PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (http://bmjopen.bmj.com/site/about/resources/checklist.pdf) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

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<th>Body mass index, waist circumference and pre-frailty/frailty: The Tromsø study 1994–2016</th>
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<td>AUTHORS</td>
<td>Uchai, Shreeshti; Andersen, Lene; Hopstock, Laila; Hjartaker, Anette</td>
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VERSION 1 – REVIEW

| REVIEWER | Sommer, Isolde Donau-Universitat Krems, Department for Evidence-based Medicine and Evaluation |
| REVIEW RETURNED | 10-Aug-2022 |

| GENERAL COMMENTS | My main concerns relate to the use of low physical activity as one indicator for prefrailty. If prefrailty was mainly established by low physical activity, the association with obesity is not a surprise. It would have also been important to rule out that pre/frailty was present at baseline, which is one of the key characteristics of a cohort study. |

| REVIEWER | Saxena, Vartika AIIMS Rishikesh, Community And Family Medicine |
| REVIEW RETURNED | 27-Aug-2022 |

| GENERAL COMMENTS | This is a very well-analysed research article. Frailty is a complex issue, over the period of 21 years there must have been an effective and accelerated impact of many other environmental factors also, like changing dietary patterns, stresses and coping mechanisms, social security mechanisms etc. Hence the result of this study should be read in light of these contextual issues. |

| REVIEWER | Zupo, Roberta National Institute of Gastroenterology IRCCS Saverio de Bellis, Unit of Data Sciences and Technology Innovation for Population Health, National Institute of Gastroenterology “Saverio de Bellis,” Research Hospital, Castellana Grotte, Bari, Italy |
| REVIEW RETURNED | 27-Aug-2022 |

| GENERAL COMMENTS | I thank the authors for this interesting article. The perspective aspect and the topic are both interesting aspects. Introduction: needs to be implemented. For example, there is a lack of epidemiological data on population studies about the prevalence of frailty (look at 10.1016/j.jamda.2020.12.026). In addition, the intriguing involvement of anthropometric variables in frailty syndrome has been described as an integral part of the construct of nutritional frailty, which autoi should mention (look at 10.1016/j.arr.2020.101148 and 10.1111/joim.13384). |
Methods: multimorbidity is self-reported, and this is a major limitation, as are some domains of the frailty construct. Please add it in the limitations.

In the models in Supplementary Table 5, please also correct for other confounding factors such as education and smoking. In Supplementary Table 2, P values should be better expressed for actual value, or replaced with effect size. The same for Supplementary Table 3.

REVIEWER
Strandberg, Timo
University of Helsinki

REVIEW RETURNED
29-Aug-2022

GENERAL COMMENTS
The topic of this longitudinal study is especially important in ageing societies with simultaneous obesity epidemic: not only mortality and morbidity risks are important consequences of obesity, development of frailty may be even more important by prematurely reducing physical function reserves and thus threatening autonomy of the individual. It is also important that the present study used phenotypic frailty (a condition independent of diseases) as the outcome and may thus give clues for the origins of this geriatric syndrome.

The study is confirmatory, as long-term studies in Finland (refs #23,24) have already reported similar results. This does not, however, reduce the importance of this population-based analysis; this side of obesity is not yet fully recognized and constant reminders are needed.

The limitations (appropriately discussed by the authors) include:
1. frailty status was not assessed at baseline. This is obvious, because interest in phenotypic frailty started to grow after 2001.
2. Prefrailty and frailty were put together, because pure frailty was infrequent. However, prefailure is a clear antecedent for frailty.
3. A modified version of the Fried phenotype was used. However, several modifications (even only questionnaire-based) seem to give similar results as to prognosis.

I don't have relevant criticisms to improve this well-written paper as is. I am not a statistician and statistical review of the trajectory approach may be considered.

REVIEWER
Zhang, Xiaoyan
Shanghai Jiaotong University

REVIEW RETURNED
31-Aug-2022

GENERAL COMMENTS
This study evaluated the relationship between BMI/WC and the risk of developing pre-frailty and frailty over an extended follow-up in a large cohort. It especially explored changes in BMI/WC and its association with frailty, which highlights the importance of maintaining optimal BMI and WC throughout adulthood to lower the risk of frailty in older age. However, I still have some questions about this manuscript.

