Amlodipine or lisinopril was not better than chlorthalidone in lowering CHD risk in hypertension

Although not mentioned by your commentator, Dr Psaty,1 concerns have been raised over the heart failure results in ALLHAT.2 Asymptomatic left ventricular (LV) systolic dysfunction is common in older patients, particularly in men and in patients with cardiovascular risk factors.3–4 ALLHAT participants were high risk patients, and many may have had asymptomatic LV dysfunction that could have been unmasked at the start of the study by withdrawal of diuretic therapy. The early difference in heart failure (HF) incidence observed between the lisinopril and chlorthalidone groups, as well as the merging of the HF curves towards the end of the trial, is consistent with this possibility. Furthermore, a true difference in HF incidence over 5 years should have resulted in greater mortality in the lisinopril group; this did not occur. A second concern is the validation of the HF endpoint, the diagnosis of which was up to the local ALLHAT investigator. An ALLHAT subcommittee, which reviewed a small fraction of HF hospital admissions, only agreed with 85% of diagnoses.5 In contrast, blinded endpoint committees in STOP-Hypertension 26 and in ANBP27 both of which included an angiotensin converting enzyme (ACE) inhibitor group, found no difference in HF incidence. In the latter study, men appeared to benefit more from ACE inhibitors than diuretics, consistent with the epidemiology of asymptomatic LV dysfunction.2 Thirdly, there seem to be race based differences between the lisinopril and chlorthalidone groups with respect to the risks for stroke, and possibly combined coronary heart disease, combined cardiovascular disease, as well as HF. Though the statistical significance of these apparent interactions is not provided in the original report, they are not unexpected.9 The ALLHAT results emphasise the importance of diuretics in hypertension treatment. However, data do not support Dr Psaty’s assertion that “If BP is controlled with a nondiuretic, the patient should be switched to a low dose diuretic." By ignoring the arguments for and against the ALLHAT results, we may neglect to pursue potentially important racial and sex differences in hypertension treatment.

GEORGE A HECKMAN, MD, FRCP
Geriatrics and Internal Medicine
McMaster University
Hamilton, Ontario, Canada

In response:

Heckman reiterates a number of published criticisms of ALLHAT. In the Cardiovascular Health Study,1 only 46 (1.5%) of 3579 older adults without clinical cardiovascular disease had an abnormal ejection fraction on echocardiogram. New HF events in older adults usually occur with preserved systolic function.1 ACE inhibitors have not been evaluated in the setting of HF with preserved systolic function, so generalisations from the existing HF trials may well be uninformative. Except in the setting of a myocardial infarction, the case fatality for new HF does not occur. A second concern is the validation of the HF endpoint, the diagnosis of which was up to the local ALLHAT investigator. An ALLHAT subcommittee, which reviewed a small fraction of HF hospital admissions, only agreed with 85% of diagnoses.5 In contrast, blinded endpoint committees in STOP-Hypertension 26 and in ANBP27 both of which included an angiotensin converting enzyme (ACE) inhibitor group, found no difference in HF incidence. In the latter study, men appeared to benefit more from ACE inhibitors than diuretics, consistent with the epidemiology of asymptomatic LV dysfunction.2 Thirdly, there seem to be race based differences between the lisinopril and chlorthalidone groups with respect to the risks for stroke, and possibly combined coronary heart disease, combined cardiovascular disease, as well as HF. Though the statistical significance of these apparent interactions is not provided in the original report, they are not unexpected.9 The ALLHAT results emphasise the importance of diuretics in hypertension treatment. However, data do not support Dr Psaty’s assertion that “If BP is controlled with a nondiuretic, the patient should be switched to a low dose diuretic." By ignoring the arguments for and against the ALLHAT results, we may neglect to pursue potentially important racial and sex differences in hypertension treatment.

BRUCE M PSATY, MD, PHD
University of Washington
Seattle, Washington, USA

1 Psaty BM. Amlodipine or lisinopril was not better than chlorthalidone in lowering CHD risk in hypertension. Evid Based Medicine 2003;8:105.