

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

TITLE (PROVISIONAL)	All-cause mortality among young men 24 to 26 years after a lifestyle health dialogue in a Swedish primary care setting: a longitudinal follow-up register study
AUTHORS	Lingfors, Hans; Persson, Lars-Göran

VERSION 1 – REVIEW

REVIEWER	Cecilia Björkelund Dep of Primary Health Care, Institute of Medicine, University of Gothenburg, Sweden
REVIEW RETURNED	22-Apr-2018

GENERAL COMMENTS	<p>This is a paper that compares mortality and morbidity ratios for men in all Sweden during a 25 year period with ratios in a small rural Swedish community. The lower ratios in the small community of Habo are interpreted as an effect of individual and community interventions during the 80ies in Habo.</p> <p>It is not possible to draw the conclusion whether the intervention activities are the reason for the lower ratios in Habo, although the lower education levels in Habo could indirectly be a further reason to accept the hypothesis. The comparisons must be made to the same type of rural communities in Sweden to be more robust. The authors have earlier published this type of follow-up (reference 25), and this would strengthen the analysis and the manuscript. It would be interesting to compare to a similar type of rural Swedish region in e.g. Region Halland, where epidemiological studies have shown lower mortality ratios than all Sweden during several decades. (e.g. Baigi A, et al. Cardiovascular mortality focusing on socio-economic influence...).</p> <p>Although the lower ratios for the participants in the individual intervention are impressive, the 3 times higher ratios of the non-participating individuals in Habo are worth commenting.</p> <p>The table captions of table 3 and 4 should be changed. It's easy to interpret the text that the follow-up concerns the life-style habits, and that a follow-up of life-style habits has been performed after 26 years.</p> <p>Odds Ratio is not a genitive – it's a plural, and consequently should not be spelled Odd's.</p> <p>There was a significantly (not: significant) higher proportion of men in Habo with a short education...</p> <p>The register is identified as the National Patient Register.</p> <p>The authors use "patient" several times. The participants were persons invited from the population of Habo and should actually</p>
-------------------------	--

	<p>not be identified as patients. Participants or persons should be a better way to describe the individuals.</p> <p>If the doctor described in Methods was a GP, I think this should be stated.</p> <p>There are many language flaws in the text and the authors should engage a language editor.</p> <p>The references should be edited and written according to the BMJOpen guidelines.</p> <p>Presently, the manuscript does not reach the standards appropriate for BMJOpen.</p>
--	---

REVIEWER	Mai-Lis Hellenius Karolinska Institutet, Sweden
REVIEW RETURNED	23-Apr-2018

GENERAL COMMENTS	<p>The objectives were to compare all-cause mortality and socioeconomic status (SES) among young men, invited from the population-registry to the primary health care for a dialogue on lifestyle, with men from all Sweden after 24 years. Furthermore, the objective was also to analyse associations between reported lifestyle and all-cause mortality, incidence of cardiovascular disease (CVD) and cancer.</p> <p>The study is a longitudinal follow-up register study of men, 33-42 years at baseline carried out in primary health care in a community, Habo, in southern Sweden. All 757 men, living in the community in 1985, and all 652 men participating in a health examination between 1985 and 1987 were included.</p> <p>The intervention contained a health examination, a lifestyle directed health dialogue and also group activities carried out by primary health care professionals in cooperation with local associations.</p> <p>The primary and secondary outcomes were all-cause mortality and income and educational level. Associations between lifestyle at baseline and all-cause mortality, incidence of CVD and cancer. At follow-up after approximately 25 years all-cause mortality was 29 % lower, OR=0.71 (0.53 to 0.95), among the 757 men invited to the health dialogue compared to all men from the same age cohort in all Sweden (intention to treat) and 43% lower, OR=0.57 (0.40 to 0.81) among the 652 men participating in the health dialogue (on treatment). A healthy lifestyle was associated with lower mortality, OR=0.16 (0.07 to 0.36). The strongest association was noted for no smoking, OR=0.38 (0.21 to 0.68), and a healthy diet, OR=0.37 (0.20 to 0.68). A healthy lifestyle was also significantly associated with decreased incidence of CVD and cancer. There was a significantly higher proportion with short education among the invited men compared to men from the same age cohort in all Sweden.</p> <p>In general</p> <p>There is today a great focus on prevention in cardiovascular medicine. Lifestyle interventions form the basis for both prevention and treatment of cardiovascular diseases (CVD). The knowledge about the importance of lifestyle factors have increased considerably and national and international guidelines for CVD prevention emphasize the role of lifestyle intervention. However, there is a need for an increased knowledge on how experiences from epidemiology, clinical trials and mechanistic studies can be</p>
-------------------------	--

