







BRIEF COMMUNICATION

Angiotensin-Converting Enzyme Inhibitors or Angiotensin Receptor Blockers Use and COVID-19 Infection Among 824 650 Patients With Hypertension From a US Integrated Healthcare System

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BACKGROUND: Previous reports suggest that the use of angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs) may upregulate angiotensin-converting enzyme 2 receptors and increase severe acute respiratory syndrome coronavirus 2 infectivity. We evaluated the association between ACEI or ARB use and coronavirus disease 2019 (COVID-19) infection among patients with hypertension.

METHODS AND RESULTS: We identified patients with hypertension as of March 1, 2020 (index date) from Kaiser Permanente Southern California. Patients who received ACEIs, ARBs, calcium channel blockers, beta blockers, thiazide diuretics (TD), or no therapy were identified using outpatient pharmacy data covering the index date. Outcome of interest was a positive reverse transcription polymerase chain reaction test for COVID-19 between March 1 and May 6, 2020. Patient sociodemographic and clinical characteristics were identified within 1 year preindex date. Among 824 650 patients with hypertension, 16 898 (2.0%) were tested for COVID-19. Of those tested, 1794 (10.6%) had a positive result. Overall, exposure to ACEIs or ARBs was not statistically significantly associated with COVID-19 infection after propensity score adjustment (odds ratio [OR], 1.06; 95% CI, 0.90–1.25) for ACEIs versus calcium channel blockers/beta blockers/TD; OR, 1.10; 95% CI, 0.91–1.31 for ARBs versus calcium channel blockers/beta blockers/TD). The associations between ACEI use and COVID-19 infection varied in different age groups (P -interaction=0.03). ACEI use was associated with lower odds of COVID-19 among those aged ≥ 85 years (OR, 0.30; 95% CI, 0.12–0.77). Use of no antihypertensive medication was significantly associated with increased odds of COVID-19 infection compared with calcium channel blockers/beta blockers/TD (OR, 1.32; 95% CI, 1.11–1.56).

CONCLUSIONS: Neither ACEI nor ARB use was associated with increased likelihood of COVID-19 infection. Decreased odds of COVID-19 infection among adults ≥ 85 years using ACEIs warrants further investigation.

Key Words: angiotensin-converting enzyme inhibitors ■ angiotensin receptor blockers ■ COVID-19 ■ hypertension

The coronavirus disease 2019 (COVID-19) pandemic has generated concerns that use of angiotensin-converting enzyme inhibitors (ACEIs)

or angiotensin receptor blockers (ARBs) may increase risk of COVID-19 infection or disease severity. Some animal models suggest that ACEIs or ARBs

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may upregulate angiotensin-converting enzyme 2 receptors and increase severe acute respiratory syndrome coronavirus 2 infectivity.¹ However, data from human studies are largely based on the shed form of angiotensin-converting enzyme 2 in plasma or urine and show complex results.² Other research suggests that ACEIs and ARBs may be protective against COVID-19 by upregulating angiotensin-converting enzyme 2 and mitigating the inflammatory response in the lungs of infected patients.³

Epidemiologic studies have emerged to address this question, and these reports showed no increased risk of severity of COVID-19 associated with ACEI or ARB exposure.^{4–9} However, most focused on those hospitalized for COVID-19¹⁰ and had limited information on the susceptibility of COVID-19. This study's purpose was to determine the risk of COVID-19 infection among patients with hypertension taking ACEIs or ARBs compared with other frequently used antihypertensive medications (calcium channel blockers [CCB], beta-blockers [BB], thiazide diuretics [TD]).

METHODS

Anonymized data that support the findings of this study are made available from the corresponding author on reasonable request from qualified researchers with documented evidence of training for human subjects protections.

Study Cohort

The study cohort was drawn from the hypertension registry of Kaiser Permanente Southern California (KPSC), a large US integrated healthcare system. The hypertension registry consists of patients who were diagnosed with hypertension and used antihypertensive medications (Table S1).¹¹ Eligible individuals were identified on March 1, 2020 (index date), aged ≥ 18 years, and not pregnant. We required 12 months of continuous membership before the index date (baseline). The study was approved by the KPSC institutional review committee and informed consent was waived.

Antihypertensive Medication Exposure

Based on pharmacy records, a fill of antihypertensive medication covering the index date defined medication exposure allowing a 20-day grace period. Antihypertensive medication groups were (1) any ACEIs; (2) any ARBs; (3) CCB, BB, or TD without the use of ACEIs or ARBs; (4) others (loop diuretics, potassium-sparing diuretics, centrally acting agents, alpha-blockers, and mineralocorticoid receptor antagonists) without the use of ACEIs or ARBs; and (5) no

antihypertensive medication. Patients who had antihypertensive medication dispenses and had a gap longer than 20 days from the index date was considered as having no antihypertensive medication.

Outcomes

The primary outcome was COVID-19 infection defined as a laboratory-confirmed, positive reverse transcription polymerase chain reaction test for COVID-19 between March 1 and May 6, 2020. KPSC members were tested for COVID-19 according to guidelines from the Centers for Disease Control and Prevention.¹² Sensitivity analysis included patients with a diagnosis code for COVID-19 but without test results at KPSC. The secondary outcome was hospitalization within 14 days after COVID-19 infection.

Covariates

Age at index, sex, race/ethnicity, neighborhood income and education, insurance, body mass index, and smoking status were included. Outpatient blood pressure and laboratory measures closest to the index date among those before the index date were used as baseline values. We used the lowest blood pressure if there were multiple blood pressure measures during the same encounter. Baseline comorbidities and outpatient medication use were evaluated.

Statistical Analysis

Descriptive statistics compared patient and clinical characteristics by COVID-19 testing, test results, and antihypertensive medication classes. The incidences of COVID-19 infection and hospitalization were calculated among all patients with hypertension and among patients with hypertension who were tested.

The primary analysis was conducted among patients with hypertension and COVID-19 test results. Propensity scores for receiving CCB/BB/TD were estimated using logistic regression considering age; sex; race/ethnicity; Elixhauser comorbidity index; body mass index; socioeconomic status; other comorbidities such as pneumonia, diabetes mellitus, heart failure, asthma, interstitial lung disease, and chronic obstructive pulmonary disease; and other medication use at baseline. Three 1:1 propensity score-matched populations were established in comparison to patients on CCB/BB/TD: (1) ACEIs, (2) ARBs, and (3) no antihypertensive medication use. Doubly robust logistic regression models accounted for covariates with standardized mean differences >0.1 to reduce residual imbalance. Sensitivity analyses were conducted using multivariable logistic regression and inverse probability treatment weights. A priori stratified analyses were conducted by several demographic and clinical characteristics such as sex,

Table 1. Patient and Clinical Characteristics by Antihypertensive Drug Exposure Among Patients Tested for COVID-19 (N=16 898)

	ACEI (N=4878)	ARB (N=3473)	Calcium Channel Blockers, Beta Blockers, or Thiazide diuretics (N=4177)	Other Antihypertensives* (N=377)	No Antihypertensives (N=3993)
	Row Percent=29%	21%	25%	2%	24%
Age, y	64 (13)	66 (13)	65 (15)	71 (14)	61 (16)
18–39	159 (3%)	76 (2%)	195 (5%)	8 (2%)	335 (8%)
40–64	2273 (47%)	1447 (42%)	1797 (43%)	108 (29%)	2032 (51%)
65–85	2162 (44%)	1723 (50%)	1842 (44%)	208 (55%)	1322 (33%)
85+	284 (6%)	227 (7%)	343 (8%)	53 (14%)	304 (8%)
Men	2574 (53%)	1404 (40%)	1617 (39%)	218 (58%)	1777 (45%)
Race/ethnicity					
Asian	528 (11%)	699 (20%)	566 (14%)	27 (7%)	495 (12%)
Black	605 (12%)	470 (14%)	759 (18%)	56 (15%)	547 (14%)
Hispanic	1743 (36%)	1068 (31%)	1138 (27%)	107 (28%)	1548 (39%)
Other†/unknown	105 (2%)	85 (2%)	90 (2%)	6 (2%)	88 (2%)
White	1897 (39%)	1151 (33%)	1624 (39%)	181 (48%)	1315 (33%)
Neighborhood income					
\$0–49k	976 (20%)	635 (18%)	753 (18%)	75 (20%)	922 (23%)
\$50–79k	1861 (38%)	1281 (37%)	1530 (37%)	141 (37%)	1536 (39%)
\$80–99k	984 (20%)	772 (22%)	856 (21%)	77 (20%)	749 (19%)
≥\$100k	1054 (22%)	780 (23%)	1031 (25%)	84 (22%)	783 (20%)
Missing	3 (0.1%)	5 (0.1%)	7 (0.2%)	...	3 (0.1%)
Neighborhood education (% of ≥ high school graduate)					
0%–50%	189 (4%)	104 (3%)	108 (3%)	12 (3%)	151 (4%)
51%–75%	1299 (27%)	865 (25%)	989 (24%)	95 (25%)	1115 (28%)
76%–100%	3388 (70%)	2499 (72%)	3073 (74%)	270 (72%)	2724 (68%)
Missing	2 (0.0%)	5 (0.1%)	7 (0.2%)	...	3 (0.1%)
Insurance type					
Commercial	2373 (49%)	1523 (44%)	1955 (47%)	119 (32%)	2219 (56%)
Private pay	1581 (32%)	1149 (33%)	1365 (33%)	161 (43%)	1157 (29%)
Medicare	767 (16%)	696 (20%)	731 (18%)	87 (23%)	418 (11%)
Medicaid	157 (3%)	104 (3%)	126 (3%)	10 (3%)	198 (5%)
Other/missing	...	1 (0.0%)	1 (0.0%)
Body mass index, kg/m ²					
<25	32 (7)	32 (7)	31 (7)	31 (8)	31 (8)
25–29.9	783 (16%)	555 (16%)	888 (21%)	79 (21%)	852 (21%)
30–34.9	1403 (29%)	991 (29%)	1272 (31%)	124 (33%)	1070 (27%)
35–39.9	1242 (26%)	925 (27%)	924 (22%)	84 (22%)	827 (21%)
35–39.9	646 (13%)	488 (14%)	535 (13%)	40 (11%)	437 (11%)
≥40	554 (11%)	393 (11%)	402 (10%)	42 (11%)	412 (10%)
Missing	250 (5%)	121 (4%)	156 (4%)	8 (2%)	395 (10%)
Smoking					
Current	345 (7%)	132 (4%)	211 (5%)	22 (6%)	245 (6%)
Former	1733 (36%)	1202 (35%)	1480 (35%)	181 (48%)	1277 (32%)
Never	2792 (57%)	2135 (62%)	2475 (59%)	174 (46%)	2435 (61%)
Missing	8 (0.2%)	4 (0.1%)	11 (0.3%)	...	36 (0.9%)
Blood pressure, mm Hg					
Systolic BP	128 (15)	130 (15)	128 (15)	125 (16)	129 (15)
Diastolic BP	71 (12)	71 (12)	72 (13)	69 (14)	74 (13)

