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Managing Patients with Concomitant Hypertension and Diabetes

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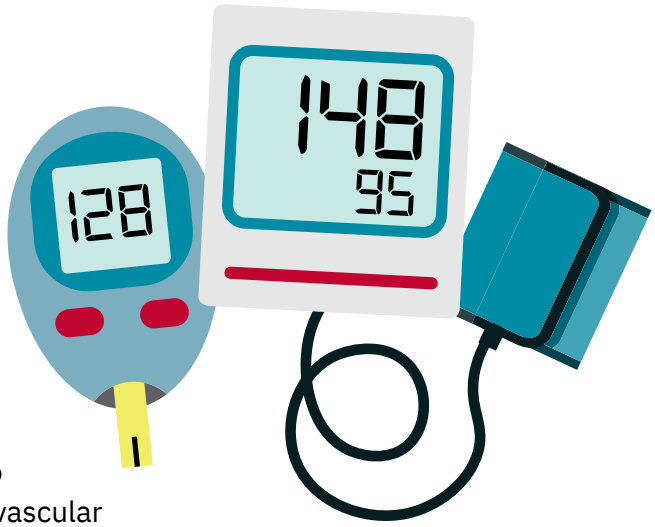


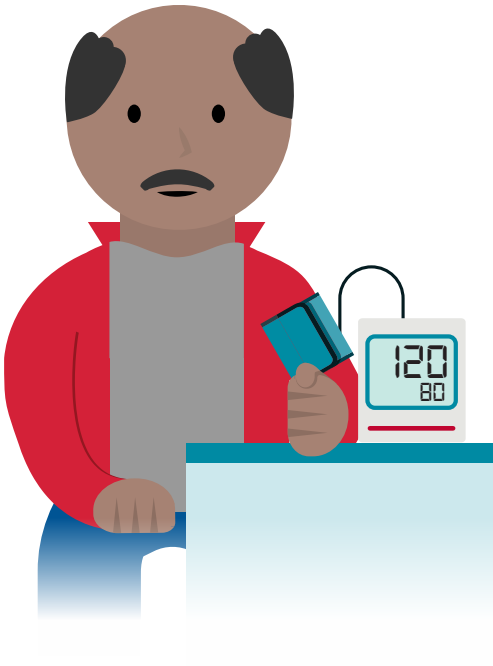
Hypertension and diabetes often occur concomitantly with hypertension prevalence of approximately 71% in patients with type 2 diabetes.[1]

Patients with hypertension are 2.5 times more likely to develop diabetes, and hypertension has been estimated to account for up to 75% of the added atherosclerotic cardiovascular disease (ASCVD) risk in those with diabetes.[2]

In addition, treatment to lower elevated blood pressure (BP) in these patients is at least as effective in reducing adverse diabetic clinical outcomes as treatment to lower blood glucose (Table 1). For every 10 mm Hg systolic blood pressure (SBP) reduction, there is a significant reduction in major cardiovascular events, coronary events, strokes, heart failure, eye disease, albuminuria, and all-cause mortality.[3] In addition to a marked increase in heart attacks, kidney disease, and peripheral vascular disease, the increases in risk of heart failure and stroke in patients with concomitant hypertension and diabetes are particularly noteworthy and responsive to BP lowering.

Guideline recommendations on hypertension management in patients with diabetes are similar to those recommended in patients without diabetes, yet there are differences in terms of evaluation, treatment, and disease outcomes. There are also some differences between recommendations published by the American Diabetes Association (ADA) and the American College of Cardiology/ American Heart Association (ACC/AHA) guideline for defining hypertension diagnosis and treatment in patients with diabetes.[4,5] However, as shown below, these differences are relatively minor in most patients with diabetes, and there is broad agreement in the recommended approach to management.