	<p>implemented into clinical practice. Therefore, I welcome a study of this kind.</p> <p>The authors conclude that combining a low and high-risk strategy comprising a health examination with a lifestyle directed health dialogue conducted in ordinary work in a primary health care setting in cooperation with local associations may contribute to reduced premature mortality. As I can understand from reading the manuscript, such a statement is correct. The findings are important having in mind that the health care all over the world is facing a new period with a greater focus on prevention and promotion of a healthy lifestyle.</p> <p>In more detail</p> <p>The manuscript reads easily. Only minor corrections of the language are needed. The study seems to be carefully carried out, the methods used are adequate for the purpose and the interpretation of the data is fair.</p> <p>However, the manuscript raises some questions to the reader. It would be interesting with some international comparisons. In the discussion section the authors discuss their finding in relation to other Swedish programmes only.</p> <p>A somewhat more detailed description of the area Habo as well as the study population in relation to the reference group (rest of Sweden) would facilitate the reading and judgement of the results. The design of the study is a strength. Would it have been possible to match the reference group for socioeconomic factors (educational levels for example)? A higher proportion of the men in the study cohort had short education compared to the corresponding age cohort in all Swede (the reference group). Would that have affected the results?</p> <p>The screening programme was directed towards men only. Are the results valid for women? Difficult to answer probably, but worth discussing.</p>
--	---

VERSION 1 – AUTHOR RESPONSE

Reviewer(s)' Comments to Author:

Reviewer: 1

Reviewer Name: Cecilia Björkelund

Institution and Country: Dep of Primary Health Care, Institute of Medicine, University of Gothenburg, Sweden

Please state any competing interests or state 'None declared': None Declared

Please leave your comments for the authors below

This is a paper that compares mortality and morbidity ratios for men in all Sweden during a 25 year period with ratios in a small rural Swedish community. The lower ratios in the small community of Habo are interpreted as an effect of individual and community interventions during the 80ies in Habo. It is not possible to draw the conclusion whether the intervention activities are the reason for the lower ratios in Habo, although the lower education levels in Habo could indirectly be a further reason to accept the hypothesis.

Answer: This is a relevant comment, but we don't claim that the intervention is the reason for the lower mortality rate in Habo. We instead say that the study indicates that the intervention may have contributed to reduced mortality. We cannot exclude that there may be other factors explaining the lower mortality rate in Habo. We have looked at two socioeconomic factors known to be of great importance concerning mortality. We found that the income level was equal in Habo and all Sweden for the studied age cohort. We also found that there were a significantly higher proportion of men with short education in Habo in comparison to all Sweden. It is well known that men in Sweden with short education have at least five years shorter life expectancy compared to men with long education (see ref 10). Therefore you would expect a higher mortality rate among the men in Habo compared to all Sweden. But we found the opposite with a lower mortality rate among the men in Habo compared to men in the rest of Sweden analysed both as intention-to-treat and on treatment. This means that the results may be underestimated rather than overestimated. So we think we have been rather modest in our conclusions.

The comparisons must be made to the same type of rural communities in Sweden to be more robust. The authors have earlier published this type of follow-up (reference 25), and this would strengthen the analysis and the manuscript.

This is true, but since that earlier follow-up the division of community types have been changed several times and this is also true for Habo. This means that the communities since 1985 have changed a lot in different directions making it hard to make that kind of comparison.

It would be interesting to compare to a similar type of rural Swedish region in e.g. Region Halland, where epidemiological studies have shown lower mortality ratios than all Sweden during several decades. (e.g. Baigi A, et al. Cardiovascular mortality focusing on socio-economic influence...).

