PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Socioeconomic Inequalities in the Prevalence of Complex Multimorbidity in a Norwegian Population: Findings from the Cross-sectional HUNT Study
AUTHORS	Vinjerui, Kristin Hestmann; Bjerkeset, Ottar; Bjorngaard, Johan; Krokstad, Steinar; Douglas, Kirsty; Sund, Erik

VERSION 1 – REVIEW

REVIEWER	Herzig Lilli Switzerland
REVIEW RETURNED	26-Jan-2020

GENERAL COMMENTS	This is a very interesting and well written paper. Only some minor comments Article Summary: You relay only one limitation in this summary – whereas some other important limitations are detailed in the limitation section. Please complete Introduction: Second paragraph and second sentence: typos? Study population: Included persons need to have an identified occupation, also if you exclude persons without such an occupation, you may underestimate the low social group. Maybe you need to add this in the limitation – however it's not clear how many people do not have an identified occupation in the study population. Table 1 Circulatory system; how can you include "undetected hypertension?" – whereas detected hypertension should surely be included in the circulatory organ system Results: Did you imagine stratifying the complexity of MM in your analyses? There may be a difference if a person suffered from 3 organ system – or from 5 or 6 or more? Discussion Interpretation of the gender differences would be interesting.

REVIEWER	Professor Tim Stokes University of Otago New Zealand

REVIEW RETURNED	28-Jan-2020

GENERAL COMMENTS	This study reports the prevalence of complex multimorbidity in a Norwegian population, using a large population-based health survey (HUNT-3: 2006-2008). It is a secondary analysis of this dataset. Overall, there is now a large body of evidence on the prevalence of multimorbidity and complex multimorbidity in a wide range of populations and using different populations (e.g., data extraction from GP records; self-completion population surveys). he study is therefore not original, though it is accepted that it adds to what we know about the prevalence of complex multimorbidity due to its county wide general population health survey approach. Overall, the methods are appropriate and the results are reported appropriately. The discussion section is well structured and the strengths and limitations of the study are clearly set out. I have several minor suggested revisions: 1. There is a lack of clarity of the definition of "complex multimorbidity" in the abstract and body of the paper. First, it is not strictly correct to define multimorbidity as "the co-occurence of multiple LTCs in which none is more important". The source reference for this quote is both more precise and more nuanced - Boyd & Fortin Ref 1 - "Multimorbidity is defined as the co-existence of two or more chronic conditions, where one is not necessarily more central than the others". Note the need for 2 or more and "one is not necessarily more central than the others" is not the same as saying "none is more important". I would therefore suggest that the Boyd and Fortin wording is either quoted verbatim or paraphrased in such a way as to keep the original intended meaning. second, when term "complex multimorbidity" is used it is important that its use is consistent with that recommended by Harrison et al. (Ref 13). 2. Introduction p.5, LL23-31. This section needs rewording to make it clear the focus is on cross-sectional prevalence studies of MM. 3. Introduction p.5, LL23-31. The second half of this para needs rewording so as to state there is a need to define the prevalence of complex multimorbidity, why describing this prevalence matters and to define what is meant by this term here.

VERSION 1 – AUTHOR RESPONSE

Reviewer 1
Reviewer Name: Herzig Lilli
Institution and Country: Switzerland
Please state any competing interests or state ‘None declared’: None competing interest d

Please leave your comments for the authors below:
This is a very interesting and well written paper. Only some minor comments.

Overall response
Thank you for the positive evaluation of our paper. Your review offered valuable considerations with regards to the study population, outcome and results, hereby improving the original article. Thank you also for notifying us of an inconsistency between table 1 and appendix A.

Comment 1
Article Summary:
You relay only one limitation in this summary – whereas some other important limitations are detailed in the limitation section. Please complete
Response 1
For a more balanced summary, we replaced bullet point 4 from:
"Socioeconomic differences in association with complex multimorbidity are reported with both absolute and relative measures for women and men separately."
to:
"Non-participants have lower socioeconomic position and higher mortality, thus the social gradients in prev

Comment 2
Introduction:
Second paragraph and second sentence: typos?
Response 2
We consulted a manuscript editor, who claims we can leave the sentence as it is.

