Reviewer's report

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

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Reviewer: Philippe Autier

Reviewer's report:

The paper by B Simone and Colleagues reviews the quality of guidelines for genetic counseling, screening and management of subjects with probable heredity for breast cancer. The topic is timely and relevant, due to the number of guidelines on hereditary cancers circulating in the literature and on the web. The authors have a good mastery of the AGREE instrument. However, the work is not satisfactory and incomplete for three reasons.

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.

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.

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.

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

None to declare