PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Impact of noncommunicable disease multimorbidity on health service use, catastrophic health expenditure, and productivity loss in Indonesia: a population-based panel data analysis study
AUTHORS	Marthias, Tiara; Anindya, Kanya; Ng, Nawi; McPake, Barbara; Atun, Rifat; Arfyanto, Hafiz; Hulse, Emily; Zhao, Yang; Jusril, Hafizah; Pan, Tianxin; Ishida, Marie; Lee, John

VERSION 1 – REVIEW

REVIEWER	Barbara de Graaff Menzies Institute for Medical Research University of Tasmania Australia
REVIEW RETURNED	16-Oct-2020

| GENERAL COMMENTS | A very interesting study that is generally very well written, with methods clearly described. Overall- a pleasure to read. One of my main comments is that I think the authors should consider the influence of BMI on their results. More information provided in a specific comment below.
Abstract: Please add information about the statistical methods used. Also, the start of the sentence "Multimorbidity increased with sex…" what does this actually mean?
Please specify in the abstract that only NCDs are considered to be multimorbid conditions.
Introduction: please include some background information on the health system in Indonesia- including who pays for what types of services that are relevant to this study and health insurance.
Methods
Were costs for medication collected?
Was ethical approval required/obtained for this study? Please comment in the paper.
Results
line 240: The authors state "Overall the prevalence of multimorbidity increased…" Given the 95%CI that overlap, was there really an increase or did the rate remain stable?
The results are interesting- higher multimorbidity associated with higher socioeconomic status. I am interested to know if overweight/obesity was more common across the higher SES groups? As high BMI is associated with increased multimorbidity (particularly most of the NCDs included in this study), and high BMI in LMICs is frequently observed amongst higher SES groups, it would be interesting to know if this is an explanatory factor. Is multimorbidity a function of high BMI (yes!)?
Without understanding the health system and costs in Indonesia, it is difficult to clearly understand the health service use. What are the barriers for low SES people accessing health services? |

Regarding multimorbidity and productivity loss (line 316), the authors state … "among those aged 50-60 years old, only 49.8% of responders with three or more NCDs were employed, compared with 84.3% of respondents with no NCDs." And line 325 notes that 3+ NCDs was associated with lower rate of employment. The authors report that multimorbidity is higher in females- I am wondering if the relatively low ~50% female labor force participation rate may influence this observation. Was this addressed in any way?

Discussion

The section begins by stating almost one in four Indonesian people …. have at least 2 NCDs. In line 224 the authors state that the statistical method used was selected to test associations- not to provide nationally representative estimates. In addition, as the initial sampling strategy was developed in 1993 and rapid and substantial changes have occurred in the demographics of Indonesia, is this statement above valid?

The finding that more NCDs are observed in higher SES groups (line 350)- I strongly recommend the authors explore the impact of obesity relating to this finding. In turn- the observation that higher numbers of NCDs are associated with higher use of healthcare use- is this a function of their ability to pay, compared with people

REVIEWER	Ingmar Schäfer
	University Medical Center Hamburg-Eppendorf, Germany
REVIEW RETURNED	11-Nov-2020

GENERAL COMMENTS	This is an interesting article about the multimorbidity in the specific situation in Indonesia. However, I have some concerns, which you should address.
	My biggest concern is the positive association between socioeconomic status and multimorbidity (line 354-362). You should shed more light on this association. Please discuss which diseases are responsible for the increase of multimorbidity in patients with higher socioeconomic status. Please emphasise in the limitations section that you measure multimorbidity by diagnosis and not by disease burden. Could it be that patients with lower socioeconomic status have a higher disease burden because diseases become diagnosed if they have progressed much further than diseases in higher status groups? I would also be interested if catastrophic health expenditure and productivity loss is higher in patients with lower socioeconomic status – an analysis of the interaction between these variables would be helpful.
	My second concern relates to the implications of the study results. I am not convinced that a guideline for multimorbidity would improve care as much as the authors suggest (line 400-414). There are much too many possible diseases and disease interactions to consider, so that recommendations in the published multimorbidity guideline are usually very general and rarely give specific advise. It therefore will still be necessary to use the disease-specific guidelines. While a guideline for multimorbidity may be a first step to improve care, disease-specific guidelines also need to consider multimorbidity and give recommendations for known constellations of comorbid diseases.
	Further points that need revision:

	- ln. 47: "Multimorbidity increased with sex, …" Sex is no hierarchical variable – better use a sentence like "Women were more likely to have multimorbidity than men." - ln 49: Please explain NCD in the abstract. - ln 176-185: Please clarify how the thresholds apply in the formula. It is not clear, if cataH=1 under the condition HSh/THEh>10% or HSh/CTPh>25%? Or is cataH=1 under the condition HSh/THEh>10% or >25% or HSh/CTPh>40%? In the results sections this becomes clearer, but it needs to be better explained in the methods section. - ln. 420-422: Self-repots may not only lead to underreporting, but also to over- or misreporting. - The article needs professional copyediting by a native speaker.

VERSION 1 – AUTHOR RESPONSE

Comments from Reviewer # 1:

Reviewer: 1
Reviewer Name: Barbara de Graaff
Institution and Country: Menzies Institute for Medical Research
University of Tasmania
Australia
Competing interests: None declared

General comments:

A very interesting study that is generally very well written, with methods clearly described. Overall- a pleasure to read. One of my main comments is that I think the authors should consider the influence of BMI on their results. More information provided in a specific comment below.

Thank you for the constructive comments, please see our response below.

Abstract:

Q1. Please add information about the statistical methods used.

We have now revised the abstract section, highlighting the statistical approaches used in this study.

Q2. Also, the start of the sentence "Multimorbidity increased with sex…" what does this actually mean?

We apologise for being unclear. Our results indicated that a higher prevalence of NCD multimorbidity was observed among women compared to men. We have changed the wording to clarify this throughout the paper.

Q3. Please specify in the abstract that only NCDs are considered to be multimorbid conditions.

Thanks for the helpful suggestion. We have added the term 'NCD' in the abstract and the title of the manuscript to make this clearer.

Introduction:

Q1. Please include some background information on the health system in Indonesia- including who pays for what types of services that are relevant to this study and health insurance.

Thank you for this important point. We have revised our introduction section highlighting health system in Indonesia, including information on health financing and health service coverage in the public health insurance programme (page 5 and 6).

Methods
Q1. Were costs for medication collected?

We would like to confirm that the total OOP variable used in our study include all costs associated with inpatient/outpatient visit, including medication, medical consultation, etc. We have also included this information in the Methods section (on page 9).

Q2. Was ethical approval required/obtained for this study? Please comment in the paper.

This study utilised an existing dataset, Indonesia Family Life Survey (IFLS), that is publicly available and did not contain any identification of the respondents, therefore does not require ethical review. However, the IFLS survey itself was conducted under the approval of the ethics review boards at RAND Corporation and the Gadjah Mada University in Indonesia. And thus, the survey complied to ethical standards and sought informed consent from all respondents prior to data collection. We have now included this information in the Ethics Approval section on page 22.

Results
line 240: The authors state "Overall the prevalence of multimorbidity increased…" Given the 95%CI that overlap, was there really an increase or did the rate remain stable?

We agree with the comment, and we have now revised our original sentence to the following: 'A similar prevalence of NCD multimorbidity was observed between 2007 (21.0%, 95% CI 19.6-22.6) and 2014 (22.0%, 95% CI 20.6–23.6).' (page 12, line 257).

The results are interesting- higher multimorbidity associated with higher socioeconomic status. I am interested to know if overweight/obesity was more common across the higher SES groups? As high BMI is associated with increased multimorbidity (particularly most of the NCDs included in this study), and high BMI in LMICs is frequently observed amongst higher SES groups, it would be interesting to know if this is an explanatory factor. Is multimorbidity a function of high BMI (yes!)?

We thank you for this comment. We have now tested whether BMI was associated with multimorbidity in our dataset and found a positive relationship between BMI and prevalence of multimorbidity as expected. However, we would like to clarify that the purpose of the study is to understand the effect of multimorbidity on health service utilisation and employment productivity. Therefore, to avoid over-adjusting and potential multicollinearity, we did not include behavioural risk factors as covariates in our regression models. This approach (i.e. not include behaviour risk factor as covariates) was similar to other studies that look at the economic burden of multimorbidity in other countries (Lee et al. 2015; Kuo & Lai 2013; Schäfer et al. 2012; Picco et al. 2016).

