Letter to the editor, "Validation and clinical value of the MANAGE-PD tool

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ABSTRACT

The MANAGE-PD tool may help general neurologists in deciding whether a patient with advanced Parkinson's disease should be referred for an advanced therapy. Although the development and clinical validation of MANAGE-PD would appear to serve an important need, we urge the reader to be aware of several methodological concerns.

Dear editor,

We have read with great interest the article entitled, "Validation and clinical value of the MANAGE-PD tool: A clinician-reported tool to identify Parkinson's disease patients inadequately controlled on oral medications" by Antonini et al. [1]. The authors highlight the need for an easy-to-use clinical decision tool to screen patients with advanced Parkinson's disease (PD) who may benefit from treatment optimization, such as starting treatment with an advanced therapy (AT). Their contribution through development and clinical validation of the so-called MANAGE-PD would appear to serve an important need in current practice. Accordingly, we would like to elaborate on the potential merits of the MANAGE-PD initiative, but also point out several methodological issues that will impede a widespread use of this tool.

We fully support the objective of the project that resulted in MANAGE-PD tool. In a survey we conducted among general neurologists in the Netherlands [unpublished results], almost half of the neurologists did not consider themselves competent to determine whether a PD patient would be eligible for *any* AT. Importantly, the survey revealed that general neurologists often considered in/exclusion criteria specifically indicative for Deep Brain Stimulation (such as treatment-resistant tremor and cognitive impairment) as primary eligibility criteria for *any* AT. Hence, should the MANAGE-PD tool indeed help determine whether PD patients may be suitable candidates for referral for one of the ATs, that would fulfill a dire clinical need. Upon timely referral, the specialized center could subsequently assess the patient in more detail, and subsequently determine whether a specific AT would be indicated.

We think, however, that the tool presented may not perform as intended, and might result in either too early or too late referral for AT. Our concerns boil down to incomplete adherence to international recommendations for the development of multivariable clinical decision tools as outlined in the so-called TRIPOD statement [2]. In short, TRIPOD recommends the use of statistical procedures identifying associations between clinical characteristics and the outcome of interest. In the past, various clinical decision tools were developed based expert opinion, some with proven merit such as the well-known Apgar-score in neonates, while others leading to false conclusions [3].

Indeed, the description of the development of MANAGE-PD is quite brief (only section 2.2 and section 3.1). As readers, we may assume that the tool is based on reviewing scientific literature and survey-derived clinical indicators. However, the authors make reference to only one article with Delphi consensus-based criteria [4]. We believe that it would have been insightful if the authors had elaborated more on how they selected the current items of MANAGE-PD. For example, it remains unclear why the tool comprises more items than the so-called 5-2-1 criteria that were previously proposed by some of the authors, and which were based on the same Delphi consensus criteria [4,5]. In addition, it seems to us that the model presented is not the most simple tool with the highest predictive value (i.e. a parsimonious model), as the authors mention that the items of dystonia with pain and impulse control disorders are not associated with the outcome of interest.

Furthermore, the validation process seems to be suboptimal. For example, it is not clear whether the MANAGE-PD panelists were involved in both the development and validation of the tool. Did the 17 panelists of international PD specialists formulate the criteria for MANAGE-PD, while also serving as an independent 'gold standard' for assessing the performance of the tool in the vignette assessment?

Finally, the authors assess the added value of the MANAGE-PD in a research sub-group of patients with a high proportion eligible for AT. More specifically, 50% of the patient vignettes were deemed eligible for

Abbreviations: PD, Parkinson's disease; AT, advanced therapy.

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referral for AT. In daily practice (i.e. PD patients visiting the outpatient clinic of a general neurologist), this percentage is much lower, as the authors show in their real-world data, in which only 26% of 2546 patients are eligible for referral for AT. If a screening tool is tested in a population in which the condition of interest is highly prevalent, the chance of false positives will appear to be low, which in turn might lead to overly optimistic conclusions regarding the positive predictive value of the MANAGE-PD tool. In fact, the article does not present any data on the number of false positives and false negatives when using the MANAGE-PD tool.

In conclusion, MANAGE-PD is a great initiative, which fulfills an unmet need, but to prove its added value, it needs a more solid validation in appropriate PD populations.

Author disclosures

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- Teus van Laar: none.

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