PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Prevalence of chronic conditions and multimorbidity in Estonia: a population-based cross-sectional study
AUTHORS	Jürisson, Mikk; Pisarev, Heti; Uusküla, Anneli; Lang, Katrin; Oona, M; Kalda, Ruth

VERSION 1 – REVIEW

REVIEWER	Nunes, BP Universidade Federal de Pelotas, Department of Nursing
REVIEW RETURNED	25-Mar-2021

GENERAL COMMENTS	The paper is well designed, written and fits all reporting requirements. However, there is no huge novelty apart of the quality of administrative health data. The authors have cited several papers which inform MM prevalence (including a systematic review) and results from Estonia (Share study). The background section presented this context but the rationale for the study is poorly addressed. Furthermore, authors did not use additional variables to figure out a big picture of multimorbidity in Estonia (e.g., education, wealth index, effects on health services utilization…). The study has a one greater strength but could be improved by more clear rationale and additional analysis to fill gaps in the literature better contextualizing Estonia's scenario. Minor comments: - The term "multimorbid" could be avoided. - Page 13, Line 30: see "82/3"

REVIEWER	Nicholson, Kathryn Western University
REVIEW RETURNED	18-Apr-2021

GENERAL COMMENTS	Thank you for the opportunity to review the manuscript entitled "Prevalence of chronic conditions and multimorbidity in Estonia: a population-based cross-sectional study" -- requested revisions are included below and I would be happy to review a resubmission. Abstract -Please change "gender" to "sex" -Please change "during 2015-2017" to "from 2015 to 2017" -Please change "(≥85)" to "(≥85 years)" -Please change "was by far the most" to "was the most" -Please change "this leading MM" to "this most common condition within the context of MM"

Background
-Please change "as most of those with long-term disorders are multimorbid" to "as most individuals with long-term conditions are living with multiple long-term conditions"
-Please change "management of patients with multimorbidity (MM)" to "management of patients with MM"
-Please remove "as most individuals presenting with long-term chronic conditions are MM"
-Please change "distribution of comorbid conditions" to "distribution of co-occurring conditions"
-Please change "of patients were multimorbid" to "of patients were living with multimorbidity"
-Please clarify if the prevalence estimates "37.9% adn 29.7%" were for the overall sample and for which specific age range
-Please move the "SHARE" acronym directly after the study name
-Please change "administrative health data is necessary" to "the use of administrative health data is necessary"
-Please change "burden of multimorbid chronic disease" to "burden of co-occurring chronic disease"
-Please change "be an important contributor" to "is an important contributor"
-Please change "by age and gender" to "by age and between males and females"

Methods
-While the background about the health of men and women in Estonia is very much appreciated, please how individuals may be uninsured
-Please change "prevalence of chronic disorders" to "prevalence of chronic conditions"
-Please change "mean number of disorders" to "mean number of chronic conditions"

Results
-Please change "prevalence of chronic conditions increased" to "prevalence of MM increased"
-Please change "in the age of 0-24" to "among those younger than 25 years"
-Please change "among those aged 85+" to "among those 85 years and older"
-Please change "was by far the most frequent" to "was the most frequent"

Discussion
-Please clarify what is meant by "82/3"
-Please change "hypertension is the most" to "hypertension was the most"
-Please change "resulted in an overall" to "calculated an overall"
-Please change "by far the most frequent" to "the most frequent"

VERSION 1 – AUTHOR RESPONSE

Reviewer 1
Dr. BP Nunes, Universidade Federal de Pelotas

Response:

Thank you for the comment. We agree that this rationale is poorly articulated. We had initially addressed this issue in the Background session as follows:

"Although research is beginning to elucidate the distribution of comorbid conditions in these countries, the comparability of findings is limited by methodological differences. This study presents an important contribution to this developing literature with a comprehensive set of prevalence estimates for MM in Eastern Europe."

