PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Associations of primary care structures with polypharmacy and patient-reported indicators in patients with complex multimorbidity: a multicentre cross-sectional study in Japan
AUTHORS	Aoki, Takuya; Fujinuma, Yasuki; Matsushima, Masato

VERSION 1 – REVIEW

REVIEWER	Smith, Susan RCSI, General Practice
REVIEW RETURNED	27-Jul-2021

GENERAL COMMENTS	Thanks you for asking me to review this paper which reports a cross sectional survey of patient experience (PREM) and self-reported health (PROM) for patients with complex multimorbidity attending different primary care settings in Japan. The paper is well written and the authors do acknowledge the limitations of a cross sectional design but there is still a potentially major confounding issue in relation to the type of patient that attends the different types of services. It may just be patient preference but there is very limited presentation of this issue which is really key for international understanding and generalisability. The following points need to be addressed: • More presentation of the types of patients that attend each type of PC service, any barriers to attending each in terms of cost, access, waiting times etc Need clear definition of primary care services and entitlements in Japan • Those attending the hospital based PC services seem more likely to have been hospitalised in the previous 6 months, which is a likely marker of severity but may also indicate that follow up following an admission is more likely to take place in the same system. This is controlled for in the analysis but may still indicate an important difference in patient type • Abstract: important to remember to keep stating that the findings are associations given the study design and uncertainties around confounding • The use of a PREM and a PROM implies a single measure when there are multiple options for each – this may just be a wording issue • 25 facilities included - of how many in network. ? representative • The PREM used has 6 domains but the reporting concentrates on the 2 found to be significantly different • The PREM item first contact is unclear. Methods say those visiting a facility for the first time were excluded from the survey so how does this effect the first contact domain? • The PROM used SRH was expanded to a 100 point scale so a difference of 6 points may not be clinically significant. Also both groups seem to have quite high SRH anyway. Can this be

	compared to any population norms though this may be a challenge for a complex MM group • Discussion para 2: The study design does not support this statement about low value care - possible association which may be explained by different patient populations • Discussion and presentation of results in abstract: Only two of the six PREM domains were significantly different between groups. Need to comment on negative findings as well throughout for balance • Conclusion refers to lower risk of polypharmacy – this should be lower prevalence, can't determine risk with this study design • STROBE checklist is empty

REVIEWER	Karimova, Kateryna Goethe-Universitat Frankfurt am Main
REVIEW RETURNED	12-Oct-2021

GENERAL COMMENTS	A clear and well written paper. Sound approach and correct statistical analysis with accompanying conclusions. One of the important aspects is the polypharmacy and patient-reported indicators in patients with complex multimorbidity, with a focus on differences between community clinics and hospitals The authors also addressed the important initial comments of the editor satisfactorily. Some remarks and maybe additional statistical analysis however need to be clarified/added. Introduction: well und clearly written Statistical analysis: the urban and rural areas of patients and clinics/ hospitals are not included as confounding variable, which are very important in those analysis. Charlson Score as common comorbidity score, and also separate chronic conditions (diseases) which are differently distributed in the both groups (Digestive, Respiratory, Eye and adnexa) could be added in to the multivariable analysis. Results/ Tables: please add the reference variable in the tables 3 and 4. It's not really self-explanatorily for the readers, which group was as reference. Discussion: well und clearly written

VERSION 1 – AUTHOR RESPONSE

Responses to the comments of Reviewer #1

Thanks you for asking me to review this paper which reports a cross sectional survey of patient experience (PREM) and self-reported health (PROM) for patients with complex multimorbidity attending different primary care settings in Japan. The paper is well written and the authors do acknowledge the limitations of a cross sectional design but there is still a potentially major confounding issue in relation to the type of patient that attends the different types of services. It may just be patient preference but there is very limited presentation of this issue which is really key for international understanding and generalisability. The following points need to be addressed:

Response: We wish to express our appreciation to you for your insightful comments on our paper. The comments have helped us significantly improve the paper.

1. More presentation of the types of patients that attend each type of PC service, any barriers to attending each in terms of cost, access, waiting times etc Need clear definition of primary care services and entitlements in Japan

Response: Thank you for your suggestions. We agree that these points require clarification. Accordingly, we have improved the 3rd paragraph of the Introduction as follows.

Although the Japanese health care system does not necessarily distinguish between primary and secondary care and there is no gate-keeper system, primary care services are generally provided in both community clinics and outpatient departments of small- and medium-sized hospitals with less than 200 beds that are predominantly privately owned and managed.9,11 Japanese community clinics are generally run by a small team consisting of one full-time physician and a small number of nurses and medical assistants. On the other hand, primary care departments of small- and medium-sized hospitals are run by a large team consisting of more physicians, nurses, medical assistants, and other healthcare professionals than clinics.10 Patients can visit any of these facilities without restricted access and additional out-of-pocket costs.10

2. Those attending the hospital based PC services seem more likely to have been hospitalised in the previous 6 months, which is a likely marker of severity but may also indicate that follow up following an admission is more likely to take place in the same system. This is controlled for in the analysis but may still indicate an important difference in patient type

Response: We appreciate the reviewer's concerns on this point. In accordance with your suggestions, we have improved the descriptions of the limitations (the 5th paragraph of the Discussion) as follows.

