Author's response to reviews

Title: Societal and individual burden of illness among fibromyalgia patients: correlations with disease severity and OMERACT core domains for fibromyalgia: a cross sectional study in France

Authors:

Serge Perrot (serge.perrot@htd.aphp.fr)
Caroline Schaefer (caroline.schaefer@covance.com)
Tyler Knight (tyler.knight@covance.com)
Meghan Hufstader (meghan.hufstader@gmail.com)
Arthi B. Chandran (Arthi.B.Chandran@pfizer.com)
Gergana Zlateva (Gergana.Zlateva@pfizer.com)

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Author's response to reviews: see over
Re: Manuscript 9665017975860055 - Societal and individual burden of illness among fibromyalgia patients in France: association between disease severity and OMERACT core domains

Dear Ms. Mellins-Cohen

My co-authors and I thank the Reviewers for their constructive comments regarding our above titled manuscript submitted for consideration for BMC Musculoskeletal Disorders. We have addressed their comments and have included a summary detailing the associated revisions to the manuscript in the accompanying document. To aid your review, the amends made in response to the Reviewers’ comments are shown as track-change. I can confirm that all co-authors have read and approved the revised manuscript for resubmission.

We hope you find our paper improved for these revisions, and I look forward to hearing from you regarding the suitability for publication in BMC Musculoskeletal Disorders.

Arthi B. Chandran, MS, MPH (corresponding author)
Associate Director, Primary Care Health Economics & Outcomes Research
Pfizer Inc. 235 East 42nd Street, New York, NY 10017
Office: (212) 733-3288; Fax: (212) 808-8832; Email: Arthi.B.Chandran@pfizer.com
Editor’s comment:

1. The manuscript has been evaluated by two reviewers and they have pointed at a few essential aspects that the authors should look carefully at and revise accordingly. I will particularly emphasize the comments and questions regarding the sample size and the possible lack of power and in your analyses and the limitations in your calculation of health care costs.

- The Limitations have been expanded on Page 20-21 to highlight that the severity analyses, particularly for patients in work, would be strengthened if repeated with larger sample sizes to confirm results (and please see response to Reviewer 2, Point 3). In addition, we have conducted non-parametric tests and added P-values to account for the unequal and small sample sizes in the severity analyses.

2. The question regarding generalizability should also be considered carefully.

- The manuscript has been edited throughout to ensure that these results are applicable to the population of FM subjects studied, and that the generalizability of our observations to the FM population as a whole is unknown.

- We note in the Limitations (Page 20-21) that larger studies are needed to support some of our observations; however given that data on the FM population in France are sparse, and furthermore that our study incorporates the full patient experience of disease function, health-related quality of life, and costs we feel that our small study presents important information for the health provider community in France, and provides key data for comparison with other similar studies conducted in other countries.

3. As suggested by one of the reviewers, clarity would probably be improved by cutting down the extent of results presented.

- We have edited back some of the text in the Results section in response to this point and in response to Reviewer 2, Point 5, below. In addition we have removed some of the $P$-values in the tables in response to Reviewer 1, Point 5.
Reviewer's 1

General comments
This study is important in enhancing knowledge of the medical readership. The patient group with fibromyalgia is indeed in need of further studies. Basically this manuscript is understandable, appropriate methods have been used, limitations have been discussed and the paper is quite well written. However, I have some comments to be considered by the authors.

Major compulsory revisions
1. In the abstract aim the authors claim that they will provide a comprehensive assessment of burden associated with Fibromyalgia in France. However, they included only 88 of 680 000 patients in France and thus can hardly claim that they are describing the situation of FM patients in France. I recommend the authors to check the whole manuscript and be modest in their statements about generalizability of this study results.
   - The Abstract has been edited and ‘comprehensive’ has been removed from the manuscript text.
   - The manuscript has been edited throughout in response to this point, to ensure that generalizability of our results is not over-stated. Extrapolation of our observations to the FM population as a whole in France is ultimately unknown, and therefore we acknowledge that larger studies are needed to confirm the observations presented in the manuscript.
2. In the “Method” section there is no information of the reliability of the different measures used in the study. This should be clarified with appropriate references for each measure.
   - We have already noted that the scales are validated on Page 6, and provided references to support each scale. However, we acknowledge that not all the scales have been validated in the FM population, although they are widely used in clinical trials of FM patients to assess subjective outcomes. We have clarified this in the Limitations on Page 20-21.
3. In “Healthcare costs” what is the reason why treatment costs are limited only to medications? This patient group uses a lot for example Physiotherapist’s services and
also Psychologist services. There could have been differences between severity groups in using these services. In my opinion, a lot of costs are most probably missing due to this bias in data collection. This is also important information since the patients were not very satisfied with the effect of medications. Is it possible to find this data in patient records?

- Patients were asked how much money they had spent on prescription medications, non-prescription medications and other treatments for fibromyalgia, over the past 4 weeks. Although we did not specifically ask for costs associated with physiotherapy or psychological services, any out-of-pocket costs incurred by the patient for other treatments should have been captured by this question. We have clarified this in the Methods on Page 9.

4. In the “Results”, “Impact of FM on health-related quality of life and core symptoms” the second sentence include a measure (The Current Overall Health) that has not been described in the method section. Also, what was the reason to ask the patients their Pain Free Overall Health?

- We have added the detail into the Abstract and the Methods on Page 7, for the Current Overall Health scale. Patients were asked to rate their current overall health and overall health if they had complete relief from their FM, on a scale from 0 to 100, where 0 represents “worst possible health” and 100 represents “perfect health”.