1. The authors Modified Fried's frailty scale to diagnose frailty or pre-frailty; however, it should measure the reliability and validity of those that delete or revise the original index system. Although the author discussed each frailty indicator they used had been validated in different research contexts, Modified Fried's frailty scale still needs to be Verified as a new scale.
2. The prevalence of frailty was very low in the study (<1.1%), given that 27,158 participants aged 25–97 years were included in
Tromsø4: many old participants may have died during 21 years of follow-up. The conclusion of this study may be biased.

3. The title of this manuscript is "Body mass index and waist circumference as predictors of pre-frailty/frailty among older adults: A prospective cohort study", according to the title, it means this study should be done in an old population, and the BMI or WC should be tested during their senior period, actually, for part of the subjects the data came from the middle age, and the results were the predictive value of midlife overweight and obesity to the risk of pre-frailty and frailty when they get old than 65 years.

4. Frailty is a complex age-related clinical condition. It was reported the prevalence of frailty is about 10%-25% in people over 65 years old and as high as 30%-45% over 85 years old. Previous studies showed a U-shaped association between BMI and (physical) frailty. The risk factor or prediction factor should differ among older adults over 80 and less than 80. The authors should divide the participants into different subgroups according to their age when they observe the predicted performance of BMI and WC on pre-frailty/frailty.

REVIEWER
Isanejad, Masoud
University of Liverpool, MSB
REVIEW RETURNED
02-Sep-2022

GENERAL COMMENTS

Major
The study although explaining a common phenomenon has an important public health message and in that aspect may be of interest.

Discussion requires a major revision based on additional data analysis:
- a psychological and mechanism explanation.
- Also, as author stated frailty is a state of disease and has a trajectory nature, how the authors controlled for this. Frailty was the outcome defined as a modified frailty phenotype definition, but what aspect of frailty was correlated strongly with BMI and WC should be analysed and discussed. How does obesity predict the lower walking speed and muscle strength, what about the mental health aspect of frailty? It is quite a narrow angle if we think just the score can be used to make a judgment on frailty!

This study is conducted carefully but incomplete, to add novelty the above questions should be addressed. It is not a surprise that obesity predicts frailty and it is odd that authors suggest that there is limited evidence on this! Also, author claim their strength is repeated assessments which is tru about BMI, and WC but not from frailty. lot of factors are changing in life from age of 49 over 20 years, ofcourse healthy wieght is important.

Minor

Line 23 and through all manuscripts: please make sure that this study can not suggest estimating effect /Or impact, but rather an estimation of association, effect needs to be replaced with the association.
An explanation of modified frailty/pre-frailty is required for the abstract.
Line 39-40: it is unclear how these trajectories were defined given the 4 times assessment, was this baseline compared to the 2007-8 assessment?
VERSION 1 – AUTHOR RESPONSE

Major

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An explanation of modified frailty/pre-frailty is required for the abstract.
Line 39-40: it is unclear how these trajectories were defined given the 4 times assessment, was this baseline compared to the 2007-8 assessment?
Suggest changing life course to adulthood?
May I suggest authors read the work carefully to eradicate grammatical mistakes, these could lower the enthusiasm of readers.
Line 180-22 seems to be redundant. Why discuss muscle and fat where there is no data presented in this work/
For frailty assessments please give the exact numbers used as the cut-off.

VERSION 2 – REVIEW

REVIEWER
Sommer, Isolde
Donau-Universitat Krems, Department for Evidence-based Medicine and Evaluation
The authors have thoroughly addressed all comments. I have no further comments.

Zhang, Xiaoyan
Shanghai Jiaotong University

All my concerns have been totally revised, thank you very much!

Isanejad, Masoud
University of Liverpool, MSB

The title accordingly needs to be tuned down and changed, prediction is not what this study could provide, at best the study shows BMI and WC are linked with frail odds ration at one follow-up time

Reviewer: 1
Dr. Isolde Sommer, Donau-Universitat Krems
Comments to the Author:
The authors have thoroughly addressed all comments. I have no further comments.

Authors’ response:
Thank you very much.

Reviewer: 5
Dr. Xiaoyan Zhang, Shanghai Jiaotong University
Comments to the Author:
All my concerns have been totally revised, thank you very much!

Authors’ response:
Thank you very much.

Reviewer: 6
Dr. Masoud Isanejad, University of Liverpool
Comments to the Author:
The title accordingly needs to be tuned down and changed, prediction is not what this study could provide, at best the study shows BMI and WC are linked with frail odds ration at one follow-up time

Authors’ response:
Thank you very much. We agree with you and have decided to remove “predictors” from our title to avoid confusing readers. Our modified title is: Body mass index, waist circumference and pre-frailty/frailty: The Tromsø study 1994–2016.