

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	The association between submarine service and multi-morbidity: a cross-sectional study of Korean naval personnel
AUTHORS	Kang, Jihun; Song, Yun-Mi

VERSION 1 - REVIEW

REVIEWER	Amy Flaxman University of Oxford, UK
REVIEW RETURNED	20-May-2017

GENERAL COMMENTS	<p>General Comment: This manuscripts compares multimorbidity and disease burden in a Korean submarine population. The study is well designed and the data well presented. The authors find that submarine service was significantly associated with increased risk of multimorbidity and disease burden compared to non-submarine navy personnel. There is no comparison to non-naval personnel of the same age group. This should be discussed as a limitation, since differences in multimorbidity and disease burden may well exist between non-navy personnel and non-submarine and submarine personnel.</p> <p>Specific Comments:</p> <ol style="list-style-type: none">1. In your description of Table 2 in the results, state that number of Chronic health problems and CIRS scores were significantly higher in submariners versus non-submariners, across all age groups.2. First sentence of the Discussion "compared to previous studies", please provide references to examples of previous studies.3. The sentence in the Discussion which begins "When we excluded current smokers and obese subjects from each CIRS domain" would be better placed in the results section. Also, can the data described here be made available in a Supplementary Table?4. In the Discussion "the duration of submarine service was positively associated with the prevalence of multi-morbidity" it would be beneficial to include a sentence discussing the fact that whilst overall duration of submarine service is positively associated with multi-morbidity, multi-morbidity actually falls from the 1-4years and 5-9years and then increases further in the >10years group.5. In the Discussion "submarine duty did not increase the risk of hospitalization in 16 major diagnostic categories and submarine-associated diagnoses", the list of these 16 categories and diagnoses is unnecessary.6. I believe the STROBE checklist for cohort studies should be completed.
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REVIEWER	Trousselard Marion Institut de recherche biomédicale des armées Brétigny sur orge cedex France
REVIEW RETURNED	05-Jun-2017

GENERAL COMMENTS	<p>Authors did not take into account prolonged shift and night work and with as a risk factors. This point must be discussed.</p> <p>The importance of social isolation from the real world (with no phone or internet contact with families or friends during a routine mission) may be evaluated by the number of children and the marital status ? Information about the number of mission stressful events should be of interest for exploring health status difference between the two populations</p>
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REVIEWER	Dr Michael Waller School of Public Health, University of Queensland, Australia
REVIEW RETURNED	23-Jun-2017

GENERAL COMMENTS	<p>1. It would be good to know what proportion of Submariners would access the primary care clinic to understand whether the study results are generalisable to 'all Korean submariners' or whether this group is likely to be in poorer health than other submariners?</p> <p>Methods</p> <p>2. Are the conditions listed in page 7 last paragraph, the full list of conditions? It is good practice to include a full list of conditions considered for extraction.</p> <p>3. Expand the methods to include details on how medical records were used to extract diagnosis of multimorbidity (e.g. pathology reports, listed as an ongoing condition). How far back did you review their medical history based on their records? How complete were the records? For the questionnaire, provide details of how the questions were asked and coded (e.g. Has a Doctor diagnosed or treated you for the following conditions? response Present or absent). Explain how data extraction was blinded so that submariner status was not known when collecting information on medical conditions. If this was not the case, acknowledge this as a potential source of bias in the Discussion.</p> <p>3. Give information on the age-strata Page 9 line 4.</p> <p>4. How was alcohol use measured.</p> <p>5. Page 8: Describe how disease burden is used and categorised in the methods section. Why CIRS\geq3?</p> <p>6. From table 3, it seems like non-submariners are included in the analysis. Are all zero years of submarine service non-submariners? Given the health and recruitment differences between submariners and non submariners, it might be worthwhile to perform your "model 1 and 2" by year of submarine service limited to submariners as a sensitivity analysis or the primary analysis. Without the inclusion of the non-submariners I imagine the relationship between submarine service length and multimorbidity would be markedly reduced. From</p>
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	<p>the results currently shown, although the test for trend is significant there is no consistent dose response relationship between length of service and multimorbidity.</p> <p>7. Is your study population exclusively male? If so state this.</p> <p>Results</p> <p>8. Clarify who "Other ranks" are? Lower ranks?</p> <p>9. "With increasing years of submarine service, the risk of having multi-morbidity and high disease burden (CIRS score of ≥ 3) tended to increase (P for trend (< 0.001))." This statement can be considered misleading as it implies submariner population but non-submariners are included in the analysis. (See point 6).</p> <p>10. Table 2. I presume 2+ is intended instead of 2 Chronic Health Problems?</p> <p>Discussion</p> <p>11. How generalizable are your findings on the prevalence of Disease burden and multimorbidity in submariners?</p> <p>12. "However, a previous study has confirmed that multi-morbidity prevalence is comparable between studies when multimorbidity is defined as ≥ 2 disease entities, regardless of the specific disease entity definitions in each study"</p> <p>This study is based on primary care populations, as is your study. Perhaps consider including this information in your sentence? In community setting populations this may not be the case.</p> <p>13. Do not introduce new analyses into the Discussion. e.g. exclusion of elderly subjects, obese and smokers excluded. Include all analyses referred to in the Discussion in the Results too.</p> <p>14. Page 12. How is obesity defined in your study compared to the comparative literature? In your methods obesity is describes as BMI 25+, however it may be described as BMI 30+ in comparative studies e.g. ref 26, 27? Further clarification is need. What were the cut points used for the Korean population (ref 25)?</p> <p>15. Is there any explanation as to why symptoms of the the eyes, ear, nose and throat were higher in non-submariners?</p> <p>16. What does 'temporary service commission" mean?</p>
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VERSION 1 – AUTHOR RESPONSE

