

## Impact Analysis of Drug-Eluting Stent in the Unified Health System Budget

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### Summary

**Background:** Drug-eluting stents represent an additional option to treat coronary artery disease. This technology represents a major breakthrough that may require additional funding in the short-term to enable its inclusion in procedures of the Unified Health System.

**Objective:** To estimate the impact on the Unified Health System budget in the first year of use of drug-eluting stents.

**Methods:** A Budget Impact Model was designed to predict the economic impact of the inclusion of drug-eluting stents in the Unified Health System budget. Data about costs and local procedures were collected in multiple sources, specifically procedure volume data, hospital costs, cost of stents, drug costs and number of stents used in single and multi-vessel procedures.

**Results:** The results in the first year indicate that the impact on the Unified Health System is of 12.8% in the best scenario and 24.4% in the worst scenario, representing an increase by R\$ 24 to 44 million in the total projected budget.

**Conclusion:** Drug-eluting stents have an additional cost compared with standard stents in the first year of use in the Unified Health System.

**Key word:** Stents – angioplasty, transluminal, percutaneous coronary – technology, high-cost.

### Introduction

In 2003, the Brazilian Unified Health System (SUS) financed 30,666 coronary angioplasties with stent placement and 19,909 myocardial revascularization surgeries with a total cost of approximately R\$ 281 million.

The introduction of standard stents in the SUS, in 1999, represented a significant change in the interventional treatment of patients with ischemic cardiomyopathy. Until 1999, myocardial revascularization surgery represented the main type of interventional treatment. In the three subsequent years, the number of coronary angioplasty procedures increased by over 100%, with a significant decrease in the number of myocardial revascularization surgeries during this period. The benefits of treatment with standard stents were important although there were limitations in some subgroups, especially among patients with diabetes, who presented long lesions (>20 mm) and small caliber vessels (<3 mm), in which restenosis is significant in the first six months after the procedure.

The development of drug-eluting stents, still not available in the SUS, led to significantly lower rates of intra-stent restenosis in these subgroups of patients, but with an increase in initial cost of treatment. The dilemma that SUS faces is to match the

budget restriction with the need to evaluate and integrate new cardiovascular technologies.

Health economic analyses (e.g. cost-effectiveness) are efficient resource allocation tools for policy makers and financiers of the Unified Health System; however, they are not able to answer the specific financing questions for the object of analysis. Therefore, in addition to maximizing efficiency in resource allocation, financiers shall analyze if the introduction of new technology is compatible with their budget. There are specific economic models for budget impact analysis, in which the financier estimates the amount of resources needed to absorb a new technology based on the additional number of patients benefited and the prevalence of the disease.

The objective of this analysis is to provide health policymakers and managers with tools for decision making on the introduction of drug-eluting stents as a procedure to be reimbursed by the SUS.

### Methods

The model of decision analysis of the budget impact was developed with data obtained from a critical analysis of multicenter randomized clinical trials<sup>2,3</sup>, meta-analysis<sup>4</sup>, systematic review<sup>5</sup>, data on cardiovascular procedures performed by the SUS, data on expenses available at DATASUS, database of the *Central Nacional de Dados* (CENIC) [National Data Center] of the Brazilian Society of Hemodynamics and Interventional Cardiology (2003 report). A panel with experts and members of the Brazilian Society of Hemodynamics and Interventional Cardiology (SBHCI) was

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held to define the reality of cardiology practice in Brazil.

The assumptions of the budget impact model were: conversion rate of conventional to drug-eluting stents, number of stents/patients/procedures; percentage of reinterventions due to restenosis in standard stents; percentage of reinterventions due to restenosis in drug-eluting stents; prices of stents; values of AIH (Hospitalization Authorization) paid by the SUS to hospitals for procedures including angioplasty and myocardial revascularization surgery, price of post-procedure clopidogrel.

The number of myocardial revascularization surgery and coronary angioplasty procedures with placement of standard stents performed in 2003, by the SUS, was used to estimate the increase in budget in face of the hypothetical migration to the use of drug-eluting stents.

