Author’s response to reviews

Title: Methodological quality of English language genetic guidelines on hereditary breast cancer screening and management: an evaluation using the AGREE instrument

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Author’s response to reviews: see over
Reviewer 1

1/ The review focuses on guidelines available in English. This is a strong limitation since many guidelines are not written in English. I was surprised by the oversight of possible Italian guidelines, as indeed, these are not written in English. I can understand that authors cannot cover guidelines written in non English, non Italian languages, but then the title should be specific about this. Having a review of guidelines showing the considerable diversity of interpretation of the few data available would be much more informative, as now the focus is on essentially North American guidelines. If addressing guidelines in non-English language is insurmountable, then authors could think of focusing their paper on variations across North American guidelines, when the knowledge base is essentially the same for all.

We thank the reviewer for the comment. As the reviewer rightly argued, we found ourselves in the impossibility of analysing guidelines in languages other than English and Italian.

Our choice to focus on English guidelines only was also based on most of the previous studies published in literature on AGREE evaluations (e.g.: Schmidt et al. Critical appraisal of clinical practice guidelines for diagnosis and treatment of hepatocellular carcinoma. J Gastroenterol Hepatol. 2011; Azemai et al. Systematic appraisal of dementia guidelines for the management of behavioural and psychological symptoms. Ageing Res Rev. 2012; Tavender et al. Quality and consistency of guidelines for the management of mild traumatic brain injury in the emergency department. Acad Emerg Med. 2011. etc. Please note that in many cases the authors come from non-English speaking countries).

Furthermore, we felt that having one set of guidelines in Italian amidst only English-language guidelines might raise methodological issues, as the Italian guidelines refer to the English-language ones, of which the Italian guidelines might be argued to be a “duplication”.

We have however amended the title to specify that all guidelines retrieved are in English, and we thank the reviewer for the indication.

As for the second observation, we do acknowledge that the evidence base is almost the same for all guidelines, North American or otherwise (from Australia, New Zealand, Singapore, United Kingdom). This is explained at page 11, first paragraph.

As for variations across guidelines, these were explored as much as possible (table 1 and 2): we have investigated how evidence-based each guideline was, who produced it, whether the guideline was endorsed by National agencies or not; we have identified the target population and the objectives for each guideline; finally, in the discussion we have provided a summary of the “recurrent” recommendations across different guidelines.

2/ Authors state that the quality of the evidence which the guidelines are built upon was beyond their objective. In fact, authors should have tried to dissect some key features of guidelines, with looking for instance on interpretations of existing data for recommending monitoring using MRI (does it really save lives? Or many just believe MRI might save life, and also create lots of anxiety and overdiagnosis? Are guidelines involving radiologists of a different tone than those not including radiologists [a recently published AGREE review of US colorectal cancer screening guidelines is very informative on this: Qaseem et al, Ann Intern Med 2012]). A same approach could be used for the counseling of men that may be mutation carriers. Psychological support could also be examined. This would add substance to the work and illustrate the variability of interpretations.

We thank the reviewer for the comment, although we are not adequately equipped to deal with this issue in this manuscript, as it would imply a systematic analysis of all the studies upon which the guidelines are based using a validated tool like GRADE. We feel that the issue raised by the
reviewer is of great importance and deserves more attention than one or two paragraphs in the discussion section of this paper. We are already considering to work on it in the future, in ad hoc paper.

Our point, for the moment, was to focus on methodological quality of the development of guidelines, which we believe is worth in itself attention from the scientific community.

3/ Authors picked up the fundamental issue of the paucity of sound data on which genetic guidelines for counseling and management of subjects with hereditary cancer background are based on. A general rule in medicine is that variations in recommendations or guidelines will be proportional to the lack of firm data indicating what is worth to do or not. The other crucial factor is the stakeholder involvement (conflict of interests). Hence, this work cannot escape form the need to provide an idea of the type of data on which to base guidelines. An approach suggested in point 2 could be adopted, with selection of few key topics and then juxtaposing the evidence with the variability for the 6 domains of the AGREE instrument.

We thank the reviewer for the observation, and we believe it is, again, a very important topic. Yet again, we feel that it is impossible to give a scientific definition of how well substantiated each recommendation, lest using a validated tool such GRADE to evaluate the sources of evidence. Furthermore, there is abundance of studies in literature that, like ours, focus on the objective of analysing methodological quality of the development of guidelines.

Reviewer 2

In this manuscript Simone and colleagues utilized the AGREE instrument to examine recommendations for the management of breast cancer screening for patients at increased genetic risk. Defining optimal screening for these patients is of importance. Individual studies are summarized and the results of interest. Overall the methodology is sound and of interest. The authors should add a table summarizing common recommendations and less well substantiated recommendations. The authors should also clearly identify best evidence recommendations.

We thank the reviewer for the appreciation and for the comment. We found ourselves in the impossibility of providing such a table, because the objectives of each guideline are different and because different guidelines target different stakeholders. Recommendations, therefore, are not always fully comparable. In the discussion, however, as much possible, we provided a list of ‘recurrent’ recommendations (second paragraph, page 11), and in tables 1 and 2 we have investigated how evidence-based each guideline was, who produced it, and the other sources of variability across guidelines.

Assessing whether recommendations are more or less well substantiated would imply a systematic analysis of all the studies upon which each guideline is based, using a validated tool such as would be GRADE. This is very important and useful, but our point, for the moment, was to focus on methodological quality of the development of guidelines, which we believe is worth in itself attention from the scientific community.