

Cost-Effectiveness of Drug-Eluting Stents: Implications for Clinical Practice and Healthcare Costs

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Drug-eluting stents (DESs) have been central focused area of interest interventional cardiology ever since the RAVEL study was presented at the meeting of the European Society of Cardiology in September 2001. Their novelty, along with the promising preliminary results published for that study, aroused many expectations.¹ Although these expectations have not been fully met and the rate of restenosis is not 0%, a substantial reduction is nonetheless achieved in most patients (including those with not so favorable clinical or angiographic characteristics).

In implanted in Spain 2004, 36.5% of all stents placed were DESs. There is still a long way to go before DESs completely replace bare-metal stents, but this does represent a substantial increase in the third year after their introduction. Usage of these new stents in the different autonomous regions of Spain ranges from 56% to 23%.²

In addition to the rapamycin-eluting stent (Cypher[®]) and paclitaxel-eluting stent (Taxus[®]) already on the market in Spain, 2 further stents launched in 2005: a tacrolimus-eluting stent (Janus[®]) and an ABT-578-eluting stent (Endeavour[®]). Other stents are under investigation or in the process of applying for regulatory approval.³

Clinical Implications: Will Drug-Eluting Stents Change Clinical Practice?

The low rate of restenosis achieved with the use of DESs could lead to important changes in clinical practice in cardiology. The key clinical implications may include a broadening of the indications of angioplasty to patients with more extensive and severe

coronary artery disease.^{3,4} As a result, the number of patients undergoing surgery would decrease.⁵

So far, the prevention of restenosis has not been shown to be associated with a lower death rate. The theoretical advantages of decreasing the rate of restenosis are therefore an improvement in the health-related quality of life (although no studies have been done to test this) and also a lower burden on health resources because fewer repeat revascularization procedures are needed.

With the results obtained in randomized clinical trials, expectations are now greater and clinicians are beginning to question some of the old paradigms that guide treatment of patients with severe multivessel disease with involvement of the left anterior descending coronary artery—patients who used to be clear candidates for surgery.⁵

Nevertheless, for the time being, it is recommended to follow the clinical guidelines for percutaneous coronary interventions issued by the corresponding Task Force of the European Society of Cardiology. These guidelines recommend the use of DESs according to the inclusion and exclusion criteria of the SIRIUS, TAXUS-IV, and TAXUS-VI studies, in which the rates of repeat revascularization events remained below 10%.⁶

Although the findings of studies of small-vessel lesions and diabetic patients are encouraging, and the registries with in-stent restenosis and in high-risk lesions for in-stent restenosis also provide reason for optimism, more randomized studies are needed to provide firmer evidence in these groups of patient.

Economic Implications of Use of Drug-Eluting Stents

Cost is generally recognized as the true limiting factor in the use of DESs. In Spain, the acquisition cost of DESs is 60%-80% times higher than that of bare-metal stents. Furthermore, the indirect cost arising from administration of thienopyridines for a longer period should be added, and it is also necessary to account for the number of stents placed per procedure—1.51 in Spain in 2004.² The clinical benefit

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derived from using DESs may not be large enough to offset such a large difference in price (we should not forget that DESs do not reduce mortality or the rate of infarction).⁷

In recent years, interest has grown in studies that provide an economic evaluation of health technologies, and the number of reports of such studies published in biomedical journals has been growing. However, the increased quantity of such studies has not been accompanied by improvements in their quality, and a lack of rigorous methodology has generally been apparent.⁸ This is because the field is relatively new (with few exceptions, the application of such studies to health care started in the 90s when health costs skyrocketed and new and increasingly costly technologies appeared). Such studies require methods and concepts alien to general medical knowledge, leading to confused terminology and aims.

Economic evaluation aims to determine which technology is more efficient or, what amounts to the same thing, which provides better health outcomes for the resources used once the costs, risks, and benefits have been identified, measured, and compared. We can divide economic studies into 4 types: analysis of cost minimization, analysis of cost-effectiveness, analysis of cost-usefulness, and analysis of cost-benefit.

We will focus on the analysis of cost-effectiveness, the analysis favored by health care professionals. In cost-effectiveness analyses, the health benefit of the outcome is measured in usual clinical units. If those units are used in clinical trials or everyday clinical practice, the medical interpretation of the outcome is made easier. Whereas a cost-effectiveness analysis can only compare technologies that present outcomes in the same unit of effectiveness, analysis of cost-utility (a special type of cost-effectiveness analysis in which the health outcomes are measured in quality-adjusted life-years [QALY]) allows comparison of the cost/effectiveness ratio of all technologies whose outcome has been measured in QALY.

