

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	The prevalence of metabolic syndrome and diabetes mellitus in Sami and Norwegian populations. The SAMINOR-a cross sectional study.
AUTHORS	Broderstad, Ann Ragnhild; Melhus, Marita

VERSION 1 - REVIEW

REVIEWER	Ellen L. Toth, MD University of Alberta, Edmonton, AB
REVIEW RETURNED	26-Aug-2015

GENERAL COMMENTS	<p>The study clearly involved considerable effort and cost, and the authors are commended in the carrying out of a large survey including physical and biochemical measures.</p> <p>I have 2 major concerns, first there is no real description for an International audience, of who the Sami people are, and why it is justified to identify them in the study. Secondly there is considerable controversy as to the rationale for identifying the "condition" metabolic syndrome, rather than its separate risk factors, and this paper lends little further stimulus for continuing to focus on the constellation of risk factors. Metabolic syndrome is still a condition awaiting a treatment or even an approach that is not the approach to the individual risk factors. Whether there is a common pathogenesis is an interesting question, and leads back to concern #1.</p> <p>Indigenous peoples in other parts of the world notably USA, Canada, Australia and New Zealand suffer inferior health status to the dominant societies in those countries. There are more (Canada and USA) or less structured inequalities in health systems in those countries, including the administrative burdens of different funders of health care and the segregation into Reservations or Reserves (USA and Canada respectively). Further there is a history of sometimes brutal colonization (Australia) military conflict (USA) or "genocide" in the name of education (The Residential School system in Canada). I assume the Sami did not escape some form of oppression by the newer Norwegian inhabitants, and while I do not expect a full accounting, I would expect some reference to this and the commonalities or differences with the other countries mentioned. This is because the health status gaps in the 4 countries mentioned are widely believed to be the result of various degrees of cultural destruction, failed attempts at assimilation, resultant poverty and inferior educational and economic status, all acknowledged as the "social determinants of health" which are particularly associated with chronic diseases such as "obesity" (if it is a disease), diabetes, heart disease (which some say diabetes is part of!) and metabolic syndrome (which is not a disease).</p> <p>Thus the authors are not giving the context, in Norway, as to what</p>
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	<p>percent of the population is Sami, how much admixture is there, is the health system the same or different, what is access to care like, how do income and education affect these survey results, not to mention the response rates to the survey, which is likely to be biased in favour of the most educated and I would guess the least likely to be Sami. Thus, the Sami who self identify in this study may or may not be representative of the Sami population as a whole.</p> <p>Back to the definition or characterization of metabolic syndrome, as the authors acknowledge, their definition of diabetes is not ideal, and the absence of information about drug treatments for both diabetes and hypertension make these 2 parameters lack rigour.</p> <p>In summary I do not see that this 10 year old survey is a useful contribution to an international journal at this stage. The results may be better understood in terms of ethnicity issues and health system issues amongst the authors themselves, and therefore may be useful for a Norwegian primary care audience concerned with health care planning.</p>
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REVIEWER	Charlotte Jeppesen Dep. of Public Health, Aarhus University and affiliated to the Danish Diabetes Academy
REVIEW RETURNED	04-Sep-2015

GENERAL COMMENTS	<p>Overall comments: Generally an interesting and relevant paper but throughout the paper there are some linguistic errors and sentences that are hard to read. The aim should be further elaborated and it should be clearer from the beginning why the two WC cut points are included and compared. This is not clear before the reader has reached the discussion part.</p> <p>I have some specific comments listed beneath, abbreviations P= page, li= line</p> <p>P 5, Aim in li 8—12 Throughout the paper the two different cut points of WC is one of your main focus points, but why is this part left out in your aim. Please rewrite your aim and it might be clearer for you reader from the beginning why you operate with the two WC cut points</p> <p>P 5, li 51 and 52 you mention two questionnaires. Were these validated or did you test them in a pilot study? And what language were they performed in? I ask because you do not write if all SAMI understand Norwegian and you do not give the questionnaire language. Not all original populations understand the national language of their country.</p> <p>P 6; li 18 Data = plural and the verb should be in past tense => were</p> <p>P6; li 18, 32, 38: Between 2003 and 2004 the en dash (-) should be an Em Dash (—) instead of because it means <i>from 2003 to 2004</i>.</p> <p>P 7, li 25 is the study registered with a number at the National Data Protection Authority, please give the number. Also, did the</p>
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participants give oral and written consent and how were they informed about the study before deciding their potential participation.