(Continued)

Table 1. Continued

	ACEI (N=4878)	ARB (N=3473)	Calcium Channel Blockers, Beta Blockers, or Thiazide diuretics (N=4177)	Other Antihypertensives* (N=377)	No Antihypertensives (N=3993)
	Row Percent=29%	21%	25%	2%	24%
SBP/DBP <140/90	4006 (82%)	2769 (80%)	3424 (82%)	326 (87%)	2884 (72%)
SBP/DBP <130/80	2131 (44%)	1371 (40%)	1779 (43%)	200 (53%)	1417 (36%)
Laboratory tests					
Hemoglobin A1c, %	6.8 (1.6)	6.7 (1.4)	6.3 (1.4)	6.4 (1.6)	6.6 (1.8)
Total cholesterol, mg/dL	164 (46)	164 (43)	170 (47)	156 (43)	176 (47)
High-density lipoprotein cholesterol, mg/dL	48 (14)	49 (15)	50 (16)	50 (16)	49 (15)
Low-density lipoprotein cholesterol, mg/dL	91 (36)	89 (35)	95 (37)	84 (34)	102 (39)
Triglycerides, mg/dL	146 (108)	151 (157)	139 (107)	121 (69)	145 (122)
Preexisting conditions					
Elixhauser comorbidity score					
0	127 (3%)	57 (2%)	113 (3%)	16 (4%)	455 (11%)
1–3	2079 (43%)	1264 (36%)	1744 (42%)	85 (23%)	1820 (46%)
4+	2672 (55%)	2152 (62%)	2320 (56%)	276 (73%)	1718 (43%)
Diabetes mellitus	2232 (46%)	1710 (49%)	1209 (29%)	145 (39%)	1130 (28%)
Heart failure	328 (7%)	283 (8%)	397 (10%)	70 (19%)	105 (3%)
Coronary artery disease	538 (11%)	446 (13%)	557 (13%)	62 (16%)	270 (7%)
Chronic kidney disease	467 (10%)	470 (14%)	576 (14%)	67 (18%)	249 (6%)
Asthma	619 (13%)	621 (18%)	721 (17%)	76 (20%)	511 (13%)
Chronic obstructive pulmonary disease	378 (8%)	367 (11%)	478 (11%)	84 (22%)	254 (6%)
Arrhythmia	842 (17%)	658 (19%)	1085 (26%)	121 (32%)	552 (14%)
Valvular disease	325 (7%)	263 (8%)	388 (9%)	54 (14%)	147 (4%)
Pulmonary circulation disease	154 (3%)	148 (4%)	213 (5%)	41 (11%)	106 (3%)
Peripheral vascular disease	1506 (31%)	1282 (37%)	1565 (38%)	205 (54%)	1085 (27%)
Cancer	101 (2%)	82 (2%)	101 (2%)	8 (2%)	80 (2%)
Outpatient medications before the index date					
Lipid lowering	3417 (70%)	2530 (73%)	2460 (59%)	237 (63%)	1577 (40%)
Antiplatelets	568 (12%)	471 (14%)	481 (12%)	42 (11%)	239 (6%)
Insulin	892 (18%)	643 (19%)	452 (11%)	57 (15%)	386 (10%)
Oral hypoglycemics	1806 (37%)	1278 (37%)	822 (20%)	78 (21%)	739 (19%)

Mean (SD) or N (%) are reported. ACEI indicates angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; BP, blood pressure; COVID-19, coronavirus disease 2019; DBP, diastolic blood pressure; and SBP, systolic blood pressure.

*Other antihypertensive medications include loop diuretics, potassium-sparing diuretics, centrally acting agents, alpha blockers, and mineralocorticoid receptor antagonists, without the use of ACEIs or ARBs.

†Multi-racial, specific races not reported, or Native American/Alaska Native.

age, race/ethnicity, presence of chronic kidney disease, heart failure, and diabetes mellitus.

The secondary analyses were conducted to determine the association between use of ACEIs or ARBs and COVID-19 infection among all patients with hypertension. We assessed the robustness of the study findings by assessing E-value and plausibility of magnitude of unmeasured confounders.¹³ $P < 0.05$ was considered as statistically significant with no adjustment for multiplicity.

RESULTS

Our study included 824 650 patients with hypertension (mean age=64.4 years), of whom 16 898 (2.0%) were tested for COVID-19 at KPSC and 1794 (10.6%) tested positive (Figure S1). A higher proportion of women were tested than men, and a higher proportion of patients who lived in lower income or education neighborhoods tested positive compared with those who lived in higher income or education neighborhoods (Table S1).

Among the 16 898 patients with hypertension and COVID-19 testing, 28.9% were on ACEIs, 20.6% were on ARBs, 24.7% were on CCB/BB/TD, 2.2% were on other antihypertensive medications, and 23.6% were not on any antihypertensive medications (Table 1). Compared with patients on CCB/BB/TD, a higher percentage of patients on ACEIs were male and Hispanic, and a higher percentage of patients on ARBs were Asian and had diabetes mellitus.

Among all patients with hypertension, crude incidence (95% CI) of laboratory-confirmed COVID-19 infection per 1000 patients was similar among those on ACEIs (1.9 [1.7–2.0]), ARBs (2.2 [2.0–2.5]), and CCB/BB/TD (1.9 [1.7–2.1]) (Table 2). The crude rates (95% CI) of hospitalization per 1000 patients were also similar among those on ACEIs (274.3 [233.0–323.0]), ARBs (355.7 [299.0–423.3]), and CCB/BB/TD (315.8 [261.5–381.3]) among those tested positive for COVID-19.

Through propensity score matching (Figure S2), we balanced patient characteristics between groups (Tables S2 through S4, Figures S3 through S5). Overall, exposure to ACEIs or ARBs was not statistically significantly associated with COVID-19 infection (odds ratio [OR] [95% CI], 1.06 [0.90–1.25] for ACEIs versus CCB/BB/TD; OR, 1.10 [0.91–1.31] for ARBs versus CCB/BB/TD) (Figure). The associations between ACEI use and COVID-19 infection varied in different age groups (*P*-interaction=0.03). The odds of COVID-19 infection associated with ACEIs were greater among those aged 18 to 39 years (OR, 1.86 [0.73–4.79]) but became lower among those aged ≥85 years (OR, 0.30 [0.12–0.77]) when compared with CCB/BB/TD. Sensitivity analyses using multivariable logistic regression and inverse probability treatment weights showed consistent results. In all stratified analyses, ACEIs or ARBs were not associated with increased odds of COVID-19. Secondary analyses also showed no increased odds of infection among all patients with hypertension (OR=0.92 [0.80–1.06] for ACEIs versus CCB/BB/TD; OR=1.04 [0.89–1.21] for ARBs versus CCB/BB/TD) (Table S5). Use of no antihypertensive medication was significantly associated with increased odds of infection.

DISCUSSION

This study evaluated COVID-19 infection among a large cohort of patients with hypertension using electronic health records with comprehensive outpatient pharmacy data. We found that ACEI or ARB use was not associated with increased risk of COVID-19 infection compared with use of other antihypertensive medications.

