization (12).

Study Measures

Self-report measures came from questionnaires administered via telephone by trained interviewers. In addition, information regarding comorbid conditions and medication classes were obtained from the administrative databases of the managed care organization.

Medication Adherence—Data for the outcome variable, antihypertensive medication adherence score, was ascertained using the self-report eight-item Morisky Medication Adherence Scale (MMAS-8). This measure was designed to facilitate the identification of barriers to and behaviors associated with adherence to chronic medications, and scores on the MMAS-8 can range from zero to eight (13). An established cutpoint of <6 was used to define low medication adherence score. In previous validation studies, a score of <6 on the MMAS-8 was associated with uncontrolled blood pressure (12;13). An MMAS-8 score of <6 has also shown to be associated with poor antihypertensive medication pharmacy fill rates (i.e. non-persistent medication possession ratio of <0.8)(12;14).

Socio-demographic and Clinical Factors—Age, race, marital status, education, height and weight (for calculation of body mass index), and duration of hypertension were obtained through self-report. Hypertension knowledge was assessed using a validated tool. Participants with scores in the lowest tertile were defined as having low knowledge (15;16). Comorbid conditions were identified, the Charlson comorbidity index was calculated, and dichotomized as <2 versus ≥2 (17;18). The classes of antihypertensive medications filled in the year prior to the baseline survey and the number of classes being taken were categorized as <3 versus ≥ 3.

Healthcare System Variables—Dissatisfaction with healthcare was defined as a score which corresponded to poor or fair satisfaction using three scales of the Group Health Association of America Consumer Satisfaction Survey (overall health care, communication with provider, and access to care)(19). Participants were asked if they had reduced antihypertensive medication because of the cost. Number of visits to a primary healthcare provider in the year prior to the survey was captured by self-report and dichotomized as <6 versus ≥6.

Psycho-social/Behavioral variables—Cigarette smoking (20) and alcohol use were assessed using self report. Reduced sexual functioning was defined as values below the median for the sample using the Massachusetts General Hospital Sexual Functioning Questionnaire (21). The presence of depressive symptoms was defined as a score ≥16 using the 20 item Center for Epidemiologic Studies Depression Scale(22). Low social support was defined as scores in the lowest tertile using the RAND Medical Outcomes Study Social Support Survey (23–25). Low coping was defined as scores below the median using a shortened version of the John Henry Active Coping scale (26). High perceived stress levels were defined as having a score in the highest tertile for the sample using the Perceived Stress Scale (27).

Self-management Behaviors—The use of lifestyle modifications (weight control; salt reduction, fruit and vegetable consumption) and complementary and alternative therapies (including general use, health food and herbal supplements, and relaxation techniques) to lower blood pressure were ascertained by self-report (28).

Statistical Analysis

Baseline characteristics and rates of low medication adherence scores were calculated for men and women, and Chi-square tests were used to determine the statistical significance of differences. Then, in sex-stratified bivariate analyses, we assessed the relationship between each participant characteristic and medication adherence score. Separate multivariable models for men and women were developed by entering variables that were significant at the $p<0.05$ for either sex in bivariate analyses and using forced entry for age, race, marital status, education and comorbidity. Participants who refused to answer the sexual functioning questions (n=301) were coded as not having "reduced functioning," and in sensitivity analyses, alternate coding schemes were used. Perceived stress and satisfaction with overall health care were not considered for inclusion in final multivariable models because of their high collinearity with depressive symptom scores and satisfaction with communication, respectively. Finally, sex differences in the associations between participant characteristics and medication adherence score were assessed by including men and women in a regression model along with interaction terms (e.g., sex*depressive symptoms). All analyses were performed using SAS version 9.2 (SAS Institute, Cary, NC).

RESULTS

The mean age of all study participants was 75.0 ±5.5 years, 30.5% were black, 58.5% were women, and 14.2% had low antihypertensive medication adherence scores (data not shown). The prevalence of participant characteristics, stratified according to sex, is shown in Table 1. Compared to men, women were significantly more likely to be black, unmarried, and non-smokers, and to have fewer comorbid conditions, practice more lifestyle modifications for blood pressure (B P) control, and have lower BMI. Women were also significantly more likely to report more depressive symptoms, lower social support, higher stress, and lower levels of sexual functioning. The prevalence of low antihypertensive medication adherence scores did not differ according to sex: 15.0% of women and 13.1% of men were classified as having low adherence scores, (p=0.208).