However, we have more fully articulated the specific rationale for the study by including these additional references and content such that this section now reads as follows:

"Although research is beginning to elucidate the distribution of comorbid conditions in these countries, the comparability of findings is limited by methodological differences. This work demonstrates the utility of administrative data for constructing prevalence estimates, an approach that is particularly helpful for middle and high-to-middle-income-countries where resource limitations make administrative data not only immediately useful but also scalable, allowing for rate comparisons with other countries. In addition, the transition from a hospital-centric system in Estonia following independence from the Soviet Union was motivated by a desire to strengthen primary health care and thereby improve population health [1]. Having a set of prevalence estimates for MM is essential for measuring the ongoing success of this transition, adjusted by the prevalence of various conditions amenable to outpatient treatment. Finally, and perhaps most importantly, the SARS-CoV-2 pandemic drew attention to the important contribution of MM to the need for sound public health measures and rapid identification of effective medical interventions based on risk stratification. Frailty has been linked to infection [2], severity [2,3], geographic differences in severity and mortality by MM [4], prompting a renewed focus on improving global health and access to care, probabilistic modelling [5], the triage of care and shielding of the most vulnerable [6]. This study presents an important contribution to this developing literature with a comprehensive set of prevalence estimates for MM in Eastern Europe."

References:

1 Atun R, Gurol–Urganci I, Hone T, et al. Shifting chronic disease management from hospitals to primary care in Estonian health system: analysis of national panel data. J Glob Health 2016;6. doi:10.7189/JOGH.06.020701

2 Chudasama Y V., Gillies CL, Appiah K, et al. Multimorbidity and SARS-CoV-2 infection in UK Biobank. Diabetes Metab Syndr 2020;14:775. doi:10.1016/J.DSX.2020.06.003

3 M H, L J, R A, et al. The Association between Presence of Comorbidities and COVID-19 Severity: A Systematic Review and Meta-Analysis. Cerebrovasc Dis 2021;50:132–40. doi:10.1159/000513288

4 Thakur B, Dubey P, Benitez J, et al. A systematic review and meta-analysis of geographic differences in comorbidities and associated severity and mortality among individuals with COVID-19. Sci Reports 2021 111 2021;11:1–13. doi:10.1038/s41598-021-88130-w

5 Clark A, Jit M, Warren-Gash C, et al. Global, regional, and national estimates of the population at increased risk of severe COVID-19 due to underlying health conditions in 2020: a modelling study. Lancet Glob Heal 2020;8:e1003–17. doi:10.1016/S2214-109X(20)30264-3

6 Fernández-Niño JA, Guerra-Gómez JA, Idrovo AJ. Multimorbidity patterns among COVID-19 deaths: proposal for the construction of etiological models. Rev Panam Salud Pública 2020;44. doi:10.26633/RPSP.2020.166

7 Fortin M, Stewart M, Poitras M-E, et al. A systematic review of prevalence studies on multimorbidity: toward a more uniform methodology. Ann Fam Med 2012;10:142–51. doi:10.1370/afm.1337

Six papers (manuscript references 15 to 20) have now been added to the paper.

Comment 2:

Furthermore, the authors did not use additional variables to figure out a big picture of multimorbidity in Estonia (e.g., education, wealth index, effects on health services utilization…). The study has one greater

strength but could be improved by a more clear rationale and additional analysis to fill gaps in the literature better contextualizing Estonia's scenario.
Response:
Thank you for the comment. We acknowledge that MM is a complex phenomenon with a mix of various causes and modifiers that can be used for better defining the risk groups and understanding different aspects of the condition. Using patient-reported data provides an important insight into the patient-reported outcome measures and socioeconomic/health behavior-related variables (such as education, income, cohabitation, physical activity, body mass index) at the cost of precision of the estimates. Using administrative health data, on the other hand, increases the precision of estimates, but reduces the number of assessed variables as the data are not readily available from the administrative databases. For example, the income estimates are not routinely collected from all individuals in the health system framework. Alternatively, we could use Electronic Health Records to assess the basic health parameters that are not available from the routine administrative data (such as systolic blood pressure, cholesterol level, etc), but that type of population-based analysis is a major undertaking associated with additional IT and data privacy related questions that can be addressed in future study programs. The wealth index is another valuable source of information, but considering the small low-density population and geography the index is not available in Estonia.
However, we believe that using the population-based administrative health data including all diagnoses on in- and outpatient health care claims and prescriptions is a valuable source of assessing the prevalence of MM in the country and provides valid comparisons.

