

A Simple Question with a Multivariate Answer

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Discussion of the cost-effectiveness analysis of drug-eluting stents (DES) is both extremely important and necessary, although challenging. Perhaps this urgency contradicts what research has recently demonstrated regarding such devices: the obvious clinical benefit of DES in all analysed subgroups in randomised experimental scenarios and in real patients.^{1,2} This year marked the tenth anniversary of the use of this ground-breaking technology in our field. Several studies have shown both the efficacy and safety of these devices for coronary restenosis reduction compared with bare-metal stents (BMS).³⁻⁵ Data favouring their use have led to increased deployment. Cardiologists must consider the novelty and high cost of this technology; conversely, they must consider the undeniable benefits it provides. The question must be asked: is this treatment cost-effective?

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In the study published in this issue of the *Revista Brasileira de Cardiologia Invasiva*, Ferreira et al.⁶ compared the performance of the Taxus® DES and the Liberté® BMS in consecutive, non-randomised patients. Even in countries where the DES/BMS relationship is not as heavily promoted as in this sample, and despite the reduction of restenosis with DES in all subgroups analysed, the development of a model of maximal benefits is necessary. In one of these recently published models,⁷ the number needed to treat (NNT) with DES to avoid new revascularisation of the target vessel ranged from 6 to 80. This finding means that in certain subgroups, restenosis with BMS was so low that it would be necessary to treat 80 patients with DES in order to avoid a new procedure. Conversely, in other subgroups, restenosis with BMS was high, and the NNT with DES to avoid a new procedure was only 6. These concepts generate a proper discussion regarding the moment at which a decision must be made, and the clinician must compare the clinical benefit of using a device

versus public health policies in order to optimize the incorporation of new technologies.

The cost-effectiveness concept can be defined as the difference between the cost of the two interventions, expressed in monetary value, divided by the difference between their effectiveness, expressed in years of life gained (life expectancy) or in order less important outcomes, such as the number of prevented complications and the number of averted non-fatal events.⁸ Regarding BMS, the following question must be asked: what is the additional cost for each new averted revascularisation? In Brazil, the values obtained in order to avoid either a new revascularisation or an event in the target vessel were R\$ 47,000 in the analysis by Polanczyk et al.,⁹ R\$ 131,000 in the analysis by Ferreira et al.,¹⁰ and the incredible value of R\$ 190,000 was obtained in the study by Quadros et al.¹¹ Two variables influence these large figures, which are substantially higher than the US \$1,650 was found in the North-American study by Cohen et al.¹² These variables are the following: the low incidence of clinical restenosis with BMS, which is exactly what we have seen in a study published in this issue (consequently, a higher number of patients need to be treated with DES to avoid restenosis); and the high prices of both stents in addition to the high DES/BMS cost ratio, which is always greater than 3, or in absolute terms, with a price difference between the two of greater than R\$ 8,000.

In Ferreira et al.,⁶ we observe that the comparison was based on high figures, either that of DES (approximately R\$ 11,000) or of BMS (approximately R\$ 4,000 – extremely expensive!). Despite the cost relationship between the two treatments, this has not been commonly observed by us.

A less relevant aspect of the proposed analysis, albeit considerable given the vision of utilising the best technology available, was the deployment of the Taxus® paclitaxel-eluting stent. This is a first-generation

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DES that has yielded inferior results compared to those of the second-generation stents.¹³

Ferreira et al.⁶ used an observational, non-randomised, consecutive design, whose results were not monitored or even adjudicated by an independent external committee. Data are analysed under such considerations.

In an observational, non-randomised study, variables evaluated before performing an intervention that is under analysis and non-modifiable or non-affected variables are called covariants.

The propensity score¹⁴ is a method that seeks to balance these covariants to provide independence to the analysed variable. In other words, this method evaluates the impact selection bias over the effect of the treatment. This tool is applied in the beginning of the analysis, and has an effect similar to that of multivariate analysis deployed by regression, moving backwards from the events to its determinants.

This score subsequently provides a 'randomisation' effect for the known variables. It is limited by the unknown covariants, which are not included in the analysis. Its use does not preclude the specification of the suggested analyses or the sample calculation regarding the power and precision of the tool.

That study proposes a comparison of the two interventions that cannot be randomised due to ethical issues. Therefore, covariant control tools, such as propensity score, are useful.

The results presented so far qualify only as hypothesis generators due to the weakness imposed by the selection bias.

The authors comment about this limitation, which is inherent to the propensity score.

It must also be noted that, even within this environment, sample calculation is fundamental to establish sample power and precision. That is, in considering the balancing capacity of the propensity score, does the sample size allow for the denial of null hypothesis?

Therefore, in this issue, more information is provided to the literature to judge a complex theme. Its interpretation deserves consideration regarding the study design, the selection bias attenuation method the DES type used, and the cost relationship between the two types of stents, before absolute conclusions can be reached.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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