The prevalence of low medication adherence score for each characteristic, stratified according to sex, are shown in Tables 2 and 3, and the results of sex-specific multivariable models are shown in Table 4. In multivariable models, having issues with medication cost and practicing fewer lifestyle modifications for blood pressure control were associated with low adherence scores for both men and women. Factors associated with low medication adherence scores in men but not women included reduced sexual functioning (OR = 2.03; 95% CI: 1.31, 3.16 for men and OR = 1.28; 95% CI: 0.90, 1.82 for women), and BMI ≥25 (OR = 3.23; 95% CI: 1.59, 6.59 for men and 1.23; 95% CI: 0.82, 1.85 for women). Factors associated with low medication adherence scores in women but not men included dissatisfaction with communication with their healthcare provider (OR = 1.75; 95% CI: 1.16, 2.65 for women and OR =1.16 95% CI: 0.57, 2.34 for men) and depressive symptoms (OR = 2.29; 95% CI: 1.55, 3.38 for women and OR = 0.93; 95% CI: 0.48, 1.80 for men). P-values for interaction were: p=0.041 and p=0.067 for sex*sexual functioning and sex*BMI, respectively, and p=0.133 and p=0.115 for sex*communication and sex*depressive symptoms, respectively.

DISCUSSION

Numerous studies have assessed barriers to adherence in combined samples of men and women (10), yet analyses stratified according to subgroup are sparse. Using data from a large cohort of older adults with hypertension, we examined whether socio-demographic, clinical, health care system and psychosocial/behavioral factors are differentially associated with low antihypertensive medication adherence scores in men and women. In accordance

with previous research, rates of low medication adherence scores did not differ between men and women in the CoSMO sample (29;30). However, we identified sex differences in factors associated with low medication adherence scores.

Factors Associated with Low Adherence Scores among Men but not Women

Our study identified lower sexual functioning as a barrier to antihypertensive medication adherence in men, but not women. Numerous studies have shown that sexual dysfunction is prevalent in hypertensive adults (31–35): low sexual functioning in this population could stem from both the physiological impact of hypertension itself, and/or side effects of the medications used to treat high blood pressure (36). Earlier work revealed an association in hypertensive men between not reporting difficulties with maintaining an erection and better health status(37). Previous research has also shown that hypertensive patients who perceive that their medication therapy is causing sexual problems may be less apt to show sustained compliance (38). A 2005 retrospective analysis of prescription claims also showed that when erectile dysfunction in men was treated with sildenafil (Viagra), adherence to hypertensive treatments subsequently improved (39). Identifying and addressing any perceived sexual side effects of antihypertensive medications might successfully improve adherence behavior in men

Results from our study also showed that among men, higher BMI (BMI $\geq$25 kg/m^2) was associated with lower medication adherence scores. There have been few previous research studies investigating the association BMI and adherence: using data from NHANES, Bautista et al showed no association between BMI and persistence to antihypertensive medication; however, sex differences were not reported (40). In our study, we explored whether the association between higher BMI and lower adherence score could be attributed to psychosocial problems. We found that even after adjusting for depression and stress, the association between BMI and medication adherence score in men remained significant. One possible explanation is that patients who do not take their medications may also be less likely to exercise and follow dietary restrictions. Further research is needed to elucidate the link between BMI and adherence behavior, particularly among men.

Factors Associated with Low Adherence Scores among Women but not Men

The presence of depressive symptoms has been identified as an important correlate of low adherence (25;41;42). Our results confirmed this association; however, while there was a strong and significant association among women, no association was present among men. In further analyses, we explored whether this finding was related to the fact that women in our sample did not have an adequate support network to “buffer” the impact of depressive symptoms on adherence: compared to men, women in our sample had lower levels of social support and were less likely to be married. However, adjustment for marital status and social support did not affect the independent association between depression and low adherence score in women. Our results extend upon previous research identifying depressive symptoms as an important risk factor for poor adherence by showing that this relationship may be most important among women. Further exploration is needed to explain how psychosocial factors such as depression can impact health behavior differently in women than in men.

Previous research has shown that physician trust is an important driver of medication adherence, suggesting that improving patient-physician communication regarding inconveniences, doubts or concerns about medication may be an effective strategy for improving adherence and blood pressure control (43;44). In our study, patients’ dissatisfaction with communication with their health care provider was identified as a barrier to adherence in women but not men. It is possible that this could be due to sex differences in patients’ communication preferences and styles. Previous studies have documented that

compared to male patients, female patients place more value on time and explanations from physicians and prefer more "feeling-oriented" doctors (45;46). Providers who allow adequate time for explanation and conversations about medication adherence – particularly during clinic visits with women - may be able to effectively improve patients' adherence and blood pressure control.