Patient Evaluation Specific to Diabetes



- Blood pressure should be measured at every routine clinical care visit. Patients with elevated BP should have it confirmed using multiple readings, including measurements on a separate day, to diagnose hypertension.[4]
- All hypertensive patients with diabetes with discordant office and home BP should have home BP monitored to identify white-coat hypertension.
- When symptoms of orthostatic hypotension are present, orthostatic blood pressure measurement should be performed during the initial evaluation of hypertension and periodically at follow-up. If orthostatic hypotension has been diagnosed, orthostatic blood pressure measurement should be performed regularly.
- Lifestyle measures are recommended for all hypertensive patients, especially those with diabetes, including reducing salt intake to less than 1.5 grams per day, losing excess weight through caloric restriction, increasing consumption of fruits and vegetables (8-10 servings per day) and low-fat dairy products (2-3 servings per day), and increasing activity levels/engaging in regular aerobic physical activity (e.g., brisk walking 30 minutes per day).
- Ten-year ASCVD risk should be assessed to determine the BP level defining when to initiate antihypertensive drug therapy and the BP treatment target. (Figure 1)

Indications for Drug Treatment and Treatment Targets According to ADA and ACC/AHA Guidelines

The ADA and ACC/AHA guidelines differ in two significant areas:

1. The 10-year ASCVD risk level defining “high risk.”
    - High risk is defined by the ACC/AHA guideline as either the presence of ASCVD or a 10-year risk of ≥ 10%; whereas the ADA guideline defines high risk as either the presence of ASCVD or 10-year risk of ≥ 15%.
    - Because of the impact of age on ASCVD risk:
        - Rephrase: According to both the ADA and ACC/AHA guidelines, most women > 65 years of age (African American women > age 50) and men > 55 years (African American men > age 45) will meet the ASCVD risk criteria for the < 130 mm Hg target (even without considering other risk factors).
        - Rephrase: According to the ACC/AHA guidelines only, most women > 60 years of age (African American women > age 50) and men > 50 years (African American men > age 45) will only meet the ASCVD risk criteria for the < 130 mm Hg.

2. Blood pressure level defining the criteria for the initiation of antihypertensive drug treatment and treatment goal of < 130/80 mm Hg.

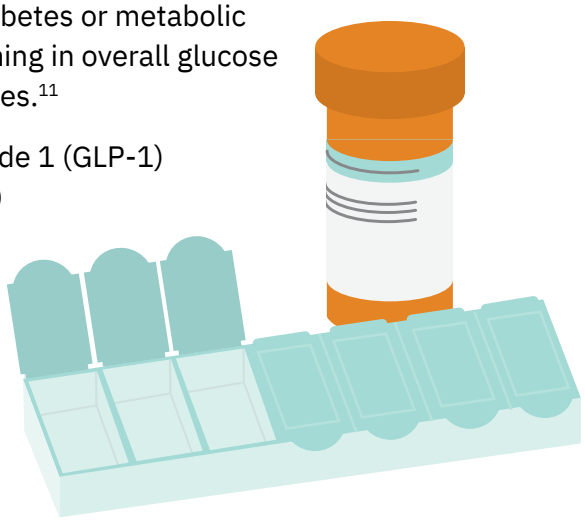
   - Both guidelines recommend initiating antihypertensive drug therapy in addition to lifestyle changes in low-risk patients with diabetes and a SBP ≥ 140 mm Hg or diastolic blood pressure (DBP) ≥ 90 mm Hg, though the ACC/AHA but not the ADA guideline would recommend treatment to a target of < 130/80.

   - In addition to lifestyle changes, antihypertensive drug treatment is recommended in high-risk patients with diabetes and a SBP ≥ 130 mm Hg or DBP ≥ 80 mm Hg with treatment goals to below those levels. (Recommendation Grade 1A and Grade C per the 2017 ACC/AHA and ADA guidelines, respectively).