Although recent epidemiologic studies reported no or lower associations between ACEI or ARB exposure and COVID-19 infection, these studies

Table 2. Incidence of COVID-19 Infection and Hospitalization Per 1000 Patients by Antihypertensive Drug Exposure

	ACEI	ARB	Calcium Channel Blockers, Beta Blockers, or Thiazide Diuretics	Other Antihypertensives*	No Antihypertensive Medications
Patients with hypertension, N	279 380	159 248	184 365	11 457	190 200
COVID-19 testing per 1000 patients (95% CI)	17.5 (17.0–18.0)	21.8 (21.1–22.5)	22.7 (22.0–23.4)	32.9 (29.7–36.4)	21.0 (20.4–21.7)
COVID-19 infection (laboratory confirmed) per 1000 patients (95% CI)	1.9 (1.7–2.0)	2.2 (2.0–2.5)	1.9 (1.7–2.1)	1.9 (1.3–2.9)	2.9 (2.6–3.1)
COVID-19 infection (laboratory or clinically confirmed) per 1000 patients (95% CI)	2.2 (2.0–2.4)	2.5 (2.3–2.8)	2.1 (1.9–2.3)	2.4 (1.7–3.5)	3.2 (3.0–3.5)
Patients with hypertension tested for COVID-19, N	4878	3473	4177	377	3993
COVID-19 infection per 1000 tested patients (95% CI)	107.6 (98.8–117.2)	102.8 (92.7–114.0)	81.9 (73.6–91.0)	58.4 (38.4–88.6)	137.2 (126.2–149.2)
Patients with hypertension tested positive for COVID-19, N	525	357	342	22	548
Hospitalization per 1000 tested positive patients (95% CI)	274.3 (233.0–323.0)	355.7 (299.0–423.3)	315.8 (261.5–381.3)	409.1 (212.9–786.2)	295.6 (253.4–344.8)

ACEI indicates angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; and COVID-19, coronavirus disease 2019.

*Other antihypertensive medications include loop diuretics, potassium-sparing diuretics, centrally acting agents, alpha blockers, and mineralocorticoid receptor antagonists, without the use of ACEIs or ARBs.

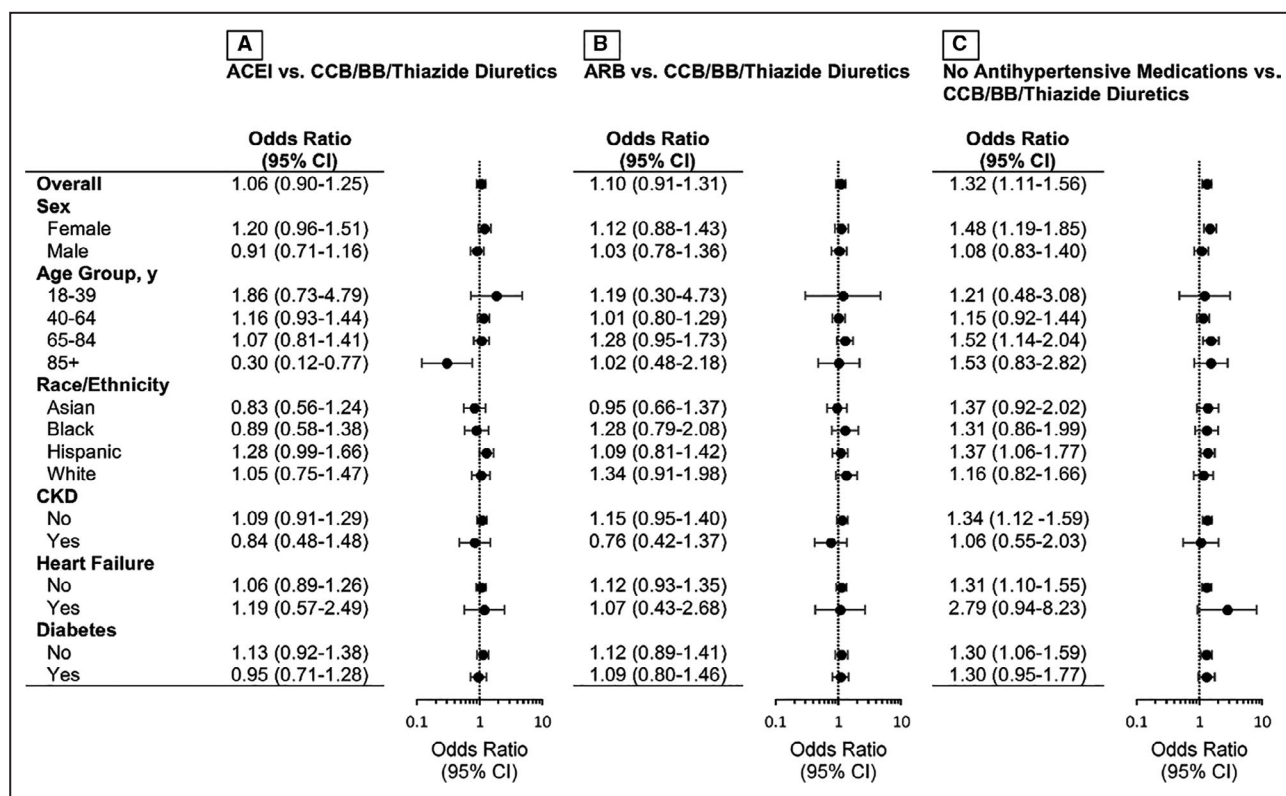


Figure. Odds ratio (95% CI) of COVID-19 infection associated with antihypertensive drug exposure stratified by sex, age, race/ethnicity, and comorbidities after propensity score matching.

A, *P*-interaction <0.05 for age-stratified analysis. **A** through **C**, Additional variables included in the model after propensity score matching: age, sex, race/ethnicity, and covariates with standardized mean difference >0.1 (Figures S3 through S5). ACEI indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BB, beta blocker; CCB, calcium channel blocker; CKD, chronic kidney disease; and COVID-19, coronavirus disease 2019.

investigated racially/ethnically homogenous populations,^{4-6,9} included patients without hypertension,^{7,14} and did not investigate patients without antihypertensive medication use separately.^{5,7,8,14} To address these limitations, we investigated a racially/ethnically diverse cohort of patients with hypertension who had similar access to care and evaluated use of antihypertensive medications.

We found that the associations between ACEI use on COVID-19 infection varied in different age groups. For adults ≥85 years, patients taking ACEIs, but not ARBs, had lower odds of infection compared with those with CCB/BB/TD. Although this finding is intriguing and warrants further investigation, we cannot rule out potential unmeasured confounding and potential inflation of type I errors due to multiple testing. However, this result is consistent with a previous study showing a lower risk of hospitalization associated with ACEIs but not ARBs among Medicare beneficiaries.¹⁵ Also, the *E*-value was substantially greater than accepted risk factors for COVID-19 infection. Thus, it is unlikely that unmeasured confounders modified the conclusion of this study.

This study showed an increased likelihood of COVID-19 infection for those without antihypertensive

medications compared with those with CCB/BB/TD. These findings are reassuring that appropriate treatment with antihypertensive medications is important in patients with hypertension. However, unmeasured confounding may contribute to these findings. Before propensity score matching, a higher percentage of patients without antihypertensives had uncontrolled blood pressure, had higher cholesterol levels, and lived in a neighborhood with lower levels of income or education compared with those with CCB/BB/TD, suggesting poor health behaviors and/or adverse social determinants of health may drive these findings. Although it is likely that these patients were nonadherent to antihypertensive medications, we were not able to distinguish between patients who discontinued or did not initiate their medications and patients who were on lifestyle modifications.

This study has limitations. First, COVID-19 testing criteria changed during the study period. From March through early April, testing was prioritized for health-care personnel and for patients who presented signs and symptoms of COVID-19.¹² In late April, testing was performed for all patients, symptomatic or not, who entered the hospital. Additionally, Los Angeles County

expanded testing on April 29 for all residents. With testing available outside KPSC, our study did not capture all testing data. Second, <5% of patients who receive medications outside KPSC may not be captured in this study. Third, we cannot confirm medication adherence. Lastly, although we assessed hospitalization after COVID-19, we did not have a sufficient number of patients with hypertension and who tested positive for COVID-19 to compare hospitalization outcomes across different drug exposures or other severity levels of COVID-19. Future studies should evaluate morbidity and mortality of COVID-19 in this population.

Neither ACEI nor ARB use was associated with COVID-19 infection. The decreased odds of infection among adults ≥ 85 years using ACEIs warrants further investigation. Our study reinforces that patients with hypertension should continue their ACEIs or ARBs as recommended by scientific communities.

ARTICLE INFORMATION

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Supplementary Material

Tables S1–S5
Figures S1–S5

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Supplemental Material

Table S1. Patient and Clinical Characteristics by Covid-19 Testing, and Test Results Among Patients with Hypertension* (N=824,650).

