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Uncertainty

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The March 8 2007 issue of *The New England Journal of Medicine* contains five original articles, two perspectives and one editorial on the debate over the comparative safety and efficacy of drug-eluting coronary stents. So why would a gastroenterologist want to write an editorial on this subject? There are two components to this debate that I find intriguing—the first is intellectual and the second is practical.

Intellectually, in an era of evidence-based medicine and from a regulatory standpoint, it is necessary to emphasize that one must always ask the right question and make certain that the resulting evidence applies to that question. The question being asked that led to the development of drug-eluting stents was whether, compared with bare-metal versions, stents coated with sirolimus or paclitaxel could reduce rates of target-vessel failure, revascularization, or both at 9 months in patients with discrete, previously untreated lesions in native coronary vessels. The results of pivotal trials that enrolled more than 1,000 patients each were unequivocally in favor of drug-eluting stents.

Now skip ahead to 4 years after initial FDA approval of the sirolimus-eluting stent, and 3 years after approval of the paclitaxel-eluting stent. It seems that medium-term data call into question the safety of drug-eluting stents, by virtue of elevated rates of nonfatal myocardial infarctions, death from cardiac causes and angiographically documented stent thromboses. The findings prompted the FDA to note that "…the data we currently have do not allow us to fully characterize the mechanism, risks and incidence of [drug-eluting-stent] thrombosis." and to convene a Circulatory System Devices Advisory Panel meeting in December 2006, that sought to identify the issues that led to the controversial findings and the mixed messages they engendered despite the large amount of published data available. The issues they identified were the variable definitions used for outcome measures and key differences in the characteristics of patients and coronary lesions (*N Engl J Med* [2007] 356: 981–984).

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The controversy over the safety and efficacy of drug-eluting stents has an exponential impact, given that millions of drug-eluting stents have been put in place and, for more than 60% of cases, used 'off-label' in patients with characteristics different to those of the patients enrolled in the original clinical trials (most often they have more extensive or complex coronary artery disease or concomitant medical problems, such as acute myocardial infarctions or diabetes). Although long-term data and ongoing clinical trials might clarify how these differences lead to the observed outcomes, the debate regarding the relative safety and efficacy of drug-eluting stents continues.

Practically, there has been the significant recommendation from the FDA panel (based on data from nonrandomized studies) that dual antiplatelet therapy with aspirin and clopidrogel should be continued for 12 months in patients treated with drug-eluting stents who are not at high risk for bleeding. Indeed, while clearly elucidating the lessons learned and questions that need to be addressed, Dr Farb and Ms Boam from the FDA state that "Health care providers who are considering discontinuation of antiplatelet therapy in order to perform invasive procedures [Ed: enter the gastroenterologist!] should also consult with the patient's cardiologist." (*N Engl J Med* [2007] 356: 984–987). Given the absence of data on the risks and benefits of continuing versus withholding clodiprogel or low-dose aspirin for gastrointestinal procedures, what will be the basis for the cardiologist's recommendation?

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Competing interests
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