Specific Drug Treatment Related Issues

- Angiotensin-converting enzyme inhibitors (ACEi), angiotensin receptor blockers (ARB), calcium channel blockers (CCB), and thiazide-type diuretics (THZD), alone or in combination are recommended by most guidelines for hypertension management in this population, though the combination of ACEi and ARB should be avoided. In African American patients, either a THZD and/or a CCB should be included. In patients with diabetes and albuminuria, either an ACEi or ARB should be included in the regimen regardless of race/ethnicity. An ACEi or ARB should also be included in the regimen in the presence of left ventricular dysfunction and in those with a previous stroke history. Beta blockers are recommended in patients with coronary artery disease, or heart failure, but they are less effective than THZD, CCB, or renin-angiotensin system inhibitors (RASI) in preventing cardiovascular outcomes in the absence of these disorders.

- There continues to be reluctance to use THZD in patients with diabetes because of their modest adverse metabolic effects on glucose and lipid metabolism, especially compared to inhibitors of the renin angiotensin system. The Antihypertensive and Lipid Lowering to Prevent Heart Attack Trial (ALLHAT), with more than 42,000 participants, randomized between 9,000-15,000 participants (36% having diabetes and more than 54% with the metabolic syndrome) to regimens containing either the THZD chlorthalidone, the ACEi lisinopril, the CCB amlodipine, and the alpha blocker doxazosin. The antihypertensive regimens containing the THZD was shown in ALLHAT and other trials to be at least as effective in reducing cardiovascular disease (CVD) outcomes compared to the ACEi, CCB, and alpha blocker regimens, including in patients with diabetes or metabolic syndrome.[10,11] (Figure 2 and Figure 3) Despite a modest worsening in overall glucose metabolism, this did not result in differences in clinical outcomes.[11]



- Some glucose lowering agents, particularly glucagon-like peptide 1 (GLP-1) receptor agonists and sodium glucose cotransporter 2 (SGLT 2) inhibitors are associated with a significant decrease in BP and decrease in cardiovascular events. Sodium glucose cotransporter 2 inhibitors seem to have the largest effect on BP of these medication classes.[12,13] The magnitude of BP lowering (2-4 mm Hg on 24-hour ambulatory blood pressure monitoring (ABPM)) is less than most first line antihypertensives, and their greater cost reinforces their primary role in glucose or cardiorenal outcomes rather than BP lowering.