	Total (N=824,650) Row Percent= 100%	Covid-19 Testing, No (N=807,752) 98%	Covid-19 Testing, Yes (N=16,898) 2.0%	Test Negative (N=15,104) 89.4%	Test Positive (N=1,794) 10.6%
Age in years	64.4 (13.56)	64.4 (13.54)	64.3 (14.37)	64.7 (14.44)	61.3 (13.42)
18-39	35067 (4.3%)	34294 (4.2%)	773 (4.6%)	683 (4.5%)	90 (5%)
40-64	363493 (44.1%)	355836 (44.1%)	7657 (45.3%)	6635 (43.9%)	1022 (57%)
65-85	382794 (46.4%)	375537 (46.5%)	7257 (42.9%)	6659 (44.1%)	598 (33.3%)
85+	43296 (5.3%)	42085 (5.2%)	1211 (7.2%)	1127 (7.5%)	84 (4.7%)
Men	397941 (48.3%)	390351 (48.3%)	7590 (44.9%)	6743 (44.6%)	847 (47.2%)
Race/ethnicity					
Asian	105040 (12.7%)	102725 (12.7%)	2315 (13.7%)	1976 (13.1%)	339 (18.9%)
Black	102667 (12.4%)	100230 (12.4%)	2437 (14.4%)	2208 (14.6%)	229 (12.8%)
Hispanic	270287 (32.8%)	264683 (32.8%)	5604 (33.2%)	4743 (31.4%)	861 (48%)
Other/Unknown	26053 (3.2%)	25679 (3.2%)	374 (2.2%)	343 (2.3%)	31 (1.7%)
White	320603 (38.9%)	314435 (38.9%)	6168 (36.5%)	5834 (38.6%)	334 (18.6%)
Neighborhood Income					
\$0-49k	152205 (18.5%)	148844 (18.4%)	3361 (19.9%)	2847 (18.8%)	514 (28.7%)
\$50-79k	308061 (37.4%)	301712 (37.4%)	6349 (37.6%)	5670 (37.5%)	679 (37.8%)
\$80-99k	165677 (20.1%)	162239 (20.1%)	3438 (20.3%)	3106 (20.6%)	332 (18.5%)
≥\$100k	197393 (23.9%)	193661 (24%)	3732 (22.1%)	3467 (23%)	265 (14.8%)
Missing	1314 (0.2%)	1296 (0.2%)	18 (0.1%)	14 (0.1%)	4 (0.2%)
Neighborhood Education (% of ≥High School Graduate)					
0-50%	25674 (3.1%)	25110 (3.1%)	564 (3.3%)	448 (3%)	116 (6.5%)
51-75%	202823 (24.6%)	198460 (24.6%)	4363 (25.8%)	3726 (24.7%)	637 (35.5%)
76-100%	594879 (72.1%)	582925 (72.2%)	11954 (70.7%)	10917 (72.3%)	1037 (57.8%)
Insurance Type					
Commercial	388737 (47.1%)	380548 (47.1%)	8189 (48.5%)	7086 (46.9%)	1103 (61.5%)
Private pay	281441 (34.1%)	276028 (34.2%)	5413 (32%)	4928 (32.6%)	485 (27%)
Medicare	131260 (15.9%)	128561 (15.9%)	2699 (16%)	2556 (16.9%)	143 (8%)
Medicaid	22935 (2.8%)	22340 (2.8%)	595 (3.5%)	532 (3.5%)	63 (3.5%)
Other/Missing	277 (0.03%)	275 (0.03%)	2 (0.01%)	2 (0.01%)	-
Body Mass Index (kg/m ²)	30.8 (6.93)	30.8 (6.92)	31.1 (7.53)	31.0 (7.55)	32.0 (7.28)
<25	136795 (16.6%)	133638 (16.5%)	3157 (18.7%)	2923 (19.4%)	234 (13%)
25-29.9	241392 (29.3%)	236532 (29.3%)	4860 (28.8%)	4376 (29%)	484 (27%)
30-34.9	185222 (22.5%)	181220 (22.4%)	4002 (23.7%)	3555 (23.5%)	447 (24.9%)
35-39.9	95157 (11.5%)	93011 (11.5%)	2146 (12.7%)	1889 (12.5%)	257 (14.3%)
≥40	69271 (8.4%)	67468 (8.4%)	1803 (10.7%)	1603 (10.6%)	200 (11.1%)
Missing	96813 (11.7%)	95883 (11.9%)	930 (5.5%)	758 (5%)	172 (9.6%)
Smoking					
Current	45961 (5.6%)	45006 (5.6%)	955 (5.7%)	906 (6%)	49 (2.7%)
Former	255451 (31%)	249578 (30.9%)	5873 (34.8%)	5384 (35.6%)	489 (27.3%)
Never	521628 (63.3%)	511617 (63.3%)	10011 (59.2%)	8764 (58%)	1247 (69.5%)
Missing	1610 (0.2%)	1551 (0.2%)	59 (0.3%)	50 (0.3%)	9 (0.5%)
Blood Pressure (BP) (mm Hg)					
Systolic BP (SBP)	129.4 (13.7)	129.4 (13.67)	128.6 (14.91)	128.4 (14.96)	129.9 (14.33)

	Total (N=824,650) Row Percent= 100%	Covid-19 Testing, No (N=807,752) 98%	Covid-19 Testing, Yes (N=16,898) 2.0%	Test Negative (N=15,104) 89.4%	Test Positive (N=1,794) 10.6%
Diastolic BP (DBP)	72.6 (11.8)	72.6 (11.79)	72.0 (12.53)	71.8 (12.59)	73.3 (11.86)
SBP/DBP <140/90	640878 (77.7%)	627469 (77.7%)	13409 (79.4%)	12046 (79.8%)	1363 (76%)
SBP/DBP <130/80	303924 (36.9%)	297026 (36.8%)	6898 (40.8%)	6263 (41.5%)	635 (35.4%)
Labs					
HbA1c (%)	6.5 (1.37)	6.5 (1.36)	6.6 (1.55)	6.6 (1.52)	6.9 (1.74)
Serum creatinine	0.9 (0.36)	0.9 (0.36)	1.0 (0.48)	1.0 (0.49)	0.9 (0.43)
Total Cholesterol (mg/dL)	169.8 (43.22)	169.9 (43.16)	167.6 (45.88)	167.2 (45.52)	171.3 (48.75)
HDL-C (mg/dL)	50.1 (14.36)	50.1 (14.35)	49.1 (14.98)	49.2 (15.13)	47.6 (13.55)
LDL-C (mg/dL)	95.0 (36.22)	95.0 (36.20)	93.5 (37.09)	93.1 (37.10)	96.7 (36.92)
Triglycerides (mg/dL)	139.0 (107.70)	138.9 (107.37)	144.7 (122.74)	143.8 (125.45)	151.7 (97.44)
Pre-existing conditions					
Elixhauser comorbidity score					
0	68139 (8.3%)	67371 (8.3%)	768 (4.5%)	624 (4.1%)	144 (8%)
1-3	459962 (55.8%)	452970 (56.1%)	6992 (41.4%)	6058 (40.1%)	934 (52.1%)
4+	296549 (36%)	287411 (35.6%)	9138 (54.1%)	8422 (55.8%)	716 (39.9%)
Diabetes	246744 (29.9%)	240318 (29.8%)	6426 (38%)	5726 (37.9%)	700 (39%)
Heart failure	22574 (2.7%)	21391 (2.6%)	1183 (7%)	1119 (7.4%)	64 (3.6%)
CAD	49481 (6%)	47608 (5.9%)	1873 (11.1%)	1758 (11.6%)	115 (6.4%)
CKD	52923 (6.4%)	51094 (6.3%)	1829 (10.8%)	1703 (11.3%)	126 (7%)
Asthma	71275 (8.6%)	68727 (8.5%)	2548 (15.1%)	2420 (16%)	128 (7.1%)
COPD	34268 (4.2%)	32707 (4%)	1561 (9.2%)	1506 (10%)	55 (3.1%)
Pneumonia	32988 (4%)	31373 (3.9%)	1615 (9.6%)	1505 (10%)	110 (6.1%)
Lung disease	6829 (0.8%)	6472 (0.8%)	357 (2.1%)	345 (2.3%)	12 (0.7%)
Arrhythmia	94680 (11.5%)	91422 (11.3%)	3258 (19.3%)	3065 (20.3%)	193 (10.8%)
Valvular Disease	28168 (3.4%)	26991 (3.3%)	1177 (7%)	1121 (7.4%)	56 (3.1%)
Pulmonary	13224 (1.6%)	12562 (1.6%)	662 (3.9%)	623 (4.1%)	39 (2.2%)
Circulation Disease					
PVD	191739 (23.3%)	186096 (23%)	5643 (33.4%)	5259 (34.8%)	384 (21.4%)
Cancer	8892 (1.1%)	8520 (1.1%)	372 (2.2%)	353 (2.3%)	19 (1.1%)
Paralysis	6010 (0.7%)	5690 (0.7%)	320 (1.9%)	301 (2%)	19 (1.1%)
Neurological	31001 (3.8%)	29708 (3.7%)	1293 (7.7%)	1209 (8%)	84 (4.7%)
Disorders					
Hypothyroidism	90429 (11%)	88188 (10.9%)	2241 (13.3%)	2087 (13.8%)	154 (8.6%)
Peptic Ulcer	3572 (0.4%)	3388 (0.4%)	184 (1.1%)	174 (1.2%)	10 (0.6%)
AIDS/HIV	1444 (0.2%)	1384 (0.2%)	60 (0.4%)	56 (0.4%)	4 (0.2%)
Lymphoma	4572 (0.6%)	4379 (0.5%)	193 (1.1%)	182 (1.2%)	11 (0.6%)
Solid Tumor	35228 (4.3%)	34092 (4.2%)	1136 (6.7%)	1078 (7.1%)	58 (3.2%)
Rheumatoid	24733 (3%)	23816 (2.9%)	917 (5.4%)	855 (5.7%)	62 (3.5%)
Arthritis					
Mild liver disease	43008 (5.2%)	41499 (5.1%)	1509 (8.9%)	1368 (9.1%)	141 (7.9%)
Coagulopathy	21749 (2.6%)	20795 (2.6%)	954 (5.6%)	905 (6%)	49 (2.7%)
Electrolyte	81218 (9.8%)	78096 (9.7%)	3122 (18.5%)	2916 (19.3%)	206 (11.5%)
Disorders					
Anemia	28019 (3.4%)	26797 (3.3%)	1222 (7.2%)	1133 (7.5%)	89 (5%)

