Author’s response to reviews

Title: Measuring the burden of herpes zoster and post herpetic neuralgia within primary care in rural Crete, Greece

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Response to reviewers

Title: Measuring the burden of herpes zoster and post herpetic neuralgia within primary care in rural Crete, Greece

Reviewer: 1

Reviewer’s report:

P1: The authors do not give the definition they used for postherpetic neuralgia (any pain one month after rash onset, as mentioned in the Background?), nor for the acute phase of herpes zoster (the first month after rash onset?). In the literature the definition of PHN is not uniform (e.g. Oxman et al. (reference 29) define PHN as pain persisting 3 months after rash onset with a severity of 30 or higher on a 0-100 scale).

R1: We thank the reviewer for this important comment. We used the 30 day definition for postherpetic neuralgia and have included this in the methods section of the revised manuscript (lines: 114-116)

P2: Combining cases of HZ and cases of PHN may overestimate the incidence of HZ.

R2: It is an important methodological comment also and we thank again the reviewer. We agree with that comment and we have noted this in the strengths and limitations section (lines 297-298). However, the main aim of the paper is to measure the burden of HZ and that distinction cannot influence the study results.

P3: The reported incidence of HZ is rather low. This may be caused by a deficient monitoring system, or selection, or a combination of both. Could the authors discuss this aspect more thoroughly?

R3: Research is ambiguous in this aspect as prevalence has been measured to be lower or higher in other settings, a fact which we have previously noted in the introduction and in the discussion. It is possible though that the incidence of HZ could have been affected by various factors including the lack of an electronic patient system that would facilitate the disease’s monitoring. We have noted this also in the strengths and limitations section (lines 298-301).

P4: As far as selection is concerned: are the healthcare facilities in Crete freely accessible for all inhabitants? If not, could this cause selection?

R4: Thanks again the reviewer for that comment. Greece does not use a gatekeeping system to regulate the contact of the population with the health care system, the population may access any hospital in any area, not only for secondary and tertiary care but also for primary
health care services in the private sector. Certainly, it can introduce a selection bias in any epidemiological study that is based on the utilization of health care services. We have included this factor in the strengths and weaknesses paragraph (lines 305-309) as below and we repeat again that this study mainly contributes to the measurement of the burden that the selected primary care services are invite to manage.

P5. The mean duration between the development of pain and the HZ attributed rash was 5.2 + or - 5.8 days. This implies that in some patients, the pain started after the onset of the rash. For clarity, the authors should mention this in the text.

R5: No, the fact that the SD was larger than the mean indicated that the results were skewed to the left, however we could have written this clearer in the previous version. So as to completely avoid that the readers do not falsely interpret the result in this manner, we have changed the presentation of the descriptive statistics (lines: 184-186) and now provided mean and ranges (minimum-max) instead of mean and standard deviations for this result. Thank you for making the manuscript clearer in this aspect.

P6. This is a cross-sectional study. Therefore, any causal relation between increased anxiety or depression and the occurrence of PHN cannot be assessed (or even suggested, as the authors do). Moreover, there are also some prospective studies which did not find this relation (e.g. Opstelten et al. Pain 2007).

R6: We thank again the reviewer and we agree with that comment and suggestion. We have included this point in the end of the strengths and limitations section of the revised manuscript, while we have referenced also the suggested prospective study in the text (lines 316-319)

P7. I advise the authors to include the following references:


R7: We have included the suggested literature as references 15, Thomas SL et al (line 230-231) and reference 20, Fleming DM et al (lines 300-303 and lines 243-245) in the main text. They are very relevant to our study and we thank very much the reviewer for that important comment and suggestion.

Reviewer: 2

Reviewer's report:
P1. I would like to mention that there are very few original research articles on the subject. Furthermore the study is planned and conducted by primary care physicians. Good subject, better to publish it as there is a lot of effort despite the problems in the primary care infrastructure of the country.

R1: We thank the reviewer for this pleasant comment; indeed there is little research in primary health care and the burden of HZ/PHN from the perspective of GPs.

P2. The data set could be much better with better selection criteria and more patients/GPs. The sample size is too small to generate the results, and there may be a selection bias as the authors are aware of it.

R2: We thank the reviewer for that comment and we agree that the sample size is relatively small and it would have been nice to have an even larger catchment area. However this was not feasible so as to increase recruitment and increase statistical strength. We have noted these points in the strengths and weaknesses section of the revised manuscript (lines 296-321).