Comment 3:
The term "multimorbid" could be avoided. Response: Corrected, thank you.
Comment 4:
Page 13, Line 30: see "82/3". Response: changed to "66%".

Reviewer 2
Dr. Kathryn Nicholson, Western University

Comments:
Abstract
Please change "gender" to "sex". Response: Changed
Please change "during 2015-2017" to "from 2015 to 2017". Response: Changed
Please change "(≥85)" to "(≥85 years)". Response: Changed
Please change "was by far the most" to "was the most". Response: Changed
Please change "this leading MM" to "this most common condition within the context of MM". Response: Changed
Background
Please change "as most of those with long-term disorders are multimorbid" to "as most individuals with long-term conditions are living with multiple long-term conditions". Response: Changed
Please change "management of patients with multimorbidity (MM)" to "management of patients with MM". Response: Changed
Please remove "as most individuals presenting with long-term chronic conditions are MM". Response: removed
Please change "distribution of comorbid conditions" to "distribution of co-occurring conditions". Response: Changed
Please change "of patients were multimorbid" to "of patients were living with multimorbidity". Response: Changed
Please clarify if the prevalence estimates "37.9% and 29.7%" were for the overall sample and for which

specific age range. Response: the pooled estimates for HIC and LMIC were for both men and women of all ages. To enable the meta-analysis of data from various studies with different age ranges with no uniformity in the way age and sex were presented the authors adjusted for those variables using the method by Fortin, et al [7].

Please move the "SHARE" acronym directly after the study name. Response: corrected.

Please change "administrative health data is necessary" to "the use of administrative health data is necessary". Response: Changed

Please change "burden of multimorbid chronic disease" to "burden of co-occurring chronic disease". Response: Changed

Please change "be an important contributor" to "is an important contributor". Response: Changed

Please change "by age and gender" to "by age and between males and females". Response: Changed

Methods

While the background about the health of men and women in Estonia is very much appreciated, please how individuals may be uninsured.

Response: the Estonian Health Insurance Fund provides insurance for children and students, working adults, and those in retirement (aged 64 and above). For the unemployed, the health insurance will terminate after nine months from the start of the unemployment period.

Please change "prevalence of chronic disorders" to "prevalence of chronic conditions". Response: Changed

Please change "mean number of disorders" to "mean number of chronic conditions". Response: Changed

Results

Please change "prevalence of chronic conditions increased" to "prevalence of MM increased". Response: The prevalence of chronic conditions refers to the prevalence of any chronic condition that includes (besides MM) also the individuals with one chronic condition. We, therefore, changed the "prevalence of chronic conditions" to "prevalence of any chronic condition".

Please change "in the age of 0-24" to "among those younger than 25 years". Response: Changed

Please change "among those aged 85+" to "among those 85 years and older". Response: Changed

Please change "was by far the most frequent" to "was the most frequent". Response: Changed

Discussion

Please clarify what is meant by "82/3". Response: we corrected that to "66%".

Please change "hypertension is the most" to "hypertension was the most". Response: Changed

Please change "resulted in an overall" to "calculated an overall". Response: Changed

Please change "by far the most frequent" to "the most frequent". Response: Changed

VERSION 2 – REVIEW

REVIEWER	Nunes, BP
	Universidade Federal de Pelotas, Department of Nursing
REVIEW RETURNED	26-Jul-2021

| GENERAL COMMENTS | The authors have addressed all my comments. |

REVIEWER	Nicholson, Kathryn
	Western University
REVIEW RETURNED	13-Aug-2021

| GENERAL COMMENTS | Thank you for the opportunity to review the manuscript entitled "Prevalence of chronic conditions and multimorbidity in Estonia: a population-based cross-sectional study" -- I have included |

suggested revisions below and I would be happy to review a resubmission.