Comment 3
Study population:
Included persons need to have an identified occupation, also if you exclude persons without such an occupation, you may underestimate the low social group. Maybe you need to add this in the limitation – however it's not clear how many people do not have an identified occupation in the study population.
Response 3
We agree that unidentifiable occupation was a challenge in our study.
The flowchart (fig. 1) for the sample selection shows that only 25 individuals were excluded based on unidentifiable occupation(s). However, 1571 had missing data on occupation, that is, their occupation was not possible to categorize in the Standard Classifications of occupations by Statistics Norway.1 Originally, table C1 in appendix C shows the distribution of occupational groups, sex and age by participation status and missing. We have now replaced appendix C with an addition to Methods, Study population removing:
Further sociodemographic characteristics of non-eligible and missing are provided in appendix C
And adding:
"Participation in the HUNT3 Survey varied with socioeconomic position, age and sex.2 The distribution of occupational groups in the sample were; 24% (high), 27% (middle) and 49% (low) and in non-eligible; 17% (high), 20% (middle), 52% (low) and 11% (missing). The average age (SD) in the sample was 55 (14) years, in the non-eligible group 44 (18) years and among missing 66 (18) years. Women constituted 55% (n=20813 of 38027) of the sample, 51% (n=5662 of 11203) of the non-eligible and 81% of the missing (n=1281 of 1576)."
We also added these considerations to Discussion, Strengths and limitations, stating:

“This study excludes those never having worked, which will underestimate social gradients in complex comorbidity.
3 Further, participants with missing information due to unclassifiable occupation, more common in elderly women, were excluded.”

Comment 4
Table 1
Circulatory system; how can you include “undetected hypertension?” – whereas detected hypertension should surely be included in the circulatory organ system
Response 4
We agree. There is an inconsistency in table 1 presenting the conditions by ICD-10 chapter and appendix A and we are grateful that you notified us. In table 1 we changed as follows:
~~Undetected~~ Hypertension

Comment 5
Results:
Did you imagine stratifying the complexity of multimorbidity in your analyses? There may be a difference if a person suffered from 3 organ system – or from 5 or 6 or more?
Response 5
This is a good comment and something that we would like to pursue in forthcoming work. We mention the importance of exploring more measures of multimorbidity in the Discussion, Further research. However, in this study we sought to investigate one definition of complex multimorbidity, as stated at the end of Introduction. The rationale was that this measure is in line with former recommendations4 which also should have increased comparability.4
We find it valuable to add this concern to Discussion, Strengths and limitations:
The number of separate organ systems affected, could have been explored as a continuous measure or at other thresholds with assumed increasing severity, however this was beyond the scope of this study.

Comment 6
Discussion
Interpretation of the gender differences would be interesting.
Response 6
We agree that sex differences are important and stratifying by age and sex are considered minimum requirements for proper reporting of multimorbidity.15 We present prevalences by sex and age groups (table 3). However, in the main analysis on association between complex multimorbidity and occupational group, continuous age and an interaction term between occupational group and age was included in the models stratified by sex. Thus, the calculated prevalence differences and ratios between occupational groups are comparable within sex and age group, yet not between the sexes.
We notice that Discussion, Main findings, exaggerated the results from table 4. We have changed the last sentence of that paragraph from:
“Occupational group prevalence differences and ratios in complex multimorbidity were present in women until age 75 years and in men until age 90 years.”
to:
“Occupational group prevalence differences and ratios in complex multimorbidity were diminishing in women, while still present in men at age 75 years.”

Reviewer 2
Reviewer Name: Professor Tim Stokes
Institution and Country: University of Otago, New Zealand
Please state any competing interests or state ‘None declared’: None declared

Please leave your comments for the authors below
This study reports the prevalence of complex multimorbidity in a Norwegian population, using a large population-based health survey (HUNT-3: 2006-2008). It is a secondary analysis of this dataset.
Overall, there is now a large body of evidence on the prevalence of multimorbidity and complex multimorbidity in a wide range of populations and using different populations (e.g., data extraction from GP records; self-completion population surveys).
The study is therefore not original, though it is accepted that it adds to what we know about the prevalence of complex multimorbidity due to its county wide general population health survey approach.
Overall, the methods are appropriate and the results are reported appropriately. The discussion section is well structured and the strengths and limitations of the study are clearly set out. I have several minor suggested revisions.