	Total (N=824,650) Row Percent= 100%	Covid-19 Testing, No (N=807,752) 98%	Covid-19 Testing, Yes (N=16,898) 2.0%	Test Negative (N=15,104) 89.4%	Test Positive (N=1,794) 10.6%
Alcohol Abuse	16412 (2%)	15747 (1.9%)	665 (3.9%)	625 (4.1%)	40 (2.2%)
Drug Abuse	10213 (1.2%)	9684 (1.2%)	529 (3.1%)	504 (3.3%)	25 (1.4%)
Outpatient Antihypertensive Medication Use Prior to the Index Date					
ACEI	279380 (33.9%)	274502 (34.0%)	4878 (28.9%)	4353 (28.8%)	525 (29.3%)
ARB	159248 (19.3%)	155775 (19.3%)	3473 (20.6%)	3116 (20.6%)	357 (19.9%)
BB or CCB or TD	184365 (22.4%)	180188 (22.3%)	4177 (24.7%)	3835 (25.4%)	342 (19.1%)
Other Antihypertensives	11457 (1.4%)	11080 (1.4%)	377 (2.2%)	355 (2.4%)	22 (1.2%)
No Antihypertensives	190200 (23.1%)	186207 (23.1%)	3993 (23.6%)	3445 (22.8%)	548 (30.5%)
Outpatient Medications Prior to the Index Date Other than Antihypertensives					
Lipid lowering	486243 (59%)	476022 (58.9%)	10221 (60.5%)	9198 (60.9%)	1023 (57%)
Antiplatelets	66093 (8%)	64292 (8%)	1801 (10.7%)	1639 (10.9%)	162 (9%)
Nitrates	28039 (3.4%)	26980 (3.3%)	1059 (6.3%)	999 (6.6%)	60 (3.3%)
Antiarrhythmic Agents	7422 (0.9%)	7151 (0.9%)	271 (1.6%)	255 (1.7%)	16 (0.9%)
Insulin	73776 (8.9%)	71346 (8.8%)	2430 (14.4%)	2183 (14.5%)	247 (13.8%)
Oral hypoglycemics	202842 (24.6%)	198119 (24.5%)	4723 (28%)	4146 (27.4%)	577 (32.2%)

Mean (SD) or N (%) are reported. Abbreviations: ACEI = angiotensin-converting enzyme inhibitors; ARB = angiotensin receptor blockers; BP = blood pressure; CCB = calcium channel blockers; BB = beta-blockers; CAD = coronary artery disease; CKD = chronic kidney disease; COPD = chronic obstructive pulmonary disease; DBP = diastolic blood pressure; HbA1c = hemoglobin A1c; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; PVD = peripheral vascular disease; SBP = systolic blood pressure; TD = thiazide diuretics. *Patients with hypertension was identified from the Kaiser Permanente Southern California (KPSC) hypertension registry as of March 1st, 2020. The KPSC hypertension registry includes adult members having one of the following criteria: 1) hypertension diagnosis on the active problem list, 2) ≥ 2 outpatient visits with a diagnosis code of hypertension within 365 days of each other, 3) ≥ 1 outpatient visit and ≥ 1 hospital discharge with a diagnosis code of hypertension within 365 days of each other, 4) ≥ 1 antihypertensive medication dispensing in the past 6 months and ≥ 1 outpatient visit with a diagnosis code of hypertension within 365 days of the dispensing date, or 5) ≥ 1 outpatient visit with a diagnosis code of hypertension and having comorbidities of heart failure, diabetes, coronary artery disease, chronic kidney disease, or cerebrovascular accident.

Table S2. Baseline Characteristics Before and After Matching (between ACEIs and CCB/BB/TD).

	Before Matching		After Matching	
	ACEIs N=4,875	CCB/BB/TD N=4,170	ACEIs N=3,598	CCB/BB/TD N=3,598
Age in years				
18-39	159 (3.3%)	195 (4.7%)	126 (3.5%)	136 (3.8%)
40-64	2271 (46.6%)	1794 (43%)	1502 (41.7%)	1592 (44.2%)
65-85	2161 (44.3%)	1840 (44.1%)	1703 (47.3%)	1609 (44.7%)
85+	284 (5.8%)	341 (8.2%)	267 (7.4%)	261 (7.3%)
Women	2302 (47.2%)	2557 (61.3%)	1935 (53.8%)	2050 (57%)
Race/Ethnicity				
White	1896 (38.9%)	1621 (38.9%)	1485 (41.3%)	1421 (39.5%)
Asian	528 (10.8%)	565 (13.5%)	421 (11.7%)	457 (12.7%)
Black	603 (12.4%)	758 (18.2%)	559 (15.5%)	555 (15.4%)
Hispanic	1743 (35.8%)	1136 (27.2%)	1068 (29.7%)	1086 (30.2%)
Other/Unknown	105 (2.2%)	90 (2.2%)	65 (1.8%)	79 (2.2%)
BMI category				
<25	782 (16%)	887 (21.3%)	666 (18.5%)	699 (19.4%)
25-29.9	1403 (28.8%)	1270 (30.5%)	1102 (30.6%)	1101 (30.6%)
30-34.9	1242 (25.5%)	921 (22.1%)	861 (23.9%)	822 (22.8%)
35-39.9	645 (13.2%)	535 (12.8%)	472 (13.1%)	464 (12.9%)
≥40	554 (11.4%)	402 (9.6%)	356 (9.9%)	362 (10.1%)
Missing	249 (5.1%)	155 (3.7%)	141 (3.9%)	150 (4.2%)
Smoking status				
Never	2791 (57.3%)	2472 (59.3%)	2114 (58.8%)	2121 (58.9%)
Current	345 (7.1%)	211 (5.1%)	197 (5.5%)	203 (5.6%)
Former	1731 (35.5%)	1476 (35.4%)	1279 (35.5%)	1265 (35.2%)
Missing	8 (0.2%)	11 (0.3%)	8 (0.2%)	9 (0.3%)
Medicaid indicator	383 (7.9%)	342 (8.2%)	260 (7.2%)	291 (8.1%)
Household income				
\$0-49k	976 (20%)	753 (18.1%)	643 (17.9%)	666 (18.5%)
\$50-79k	1861 (38.2%)	1530 (36.7%)	1340 (37.2%)	1330 (37%)
\$80-99k	984 (20.2%)	856 (20.5%)	751 (20.9%)	737 (20.5%)
≥\$100k	1054 (21.6%)	1031 (24.7%)	864 (24%)	865 (24%)
Neighborhood education				
<75%	1487 (30.5%)	1097 (26.3%)	962 (26.7%)	985 (27.4%)
76-100%	3388 (69.5%)	3073 (73.7%)	2636 (73.3%)	2613 (72.6%)
Elixhauser score				
0	127 (2.6%)	112 (2.7%)	99 (2.8%)	98 (2.7%)
1-3	2079 (42.6%)	1744 (41.8%)	1546 (43%)	1515 (42.1%)
4+	2669 (54.7%)	2314 (55.5%)	1953 (54.3%)	1985 (55.2%)
Pre-existing comorbidities				
Pneumonia	393 (8.1%)	456 (10.9%)	331 (9.2%)	337 (9.4%)
Lung disease	82 (1.7%)	105 (2.5%)	71 (2%)	75 (2.1%)
Diabetes	2231 (45.8%)	1206 (28.9%)	1280 (35.6%)	1162 (32.3%)
Heart Failure	328 (6.7%)	395 (9.5%)	292 (8.1%)	298 (8.3%)
Asthma	618 (12.7%)	719 (17.2%)	541 (15%)	545 (15.1%)
COPD	378 (7.8%)	476 (11.4%)	348 (9.7%)	361 (10%)
Cancer	342 (7%)	333 (8%)	274 (7.6%)	278 (7.7%)
Outpatient Medications Prior to the Index Date				
Antiarrhythmic Agents	73 (1.5%)	112 (2.7%)	70 (1.9%)	71 (2%)
Antiplatelets	568 (11.7%)	479 (11.5%)	412 (11.5%)	408 (11.3%)
Insulin	892 (18.3%)	450 (10.8%)	491 (13.6%)	436 (12.1%)
Lipid lowering agents	3414 (70%)	2454 (58.8%)	2328 (64.7%)	2241 (62.3%)
Nitrates	318 (6.5%)	322 (7.7%)	280 (7.8%)	265 (7.4%)
Oral hypoglycemics	1805 (37%)	821 (19.7%)	887 (24.7%)	813 (22.6%)

SBP/DBP <140/90 mm Hg	4004 (82.1%)	3419 (82%)	2952 (82%)	2941 (81.7%)
SBP/DBP <130/80 mm Hg	2130 (43.7%)	1775 (42.6%)	1586 (44.1%)	1540 (42.8%)
Labs				
Serum creatinine	1.0 (0.39)	1.0 (0.56)	1.0 (0.41)	1.0 (0.57)
HDL-C (mg/dL)	47.9 (13.97)	50.2 (16.14)	49.4 (14.36)	49.5 (15.57)
HbA1c (%)	6.8 (1.62)	6.3 (1.35)	6.5 (1.44)	6.4 (1.39)
LDL-C (mg/dL)	90.8 (36.39)	94.7 (37.33)	92.5 (35.71)	93.9 (37.31)
Total Cholesterol (mg/dL)	164.0 (45.91)	169.6 (46.74)	166.2 (43.50)	168.4 (46.64)
Triglycerides (mg/dL)	146.1 (107.58)	138.7 (107.34)	136.9 (81.82)	141.1 (111.73)

Mean (SD) or N (%) are reported. Abbreviations: ACEI = angiotensin-converting enzyme inhibitors; ARB = angiotensin receptor blockers; BP = blood pressure; CCB = calcium channel blockers; BB = beta-blockers; CAD = coronary artery disease; CKD = chronic kidney disease; COPD = chronic obstructive pulmonary disease; DBP = diastolic blood pressure; HbA1c = hemoglobin A1c; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; PVD = peripheral vascular disease; SBP = systolic blood pressure; TD = thiazide diuretics.

