

Racial/Ethnic Differences in the Use of Angiotensin II Receptor Stimulatory Vs. Inhibitory Antihypertensive Among US Adults with Hypertension

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Introduction

- Hypertension, affecting nearly half of adults in the US, is a leading modifiable risk factor for cognitive impairment.¹
- No curative treatments are available for cognitive impairment, but optimizing antihypertensive treatment is a potentially promising, and inexpensive, strategy to reduce cognitive impairment incidence.²
- Thiazide diuretics and DiCCBs are generally thought to upregulate angiotensin II production, thereby stimulating activity at the AT2 and AT4 receptors.³
- BBs and non-DiCCBs are generally thought to downregulate angiotensin II production, thereby diminishing the positive activity at the AT2 and AT4 receptors.³
- Stimulatory antihypertensives were associated with a 24% lower risk of incident amnesic MCI or probable dementia during 4.8 years of follow-up.⁴
- Angiotensin II–stimulating antihypertensive use was associated with an approximately 42% lower risk of incident dementia compared to angiotensin II–inhibiting antihypertensive use over 6.7 years of follow-up.³
- Angiotensin II–stimulating antihypertensive use was associated with an approximately 17% lower risk of incident cognitive impairment compared to angiotensin II–inhibiting antihypertensive use over 5.4 years of follow-up.⁵

Objectives :

- To identify the health disparities among adult individuals prescribed type 2 and type 4 angiotensin II–inhibiting or type 2 and type 4 angiotensin II–stimulating antihypertensive agents.
- To describe the prevalence and patient characteristics among U.S adults prescribed type 2 and type 4 angiotensin II–inhibiting or type 2 and type 4 angiotensin II–stimulating antihypertensive agents.

Methods

- Cross-sectional study using the Medical Expenditure Panel Survey (MEPS) database from 2016 to 2019.

Included:

- Patients with hypertension.
- Age ≥ 45.

Excluded:

- Pregnancy.
- Patients with dementia and Alzheimer’s disease.

Exposure:

- Type 2 and 4 angiotensin II–stimulating group (i.e., thiazide diuretics, DiCCBs, and ARBs)
- Type 2 and 4 angiotensin II–inhibiting group (i.e., BB, non-DiCCBs, and ACEI).
- Other groups (i.e., vasodilators, diuretics other than thiazide, antiadrenergic agents centrally or peripherally acting, unknown combination antihypertensive, not on antihypertensive agents).

Analysis:

- Two multivariate logistic regression analyses were applied.
- 1st regression stimulatory vs (inhibitory and others) antihypertensives.
- 2nd regression inhibitory vs (stimulatory and others) antihypertensives.

Three adjusted models were used:

- 1st model: adjusted for age, sex, and race.
- 2nd model: adjusted for, age, sex, race, and comorbidities.
- 3rd model: adjusted for all variables.

