province, were used. In a cohort of 27,000 newly diagnosed hypertensive patients followed for five years, the relationship of continued use (persistence) with antihypertensive therapy to the choice of initial agent was examined. After one year of observation, only 74% of those starting on diuretics were still persistent compared to 78% on beta blockers, 81% calcium channel blockers (CCB), and 83% on angiotensin converting enzyme inhibitors (ACEI) ($p < 0.001$). These relationships remained significant in Cox proportional hazards analysis controlling for confounding by age, sex and proxy measures of prior health status. Almost half of all patients who discontinue medication were found to do so early during receiving fewer than four prescriptions, with the worst discontinuation patterns found in those starting with a diuretic, and the best with ACEI ($p < 0.001$). Turbulence of the therapeutic course (medication switches, additions, discontinuations) was also found to be inversely associated with persistence. Thus, the choice of initial agent, of one more tolerable and less prone to require changes, may be important in achieving persistence and, therefore, effectiveness. These findings indicate that evidence from studies of antihypertensive use in actual practice is needed to enhance therapeutic outcomes.

1026-67 Time Trends in the use of Antihypertensives in Patients With Initial Acute Myocardial Infarction (AMI) (1986–95): The Worcester Heart Attack Study

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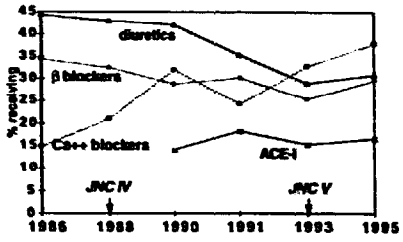
Background: JNC IV, published in 1988, classified calcium channel blockers (CCBs) and angiotensin converting enzyme inhibitors (ACE-i), among others, as first line agents, while JNC V, published in 1993, classified diuretics and β blockers as "preferred" therapy.

Methods: In order to study time trends in antihypertensive use and to assess the impact of the Joint National Committee (JNC) guidelines on clinical practice patterns, we studied 1589 patients (pts) with an initial validated AMI in all metropolitan Worcester hospitals between 1986 and 1995; these pts were investigated as part of an ongoing community-wide surveillance study. Only pts with a history of hypertension were included.



Results: The percentage of pts prescribed CCBs, β blockers, diuretics, and ACE-i), as mono-or combination therapy by year is shown at right. CCB use among hypertensives with first AMI increased dramatically ($p < 0.001$) during the study period, such that CCBs were the most commonly prescribed agent after 1993. The advent of CCBs and ACE-i coincided with an overall decrease in β blocker and diuretic use, though from 1993–5, following publication of JNC V, this trend reversed. CCB use appeared unaffected by JNC V recommendations.

Conclusion: These population-based findings suggest marked changes in practice patterns in hypertensives at risk for AMI.

1026-68 Active Control Trials: What About a Placebo? A Method Illustrated With Clopidogrel, Aspirin and Placebo

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Background: Cardiovascular drug approval is increasingly dependent on active control trials for ethical reasons. For regulatory approval it is necessary to illustrate that a drug would have beaten placebo. Supportive analyses to an active control trial(s) are needed in order to estimate what might have happened if there had been a placebo treatment arm.

Methods: A new method combines an active control trial with a number of separate placebo controlled trials against the active comparator. The method uses the logarithm of the odds ratio for the first occurrence of an event and estimates: i) the odds ratio for the new drug versus placebo and ii) a 95% confidence interval for the estimate.

Illustration: The CAPRIE trial of 75 mg of Clopidogrel versus 325 mg of Aspirin studied more than 19,000 patients with recent prior ischemic stroke, myocardial infarction or peripheral arterial disease, (Lancet, 1996; 348: 1329–39). Aspirin versus placebo was evaluated in a meta-analysis: Antiplatelet Trialists Collaboration (BMJ, 1994; 308: 81–106). These two sources are used to illustrate the method with four endpoints: i) the cluster of all strokes, MI or vascular death; ii) as in i) plus death from any cause, iii) vascular death and iv) death from any cause. The method and graphic presentation of the results are given, estimating very highly statistically significant Clopidogrel versus placebo results ($p < 0.0001$ for the cluster of events). The scientific cogency, strengths and weaknesses of such analyses are discussed.

1026-69 Point of Care Testing for aPTT Improves Cost Outcomes Following Coronary Intervention

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The central laboratory aPTT is currently the leading method for monitoring heparin therapy following percutaneous coronary intervention (PCI). Delays using central laboratory results may limit the ability to establish and maintain therapeutic anticoagulation. This delay, as well as the potential exposure to periods of inadequate or excessive anticoagulation, may adversely affect clinical outcomes, cost and hospital length of stay (LOS). Point of care testing (POCT) for rapid, bedside determination of aPTT has recently become available. No prior study has directly compared central laboratory guided heparin therapy with POCT among PCI patients. The purpose of this study was to prospectively compare clinical outcome, cost per case and LOS between two patient groups cared for under these monitoring systems. We studied 694 patients undergoing PTCA at our institution over 12 consecutive months. In the first 6-month phase, 466 patients were cared for with central laboratory assessed aPTT, whereas in the subsequent phase, 228 patients were monitored with bedside POCT (Coaguchek, Boehringer Mannheim). There were no statistically significant differences between the groups, including baseline predictors of bleeding and ischemia. No difference in clinical in-hospital outcome was observed between the two groups with respect to Q wave MI, stroke, death, acute closure, transfusion and hematoma. POCT reduced LOS by 22% and cost per case by 15%.

	Lab	POCT	p-Value
Mean LOS (days)	5.22 (6.19)	4.09 (3.35)	0.001
Direct Cost/Case	$8,403	$7,164	0.003

In conclusion, a large economic benefit without decrease in quality of care was noted with the use of POCT for management of heparin therapy following coronary intervention.

1026-70 Calcium Channel Blockers and Cancer. No Evidence of an Increased Risk.

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Background: The epidemiologic studies have suggested that calcium channel blockers (CCBs) increase the risk of several cancers. One study has suggested that CCBs may cause breast cancer, and interact with estrogen supplements.

Methods: In a large case-control study of many cancers conducted during 1983–1996 among patients 40 to 69 years of age in hospitals in Baltimore, New York and Philadelphia, 9513 cancer cases were compared with 6492 controls.

Results: The use of CCBs (mean duration 3.8 years) was not associated with cancer overall (relative risk, 1.1%; 95% confidence interval 0.9–1.3). Nor were CCBs associated with individual cancers, including those previously implicated, with the exception of renal cancer. Again with the exception of renal cancer, beta-blockers and angiotensin-converting enzyme inhibitors were also unrelated to cancer risk. Renal cancer has been associated with hypertension (and drugs used to treat hypertension) in previous studies. Among 2893 cases of breast cancer the relative risk for CCB use was 1.1 (95% confidence interval 0.8–1.4) and there was no evidence of interaction with estrogen supplements.

Conclusions: The findings suggest that CCBs do not cause cancer.