Author's response to reviews

Title: Simplified scoring of the Actionable 8-item screening questionnaire for neurogenic bladder overactivity in multiple sclerosis: a comparative analysis of test performance at different cut-off points

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Author's response to reviews:

Dear editor,

We thank the reviewers for their constructive comments. We have handled the points raised by them as follows.

Reviewer 1

1. Obviously one of the most important aspects should be to understand which are the changes of the questionnaire’s scores in positive patients after urological treatment. This consideration could help to understand if the questionnaire well correlates with clinical improvement in patients that have been urologically treated basing on the questionnaire’s outcomes.

We agree with this point concerning the changes of the questionnaire’s scores in positive patients after urological treatment. We further address this point in our answer to the similar comment of reviewer 2.

2. To further validate the outcomes of this type of investigations, it should be proposed a specific study in which the 2 forms of the questionnaire might be administrated to MS patients that also are submitted to instrumental evaluation (such as flowmetry, post-void residual assessment or cystometry) and definitively discriminate how much are these questionnaires reliable and if there is somewhat difference between the two forms (simplified and original).

However, I consider these comments discretionary because are not strongly related to the specific content and aim of the manuscript. Therefore, If the
authors would like to insert some considerations about them in the discussion I surely appreciate. On the contrary, if not, I consider that manuscript can proceed.

We agree with this point concerning a specific study in which the 2 forms of the questionnaire are administered to MS patients, who are also submitted to instrumental evaluation such as flowmetry, post-void residual assessment or cystometry. As with the previous point, this comment will also be further addressed in our answer to a similar comment of reviewer 2.

We have added the following text to the section Discussion:

‘It is our intention to perform a prospective study on the use and the added value of the Actionable questionnaire in real-life practice in The Netherlands, with instrumental urological assessments, such as flowmetry, post-void residual assessment or cystometry, and a comparison of the original scoring with the two simplified scorings.’

Reviewer 2

1. The question made by the authors is pretty well defined and the manuscript sounds to be acceptable with few major revisions. In my opinion the major limit of this study, as briefly report by the authors on their discussion, was that data were not related to the clinician assessment. Another limit that might be reported it was that neither a concurrent validity, correlating results with other validated tools was performed.

We agree that ideally we should have collected data about the urological assessment as well, and correlated these with the screening data (see also the comment of reviewer 1). It is our intention to perform a prospective study on the use and the added value of the Actionable questionnaire in real-life practice in The Netherlands, to also obtain data on instrumental urological assessments, such as flowmetry, post-void residual assessment or cystometry (as also suggested by reviewer 1), and to compare the original scoring with the two simplified scorings.

We have added the following text to the section Discussion:

‘It is our intention to perform a prospective study on the use and the added value of the Actionable questionnaire in real-life practice in The Netherlands, with instrumental urological assessments, such as flowmetry, post-void residual assessment or cystometry, and a comparison of the original scoring with the two simplified scorings.’

The concurrent validity of the Actionable questionnaire is described in another paper, which was added as a separate file in the submission.

In the section Introduction, Study design and setting, we refer to this paper via the following text:

‘The study was part of the Dutch Actionable validation study, an observational
non-interventional web-based study in The Netherlands in the period January 2015 to May 2015. The Dutch Actionable validation study assessed the test-retest reliability and concurrent validity of a Dutch version of the English Actionable questionnaire'.

In fact, we initially considered to also compare the two simplified scoring systems by evaluating their correlations with disability (EDSS) and health-related quality of life (HRQoL). But it was methodologically inappropriate to use overall clinical measures (in addition to the ‘urological referral status’ and ‘bladder medication status’) for the assessment of the cut-off points’ validity. The EDSS is an overall measure of disability, and the HRQoL is a comprehensive measure of subjective well-being. As urological problems constitute only one of many components of the EDSS and the HRQoL scales, the use of these measures would be unacceptably hampered by a ceiling effect, and predictably lead to weak correlations.

Major revisions:

2. Patient demographic and clinical characteristics should be better defined and reported, whether they were recorded.

We agree with the reviewer that the demographic and clinical description of the patients is insufficient.

Therefore, in addition to the information about the number of female vs. male patients, the patients’ age (mean, standard deviation, minimum, maximum) and the clinical type of disease (relapsing remitting vs. progressive vs. unknown), we have now also presented, as demographic information, the disease duration (years) (mean 10.1, standard deviation 8.0, minimum 0, maximum 35) and, as disease characteristic, the Expanded Disability Status Scale (EDSS) score (mean 4.30, standard deviation 1.78, minimum 0.00, maximum 7.50), a measure of MS-related neurological disability (section Results, first paragraph).

The following text has been added to the first paragraph of the section Results:

... the mean (SD) disease duration 10.1 (8.0) years (minimum 0 years, maximum 35 years), and the mean (SD) EDSS score 4.3 (1.8) (minimum 0.00, maximum 7.5).