Responses to Reviewer #1's comments

Reviewer Name: Amy Flaxman

Institution and Country: University of Oxford, UK

Competing Interests: None declared

General Comment: This manuscript compares multimorbidity and disease burden in a Korean submarine population. The study is well designed and the data well presented. The authors find that submarine service was significantly associated with increased risk of multimorbidity and disease burden compared to non-submarine navy personnel. There is no comparison to non-naval personnel

of the same age group. This should be discussed as a limitation, since differences in multimorbidity and disease burden may well exist between non-navy personnel and non-submarine and submarine personnel.

[Answer] Agreeing with reviewer's advice, we have acknowledged this point in the Discussion as one of the limitations.[Page 16]

Specific Comments:

1. In your description of Table 2 in the results, state that number of Chronic health problems and CIRS scores were significantly higher in submariners versus non-submariners, across all age groups.

[Answer] We revised the Result section regarding Table 2, according to reviewer's comment. [Page 10]

2. First sentence of the Discussion "compared to previous studies", please provide references to examples of previous studies.

[Answer] We have added the relevant references [Page 11].

3. The sentence in the Discussion which begins "When we excluded current smokers and obese subjects from each CIRS domain" would be better placed in the results section. Also, can the data described here be made available in a Supplementary Table?

[Answer] We have placed this statement in the Results section and have presented the data in a Supplementary Table 2.

4. In the Discussion "the duration of submarine service was positively associated with the prevalence of multi-morbidity" it would be beneficial to include a sentence discussing the fact that whilst overall duration of submarine service is positively associated with multi-morbidity, multi-morbidity actually falls from the 1-4years and 5-9years and then increases further in the >10years group.

[Answer] Agreeing with reviewer's comment, we repeated the analysis in subgroup of submariners after excluding non-submariners. In the subgroup analysis limited in submariners, there was no difference in the risk according to the years of submarine service. We presented this findings in the Supplementary Table 1. We revised result section. In addition, we deleted the sentences describing the relationship of submarine service duration and with multi-morbidity and disease burden.

5. In the Discussion "submarine duty did not increase the risk of hospitalization in 16 major diagnostic categories and submarine-associated diagnoses", the list of these 16 categories and diagnoses is unnecessary.

[Answer] We have removed this information from the paragraph.

6. I believe the STROBE checklist for cohort studies should be completed.

[Answer] We have completed the STROBE checklist and attached it to this submission.

Responses to Reviewer #2's comments

Reviewer: 2

Reviewer Name: Trousselard Marion

Institution and Country: Institut de recherche biomédicale des armées, Brétigny sur orge cedex, France

Competing Interests: no competing interest

1. Authors did not take into account prolonged shift and night work and with as a risk factors. This point must be discussed.

[Answer] Thank you for this comment. We have described circadian misalignment as a potential risk factor for poor submariner health in the Discussion [Page 13].

2. The importance of social isolation from the real world (with no phone or internet contact with

families or friends during a routine mission) may be evaluated by the number of children and the marital status?

[Answer] Although we agree that these factors would be useful surrogate markers for evaluating the effects of social isolation during deployment, we could not access to this information. We believe that it will be an interesting factor to incorporate into future studies.

3. Information about the number of mission stressful events should be of interest for exploring health status difference between the two populations

[Answer] We completely agree with your valuable comment. However, we could not evaluate this issue because the information was not available for the present study.

