



Interpreting desirability of outcome ranking (DOOR) analyses in observational studies in infectious diseases: caution still needed

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Dear Editor,

Desirability of outcome ranking (DOOR) is a new methodology to assess the effect of interventions in clinical trials in a more pragmatic way compared with conventional methods. This occurs by taking into account efficacy and safety as a composite, ranked endpoint, rather than as two independent, marginal outcome measures [1]. Briefly, with DOOR methods, different strategies/treatments are compared according to the desirability of the composite outcome registered in each patient, e.g., from the most to the least desirable: (i) survival without major adverse events; (ii) survival with major adverse events; (iii) death. This allows for a patient-centered perspective, avoiding the frequently unsatisfied assumption (in conventional analyses) that benefits and harms are not associated [1]. However, by doing this, the issue of arbitrariness inevitably arises, and a careful, standardized consensus definition of the ordinal outcome a priori should become the rule rather than the exception in DOOR analyses [2].

The first published reports of application of DOOR methods involved randomized interventions in investigational trials. However, some authors, including ourselves, have also started to explore their possible use in observational studies, mostly in patients with infectious diseases [3–5]. In our opinion, the application of DOOR methods to observational studies raises some additional considerations. For example, it is plausible that biases inherent to observational studies (e.g., selection biases) could impact in a different way conventional and

DOOR analyses conducted in the same population and with similar objectives (e.g., for evaluating which among 2 antibiotics is more effective and which among the same 2 antibiotics is more desirable in terms of outcome). This could make it more difficult to draw firm interpretations from the results of the two analyses, especially if conflicting (e.g., more effective but less desirable), since biases might participate, theoretically and elusively, in determining the difference. This adds to the concerns regarding the lack of standardization, also noticed in the first experiences with DOOR analyses against an observational backdrop that were indeed classified just as experiments of the possible use of DOOR techniques in observational studies [3, 5]. Furthermore, this is just an example of a possible new issue to be considered when applying DOOR analyses to observational studies, but it is likely that more will arise with further experience, as with all new methodologies.

In conclusion, although the innovative idea inherent to DOOR methods is certainly promising, in our opinion caution still remains essential when attempting to generalize results from DOOR analyses in observational studies, at least pending further experience and standardization.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with human participants performed by any of the authors.

Informed consent For this type of study, formal consent is not required.

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