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Research Article

The Association of Beta-Blocker Use to Cognitive Impairment among Adults with Hypertension or Cardiovascular Diseases in the United States

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Abstract

Background: Some studies have shown that beta-blocker use is associated with better cognitive impairment. However, these studies did not control for pain. The relationship between pain and cognitive impairment has been exhaustively investigated. The association of beta blockers to cognitive impairment in the presence of chronic pain is still unknown.

Objective: To examine the independent association of beta-blocker use to cognitive impairment among adults with hypertension or Cardiovascular Diseases (CVDs).

Methods: We used a cross-sectional study design. We derived data on 8,279 adults from the 2015 Medical Expenditure Panel Survey (MEPS). Study participants were adults (age ≥ 21 years), with hypertension or CVDs and without intracranial injury, Parkinson, Alzheimer's disease and Related Dementia. Cognitive impairment was measured based on 1) confusion or memory loss; 2) problems making decisions, or 3) supervision for participant's safety. Anti-hypertensive medications were categorized into 1) beta-blockers; 2) other anti-hypertensives; and 3) no antihypertensive medication. We used multivariable survey logistic regressions to examine the association between beta-blockers and cognitive impairment after controlling for biological factors, pain, chronic conditions, socioeconomic status, access to healthcare services, behavioral, socio-cultural and external environmental factors.

Results: Overall, 24.2%, 41.9%, and 33.9% reported using beta-blockers, other antihypertensives, and no antihypertensive medications, respectively; 18.1% participants reported cognitive impairment. After controlling for pain, beta-blocker use was not significantly associated with cognitive impairment (AOR= 1.22, 95%CI= 1.00-1.49). In fully adjusted models, the AOR for beta-blockers use was 1.05 (95%CI = 0.84-1.31).

Conclusion: In this first large cross-sectional study, we found that the use of beta-blockers was not associated with cognitive impairment. Future prospective studies that include pain management and blood pressure control are needed to confirm the findings.

Keywords: Antihypertensive medicines; Beta-blockers; Cardiovascular diseases; Cognitive impairment; Pain

Introduction

Cognitive impairment, defined as difficulties in learning new things, remembering, concentrating, and making rational decisions affects nearly 16 million adults in the United States (US) [1]. Cognitive impairment has profound negative effects on patients, caregivers, healthcare providers, payers, and society [1-3]. Mild Cognitive Impairment (MCI) is a risk factor for Alzheimer disease and other dementias (ADRD) [4,5] and places excessive humanistic and financial burdens on both adults and their caregivers [6,7].

Many factors have been known to affect cognitive functioning, including age, race, sex, family history,, physical and mental health conditions, head trauma, smoking, physical inactivity, environmental factors, pain [8-14] and pharmacotherapies [15].

There are several plausible explanations of why the use of beta-blockers may favorably affect cognition. Beta-blockers inhibit the sympathetic nervous system by binding to beta-adrenergic receptors which lowers the hearts' contractile force, dilates arterial vasculature, and lowers blood pressure [16]. As high blood pressure [17,18] and pathological vascular systems [19] have been shown to have harmful effects on cognitive function, it is plausible that beta-blockers may improve blood pressure and indirectly improve cognitive functioning. Gelber [20] and White [21] reported that beta-blocker use was associated with lower risks of cognitive impairment due to the effect of beta blockers on improved brain tissue functions.

Other studies have hypothesized that the use of adrenergic receptor antagonists may affect cognitive function through the pain pathway [15,22]. It is important to note that the association between pain and cognitive impairment is complex and involves changes to brain morphology, electrophysiology, neurotransmitters and receptors, glial cells, cytokines, enzymes, and neurotrophic factors [15]. Several pre-clinical and clinical studies have documented the association of chronic pain to cognitive impairment [14,15,23]. Whitlock and colleagues reported that respondents with persistent pain had 15% higher rates of memory decline compared to participants without pain [24]. In addition, higher levels of pain have been correlated with increased depressive symptoms and reduced neuropsychological test scores [25].