Factors Associated with Low Adherence Scores among Both Men and Women

Results from the current study show that patients practicing fewer lifestyle modifications for blood pressure control are more likely to have low adherence scores, and that this association is consistent among both men and women. Previous research has indicated a patient's underlying "health lifestyle" philosophy is related to not only their medication adherence behavior but also their involvement in self-management behaviors such as diet, exercise, weight control, and smoking (47). Correlations between adherence and lifestyle behaviors have been previously documented: analysis of data from NHANES shows that patients with hypertension separate into distinct subgroups - including subgroups of patients with lower rates of medication non-persistence and increased practice of healthy lifestyle behaviors, and subgroups who have both higher rates of medication non-persistence, and more difficulty complying with lifestyle changes for blood pressure control (48). Because adherence to antihypertensive medications and lifestyle modifications are important cornerstones of blood pressure control (3), strategies which identify and address these behaviors could simultaneously lead to improvements in blood pressure control among populations of both men and women.

Cost was also identified as an important barrier to adherence among both men and women. Prescription cost has consistently been associated with low medication adherence measures in previous studies (49;50). Previous research has shown that cost-related underuse of medications for older adults with chronic disease is associated with health care coverage factors (increasing out of pocket costs and/or inadequate prescription coverage) as well as the quality of the physician / patient relationship (49;50). Yet, older patients and their providers often fail to discuss cost-related non-adherence issues during clinic visits: results from a national sample of Medicare Beneficiaries age 65 years of age and older showed that 39% of seniors who reported cost-related non-adherence on a national survey had not talked with their physicians about this barrier (51). Providers should consider initiating discussions to identify cost-related adherence issues and switching patients to lower cost alternatives.

Strengths and Limitations

This study has many strengths, including its large sample size, broad range of data collected (survey, administrative, and clinical data) and diversity of the sample with respect to socio-demographics and the presence of risk factors, which allowed for the conduct of sex-stratified analyses assessing a comprehensive list of variables. 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; however, generalizability to patients without insurance or with other types of insurance may be limited. Finally, because hypertension is a prevalent disease, the results of this study may be useful in the evaluation and management of a substantial segment of the population.

The results of the study should be interpreted in light of its limitations. The cross-sectional and observational nature of the study does not allow for causal inferences. Thus, while the factors identified in these analyses can be used as markers for low adherence, further research is needed to determine whether or not modification of the factors associated with low adherence scores in this study lead to improved adherence. There are also limitations inherent in some of the scales used in the study. A number of measures used in the survey

relied on self report, including the main outcome measure, medication adherence score. This could have led to the over-estimation of adherence due to social desirability and recall biases. However, our prior work has revealed an association between the MMAS-8 and antihypertensive pharmacy fill data (23). Finally, a large number of participants (245 women and 56 men) did not provide responses to the survey questions about sexual functioning. It is possible that their non-response was due to lack of a partner (66% of women who did not answer these questions were not married/living with a partner). However, we were unable to confirm the exact reasons for these patients' non-response. Importantly, results of sensitivity analyses treating non-response on these questions as 1) missing 2) having "reduced functioning", and 3) having "normal functioning", were all qualitatively similar.

CONCLUSION

In the current analysis, we used baseline data from a large cohort of older adults to identify factors associated with low antihypertensive medication adherence scores among men and women. This study adds to the body of literature on barriers to adherence, highlighting sex differences that may have been previously obscured in combined analyses. Interventions designed to reflect gender differences could be effective in improving antihypertensive medication adherence among older adults.

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Table 1

Participant characteristics according to sex

Participant Characteristics	Men (N = 911)	Women (N =1,283)
Socio-Demographics and Patient Characteristics	**%**	
Age ≥ 75 years	47.0	50.4
Black race	21.4	37.0‡
Married	77.2	42.4‡
High school education or greater	81.0	78.1
Low hypertension knowledge	32.8	31.8
Clinical / Treatment Variables		
Hypertension duration ≥ 10 Years	65.4	61.3
Charlson Comorbidity Index score ≥ 2 §	56.4	44.8‡
Body mass index: ≥ 25 kg/m^2	80.0	74.1‡
3+ classes of antihypertensive medication§	44.8	43.5
Health Care System Variables		
Not satisfied with overall health care	4.8	4.8
Not satisfied with communication	10.1	11.1
Not satisfied with access to healthcare	4.7	4.4
Reduced antihypertensive medications due to cost	3.4	3.7
6+ visits to primary care physician §	24.2	22.1
Psychosocial / Behavioral Variables		
Current or former smoker	67.4	39.3‡
≥ 2 alcoholic beverages per week	32.8	12.7‡
Reduced sexual functioning	51.3	64.8‡
Depressive symptoms	10.6	14.9‡
Low Social Support	30.4	36.4‡
Low Coping	46.5	48.8
High Stress, %	28.8	37.6‡
Hypertension Management Behaviors		
Complementary and alternative medicine use	25.6	26.9
< 2 Lifestyle Modifications	20.5	16.5†