Responses to Reviewer #3's comments

Reviewer: 3

Reviewer Name: Dr Michael Waller

Institution and Country: School of Public Health, University of Queensland, Australia

Competing Interests: None declared

1. It would be good to know what proportion of Submariners would access the primary care clinic to understand whether the study results are generalisable to 'all Korean submariners' or whether this group is likely to be in poorer health than other submariners?

[Answer] We agree that understanding the proportion of individuals who visited a primary care clinic would be an important factor to consider for assessing the generalizability of study finding.. However, given the current critical political situation between South Korea and North Korea, and it is impossible to report the data that you are requesting, as the data would inevitably make it possible to calculate the total population of South Korean submariners (this information is inappropriate for public release).

Methods

2. Are the conditions listed in page 7 last paragraph, the full list of conditions? It is good practice to include a full list of conditions considered for extraction.

[Answer] Yes, that it is the full list of conditions. Patients were asked to self-report all of their medical conditions and then an additional physician-led examination was followed to identify any unreported conditions. In addition, we reviewed medical record of each study subjects. We described this process in detail in the manuscript (Page 7-8).

3. Expand the methods to include details on how medical records were used to extract diagnosis of multimorbidity (e.g. pathology reports, listed as an ongoing condition). How far back did you review their medical history based on their records? How complete were the records? For the questionnaire, provide details of how the questions were asked and coded (e.g. Has a Doctor diagnosed or treated you for the following conditions? response Present or absent). Explain how data extraction was blinded so that submariner status was not known when collecting information on medical conditions. If this was not the case, acknowledge this as a potential source of bias in the Discussion.

[Answer] We have revised the Method section regarding data extraction and the questionnaire for identifying chronic diseases.(Page 8) Furthermore, we have described several limitations that are related to data collection in the Discussion. (Page 15-16)

3. Give information on the age-strata Page 9 line 4.

[Answer] We have added the information that you requested.(Page 8)

4. How was alcohol use measured.

[Answer] We have explained how alcohol consumption was measured in the Methods.(Page 7)

5. Page 8: Describe how disease burden is used and categorized in the methods section. Why

CIRS \geq 3?

[Answer] As there is no standardized cut-off value for high disease burden based on the CIRS score, and we arbitrarily defined the upper tertile of CIRS scores (≥ 3) as a status of high disease burden.

6. From table 3, it seems like non-submariners are included in the analysis. Are all zero years of submarine service non-submariners? Given the health and recruitment differences between submariners and non-submariners, it might be worthwhile to perform your "model 1 and 2" by year of submarine service limited to submariners as a sensitivity analysis or the primary analysis. Without the inclusion of the non-submariners I imagine the relationship between submarine service length and multimorbidity would be markedly reduced. From the results currently shown, although the test for trend is significant there is no consistent dose response relationship between length of service and multimorbidity.

[Answer] Agreeing with reviewer's comment, we repeated the analysis in subgroup of submariners after excluding non-submariners. In the subgroup analysis limited in submariners, there was no difference in the risk according to the years of submarine service. We presented these findings in the Supplementary Table 1. We revised result section. In addition, we deleted the sentences describing the relationship of submarine service duration and with multi-morbidity and disease burden from the Discussion section.

7. Is your study population exclusively male? If so state this.

[Answer] Yes, all of study subjects were male. We have addressed this point in the revised text.

Results

8. Clarify who "Other ranks" are? Lower ranks?

[Answer] This category included civilians who worked for the navy but did not belong to the navy. Most of these individuals had previously completed active duty assignments, and continued to work as employees of the Ministry of National Defense after they were discharged. For better understanding, we changed 'other' to 'Navy civilian' in Table 1.

9. "With increasing years of submarine service, the risk of having multi-morbidity and high disease burden (CIRS score of ≥ 3) tended to increase (P for trend (< 0.001))." This statement can be considered misleading as it implies submariner population but non-submariners are included in the analysis. (See point 6).

[Answer] As described in our response to the comment by you (#6) and other reviewer 1(#4), we revised the text in the Result section. In addition, we deleted the sentences describing the relationship of submarine service duration and with multi-morbidity and disease burden from the Discussion section. and in the revised text.

10. Table 2. I presume 2+ is intended instead of 2 Chronic Health Problems?

[Answer] Thank you for this comment. We have corrected this issue.

Discussion

11. How generalizable are your findings on the prevalence of Disease burden and multimorbidity in submariners?

[Answer] We agree with your comment regarding the generalizability of the prevalence of Disease burden and multimorbidity in submariners observed in our study. However, given the current critical political situation between South Korea and North Korea, and it is impossible to report the data that you are requesting, as the data would inevitably make it possible to calculate the total population of South Korean submariners (this information is inappropriate for public release).