Recent observational studies have found that beta-blockers may reduce pain. For example, Valdes et al, used data from the Genetics of Osteoarthritis and Lifestyle study and found that among adults with osteoarthritis, those who used beta-blockers reported less joint pain and were less likely to use opioids and other analgesics compared to those who did not use beta-blockers [22].

To date, no study has evaluated the association of beta-blockers to cognitive impairment after controlling for chronic pain. Therefore, the primary objective of the current study is to explore the association of beta-blocker medication use to cognitive impairment after controlling for pain among adults with cardiovascular diseases (CVDs) or hypertension using a nationally representative sample of adults in the United States. Adults with hypertension or CVDs were chosen because they are more likely to receive beta-blockers for treatment of these conditions [16].

Methods

Study design

This study adopted a cross-sectional design.

Data source

We used data from the 2015 Medical Expenditure Panel Survey (MEPS), a household survey of non-institutionalized adults in the US [26]. The survey collects a variety of health-related information including individual socio-demographic characteristics, health conditions, healthcare use and expenditures, sources of payment and health insurance coverage. We combined data from MEPS Household Survey, Prescribed Medicines, and Medical Condition Files to create our analytical dataset.

Sample

Study participants were adults (21 years or older) with CVDs or hypertension. The cardiovascular conditions included were pulmonary heart disease, acute myocardial infarction, cardiomyopathy, coronary atherosclerosis, conduction disorders, cardiac dysrhythmias, congestive heart failure, cardiac arrest, ventricular fibrillation, and other ill-defined heart diseases. These conditions were measured based on Clinical Classification Code, International Classification of Diseases, Ninth Revision (ICD-9), and self-reported data (especially for hypertension) on MEPS. We excluded adults with missing information on cognitive impairment, (n = 158) individuals with intracranial injury, (n = 59) Parkinson's disease or ADRD (n = 199) and individuals who died during the calendar year. The final sample size consisted of 8,279 adults with CVDs or hypertension.

Measures

Dependent variable: Cognitive Impairment

We identified the presence or absence of cognitive impairment from the household (full year consolidated) file based on the questions asking if the person (1) experienced confusion or memory loss, (2) had problems making decisions, or (3) required supervision for their own safety. We used codes COGLIM31, COGLIM53 – representing cognitive limitations (round 3/1 and 5/3), and Code DFCOG42 – representing serious cognitive difficulties (round 4/2). We categorized this into a binary variable Yes (cognitive limitation) and No (no cognitive limitation)

Key Independent Variables

Use of Beta-Blockers

We identified Beta-blockers and other antihypertensive medications using the prescribed medicines file. This file contains information on drug names, national drug code, drug-supplied and other medication related information. Prescription drugs were classified into various therapeutic classes based on the proprietary "Multum Lexicon" files. Multum Lexicon provides a 3-level nested category system for each drug based on the ingredients [27]. Therapeutic classification code 47 represented beta-blockers and codes 42, 43, 48, 49, 53, 55, 56 represented other antihypertensives (ACE-inhibitor, alpha-adrenergic blockers, calcium channel blockers, diuretics, vasodilators, angiotensin receptor blockers, antihypertensive combinations, and angiotensin II inhibitors). This variable was categorized into three groups: (1.) Beta-Blockers (2.) other antihypertensives (3.) No antihypertensive medication.

Pain

A self-administered questionnaire was used to collect information on pain and other domains of health-related quality of life. Pain was measured using one item from the Short Form (SF)-12, asking how much pain "interfered with normal work (including both work outside the home and housework)" during the past 4 weeks prior to the interview. Responses were recorded using a 5-item Likert scale: 1) 'Not at all'; 2) 'A little bit'; 3) 'Moderate';
4) 'Severe'; and 5) 'Extreme'. We used this pain interference with activities as a proxy for chronic pain [28,29].