Likewise, it is important to point out that the incremental cost/effectiveness or cost/utility ratios are what really matters for providing useful information for decision making; we are not so much interested in the cost of achieving a given health outcome as in the extra cost for each additional unit of effectiveness obtained by applying a more expensive but more effective technology. At this point, the decision maker should be the one to decide how many resources he or she is prepared to assign for each additional unit of improved outcome.

This issue of the REVISTA ESPAÑOLA DE CARDIOLOGÍA has published an economic evaluation of the use of the Taxus DESs versus bare-metal stents from the perspective of a Spanish hospital (although the title suggests the study is from the perspective of the financing body of public health services).⁹ Three

analyses were performed in this study. First, there is an analysis of the impact of the cost per patient of DES placement compared with bare-metal stents in the general population and in a subgroup at a high risk of restenosis (diabetic patients and those with small-vessel and large lesions) over a 2-year period. Second, the incremental cost per repeat revascularization avoided is analyzed. Finally, the investigators assess the impact on the costs incurred by a Spanish hospital in which 370 patients a year on average undergo repeat revascularization.

Although many studies on the cost-effectiveness of DESs have been published in the last 2 years in different countries, the study of Russell et al⁹ is the first to be done in Spain and we should congratulate the authors and encourage other investigators to conduct similar studies. When the studies have been done in certain countries with different health systems, costs, and health conditions, the information on cost-effectiveness available is not always applicable to other countries for guiding decisions.

In a previous study, also in Spain, an analysis was done on the economic impact of use of DESs in comparison with bare-metal stents in the cohort of patients treated in 2002 in Spain. A break-even price was calculated for the new device, which is, the price of the DESs that would be needed so that the overall budget did not increase through use of the DESs. The break-even price was €1448 for 2004, with a price of €1000 for the bare-metal stents and €2000 for DESs.¹⁰

In the study by Russell et al,⁹ the expected costs per patient for the general population were €6934 for DESs and €6756 for the bare-metal stents after 12 months, which is, 2.6% higher for DESs. After 24 months, those costs were €6991 and €6887, respectively, that is, 1.5% larger for DESs. For high-risk patients, the difference in the cost of the initial procedure had been canceled out after 12 to 24 months. The incremental cost per repeat revascularization avoided was €1568 after 12 months and €811 after 24 months, taking €712 as the additional cost of a Taxus stent compared to a bare-metal one. The calculation of the impact on a hospital budget was compared in 3 hypothetical situations: the base-case scenario (prior to DES placement), in which the patients underwent percutaneous coronary intervention with a bare-metal stent or coronary artery bypass grafting; scenario 1, with a 90% switch from bare-metal stents to DESs for high-risk groups; and scenario 2, with a 90% switch from bare-metal stents to DESs for the entire population and a 20% switch to DESs for patients who underwent bypass grafting in the base-case scenario. The authors obtained more favorable results in the scenario of DESs for high-risk groups (scenario 1) and less favorable ones for the overall population (scenario 2), although the increase was only 0.5% with respect to the base-case scenario.

The study shows that most of the initial excess cost of DESs is compensated for by savings arising from fewer repeat revascularization procedures. For the patients at greatest risk, the balance in favor of the DESs is larger even greater. It should be highlighted that the analysis is very sensitive to changes in the rate of repeat revascularization for the bare-metal stent and the DESs, differences in cost between the two, and number of stents used per patient.

An important factor when analyzing cost-effectiveness studies is the sources of information used to calculate the associated costs. Although considerable effort has gone into implementing cost accounting in hospitals in the Spanish health system in recent years, information sources on the true costs of the different interventions or procedures generally remain limited. Therefore, approximate data tend to be used from unit acquisition costs or price lists established by the bodies that finance the health services. In the case of the study by Russell et al.⁹ the Spanish health costs database Soikos was used (available for a fee). As in many of the publications on economic analyses, more detail of the costs included would be helpful for greater clarity and better reproducibility of the analysis. Moreover, although there are different types of DESs on the market, the authors of the study only compared the TAXUS stent with bare-metal stents. A manager would want to know the cost-effectiveness of all products available on the market.