12. "However, a previous study has confirmed that multi-morbidity prevalence is comparable between studies when multimorbidity is defined as ≥ 2 disease entities, regardless of the specific disease entity

definitions in each study”

This study is based on primary care populations, as is your study. Perhaps consider including this information in your sentence? In community setting populations this may not be the case.

[Answer] Agreeing with this comment, We have revised the sentences with further consideration of the study setting.

13. Do not introduce new analyses into the Discussion. e.g. exclusion of elderly subjects, obese and smokers excluded. Include all analyses referred to in the Discussion in the Results too.

[Answer] We have placed the statement related to the result of analysis in the Results section and have presented the data in a Supplementary Table.

14. Page 12. How is obesity defined in your study compared to the comparative literature? In your methods obesity is describes as BMI 25+, however it may be described as BMI 30+ in comparative studies e.g. ref 26, 27? Further clarification is need. What were the cut points used for the Korean population (ref 25)?

[Answer] The WHO recommended cut-off for obesity in Korean populations is 25 kg/m², as Asian individuals have higher body fat composition compared to Caucasian individuals. Moreover, increased all-cause mortality in the Korean population is associated with a BMI of ≥ 25 kg/m² 1 2. We added this point in Discussion section (Page 13).

15. Is there any explanation as to why symptoms of the eyes, ear, nose and throat were higher in non-submariners?

[Answer] It is possible that low air quality in an enclosed space and the high rate of current smokers may partially explain the prevalence of ear/nose/throat symptoms among submariners. We added relevant discussion in Discussion section. (Page 12)

16. What does 'temporary service commission" mean?

[Answer] These individuals receive their commission through a conscription system, complete approximately 20 months of naval service, and are then discharged. We used the term 'temporary service commission" to distinguish these individuals from 'permanently commissioned naval personnel' (which includes the submariners in this study).

References

1. Deurenberg P, Yap M, Van Staveren WA. Body mass index and percent body fat: a meta analysis among different ethnic groups. International Journal of Obesity & Related Metabolic Disorders 1998;22.
2. Jee SH, Sull JW, Park J, et al. Body-mass index and mortality in Korean men and women. New England Journal of Medicine 2006;355:779-87.

VERSION 2 – REVIEW

REVIEWER	Amy Flaxman University of Oxford, UK
REVIEW RETURNED	18-Jul-2017

GENERAL COMMENTS	Thank you for addressing my comments from my previous review. The manuscript is improved through these changes and those recommended by the other reviewers and editor. I now recommend your manuscript for publication.
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REVIEWER	Michael Waller School of Public Health University of Queensland Australia
REVIEW RETURNED	17-Jul-2017

GENERAL COMMENTS	<p>I have a small number of further suggested changes.</p> <p>The abstract still states: "Significant positive age-adjusted associations were observed between the overall years of submarine service and multi-morbidity or high disease burden (a CIRS score of ≥ 3) (P for trend < 0.001)."</p> <p>This contradicts the statement in the results "However, a dose-response relationship according to submarine service duration was not evident (Supplementary Table 1)."</p> <p>In light of the updated manuscript the abstract should be modified to be consistent with the results section.</p> <p>Methods: If as stated the list of conditions is a "full list" of those considered, then remove "such as" from the following sentence:</p> <p>"First, we asked the study subjects to answer "yes" or "no" to each question regarding whether they had experienced or had received treatment for the chronic conditions such as such as diabetes,....."</p> <p>and say instead</p> <p>"First, we asked the study subjects to answer "yes" or "no" to each question regarding whether they had experienced or had received treatment for the following chronic conditions; diabetes,....."</p>
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VERSION 2 – AUTHOR RESPONSE

1. The abstract still states: "Significant positive age-adjusted associations were observed between the overall years of submarine service and multi-morbidity or high disease burden (a CIRS score of ≥ 3) (P for trend < 0.001)." This contradicts the statement in the results "However, a dose-response relationship according to submarine service duration was not evident (Supplementary Table 1)." In light of the updated manuscript the abstract should be modified to be consistent with the results section.

[Response] We have corrected the abstract to conform with our findings in the results section.

2. Methods: If as stated the list of conditions is a "full list" of those considered, then remove "such as" from the following sentence:

"First, we asked the study subjects to answer "yes" or "no" to each question regarding whether they had experienced or had received treatment for the chronic conditions such as such as diabetes,....." and say instead

"First, we asked the study subjects to answer "yes" or "no" to each question regarding whether they had experienced or had received treatment for the following chronic conditions; diabetes,....."

[Response] As the sentence included a full list of conditions, we have revised the text according to your suggestion.