Other Independent Variables

Other variables that may influence cognitive impairment were selected based on *the determinants of health model initially proposed by Park in the Textbook of Preventive and Social Medicine (2015)* and published studies that examined factors associated with cognitive impairment. These included: biological characteristics like sex (female vs. male), age, categorized into 4 groups (21-44, 45-54, 55-64, 65 and older) and race (White, African American, Latino, and other), socio-economic factors like education (Less than high school, high school, and above high school) and poverty status (poor, near poor, middle income, and high income measured in terms of percentages of federal poverty line), socio-cultural factors like marital status (married, widowed, divorced/separated, and not married)], and behavioral factors like body mass index (underweight, normal, overweight, obese), physical activity (exercising five times/week and others), and smoking status (yes/ no). We also included variables of access to healthcare services, measured by health insurance (public, private, and uninsured) and prescription coverage (yes/no), medical condition including the presence of asthma, chronic obstructive pulmonary disease (COPD), cancer, diabetes mellitus, mental health conditions (depression and anxiety), hypercholesterolemia, and arthritis (yes/no), and region of residence (Northeast, Midwest, South and West).

Statistical analysis

Statistically significant differences in cognitive impairment by type of antihypertensive medications were determined by Rao-Scott chi-square tests. Multivariable logistic regression models were used to assess the relationship between type of antihypertensive medications and cognitive impairment after controlling for sex, age, race, pain, education, poverty status, marital status, body mass index, physical activity, smoking status, health insurance, prescription coverage, asthma, Chronic Obstructive Pulmonary Disease (COPD), cancer, diabetes mellitus, mental health conditions (depression and anxiety), hypercholesterolemia, arthritis, region of residence. Since MEPS uses as complex survey design with clustering, stratification, and weights, we conducted all the analyses using the survey procedure in SAS version 9.4. Because pain information was assessed from self-administered questionnaires, we applied appropriate weights for the responses derived from those self-administered questionnaires.

Results

Our study participants consisted of 8,279 adults (Wt. N= 94,815,011) with hypertension or cardiovascular disease. Majority of the respondents were female (50.8%), white (67.6%) and married (58.8%). Thirty-seven percent of the participants were 65 years or older and 54.3% had greater than high school education. About 52.9% of the sample had prescription medicine coverage and only 5.9% were uninsured (Table 1).

Overall, 24.2% of the participants reported using beta-blockers and 41.9% used other antihypertensives (Appendix 1). A higher percentage of elderly participants (65 years or older) used beta-blockers compared to adults aged 21-44 years (36.3% vs 9.2%). A similar trend was also observed among individuals with chronic conditions. Compared to individuals without chronic conditions, respondents with chronic conditions such as COPD (31.9% vs 23.3%), cancer (32.8% vs 22.9%), diabetes mellitus (32.7% vs 21.4%), hypercholesterolemia (30.1% vs 16.0%), and arthritis (28.8% vs 17.6%) were more likely to use beta blockers. We found statistically significant differences in reported pain and cognitive impairment between groups of individuals who used beta-blockers, other antihypertensive medications, compared to those who did not use antihypertensive medications.

Table 1: Description of Sample Characteristics Adults with hypertension or Cardiovascular diseases Medical Expenditure Panel Survey, 2015.

	N	Wt. %
ALL	**8,279**	**100.0**
Anti-Hypertensive Medications		
Beta-blockers	1,917	24.2
Other Antihypertensives	3,451	41.9
No Antihypertensives	2,911	33.9
Cognitive Impairment		
Yes	1,496	18.1
No	6,783	81.9
Pain		
No Pain	3,290	40.8
A Little bit	2,116	26.8
Moderate	1,164	14.2
Severe	1,141	12.7
Extreme	457	4.5
Biological Factors		
Sex		
Female	4,489	50.8
Male	3,790	49.2
Race/Ethnicity		
White	3,855	67.6
African American	1,950	13.6
Latino	1,728	11.6
Other	746	7.3
Age		
21-44 years	1,778	20.3
45-54 years	1,615	18.8
55-64 years	2,042	24.0
65 years and older	2,844	37.0
Socio-economic Factors		
Poverty Status		
Poor	1,526	11.3
Near Poor	1,877	18.7
Middle Income	2,404	28.2
High Income	2,472	41.8
Education		
Less than High School	1,673	13.3
High School	2,673	31.8
Greater than High School	3,869	54.3
Socio-cultural Factors		
Marital Status		
Married	4,234	58.8
Widowed	982	11.0
Divorced/Separated	1,625	16.4
Not Married	1,438	13.8
Behavioral Factors		
Body Mass Index		
Underweight	82	1.0
Normal	1,761	22.3
Over	2,673	33.0
Obese	3,642	42.4

