Drug-eluting stents

In their recent systematic review, Suzanne Ligthart and associates compared analyses of the cost-effectiveness of drug-eluting stents.¹ They found that in most studies in which an incremental cost-effectiveness ratio greater than \$50 000 per quality-adjusted life-year was calculated the study authors recommended against the widespread use of drug-eluting stents. However, we believe that previously published cost analyses of drug-eluting stents, including those mentioned by Ligthart and associates, may have failed to consider the potential costs of lifetime therapy with clopidogrel.

Recent evidence suggests that cessation of clopidogrel therapy in patients with drug-eluting stents can lead to severe adverse outcomes such as in-stent thrombosis and may pose an increased mortality risk.² As a result, the duration of clopidogrel therapy in these patients has become controversial, leading most physicians to treat these patients indefinitely. A cost analysis of 1 year of clopidogrel therapy in the PCI-CURE and CREDO trials showed diminishing returns after 4 weeks of therapy and that an expenditure ranging from \$70 000 to \$350 000 was required to avoid a single myocardial infarction.³

Given that the only proven benefit of drug-eluting stents over conventional bare-metal stents is the reduction in target vessel restenosis,⁴ we feel that the additional cost of lifetime clopidogrel therapy makes drug-eluting stents even less desirable. In a publicly funded health care system with limited re-

sources, such as ours, interventions that provide marginal benefit at a high cost should be carefully scrutinized.

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The results of the cost-effectiveness study by Suzanne Ligthart and associates¹ bring into question the independence and validity of the science generated by health services researchers working with industry support, even in cases in which the support is unrestricted and the research is performed without any direct input from the funder. We suggest that important biases might have affected the authors' conclusions.

It is possible that the quality rating of the studies was biased by knowledge of the studies' conclusions and funding source. Indeed, it is surprising that some cost-effectiveness studies published in high-impact journals, especially the one by Cohen and colleagues,² were rated poorly by the reviewers. In addition, researchers may have undisclosed relationships with the government agencies that support some of their cost-effectiveness research. Interestingly, most of the highly rated cost-effectiveness analyses were requested and financed by health technology assessment agencies, whose

mandate is to provide policy guidance to third-party payers. We believe such funding may influence studies' conclusions about cost-effectiveness, given that researchers are expected to provide responsible policy statements in the name of the health technology agency. Therefore, an alternative conclusion to that proposed by Ligthart and associates could be that publicly funded studies of the cost-effectiveness of drug-eluting stents are not likely to encourage widespread adoption of this technology unless it is expected to save costs. Finally, other factors such as geographic variation in the pricing of drug-eluting stents and repeat procedure costs (which are very different in the United States and Canada) or variations in the baseline risk of clinical restenosis in the population of interest may have had at least as much impact on the studies' conclusions as the source of funding.

In a 2006 industry-sponsored study³ based on the results of the C-SIRIUS trial,⁴ which was not included in the study by Ligthart and colleagues, we concluded that the cost-effectiveness of drug-eluting stents was borderline in high-risk patients. We clearly stated that drug-eluting stents would only be cost-effective in Canada in patients with a 12% or higher risk of repeat procedures. This is a clear example of responsible and unbiased conclusions reached by independent researchers who work with various sources of funding, including the medical device industry.

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