Third, although we adjusted for the possible confounding variables, unmeasured patient characteristics might have influenced the results. For example, we adjusted for hospitalization in the past six months, which potentially reflects the severity of chronic conditions; however, confounding by the severity of individual chronic conditions was not fully accounted for in the analyses. This might have overestimated the associations of the types of primary care facilities with polypharmacy and SRH.

3. Abstract: important to remember to keep stating that the findings are associations given the study design and uncertainties around confounding

Response: Accordingly, we have improved the Conclusion of the abstract as follows.

Clinic-based primary care practices were associated with a lower prevalence of polypharmacy, better patient experience of coordination and community orientation, and better SRH in patients with complex multimorbidity compared with hospital-based primary care practices.

4. The use of a PREM and a PROM implies a single measure when there are multiple options for each – this may just be a wording issue

Response: Accordingly, we changed the expressions PREM and PROM in the Measures, Results, and Discussion sections to the JPCAT-SF and SRH.

5. 25 facilities included - of how many in network. ? representative

Response: Accordingly, we have added this point to the Design, setting, and participants as follows.

The participating facilities included seven facilities from three networks of medical institutions.

6. The PREM used has 6 domains but the reporting concentrates on the 2 found to be significantly different

Response: Thank you for your comment. We have improved the descriptions of the Results (Facility types and patient-reported indicators) as follows.

The associations between the types of primary care facilities and JPCAT-SF scores in longitudinality and comprehensiveness were not statistically significant.

According to the other reviewer's comment, we have added municipality population size where the participating facility was located as a confounding variable. Newly, the association between primary care facility types and community orientation became significant as shown in Table 4.

7. The PREM item first contact is unclear. Methods say those visiting a facility for the first time were excluded from the survey so how does this effect the first contact domain?

Response: Accordingly, we have added the description of the first contact to the Japanese version of Primary Care Assessment Tool section as follows.

The first contact domain reflects accessibility including out-of-hours care.

We excluded patients who were seen for the first time at the participating facilities because it is difficult for them to assess their primary care experience including the first contact domain in the first place. We have added this point to the Design, setting, and participants section as follows.

We excluded patients who were seen for the first time at the participating facilities because it is difficult for them to assess their primary care experience.

8. The PROM used SRH was expanded to a 100 point scale so a difference of 6 points may not be clinically significant. Also both groups seem to have quite high SRH anyway. Can this be compared to any population norms though this may be a challenge for a complex MM group

Response: We appreciate the reviewer's concerns on this point. In view of the clinical significance, we have changed our method of analysis of SRH. According to previous studies, we created a dichotomous variable for SRH (0 if excellent, very good, or good; 1 if fair or poor) and performed analyses as shown in Self-rated health status and Statistical analysis sections. As the result, clinic-based practices were significantly associated with a lower prevalence of poor or fair SRH compared with hospital-based practices (aOR = 0.53, 95%CI 0.35 to 0.80) as shown in Facility types and patient-reported indicators section and Table 4. SRH in patients with complex multimorbidity was poorer than that in Japanese representative sample (reference #23).

9. Discussion para 2: The study design does not support this statement about low value care - possible association which may be explained by different patient populations

Response: Accordingly, we have removed this sentence about low value care.

10. Discussion and presentation of results in abstract: Only two of the six PREM domains were significantly different between groups. Need to comment on negative findings as well throughout for balance

Response: We have added this point to the Results in the abstract and the Discussion section as follows.

Results in the abstract
The associations between the types of primary care facilities and JPCAT-SF scores in longitudinality and comprehensiveness were not statistically significant.

Discussion (first paragraph)
In contrast, the JPCAT-SF score in first contact evaluating out-of-hours care was lower in clinic-based practices and the differences in longitudinality and comprehensiveness were not statistically significant, as seen in the findings from our previous study on non-selective primary care patients.10

11. Conclusion refers to lower risk of polypharmacy – this should be lower prevalence, can't determine risk with this study design

Response: Thank you for your comments. Accordingly, we have improved this sentence as follows.

Clinic-based primary care practices were associated with a lower prevalence of polypharmacy, better patient experience of coordination and community orientation, and better SRH in patients with complex multimorbidity compared with hospital-based primary care practices.

12. STROBE checklist is empty

Response: Accordingly, we have improved this point.

Responses to the comments of Reviewer #2

A clear and well written paper. Sound approach and correct statistical analysis with accompanying conclusions.
One of the important aspects is the polypharmacy and patient-reported indicators in patients with complex multimorbidity, with a focus on differences between community clinics and hospitals
The authors also addressed the important initial comments of the editor satisfactorily.
Some remarks and maybe additional statistical analysis however need to be clarified/added.

Response: We wish to express our appreciation to you for your insightful comments on our paper. The comments have helped us significantly improve the paper.