5. In the “Results” “Impact of FM severity” section, fourth paragraph it says that “Comparisons across FM severity level for the FIQ are not made…” However, these comparisons are presented in table 4. What is the reasoning with these contradictory results?

- As FM severity level was developed based on FIQ total scores, we have removed the $P$-values from Table 4 in response to this point.

6. The word “correlation” is used in the abstract aim. Correlation leads the reader to think of correlation analyses. The authors studied differences between FM severity groups thus association would be better word to use.
• We agree with this point and the text and title have been updated using ‘association’ in place of correlation as suggested, as statistical correlations were not conducted in this study.

7. In Methods, “Study design” section includes information of participants, how the study was conducted (procedure), and ethics. This section should be clarified through adding appropriate sub-headings.
   - **Subheadings have been added to the Study Design paragraph section in response to this point.**

8. In section “Patient questionnaires”, the first sentence claims that there were five health related quality of life measures. Obviously this is not true, only one measures HRQoL. Clarify this, please.
   - **The text has been updated to clarify on Page 6**

9. Change the colours to different structures in figure 2 and 3. This would help to understand the figures better.
   - **Figures have been amended as requested to improve differentiation between the 5 groups**

**Discretionary revisions**

10. Consider shortening and focusing the title of this paper.
    - **The title has been edited in response to this point**
Second Reviewer’s report:

In my opinion this is an interesting and mostly well-written article about the burden of illness among fibromyalgia patients. The study is perhaps a little too small for some of the analyses presented?

Major Compulsory Revision:

1. I have one major item that has to be justified. In the analyses of patient perception of treatment effectiveness and satisfaction treatment seems to mean medication, and nothing else. In my part of Europe (in the North) several treatment modalities are used for FM patients like physiotherapy, self-management courses, psychological cognitive treatments, paced physical activity and others. Perhaps medication is the dominating form of therapy in France, but that has to be justified and commented.
   - Survey questions related to patients’ perceived effectiveness and satisfaction with their FM treatment, which included questions on prescription medications, non-prescription medications, and other treatments for fibromyalgia. Specific questions on non-prescription medications (over-the-counter), physical treatments, such as physical therapy/massage, acupressure/acupuncture, or chiropracty, and including herbs, vitamins or other supplements were asked. Data presented in the Figures relate specifically to the questions regarding effectiveness and satisfaction with prescription medications only. The text has been clarified in the Methods on Page 7 and in the Results on Page 12 in response to this point.

2. Minor Essential Revisions: The use of n in both heading and content of tables seems to be unnecessary. Sometimes the n inside the table differs from the heading probably due to missing values. But I suggest to present n only once in each table.
   - We have simplified the tables, removing denominator N-numbers from inside the table, and adding an explanatory footnote e.g., to Table 2.

3. In the discussion on limitations of the study I suggest to add comments about the size of the study and especially the appropriateness of analyzing the data about work stratified on the three severity levels. Or alternatively do these analyses where n is rather small on sample not divided into severity groups? Trends that were non-
significant are probably due to the low (and very low power) [power] in these analyses?

- The Limitations have been expanded on Page 21 to highlight that the severity analysis, particularly those in work, need to be repeated with larger sample sizes to confirm results. In addition, we have conducted non-parametric tests and added P-values to account for the unequal and small sample sizes in the severity analyses. The Methods, Results and tables have been updated.

4. My comment under major compulsory revision about definition of treatment might also be discussed under limitations?

- Please see response to Point 1 above

Discretionary revisions:

5. In my opinion this article would gain on presenting fewer results in tables and in the result presentation. A more careful selection of the main results will give a more reader friendly article, in my opinion.

- We have edited back the Results section to reduce overlap and focus the text on key points of the survey

6. Figure 2 and 3 might be better presented in a table? Table 4 in my opinion present too much information for one table.

- Given that the paper already contains 6 tables, we feel that the figures are important for displaying the observations in a more accessible format for the reader. However, we have made edits to the formatting of the Figures according to Reviewer 1, point 9.

- We feel that all the scales (including the individual components of these scales) listed in Table 4 are key to the overall objective of this study as they provide a detailed assessment of different aspects of disease burden in these patients with FM. However, according to Reviewer 1 point 5, P-values have been removed for the FIQ data to simplify this section

7. The abbreviated term HRU is used in the text without being defined and explained, or did I miss the definition?
• Please note the definition of Health Resource Utilization (HRU) is provided on Page 7.

8. In the description of health professional use by FM patients it might once again be cultural differences, but I still wonder: do not FM patients in France use a lot of other health professionals than doctors?

• Patients were asked questions relating to other treatments for their FM, which included the example of physical therapy/massage, acupressure/acupuncture, or chiropracty. Therefore these aspects of treatment were captured within the questions relating to treatment satisfaction and effectiveness. Visits to ‘other’ healthcare professionals are included in Table 3, although these were not defined further.

• As outlined in response to Reviewer 1, Point 3, healthcare costs related to prescription medications, non-pharmacological treatments, and other treatments, which could have included use of other healthcare professionals including those given as examples in the treatment questions (e.g., relating to physical therapy/massage, acupressure/acupuncture, or chiropracty). These points have also been noted in response to Point 1, above, and the text clarified on Page 7.

9. I also got curious about the fact that 18 centers recruited only 88 patients. Why did each center recruit so few patients (short time for inclusion, many patients did not want to participate, problems with motivation in staff or something else?).

• Although we do not know the complete reason for this, similar surveys were conducted in different countries across Europe; however due to regulatory steps in France the study presented in the current manuscript took longer to start compared with these other studies, and therefore when the target number of patients had been reached all studies were closed.