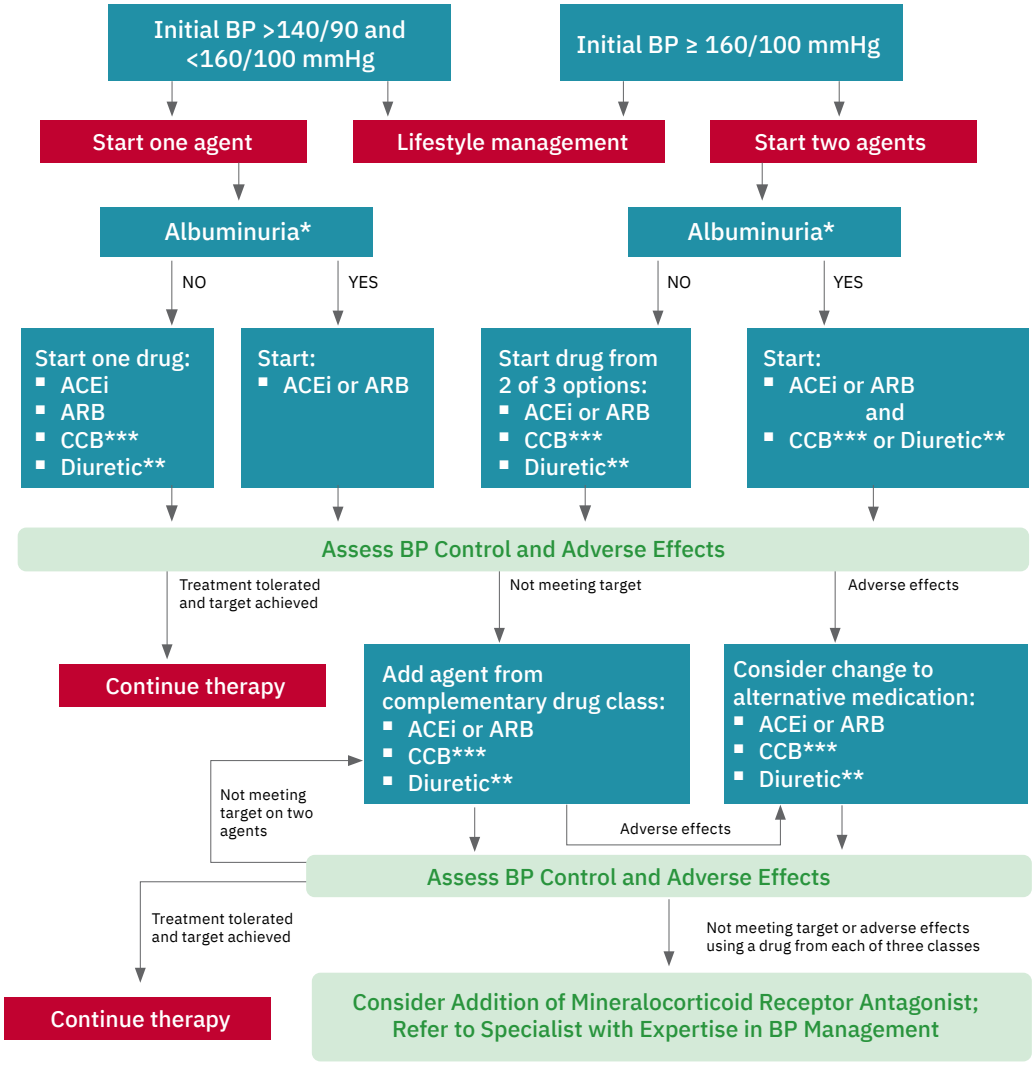
Table 1: Clinical Trials of Blood Pressure Lowering in Diabetes/ Non-Diabetes Patients: Systolic Blood Pressure

	N	Mean SBP Less intense	Mean SBP More intense	CVD Risk Reduction (Overall)	CVD Risk Reduction (Diabetes)
SHEP[14]	583/4,736	155*	146*	27-33%	22-56%
Syst-Eur[15]	492/4,695	162	153	26-44%	62-69%
HOT[16]	1,501/18,790	144**	140**	4%	30-67%
UKPDS[17]	1,148/1,148	154	144	N/A	32-44%
ABCD[18]	470/470	138	132	N/A	No CVD reduction
ACCORD[9]	4,733/4,733	134	119	N/A	No CVD reduction

* Personal communication, Sara Pressel: mean BP at 3 years of follow up
** Mean SBP in overall population (with and without diabetes)

Figure 1: 2020 ADA Guideline BP Treatment Algorithm[4]

Recommendations for the treatment of confirmed hypertension in people with diabetes



*An ACE inhibitor (ACEi) or angiotensin receptor blocker (ARB) is suggested to treat hypertension for patients with urine albumim-to-creatinine ratio of 30-299 mg/g creatinine and strongly recommended for patients with urine albumin-to-creatinine ratio ≥ 300 mg/g creatinine. **Thiazide-like diuretic; long-acting agents shown to reduce cardiovascular events, such as chlorthalidone and indapamide, are preferred. ***Dihydropyridine calcium channel blocker (CCB). BP, blood pressure. Adapted from de Boer et al.