† p<0.05

‡ p<0.01 for comparisons between men and women

§ in the prior year

Table 2

Relationship between participant characteristics (patient and health care system variables) and low antihypertensive medication adherence score, stratified according to sex

	% w/low medication adherence score (MMAS-8)	
	Men (N=911)	**Women (N =1,283)**
Socio-Demographics and Patient Characteristics		
Age ≥ 75 years	10.5†	12.7
Age <75 years	15.3	17.3
Black race	16.4	19.2†
White/Other Race	12.2	12.5
Married	12.5	15.6
Not Married	14.9	14.5
<High School Graduate	13.1	14.6
≥High School Graduate	12.7	16.4
Low hypertension knowledge	13.4	16.7
Not low hypertension knowledge	12.9	14.2
Clinical / Treatment Variables		
Hypertension duration ≥ 10 Years	12.9	14.1
Hypertension duration < 10 Years	13.3	16.4
Charlson Comorbidity Index score ≥ 2§	14.2	15.2
Charlson Comorbidity Index score < 2§	11.6	14.8
Body mass index: ≥ 25 kg/m^2	14.8‡	16.1
Body mass index: < 25 kg/m^2	6.0	11.5
3+ classes of antihypertensive medication§	13.1	14.5
<3 classes of antihypertensive medication§	12.5	15.6
Health Care System Variables		
Not satisfied with overall health care	18.2	24.6†
Satisfied with overall health care	12.8	14.5
Not satisfied with communication	13.0	23.2‡
Satisfied with communication	13.1	14.0
Not satisfied with access to healthcare	11.6	25.0†
Satisfied with access to healthcare	13.1	14.5

	% w/low medication adherence score (MMAS-8)	
	Men (N=911)	**Women (N =1,283)**
Reduced medications due to cost	45.2‡	39.6‡
Did not reduce medications due to cost	11.9	13.9
6+ visits to primary care physician§	13.2	14.5
<6 visits to primary care physician	13.0	15.0

† p<0.05

‡ p<0.01 for comparisons between men and women

§ in the prior year. Low MMAS-8 defined as a score <6 on the Morisky Medication Adherence Scale

Table 3

Relationship between participant characteristics (psychosocial/behavioral and hypertension management variables) and low antihypertensive medication adherence score, stratified according to sex

	% w/low medication adherence score (MMAS 8)	
	Men (N= 911)	**Women (N= 1,283)**
Psychosocial / Behavioral Variables		
Current or former smoker	16.4	14.1
Never smoker	14.1	11.2
≥ 2 alcoholic beverages per week	12.5	19.0
<2 alcoholic beverages per week	13.0	14.4
Reduced sexual functioning	16.7‡	15.9
Normal sexual functioning	9.2	13.3
Depressive symptoms	17.7	26.7‡
No Depressive symptoms	12.5	12.9
Low Social Support	17.3†	17.3
Med/High Social Support	11.2	13.6
Low Coping	13.0	15.8
Med/High Coping	13.1	14.0
High Stress	19.5‡	19.3‡
Med/Low Stress	10.5	12.4
Hypertension Management Behaviors		
Complementary / alternative medicine use	15.0	18.6
No Complementary / alternative medicine	12.4	13.7
< 2 Lifestyle Modifications	18.2‡	19.0†
≥ 2 Lifestyle Modifications	11.7	14.2

† p<0.05

‡ p<0.01 for the relationship between each characteristic and medication adherence score within each sex (p-values adjusted for age, race, marital status, education, and comorbidity (Charlson).

§ in the prior year

Low medication adherence score defined as a score <6 on the Morisky Medication Adherence Scale

Table 4

Sex-stratified multivariable models showing the association between participant characteristics and low antihypertensive medication adherence score

	Men (N=911)	Women (N=1,283)
	OR (95% CI)*	OR (95% CI)*
Reduced antihypertensive medications due to cost	5.89(2.65,13.07)‡	3.51(1.84,6.68)‡
< 2 Lifestyle modifications	2.32(1.44,3.74)‡	1.73(1.15,2.60)‡
Not satisfied with provider communication	1.16(0.57, 2.34)	1.75(1.16,2.65)†
Depressive symptoms	0.93(0.48,1.80)	2.29(1.55,3.38)‡
Reduced sexual functioning	2.03(1.31,3.16)‡	1.28(0.90,1.82)
Body mass index: ≥ 25 functioning	3.23(1.59,6.59)‡	1.23(0.82,1.85)

*OR's adjusted for all variables shown, as well as age, race, marital status, education, and comorbidity (Charlson)

†p<0.05

‡p<0.01. Low medication adherence score defined as a score <6 on the Morisky Medication Adherence Scale