	N	Wt. %
ALL	**8,279**	**100.0**
Current Smoking Status		
Current Smoker	1,311	15.1
Other	6,768	82.7
Exercise		
5/week	3,548	44.9
No exercise	4,688	54.6
Access to Healthcare		
Insurance Coverage		
Public	4,639	65.6
Private	2,952	28.6
Uninsured	688	5.9
Prescription Coverage		
Yes	3,739	52.9
No	4,540	47.1
Health Status (Chronic Conditions)		
Asthma		
Yes	1,141	12.9
No	7,137	87.1
COPD		
Yes	732	9.8
No	7,547	90.2
Cancer		
Yes	861	12.9
No	7,418	87.1
Diabetes Mellitus		
Yes	2,212	24.2
No	6,066	75.8
Mental Health Condition		
Yes	2,094	26.9
No	6,185	73.1
Hypercholesterolemia		
Yes	4,674	58.1
No	3,601	41.9
Arthritis		
Yes	4,771	58.6
No	3,507	41.4
External Environment		
Region		
Northeast	1,258	17.0
Midwest	1,670	22.1
South	3,443	39.7
West	1,908	21.2

Notes: Based on 8,279 adults age 18 years or older, who participated in the survey in 2015, observed during the entire calendar year and reported having hypertension or cardiovascular diseases.
COPD: Chronic Obstructive Pulmonary Disease.
Wt. %: Weighted Percentage.

As many as 18.1% of the participants reported having cognitive impairment. Individuals who reported cognitive impairment differed significantly from those who did not with respect to all the independent variables included in the study except race/ethnicity, cancer, and region (Table 2). For example, compared to adults with no antihypertensive medications, a higher percentage of those with beta-blocker use had cognitive impairment (13.2% vs 20.2%). The Unadjusted Odds Ratios (UOR) indicated that adults who used beta-blockers had significantly higher odds of cognitive impairment (OR = 1.67; 95%CI= 1.39, 2.01, p <.0001) compared to individuals who did not use any anti-hypertensive medication. We did not find significantly higher odds of cognitive impairment among individuals who used other antihypertensive medications (OR=1.17; 95%CI= 0.97, 1.41, p = 0.0920). Pain was significantly associated with cognitive impairment; adults who reported extreme pain (UOR = 13.52; 95%CI = 9.99, 18.30, p= <0.001), severe pain (UOR = 8.70; 95%CI = 6.85, 11.06, p= <0.001), and moderate pain (UOR = 4.47; 95%CI = 3.49, 5.73, p= <0.001) all had higher odds of having cognitive impairment compared to those with no pain.

After controlling for pain in our model, beta-blocker use was not significantly associated with cognitive impairment (AOR= 1.22, 95%CI= 1.00-1.49). Adults who reported extreme pain were 13.2 times more likely to report impaired cognition (95%CI= 9.71, 17.92, p <.001) compared to those with no pain. In the fully adjusted model, the use of beta-blockers was not associated with cognitive impairment. (OR=1.05, 95% CI = 0.84-1.31, p=0.6901) (Table 3).

Table 2: Unweighted N and Weighted Percentages of Adults with Hypertension or Cardiovascular Diseases by Cognitive Impairment status Medical Expenditure Panel Survey, 2015.