Overall response
Thank you for approving the methods and presentation of the results in this study and for considering it to add knowledge on complex multimorbidity in a general population. Your precise comments on fundamental parts of the paper (abstract and introduction), definitions and references, were much appreciated. We find them to have enhanced the consistency, readability and appropriateness of the original manuscript.
Comment 1
There is a lack of clarity of the definition of "complex multimorbidity" in the abstract and body of the paper.
First, it is not strictly correct to define multimorbidity as "the co-occurrence of multiple LTCs in which none is more important". The source reference for this quote is both more precise and more nuanced - Boyd & Fortin Ref 1 - "Multimorbidity is defined as the co-existence of two or more chronic conditions, where one is not necessarily more central than the others". Note the need for 2 or more and "one is not necessarily more central than the others" is not the same as saying "none is more important".
I would therefore suggest that the Boyd and Fortin wording is either quoted verbatim or paraphrased in such a way as to keep the original intended meaning.
Second, when term "complex multimorbidity" is used it is important that its use is consistent with that recommended by Harrison et al. (Ref 13).

Response 1
It is unfortunate if the definitions of multimorbidity and complex multimorbidity seem different in the Abstract, Introduction and Methods section.
With regards to the first comment, we agree that, after several rounds of paraphrasing, the definition in Boyd and Fortin (ref. 1), does not reflect the content where it is quoted. We are grateful you noticed, so it could be corrected.
In the Abstract, the first sentence is altered from:
Multimorbidity, the co-occurrence of multiple long-term conditions that are all equally important, is common and increasing.
to:
Multimorbidity, the co-occurrence of multiple long-term conditions, none in priority, is common and increasing.
In the Introduction the first sentence is altered from:
“Multimorbidity, the cooccurrence of multiple long-term conditions in which none is more important,5
(Ref Boyd, 2010) is common and increasing.6, 7
”
to:

“Multimorbidity, the cooccurrence of multiple long-term conditions in which none holds priority8
(Ref Nicholson, 2019) is common and increasing.6, 7
”
As for the second comment, we agree that the definition of complex multimorbidity in the Abstract might have been unclear in terms of number of conditions needed to be identified with complex multimorbidity. In the Abstract, Objectives, the last sentence is changed from:
“We aimed to investigate complex multimorbidity (defined as chronic conditions in three or more organ systems) by sex and occupational groups throughout adulthood.”
to:
“We aimed to investigate the prevalence of complex multimorbidity by sex and occupational groups throughout adulthood.”
and in the Abstract, Outcome measure, we replaced:
“51 chronic conditions were grouped in 14 ICD-10 organ-specific chapters, and complex multimorbidity was identified as conditions in three or more organ systems.”
with the complete citation from Harrison et al, 2014:4

“Complex multimorbidity defined as “the co-occurrence of three or more chronic conditions affecting three or more different body [organ] systems within one person without defining an index chronic condition”.”
In the final paragraph in the Introduction we write:
“Our aim is to add to former knowledge by assessing the prevalence of complex multimorbidity, defined as three or more conditions in separate organ systems, in a general population health survey.”
We believe that this paraphrasing is sufficiently similar to the definition in Harrison et al, 2014,
4 although we do not specify the requirement of no index condition as this is given by the general definition of multimorbidity stated in the first sentence of the Introduction.
Comment 2
Introduction
p.5, LL23-31. This section needs rewording to make it clear the focus is on cross-sectional prevalence studies of multimorbidity.
Response 2
It is true that all content on determinants, specificity and comparability that we have referred to, are from cross-sectional prevalence studies (Uijen, 2008; Barnett, 2012; Harrison, 2014) or reviews of such observational studies (Fortin, 2012; Violan, 2014).
We altered the first sentence in the paragraph on p.5, LL23-31. from:
“Research results from multimorbidity studies has been difficult to compare because of differences in definitions, methods, and the number and types of conditions included.9, 10
”
To:
“Research results from cross-sectional studies on multimorbidity prevalence have been difficult to compare because of differences in definitions, methods, and the number and types of conditions included.9, 10
”
Comment 3
Introduction
p.5, LL23-31. The second half of this para needs rewording so as to state there is a need to define the prevalence of complex multimorbidity, why describing this prevalence matters and to define what is meant by this term here.