Results

Table 1. Sample characteristics

	Number of Observations Used ^a (24,581) Weighted (252391188)	Stimulatory N (%) 13612 (54.58)	Inhibitory types N (%) 14594 (59.54)	Others* N (%) 3976 (16.08)
Age Mean (SE)	65.42 (0.130)	66.55 (0.15)	66.51 (0.16)	61.43 (0.25)
N (%)				
Age Categorical 45-64 65+	11637 (48.21) 12944 (51.79)	5832 (43.39) 7780 (56.61)	6296 (43.86) 8298 (56.14)	1455 (64.68) 1455 (35.32)
Sex Male Female	11423 (48.79) 13158 (51.21)	5899 (45.99) 7713 (54.01)	6998 (50.26) 7596 (49.74)	1975 (51.59) 2001 (48.41)
Race/ethnicity Hispanic Non-Hispanic White Non-Hispanic Black Non-Hispanic Asian Non-Hispanic Others	3890 (10.14) 14046 (69.58) 4850 (13.26) 1112 (4.27) 683 (2.75)	1938 (9.21) 7362 (66.97) 3265 (16.40) 687 (4.79) 360 (2.62)	2184 (9.33) 8798 (72.39) 2682 (12.16) 531 (3.43) 399 (2.68)	790 (13.33) 2206 (68.05) 676 (11.34) 180 (4.45) 124 (2.84)
Tobacco use Yes No	3595(13.62) 20986 (86.38)	1828 (12.31) 11784 (87.69)	2083 (13.51) 12511 (86.49)	3265 (83.34) 3265 (16.66)
Income level Poor/negative Near poor Low income Middle income High income	4105 (11.28) 1384 (4.55) 3701 (13.43) 6829 (27.34) 8562 (43.41)	2146 (10.32) 807 (4.74) 2067 (13.48) 3788 (27.42) 4804 (44.05)	2443 (11.33) 867 (4.90) 2308 (14.45) 4144 (28.40) 4832 (40.92)	780 (14.03) 186 (3.57) 574 (12.02) 1054 (26.33) 1382 (44.05)
Educational level No Degree High school or equivalent Higher than high school	4482 (13.04) 11889 (49.23) 8016 (37.73)	2411 (12.60) 6644 (49.30) 4462 (38.10)	2794 (14.07) 7181 (50.42) 4503 (35.51)	740 (13.23) 1885 (47.69) 1307 (39.08)
Health insurance Public Private Uninsured	10281 (35.43) 13512 (62.12) 788 (2.46)	5757 (35.65) 7492 (62.28) 363 (2.08)	6468 (38.24) 7697 (59.51) 429 (2.25)	1527 (31.60) 2260 (64.73) 189 (3.67)
Region of residency Northeast Midwest South West	4183 (17.49) 5058 (21.48) 10041 (40.19) 5299 (20.84)	2298 (17.49) 2691 (20.93) 5841 (41.69) 2782 (19.88)	2542 (17.83) 3093 (22.22) 6016 (40.75) 2943 (19.20)	659 (17.02) 798 (20.24) 1515 (38.01) 1004 (24.73)
Comorbidities Coronary artery disease Congestive heart failure Atrial fibrillation Stroke Chronic kidney disease Obesity/overweight Type 2 diabetes Dyslipidemia	5067 (20.12) 561 (2.16) 857 (4.00) 2788 (10.55) 213 (0.84) 179 (0.77) 7964 (29.88) 16542 (67.44)	2593 (18.96) 288 (2.02) 458 (3.92) 1594 (10.94) 138 (1.01) 108 (0.86) 4386 (29.69) 9261 (68.36)	3800 (25.54) 490 (3.15) 731 (5.62) 1899 (12.31) 144 (0.95) 105 (0.70) 5263 (33.33) 10274 (70.60)	594 (13.65) 38 (0.86) 49 (1.58) 391 (8.81) 20 (0.45) 28 (0.85) 1138 (26.06) 2424 (60.83)
Medications Thiazide diuretics ARBs Dihydropyridine CCBs ACEIs Non-Dihydropyridine CCBs Beta blockers	3496 (13.54) 4705 (19.31) 5946 (22.99) 7599 (31.28) 939 (3.96) 7573 (30.90)	3496 (24.81) 4705 (35.39) 5946 (42.11) 2767 (20.05) 480 (3.73) 4304 (31.75)	2086 (13.59) 1953 (13.38) 3346 (21.56) 7599 (52.54) 939 (6.65) 7573 (51.90)	NA NA NA NA NA NA
¥ Number of observations with Nonpositive Weights =376 *Others=Vasodilators, diuretics other than thiazide, antiadrenergic agents centrally or peripherally acting, unknown combination antihypertensive, none on antihypertensive agents. Note: we have 194 missing values in the education				

Discussion

- The results indicated that the prevalence of using the inhibitory group was higher than the stimulatory group.
- This could be justified by the high proportion of our cohort (26.28%) were suffering from compelling indications (coronary artery disease, congestive heart failure, atrial fibrillation) which are recommended to be mainly managed by beta-blocker and ACEI^{6,7}, both of which were represented by 30.9% & 31%, respectively in our studied drugs.
- Interestingly, the regression model showed that females benefited more from the stimulatory group than males.
- Considering the observable protective effect of the stimulatory group on dementia; and the fact that they have a higher risk of developing dementia than males (25% vs 18%), this might be why healthcare professionals are prescribing more stimulatory group medications to females than males.^{8,9}
- Despite the white race being most of our cohort, our findings showed that non-Hispanic Black and non-Hispanic Asians were prescribed more types 2 & 4 angiotensin II stimulatory antihypertensive agents than the inhibitory agents.
- This finding is corroborated by the fact that the most prescribed medication in the stimulatory group is DiCCBs and this is consistent with hypertension guidelines recommending DiCCBs for Black individuals.^{6,7}

Table 2. Factors associated with the use of stimulatory types 2 and 4 angiotensin II receptor medications among adults diagnosed with hypertension