	Cognitive Impairment		No Cognitive Impairment		Sig.
	N	Wt%	N	Wt%	
ALL	**1,496**	**18.1**	**6,783**	**81.9**	
Anti-hypertensive medications					***
Beta-blockers	457	20.2	1,460	79.8	
Other antihypertensives	612	15.1	2,839	84.9	
No antihypertensives	427	13.2	2,484	86.8	
Pain					***
No pain	211	6.2	3,079	93.8	
A little bit	277	10.7	1,839	89.3	
Moderate	295	23.0	869	77.0	
Severe	458	36.6	683	63.4	
Extreme	226	47.3	231	52.7	
Biological Factors					
Sex					***
Female	905	17.2	3,584	82.8	
Male	591	14.1	3,199	85.9	
Age					***
21-44 years	221	11.1	1,557	88.9	
45-54 years	255	12.6	1,360	87.4	
55-64 years	405	16.8	1,637	83.2	
65 years and older	615	19.0	2,229	81.0	
Race/Ethnicity					
White	672	15.2	3,183	84.8	
African American	389	16.6	1,561	83.4	
Latino	308	16.9	1,420	83.1	
Other race	127	16.6	619	83.4	
Socio-economic Factors					
Poverty Status					***
Poor	524	35.3	1,002	64.7	
Near Poor	441	24.4	1,436	75.6	
Middle Income	319	13.8	2,085	86.2	
High Income	212	7.7	2,260	92.3	

	Cognitive Impairment		No Cognitive Impairment		Sig.
	N	Wt%	N	Wt%	
ALL	**1,496**	**18.1**	**6,783**	**81.9**	
Education					
Less than High School	420	24.5	1,253	75.5	
High School	527	18.0	2,146	82.0	
Greater than High School	529	12.0	3,340	88.0	
Socio-cultural Factors					
Marital Status					***
Married	466	10.0	3,768	90.0	
Widowed	269	26.9	713	73.1	
Divorced/Separated	443	25.2	1,182	74.8	
Not Married	318	19.7	1,120	80.3	
Behavioral Factors					
Body Mass Index					*
Underweight	20	23.5	62	76.5	
Normal	350	18.2	1,411	81.8	
Over	452	14.5	2,221	85.5	
Obese	658	15.3	2,984	84.7	
Current Smoking					***
Current Smoker	331	22.8	980	77.2	
Other	1,120	14.1	5,648	85.9	
Exercise					***
5 times /week	445	10.1	3,103	89.9	
No exercise	1,047	20.3	3,641	79.7	
Access to Healthcare					
Insurance Coverage					***
Public	493	9.8	4,146	90.2	
Private	925	29.5	2,027	70.5	
Uninsured	78	13.6	610	86.4	
Prescription Coverage					***
Yes	348	8.8	3,391	91.2	
No	1,148	23.4	3,392	76.6	

Health Status (Chronic Conditions)					
Asthma					***
Yes	327	25.3	814	74.7	
No	1,169	14.2	5,968	85.8	
COPD					***
Yes	259	32.2	473	67.8	
No	1,237	13.9	6,310	86.1	
Cancer					
Yes	190	17.8	671	82.2	
No	1,306	15.4	6,112	84.6	
Diabetes Mellitus					***
Yes	557	22.4	1,655	77.6	
No	939	13.5	5,127	86.5	
Mental Health Condition					***
Yes	798	32.0	1,296	68.0	
No	698	9.7	5,487	90.3	
Hypercholesterolemia					***
Yes	1,005	18.5	3,669	81.5	
No	490	11.7	3,111	88.3	
Arthritis					***
Yes	1,219	21.8	3,552	78.2	
No	277	7.0	3,230	93.0	
External Environment					
Region					
Northeast	222	12.9	1,036	87.1	
Midwest	308	15.5	1,362	84.5	
South	637	16.7	2,806	83.3	
West	329	16.2	1,579	83.8	

Notes: Based on 8,279 adults age 21 years or older, who participated in the survey in 2015, observed during the entire calendar year and reported having hypertension or cardiovascular diseases. Asterisks represent significant group differences by cognitive impairment based on Rao-Scott Chi square tests.
***p< .001; **.001 ≤ p < .01; *.01 ≤ p <.05
Unweighted N may not add to total due to missing data in pain, body mass index, exercise, smoking, asthma, diabetes mellitus, hypercholesterolemia, and arthritis.
COPD: Chronic Obstructive Pulmonary Disease; Sig: Significance, wt. %: Weighted Percentage.