Yes, it is well known that Region Halland during several decades have shown lower mortality rate than all Sweden. The conclusion in the referred study by Baigi et al mentioned above was that higher socioeconomic status was more important than geography to explain the lower mortality in Region Halland. This again means that a higher mortality rate would be expected in Habo as there were a significantly higher proportion of men in Habo with short education.

Although the lower ratios for the participants in the individual intervention are impressive, the 3 times higher ratios of the non-participating individuals in Habo are worth commenting.

This is true. We have in an earlier study characterised the non-participants thoroughly (ref 11) and we have now added some results from that study in the Discussion section.

The table captions of table 3 and 4 should be changed. It's easy to interpret the text that the follow-up concerns the life-style habits, and that a follow-up of life-style habits has been performed after 26 years.

This is true and we have now changed the captions.

Odds Ratio is not a genitive – it's a plural, and consequently should not be spelled Odd's.

We have now changed to odds ratio (plural) in the manuscript.

There was a significantly (not: significant) higher proportion of men in Habo with a short education...

This has been corrected in the manuscript.

The register is identified as the National Patient Register.

Yes, there is a register called the National Patient register, but we have used several registers from the National Board of Health and Welfare so we think our sentence is appropriate.

The authors use “patient” several times. The participants were persons invited from the population of Habo and should actually not be identified as patients. Participants or persons should be a better way to describe the individuals.

We have used the word “patient” in the manuscript, where we think this is appropriate. According to the “term bank” from The National Board of Health and Welfare a patient is “a person who receives or is registered to receive health care”. So we prefer to use that definition and keep the word “patient” where it is now mentioned in the manuscript.

If the doctor described in Methods was a GP, I think this should be stated.

We have changed doctor to GP in Methods.

There are many language flaws in the text and the authors should engage a language editor.

We have now engaged professional help to improve the language.

The references should be edited and written according to the BMJOpen guidelines.

We have now adjusted the references according to the BMJOpen guidelines.

Presently, the manuscript does not reach the standards appropriate for BMJOpen.

Reviewer: 2

Reviewer Name: Mai-Lis Hellenius

Institution and Country: Karolinska Institutet, Sweden

Please state any competing interests or state ‘None declared’: None declared

Please leave your comments for the authors below

The objectives were to compare all-cause mortality and socioeconomic status (SES) among young men, invited from the population-registry to the primary health care for a dialogue on lifestyle, with men from all Sweden after 24 years. Furthermore, the objective was also to analyse associations between reported lifestyle and all-cause mortality, incidence of cardiovascular disease (CVD) and cancer.

The study is a longitudinal follow-up register study of men, 33-42 years at baseline carried out in primary health care in a community, Habo, in southern Sweden. All 757 men, living in the community in 1985, and all 652 men participating in a health examination between 1985 and 1987 were included. The intervention contained a health examination, a lifestyle directed health dialogue and also group activities carried out by primary health care professionals in cooperation with local associations. The primary and secondary outcomes were all-cause mortality and income and educational level. Associations between lifestyle at baseline and all-cause mortality, incidence of CVD and cancer. At follow-up after approximately 25 years all-cause mortality was 29 % lower, OR=0.71 (0.53 to 0.95), among the 757 men invited to the health dialogue compared to all men from the same age cohort in all Sweden (intention to treat) and 43% lower, OR=0.57 (0.40 to 0.81) among the 652 men

participating in the health dialogue (on treatment). A healthy lifestyle was associated with lower mortality, OR=0.16 (0.07 to 0.36). The strongest association was noted for no smoking, OR=0.38 (0.21 to 0.68), and a healthy diet, OR=0.37 (0.20 to 0.68). A healthy lifestyle was also significantly associated with decreased incidence of CVD and cancer. There was a significantly higher proportion with short education among the invited men compared to men from the same age cohort in all Sweden.

In general

There is today a great focus on prevention in cardiovascular medicine. Lifestyle interventions form the basis for both prevention and treatment of cardiovascular diseases (CVD). The knowledge about the importance of lifestyle factors have increased considerably and national and international guidelines for CVD prevention emphasize the role of lifestyle intervention. However, there is a need for an increased knowledge on how experiences from epidemiology, clinical trials and mechanistic studies can be implemented into clinical practice. Therefore, I welcome a study of this kind.