Drug Class	Predictors	Odd Ratio (95% CI)		
		Model 1 ^a	Model 2 ^a	Model 3 ^a
Stimulatory	Age (ref ≥65) 45-64	0.639 (0.607-0.672)	0.624 (0.592-0.658)	0.622 (0.588-0.657)
	Sex (ref; male) Female	1.264 (1.202-1.330)	1.241 (1.179-1.306)	1.261 (1.197-1.328)
	Race/ethnicity (ref; Non-Hispanic White) Hispanic Non-Hispanic Black Non-Hispanic Asian Non-Hispanic Others	0.953 (0.887-1.024) 1.939 (1.809-2.077) 1.477 (1.302-1.674) 1.065 (0.913-1.242)	0.960 (0.893-1.032) 1.943 (1.812-2.084) 1.450 (1.278-1.644) 1.078 (0.924-1.258)	1.046 (0.965-1.134) 1.980 (1.839-2.132) 1.545 (1.356-1.761) 1.128 (0.965-1.319)
	Tobacco use (ref; No)			0.876 (0.813-0.944)
	Income level (ref; High income) Poor/Negative Near poor Low income Middle income			0.790 (0.723-0.864) 0.979 (0.864-1.109) 0.912 (0.837-0.994) 0.920 (0.860-0.985)
	Educational level (ref; Higher than high school) No Degree High school or equivalent			0.954 (0.876-1.039) 1.033 (0.973-1.098)
	Health insurance (ref; private) Public Uninsured			0.948 (0.891-1.009) 0.832 (0.716-0.967)
	Region of residency (ref; South) Northeast Midwest West			0.936 (0.868-1.008) 0.894 (0.833-0.959) 0.835 (0.778-0.897)
	Comorbidities (ref; No) Coronary artery disease Congestive heart failure Atrial fibrillation Stroke Chronic kidney disease Obesity/overweight Type 2 diabetes Dyslipidemia		0.786 (0.736-0.840) 0.821 (0.691-0.975) 0.928 (0.806-1.069) 1.029 (0.947-1.117) 1.474 (1.108-1.962) 1.246 (0.921-1.687) 0.947 (0.895-1.002) 1.104 (1.043-1.169)	0.799 (0.747-0.854) 0.822 (0.691-0.977) 0.928 (0.806-1.069) 1.063 (0.977-1.155) 1.532 (1.147-2.047) 1.227 (0.906-1.662) 0.956 (0.903-1.013) 1.100 (1.039-1.165)
	Age (ref ≥65) 45-64	0.672 (0.638-0.707)	0.769 (0.729-0.811)	0.795 (0.751-0.841)
	Sex (ref; male) Female	0.868 (0.825-0.914)	0.935 (0.887-0.986)	0.915 (0.867-0.965)
	Race/ethnicity (ref; Non-Hispanic White) Hispanic Non-Hispanic Black Non-Hispanic Asian Non-Hispanic Others	0.820 (0.763-0.881) 0.789 (0.738-0.843) 0.551 (0.487-0.622) 0.879 (0.752-1.026)	0.800 (0.743-0.862) 0.787 (0.735-0.843) 0.578 (0.510-0.655) 0.823 (0.702-0.964)	0.744 (0.685-0.808) 0.737 (0.686-0.793) 0.602 (0.529-0.685) 0.802 (0.683-0.942)
	Tobacco use (ref; No)			0.924 (0.857-0.998)
	Income level (ref; High income) Poor/Negative Near poor Low income Middle income			1.000 (0.913-1.095) 1.091 (0.960-1.239) 1.092 (1.000-1.193) 1.104 (1.030-1.183)
	Educational level (ref; Higher than high school) No Degree High school or equivalent			1.236 (1.132-1.349) 1.121 (1.055-1.193)
	Health insurance (ref; private) Public Uninsured			1.093 (1.026-1.165) 1.036 (0.891-1.205)
	Region of residency (ref; South) Northeast Midwest West			1.014 (0.939-1.095) 0.985 (0.916-1.059) 0.864 (0.804-0.929)
	Comorbidities (ref; No) Coronary artery disease Congestive heart failure Atrial fibrillation Stroke Chronic kidney disease Obesity/overweight Type 2 diabetes Dyslipidemia	1.913 (1.778-2.058) 3.038 (2.362-3.907) 2.934 (2.418-3.559) 1.157 (1.060-1.263) 1.017 (0.755-1.371) 0.942 (0.692-1.282) 1.426 (1.345-1.512) 1.118 (1.056-1.183)		1.867 (1.734-2.010) 3.009 (2.336-3.877) 2.998 (2.467-3.642) 1.125 (1.030-1.230) 1.028 (0.760-1.391) 0.952 (0.699-1.296) 1.398 (1.317-1.483) 1.111 (1.049-1.177)

Inhibitory

Stimulatory

Conclusions

- The results showed that angiotensin II–inhibitory agents were more prevalent than stimulatory ones.
- Despite the white race being most of this study cohort, the finding showed that non-Hispanic Black and non-Hispanic Asians were prescribed more stimulatory than inhibitory antihypertensive agents.

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