Table 3: Unadjusted Odds Ratios (UOR), Adjusted Odds Ratios (AOR) and 95% Confidence Intervals (CI) of The Use of Anti-hypertensive Medication and Pain Categories from Logistic Regression on Cognitive Impairment Among Adults Medical Expenditure Panel Survey, 2015.

Model 1: Unadjusted Model			
	UOR	**95% CI**	**Significance**
Anti-Hypertensive Medication			
Beta-blockers	1.67	[1.39,2.01]	<0.001***
Other Anti-hypertensive (s)	1.17	[0.97,1.41]	0.0920
No Anti-hypertensive (s)†			
Model 2: Adjusted for Pain			
	AOR	**95% CI**	**Significance**
Anti-Hypertensive Medication			
Beta-blockers	1.22	[1.00, 1.49]	0.0544
Other Anti-hypertensive (s)	0.94	[0.77, 1.15]	0.5674
No Anti-hypertensive (s)†			
Pain			
None†			
Little	1.78	[1.41, 2.25]	<0.001***
Moderate	4.38	[3.42, 5.60]	<0.001***
Severe	8.57	[6.76, 10.86]	<0.001***
Extreme	13.19	[9.71, 17.92]	<0.001***
Model 3: Fully Adjusted Model			
Anti-Hypertensive Medication			
Beta-blockers	1.05	[0.84, 1.31]	0.6901
Other Anti-hypertensive (s)	0.84	[0.67, 1.05]	0.1335
No Anti-hypertensive (s) †			
Pain			
None†			
Little	1.28	[1.01, 1.63]	0.0409*
Moderate	2.51	[1.89, 3.34]	<0.001***
Severe	3.68	[2.85, 4.74]	<0.001***
Extreme	5.41	[3.90, 7.50]	<0.001***

Note: Based on 8,279 adults age 21 years or older, who participated in the survey in 2015, observed during the entire calendar year and reported having hypertension or cardiovascular diseases. †: Reference Group. Fully adjusted model controlled for pain, sex, age, race, education, poverty status, marital status, body mass index, physical activity, smoking status, health insurance, prescription coverage, asthma, chronic obstructive pulmonary disease (COPD), cancer, diabetes mellitus, mental health conditions (depression and anxiety), hypercholesterolemia, arthritis, region of residence. Pain included a missing category as well (not presented).
***p< .001; **.001 ≤ p < .01; *.01 ≤ p <.05

Discussion

This paper examined the association of beta-blockers with cognitive impairment among adults with hypertension or CVDs. In this study, 18.1% of all participants and 19.0% of the elderly reported cognitive impairment. This finding is broadly consistent with previous studies in adults over 65 years that report rates of cognitive impairment between 5% and 36.7% [30].

After controlling for pain, the association between beta blocker use and cognitive impairment was not statistically significant. In the fully adjusted model, individuals with extreme pain were 5.4 times more likely to have cognitive impairment compared to those without pain. The prevalence of moderate and extreme pain was comparable within the anti-hypertensive medication categories (Appendix 1) Taken together, these findings suggest that pain rather than antihypertensive medication use may account for the observed association to cognitive impairment.

