Do the SBP differences between the lisinopril and chlorthalidone arms explain the differences in CVD outcomes?
BP differences: lisinopril versus chlorthalidone

- Mean follow-up SBP for L vs. C
  - 2 mm Hg higher – all participants
  - 4 mm Hg higher – Black participants

- Adjustment for follow-up SBP/DBP as time-dependent covariates in a Cox regression model slightly reduced the relative risks but they remained statistically significant
  - Stroke (1.15 → 1.12) & HF (1.20 → 1.17), overall
  - Stroke (1.40 → 1.35) & HF (1.32 → 1.26), for Blacks
BP differences: lisinopril versus chlorthalidone (continued)

- Prospective observational studies* predict that 2 mm Hg difference → 9% higher stroke mortality & 6% higher HF mortality, versus 15 & 19% higher risk (fatal + nonfatal events) observed in ALLHAT
- Based on same data, 4 mm Hg difference in blacks would predict 19% higher stroke mortality & 14% higher HF mortality, versus 40% & 32% higher risk (fatal + nonfatal events) in ALLHAT

• Although application of epidemiologic adjustments and extrapolations have limitations, seems unlikely that BP differences explain total effects.

• ALLHAT will also conduct a meta-regression analysis of BP and CVD endpoints, with clinics (1 or more) as unit of analysis. This will reduce BP measurement error.
BP differences: Future analyses

1) Divide ALLHAT into a number of large or mega-clinics, i.e. small clinics combined into mega-clinics.

2) Within each mega-clinic compute a) mean follow-up SBP difference between diuretic and other treatment arm, and b) log hazard ratio (for a given endpoint) using Cox model.

3) Do a weighted regression of log hazard ratios against follow-up SBP differences.

4) A markedly non-zero intercept indicates drug treatment effect is not entirely explained by SBP differences.