Author's response to reviews

Title: Minimum detectable and minimal clinically important changes for pain in patients with nonspecific neck pain

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Author’s response to reviews: see over
MINIMUM DETECTABLE AND MINIMAL CLINICALLY IMPORTANT CHANGES FOR PAIN IN PATIENTS WITH NONSPECIFIC NECK PAIN.

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The following are the authors’ replies to the reviewer's latest comments:

1.1
I had objections against the sentence: MDC, MCS and ROC reflect different constructs, because ROC and MCS are both methods which assess the same construct MCIC. Therefore I suggest that the authors state: MDC and MCIC reflect different constructs.

In accordance with the reviewer’s wish, the manuscript has been modified and it now reads (paragraph 7 under Discussion)

Although it is up to researchers or clinicians to decide whether MCS or ROC are more suitable to define MCIC in their specific circumstances, the consistency of ROC and MCS values across studies may help them to use these results in practice (Tables 3 and 4). The upside of using the MCS value instead of ROC is that patients with scores showing an improvement above its value have a 95% chance of having improved meaningfully. However, in general, ROC might be more suitable, since scores from patients both reporting and denying improvement are used to calculate it, and it tends to weigh equally false-positive and false-negative misclassifications. As it has been suggested, the choice between the two methods may also depend on the type of intervention or the clinical consequences of being a “false positive” or “false negative.” For instance, some researchers may prefer to anticipate a difference generally corresponding to ROC (e.g. 1.5 PI-NRS points) for sample calculations in clinical trials vs. placebo, since ROC represents “the cut-off point that best discriminates between those patients feeling and not feeling that they have improved” and, since its size is smaller than MCS, it leads to larger samples. On the contrary, some clinicians may prefer to disregard differences smaller than MCS (e.g., 4 PI-NRS points) when they have to select among treatments with different safety profiles or side effects for a given patient, since that value represents “the mean change above which most patients would feel they have improved”.

1.2.3
The reason I questioned the calculation of Standard Error of Measurement (SEM) is because SEM is equal to (or larger) than SDchange / â??2 where SDchange is the SD of the unchanged group. The formula MDC = 1.96 * â??2 * SEM can be rewritten as 1.96 * SDchange = 2.7 *1.96 = 5.3 and SEM = 1.9

In your paper MDC = 1.96 * â??2 * SEM = 4.0 so SEM = 1.44 which is smaller than expected.

In the results section the MDC values which you now removed from the tables, should also be removed from the text (page 6; 4th paragraph)
The values of MDC removed from the tables were those corresponding to subgroups of patients (in which “n” was too small). However, the results given in the text are for the entire sample. They are shown in the tables and are a major result of this study. Therefore, they should remain. As seen in 4th paragraph under Results)

As seen in those tables, MDC for neck pain is 4.0 PI-NRS points in the entire sample and it is 4.2 for patients who also complained from referred pain, and MDC for referred pain is 6.2 PI-NRS points. These values are not influenced by baseline pain severity or duration.

2.11
I agree that Farrar stated that â??In fact, MCIC seem to be consistent even across different chronic pain conditionsâ??. But I have objections about how you use this reference. You use this reference to support you statement that the MCIC is not affected by the treatment given. The sentences before and after the sentence that includes the Farrar reference are all about treatment. The reference of Farrar is about different conditions and does not say anything about different treatments.

In accordance with the reviewer’s desire, the reference to Farrar about different conditions has now been removed from that paragraph which discusses treatments, and which now reads (paragraph 10 under Discussion):

Mean duration of pain when patients entered this study was over 540 days (Table 1). During that period, they had all received many forms of treatment and many still received them during the study. Since data being analyzed in this study derive from post-marketing surveillance of neuroreflexotherapy, all of them received that specific form of treatment. No study has assessed the potential influence of any specific form of treatment on MDC or MCIC and many studies include patients receiving heterogeneous treatments, since they are participating in randomized controlled trials. In fact, MDC and MCIC calculations rely on patients’ self-assessment of their own evolution and scores from instruments used to assess evolution of symptoms, no matter what treatments are potentially influencing that evolution. Therefore, the generalizability of results from this study are not affected by the fact that these results derive from the post-marketing surveillance of a particular form of treatment. The consistency of results from this study with those from previous reports on neck pain and low back pain patients further supports their generalizability.

Minor essential revisions
Page 6, paragraph 5, line 4. Dependent of baseline severity, MCS values range from 2.5 to 4.8 instead of 4.9

Range of values for MCS refer to those found in the study. Those values range from 2.5 (neck pain in Table 4) to 4.9 (neck pain in Table 3). Therefore, what is stated in the text is correct. Perhaps the confusion arises because the minimum and maximum of that range are given in different tables (tables 3 and 4).
Based on the reviewer’s comment, the text has been modified to further clarify this, and it now reads (paragraph 5 under Results):

MCS for neck pain is 4.1 PI-NRS points, both in the entire sample and in patients who also had referred pain, and it is also 4.1 PI-NRS for referred pain. MCS remains constant across subacute and chronic patients, but it is higher for patients with more severe baseline pain. Depending on baseline severity, MCS values range from 2.5 to 4.9 PI-NRS points for neck pain, and from 2.4 to 5.3 for referred pain (Tables 3 and 4).

Page 7, line 9 from bottom, MDC is what detectable and MCIC is what is relevant. Therefore â??relevantâ?? is not the right term but is does not apply to MDC.

Based on the reviewer’s comment, that sentence has been changed and now reads (paragraph 6 under Discussion):

The low number of patients in this sample denying any change made it impossible to reliably estimate the potential effect of baseline pain severity and chronicity status on MDC values (Tables 2-4). However, results from this study show that, although MDC and MCS are different concepts and the methods used to calculate their values are also different, their size for neck pain is very similar both in all the patients and in the subset of those complaining from referred pain. This finding is also consistent with results from previous studies, both in neck and low back pain patients. It might be interpreted that the limit of what constitutes a “relevant” and a “detectable” change is similar whether it derives from the scores of patients who report improvement or deny it. However, as opposed to ROC, those calculations do not take into account false positives and false negatives.