Figure 2: ALLHAT Diabetes and Other Pre-Specified Subgroup Results: Lisinopril vs Chlorthalidone[11]

4-Year BP Difference Relative to Chlorathalidone (SBP/DBP)

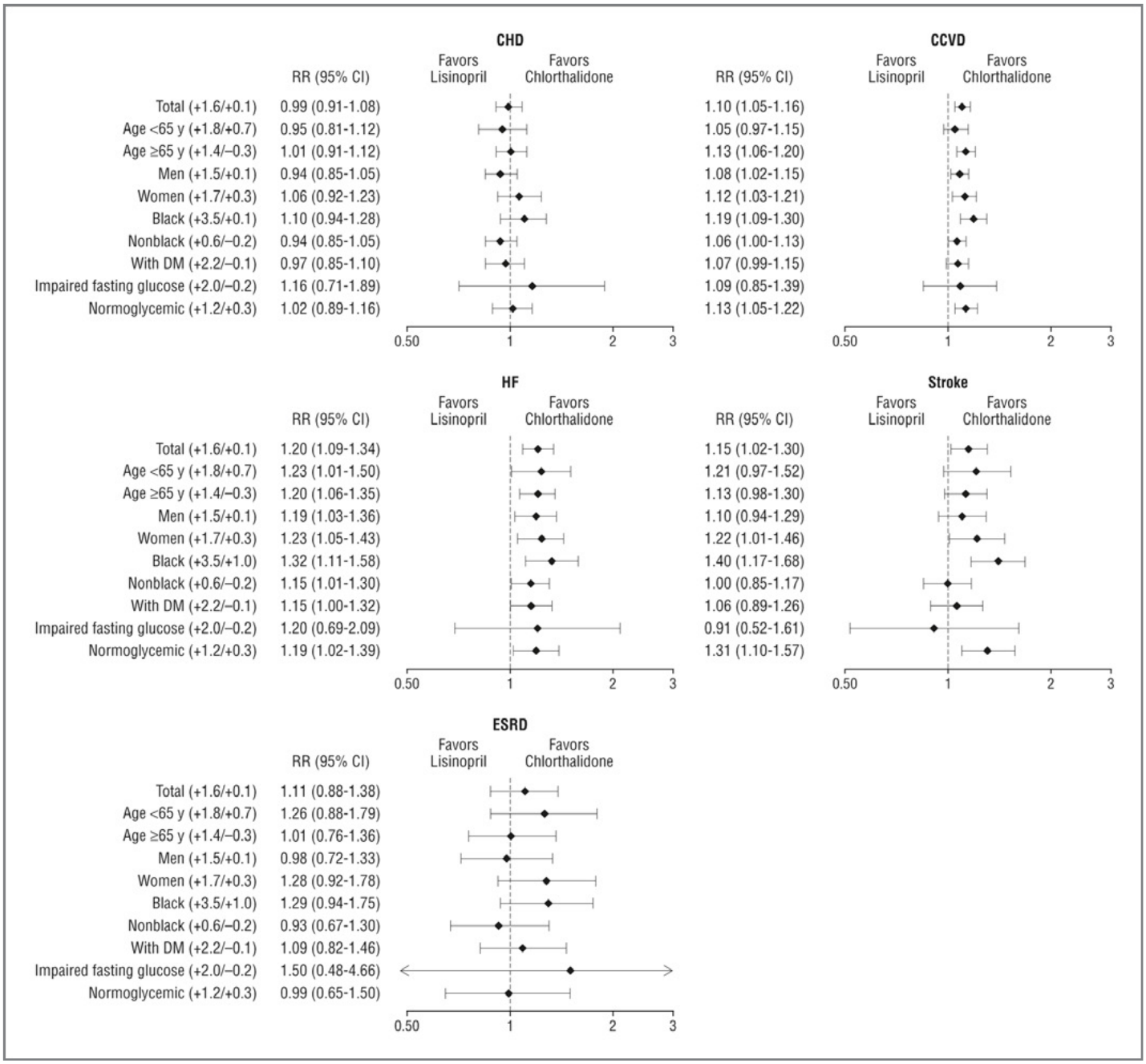
