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Comment on: "Does MCDA Trump CEA?"

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We read the article by Campillo-Artero et al 2018 (1) in the journal with great interest. The article focuses on the use of Multiple Criteria Decision Analysis (MCDA) in the context of Health Technology Assessment (HTA), outlining a number of issues perceived as limitations in relation to its use. Overall, we agree with the authors that a number of challenges remain outstanding, both methodological and policy-related, that need to be addressed for MCDA to be effectively applied in HTA and policy-making. These include ensuring that the value models are in alignment with decision science theory and that both methods and results are fit-for-purpose for HTA to serve the needs of decisionmakers.

In their article, the authors offer constructive critique to the Advance Value Framework (AVF) we have developed based on MCDA principles and its encompassing generic value tree, the Advance Value Tree (AVT), that provides the hierarchical structure of evaluation criteria (2). While we are delighted that our work is receiving attention in the literature, we also feel compelled to address some of the points the authors raise in their paper, as we fear that the authors may have mis-interpreted some of our paper's findings and recommendations. With regards to the AVF, Campillo-Artero et al focus their critique on the following issues: first, the existence of double counting and lack of "independence" between criteria, and, second, the credibility of a "holistic" multidimensional benefit measure that reflects patient preferences in the context of welfare or extra-welfare theory,

1

Campillo-Artero et al conclude "There are clear risks of double (or repeated) counting and an evident lack of independence of criteria like social impact, reduced burden, therapeutic effects and safety effects." While this may be a generic threat to validity, we are missing an explanation of where in our model there is double-counting or lack of independence; additionally, the meaning of the term "independence", is not provided, but could relate to statistical independence, preference independence or both.

Based on Multi-Attribute Value Theory (MAVT), the theoretical backbone of AVF, criteria should possess a number of properties for MCDA results to be robust and we repeatedly underscore the importance of satisfying them. These properties are not limited to being non-overlapping and preferenceindependent, but also being concise, understandable and operational (3). With regards to these criteria properties and, more specifically, to double-counting, we acknowledge that the AVT, "aims to capture a comprehensive generic set of value concerns that can be adapted to different decision-making contexts, problems, indications or treatments" (page 142). Crucially, and following the completion of the model-building phase, we forewarn about the likelihood of some of the criteria not satisfying the required properties, in which case the underlying issues should be addressed with caution. Explicit reference is made to the case of possible double-counting between two criteria leading to the recommendation that "one of the two would have to be excluded". In relation to double-counting, a number of possible cases are listed such as the inclusion of efficiency and clinical benefit criteria, burden of disease and therapeutic impact criteria, population size and unmet need criteria, overall survival and grade 5 adverse events criteria, and incidence of adverse drug events (ADEs) and treatment discontinuation criteria when the latter relates to known to ADEs that are already accounted for, among others. This is by no means an exhaustive list of plausible double-counting effects between HTA-related criteria.

With regards to the "independence" issue, only the case of preferenceindependence should be considered as part of this discussion (rather than statistical dependence), given that this is only acting as a theoretical requirement in MAVT. Similar to the case of double-counting, explicit reference is made in

2

our model to the possibility of preference-dependence, explaining the need to aggregate two criteria whose value seems to depend on each other into a single one, providing as examples the possible interdependencies between severity of disease and unmet need criteria, overall survival and health related quality of life criteria, the attributes of ADEs' seriousness and frequency, or treatment posology and delivery system criteria. Once again, this is not an exhaustive list of plausible preference-dependencies between HTA-related criteria.

Campillo-Artero et al argue that "Angelis and Kanavos and others claim that MCDA is "holistic", by which they seem to mean "more completely representative of patients' preferences" and that "In CEA, the source of value is a matter for decision makers to determine". We believe that this statement misinterprets our argument. We would agree on the "holistic" nature of MCDA (nevertheless, we did not use this term in our paper), but primarily on the basis of the multiplicity of evaluation criteria considered in the analysis, rather than solely on the grounds of wider stakeholder engagement, which, depending on the specific decision context, could include patients. In other words, "holistic" should be interpreted as "comprehensive". We have never proposed a value index that would be based solely on patient preferences, but primarily on decision-makers' preferences and those of any relevant stakeholders and key experts. It is clear that the main aim of MCDA is to enable decision-makers to reach a decision, rather than serve the needs of any particular stakeholder group. Within the strict context of cost-effectiveness analysis (CEA), different decision-makers have different preferences; from a practical standpoint, patient and other stakeholder preferences, are often considered throughout the appraisal process of different HTA agencies, including that of NICE, albeit implicitly.

Finally, Campillo-Artero et al point that "Angelis and Kanavos go on to suggest that a multidimensional index of benefit based on patient preferences should then be compared with "purchasing costs". It is hard to see what kind of welfare or extra-welfare theory could lead to such a conclusion". We would argue that reference to welfare or extra-welfare theory is irrelevant and slightly out of context, simply because MCDA in general, and AVF in particular, are based on MAVT, an extension of Value Theory, which is also relevant to decision-

3

makers. As a result, it might be fairer to appraise the use of MCDA approaches by considering their appropriate theoretical frameworks as defined within the relevant field of science. Given the interdisciplinary nature of HTA, it would probably be advisable to have some degree of flexibility.

Undoubtedly, the application of MCDA in HTA raises important methodological and empirical issues, many of which will require intense debate. Whether one method "trumps" another remains to be seen but, in the meantime, the debate needs to focus on the appropriate interpretation of theoretical and empirical findings. Our interests, as those of Campillo-Artero et al, remain firmly in the camp of providing decision-makers with improved tools for a fair resource allocation. In this context, we welcome further debate.

Compliance with ethical standards

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