

Format for ANSWERING REVIEWERS



March 5th, 2015

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: Manuscript WJC revised track change.doc).

Title: Cost-effectiveness modelling of percutaneous coronary interventions in stable coronary artery disease

Author: A. Beresniak, T Caruba, B. Sabatier, Y. Juillièrè, O. Dubourg, N. Danchin

Name of Journal: *World Journal of Cardiology*

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The manuscript has been improved according to the suggestions of reviewers:

Reviewer 1:

Comment 1: **Hard to understand for a clinician. Limited useful information without actual data.**

Response: The methodology has been clarified to be understandable by clinicians

Reviewer 2:

Comment 2: **This subject has been studied a number of times previously. Some of the efforts to analyze this kind of data were not referenced in this manuscript for example Wisloff et al (American Journal of Therapeutics 20, 596–601 2013) who reported that using trial data, it was found that sirolimus-eluting stents (SES) yield 0.003 greater life expectancy and \$3300 lower costs than do BMS (dominant strategy).**

Response: The following text and reference have been added:

Wisloff et al carried out a cost-effectiveness model comparing DES versus BMS and concluded that DES was more cost-effective over a life time horizon using life years saved as an effectiveness endpoint. However this model is based on life-time horizon projections speculating well beyond clinical trials evidence and diluting costs over years

Comment 3: **The subject has been reviewed a number of times in studies that were not quoted in this paper eg (i) Fanari Z; A Weiss S; Weintraub WS. Comparative effectiveness of revascularization strategies in stable ischemic heart disease: current perspective and literature review. Expert Review of Cardiovascular Therapy. 11(10):1321-36, 2013 (ii) Annemans L. The euros and sense of stents: do we get value for money? J Cardiovasc Med 2011;12:878**

Response: The suggested references have been included

Comment 4: **Some of the analysis is difficult to deconstruct such as the distribution of costs and success Figures 3 to 6. Fig 4 and 6 appear to be mathematically generated and independent of the data.**

Response: The key feature of the proposed methodological approach is to provide distribution parameters of the model outcome, and not only the mean. Success distributions appear to have Gaussian shape, but not costs distributions. For better understandability and simplification toward a clinician audience, costs distributions

figures have been withdrawn.

Comment 5: The data may only be relevant for France or understandable by readers in France eg “Concerning hospital costs, the French 2012 DRG system has been used by calculating mean costs weighted by patient numbers in each DRG. Then costs of coronarography alone are not been derived only from the related ambulatory DRG, even if some hospitals consider this imaging procedure as ambulatory. In this case, costs of coronarography could be lower, but does not seem to impact the overall cost-effectiveness analyses.”

Response: Diagnosis Related Groups are a system used in many countries to collect information data and derived standard costs per homogeneous patient groups.

The text has been changed as followed:

"Costs for the hospitalisation are determined using the french official hospital information system according to the specific diagnosis-related groups (DRGs) named “PCI without myocardial infarction”.

The following text has been withdrawn because difficult to understand by clinicians:

"Concerning hospital costs, the French 2012 DRG system has been used by calculating mean costs weighted by patient numbers in each DRG. Then costs of coronarography alone are not been derived only from the related ambulatory DRG, even if some hospitals consider this imaging procedure as ambulatory. In this case, costs of coronarography could be lower, but does not seem to impact the overall cost-effectiveness analyses."

Comment 6: Minor issues:

-The word Coronarography is usually coronary angiography

-9'303 €is usually presented as 9,303

- The sentence is not clear “The dichotomous approach also requires fewer assumptions than other modelling approaches and appears more methodologically robust as already published in other countries.

Response: The wording "coronarography" has been replaced by "coronary angiography"

The number formatting will be changed according to the requirement of the editorial board

The sentence has been changed as followed: "Not only the proposed dichotomous approach success/no success is clinically meaningful, but it also requires fewer assumptions than using other outcomes"

Reviewer 3:

Comment 7: The duration of dual antiplatelet agents is generally different between BMS and DES. Does this study take it into account?

Response:

Costs of Dual antiplatelet agents have been considered as followed:

- BMS: one month of clopidogrel
- DES: 12 months of clopidogrel

Comment 8: Figure legends should be added for each figure. In addition, there is no description about the unit in the longitudinal axis in figure 4-6.

Response: legends and axes description have been added for each figure. A

Reviewer 5:

Comment 9: I suggest to add some more data: -Confidence intervals and inferior limits for effectiveness of one treatment over the other one would be useful

-A specific reference that the results are difficult to extrapolate to other countries, specifically in terms of costs (not on clinical results), because of the different costs and payers in different health programs

-Even it is clearly specified, a conclusion should be incorporated to the paper

Response:

Standard deviations have been provided with the results, allowing to derive confidence intervals (± 1.96 SD)

A reference has been added for limitation of modelling approach in other countries

A conclusion has been added

Reviewer 6:

Comment 10: I would like to see a considerable section in the manuscript discussing the utility, pros and cons of biodegradable stents. Biodegradable/bioabsorbable stents may replace both bare metal and drug-eluting stents in the future.

Responses: The Objective of this cost-effectiveness study was only to compare BMS and DES strategies, explaining why a full section dedicated to biodegradable stents would be out of scope. Whatever . Whatever the proposed methodological approach would suit to assess innovative strategies such as biodegradable stents. The last sentence of the conclusion has been enriched as followed:

"Future modelling approaches should confirm these results as further comparative data in stable coronary artery disease and long-term evidence become available, but also to assess the value of innovative strategies such as biodegradable coronary stents."

Sincerely yours,



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