Three possible scenarios were created to estimate the impact on SUS budget after the introduction of drug-eluting stents. These different scenarios are the result of sensitivity analyses, where some concepts were modified within the variation found in the literature. Scenario 1 adopted a more conservative prospect; scenario 2 pictured an intermediate condition and scenario 3 presented the most expressive prospect for the introduction of drug-eluting stents. Table 1 summarizes the assumptions used in the model.

The variation in conversion of standard stent to drug-eluting stent was 30%, 40% and 50%, according to the variations found in the guidelines of the National Institute for Clinical Excellence (NICE)<sup>6</sup> and the *Agence D'Évaluation des Technologies et des Modes D'Intervention en Santé* (AETMIS)<sup>7</sup>.

The estimate of the number of stents per patient in each procedure varied between 1.3 and 1.7. This estimate was obtained from the Final Report and Recommendations of the American Task Force about Drug-Eluting Stents<sup>8</sup>, the NICE guidelines and validation by a panel of specialists of SBHCl.

Reinterventions due to restenosis in standard stents varied between 20% and 15% and in drug-eluting stents it was 4%, according to data of a meta-analysis using a hierarchical Bayesian model to compare conventional and drug-eluting stents<sup>9</sup>. These reinterventions were treated in the model - 90% of them being by coronary angioplasty and 10% by surgical myocardial revascularization. This practice standard was suggested by the panel of specialists of the SBHCl.

The price of standard stents used in the analysis was the value paid by the SUS to accredited hospitals, that is, R\$ 2,580.00. The price of drug-eluting stents was the amount reimbursed by the Medicare to the healthcare providers in the USA, at R\$5,166.00, which characterized as the lowest value in the health systems surveyed (Canada, UK, France, Australia). The exchange rate was US\$ 1 = R\$ 2.87 on June 30, 2003.

The values used for coronary angioplasty and surgical myocardial revascularization were those reimbursed by the SUS to accredited health services - R\$ 4,989.95 and R\$ 6,484.84, respectively.

The economic impact of the SBHCl guideline for the use of clopidogrel for six months after placement of a drug-eluting stent and for one month after that of a standard stent was incorporated into the model. The price used for this medication was that listed in the *Brasíndice* minus 30%, which accounts for the retail marketing margin, with a final price of R\$123.00.

## Results

The best scenario, i.e., the one with lower use of drug-eluting stents, forecasts a 30% migration from standard stent to drug-eluting stent. This scenario would represent an increase in the SUS budget by approximately 12.8% in the first year of the procedure. The additional cost of the drug, which is necessary to avoid intra-stent thrombosis in the first six months, would represent one-third 1/3 of total amount. The results of scenario 1 are shown in Table 2.

The intermediate scenario with 40% inclusion of the drug-eluting stent represents an increase in the SUS budget by approximately 20.1% in the first year of the procedure. The increase by 10% in the number of patients who are eligible to receive drug-eluting stents caused a raise by approximately 35% in budget. The results of scenario 2 are shown in Table 3.

The most dramatic scenario with 50% inclusion of drug-eluting stents would represent an increase by approximately 24.4% in the SUS budget in the first year of the procedure. In this change of scenario 2 to 3, the 10% increase in the number of patients who are illegible to receive drug-eluting stents caused an increase by only 18% in the budget. The results of scenario 3 are shown in Table 4.

Table 1 - Comparison of assumptions used in three hypothetical scenarios

Assumptions	Scenario 1	Scenario 2	Scenario 3
Patients treated (CA) com DES	9,199	12,266	15,333
Conversion from standard stent to drug-eluting stent	30%	40%	50%
Stents per patient per procedure	1.3	1.5	1.7
Percentage of reinterventions due to restenosis in standard stent	20%	17%	15%
Percentage of reinterventions due to restenosis in drug-eluting stent	4%	4%	4%
Price of drug-eluting stent (R\$)	5,166.00	5,166.00	5,166.00
Price of standard stent (R\$)	2,580.00	2,580.00	2,580.00

CA - coronary angioplasty; DES - drug-eluting stent.

