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## Evaluation of Comparative Treatment Effects Using Indirect Comparisons. Response

### Evaluación del efecto de los tratamientos utilizando comparaciones indirectas. Respuesta

#### To the Editor,

We are aware of the open debate and the position in favor of indirect comparisons of some scientific societies and the position against—or with grave reservations—of some evaluation agencies,<sup>1</sup> and we are grateful for the opportunity to continue this debate.

We also acknowledge the effort made to develop new methods for this type of comparison, such as network meta-analyses.<sup>2</sup> This statistical methodology has already been used in cardiovascular research, such as the study by Steiner,<sup>3</sup> and sometimes the results have not been confirmed when the drugs have been directly compared in randomized clinical trials specifically designed for this purpose.<sup>4,5</sup>

Dr. Catalá-López states that this type of analysis should be based on rigorous systematic reviews and meta-analyses, bearing in mind a complete network of studies guaranteeing its quality, a condition that does not seem fulfilled in our letter. We agree with this premise, and although Steiner's analysis includes 14 trials, only 3 of these (JUMBO [Joint Utilization of Medications to Block Platelets Optimally], TRITON [TRial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet Inhibition with Prasugrel–Thrombolysis In Myocardial Infarction], and PLATO [PLATelet inhibition and patient Outcomes]) provide data for comparison of ticagrelor and prasugrel, which was the example used by us. We excluded the JUMBO trial because it was designed to assess safety and had a follow-up period of only 30 days, and we believe it was not comparable with TRITON and PLATO.

Dr. Catalá-López writes that this type of study is “not advisable when there may be factors that could influence treatment effects”. In our view, this is the criterion that contributes the most to limiting the validity of network meta-analyses. In our example, 100% of the patients in TRITON were treated with invasive coronary procedures, while this percentage was 65% in PLATO. In the secondary analysis by subgroups in PLATO, the efficacy of ticagrelor therapy was greater in patients treated with invasive strategies.<sup>6</sup> That is, the efficacy of the treatment varied according to a patient characteristic—treatment with invasive procedures—which was very different between the 2 studies used for the indirect comparison and consequently the results of that comparison could be biased or not valid.

As also mentioned by Dr. Catalá-López, it is true that to avoid these biases analysis strategies such as meta-regression can be designed, although this approach is limited and is not always

feasible when the variables defining differences in the efficacy of interventions in subgroups are not known *a priori* and perhaps have not even been gathered in the study.

In view of all of the above, we continue to adopt a conservative stance in this debate and we do not believe that, at present, indirect comparisons are useful to evaluate the efficacy of 2 interventions.

#### CONFLICTS OF INTEREST

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