Response 3

We agree that the connection from the main text in Introduction to the final aim of the study could be more precise. We chose to rewrite the final paragraph of Introduction, from:

"In sum, multimorbidity represents a challenge both for the individual and clinician, as well as for the coordination of services within health care. Furthermore, demographic and socioeconomic gradients clearly operate. In Norway, multimorbidity prevalence and patterns have been partly explored.11 In this study, we investigate one definition of complex multimorbidity, three or more conditions in separate organ systems, throughout the adult life span by sex and occupational groups in a general population health survey."

to:

"In sum, multimorbidity represents a challenge both for the individual and clinician, as well as for the coordination of health care. Previous multimorbidity prevalence research suggests that demographic and socioeconomic gradients operate. In Norway, multimorbidity prevalence and patterns have been partly explored.
11 Studies
on complex multimorbidity is lacking, and no studies have investigated sociodemographic differences. Such data, can strengthen health care planning and clinical management of multimorbidity, as well as guide public health interventions. Our aim is to add to former knowledge by assessing the prevalence of complex multimorbidity, defined as three or more conditions in separate organ systems, by age, sex and occupational groups, in a general population health survey."

References

1. Statistics Norway. Standard Classification of Occupations. Oslo/Kongsvinger: Statistics Norway, 1998.
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3. Martikainen P and Valkonen T. Bias related to the exclusion of the economically inactive in studies on social class differences in mortality. Int J Epidemiol 1999; 28: 899-904. DOI: 10.1093/ije/28.5.899.
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multimorbidity: toward a more uniform methodology. Ann Fam Med 2012; 10: 142-151. 2012/03/14. DOI: 10.1370/afm.1337.
11. Tomasdottir MO, Getz L, Sigurdsson JA, et al. Co-and multimorbidity patterns in an unselected Norwegian population: Cross-sectional analysis based on the HUNT Study and theoretical reflections concerning basic medical models. European Journal for Person Centered Healthcare 2014; 2: 335-345.

VERSION 2 – REVIEW

REVIEWER	Herzig Lilli Departement of family medicine University of Lausanne Switzerland
REVIEW RETURNED	29-Mar-2020

GENERAL COMMENTS	I'm satisfied by the adaptation of the paper after the first review

REVIEWER	Professor Tim Stokes University of Otago, New Zealand
REVIEW RETURNED	16-Mar-2020

GENERAL COMMENTS	The authors have done an excellent job revising the paper and have fully addressed the reviewers' comments. I do, however, have a suggested change for the revised abstract for clarity: 1. The revision to the multimorbidity definition in the abstract now reads: "Multimorbidity, the co-occurrence of multiple long-term conditions, none in priority, is common and increasing." "none in priority" is not grammatically correct english, but more importantly, in the abstract, it is not necessary to add "none in priority". So the following will be fine in the abstract: "Multimorbidity, the co-occurrence of multiple long-term conditions, is common and increasing." The authors offer a correct definition in the introduction section.

VERSION 2 – AUTHOR RESPONSE

We found the first revision to improve the clarity of the paper and are happy that the reviewers are satisfied with how we addressed their comments. We thank for the correction and have altered the abstract as proposed by reviewer 2.
During the review process, we discovered the need to make a few minor changes as follows:
1. Overall: The name of the survey was corrected on two occasions from “the HUNT3 survey” to “the HUNT3 Survey” (capitol S).
2. Abstract, Results: Added -al to occupational.
3. Methods, Study population: Clarification of abbreviation, SD=standard deviation.
4. Figure 1: The legend was formatted according to BMJ Open recommended style.
5. Table 2: Removed “male”.

6. Discussion, Main results: Added a comma.
7. Discussion, Comparison with existing literature: Removed a hyphen.
8. Discussion, Strengths and limitations:
a. First paragraph: The reference 41 Marengoni, 2011 was replaced by 40, Willadsen, 2016.
b. Last paragraph: The reference 23 Krokstad, 2013 was added.
9. Conclusion: The heading was altered to CAPS LOCK, in line with BMJ Open formatting style.
Post manuscript:
10. Figures: Legends were changed to match figure legends in the text.
a. Figure 1: Changed from colon to semi-colon.
b. Figure 2: Changed to abbreviated form (95% CIs).
11. Funding statement: Information on funding was added:
The Liaison Committee for Education, Research and Innovation in Central Norway (17/38297) supported a research stay at the Australian National University, Canberra.
12. Supplementary files: An updated version of the appendix A was uploaded. The update includes more references on construction or accuracy of self-report of, or comparison of prevalence of the conditions to primary care and/or non-participant data.
13. References: Style was changed to "Vancouver", edited to list first 3 authors, in line with BMJ Open formatting guidelines.