Study Question: Does blood pressure reduction alone explain the effect of blood pressure lowering medications in preventing coronary heart disease (CHD) and stroke, are there differences in efficacy among various classes of blood pressure lowering medications, and is the benefit of blood pressure lowering medication use related to subject’s history of cardiovascular disease?

Methods: The authors reported the results of a rigorous meta-analysis of randomized trials of blood pressure lowering medications in which CHD events and strokes were recorded. The analysis included 108 trials comparing study drug with placebo, 46 trials comparing different antihypertensive medications, and seven trials including three randomized groups which fell into both categories. They compared the results with a large published meta-analysis of cohort studies, and looked at effective blood pressure lowering drugs on lowering blood pressure according to dose, reduction in disease events per reduction in blood pressure, and analyzed the results based on whether or not subjects had a history of vascular disease, coronary disease, or stroke.

Results: Among a total of 464,000 subjects included in these trials, the authors observed that beta-blockers had an effect above what would be expected for the blood pressure reduction achieved in preventing recurrent CHD events in people with CHD (relative risk, 29%; 95% confidence interval [CI], 22-34% versus 15%; 95% CI 11-19%) for other medications. This benefit was seen only in the first few years after MI, during which time there was a risk reduction of 31% for beta-blockers in recent myocardial infarction (MI) versus 13% with no recent MI (p = 0.04). Otherwise, the reduction in CHD events (22%; 95% CI, 17%-27%) and stroke (41%; 95% CI, 33%-48%) were similar for a blood pressure reduction of 10 mm mercury systolic or 5 mm mercury diastolic. This was similar to reductions reported in a previous large cohort study meta-analysis. All classes of blood pressure lowering medications had similar benefit in preventing CHD events and stroke, except for a slightly greater stroke reduction with calcium channel blockers. These reductions in events were similar regardless of presence of cardiovascular disease or baseline blood pressure. Calcium channel blockers were associated with a slightly lower reduction in incidence of heart failure than other blood pressure lowering medications (19% vs. 24%). There was a greater risk reduction associated with the use of two blood pressure medications at half standard dose versus one medication at standard dose, and roughly double the benefit of three medications at half standard dose when compared with one medication at standard dose.

Conclusions: The authors concluded that, with the exception of an extra protective effect of beta-blocker therapy shortly after MI, and a slightly increased protective effect of calcium channel blockers for stroke, all types of blood pressure medication have a similar, striking benefit in reducing CHD events and stroke, suggesting a lack of important pleiotropic effect. The benefit was similar regardless of pretreatment blood pressure or pretreatment cardiovascular disease status. The authors further opined that guidelines on the use of blood pressure medications could be simplified to offer medications to subjects with all levels of blood pressure, and that the results suggest blood pressure lowering is important in everyone over a certain age.

Perspective: This enormous statistical tour de force provides evidence of the dramatic benefit from blood pressure lowering therapy, regardless of the agent chosen. These data also lend strong support to the concept of adding a different class agent rather than escalating dose when increasing antihypertensive therapy. The authors make an argument for virtually universal blood pressure lowering therapy. (For example, in this meta-analysis, subjects with a pretreatment systolic blood pressure between 110 and 119 mm Hg experienced a statistically significant 22% reduction in CHD events.) These data suggest that blood pressure confers a continuum of risk and that any lowering of blood pressure confers cardiovascular and stroke risk reduction. It may be that public health resources should be diverted from hypertension case-finding to effective delivery of antihypertensive therapy to all but those with contraindications.