HYVET Ambulatory Blood Pressure Substudy
To the Editor:

We read with interest the provocative Hypertension in Very Elderly Trial (HYVET) ambulatory blood pressure (ABP) article by Bulpitt et al.1 The main result is that white-coat hypertension (WCH) was present in half of HYVET patients at baseline. The authors hypothesized that the benefits of active treatment in HYVET may partially stem from treating individuals with WCH. To test this hypothesis, subgroup analysis of outcome in the active versus placebo arms according to baseline blood pressure status (sustained hypertension and WCH) is required. Such analysis cannot be made because of the small number of patients with available ABP. In its absence, the authors rely on ill-defined expectations of benefits in relation to blood pressure reduction to support the hypothesis. We argue that the current findings may at best warrant follow-up evaluation but do not suggest that treatment of WCH should be included in guidelines for treatment of hypertension in the very elderly.

Furthermore, blood pressure in clinical trials has been traditionally measured in the office; our expectations of benefits from its reduction are based on clinical measurements, which were prone to the unrecognized white-coat effect. Thus, the rationale of realigning expected benefits with observed ABP reductions hypothesis is questionable.

We have reservations on the generalizability of the conclusions:
1. First, countries providing 72% of the ABP monitorings recruited only 15% of the participants in HYVET. The unusual HYVET geographical patient mix, together with their exceptional health, makes for suboptimal representation of this age group. In Israel, for example, only 9% of community-dwelling 80-year-olds would have been HYVET-eligible.

Second, the ABP diurnal time intervals chosen may substantially reduce daytime ABP,1 because elderly people frequently nap2 even more so in China.3

Third, we wonder whether patients might have been misclassified as having WCH. This concern arises because in the subset of subjects with repeat ABP data available, individuals classified as WCH and subsequently randomized to placebo experienced dramatic increase in ABP: 127/75 mm Hg daytime and 122/69 mm Hg nighttime at baseline versus 145/82 mm Hg daytime and 133/73 mm Hg nighttime at follow-up (see their Table S1). Accordingly, in subjects with WCH randomized to active treatment, no change in ABP was noted during follow-up, suggesting ineffectiveness of treatment in reducing ABP in patients with WCH and negating the authors’ main conclusion. This leaves open the possibility that patients derived benefit from diuretic and ACE inhibitor treatment of congestive heart failure (the most significant finding in HYVET), regardless of blood pressure.

An alternative interpretation to the substudy results could be that very elderly should be treated with low-dose indapamide and perindopril, given their high risk based on age alone even when normotensive. By a similar approach, benefits were found in PROGRESS (Perindopril pR0tection aGainst REcurrent Stroke Study) and ADVANCE (Action in Diabetes and Vascular disease: preterAx and diamicron-MR Controlled Evaluation) for stroke and diabetes mellitus patients, respectively. However, recommendations to treat WCH are premature, and until a definitive study is done the suggestion to treat WCH in the elderly or to treat elderly normotensives should be deferred.

Disclosures
None.

Ido Z. Ben-Dov
Nephrology and Hypertension Services
Hadassah-Hebrew University Medical Center
Jerusalem, Israel

Michael Bursztyn
Department of Medicine
Hadassah-Hebrew University Medical Center, Mount-Scopus
Jerusalem, Israel