Table S3. Baseline Characteristics Before and After Matching (between ARBs and CCB/BBTD).

	Before Matching		After Matching	
	ARB N=3,468	CCB/BB/TD N=4,170	ARB N=2,945	CCB/BB/TD N=2,945
Age in years				
18-39	76 (2.2%)	195 (4.7%)	73 (2.5%)	77 (2.6%)
40-64	1445 (41.7%)	1794 (43%)	1199 (40.7%)	1277 (43.4%)
65-85	1721 (49.6%)	1840 (44.1%)	1456 (49.4%)	1378 (46.8%)
85+	226 (6.5%)	341 (8.2%)	217 (7.4%)	213 (7.2%)
Women	2065 (59.5%)	2557 (61.3%)	1766 (60%)	1763 (59.9%)
Race/Ethnicity				
White	1149 (33.1%)	1621 (38.9%)	1072 (36.4%)	1064 (36.1%)
Asian	698 (20.1%)	565 (13.5%)	477 (16.2%)	504 (17.1%)
Black	469 (13.5%)	758 (18.2%)	456 (15.5%)	442 (15%)
Hispanic	1068 (30.8%)	1136 (27.2%)	877 (29.8%)	862 (29.3%)
Other/Unknown	84 (2.4%)	90 (2.2%)	63 (2.1%)	73 (2.5%)
BMI category				
<25	554 (16%)	887 (21.3%)	518 (17.6%)	510 (17.3%)
25-29.9	990 (28.5%)	1270 (30.5%)	872 (29.6%)	887 (30.1%)
30-34.9	925 (26.7%)	921 (22.1%)	721 (24.5%)	727 (24.7%)
35-39.9	487 (14%)	535 (12.8%)	409 (13.9%)	410 (13.9%)
≥40	392 (11.3%)	402 (9.6%)	319 (10.8%)	306 (10.4%)
Missing	120 (3.5%)	155 (3.7%)	106 (3.6%)	105 (3.6%)
Smoking status				
Never	2134 (61.5%)	2472 (59.3%)	1778 (60.4%)	1775 (60.3%)
Current	132 (3.8%)	211 (5.1%)	120 (4.1%)	133 (4.5%)
Former	1198 (34.5%)	1476 (35.4%)	1043 (35.4%)	1034 (35.1%)
Missing	4 (0.1%)	11 (0.3%)	4 (0.1%)	3 (0.1%)
Medicaid indicator	294 (8.5%)	342 (8.2%)	223 (7.6%)	241 (8.2%)
Household income				
\$0-49k	635 (18.3%)	753 (18.1%)	526 (17.9%)	538 (18.3%)
\$50-79k	1281 (36.9%)	1530 (36.7%)	1079 (36.6%)	1073 (36.4%)
\$80-99k	772 (22.3%)	856 (20.5%)	634 (21.5%)	641 (21.8%)
≥\$100k	780 (22.5%)	1031 (24.7%)	706 (24%)	693 (23.5%)
Neighborhood education				
<75%	969 (27.9%)	1097 (26.3%)	777 (26.4%)	784 (26.6%)
76-100%	2499 (72.1%)	3073 (73.7%)	2168 (73.6%)	2161 (73.4%)
Elixhauser score				
0	57 (1.6%)	112 (2.7%)	56 (1.9%)	72 (2.4%)
1-3	1263 (36.4%)	1744 (41.8%)	1112 (37.8%)	1156 (39.3%)
4+	2148 (61.9%)	2314 (55.5%)	1777 (60.3%)	1717 (58.3%)
Pre-existing comorbidities				
Pneumonia	340 (9.8%)	456 (10.9%)	299 (10.2%)	296 (10.1%)
Lung disease	83 (2.4%)	105 (2.5%)	77 (2.6%)	77 (2.6%)
Diabetes	1708 (49.3%)	1206 (28.9%)	1202 (40.8%)	1134 (38.5%)
Heart Failure	281 (8.1%)	395 (9.5%)	264 (9%)	268 (9.1%)
Asthma	620 (17.9%)	719 (17.2%)	531 (18%)	504 (17.1%)
COPD	366 (10.6%)	476 (11.4%)	339 (11.5%)	326 (11.1%)
Cancer	236 (6.8%)	333 (8%)	215 (7.3%)	217 (7.4%)
Outpatient Medications Prior to the Index Date				
Antiarrhythmic Agents	45 (1.3%)	112 (2.7%)	45 (1.5%)	49 (1.7%)
Antiplatelets	470 (13.6%)	479 (11.5%)	384 (13%)	367 (12.5%)
Insulin	643 (18.5%)	450 (10.8%)	456 (15.5%)	427 (14.5%)
Lipid lowering agents	2525 (72.8%)	2454 (58.8%)	2032 (69%)	1967 (66.8%)
Nitrates	291 (8.4%)	322 (7.7%)	254 (8.6%)	244 (8.3%)
Oral hypoglycemics	1275 (36.8%)	821 (19.7%)	833 (28.3%)	790 (26.8%)

SBP/DBP <140/90 mm Hg	2767 (79.8%)	3419 (82%)	2359 (80.1%)	2385 (81%)
SBP/DBP <130/80 mm Hg	1369 (39.5%)	1775 (42.6%)	1175 (39.9%)	1240 (42.1%)
Labs				
Serum creatinine	1.0 (0.51)	1.0 (0.56)	1.0 (0.43)	1.0 (0.60)
HDL-C (mg/dL)	49.0 (14.52)	50.2 (16.14)	49.9 (14.96)	49.4 (15.60)
HbA1c (%)	6.7 (1.40)	6.3 (1.35)	6.6 (1.34)	6.5 (1.45)
LDL-C (mg/dL)	89.1 (34.93)	94.7 (37.33)	90.7 (35.27)	92.8 (37.96)
Total Cholesterol (mg/dL)	163.7 (42.78)	169.6 (46.74)	165.2 (42.86)	167.3 (47.07)
Triglycerides (mg/dL)	151.1 (156.94)	138.7 (107.34)	145.2 (159.27)	140.5 (94.59)

Mean (SD) or N (%) are reported. ACEI = angiotensin-converting enzyme inhibitors; ARB = angiotensin receptor blockers; BP = blood pressure; CCB = calcium channel blockers; BB = beta-blockers; CAD = coronary artery disease; CKD = chronic kidney disease; COPD = chronic obstructive pulmonary disease; DBP = diastolic blood pressure; HbA1c = hemoglobin A1c; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; PVD = peripheral vascular disease; SBP = systolic blood pressure; TD = thiazide diuretics.

Table S4. Baseline Characteristics Before and After Matching (between No Antihypertensive Medications and CCB/BB/TD).

