PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (see an example) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below. Some articles will have been accepted based in part or entirely on reviews undertaken for other BMJ Group journals. These will be reproduced where possible.

ARTICLE DETAILS

TITLE (PROVISIONAL)	How does multi-morbidity influence health care costs? A population-based cross-sectional study of depression, back pain and osteoarthritis
AUTHORS	John, Carstensen
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VERSION 1 - REVIEW

REVIEWER	Sandra Hollinghurst
	Senior lecturer in health economics
	University of Bristol, UK
REVIEW RETURNED	08-Feb-2012

THE STUDY	The title and introduction imply that the aim is to investigate how multimorbidity influences health care costs in general. This is misleading as the analysis is restricted to three conditions so to that extent the design cannot answer the question.
	The claim in the "key message" that "multi-morbidity does not generally increase health care costs per diagnosis" does not follow from the analysis.
RESULTS & CONCLUSIONS	See comment above The interpretation of the results is limited not only by concentrating on only three diseases but the three-way interaction (patients with all three diagnoses) appears to have been ignored completely.

REVIEWER	Christine Vogeli, PhD
	Mongan Institute for Health Policy
	Massachusetts General Hosptial
	U.S.A.
REVIEW RETURNED	10-Feb-2012

THE STUDY The paper offers an interesting look at the associations between

	multiple chronic conditions and health care costs and utilization. The study relies on strong data. Methods used are very clearly described, and the discussion and implications and detailed and thoughtful. The introduction and abstract would benefit from clearer writing and perhaps more thorough review of the literature on multiple chronic conditions or rationale for conducting the present analysis. The abstract in particular would benefit from a clearer description of the study findings.
	Methods: Most studies to date have not adjusted utilization for patient factors. Adjustment for age and gender is appropriate given the clear link to overall health care utilization. But more thought should be given to other adjusters. For example, total health care utilization is clearly linked to the severity of disease, and the number of other conditions – besides those of interest to the study. In particular osteoarthritis may be associated with the presence of a number of additional chronic illness that may also require medical care. If the sample is not limited to persons with only the conditions of interest (e.g. depression, osteoarthritis and back pain) then care should be taken to at least adjust for the number of other conditions. The use of education as an adjuster should be defended in the
	approach as it is not related to health care need. Perhaps it should be considered an explanatory factor of interest in that differences in health care utilization across levels of education could be thought of as inappropriate.
RESULTS & CONCLUSIONS	Discussion: care should be used when describing the costs of care. These are total costs of care for patients with specific diagnoses, but who also may have a number of other diagnoses not analyzed in the study. So costs are not "total health care costs associated with a depression diagnosis" but rather total costs of care among patients with a depression diagnosis.
	In the discussion, final sentence of paragraph 1, note that drug costs did not "increase", but rather they were higher for patients with both diagnoses.

VERSION 1 – AUTHOR RESPONSE

Dear Editor,

We hereby resubmit our paper " How does co-morbidtiy influence health care costs? A populationbased cross-sectional study of depression, back pain and osteoarthritis"

Below follow a point-by point response to the concerns raised by the reviewers. We hope that our response will satisfy the valuable comments from the reviewers.

The tables are new and all other changes have been colored in the revised manuscript. We hope that the manuscript conforms to the journal style and that you find it valuable for publication in your journal.

Reviewer: Sandra Hollinghurst

1. "Title is misleading". We agree with the reviewer that the title is misleading. Our analysis is restricted to interactions between two health states at a time. We did not include the three-way interaction term (for those with all three diagnoses) since there were only 46 patients of this kind in the population, and with these type of highly variable outcomes the power for detecting even large effects in this group was considered too low. This is commented in our discussion on page 10 in the manuscript. Therefore, we have changed the title and replaced multi- morbiditiy with the more appropriate term: co-morbidity

2. "Key message". The comment is correct and we have omitted the whole sentence in the key

message

3. "Patients with all three diagnoses". The reason for exclusion of three-way interaction is commented above (point 1). In our analyses we have now also adjusted for all other health states (tables 1-3). For more comments: See also point 5 below.

Reviewer: Christine Vogeli

4. "The introduction and abstract would benefit from review of the literature on multiple chronic conditions or rationale for conducting the analysis. The abstract would benefit from clearer description of the study findings."

We have expanded the introduction and added new references (4,5 26,27) of relevance for our analysis of the clustering of multiple chronic conditions and the management and coordination of primary care and specialist care.

The result part of the abstract is rewritten and some of the most important study findings are added.

5. "Adjust for at least the number of other conditions and for severity"

To investigate further whether any differences in the presence of other conditions could have affected our main findings concerning the interactions, we added (page 5 in the manuscript) a variable (representing other health states) counting the number of other diagnoses in 2006 (maximum one per ICD10 chapters, excluding the entire F-chapter "mental disorders" as well as the back pain and arthroses sub-sections of the M-chapter "musculoskeletal disorders"). Adding this variable as an adjustor in the regression models produced no changes in the estimates of the interaction effects on costs and did not interfere with our main conclusions. Hence, all the calculations and the three tables are new.

We agree that severity of disease is linked to health care utilization and costs. However, we have not been able to perform such an analysis with our data register.

6. "Education as an adjuster should be defended".

We have in the method part of the manuscript (page 5) added a sentence on education as an adjuster. "Education was used to express socioeconomic status. In a former study where we used the same data register it was shown that education was an adequate covariate for the age interval." 7. "Total health care costs associated with a depression..." has now been changed to: total health care costs among patients with a diagnosis (page 8)

8. "Drug costs did not increase" has now been changed to "were higher".. (page 8)

REVIEWER	Sandra Hollinghurst Senior Lecturer in Health Economics University of Bristol
	UK
REVIEW RETURNED	23-Mar-2012

THE STUDY	The research question is given as "to analyse now co-morbidity influences health care costs per patient based on three diagnoses, back pain, depression and osteoarthritis" It would be more accurate to say "to analyse how co-morbidity among patients with back pain, depression and osteoarthritis influences health care costs per patient" This applies to the abstract (p2), the key message (p3), and the introduction (p4)
RESULTS & CONCLUSIONS	As above. The conclusion begins "The comorbidity influence on health care costs" It would be better if it read "The comorbidity influence of back pain, depression and osteoarthritis on health care costs