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Comment
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With regard to the implementation of the AGREE instrument in atrial fibrillation clinical guidelines

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Introduction

Clinical practice guidelines summarize and evaluate scientific knowledge about a particular health problem, in order to set priorities for different available diagnostic and therapeutic strategies.

To accomplish this task, clinical practice guidelines must review and thoroughly analyze the quality of clinical evidence and medical recommendations. This becomes a "quasi-detective" work; because within large studies (trials, meta-analyses, records, ant others) biases may hide [1],[2] thus limiting extrapolation of results. Another important aspect is that there will never be enough trials to represent most clinical situations of the "real world." Consequently it is not a practical strength that guidelines are based solely on this type of evidence [3].

Another feature of clinical practice guidelines is that they must also consider the ratio "cost / benefit" of each of the strategies [4]. In this regard one must highlight the suggestions of the American College of Cardiology Foundation and the American Heart Association, for the rational use of various diagnostic tests according to global cardiovascular risk in asymptomatic patients [5]. This behavior reduces not only the financial costs, but also the risks of iatrogenic actions, as the inadequate exposure to ionizing [6] radiations.

The reality is that there is variability in the quality of clinical practice guidelines. In addition, the main clinical practice guidelines about a disease, often differ in some of their key recommendations [1].

AGREE

The AGREE (Appraisal of Guidelines and Research and Evaluation) instrument was created in 2003 with the aim of analyzing the methodological rigor and "transparency" of Clinical Practice Guidelines. Currently the tool has been refined and a second version (AGREE II) has been released. The main utility of AGREE is to provide a systematic methodological standard for the development and evaluation of clinical practice guidelines [7]. Although the development and evaluation of clinical practice guidelines is a pertinent topic of growing interest, the AGREE methodology is still underutilized and/or undervalued, or even unknown, by most of the medical community.

For these reasons the appearance of initial work in Latin America on the subject should be embraced, as those of Alvarez-Vargas *et al.* [8] and Galvez-Olortegui *et al.* [9] published in Medwave. In the latter publication, the authors performed the external evaluation of three influential clinical practice guidelines (American, British and Canadian) [10],[4],[11], for atrial fibrillation [9].

The authors stress that, in general, clinical practice guidelines for the diagnosis and treatment of Atrial Fibrillation get the highest and lowest scores in the domains of Clarity of presentation (mean 93.5%) and Applicability (mean 36.1%) respectively. While specifically the lowest score corresponded to the domain Editorial Independence (4.2%) of the Canadian guidelines [9].

Finally, the authors recommend the use of the American and British guidelines, but not the Canadian ones [9]; which is controversial and contrasts with the view of some experts in the management of patients with atrial fibrillation, such as Dr. Adrian Baranchuk (Kingston General

Hospital, Canada), who believes that the Canadian guidelines are among the best.

Alerts

This controversy about and ignorance of the AGREE instrument motivates us to make the following observations:

1. AGREE should not be seen as an static instrument but rather a still developing and improvable one. The instrument AGREE II in itself recognizes that the major validity studies of the instrument are under development [7]. Logic makes us question if all six AGREE domains (1. Scope and purpose, 2. Stakeholder involvement, 3. Rigor of development, 4. Clarity and presentation, 5. Applicability and 6. Editorial independence) have similar importance to the overall evaluation of clinical practice guidelines. Perhaps domain 4, in relation to recommendations should hold more weight than others. In addition there seems to be some overlap in the boundaries of several domains.
2. The evaluation of clinical practice guidelines by means of AGREE quantifies the subjective opinion of the assessors; i.e. scores fluctuate according to the competence and performance of examiners. Rigorous evaluation of clinical practice guidelines requires expertise and is as complex as the preparation of the same guidelines. In this sense it seems appropriate to have regional multidisciplinary groups with expertise in AGREE methodology and seasoned professionals in the medical topic being addressed, as well as other professionals.
3. Galvez-Olortegui *et al.* note that "the four evaluators conducted an analysis of each set of guidelines, and discrepancies were resolved by consensus" [9]. This is a modification, as the protocols for the AGREE methodology say examiners must give their scores independently [7]. We warn that this modification is not validated and might lead to bias, especially when the opinion of an expert prevails in the consensus process.
4. The evaluation of clinical practice guidelines should include a review of their supplementary materials and in the case of an update (such as the Canadian Guide for Atrial Fibrillation) the previous guidelines should also be consulted. These documents may contain essential methodological details for AGREE evaluators. Have Galvez-Olortegui *et al.* met this standard?
5. Galvez-Olortegui *et al.* wrongly assume that the recommendations classified as conditional by the Canadian guidelines are equivalent to Class III recommendations of the American guidelines (see Table 4)[9]. For example, the Canadian conditional recommendation "we suggest that aspirin (81mg/day) is prescribed to patients under 65 years of age and CHADS2 negative but with a history of arterial disease (coronary, aortic or peripheral)" [11], is not tantamount to a ban. This sensitive bias could have led to the Canadian guideline being excessively penalized.
6. The authors note that "the British guidelines did not link their recommendations to the levels of evidence from studies" [4], which we believe is a "cardinal sin" in clinical practice guidelines. So it seems contradictory that they give the best rating in the domains 3 and 4 to the British guidelines. Although we clarify this guide has tables in which the quality of the evidence is specified according to the analyzed topic.
7. It is noteworthy that the Canadian guidelines only got one high score (in the decisive domain 4). Maybe this guide was overly penalized in the other domains. The previous paragraph may indirectly support this claim, as well as that in the domain "Applicability" the Canadian guidelines scored lower than the American ones, even though the latter did not provide algorithms in vital topics like the decision of antithrombotic treatment [10].
8. Galvez-Olortegui *et al.* in the discussion of their work, omit the message that the most important thing is not which clinical practice guidelines for atrial fibrillation are used but the degree of adherence to the selected guidelines achieved by patients. As there are no major differences in substance between the guidelines, nor is there a definitive answer to the main issues in dispute - a) assessing the risk of stroke and bleeding through the different scores, b) the use of aspirin and c) the inclusion of the new oral anticoagulants (NOAC). For instance, against CHADS2 score is the fact that it is less accurate in identifying patients with low risk of stroke; while in its favor stands that the progression in CHADS2 scores correlates better with the risk of stroke than the score CHA2DS2-VASc [10]. Perhaps a good practical alternative is the mixed algorithm proposed by the Canadian guidelines [11]; which begins assessment with age (the greater predictor of "hazard ratio"), then stratifies according to the other CHADS2 variables and finally applies the variable with the lowest "hazard ratio": the personal history of arterial disease (included in CHA2DS2 -VASc) [12].

In short, the poor overall evaluation and no recommendation of the Canadian guidelines could have been influenced by several of the above elements.

Final thoughts

- Clinical practice guidelines are documents of great interest not only to doctors and persons outlining health policy, but also for patients, industry and health insurance among other sectors. The trend of increased patient involvement in medical decisions, "invites" to consider (as the British guidelines do), variables traditionally neglected as opinion / preference of patients in gradation and selection of strategies. This represents an additional challenge for Evidence-Based Medicine.
- The British document is about 400 pages long, too much for a clinical practice guideline! However, to comply with the AGREE methodology does not necessarily imply that guidelines must be extensive; Alvarez-Vargas *et al*. recently demonstrated that the brief Canadian Hypertension Guide (20 pages) [13]adequately meets AGREE standards [8].

Finally we specify that our comments are not intended to detract from the contributions of Galvez-Olortegui*et al.* or claim a guide; but to emphasize how subtle and specialized

both processing and evaluating clinical practice guidelines must be. Hopefully, this group of researchers continue giving light to the emerging and necessary Latin American "avenues" of clinical practice guidelines based on AGREE.

Notes

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