1. Statistical analysis: the urban and rural areas of patients and clinics/ hospitals are not included as confounding variable, which are very important in those analysis. Charlson Score as common

comorbidity score, and also separate chronic conditions (diseases) which are differently distributed in the both groups (Digestive, Respiratory, Eye and adnexa) could be added in to the multivariable analysis.

Response: Thank you for your suggestions. Accordingly, we have added municipality population size where the participating facility was located as a confounding variable. Please see the results of the reanalysis (Table 3 and 4). Newly, the association between primary care facility types and community orientation became significant. Charlson scores cannot be calculated from the chronic disease data in our study. In addition, we have also tried the multivariable analyses including the variables of Digestive, Respiratory, and Eye and confirmed that the results didn't change.

2. Results/ Tables: please add the reference variable in the tables 3 and 4. It's not really self-explanatorily for the readers, which group was as reference.

Response: Thank you for your comment. We have already described in the note below Tables 3 and 4 that the reference group is hospitals, but moved it to the beginning of the note for clarity.

VERSION 2 – REVIEW

REVIEWER	Smith, Susan RCSI, General Practice
REVIEW RETURNED	02-Dec-2021

GENERAL COMMENTS	Thank you for addressing most of my comments. I think the paper is much clearer. You have acknowledged in your responses that there is likely residual confounding so I think your conclusions in the abstract and main text should reflect this, perhaps stating that while your results, controlled for multiple suggest that community care based primary care clinics with smaller teams were associated with a lower prevalence of polypharmacy, better patient experience of coordination and community orientation, and better SRH in patients with complex multimorbidity compared with hospital-based primary care practices, further research is needed to confirm these findings that control carefully for case mix and other factors that may mediate these associations. For balance the conclusions should also mention finding of significantly higher 'first contact' scores for hospital based primary care clinics reflects greater accessibility including for out of hours care.

REVIEWER	Karimova, Kateryna Goethe-Universitat Frankfurt am Main
REVIEW RETURNED	02-Dec-2021

GENERAL COMMENTS	Thank you very much for the revision. Almost all Reviewer comments have been taken into account in this revision. But I still have considerable concerns regarding Charlson Score and also separate chronic conditions (diseases) which are differently distributed in the both groups (Digestive, Respiratory, Eye and adnexa). All these influence factors were not included in

	the multivariable analysis as recommended. All these variables have been listed separately in the table 2. I would strongly recommend to include these variables in the multivariable analysis (comparability of the groups)

VERSION 2 – AUTHOR RESPONSE

Responses to the comments of Reviewer #1

Thank you for addressing most of my comments. I think the paper is much clearer. You have acknowledged in your responses that there is likely residual confounding so I think your conclusions in the abstract and main text should reflect this, perhaps stating that while your results, controlled for multiple suggest that community care based primary care clinics with smaller teams were associated with a lower prevalence of polypharmacy, better patient experience of coordination and community orientation, and better SRH in patients with complex multimorbidity compared with hospital-based primary care practices, further research is needed to confirm these findings that control carefully for case mix and other factors that may mediate these associations. For balance the conclusions should also mention finding of significantly higher 'first contact' scores for hospital based primary care clinics reflects greater accessibility including for out of hours care.

Response: Thank you for your suggestions. Accordingly, we have improved the conclusions of the main text as follows because word limits did not allow us to add more description to the abstract.

Clinic-based primary care practices were associated with a lower prevalence of polypharmacy, better patient experience of coordination and community orientation, and better SRH in patients with complex multimorbidity compared with hospital-based primary care practices. In contrast, hospital-based practices were associated with comparatively better patient experience of first contact including out-of-hours care. In the primary care setting, small and tight teams may improve the quality of care for patients with complex multimorbidity. Further research, which controls unmeasured confounding factors, is needed to confirm our findings.

Responses to the comments of Reviewer #2

Thank you very much for the revision. Almost all Reviewer comments have been taken into account in this revision. But I still have considerable concerns regarding Charlson Score and also separate chronic conditions (diseases) which are differently distributed in the both groups (Digestive, Respiratory, Eye and adnexa). All these influence factors were not included in the multivariable analysis as recommended. All these variables have been listed separately in the table 2. I would strongly recommend to include these variables in the multivariable analysis (comparability of the groups)

Response: Thank you for your suggestions. As mentioned before, Charlson scores cannot be calculated from the chronic disease data in our study. Accordingly, we have added Digestive, Respiratory, and Eye and adnexa diseases as confounding variables. Please see the results of the reanalysis (Results and Table 3 and 4). We confirmed that the results didn't change.

VERSION 3 – REVIEW

REVIEWER	Smith, Susan RCSI, General Practice
REVIEW RETURNED	20-Dec-2021

GENERAL COMMENTS	Thank you for addressing my comments. I have no further suggestions

REVIEWER	Karimova, Kateryna Goethe-Universitat Frankfurt am Main
REVIEW RETURNED	21-Dec-2021

GENERAL COMMENTS	Thank you for addressing of all my comments. In my opinion, this manuscript should be accepted for publication.