P 8, li 54. You use the word screening. That is a bit confusing screening of your study population? It is just characteristics of your study population. At baseline or enrolment in the study if you prefer a time.

P 9 for table 2 write “prevalence of self-reported type 2 diabetes”

Table 2. You performed chi² test. And the p-value is for the difference between all groups which in my opinion is not informative at all. I would prefer p-values for the difference between treatment groups. So p-value e.g. insulin treatment between SAMI and non-SAMI. Ect.

P 10, li 50 The sentence “Based on information.....” this sentence is confusing and it seems there is something missing.

P 10, li 54—56 Also hard to read. I had to read it several times before I understood what you meant.

P 11, li 14 you write: “the most prevalent risk marker....” As if there is only ne. But later you list both blood pressure and triglycerides

P11, li 18—23 this sentence is hard to read

P 11, li 19 I do not under this sentence where you write that diabetes contributed the most to MetS. MetS is a risk factor for diabetes. So how can a disease contribute to its' risk factors.

P 13, li 34 Start you discussion with a very brief summary of your findings in accordance with your aim.

P 13, li 43—45 I would prefer the word age group instead of the word age bracket

P 14. You write that obesity among SAMI women has been discussed by Njølstad. But this information is irrelevant for your reader if you leave out the discussion of Njølstad's results in relation to your own.

P15, li 7 Inuit with capital I

P15, li 10 adiposity and obesity *were*

P 15, li 23. MetS is an indicator? You mean a cluster of risk factors. There is a difference between indicators and risk factors.

P 15, li 32 I do not follow you argument for not conducting OGTT in your study. It seems you give the argument that because your study was epidemiologic you could not perform OGTT.

You write: As the study was epidemiologically designed conducting two-hour plasma glucose tolerance tests was infeasible

	<p>what do you really mean by this sentence? Numerous epidemiological studies do OGTT even under conditions like yours, e.g the population surveys in Greenland that you also refer to.</p> <p>P 15, li 47—52 again a sentence that I do not understand.</p> <p>P 15, li 56 em dash between 2007 and 2008</p> <p>P 16, li 7 you write very correctly that you have probably underestimated the real prevalence of type 2 diabetes in your population because you use self-reported data. I think the prevalence is much higher. But please write a few sentences how this underestimation affects your results.</p> <p>P16, li 23 data= plural => were</p> <p>P 16, li 37 “conversely, however,” Either use conversely or however, not both.</p> <p>P 16, li 45 Reference for the statement in line 43—45 “on the other hand,....”</p> <p>P 16, li 34—57 you part on limitations Self-reported diabetes and self-perceived ethnicity status. How do you think this affects your results?</p> <p>P 17 Conclusion seems to be a listing of your findings but I am missing a short paragraph on the clinical value of your findings. And again the use of the two WC cut points is not clearly included in your conclusion. What does the two cut points mean for the clinical value of our study. It does not leave your reader with a clear conclusion of “This is what we have to do”-solution.</p> <p>Reference 18. Lease check how you inserted WHO in your reference programme.</p> <p>P 8; li 54 The word “screening”, I would not use that here. I would prefer</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name Ellen L. Toth, MD
Institution and Country University of Alberta, Edmonton, AB

Please leave your comments for the authors below

The study clearly involved considerable effort and cost, and the authors are commended in the carrying out of a large survey including physical and biochemical measures.

I have 2 major concerns, first there is no real description for an International audience, of who the Sami people are, and why it is justified to identify them in the study.