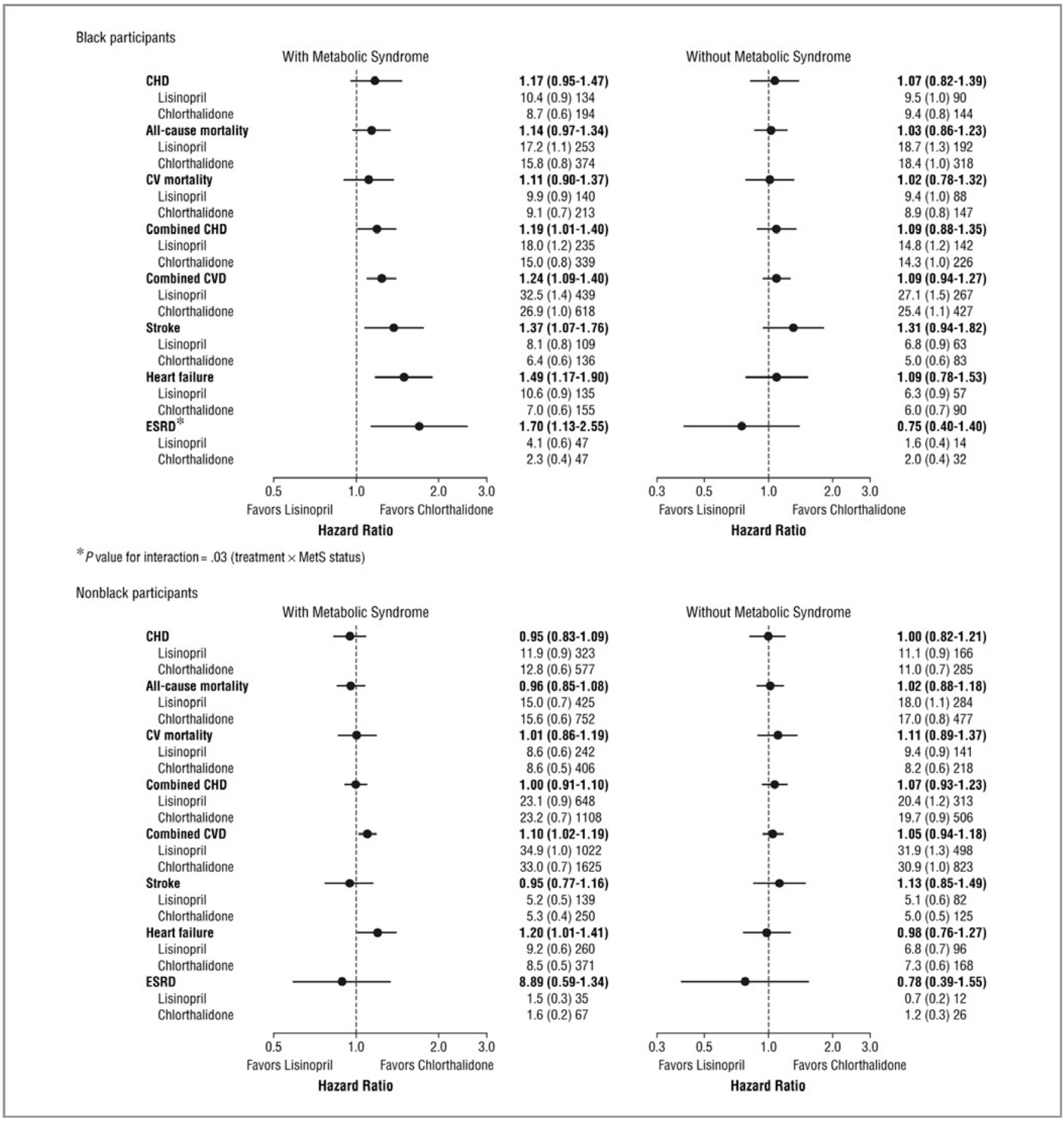


Figure 3: ALLHAT Post-hoc Results by Race and Metabolic Syndrome: Lisinopril vs. Chlorthalidone[19]



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