Our study findings are not consistent with previous studies by Gelber, et al. and White, et al. which reported that individuals who used beta blockers had lower risks of developing cognitive impairment compared to those who did not use antihypertensive medications [20,21,31]. Differences in study design, study population, cognitive impairment scales, and controlling for pain may partly explain the inconsistent findings. Gelber, et al. used a prospective cohort of Japanese American men living in Hawaii and measured cognitive impairment using a combination of the Hasegawa Dementia Screening Scale, the Folstein Mini-Mental State Examination, and the Modified Mini-Mental State Examination but did not control for pain. Several reports postulated that the mechanism behind this protective effect of beta-blocker on cognition involved the action of beta-blockers on vasculature to improve and maintain the ability of the heart and blood vessels to adjust to systemic or local physiological disturbances in the cardiovascular system [16,17]. Conversely, Gliebus and Lippa posited that beta-blockers could potentially block the activation of norepinephrine, the neurotransmitter which plays an essential role in the retrieval of memories from the hippocampus [32]. On the other hand, our main study finding that there is no significant association between beta blocker use and cognitive impairment is consistent with an analysis of published clinical trial data from 19 trials on beta-blockers [33] and a randomized, double-blind, controlled crossover trial [34].

Several factors that may account for the different findings in this study include extent of blood pressure control, which has been shown to be correlated with medication adherence [35,36], and other residual factors which were not measured in this study [37]. The cognitive impairment scale used in MEPS was relatively crude and we expect that more specific measures of cognition (such as attention, learning and memory, speed of processing, psychomotor ability and executive function) could improve the robustness the study design.

Our study findings are consistent with previous reports on the association of pain to cognitive impairment which has been exhaustively investigated [14,15]. Almost all pain categories were associated with cognitive impairment with adjusted odds ratios ranging from 1.28 for mild pain, 2.51 for moderate pain, 3.68 for severe pain, and 5.41 for extreme pain. This is consistent with a review of pre-clinical and clinical studies by Moriarty and colleagues [15].

Our study has many strengths such as the use of a representative sample of adults in the US, availability of prescription drug information, and adjustment for a comprehensive list of variables, especially pain, which could confound the relationship between antihypertensive medications and cognitive impairment. However, our study has some limitations including the use of cross-sectional data, which precludes the assumption of any causal relationship. We did not adjust for blood pressure control due to the fact that MEPS does not include clinical parameters. Other limitations are that this study utilized self-reported overall cognitive impairment as a crude measure of cognitive function and did not include data on duration of beta-blockers use. Future studies that employ a prospective study design, with robust measures of cognitive impairment and duration of beta-blocker use and medication adherence measures are needed to confirm our study findings.

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Appendix 1: Unweighted N and Weighted Percentages of Adults with Hypertension or Cardiovascular Diseases by Antihypertensive Categories Medical Expenditure Panel Survey, 2015.

