We performed a quantitative overview of the literature to investigate whether properties of antihypertensive drugs may play a role in cardiovascular protection over and beyond blood pressure (BP) lowering. We extracted summary statistics from published articles and computed pooled odds ratios (ORs) for experimental vs reference treatment from stratified 2 x 2 contingency tables after application of Zelen’s test of heterogeneity. Subsequently, we correlated ORs with BP differences across individual trials, using meta-regression. Among 5 trials in hypertension which compared cardiovascular risk on diuretics or β-blockers with that on calcium-channel blockers (CCBs) or angiotensin-converting enzyme (ACE) inhibitors, all drug classes offered similar cardiovascular protection. However, on CCBs there was more reduction in the risk of stroke (15.1%, CI 2.8–25.9%, p=0.02) and less reduction in the risk of myocardial infarction (20.1%, CI 3.90–38.9%, p=0.01). Meta-regression across 21 trials showed that for cardiovascular mortality the relationship between the ORs and BP differences was linear, whereas for other outcomes there was no further decrease in risk once the systolic/diastolic differences had reached ~15/5 mm Hg. In recent trials of doxazosin vs chlorothalidone in hypertensive patients and of ramipril vs placebo in high-risk patients, outcome was better on the diuretic and the ACE inhibitor, respectively. However, there were also 2-3/1 mm Hg BP differences between the groups. For systolic BP in the 2 trials, all ORs conformed with the regression lines. For diastolic BP, there was also no separation between predicted (0.99, CI 0.88–1.10) and observed ORs, except for the risk of all cardiovascular events on doxazosin (1.24, CI 1.15–1.33) or ramipril (0.76 CI 0.67–0.85). In conclusion, in the recent trials BP largely accounts for outcome. Older and newer antihypertensive drugs provide similar overall cardiovascular benefit, but CCBs may offer more protection against stroke than myocardial infarction. The hypothesis that ACE inhibitors or α-blockers might influence outcome over and beyond their BP lowering effects remains to be proven.

Key Words: Meta-analysis, Clinical trials, Hypertension