

found no significant differences between the study groups in compliance with protocol assessment or nonprotocol therapy administered before progression. Since censoring is affected by differences in progression-free survival, comparisons are not very meaningful. Nonetheless, we found no major differences in the number of patients for whom data were censored (31 vs. 10) or the median time from registration to censoring (29.4 months vs. 16.8 months). Finally, we found no differences in the reasons for treatment discontinuation.

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Platelet Activation and Atherothrombosis

TO THE EDITOR: In their review of platelet activation and atherothrombosis, Davì and Patrono (Dec. 13, 2007, issue)¹ state that “the clinical benefit associated with P2Y₁₂ blockade by clopidogrel in patients receiving aspirin is relatively modest and inconsistent.” However, combining aspirin and clopidogrel is beneficial in certain subgroups. In one study, after percutaneous coronary intervention, combination therapy for 1 year was associated with a 26.9% relative reduction in the combined risk of death, myocardial infarction, or stroke.² The addition of clopidogrel (300 mg in a loading dose, then 75 mg daily) to aspirin also improved patency rates for the infarct-related artery and reduced ischemic complications in patients with ST-segment elevation.³ The composite end point of arterial occlusion, death, or recurrent myocardial infarction in the study by Sabatine et al.³ was reduced by 36% with clopidogrel. Combination therapy also reduced the composite end point of death, reinfarction, or stroke as well as all-cause mortality and reinfarction among 45,852 patients presenting with an acute myocardial infarction.⁴ The clinical benefits of the combination therapy were not associated with an increased risk of bleeding. Thus, the beneficial role of dual antiplatelet therapy should not be underestimated.

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THE AUTHORS REPLY: In response to Kapoor’s comments, the relative risk reduction of major vascular events associated with the combination of clopidogrel and aspirin, as compared with single antiplatelet therapy, is relatively modest and inconsistent in the major areas of high cardiovascular risk (Fig. 1).²⁻⁴ The additional benefit of dual antiplatelet therapy versus aspirin alone is only a fraction of the benefit associated with aspirin versus placebo in the same clinical setting.^{1,5} In our article, we also suggest that the role of adenosine diphosphate (ADP) in atherothrombosis may have been underestimated on the basis of trials of ticlopidine and clopidogrel because of incomplete and variable blockade of ADP-induced platelet aggregation by these drugs. The results of the Trial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet Inhibition with Prasugrel–Thrombolysis in Myocardial Infarction (TRITON–TIMI) 386 are consistent with this hypothesis.

A new thienopyridine, prasugrel, which causes a higher level of inhibition of ADP-induced platelet aggregation and a less variable response than standard-dose clopidogrel, further reduced major vascular events by about one fifth in patients with acute coronary syndromes and scheduled percutaneous coronary intervention.

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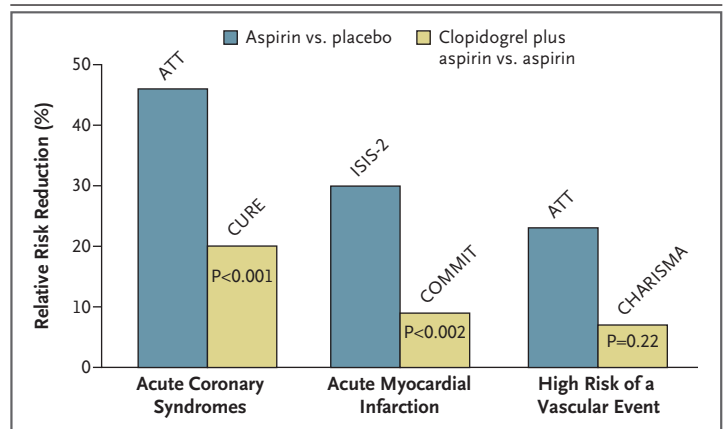


Figure 1. Relative Risk Reductions for the Combined End Point of Major Vascular Events.

Data are from individual randomized clinical trials and from a meta-analysis of trials of aspirin. ATT denotes Antithrombotic Trialists' Collaboration,¹ CHARISMA Clopidogrel for High Atherothrombotic Risk and Ischemic Stabilization, Management, and Avoidance,² COMMIT Clopidogrel and Metoprolol in Myocardial Infarction Trial,³ CURE Clopidogrel in Unstable Angina to Prevent Recurrent Events,⁴ and ISIS-2 Second International Study of Infarct Survival.⁵

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Expansion of the Health Workforce and the HIV Epidemic

TO THE EDITOR: Samb and colleagues (Dec. 13, 2007, issue)¹ call attention to the critical topic of shortages of health care workers in the developing world. One proposed solution involves shifting medical tasks to less skilled workers and laypersons. We are concerned that the rush to the bandwagon of “task shifting” takes the emphasis off the need to improve the jobs of health care workers in countries with severe epidemics of human immunodeficiency virus infection and AIDS (HIV/AIDS) and tuberculosis.

Our study involving South African nurses showed that working conditions and financial concerns were driving migration.² As part of a strategy to expand health care systems, the implication is that task shifting will allow systems to provide care with lower-cost workers.³ Are the problems that have fueled shortages of health care workers in the developing world — low pay and poor working conditions — addressed by task

shifting, or are they merely shifted onto an already overburdened community? Of additional concern is the burden of community-based care on women and its contribution to sex inequality.⁴ Integrating community members into a strengthened primary health care system is desirable, but so is the goal of decent work in the health sector.⁵

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