	Beta-blocker		Other Anti-HTN Rx		No Anti-HTN Rx		Sig.
	N	Wt%	N	Wt%	N	Wt%	
ALL	1,917	24.2	3,451	41.9	2,911	33.9	
Cognitive Impairment							***
Yes	457	20.2	612	15.1	427	13.2	
No	1,460	79.8	2,839	84.9	2,484	86.8	
Pain Interference with Normal Activities							***
No pain	572	18.7	1,306	40.6	1,412	40.8	
A little bit	512	24.8	898	41.7	706	33.5	
Moderate	332	30.4	493	41.8	339	27.8	
Severe	337	30.1	528	48.3	276	21.6	
Extreme	137	33.0	188	39.9	132	27.1	
Biological Factors							
Sex							*
Female	1,045	23.8	1,943	43.5	1,501	32.7	
Male	872	24.5	1,508	40.3	1,410	35.2	
Age							***
21-44 years	150	9.2	423	22.8	1,205	68.0	
45-54 years	253	16.8	698	42.4	664	40.8	
55-64 years	481	23.8	985	48.2	576	28.0	
65 years and older	1,033	36.3	1,345	48.1	466	15.6	
Race/Ethnicity							***
White	1,031	26.3	1,580	42.2	1,244	31.5	
African American	432	21.6	908	45.3	610	33.1	
Latino	286	16.4	653	36.6	789	47.0	
Other race	168	21.7	310	41.2	268	37.1	
Socio-Economic Factors							
Poverty Status							***
Poor	336	20.6	601	39.4	589	39.9	
Near Poor	465	27.0	743	39.6	669	33.5	
Middle Income	564	25.4	1,001	40.2	839	34.4	
High Income	552	23.1	1,106	44.8	814	32.2	
Education							*
Less than High School	392	25.2	719	42.9	562	31.9	
High School	652	25.6	1,097	41.9	924	32.6	
Greater than High School	860	23.2	1,604	41.5	1,405	35.3	
Socio-cultural Factors							
Marital Status							***
Married	950	24.0	1,828	43.3	1,456	32.7	
Widowed	318	32.3	474	50.1	190	17.6	
Divorced/Separated	419	26.1	673	40.9	533	33.0	
Not Married	230	16.2	476	30.6	732	53.1	
Behavioral Factors							
Body Mass Index							***
Underweight	21	24.5	21	26.5	40	49.0	
Normal	358	20.0	648	36.0	755	44.1	
Over	607	23.4	1,122	42.9	944	33.6	
Obese	910	27.1	1,611	44.7	1,121	28.3	
Current Smoking							***
Current Smoker	251	19.6	478	36.1	582	44.3	
Other	1614	24.9	2,887	43.0	2,267	32.2	
Exercise							***
5 times /week	710	20.0	1,509	43.3	1,329	36.7	
No exercise	1,200	27.7	1,928	40.8	1,560	31.5	

Access to Healthcare							
Insurance Coverage							***
Public	979	22.2	1,979	42.8	1,681	34.9	
Private	867	31.0	1,265	42.6	820	26.4	
Uninsured	71	12.4	207	28.3	410	59.3	
Prescription Coverage							***
Yes	753	21.5	1,609	42.5	1,377	36.0	
No	1,164	27.1	1,842	41.3	1,534	31.6	
Health Status (Chronic Conditions)							
Asthma							
Yes	283	25.1	488	43.1	370	31.8	
No	1634	24.0	2,962	41.7	2,541	34.2	
COPD							***
Yes	224	31.9	320	43.5	188	24.6	
No	1,693	23.3	3,131	41.7	2,723	34.9	
Cancer							***
Yes	297	32.8	401	48.5	163	18.7	
No	1,620	22.9	3,050	40.9	2,748	36.2	
Diabetes Mellitus							***
Yes	695	32.7	1,128	51.0	389	16.3	
No	1,222	21.4	2,322	39.0	2,522	39.6	
Mental Health Condition							
Yes	539	25.2	881	43.0	674	31.7	
No	1,378	23.8	2,570	41.5	2,237	34.7	
Hypercholesterolemia							***
Yes	1,369	30.1	2,151	46.2	1,154	23.7	
No	547	16.0	1,298	35.9	1,756	48.1	
Arthritis							***
Yes	1,340	28.8	2,145	44.5	1,286	26.7	
No	577	17.6	1,306	38.3	1,624	44.1	
External Environment							
Region							
Northeast	327	26.9	499	38.8	432	34.3	
Midwest	419	25.1	700	42.6	551	32.4	
South	805	24.3	1,475	43.2	1,163	32.6	
West	366	20.8	777	41.4	765	37.8	

Notes: Based on 8,279 adults age 21 years or older, who participated in the survey in 2015, observed during the entire calendar year and reported having hypertension or cardiovascular diseases. Asterisks represent significant group differences by cognitive impairment based on Rao-Scott Chi square tests.

$^{***}p < .001$; $^{**}.001 \leq p < .01$; $^{*}.01 \leq p < .05$

Unweighted N may not add to total due to missing data in pain, body mass index, exercise, smoking, asthma, diabetes mellitus, hypercholesterolemia, and arthritis.

AntiHTN-Rx: Antihypertensive Medications, COPD: Chronic Obstructive Pulmonary Disease; Sig: Significance, Wt. %: Weighted Percentage.