Without understanding the health system and costs in Indonesia, it is difficult to clearly understand the health service use. What are the barriers for low SES people accessing health services?

Thank you for this, we have added a brief overview of the Indonesia health system and barriers to services in the Introduction section (page 5 and 6). We also highlighted the fact that Indonesia health care delivery is highly fragmented and hospital-centred. Studies have reported that patients have to navigate through a plethora of health care provider to received treatment, and sometimes lead to a significant delay in medical diagnoses, especially among the poorer population.

Discussion
The section begins by stating almost one in four Indonesian people …. have at least 2 NCDs. In line 224 the authors state that the statistical method used was selected to test associations- not to provide nationally representative estimates. In addition, as the initial sampling strategy was developed in 1993 and rapid and substantial changes have occurred in the demographics of Indonesia, is this statement above valid?

According to IFLS website, the sample is representative of about 83% of the Indonesian population and contains over individuals living in 13 of the 27 provinces in the countries. We have now revised our manuscript by not generalising the findings to the Indonesian population.

The finding that more NCDs are observed in higher SES groups (line 350)- I strongly recommend the authors explore the impact of obesity relating to this finding. In turn- the observation that higher numbers of NCDs are associated with higher use of healthcare use- is this a function of their ability to pay, compared with people

Thank you, we have added an explanation of the prevalence of obesity across the SES groups in the Discussion section (page 16, line 357). And yes, the possible higher use of health care among higher SES groups was already explained in the Discussion section as well (page 17).

Comments from Reviewer # 2
Reviewer Name: Ingmar Schäfer
Institution and Country: University Medical Center Hamburg-Eppendorf, Germany
Please state any competing interests or state 'None declared': None declared

General Comments

This is an interesting article about the multimorbidity in the specific situation in Indonesia. However, I have some concerns, which you should address.

My biggest concern is the positive association between socioeconomic status and multimorbidity (line 354-362). You should shed more light on this association. Please discuss which diseases are responsible for the increase of multimorbidity in patients with higher socioeconomic status.

We agree with this comment and have now included the following sentence to discuss the 'mixed' findings of socioeconomic patterning on multimorbidity in LMICs (page 16).

"Analyses of socioeconomic gradients of NCDs in HICs routinely find negative socioeconomic gradients. However, this is not the case for LMICs, which have a more mixed pattern of the distribution of risk factors.[30,31] Other studies find a similar picture with diabetes and cardiovascular diseases in LMICs undergoing epidemiological transition.[31] These conditions predominate in high-income quintiles in the early stages of transition. We also found that obesity was more prevalent in wealthier quintiles (results not shown), which may explain the socioeconomic gradients of NCDs as obesity is associated with several NCDs included in this study, e.g. cardiovascular diseases, hypertension, stroke, cancer, arthritis and hypercholesterolemia.[32] Our results on socioeconomic patterning of multimorbidity can also be explained by the fact that higher-income and higher-educational groups, who have better access to healthcare services and better health literacy, are more likely to have NCDs diagnosed (or even over-diagnosed) than lower socio-income groups. Further studies are required to explore socioeconomic patterning of individual NCDs, including mental health condition, and physical-mental multimorbidity."

Please emphasise in the limitations section that you measure multimorbidity by diagnosis and not by disease burden. Could it be that patients with lower socioeconomic status have a

higher disease burden because diseases become diagnosed if they have progressed much further than diseases in higher status groups?

We appreciate this comment and have included this point as a limitation of the study (Page 18-19) as follow:

"The use of self-reported diagnoses also limit our assessment of the actual severity of the diseases, which may vary across socioeconomic status. It is warranted for future studies to consider the severity of the disease by using different datasets (such as clinical dataset from the hospital) and applying clinical metrics such as Charlson index, which could capture the diseases severity and predict the health outcomes more objectively."

I would also be interested if catastrophic health expenditure and productivity loss is higher in patients with lower socioeconomic status – an analysis of the interaction between these variables would be helpful.

While it is an interesting comment, we prefer not to include this analysis as our study primarily interested in the effect of multimorbidity for the entire population in Indonesia.

My second concern relates to the implications of the study results. I am not convinced that a guideline for multimorbidity would improve care as much as the authors suggest (line 400-414). There are much too many possible diseases and disease interactions to consider, so that recommendations in the published multimorbidity guideline are usually very general and rarely give specific advise. It therefore will still be necessary to use the disease-specific guidelines. While a guideline for multimorbidity may be a first step to improve care, disease-specific guidelines also need to consider multimorbidity and give recommendations for known constellations of comorbid diseases.