Table 2 - Scenario 1: Estimate of the impact on the SUS budget by introducing drug-eluting stent, conversion of 30%

Parameters of 2003 model	Total cost	Hypothetical scenario with drug-eluting stent	Incremental cost
Patients treated (CA)	30,666	30,666	
Total cost of initial procedure (R\$)	152,986,729	176,775,343	23,788,614
Total number of reinterventions due to restenosis (90% of CA + 10% of MRS)	6,133	4,660	-1,473
Total cost of reinterventions (90% of CA + 10% of MRS) (R\$)	31,514,741	23,949,785	-7,564,956
Use of clopidogrel after PTCA	1 month	6 months	
Total cost of clopidogrel (R\$)	5,366,550	13,415,200	8,048,650
Incremental cost in one year (R\$)			24,272,308
Impact on budget in one year (%)	189,868,020	214,140,328	12.8%

CA - coronary angioplasty; MRS - myocardial revascularization surgery.

Table 3 - Scenario 2: Estimate of the impact on the SUS budget by introducing drug-eluting stent, conversion of 40%

Parameters of 2003 model	Total cost	hypothetical scenario with drug-eluting stent	Incremental cost
Patients treated (CA)	30,666	30,666	
Total cost do initial procedure (R\$)	152,986,729	184,706,605	31,719,876
Total number of reinterventions due to restenosis (90% of CA + 10% of MRS)	4,599	3,250	-1,349
Total cost of reinterventions (90% of CA + 10% of MRS) (R\$)	23,636,429	16,700,125	-6,939,304
Use of clopidogrel after PTCA	1 month	6 months	
Total cost of clopidogrel (R\$)	5,366,550	16,569,964	11,803,414
Incremental cost in one year (R\$)			36,586,986
Impact on budget in one year (%)	181,989,708	217,976,694	20.1%

CA - coronary angioplasty; MRS - myocardial revascularization surgery.

## Discussion

The analysis of budget impact aims to help decision makers at the SUS in their task of critically evaluating the inclusion of drug-eluting stents in treatment of patients who are eligible to receive this device.

Health economic models use data of clinical outcomes obtained from critical literature analysis. Multicenter clinical trials comparing drug-eluting stents versus standard stents showed greater efficacy of the former in restenosis outcome. This data can be extended to the Brazilian scenario because the country participated in all steps of development, research and clinical trials of drug-eluting stents.

Data related to costs and clinical practice standards reflect the local features, so that the economic model be the most accurate possible.

There are some uncertainties in the assumptions that comprise the economic models in general due to scarcity of data and variability of local medical practice. Such limitations are minimized with sensitivity analyses. In the model of elaborated impact analysis, we determined the variation in the percentage of population access to drug-eluting stents and the percentage of reinterventions avoided in the 12 subsequent months, in order to help decision makers choose the possible scenarios. These variations explain the possible scenarios with increase by 12.8% to 24.4% in the budget in the first 12 months after the procedure.

Six brands of drug-eluting stents are authorized by the ANVISA (National Health Surveillance Agency) to be traded in Brazil in 2006, but only two (Cypher® and Taxus®) have long-term follow-up studies (more than three years).

**Table 4 - Scenario 3: Estimate of the impact on the SUS budget by introducing drug-eluting stent, conversion of 50%**

Parameters of 2003 model	Total cost	Hypothetical scenario with drug-eluting stent	Incremental cost
Patients treated (CA)	30,666	30,666	
Total cost of initial procedure (R\$)	152,986,729	192,637,867	39,651,138
number of reinterventions due to restenosis (90% of CA + 10% of MRS)	4,599	2,913	-1,686
Total cost of reinterventions (90% of CA + 10% of MRS) (R\$)	23,636,429	14,965,746	-8,670,683
Use of clopidogrel after PTCA	1 month	6 months	
Total cost of clopidogrel (R\$)	5,366,550	18,844,257	13,477,707
Incremental cost in one year (R\$)			44,458,162
Impact on budget in one year (%)	181,989,708	226,447,870	24.4%

CA - coronary angioplasty; MRS - myocardial revascularization surgery.

The definition of long-term performance of other brands requires the publication of randomized clinical trials with long-term follow-up.