Response; We agree in this and the “Introduction” is now paraphrased to highlight the Sami people

health issues more. The "Introduction" is added under "Response" to the Editor.

Secondly there is considerable controversy as to the rationale for identifying the "condition" metabolic syndrome, rather than its separate risk factors, and this paper lends little further stimulus for continuing to focus on the constellation of risk factors. Metabolic syndrome is still a condition awaiting a treatment or even an approach that is not the approach to the individual risk factors. Whether there is a common pathogenesis is an interesting question, and leads back to concern #1.

Response; Our feedback on this is that the metabolic syndrome is made as a diagnostic tool for use both in clinical practice and in health research world-wide. Report and recognize the syndrome facilitates a better understanding of the syndrome and, even more important, targeting of care to people who will benefit from lifestyle disease reduction. Health researcher can therefore use this syndrome to monitor and predict change in lifestyle diseases associated with the syndrome. Lifestyle change happens all over the world and interfere also on the indigenous health situation. Obesity is reported in many indigenous groups world-wide. Lack of knowledge about MetS and absent of treatment is not an argument for not continuing research on MetS, but rather a good argument to continuing the research on the extent and treatment challenges connected to the syndrome.

Indigenous peoples in other parts of the world notably USA, Canada, Australia and New Zealand suffer inferior health status to the dominant societies in those countries. There are more (Canada and USA) or less structured inequalities in health systems in those countries, including the administrative burdens of different funders of health care and the segregation into Reservations or Reserves (USA and Canada respectively). Further there is a history of sometimes brutal colonization (Australia) military conflict (USA) or "genocide" in the name of education (The Residential School system in Canada). I assume the Sami did not escape some form of oppression by the newer Norwegian inhabitants, and while I do not expect a full accounting, I would expect some reference to this and the commonalities or differences with the other countries mentioned. This is because the health status gaps in the 4 countries mentioned are widely believed to be the result of various degrees or cultural destruction, failed attempts at assimilation, resultant poverty and inferior educational and economic status, all acknowledged as the "social determinants of health" which are particularly associated with chronic diseases such as "obesity" (if it is a disease), diabetes, heart disease (which some say diabetes is part of!) and metabolic syndrome (which is not a disease).

Response; We agree that these are important issues to highlight when research are done. The revised introduction has little more about the Sami. But to include more than this in the present manuscript will increase the manuscript length considerably. Therefore these topic must be addressed in other publications. We are working with such a manuscript together with 23 other countries compering different health indicators in indigenous groups world-wide.

Thus the authors are not giving the context, in Norway, as to what percent of the population is Sami, how much admixture is there, is the health system the same or different, what is access to care like, how do income and education affect these survey results, not to mention the response rates to the survey, which is likely to be biased in favour of the most educated and I would guess the least likely to be Sami. Thus, the Sami who self identify in this study may or may not be representative of the Sami population as a whole.

Response; This is addressed under "Limitaions"

Categorizing people based on ethnicity is a contentious practice. Different studies use different criteria of ethnic categorization, which makes it difficult to compare results. Our definition of the Sami group is rather weak. This may have influenced our results. Since there are no national records with information on ethnic background, it is impossible to know if the response rate among Sami and non-Sami are different. We are therefore unable to assess whether differences in participation have

influenced the observed disease burden.

Back to the definition or characterization of metabolic syndrome, as the authors acknowledge, their definition of diabetes is not ideal, and the absence of information about drug treatments for both diabetes and hypertension make these 2 parameters lack rigour.

In summary I do not see that this 10 year old survey is a useful contribution to an international journal at this stage. The results may be better understood in terms of ethnicity issues and health system issues amongst the authors themselves, and therefore may be useful for a Norwegian primary care audience concerned with health care planning.

