

# Outcomes with Angiotensin-Converting Enzyme Inhibitors vs Other Antihypertensive Agents in Hypertensive Blacks

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## ABSTRACT

**BACKGROUND:** Angiotensin-converting enzyme inhibitors are used widely in the treatment of patients with hypertension. However, their efficacy in hypertensive blacks when compared with other antihypertensive agents is not well established.

**METHODS:** We performed a cohort study of patients using data from a clinical data warehouse of 434,646 patients from New York City's Health and Hospitals Corporation from January 2004 to December 2009. Patients were divided into the following comparison groups: angiotensin-converting enzyme inhibitors vs calcium channel blockers, angiotensin-converting enzyme inhibitors vs thiazide diuretics, and angiotensin-converting enzyme inhibitors vs  $\beta$ -blockers. The primary outcome was a composite of death, myocardial infarction, and stroke. Secondary outcomes included the individual components and heart failure.

**RESULTS:** In the propensity score-matched angiotensin-converting enzyme inhibitors vs calcium channel blocker comparison cohort (4506 blacks in each group), angiotensin-converting enzyme inhibitors were associated with a higher risk of primary outcome (hazard ratio [HR], 1.45; 95% confidence interval [CI], 1.19-1.77;  $P = .0003$ ), myocardial infarction (HR, 3.40; 95% CI, 1.25-9.22;  $P = .02$ ), stroke (HR, 1.82; 95% CI, 1.29-2.57;  $P = .001$ ), and heart failure (HR, 1.77; 95% CI, 1.30-2.42;  $P = .0003$ ) when compared with calcium channel blockers. For the angiotensin-converting enzyme inhibitors vs thiazide diuretics comparison (5337 blacks in each group), angiotensin-converting enzyme inhibitors were associated with a higher risk of primary outcome (HR, 1.65; 95% CI, 1.33-2.05;  $P < .0001$ ), death (HR, 1.35; 95% CI, 1.03-1.76;  $P = .03$ ), myocardial infarction (HR, 4.00; 95% CI, 1.34-11.96;  $P = .01$ ), stroke (HR, 1.97; 95% CI, 1.34-2.92;  $P = .001$ ), and heart failure (HR, 3.00; 95% CI, 1.99-4.54;  $P < .0001$ ). For the angiotensin-converting enzyme inhibitors vs  $\beta$ -blocker comparison, the outcomes between the groups were not significantly different.

**CONCLUSIONS:** In a real-world cohort of hypertensive blacks, angiotensin-converting enzyme inhibitors were associated with a higher risk of cardiovascular events when compared with calcium channel blockers or thiazide diuretics.

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Major national and international hypertension guidelines recommend angiotensin-converting enzyme inhibitors as one of the first-line agents for the treatment of hypertension.<sup>1-3</sup> Despite the proven efficacy of angiotensin-converting enzyme inhibitors in lowering blood pressure,<sup>4-6</sup> there is uncertainty about their effectiveness among blacks.<sup>7</sup> In the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT), blacks treated with angiotensin-converting enzyme inhibitors demonstrated poorer blood pressure control (5/2 mm Hg higher blood pressure), 40% greater risk of stroke, 32% greater risk of heart failure, and 19% greater rates of cardiovascular disease than those randomized to diuretics.<sup>7-9</sup> In addition, studies have shown that blacks are more prone to develop adverse effects associated with angiotensin-converting enzyme inhibitors, including cough, angioedema,<sup>10,11</sup> and hyperkalemia.<sup>12</sup> Consequently, the National Institute for Health and Clinical Excellence clinical practice guidelines for hypertension recommend calcium channel blockers in lieu of angiotensin-converting enzyme inhibitors for hypertensive blacks as initial therapy. If a calcium channel blocker is not tolerated because of edema or other side effects, the guidelines recommend a thiazide-like diuretic in blacks.<sup>1</sup>

Given the low representation of blacks in hypertension clinical trials, there is an urgent need for more definitive data on the real-world therapeutic effectiveness of angiotensin-converting enzyme inhibitors vs other antihypertensive agents in hypertensive blacks. Our objective was to evaluate the effectiveness of angiotensin-converting enzyme inhibitors when compared with other antihypertensive agents in hypertensive blacks.

## MATERIALS AND METHODS

### Patient Population

Data from the New York City Health and Hospital Corporation's clinical data warehouse encompassing more than 1.8 million patients from its inception on January 2004 to December 2009 were chosen. The Health and Hospital Corporation consists of 11 acute care hospitals, 6 diagnostic and treatment centers, 4 long-term care facilities, a certified home health care agency, and more than 80 community health clinics, which provide care for approximately one fifth of all general hospital discharges and more than one third of emergency department and hospital-based clinic

visits in New York City. Approximately 35% of patients seen in the Health and Hospital Corporation system are black. The institutional review boards from the New York University School of Medicine and New York City Health and Hospital Corporation approved the study.

### CLINICAL SIGNIFICANCE

- In a cohort of 25,564 propensity score-matched hypertensive black patients, angiotensin-converting enzyme inhibitors were associated with a higher risk of primary outcome, myocardial infarction, stroke, and heart failure vs calcium channel blockers (4506 matched pairs) and a higher risk of primary outcome, death, myocardial infarction, stroke, and heart failure vs thiazide diuretics (5337 matched pairs).
- In this largest cohort of hypertensive blacks, angiotensin-converting enzyme inhibitors were associated with less benefit when compared with calcium channel blockers or thiazide diuretics.

### Inclusion and Exclusion Criteria

For the current study, hypertensive black patients who met the following inclusion criteria were selected: (1) hypertension diagnosis (identified through International Classification of Diseases, 9th Revision, Clinical Modification code for hypertension, or systolic pressure >140 mm Hg, or prescribed an antihypertensive agent on at least 2 occasions); and (2) prescribed an angiotensin-converting enzyme inhibitor/ $\beta$ -blocker/thiazide diuretic/calcium channel blocker at least 6 months after their first date of entry in the system (to prevent "healthy user" effect) and with at least 1 additional refill.

The exclusion criteria included (1) age <18 years or >90 years; (2) first medication prescription <6 months of entry into the system; (3) a history of heart failure, myocardial infarction, or stroke, because these are compelling indications for angiotensin-converting enzyme inhibitor use; (4) prescription of an angiotensin receptor blocker; and (5) patients with missing follow-up.

### Antihypertensive Use and Follow-up

We identified new users (an inception cohort) for each antihypertensive medication of interest<sup>13</sup> to prevent "healthy user" effects that result from studying patients who are not treatment naïve.<sup>14</sup> A 6-month time span after their first date of entry in the system and before the first prescription was required to ensure patients are new users, to eliminate selection bias.

Patient follow-up information, including blood pressure measurements, was obtained from the electronic health records (Misys, Raleigh, N.C). The study data were derived from structured fields and codes in the electronic health records, which contain all potential confounders to be included in the models. In addition, the database was linked with the New York State Vital Statistics to determine death during follow-up.

### Outcomes

The primary outcome was a composite of death, nonfatal myocardial infarction, and nonfatal stroke. Secondary

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