PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Chronic disease multimorbidity transitions across healthcare interfaces and associated costs: a clinical-linkage database study
AUTHORS	Kadam, Umesh; Uttley, John; Jones, Peter; Iqbal, Zafar

VERSION 1 - REVIEW

REVIEWER	Jennifer St. Sauver, PhD Associate Professor of Epidemiology Mayo Clinic Rochester, MN, USA I have no conflicts of interest to disclose.
REVIEW RETURNED	09-May-2013

THE STUDY	No concerns about the supplemental documents.
GENERAL COMMENTS	Kadam and colleagues have written a clear and interesting paper focused on defining the health care utilization (emergency visits and hospitalizations) associated with multiple chronic conditions. The paper is well written and clearly presented, and was a logical way to start addressing the question of the impact of multi-morbidity on adverse health outcomes. A significant limitation was the failure to address comorbidity beyond 2x2 pairings. I would suspect there's substantial patient overlap in some of their groupings. However, overall, the paper is clear, results are logically presented, and discussion is good.

REVIEWER	Colin McCowan, Reader in Health Informatics, University of Glasgow, UK
REVIEW RETURNED	13-May-2013

THE STUDY	I felt the research question could be more clearly defined - the study answered whether there are differences in health care resource use based on defined multimorbid pairs and are associated costs higher comparing these pairs and also comparing against patients with only one of the matched conditions. It is unclear from the methods whether patients could have more than two co-morbid conditions or if the matched pairs were mutually exclusive (i.e. a patient with diabetes, COPD, CHF and CHD could be in 3 groups). There is no justification for the choice of the six conditions or for the pairs that were chosen other than to represent chronic disease through mid-life to old age. Some more information on this and whether the other 30 pairs were initially examined but discounted

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	would be of interest. I don't think it is that important that these pairs were chosen above others but more insight to the process would be helpful.
REPORTING & ETHICS	There was no supplied STROBE checklist although the paper would seem to meet these criteria anyway.
GENERAL COMMENTS	I enjoyed reading this paper but felt there were some aspects that needed addressed to add clarity to what the authors had done. The decision to examine multimorbid pairs rather than a count of diseases looks valid but could be explained further earlier than the discussion. I also thought what woudl hopefully be some simple additional statistics may place the study population in a clearer context. I had difficulty with how the authors used "transition" so would suggest it needs to be clearly defined at the start of the article. The authors report on prevalence of co-morbid pairs for those on disease registers. Can they estimate prevalence in the underlyng population? Also reporting what prevalence of those with an additional condition for the pair would be useful i.e. out of the diabetics what proportion had CHD? Did patients only have pair or could they have 3+ conditions. Unclear what happened if a patient had 4 conditions - would they be in multiple pairs? Pg6 L46 - sentence makes it unclear as to whether all contacts were known or only those from UHNS. Whilst I believe it is the former this should be clarified.

VERSION 1 – AUTHOR RESPONSE

Reviewer 1
The overall comments are positive. In response to the pairing approach, we should like to draw the reader's attention (top of page 6 – "Multimorbidity definitions"):

"Whilst multimorbidity could be characterised for the study as any number or multiple combinations, we selected 'pairs' as the basic measure of investigating multimorbidity. The 'pairs' provides the basis for clinically intuitive understanding of how two chronic disease pathways might combine together, but with six study chronic diseases chosen, the potential number of pairs could be 6x(6-1)/2=15 distinct pairs. Presentation of data for 15 pairs would have been cumbersome. Instead, we chose six pairs as common examples to represent the range of chronic diseases onsets from mid-life to old-age.

Reviewer 2

(i) Research question more clearly defined – the final sentence to the background section has been re-phrased and clarified (page 5).

(ii) Study group construction – In the methods section under "Multimorbidity definitions we do state that "Each multimorbid group and their respective 'index' conditions represent a within group (see Table 1 for annotation of all study defined groups) and separate clinical hypothesis of the association between multimorbidity and healthcare outcomes."
Whilst there could be overlap between the multimorbid pairs, each study pair population and comparator groups were selected by the index conditions of interest, as the primary interest in this study was to investigate and test influence of an overall pair combination on cost.

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We have now added a sentence to this section to clarify the approach (page 6).

(iii) Choice of pairs – As stated in our response to Reviewer 1 we could have investigated any number of pairs, but we selected the six empirically in this proof-of-principle test. Our future work is now investigating more complex definitions of multimorbidity.

(iv) Strobe criteria – We should have completed this list and it is now attached.

(v) Study population prevalence – We had wondered about including these in the original submission, but have now added these as supplementary tables as these have been specifically requested, and will be helpful to the reader to understand the broader population. We have, however, not made detailed comments on these tables in the main text.
We have now added a sentence to the analyses section and a sentence at the start of the results section, on information given as supplementary tables.

(vi) Definition of transition – a sentence has been added to the background (page 4).

(vii) Sentence clarity – the admissions data relate to any hospital and England and Wales and not just UHNS, so the sentence in “Healthcare transitions data: A&E episodes and hospital admissions” section has been amended (page 6).

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