Response; Some of these remarks are addressed under "Introduction" and "Limitation". Even though the information is ten years old it is still of great value for the health care system and the health administrators in Northern Norway, but also for Health Authority in Sweden and Finland as well. Therefore our research knowledge are frequently requested. The lifestyle and living conditions in Norway have not changed considerably the last 10 years and the SAMINOR study still provide substantial health information.

In addition, the first SAMINOR study done ten years ago, give solid health information which we can use in the future as well.

Reviewer: 2

Reviewer Name Charlotte Jeppesen

Institution and Country Dep. of Public Health, Aarhus University and affiliated to the Danish Diabetes Academy

Please leave your comments for the authors below I have attached a list of recommendations for you.

Review comments for the BMJ Open paper "The prevalence of metabolic syndrome and diabetes mellitus in Sami and Norwegian populations. The SAMINOR study".

Authors: Broderstad and Melhus

Overall comments: Generally an interesting and relevant paper but throughout the paper there are some linguistic errors and sentences that are hard to read. The aim should be further elaborated and it should be clearer from the beginning why the two WC cut points are included and compared. This is not clear before the reader has reached the discussion part.

I have some specific comments listed beneath, abbreviations P= page, li= line

P 5, Aim in li 8—12 Throughout the paper the two different cut points of WC is one of your main focus points, but why is this part left out in your aim. Please rewrite your aim and it might be clearer for you reader from the beginning why you operate with the two WC cut points

Response; The aim is now rewritten as follow;

In order to evaluate the health of indigenous and non-indigenous populations of Norway (inhabiting the same geographic area) it was necessary to conduct an epidemiological survey. The SAMINOR study provides unique information on lifestyle diseases and risk factors. The present study aims to evaluate the prevalence of MetS and diabetes mellitus in Sami and non-Sami populations residing in selected areas of North Norway. In addition, we will discuss different cut-off values for waist circumference (WC), and what impact this has on the prevalence of MetS.

P 5, li 51 and 52 you mention two questionnaires. Were these validated or did you test them in a pilot study? And what language were they performed in? I ask because you do not write if all SAMI

understand Norwegian and you do not give the questionnaire language. Not all original populations understand the national language of their country.

Response; No such validation has been done. We have added information about the questionnaire language:

The questionnaires were available in Norwegian and the three main Sami languages, Northern, Lule and South Sami languages. However, only 1.6% of the participants chose to use the Sami version of the questionnaire.

P 6; li 18 Data = plural and the verb should be in past tense => were

Response; We assume that you mean page 5, line 42:

The sentence "Data was obtained from physical tests and blood samples." has been changed to "Data were obtained from physical tests and blood samples."

On P6 li 8 we have changed the sentence to past;
The "Non-Sami" comprised the remainder of the participants.

P6; li 18, 32, 38: Between 2003 and 2004 the en dash (-) should be an Em Dash (—) instead of because it means from 2003 to 2004.

Response; This remark fit the lines on page 5, so I will answer for page 5. We have corrected this, The (-) is now replaced to an EM Dash (—).

P 7, li 25 is the study registered with a number at the National Data Protection Authority, please give the number. Also, did the participants give oral and written consent and how were they informed about the study before deciding their potential participation.

Response; This remark fit li 25 at page 5 and the text is revised;

The study was accredited by the Regional Board of Research Ethics in Northern Norway, and by the Board's Sami Consultant. The survey is in accordance with the Helsinki Declaration of 1975. The National Data Protection Authority (Datatilsynet) approved the use of personal information and the study are registered with the number 2002/1525-2.

A personal invitation was mailed several weeks before the survey arrived the municipality. The invitation contained information about the time and place, together with a five-page questionnaire. They were asked to bring the questionnaire with them when they attended the clinical examination.. After the consultation, the participants were asked to complete a new questionnaire.

P 8, li 54. You use the word screening. That is a bit confusing screening of your study population? It is just characteristics of your study population. At baseline or enrolment in the study if you prefer a time.

Response: This is now corrected to;
Table 1 shows gender-specific and ethnicity-specific characteristics of the study sample.

