PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	A Cross-Sectional Assessment of the Prevalence of Multiple Chronic Conditions and Medication Use in a Sample of Community-Dwelling Adults with Fibromyalgia in Olmsted County, Minnesota
AUTHORS	Vincent, Ann; Whipple, Mary; McAllister, Samantha; Aleman, Katherine; St Sauver, Jennifer

VERSION 1 - REVIEW

REVIEWER	Peter Przekop Loma Linda University Medical School Hazelden Betty Ford Foundation United States
REVIEW RETURNED	06-Oct-2014

GENERAL COMMENTS	The paper needs minor revisions. I believe that tramadol is an opioid and should be included as such. In the results section page 10 should reflect this change under medications. Also, it may be helpful and if possible, to separate sleep aids into those with and without potential for dependency. Page 13 line 33 "is" should be omitted. This paper exposes some interesting problems that we all struggle with. Is it possible to determine how many physicians are prescribing the medications per patient? The paper needs minor revisions. I believe that tramadol is an opioid and should be included as such. In the results section page 10 should reflect this change under medications. Also, it may be helpful and if possible, to separate sleep aids into those with and without potential for dependency. Page 13 line 33 "is" should be omitted. This paper exposes some interesting problems that we all struggle with. Is it possible to determine how many physicians are prescribing the medications per patient? This paper, although viewed with caution due to the experimental design, reveals that many patients with fibromyalgia have multiple co-morbidities and are prescribed multiple medications. For example as many as 1/3 of the patients studied receive opioids which have no proven role in the treatment of fibromyalgia and possess far too many dangerous side-effects. The results call into question the utility of current management strategies used to treat these patients and exposes the need for research into novel treatments strategies.

REVIEWER	Marcus Beasley University of Aberdeen, United Kingdom
REVIEW RETURNED	15-Dec-2014

GENERAL COMMENTS	Item 9, and 13 (b) on the STROBE checklist could still be answered despite the design of the study being a review of medical records. For example, for item 9, a source of bias could be from not including those who did not authorize researchers to view their medical records. And again reference to this group of people should be made to answer item 13 (b), reasons for non-participation. The main thing lacking from this paper was a comparison with an age, gender, and location matched general population for the prevalence of these multi-comorbidities and polypharmacy. We just can't tell if there is anything specific to patients with fibromyalgia in what is observed here. For example, degenerative arthritis is very common among those in their 50s and 60s, but we cannot tell from this study if this is more or less so in those with fibromyalgia. The best thing the authors could do is add to table 1 a column which gives the same numbers of people with each condition or taking each medicine among those in the Rochester Epidemiology Project matched for age and gender, but having no diagnosis of fibromyalgia. Also, similar pie charts could be produced for figure 1 for those without fibromyalgia for comparison. Minor points to consider: - Including a diagnosis of metabolic syndrome that is derived from other conditions means there is some 'double-counting' and the total number of conditions might be inflated. The authors should consider not including metabolic syndrome as a separate condition, but could use type 2 diabetes instead (diabetes mellitus is given in the table, but type 1 or 2 is not stated). - Figure 1 should include the numbers and percentages in the key. Item 9, and 13 (b) on the STROBE checklist could still be answered despite the design of the study being a review of medical records. For example, for item 9, a source of bias could be from not including those who did not authorize researchers to view their medical records. And again reference to this group of people should be made to answer item 13 (b), reasons for non-participation. Thank you for this very nice study. The main thing that I would like to see in the paper is a comparison with other patients in the Rochester Epidemiology Project. The prevalences quoted for multi-morbidities and polypharmacy might not be specific to those with fibromyalgia. You conclude that there is a high prevalence of polypharmacy in fibromyalgia but there is nothing to judge this against to determine whether it is particularly high or not. Comparison with a reference group would allow us to see where prevalences in fibromyalgia are particularly high. For example, in table 1, it would be really useful to have an extra column giving the prevalence estimates for each condition, or medication, from a sample of patients of similar age and gender but without a diagnosis of fibroymyalgia. The same procedures could be used among those without fibromyalgia to calculate the extent of multi-morbidities and polypharmacy and shown in additional pie charts in figure 1. Minor points to consider: - Including a diagnosis of metabolic syndrome that is derived from other conditions means there is some 'double-counting'. You could consider not including metabolic syndrome as a separate condition, but just have type 2 diabetes instead (diabetes mellitus is given in the table, but type 1 or 2 is not stated). You could mention the derived prevalence of metabolic syndrome in the text, but leave it out of calculations for total number of morbidities.

	- Figure 1 should include the numbers and percentages in the key for clarity.

VERSION 1 – AUTHOR RESPONSE

Reviewer 1 Comments

Reviewer 1, Comment 1. The paper needs minor revisions. I believe that tramadol is an opioid and should be included as such. In the results section page 10 should reflect this change under medications.

Reviewer 1, Response 1. The reviewer is correct, tramadol acts as an opioid. Our rationale for evaluating the prevalence of tramadol use separately was two-fold. First, in our experience, tramadol is the most frequently prescribed medication for fibromyalgia pain. Therefore, we felt it important to evaluate the use of tramadol by itself. Second, at the time the data were collected and medications classified (2013), tramadol was not classified as a controlled substance, despite its opioid-like properties. The change in regulatory status occurred in August 2014. Recognizing that tramadol is prescribed in a similar fashion to other opioids, while we include tramadol and other opioids separately in the table, we also report the total percentage of patients using either tramadol or an opioid in the text ("Overall, 31.4% of our sample was taking either tramadol or an opioid.") (pg. 12).

