Reviewer’s report

Title: Multiple Criteria Decision Analysis in the Context of Health Technology Assessment: A Simulation Exercise on Metastatic Colorectal Cancer with Multiple Stakeholders in the English Setting

Version: 0 Date: 27 Apr 2017

Reviewer: Martina Garau

Reviewer's report:

Thank you for asking me to review this paper, which provides robust and timely evidence on the application of MCDA in HTA. The paper is well written and documented. Details of the approach followed are very well reported in both the main text of the article and the Appendix, particularly in the result section where discussions that took place at the workshop and changes in the initial model where made. It nicely refers to a previously published paper (Angelis and Kanavos; 2016) presenting the theoretical foundations and possible development of the framework. For the purpose of the review it would have been useful to have access also to the most recent Angelis and Kanavos (currently under review) which focuses on the AVF.

The article should be published subject to some clarifications that I outline below.

* The authors clearly explain the theoretical foundations of the approach used, from an operational research perspective. There are references of existing MCDA approaches and Angelis and Kanavos (2016) provides an extensive discussion about different techniques. However, in this article there is a need to explaining why that specific method was selected and deemed appropriate in the context of HTA. In a way the issue of applying MCDA in HTA is not so much the lack of empirical studies and applications but the lack of agreement among health economists and decision makers on the most appropriate approach to implement. Overall the paper would benefit from an indication on how its results can position in the current debate: should this approach replace or complement NICE or more generally HTA decision making?

* For non-UK readers, it might be useful to expand on the problem structuring section by reminding what NICE's remit is (i.e. develop recommendations on appropriate use of new technologies within the NHS based on clinical, cost effectiveness and other considerations) and how that is different from the aim of this exercise (i.e. value ranking treatments in the same indications or disease area). This is a fundamental issue that should be discussed in the paper. Although the authors did mention the issue of opportunity cost and potential need to estimate a cut-off point also when applying MCDA (on page 25), the paper would benefit
from an expanded discussion on how the results of the exercise can be interpreted and used in the context of repeated HTA decisions affecting a fixed budget such as those developed by NICE.

* Related to the point above, it would be interesting to see a comparison between the results of this exercise and the published NICE decisions. This would provide a useful comparison between the traditional cost per QALY driven approach and a "clean slate" MCDA (as defined in the Angelis and Kanavos (2016)). I noticed that the treatment that scored the highest (cetuximab) was not recommended by NICE in TA 242. This should be mentioned and discussed.

* It is unclear why direct costs are separated into medical costs and drug purchasing costs and why the first are included as a criterion contributing to the composite value measure (WPV) and the second are presented separately and plot against the WPV. From an economic point of view, should all the relevant costs and savings (incremental costs) be considered against the benefits? This is for example done in the Golan and Hansen (2012).[Golan and Hansen (2012). Which health technologies should be funded? A prioritization framework based explicitly on value for money. Israel Journal of Health Policy Research 1:44]

Minor points include:

Page 2, sentences in line 24 to 34 does not have a verb

Page 5, line 32, reference 1: there are a number of articles in the health economics literature looking at value beyond QALY so I think that at least a couple of additional references should be included.

Page 6, line 5, reference 3-8: the references included as examples of uses of MCDA in HTA do not include the more recently published reports of the ISPOR MCDA Emerging Good Practices Task Force, which include other MCDA pilots. The article is an important milestone for the development of a common definition of MCDA and guidelines for implementation in health care decision making. One of the reports (Marsh et al (2016) ref [51]) is actually mentioned in the discussion section.

Page 9, line 24-34. The paper claims that the attributes possess the right decision theory properties. Can the author expand on the relationship between Overall Survival (OS) and Progression Free Survival (PFS) and explain why this does not lead to issues of overlapping between the two attributes? I understand that they might be statistically dependent but preference independent. However, PFS is a surrogate endpoints that, in the absence of long term effects, it is used to answer the same question "what is the impact on length of life"? As discussed in the context of HRQoL measures, a distinction should be made between preferences across endpoints.
and measures of the same criteria (which can inform for example trial design or evidence generation) versus preferences across criteria relevant for resource allocation decisions (for example, incremental survival or QoL).

Page 9, reference to Table 1. One of the key motivations of the paper is that the QALY is "inadequate to express the wider patient perspective because it does not reflect other dimensions of social value relating to the burden of the disease, the innovation level of interventions and their wider socioeconomic impact". Similarly Angelis and Kanavos (2016), point out that "the reliance on generic tool such as the EQ-5D may not reflect patient experience adequately". It is then stated that MCDA can address these issues. However, the framework presented rely on EQ-5D scores as a measure of Health Related Quality of Life (HRQoL) similarly to NICE. Presenting EQ-5D scores has potentially two issues. First it is an aggregate measure so it does not allow patients and other stakeholders to make explicit trade off among different levels of individual dimensions. Second, EQ-5D utility values capture already the preferences of the general public so consideration of unweighted health states might be more appropriate. Those issues are addressed only partially by the consideration of further two dimensions relevant to patients (safety and patient convenience/posology). I understand that this was probably driven by the evidence available but it might be worth stressing that MCDA does not solve the challenges of measuring and developing robust evidence on patient experience.

Page 16, line 7 refers to "clinical attributes". It would be helpful to specify which ones they are (all therapeutic impact attributes?)

Page 21, line 17-52. As mentioned before, the discussion about selection of the preferred treatment option should be made in the context of the published NICE decisions on the treatments considered. The approach presented seems to provide a value ranking of the treatment options where you choose the one with the best cost per unit of value among the set of options (cetuximab). This is not in line with the current NICE remit, which is that of repeated decisions, where it is assessed whether or not an intervention provides good value for money given the alternative health investments possible given the cost. Therefore while in the case of this exercise, the top-ranked option is recommended; in the case of NICE, an intervention is recommended only if it represents an efficient use of health care resources so there might be the case that none of the therapy options are recommended for use (such as in the case of the considered treatments).

Page 23, line 51: there is a typo ("had" should be "have")

page 24, line 34-54. It is unclear why the QALY measure is mentioned here for the first time (apart from the reference in the introduction). Based on the framework presented on pages 50 and 51 it seems like that the QALY is not used but disaggregated into objective and subjective endpoints.
Finally, the Appendix needs page number. It is not clear whether there is an additional reference list to consider. For example, reference [67] does not appear in the main reference list.

Martina Garau
Principal Economist
The Office of Health Economics
Email: mgarau@ohe.org

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.
Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.
Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.
Yes

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