P 9 for table 2 write "prevalence of self-reported type 2 diabetes"

Table 2. You performed chi2 test. And the p-value is for the difference between all groups which in my opinion is not informative at all. I would prefer p-values for the difference between treatment groups. So p-value e.g. insulin treatment between SAMI and non-SAMI. Ect.

Response; In table 2 we have analysed for differences in total diabetes prevalence between the two ethnic groups. We have not analysed differences between treatment groups because this is not the main aim in the manuscript, rather an additional information.

P 10, li 50 The sentence “Based on information.....” this sentence is confusing and it seems there is something missing.

Response; The sentence is now paraphrased;

Diabetes was significant more frequent among the Sami participants than the non-Sami in both gender. Ethnicity appeared therefore to affect diabetes prevalence.

P 10, li 54—56 Also hard to read. I had to read it several times before I understood what you meant. Response; The sentence is now paraphrased;

The prevalence of the various diagnostic tools for MetS is presented in Figures 1 (males) and 2 (females).

P 11, li 14 you write: “the most prevalent risk marker....” As if there is only one. But later you list both blood pressure and triglycerides

Response; The sentence is now paraphrased

The most prevalent risk marker for MetS (aside from central obesity) was elevated systolic blood pressure and high triglyceride levels independent of gender and ethnicity.

P11, li 18—23 this sentence is hard to read

P 11, li 19 I do not understand this sentence where you write that diabetes contributed the most to MetS. Response; The sentence is now removed

MetS is a risk factor for diabetes. So how can a disease contribute to its' risk factors.

Response; We used the consensus Statement of MetS from the International Diabetes Federation.

P 13, li 34 Start your discussion with a very brief summary of your findings in accordance with your aim. Response; This is done as follows;

The prevalence of MetS was high in both ethnic groups. Diabetes prevalence was significantly higher among both Sami men and women compared to the non-Sami participants. The two different WC cut-off values greatly influenced the measured prevalence of MetS. The present study demonstrates that ethnicity is a significant factor for MetS in participants belonging to the lowest age bracket.

P 13, li 43—45 I would prefer the word age group instead of the word age bracket

Response; yes, I agree, but we used an experienced language translator who claimed that bracket was better to use than group. I can not argue against his suggestion.

P 14. You write that obesity among SAMI women has been discussed by Njølstad. But this information is irrelevant for your reader if you leave out the discussion of Njølstad's results in relation to your own.

Response; The sentence is now paraphrased

General obesity in Sami females has also been discussed by Njølstad et al (1998) and show that obesity has existed as risk factor among Sami women over time is not [27]

P15, li 7 Inuit with capital I

Response; The word has been revised.

P15, li 10 adiposity and obesity were

Response; The word has been revised

P 15, li 23. MetS is an indicator? You mean a cluster of risk factors. There is a difference between indicators and risk factors.

Response; The sentence is now paraphrased

...the syndrome itself is not a disease, but consists of a cluster of risk factors increasing the hazard for developing diseases.

P 15, li 32 I do not follow your argument for not conducting OGTT in your study. It seems you give the argument that because your study was epidemiologic you could not perform OGTT.

You write: As the study was epidemiologically designed conducting two-hour plasma glucose tolerance tests was infeasible what do you really mean by this sentence? Numerous epidemiological studies do OGTT even under conditions like yours, e.g. the population surveys in Greenland that you also refer to.

Response; Yes, we agree that this sentence was too imprecise and is now paraphrased; As the study had a large number of participants, up to 140 per day, conducting two-hour plasma glucose tolerance tests was considered infeasible.
P 15, li 47—52 again a sentence that I do not understand.

Response; The sentence is now paraphrased;
This figure is expected to increase due to lifestyle changes.

P 15, li 56 em dash between 2007 and 2008

Response; This is now corrected

P 16, li 7 you write very correctly that you have probably underestimated the real prevalence of type 2 diabetes in your population because you use self-reported data. I think the prevalence is much higher. But please write a few sentences how this underestimation affects your results.