3. How many patients were on bladder medications?

Forty-five (31.91%) patients were on bladder medication, whereas 96 (68.09%) were not. This information is given in the section Results, first paragraph.

4. How many patients were already seen by clinicians for OAB symptoms?

Fifty-six (39.72%) patients were seen by an urologist for OAB symptoms, whereas 85 (60.28%) were not. This information is given in the section Results, first paragraph.

5. Any data about co-morbidities?
We did not collect data about co-morbidities.

6. What do the authors mean with that disability was assessed by phone? What did they specifically assess and what not?

The Expanded Disability Status Scale (EDSS) score was assessed by phone. The EDSS is a generally accepted and widely used measure of MS-related disability. The classical EDSS is based on symptoms and neurological examination. An EDSS version for use by telephone via a structured interview has been developed and validated (Lechner-Scott J, Kappos L, Hofman M, Polman CH, Ronner H, Montalban X, Tintore M, Frontoni M, Buttinelli C, Amato MP, et al: Can the Expanded Disability Status Scale be assessed by telephone? Mult Scler 2003, 9:154-159).

To elucidate this point we have changed ‘having disability assessed by phone’ into ‘having the Expanded Disability Status Scale (EDSS) score assessed by phone’ (section Methods).

To answer the question on what specific items were addressed, and which not, we have added the following text to the Methods section:

‘Disability was assessed by use of the EDSS score via telephone. The EDSS is a generally accepted and widely used measure of MS-related disability. The classical EDSS is based on a neurological examination that provides the basis for the assessment of several functional systems (visual, brainstem, pyramidal, cerebellar, sensory, bowel and bladder, cerebral) that, according to predefined algorithms, contribute to the EDSS score. An EDSS version for use by telephone via a structured interview has been developed and validated (Lechner-Scott J, Kappos L, Hofman M, Polman CH, Ronner H, Montalban X, Tintore M, Frontoni M, Buttinelli C, Amato MP, et al: Can the Expanded Disability Status Scale be assessed by telephone? Mult Scler 2003, 9:154-159)’. The reference has been added to the section References.

7. How did the authors assess the cognitive status, whether it is was done? Otherwise, authors could better define such lack of data as possible limitation of the study.

The cognitive status was not assessed. This point is now discussed in the section Discussion, to which we have added the following text:

‘The study data were acquired via patients’ self-report. Given the well-known prevalence of cognitive impairment in patients with MS (Langdon DW: Cognition in multiple sclerosis. Curr Opin Neurol 2011, 24:244-249), it may be thought that cognitive impairment may have interfered with the quality of our data, and thus with the study’s conclusions. However, Gold et al. have demonstrated that cognitive impairment in MS patients does not affect the reliability and validity of self-report health measures (Gold SM, Schulz H, Monch A, Schulz KH, Heessen C: Cognitive impairment in multiple sclerosis does not affect reliability and validity of self-report health measures. Mult Scler 2003, 9(4):404-410). Therefore, we are
confident that the quality of our outcomes were not affected by cognitive dysfunction.'

The reference has been added to the section References.

Discretional revisions

8. In the introduction and discussion authors referred to Cardozo et al as the study in which was established 3 as cut-off value in urogynecological patients. While, in Cardozo’s study it’s been deduced that her group only confirmed such cut-off in their cohort which was already determined by expert clinicians in Burks et al validation study for MS population. Please, can authors check the right reference about this important issue?

In their paper Cardozo et al. (Int Urogynecol 2014) refer to Burks et al. (Int J MS Care 2013). However, this latter paper describes the development of the original 16-item version of the questionnaire, and does not mention the shortened 8-item version (Actionable), nor the simplified scoring algorithm (0-1; cut-off 3) for the 8-item version. The information that ‘… for the MS population, … the cut-off score of #3 was determined by expert clinicians’ given by Cardozo et al. (page 1661) is not accompanied by a reference.

The paper by Bates et al. (BMC Neurol 2013) describes the development of the 8-item questionnaire, and uses the same scoring algorithm (0-4) as in the 16-item version; the cut-off is 6. The authors do not describe or refer to a simplified scoring algorithm, and the sentence on ‘The simplified scoring method for bladder problem assessment developed here... ’ (page 7) must be understood to refer to the development of the 8-item version, being a simplified scoring method indeed, and not to the development of a simplified scoring algorithm. To our knowledge there is no published report on the development of the simplified scoring algorithm (0-1; cut-off 3) by expert clinicians. To stress this point, we added ‘to our knowledge’ and the references Burks et al. and Bates et al. to the first sentence of the section Discussion.

9. Needs some language corrections before being published

The English language has now been reviewed by a native speaker, and we have made several corrections which are indicated in the text.

Other changes we made:

1. Affiliation of author MH added.
2. ‘Nationaal Multiple Sclerose Fonds’ has been changed into ‘National MS Foundation The Netherlands’ in the section Acknowledgements.
3. ‘from Allergan’ added to the section Competing interests.

Kind regards,
Peter Joseph Jongen PhD, neurologist