Introduction:
-it is suggested that social deprivation and ethnicity are listed with the other sociodemographic factors

Methods:
-please clarify how a 6-week interval between the diagnoses would reduce double-counting as this interval is only used within diagnoses (for example, would a hypertension diagnosis only be counted once, regardless of the timing of the diagnoses)
-it is suggested that the authors incorporate an assessment of which conditions tend to co-occur together most frequently, especially with the large sample size (or please clarify why this was not done)

Results:
-it is suggested that either one or two decimal points are used throughout

Discussion
-it would be helpful to add age comparisons between the study in Scotland and this study in Estonia when comparing MM prevalence
-please change "age 25+" to "aged 25+ years"
-please clarify if "to reflect diagnostic practices" refers to regional diagnostic practices

VERSION 2 – AUTHOR RESPONSE

Reviewer 1, Dr. BP Nunes, Universidade Federal de Pelotas
Comments to the Author:
The authors have addressed all my comments.
Response: thank you very much for your suggestions throughout the submission.

Reviewer 2, Dr. Kathryn Nicholson, Western University
Comments to the Author:
Thank you for the opportunity to review the manuscript entitled "Prevalence of chronic conditions and multimorbidity in Estonia: a population-based cross-sectional study" -- I have included suggested revisions below and I would be happy to review a resubmission.
Comment 1. Introduction: it is suggested that social deprivation and ethnicity are listed with the other sociodemographic factors.
Response: Thank you for this comment, we have amended the text accordingly: "In addition to aging, MM is associated with other sociodemographic factors, such as female sex, lower education, lower household income, living alone, social deprivation and ethnicity, as well as health conditions, such as obesity, hypertension, having one chronic condition at baseline."
Comment 2. Methods: Please clarify how a 6-week interval between the diagnoses would reduce double-counting as this interval is only used within diagnoses (for example, would a hypertension diagnosis only be counted once, regardless of the timing of the diagnoses).

Response: Thank you for the comment, we recognized that the issue of double-counting was misleading and removed it from the text which now appears like this: "The 6-week interval between the diagnoses reduced over-ascertainment of cases."

Comment 3. 'Methods: It is suggested that the authors incorporate an assessment of which conditions tend to co-occur together most frequently, especially with the large sample size (or please clarify why this was not done).

Response: Thank you for the recommendation. We agree that the clustering analysis is very important for revealing the frequently co-occurring conditions, and confirm that the respective analysis is in the process. However, as the objective of the current paper was to estimate the MM burden in general, we are planning to elaborate on clustering in a forthcoming research paper.

Comment 4. Results: It is suggested that either one or two decimal points are used throughout.

Response: We have used one decimal point for prevalence percentage, and two decimal points for the means (along with 95% CI-s). The reason is that while the prevalence numbers are relatively high the numbers of conditions are small and require two decimals for precision. For better comparison, we followed the research practice from Scotland (Barnett, et al) who used a similar categorization for multimorbidity estimates (Table 1).

Table 1. Mean number of morbidities and the prevalence of multimorbidity [1]
1 Barnett K, Mercer SSW, Norbury M, et al. Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study. Lancet 2012;6736:37–43. doi:10.1016/S0140-6736(12)60240-2.

Comment 5. Discussion: It would be helpful to add age comparisons between the study in Scotland and this study in Estonia when comparing MM prevalence.

Response: Thank you for the suggestion. We have added a sentence about age comparison:

Age group comparisons reveal that MM is more prevalent in Estonia in all age groups, especially in 45-64 years (41.0% in Estonia vs 30.4% in Scotland) and 65-84 years (71.1% vs 64.9%), except for the ≥85 years age group, where it is very similar (80.4% vs 81.5%).

Comment 6. Please change "age 25+" to "aged 25+ years"

The wording has been changed accordingly: "We found that in women aged 25+ years,"

Comment 7. Please clarify if "to reflect diagnostic practices" refers to regional diagnostic practices

Yes, the diagnostic practices refer to the regional practices. We have corrected the wording accordingly: "We used the list of conditions from previous research with only minor adjustments to reflect the regional diagnostic practices".

VERSION 3 – REVIEW

REVIEWER	Nicholson, Kathryn Western University
REVIEW RETURNED	19-Sep-2021

GENERAL COMMENTS	Thank you for the opportunity to review the manuscript entitled "Prevalence of chronic conditions and multimorbidity in Estonia: a population-based cross-sectional study". I have no other requested revisions following the authors' responses and I believe that the manuscript is ready for publication.