Author's response to reviews

Title: High prevalence of obesity, central obesity and abnormal glucose tolerance in the middle-aged Finnish population

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Author's response to reviews: see over
Dear Editor,

Thank you very much for the opportunity to revise our manuscript according to the reviewers’ suggestions and advice. We went carefully through the reviewers’ comments and have addressed them one by one. All changes in the manuscript (except for tables) are indicated in **BOLD** letters.

Please find enclosed our revised manuscript.

*Please note, that the file “Saaristo_TablesRevised_Final240608.doc” containing tables 1-5 has been uploaded as additional file because the tables are too big to be displayed in portrait format. However, tables are referred to in the text and are intended to appear within the body of the article. If this is not accepted or suitable for publication we will need your advice how to edit the tables: for example by using screenshot, rotating the picture by 90 degrees and submitting the tables as jpeg or splitting the tables into several tables.*

On behalf of the research group.

Tampere, the 24\textsuperscript{th} of June 2008

Yours sincerely,

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Response to reviewers

Response to reviewer 1

**Serious flaw**

Although the research question is clear and well defined, the paper contains a serious flaw: the sampling of the study population is done in strata of age, which does not represent the age distribution of the population. Therefore the presented population prevalence figures are incorrect. The analyses should be based on the survey design (which is available within the used Stata package).

We thank Reviewer 1 for constructive advice. We re-analysed the data based on the reviewer’s comment taking into account the age distribution of the population. Tables 1 and 2 have been corrected as well as the corresponding numbers reported in the text. We added a new sentence in the Methods/statistical methods part as following:

Page 7, Methods/Statistical methods, paragraph 1, line 2
“The estimates of total prevalences in the age group 45-74 years were calculated taking into account the stratified sampling design used in the study”

**A minor flaw**

A minor flaw is the lack of comparison between those who did and who did not participate in the study.

This is an important comment. Unfortunately we had no possibility to carry out a loss analysis in this kind of population based survey by comparison between those who did and who did not participate in the study. This issue has been addressed as a weakness in the discussion part of the revised manuscript as following:

Page 11, Discussion, paragraph 8, line 3:
“However, several limitations of this study need to be considered. Despite efforts to increase the response rate, only 56% of the men in the age-group 45 to 54 years agreed to participate. The response rate was higher in women and among older men. Non-participants might have had already diabetes, and thus they have considered unnecessary to take part in the survey. Therefore, the prevalence of known type 2 diabetes might have been underestimated”
Response to reviewer 2

Major Compulsory Revision 1

The authors do not distinguish between type 1 and type 2 diabetes, but state that all with diabetes had T2D. In Background, paragraph 2, they refer to the study by Ylihärsilä et al as showing the prevalence of type 2 diabetes, while that paper do not distinguish between type 1 and 2, but say that “although we did not separate type 1 and type 2 diabetes, the observed prevalences in the present study may be generalized to represent PRIMARILY (marked by referee) type 2 diabetes”.

In the current paper the authors state (Methods/Definitions, paragraph 1): “Individuals who reported that they have diabetes were not included in the OGTT and were classified as known T2D”.

In Norway type 1 diabetes in the adult population constitutes about 15-20% of the diabetic persons; in the present population of 45-75 is should be at least that much, and this should be commented by the authors.

The Methods section was not clear on this issue. Individuals who reported that they had diabetes onset at the age of younger than 35 years, and were treated with insulin from the beginning of their disease were classified as having type 1 diabetes. They constituted approximately 5% of all individuals who reported having diabetes, and they were not included in the type 2 diabetes prevalence calculations as persons with disease. This has been clarified in the Methods section:

Page 5, Methods/definitions, paragraph 1, line 2:
“Individuals who reported that they had diabetes onset at the age of younger than 35 years, and were treated with insulin from the beginning of their disease were classified as having type 1 diabetes. They constituted approximately 5% of all individuals who reported having diabetes, and they were not included in the type 2 diabetes prevalence calculations as persons with disease.”