Response; The sentence is now paraphrased;

It is therefore likely that the present study underreports the diabetes prevalence maybe as much as up to 50 percent.

P16, li 23 data= plural => were

Response; This is now corrected

P 16, li 37 “conversely, however,” Either use conversely or however, not both.

Response; This is now corrected as follow;

Conversely the design preven

P 16, li 45 Reference for the statement in line 43—45 “on the other hand,.....” Response; We have removed this sentence

P 16, li 34—57 you part on limitations Self-reported diabetes and self-perceived ethnicity status. How do you think this affects your results?

Response; The text under “Limitation” is now revised as followed and a new reference is added;
Limitations

The cross-sectional study design is suitable for the examination of associations in order to generate hypotheses that may be explored in longitudinal studies. Conversely, however, the design prevents the establishment of causality. Due to the nature of the design, people with severe disease may be missed because they are diseased at home, in long-term hospitalization or having died in the time since the sample list was prepared (i.e., selection bias). The SAMINOR study has used questionnaires to survey self-reported diseases. This approach cannot detect people with undiagnosed symptoms and is limited by recall bias. In Norway, it is estimated between 90 000 to 120 000 people with diabetes and nearly as many have undiagnosed disease. [39]

Categorizing people based on ethnicity is a contentious practice. Different studies use different criteria of ethnic categorization, which makes it difficult to compare results. Our definition of the Sami group is rather weak. This may have influenced our results. Since there are no national records with information on ethnic background, it is impossible to know if the response rate among Sami and non-

Sami are different. We are therefore unable to assess whether differences in participation have influenced the observed disease burden.

In summary, cross-sectional studies may be used in the measurement of the burden of disease in a population. However, cross-sectional data cannot assess the effect of lifestyle on the incidence of MetS, and longitudinal cohort studies are therefore needed.

P 17 Conclusion seems to be a listing of your findings but I am missing a short paragraph on the clinical value of your findings. And again the use of the two WC cut points is not clearly included in your conclusion. What does the two cut points mean for the clinical value of our study. It does not leave your reader with a clear conclusion of “This is what we have to do”-solution.

Response; We totally agree. The conclusion is now paraphrased;

Without question, the prevalence rates for several negative health factors were high in the Sami and non-Sami population. Overweight and obesity were common, especially in the case of Sami females. The prevalence of diabetes was higher among the Sami participants than the non-Sami in both genders, even though the presents of MetS among men were higher among the non-Sami men. However, the prevalence of MetS were in general high among participants in the SAMINOR study, with the highest prevalence for the European cut off values. The syndrome has important health implication but a cross sectional study cannot be used to validate the best ethnic specific values for WC used in the definition of MetS and more data on this issue must be obtained. In addition, determining preventive initiatives is important in the primary and specialist health care system. These initiatives must be made culture and linguistic specific, in order to reduce differences and improve health status in the whole population.

Reference 18. Lease check how you inserted WHO in your reference programme.

Response; This is now corrected

P 8; li 54 The word “screening”, I would not use that here. I would prefer

Response; We suppose the above sentence is a writing error

VERSION 2 - REVIEW

REVIEWER	Charlotte Jeppesen Department of Public Health, Aarhus University
REVIEW RETURNED	25-Feb-2016

GENERAL COMMENTS	In the table text for the revised table 2 is written: Table 2. Prevalence of diabetes mellitus in the SAMINOR study (N=15112). However, I suggest you revise this to include the new outcome of diabetes treatment.
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VERSION 2 – AUTHOR RESPONSE

Thank you for giving us the opportunity to revise the article.

In the table text for the revised table 2 is written: Table 2. Prevalence of diabetes mellitus in the SAMINOR study (N=15112). However, I suggest you revise this to include the new outcome of diabetes treatment.

Response; The text (heading) in table 2 is now changed to following text;

Prevalence of diabetes mellitus and diabetes treatment in the SAMINOR study (N=15112)