Author's response to reviews

Title: Detecting the neuropathic pain component in the clinical setting: A study protocol for validation of screening instruments for the presence of a neuropathic pain component

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Author's response to reviews: see over
Dear Mr. Jhonell De Los Santos,

Hereby we send you our revised manuscript: ‘Detecting the neuropathic pain component in the clinical setting: A study protocol for validation of screening instruments in the clinical setting’ for publication as an original research protocol in ‘BMC Neurology’.

We would like to thank the reviewer(s) for their comments to our manuscript. In the supplement you will find the respond to the reviewer.

We declare that the authors have all participated in development of the study and writing the submitted protocol, and that they have seen and approved the final version. Furthermore we confirm that this protocol has not been published in whole or part elsewhere. No specific conflicts of interest are present for the authors.

With kind regards,

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Supplement: Respond to the comments made by the reviewers

We would like to thank the reviewer(s) for reading our manuscript carefully, and giving valuable advice. Below we have answered to the questions and concerns to our best capability.

Reviewer 1: Daniel Giampi de Andrade

"This is a very well designed study intended to detect neuropathic pain components in prevalent pain syndromes such as LBP and NSP. I believe the authors should separate two main objectives: one is to validate the screening tools (DN4 and PDQ) which were already translated into Dutch. Here, the gold standard must be the current IAPS criteria.

Of course we used the IASP criteria as the definition of neuropathic pain as the standard for the diagnosis of neuropathic pain by the physicians. This is stated in the first lines of the background. Moreover, we changed the sentence (measurements part in the method section): "At the first visit, each patient will be seen by two physicians who will examine and diagnose patients' pain as pain with or without NeP components, accordingly to the standardized assessment form" into "At the first visit, each patient will be seen by two physicians who will question and examine the patients. They will then independently classify the patients' pain as pain with or without a NePC (neuropathic pain component), based in the IASP NeP criteria and supported by a standardized assessment form."

A second aim of the study would be to validate these two tools to detect neuropathic pain component, which is a clinical entity still ill understood and poorly studied." "A it is, there is some circularity, since neuropathic components stem from neuropathic pain, screening tools need first to be validated to detect NeP itself, and then these so called "components.""

We added a few sentences to make this more clear to the reader in the background section: "Strictly speaking, the diagnosis of neuropathic pain is a patho-anatomical diagnosis presuming knowledge regarding nerve injury which is difficult to obtain in the clinical patient. Thus in the clinical context it is better to speak of a neuropathic pain component (NePC), which is a clinical syndrome based on a typical set of clinical symptoms and signs. Clinically, a NePC is characterized by spontaneous pain and abnormal pain sensations [9]. NeP is typically described as a spontaneous
ongoing burning or shooting pain with spontaneous sharp exacerbations and somatosensory abnormalities after a (non-) noxious stimulus [10]."

*I could not understand the use of SAF as a gold standard instead of the proposed definition (irrespective of the grading system). By the way, the SAF is not displayed nor explained in the manuscript.*

The SAF is not used as a gold standard, but just a form to write down the findings during the assessment of the patient. This to not miss essential data. In the text we’ve added a few sentences to make this more clear to the reader. We changed the name SAF in ‘standardized assessment form’ to make more clear it is just a form, not an instrument.

**Reviewer 2: Constanza Pazzaglia**

"In my opinion, when performing a validation of an existing questionnaire for neuropathic pain, the sample of patients have to a diagnosis of neuropathic pain and the result of questionnaire has to compare with that of already validated pain questionnaires. I think that the study design is not well constructed to reach this aim."

The diagnosis of a NePC is a clinical diagnosis so we chose to use the opinion of two independent physicians to act as a standard for the diagnosis of NePC. This standard is also used in the original validation studies by Bouhassira (DNP) and Freynhagen (PainDETECT). The use of a validated questionnaire for neuropathic pain as a ‘gold standard’ for another questionnaire for neuropathic pain is, to our opinion, not the right way to become a validated instrument.

"Also the title is misleading if the authors concluded the background with this sentence: "The final aim is to assess the prevalence of NeP components in patients with LBP and NSP in the Netherlands. What is the real aim of the study? Validate the questionnaires in Dutch language or assess the prevalence of NeP components in patients with LBP and NSP in the Netherlands?"

We skipped this aim, because it is confusing indeed. We added it to the additional data which will be collected (last paragraph background section).
"Moreover, LBP and NSP are considered examples of mixed pain condition, in which neuropathic and nociceptive pain coexists. For that reason, these conditions cannot considered a relevant example of neuropathic pain, as for example diabetic polyneuropathy."

The aim of our study is to detect the NePC in patients with low back pain, neck-shoulder pain or in patients suffering from a known peripheral nerve damage (such as diabetes mellitus, trigeminal neuralgia etc.). We chose specifically for a non-selective consecutive patient recruitment in specialized pain clinics, neurology clinics and in general physician practices. This because of the fact that almost all screening questionnaires to detect the NePC in patients suffering from pain are performed in two groups who were expected to have a NePC or to have, for sure, no NePC. This study will provide more and new information relevant to the general population.