	Before Matching		After Matching	
	No Antihypertensive Medications N=3,990	CCB/BB/TD N=4,170	No Antihypertensive Medications N=3,110	CCB/BB/TD N=3,110
Age in years				
18-39	335 (8.4%)	195 (4.7%)	192 (6.2%)	143 (4.6%)
40-64	2031 (50.9%)	1794 (43%)	1507 (48.5%)	1531 (49.2%)
65-85	1321 (33.1%)	1840 (44.1%)	1173 (37.7%)	1176 (37.8%)
85+	303 (7.6%)	341 (8.2%)	238 (7.7%)	260 (8.4%)
Women	2215 (55.5%)	2557 (61.3%)	1879 (60.4%)	1850 (59.5%)
Race/Ethnicity				
White	1314 (32.9%)	1621 (38.9%)	1125 (36.2%)	1134 (36.5%)
Asian	495 (12.4%)	565 (13.5%)	415 (13.3%)	387 (12.4%)
Black	547 (13.7%)	758 (18.2%)	487 (15.7%)	503 (16.2%)
Hispanic	1546 (38.7%)	1136 (27.2%)	1010 (32.5%)	1026 (33%)
Other/Unknown	88 (2.2%)	90 (2.2%)	73 (2.3%)	60 (1.9%)
BMI category				
<25	851 (21.3%)	887 (21.3%)	688 (22.1%)	700 (22.5%)
25-29.9	1070 (26.8%)	1270 (30.5%)	909 (29.2%)	886 (28.5%)
30-34.9	827 (20.7%)	921 (22.1%)	666 (21.4%)	666 (21.4%)
35-39.9	435 (10.9%)	535 (12.8%)	385 (12.4%)	371 (11.9%)
≥40	412 (10.3%)	402 (9.6%)	308 (9.9%)	315 (10.1%)
Missing	395 (9.9%)	155 (3.7%)	154 (5%)	172 (5.5%)
Smoking status				
Never	2434 (61%)	2472 (59.3%)	1895 (60.9%)	1889 (60.7%)
Current	245 (6.1%)	211 (5.1%)	177 (5.7%)	175 (5.6%)
Former	1275 (32%)	1476 (35.4%)	1027 (33%)	1030 (33.1%)
Missing	36 (0.9%)	11 (0.3%)	11 (0.4%)	16 (0.5%)
Medicaid indicator	457 (11.5%)	342 (8.2%)	296 (9.5%)	283 (9.1%)
Household income				
\$0-49k	922 (23.1%)	753 (18.1%)	600 (19.3%)	623 (20%)
\$50-79k	1536 (38.5%)	1530 (36.7%)	1195 (38.4%)	1194 (38.4%)
\$80-99k	749 (18.8%)	856 (20.5%)	615 (19.8%)	616 (19.8%)
≥\$100k	783 (19.6%)	1031 (24.7%)	700 (22.5%)	677 (21.8%)
Neighborhood education				
<75%	1266 (31.7%)	1097 (26.3%)	885 (28.5%)	894 (28.7%)
76-100%	2724 (68.3%)	3073 (73.7%)	2225 (71.5%)	2216 (71.3%)
Elixhauser score				
0	455 (11.4%)	112 (2.7%)	105 (3.4%)	251 (8.1%)
1-3	1820 (45.6%)	1744 (41.8%)	1450 (46.6%)	1400 (45%)
4+	1715 (43%)	2314 (55.5%)	1555 (50%)	1459 (46.9%)
Pre-existing comorbidities				
Pneumonia	356 (8.9%)	456 (10.9%)	294 (9.5%)	282 (9.1%)
Lung disease	69 (1.7%)	105 (2.5%)	58 (1.9%)	59 (1.9%)
Diabetes	1129 (28.3%)	1206 (28.9%)	859 (27.6%)	893 (28.7%)
Heart Failure	105 (2.6%)	395 (9.5%)	114 (3.7%)	99 (3.2%)
Asthma	511 (12.8%)	719 (17.2%)	459 (14.8%)	453 (14.6%)
COPD	254 (6.4%)	476 (11.4%)	242 (7.8%)	238 (7.7%)
Cancer	233 (5.8%)	333 (8%)	217 (7%)	213 (6.8%)
Outpatient Medications Prior to the Index Date				
Antiarrhythmic Agents	26 (0.7%)	112 (2.7%)	30 (1%)	25 (0.8%)
Antiplatelets	239 (6%)	479 (11.5%)	240 (7.7%)	227 (7.3%)
Insulin	386 (9.7%)	450 (10.8%)	300 (9.6%)	322 (10.4%)
Lipid lowering agents	1577 (39.5%)	2454 (58.8%)	1508 (48.5%)	1460 (46.9%)

Nitrates	88 (2.2%)	322 (7.7%)	98 (3.2%)	88 (2.8%)
Oral hypoglycemics	739 (18.5%)	821 (19.7%)	592 (19%)	587 (18.9%)
SBP/DBP <140/90 mm Hg	2881 (72.2%)	3419 (82%)	2459 (79.1%)	2404 (77.3%)
SBP/DBP <130/80 mm Hg	1416 (35.5%)	1775 (42.6%)	1238 (39.8%)	1197 (38.5%)
Labs				
Serum creatinine	0.9 (0.44)	1.0 (0.56)	1.0 (0.55)	0.9 (0.43)
HDL-C (mg/dL)	49.3 (15.18)	50.2 (16.14)	50.3 (16.23)	50.1 (15.42)
HbA1c (%)	6.6 (1.75)	6.3 (1.35)	6.3 (1.36)	6.6 (1.70)
LDL-C (mg/dL)	101.5 (38.96)	94.7 (37.33)	97.9 (37.08)	101.0 (40.03)
Total Cholesterol (mg/dL)	175.7 (46.96)	169.6 (46.74)	173.1 (46.48)	175.3 (47.92)
Triglycerides (mg/dL)	145.0 (122.04)	138.7 (107.34)	141.0 (114.92)	140.3 (113.01)

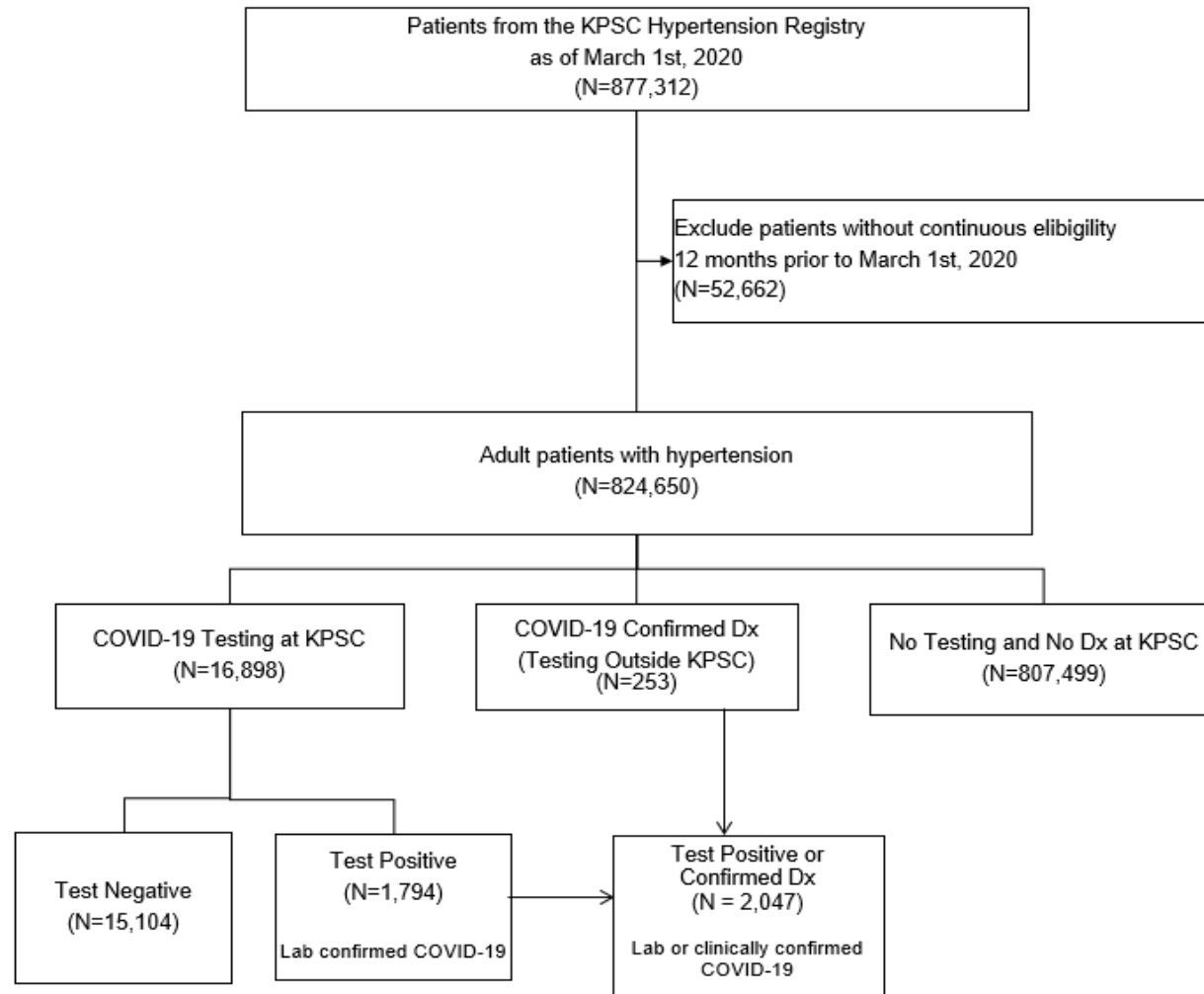
Mean (SD) or N (%) are reported. ACEI = angiotensin-converting enzyme inhibitors; ARB = angiotensin receptor blockers; BP = blood pressure; CCB = calcium channel blockers; BB = beta-blockers; CAD = coronary artery disease; CKD = chronic kidney disease; COPD = chronic obstructive pulmonary disease; DBP = diastolic blood pressure; HbA1c = hemoglobin A1c; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; PVD = peripheral vascular disease; SBP = systolic blood pressure; TD = thiazide diuretics.

Table S5. Odds Ratio (95% CI) of Covid-19 Infection Associated with Antihypertensive Drug Exposure Among All Patients with Hypertension (Outcome = Covid-19 Infection; Reference group: CCB/BB/TD).