An increasing number of countries are developing their own clinical guideline for multimorbidity to suit local population and context. We would like to clarify that while clinical guideline for multimorbidity is essential for the prevention and treatment of multimorbidity in Indonesia, existing clinical guideline for single NCD (such as diabetes) still has a very important role to play. We have now revised our discussion section as the following (page 19-20):

"Similar to many LMICs and neighbouring countries in Asia, healthcare delivery in Indonesia remains fragmented and hospital centred, with little coordination among healthcare providers across different tiers of the system.[1] Health systems need to shift from single-disease models to new methods of financing and service delivery to more effectively manage multimorbidity.[1,2] Strong primary health care, underpinned by multidisciplinary teams lead by a general practitioner, is also crucial for the improved prevention and treatment of multimorbidity.[1] Evidence from high-income countries (HICs) suggested that people-centred integrated care for multimorbidity patients can sometimes be cost-effective. However, there may be dangers in extrapolating findings from HICs to LMICs where

healthcare delivery differs significantly. It is also worth noting that Indonesia are still facing the double burden of infectious and chronic diseases. Therefore, multimorbidity care delivery model in LMICs also needs to pay attention to the management of NCDs with infectious disease. Rigorous evaluation of these new healthcare delivery models is warranted to ensure effectiveness, efficiency, and quality of care."

- ln. 47: "Multimorbidity increased with sex, …" Sex is no hierarchical variable – better use a sentence like "Women were more likely to have multimorbidity than men."

Thank you for this comment. We would like to clarify that we observed a higher prevalence of NCD multimorbidity among women compared to men. We have changed the abstract accordingly.

- ln 49: Please explain NCD in the abstract.

We have clarified in the abstract that this study is about NCD multimorbidity.

- ln 176-185: Please clarify how the thresholds apply in the formula. It is not clear, if cataH=1 under the condition HSh/THEh>10% or HSh/CTPh>25%? Or is cataH=1 under the cond'ition HSh/THEh>10% or >25% or HSh/CTPh>40%? In the results sections this becomes clearer, but it needs to be better explained in the methods section.

Thank you for the comment, we have added clarifications in the Methods section 'In using the proportion of total OOPE for health to total household expenditure (THE), the threshold z was set at 10% and 25%. Further, in using the proportion of OOPE for health to capacity to pay (CTP), the threshold z was set at 40%.' (page 9, line 202–205).

- ln. 420-422: Self-repots may not only lead to underreporting, but also to over- or misreporting.

Thank you, and we agree with this, previous studies have also stated such biases. We have amended our statement on this 'This may cause misreporting of the true diagnoses and prevalence of multimorbidity.' (page 18, line 425-426).

- The article needs professional copyediting by a native speaker.

Thank you for this comment. The revised manuscript has now been carefully copyedited by two co-authors who are native speakers.

VERSION 2 – REVIEW

REVIEWER	Barbara de Graaff Menzies Institute for Medical Research University of Tasmania Australia
REVIEW RETURNED	02-Jan-2021

GENERAL COMMENTS	Thank you for addressing my comments. I am happy with all changes. There remains a small number of language edits to be undertaken. The only question that I have, is on pg 17 line 340: for which year are these OOPE costs related to?

VERSION 2 – AUTHOR RESPONSE

Comments from Reviewer 1:

Reviewer Name: Barbara de Graaff

Institution and Country: Menzies Institute for Medical Research

University of Tasmania

Australia

Competing interests: None declared

Thank you for addressing my comments. I am happy with all changes. There remains a small number of language edits to be undertaken.

Thank you. The revised manuscript has now been carefully edited.

The only question that I have, is on pg 17 line 340: for which year are these OOPE costs related to?

We appreciate this question. We would like to clarify that the recall period of OOPE for outpatient and inpatient care was four weeks and a year prior to the interview, respectively. The OOPE shown in the "Multimorbidity and financial burden" sub-section was based on the 2014 IFLS (Wave 5), which conducted between September 2014–March 2015. We have now included this information on page 13:

"Table 2 presents the mean OOPE based on 2014 IFLS." (page 13, line 298)