The authors conclude that combining a low and high-risk strategy comprising a health examination with a lifestyle directed health dialogue conducted in ordinary work in a primary health care setting in cooperation with local associations may contribute to reduced premature mortality. As I can understand from reading the manuscript, such a statement is correct. The findings are important having in mind that the health care all over the world is facing a new period with a greater focus on prevention and promotion of a healthy lifestyle.

In more detail

The manuscript reads easily. Only minor corrections of the language are needed. The study seems to be carefully carried out, the methods used are adequate for the purpose and the interpretation of the data is fair.

However, the manuscript raises some questions to the reader.

It would be interesting with some international comparisons. In the discussion section the authors discuss their finding in relation to other Swedish programmes only.

There are sparse with international programmes resembling the Swedish ones, but we now have added one interesting reference from USA in the Discussion section.

A somewhat more detailed description of the area Habo as well as the study population in relation to the reference group (rest of Sweden) would facilitate the reading and judgement of the results.

We now have added a more detailed description of Habo in the Introduction section. We have also added information about the non-participants.

The design of the study is a strength. Would it have been possible to match the reference group for socioeconomic factors (educational levels for example)?

A higher proportion of the men in the study cohort had short education compared to the corresponding age cohort in all Swede (the reference group). Would that have affected the results?

This would have been interesting but we don't have enough details on an individual level to make such a matching and we don't have the possibility to adjust or stratify the material.

The screening programme was directed towards men only. Are the results valid for women? Difficult to answer probably, but worth discussing.

This is of course of great interest and we have added this aspect of the study in the Discussion section.

VERSION 2 – REVIEW

REVIEWER	Cecilia Björkelund Department of Primary Health Care, Institute of Medicine, University of Gothenburg, Sweden
REVIEW RETURNED	17-Jul-2018

GENERAL COMMENTS	<p>Thank you for the revised manuscript. The authors have improved the manuscript, but I still think it needs further revision.</p> <p>1. The authors answer, that they do not claim that the intervention has had impact on reduced morbidity - but that the study indicates that the intervention may have contributed to reduced mortality, which might be a slightly milder way to indicate causative association. It would be preferable if the authors also in the manuscript added the rest of their review answer: The study indicates that the intervention may have contributed to reduced mortality, but we cannot exclude that there may be other factors explaining the lower mortality rate in Habo. This should be formulated also in the Conclusions in the main manuscript, not only in the Abstract. The design of the study does not give possibility to show causal association.</p> <p>2. The authors have changed Odds Ratio in most places, but it's still wrong in Table 3.</p> <p>3. I still don't think it is appropriate to use the word "patient" in connection with participants who have been invited to health checks and health dialogues, which is participating in screening on a population level. Participants or persons or individuals should be a better way to describe the participants. If the screening program was emanating from primary care and only concerned those individuals who had attended primary care, the term patient could be relevant, but then it would not have been a community based intervention program. You also identify the group of individuals as 'participants' in Aims and also mostly use 'participants' in the manuscript, and I think it is only confusing to use the denomination 'patient' in some places.</p> <p>4. Some more details: In abstract -Confidence Interval should be identified when first presented in Abstract (page 2 line 41). - A limitation should be added concerning no comparison with similar demographic cohort. Main manuscript: Background: The Live for Life program is presented as a CVD and cancer prevention program (page 6 line 3) but is presented as a cardiovascular prevention program in the reference (nb 11), and also most of the background text refers to cardiovascular prevention. In Background it would be relevant to present facts why and how it also aimed at cancer prevention.</p> <p>On page 8 – first bullet point: It's hard to understand if the participants is a subgroup of those who participated - or a subgroup of the target group. Please change - for example "Compare mortality rate from 1987 up to 2010 for all men aged 33 to 42 (born between 1943 and 1952) who while living in Habo between 1985 and 1987 were invited to a health dialogue (target group), as well as a subgroup of the target group: those who participated in the health dialogue (participants), with mortality rate</p>
-------------------------	--