	Crude OR	Age- and Sex- Adjusted OR	Multivariable Adjusted OR*
ACEI	1.01 (0.88-1.16)	0.98 (0.86-1.13)	0.92 (0.80-1.06)
ARB	1.20 (1.04-1.40)	1.15 (0.99-1.33)	1.04 (0.89-1.21)
No Antihypertensive Medication	1.55 (1.36-1.78)	1.38 (1.21-1.59)	1.44 (1.25-1.65)

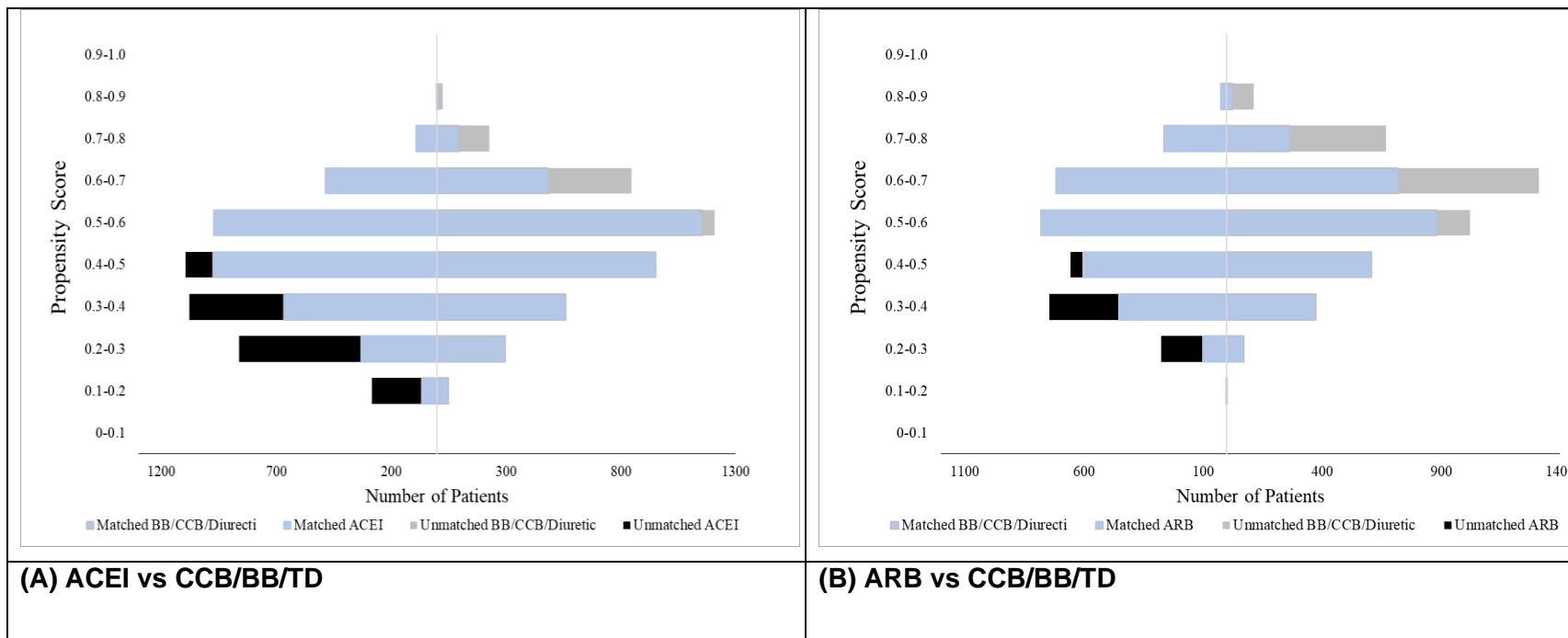
ACEI = angiotensin-converting enzyme inhibitors; ARB = angiotensin receptor blockers; BB = beta blocker; CCB = calcium channel blocker; *Patient demographics, neighborhood income and education, insurance, body mass index, smoking status, outpatient blood pressure, baseline comorbidities, and outpatient medication use were adjusted.

Figure S1. Study Cohort.



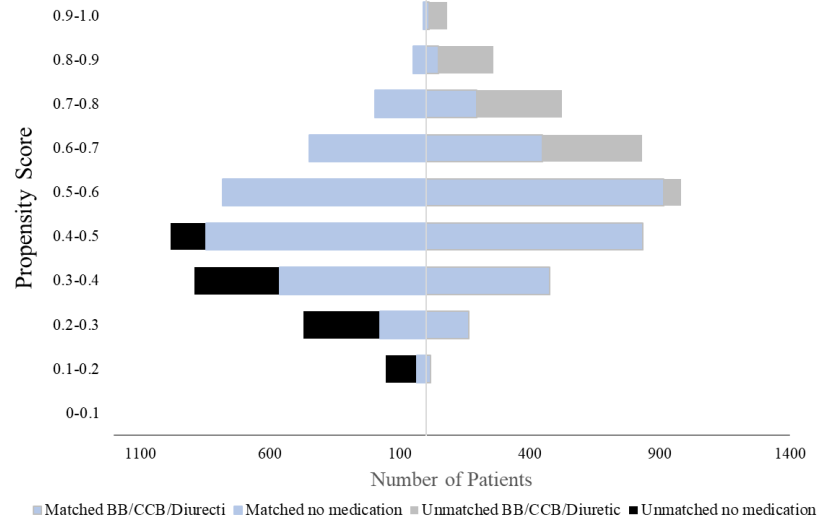
KPSC = Kaiser Permanente Southern California; Dx = diagnosis; COVID-19 Testing period = March 1-May 6, 2020; Test positive = Ever positive results

Figure S2. Propensity Score Distribution.



(A) ACEI vs CCB/BB/TD

(B) ARB vs CCB/BB/TD



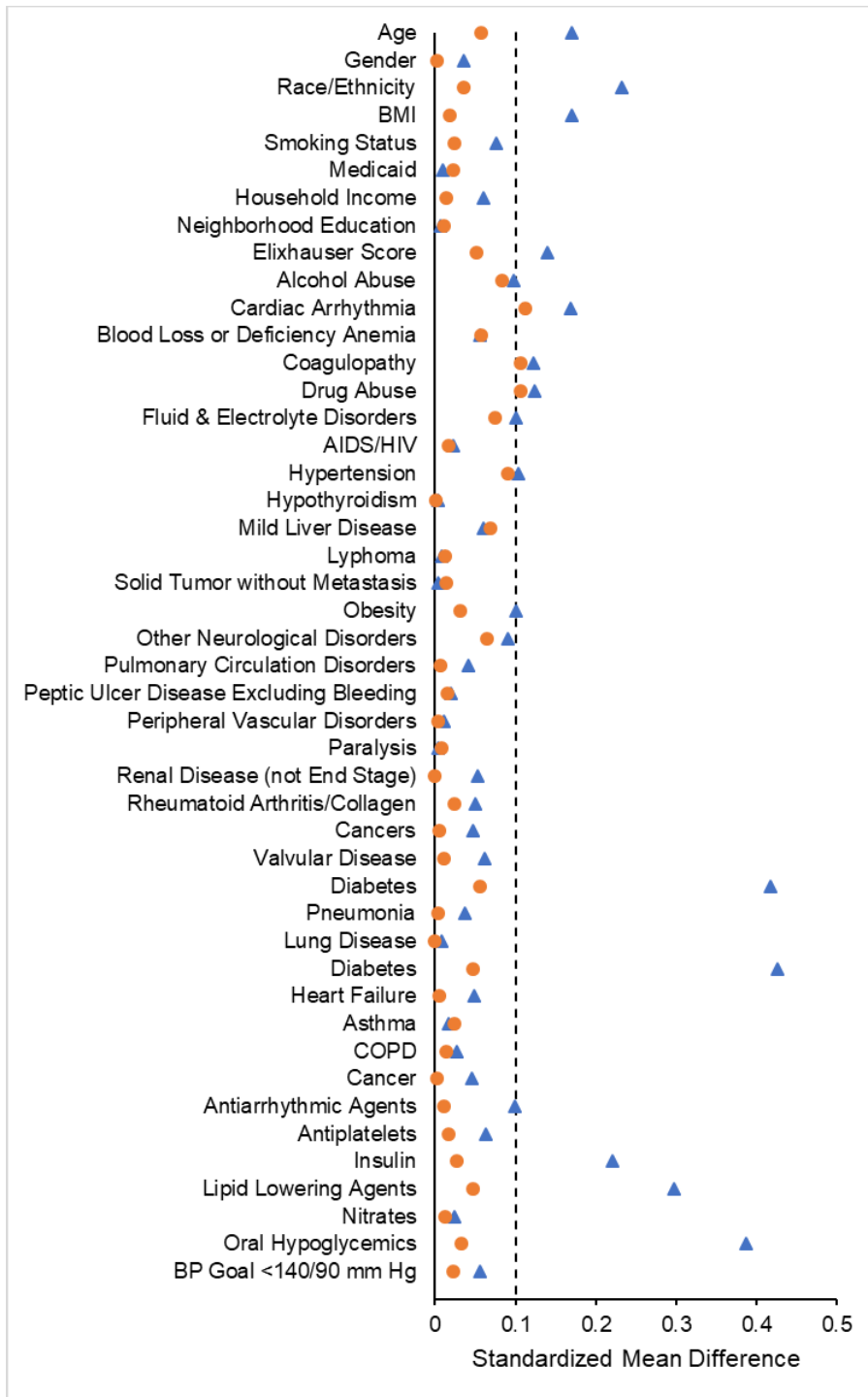
(C) No antihypertensive medication vs CCB/BB/TD

Figure S3. Standardized Mean Difference Comparison Before and After Propensity Score Matching among Patients Taking ACEI or BB/CCB/TD.



Blue triangle represents standardized mean difference (SMD) before matching, and orange circle represents SMD after matching. Hypertension refers to ≥ 1 outpatient visits with hypertension diagnosis codes.

Figure S4. Standardized Mean Difference Comparison Before and After Propensity Score Matching among Patients Taking ARB or BB/CCB/TD.



Blue triangle represents standardized mean difference (SMD) before matching, and orange circle represents SMD after matching. Hypertension refers to ≥ 1 outpatient visits with hypertension diagnosis codes.

Figure S5. Standardized Mean Difference Comparison Before and After Propensity Score Matching among Patients Not Taking Antihypertensive Medications or Taking BB/CCB/TD.



Blue triangle represents standardized mean difference (SMD) before matching, and orange circle represents SMD after matching. Hypertension refers to ≥ 1 outpatient visits with hypertension diagnosis codes.