The result of a small long-term follow-up trial (18 months to three years after placement of drug-eluting stents), with the purpose of analyzing cost-effectiveness of drug-eluting stents with rapamycin and paclitaxel *versus* standard stents (Study BASKET-LATE)<sup>10</sup> showed that, in up to one year after discontinuation of clopidogrel, the group of patients with drug-eluting stents presented two to three times more events related to late thrombosis than the group of patients who received standard stents.

A meta-analysis conducted by Nordmann *et al*<sup>11</sup> compared the first generation drug-eluting stents *versus* standard stents in the outcomes of mortality and Q-wave myocardial infarction. These authors reported a higher incidence of death and Q-wave myocardial infarction in patients who received the first generation drug-eluting stents *versus* standard stents.

The study BASKET-LATE and the meta-analysis conducted by Nordmann *et al* demonstrated the need to re-evaluate the onset time and maintenance time of clopidogrel therapy after placement of drug-eluting stents to avoid late thrombosis episodes. The study CREDO<sup>12</sup> estimated the ideal time to start administration of the loading dose of 300 mg clopidogrel in patients who underwent coronary angioplasty in order to reduce the primary outcomes: death, myocardial infarction and urgent revascularization of target lesion. There was a reduction by 58.8% in primary outcomes in patients who were pre-treated with clopidogrel for  $\geq 15$  hours before the procedure when compared with placebo.

The definition of ideal time of clopidogrel use after placement of drug-eluting stents is fundamental for the real estimate of the impact on the SUS budget, thus inferring that the medication shall be available to patients throughout the utilization period and with patient compliance to treatment.

Our analysis evaluated a time period of six months as per the guideline of the SBHCI at that time. However, in view of the last publications mentioned above on late thrombosis after drug-eluting stent placement, the guidelines have been under re-evaluation to standardize a longer use of clopidogrel.

Another possible effect of the inclusion of drug-eluting stents in the SUS is the migration of myocardial revascularization surgery to this procedure. Myocardial revascularization surgery in Brazil presents mortality rates that are much higher than in other countries, in addition to a higher financial cost to the SUS. A study conducted by Godoy *et al*, in Brazil, found an overall mortality rate of 7.8% for myocardial revascularization surgery adjusted to age, sex and diagnostic groups, between 1999-2003<sup>13</sup>. Migration of myocardial revascularization surgery to placement of drug-eluting stents was analyzed in a study conducted at the Mayo Clinic<sup>14</sup>. The authors concluded that up to 46% of patients who underwent myocardial revascularization surgery would be eligible for drug-eluting stents.

It is probable that in the subgroup of diabetic patients in whom the restenosis rate is higher than in non-diabetic individuals<sup>15</sup>, the cost-effectiveness ratio is more attractive for the inclusion of drug-eluting stents, with lower impact on the financier's budget.

## Conclusion

With the fast technological development, especially in the cardiovascular field, the evaluation of inclusion of new technologies is essential not only to identify the interventions relevant to the health system, but also to choose the alternatives that actually aggregate value to the health system (Table 5).

The discussion about the inclusion of new technologies in the SUS is an opportunity for the Brazilian Cardiology Society to foster the development of methods that help cardiovascular

Table 5 - Comparison of results of three hypothetical scenarios of drug-eluting stent introduction.

Parameters of 2003 model	Scenario 1	Scenario 2	Scenario 3
Patients treated (CA) = DES + CS	30,666	30,666	30,666
Total cost of initial procedure (R\$)	176,775,343	184,706,605	192,637,867
Total number of reinterventions due to restenosis (90% of CA + 10% of MRS)	4,660	3,250	2,913
Total cost of reinterventions (90% of CA + 10% of MRS) (R\$)	23,949,785	16,700,125	14,965,746
Use of clopidogrel after PTCA	6 months	6 months	6 months
Total cost of clopidogrel (R\$)	13,415,200	16,569,964	18,844,257
Incremental cost in one year (R\$)	24,272,308	36,586,986	44,458,162
Impact on budget in one year (%)	12.8%	20.1%	24.4%

CA - coronary angioplasty; MRS - myocardial revascularization surgery; DES - drug-eluting stent; CS - standard stent.

health policy makers in the process of choosing between the alternatives available, by measuring the benefits for each cost

unit and the estimated return to society with the inclusion of new diagnostic and therapeutic models.

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