Reviewer 1, Comment 2. Also, it may be helpful and if possible, to separate sleep aids into those with and without potential for dependency.

Reviewer 1, Response 2. Thank you for this suggestion. While such a separation would have been interesting (and potentially a direction for future research), this level of detail was not possible at the time of data collection. Additionally, information regarding the potential for dependency for non-benzodiazepine sleep medications is still a matter of debate. At the current time, delineating between sleep aids and other medications with and without potential for dependency is beyond the scope of this project.

Reviewer 1, Comment 3. Page 13 line 33 "is" should be omitted.

Reviewer 1, Response 3. We were unable to locate the "is" to be omitted.

Reviewer 1, Comment 4. This paper exposes some interesting problems that we all struggle with. Is it possible to determine how many physicians are prescribing the medications per patient?

Reviewer 1, Response 4. The reviewer raises a very important concern to clinicians caring for patients with chronic pain. While the medical records do include information on the number of providers involved in the patient's care, it would be labor-intensive to determine which provider wrote the original prescription. The answer to this question is beyond the scope of this paper and should be included in future research.

Reviewer 1, Comment 5. This paper, although viewed with caution due to the experimental design, reveals that many patients with fibromyalgia have multiple co-morbidities and are prescribed multiple medications. For example as many as 1/3 of the patients studied receive opioids which have no proven role in the treatment of fibromyalgia and possess far too many dangerous side-effects. The results call into question the utility of current management strategies used to treat these patients and exposes the need for research into novel treatments strategies.

Reviewer 1, Response 5. We thank the reviewer for the kind feedback. We agree that our findings do

call into question the use of multiple medications in fibromyalgia, utility of current management strategies, and the need for research to evaluate novel treatment strategies.

Reviewer 2 Comments

Reviewer 2, Comment 1. Item 9, and 13 (b) on the STROBE checklist could still be answered despite the design of the study being a review of medical records. For example, for item 9, a source of bias could be from not including those who did not authorize researchers to view their medical records. And again reference to this group of people should be made to answer item 13 (b), reasons for non-participation.

Reviewer 2, Response 1. Thank you for bringing this to our attention. We have added a sentence describing those who declined medical record review to the methods and limitations sections (pgs. 8 and 16) as well as updated the STROBE checklist to reflect inclusion of this information in the manuscript.

Reviewer 2, Comment 2. Thank you for this very nice study. The main thing that I would like to see in the paper is a comparison with other patients in the Rochester Epidemiology Project. The prevalences quoted for multi-morbidities and polypharmacy might not be specific to those with fibromyalgia. You conclude that there is a high prevalence of polypharmacy in fibromyalgia but there is nothing to judge this against to determine whether it is particularly high or not. Comparison with a reference group would allow us to see where prevalences in fibromyalgia are particularly high. For example, in table 1, it would be really useful to have an extra column giving the prevalence estimates for each condition, or medication, from a sample of patients of similar age and gender but without a diagnosis of fibromyalgia. The same procedures could be used among those without fibromyalgia to calculate the extent of multi-morbidities and polypharmacy and shown in additional pie charts in figure 1.

Reviewer 2, Response 2. Thank you for providing this feedback. Although what you are suggesting would be the ideal comparison, in order to provide this information we would need to conduct the same, extensive medical record review in a control population. This is beyond the scope of the current project. A recent publication by Rocca et al. describes the scope of multimorbidity using the Rochester Epidemiology Project (Rocca et al., 2014). As this publication does not include all of the conditions in Table 1, we were unable to include a column in Table 1 comparing prevalence estimates. We have however, added a few sentences to the discussion section regarding conditions that were assessed in both papers (pg. 15). This comparison is somewhat limited, however, as Rocca's study evaluated the general population of Olmsted County, and so includes patients with chronic pain.

Regarding polypharmacy, our focus was on medications used specifically for the management of fibromyalgia symptoms, which have not been evaluated in the general population of Olmsted County. Also, we did not collect information regarding use of medications for the treatment of other conditions, which may have allowed us to make comparisons between our sample and the general population.

Reviewer 2, Comment 3. Minor points to consider:
- Including a diagnosis of metabolic syndrome that is derived from other conditions means there is some 'double-counting'. You could consider not including metabolic syndrome as a separate condition, but just have type 2 diabetes instead (diabetes mellitus is given in the table, but type 1 or 2 is not stated). You could mention the derived prevalence of metabolic syndrome in the text, but leave it out of calculations for total number of morbidities.

Reviewer 2, Response 3. Thank you for this suggestion. We have removed metabolic syndrome from

the table and updated the calculations for number of conditions to reflect this. We have also updated the table to clarify type II, and not type I, diabetes.

Reviewer 2, Comment 4. Figure 1 should include the numbers and percentages in the key for clarity.

Reviewer 2, Response 4. This has been added.

Thank you very much for considering our revisions.

Sincerely,
Ann Vincent, MD

VERSION 2 – REVIEW

REVIEWER	Peter Przekop Loma Linda University School of Medicine Betty Ford Center
REVIEW RETURNED	21-Jan-2015

GENERAL COMMENTS	The authors report the results of a retrospective chart review in which they examine the medical records of patients with a diagnosis of fibromyalgia. The authors report the multiple chronic medical and psychiatric conditions along with the multiple prescribed medications associated with these patients. Their work points out the enormous total health burden that these patients endure along with the multiple medications associated with their treatment. The study points out the lack of a comprehensive coordinated care that many of these difficult to treat patients receive. It reveals important information that should be used to better coordinate care.