As was mentioned earlier, other countries have also performed economic assessments of DESs. The main findings are summarized below:

1. In Canada, the cost-utility study of Shrive FM et al¹¹ estimated the cost per QALY to be 58 721 Canadian dollars (CAD) (2002 prices), using a sirolimus-eluting stent instead of bare-metal stents, from the perspective of public financing. They found that DESs were more cost-effective in diabetic patients and those over 75 years old. In another study done by Brophy et al,¹² also from the perspective of financing bodies, the investigators reported that the cost per repeat revascularization avoided (assuming 100% switch from bare-metal stents to DESs) was 23 067 CAD (2003 prices). The most cost-effective strategy was in high-risk populations (7800 CAD). Another analysis of cost-effectiveness done by an agency for evaluation of medical technology in Canada¹³ found the cost per repeat revascularization avoided was between 12 527 CAD and 29 048 CAD (2003 prices) from the perspective of the hospital and between 11 133 and 27 687 CAD from the point of view of health service financing.

2. In Australia, the study by Lord et al¹⁴ found the incremental cost per repeat revascularization avoided to be 3750 Australian dollars (sirolimus-eluting stent) and 6100 Australian dollars (paclitaxel-eluting stent)

after 12 months. The cost per QALY was 46 829 Australian dollars (sirolimus-eluting stent) and 76 467 Australian dollars (paclitaxel-eluting stent) from the perspective of the body that finances the public health services. The authors concluded that limiting DES usage to high-risk patients could improve the cost-effectiveness ratio.¹⁴

3. In the United States of America, Cohen et al¹⁵ reported the cost-effectiveness analysis from the hospital perspective with 1-year of follow-up for repeat revascularization avoided to be 1650 USD and the cost per QALY to be 27 450 USD (2002 prices). A subgroup analysis suggested that DESs were more economical in patients with long lesions and small-vessel lesions.¹⁵

4. In the United Kingdom, Bagust et al¹⁶ estimated the difference in price between DESs and bare-metal stents that would ensure that the QALY was cost effective (the so-called price premium) or that would yield a break-even cost after 12 months of follow-up from the perspective of public financing. For the study, a QALY of €42 000 (30 000 pounds sterling) was considered cost effective at 2003 prices. The recommended difference was €309 (cost-effectiveness) or €204 (break-even cost) with 50% usage of DESs and €157 and €112, respectively, for 90% usage. The authors concluded that DESs are not cost effective compared with bare-metal stents at the current prices in the United Kingdom, except for a selected group of patients.

5. In Switzerland, Kaiser et al¹⁷ carried out a study in unselected patients and found that, after 6 months, the cost per patient with DESs was higher compared to bare-metal stents, with a mean (SD) of €10 544 (6849) compared to €9639 (9067), respectively ($P < .0001$) from the perspective of public health financing. The mean difference in cost between the 2 types of stent was €1702 per patient. The cost per major cardiac event avoided was €18 311 and the cost per QALY was €50 000. The subgroup analysis showed that DESs were more cost-effective in high-risk patients (those over 65 years old with multivessel disease).

6. In Sweden, Ekman et al¹⁸ analyzed the cost-effectiveness of Taxus stents compared to bare-metal stents from the perspective of public health financing. The mean cost per patient treated during 1 year was €7913 for Taxus stents compared to €7328 for bare-metal stents. The cost per major cardiac event avoided was €5126 per year and €3900 after 2 years. The results were more favorable in high-risk patients: €47 791 per QALY and €838 per repeat revascularization avoided after 12 months. The investigators also analyzed the economic impact for 2 hypothetical scenarios and a base-case scenario. In the first scenario, 80% of bare-metal stenting procedures are switched to DESs for high-risk groups and in the second scenario, there is also a 20% switch from bypass grafting to DESs in patients with multivessel disease. In the first scenario,

there was an 0.8% increase with respect to the base-case scenario whereas, in the second, a decrease of 0.8% was found.¹⁸

Conclusions and Future Perspectives

Economic assessment provides information on the impact of introducing new medical technology in a given health care setting and determines whether or not costs should be set according to criteria of comparative efficiency or according to the available budget. The responsibility lies with the physicians to choose the ideal option for each of their patients taking into account data on efficacy, effectiveness, safety, and efficiency.

Use of Cypher and Taxus stents has been associated with a substantial decrease in restenosis and the need for repeat revascularization procedures. Moreover, at present, the results of the cost-effectiveness studies of the DESs in different settings are available. Most authors agree that the high cost of DESs is a limiting factor in its use and that the most cost-effective strategy is to use such stents in patients at a high risk of restenosis. Although the technology is effective, systematic use of DESs does not seem justified unless the price differences with bare-metal stents are reduced.

The costs of the materials used today in interventional cardiology have dropped compared to 10 years ago; for example balloons and stents have decreased by 50% to 60%. Likewise, DESs may also come down in price; for this to happen, DES usage will need to become more widespread and, as new DESs appear, competition may also force the industry to reconsider its prices.