	<p>for the corresponding age cohort from all Sweden (reference group).</p> <p>Page 9 line 26: Could 'stress' be identified as 'mental stress' . Heredity for... should be changed to a family history of. FN is not a diagnose, but a surgical procedure</p> <p>Table 2 (and Table 3) – Confidence interval (CI) is not usually presented as plural (CIs) .</p> <p>- If the authors change the manuscript accordingly, I'm willing to review a revision.</p>
--	--

VERSION 2 – AUTHOR RESPONSE

Reviewer(s)' Comments to Author:

Reviewer: 1

Reviewer Name: Cecilia Björkelund

Institution and Country: Department of Primary Health Care, Institute of Medicine, University of Gothenburg, Sweden

Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below

Thank you for the revised manuscript. The authors have improved the manuscript, but I still think it needs further revision.

1. The authors answer, that they do not claim that the intervention has had impact on reduced morbidity - but that the study indicates that the intervention may have contributed to reduced mortality, which might be a slightly milder way to indicate causative association. It would be preferable if the authors also in the manuscript added the rest of their review answer: The study indicates that the intervention may have contributed to reduced mortality, but we cannot exclude that there may be other factors explaining the lower mortality rate in Habo. This should be formulated also in the Conclusions in the main manuscript, not only in the Abstract. The design of the study does not give possibility to show causal association.

We have now clarified the conclusion both in the Abstract and in the Conclusions according to the proposal.

2. The authors have changed Odds Ratio in most places, but it's still wrong in Table 3.

Odds ratio is now correct in all places.

3. I still don't think it is appropriate to use the word "patient" in connection with participants who have been invited to health checks and health dialogues, which is participating in screening on a population level. Participants or persons or individuals should be a better way to describe the participants.

If the screening program was emanating from primary care and only concerned those individuals who had attended primary care, the term patient could be relevant, but then it would not have been a community based intervention program. You also identify the group of individuals as 'participants' in Aims and also mostly use 'participants' in the manuscript, and I think it is only confusing to use the denomination 'patient' in some places.

We agree that the word patient may be confusing in some places and we have changed this to persons except for the section about "**Patient and Public Involvement**", which is obligatory according to the rules of the journal.

4. Some more details:

In abstract

-Confidence Interval should be identified when first presented in Abstract (page 2 line 41).

We have now identified Confidence Interval when first presented in Abstract.

- A limitation should be added concerning no comparison with similar demographic cohort.

We have now added “No comparison is made with a similar demographic cohort” in the Limitation section

Main manuscript:

Background: The Live for Life program is presented as a CVD and cancer prevention program (page 6 line 3) but is presented as a cardiovascular prevention program in the reference (nb 11), and also most of the background text refers to cardiovascular prevention. In Background it would be relevant to present facts why and how it also aimed at cancer prevention.

We have now excluded cancer from the aim mentioned in page 6.

On page 8 – first bullet point: It's hard to understand if the participants is a subgroup of those who participated - or a subgroup of the target group. Please change - for example “Compare mortality rate from 1987 up to 2010 for all men aged 33 to 42 (born between 1943 and 1952) who while living in Habo between 1985 and 1987 were invited to a health dialogue (target group), as well as a subgroup of the target group: those who participated in the health dialogue (participants), with mortality rate for the corresponding age cohort from all Sweden (reference group).

We think that this is a good idea and we now have clarified the aims of the study according to the proposal.

Page 9

line 26: Could ‘stress’ be identified as ‘mental stress’ .

Yes, we mean mental stress and have now changed this to ‘mental stress’.

Heredity for... should be changed to a family history of.

We have changed ‘heredity’ to ‘family history of’.

FN is not a diagnose, but a surgical procedure

That is true. We have now added an explanation in the manuscript concerning FN.

Table 2 (and Table 3) – Confidence interval (CI) is not usually presented as plural (CIs) .

We have changed this to CI, also in table 4.

VERSION 3 – REVIEW

REVIEWER	Cecilia Björkelund Institute of Medicine/Primary Health Care; University of Gothenburg, Sweden
REVIEW RETURNED	29-Oct-2018
GENERAL COMMENTS	The English is still not fully acceptable - for example, I think the table texts should be edited: Risk for.. should be risk of...