REFERENCES

1. Regar E, Serruys PW. El estudio RAVEL. Reestenosis del cero por ciento: ¿un sueño del cardiólogo hecho realidad! [editorial]. *Rev Esp Cardiol*. 2002;55:459-62.
2. López-Palop R, Moreu J, Fernández-Vazquez F, Hernández R. Registro Español de Hemodinámica y Cardiología Intervencionista. XIV Informe Oficial de la Sección de Hemodinámica y Cardiología Intervencionista de la Sociedad Española de Cardiología (1990-2004). *Rev Esp Cardiol*. 2005;58:1318-34.
3. Hernández RA, Fernández F, Moreu J, López R. Cardiología intervencionista 2005. *Rev Esp Cardiol*. 2006;59 Supl 1:38-49.
4. Moreno R. Stents recubiertos y otros dispositivos antirreestenosis. *Orthod Craniofac Res*. 2005;58:842-62.
5. van Domburg RT, Lemos PA, Takkenberg JJ, Liu TK, van Herwerden LA, Arampatzis CA, et al. The impact of the introduction of drug-eluting stents on the clinical practice of surgical and percutaneous treatment of coronary artery disease. *Eur Heart J*. 2005;26:675-81.
6. Silber S, Albertsson P, Avilés FF, Camici PG, Colombo A, Hamm C, et al. En representación del Grupo de Trabajo de la Sociedad Europea de Cardiología de intervención coronaria percutánea. Guías de Práctica Clínica sobre intervencionismo coronario percutáneo. *Rev Esp Cardiol*. 2005;58:679-728.
7. Babapulle MN, Joseph L, Belisle P, Brophy JM, Eisenberg MJ. A hierarchical Bayesian meta-analysis of randomised clinical trials of drug-eluting stents. *Lancet*. 2004;364:583-91.
8. García-Altés A. Twenty years of health care economic analysis in Spain: are we doing well? *Health Econ*. 2001;10:715-29.
9. Russell S, Antoñanzas F, Mainar V. Impacto económico del *stent* coronario Taxus: implicaciones para el sistema sanitario español. *Rev Esp Cardiol*. 2006;59:889-96.
10. Oliva G, Espallargues M, Pons JMV. Stents recubiertos de fármacos antiproliferativos: revisión sistemática del beneficio y estimación del impacto presupuestario. *Rev Esp Cardiol*. 2004; 57:617-28.
11. Shrive FM, Manns BJ, Galbraith PD, Knudtson ML, Ghali WA. Economic evaluation of sirolimus-eluting stents. *CMAJ*. 2005; 172:345-51.
12. Brophy JM, Erickson LJ. Cost-effectiveness of drug-eluting coronary stents in Quebec, Canada. *Int J Technol Assess Health Care*. 2005;21:326-33.
13. Mittmann N, Brown A, Seung SJ, Coyle D, Cohen E, Brophy J, et al. Economic evaluation of drug eluting stents. Technology report no. 53. Ottawa: Canadian Coordinating Office for Health Technology Assessment; 2005.
14. Lord SJ, Howard K, Allen F, Marinovich L, Burgess DC, King R, et al. A systematic review and economic analysis of drug-eluting coronary stents available in Australia. *Med J Aust*. 2005;183:464-71.
15. Cohen DJ, Bakhai A, Shi C, Githiora L, Lavelle T, Berezin RH, et al. Cost-effectiveness of sirolimus-eluting stents for treatment of complex coronary stenoses: results from the Sirolimus-Eluting Balloon Expandable Stent in the Treatment of Patients With De Novo Native Coronary Artery Lesions (SIRIUS) trial. *Circulation*. 2004;110:508-14.
16. Bagust A, Grayson AD, Palmer ND, Perry RA, Walley T. Cost effectiveness of drug eluting coronary artery stenting in a UK setting: cost-utility study. *Heart*. 2006;92:68-74.
17. Kaiser C, Brunner-La Rocca HP, Buser PT, Bonetti PO, Osswald S, Linka A, et al. Incremental cost-effectiveness of drug-eluting stents compared with a third-generation bare-metal stent in a real-world setting: randomised Basel Stent Kosten Effektivitäts Trial (BASKET). *Lancet*. 2005;366:921-9.
18. Ekman M, Sjögren I, James S. Cost-effectiveness of the Taxus paclitaxel-eluting stent in the Swedish healthcare system. *Scand Cardiovasc J*. 2006;40:17-24.