Major Compulsory Revision 2

There is a little uncertainty concerning the diagnosis of IGT/IFG. According to the WHO 1999 correctly referred in “Definitions”, paragraph 1, all with both IFG and IGT are classified as IGT (FPG 6.1-6.9 mmol/l and 2hrBG 7.8 to 11.0 mmol/l).

Why then the heading in table 2: “AGT= at least one of TT2D, IGT or IFG”, which seems to imply that one person might have more than one of these diagnoses, and that the total number with AGT do not represent the total no of persons. This needs clarification.

Reviewer 2 is completely right as pointing out that WHO 1999 criteria are mutually exclusive. We changed the heading in table 2 as following:

“Prevalence (95% confidence interval, CI) of type 2 diabetes (T2D), screen-detected type 2 diabetes (ST2D), total type 2 diabetes (TT2D), impaired glucose tolerance (IGT), impaired fasting
glucose (IFG), abnormal glucose tolerance (AGT= TT2D, IGT, or IFG) in the study sample according to sex and age groups”

Major Compulsory Revision 3

The tables contain overlapping categories, for instance BMI in tables 1, 3 and 5 (BMI 25-30 and BMI >= 30), and waist circumference in tables 4 and 5 (94-102 and >= 102, 80-88 and >= 88). This might be OK if a sufficient number of decimals are used in the calculation of BMI, but the table text “25-30” implies that all with a BMI of 30 are included. In waist circumference the precision in measurement is not mentioned in the methods section, but a measurement closer than to the nearest whole cm seems impractical, meaning that those with a waist of 102 and 88 cm might also fall in two categories. I suppose this may be only a misprint, but if not the calculations might have to be repeated and the tables adjusted.

This is really a regrettable misprint. We changed the inaccurate marks of the overlapping categories of BMI in tables 1, 3 and 5 (the new category BMI>30) and those of waist circumference in tables 4 and 5 (the new category >102/>88).

On account of this comment we also added a new sentence in the methods section as following:

Page 5, Methods, paragraph 2, line 4:
“Waist circumference was measured to the nearest cm”

Minor Essential Revision 1

The title and the conclusion in the paper, as well as the abstract, imply that the main aim of the study is the prevalence. This is, however, not mentioned in the aims of the study (“Background”, last paragraph), which only focus on the associations between abnormal glucose tolerance and BMI/waist circumference.

An account of this comment we modified the sentence in the last paragraph of the Background section as following:

Page 4, Background, paragraph 5, line 1:
“The aims of this study were to investigate the current prevalence of obesity, central obesity and abnormal glucose tolerance as well as the associations between body mass index (BMI), waist circumference and abnormal glucose tolerance among 45-74 year- old Finnish men and women, and to assess whether the prevalence of abnormal glucose tolerance is associated with increased central obesity among people who are normal weight, overweight or obese”
**Minor Essential Revision 2**

**Discussion, paragraph 3, points to four references (25-28) to the statement that “many cases of diabetes remain undetected for many years”. As far as I can see the references are all to cross-sectional studies not addressing the duration of unknown diabetes. Ref. no. 26 also seems a little dubious as the prevalence according to the English abstract is established in a clinical setting using a reflectometer (One-Touch, Lifescan).**

This is a very important comment. As far as we know there are no published prospective studies addressing the duration of unknown type 2 diabetes. That is the reason we had to cite papers on cross-sectional studies. However, an account of this comment we edited our text in the manuscript as following:

Page 9, Discussion, paragraph 3, line 3:
“*Our results are in line with the data from previous surveys that many cases of diabetes remain undetected in the population since no systematic screening using an OGTT is conducted [25-28]*”

Harris et al. suggested many years ago that the onset of diabetes occurs 4-7 years before the clinical diagnosis. We deleted the reference no. 26 and added a new one addressing the long preclinical phase of type 2 diabetes:

Page 15, References, ref 26:  

**Minor Essential Revision 3**

*A small detail: Results, paragraph 1, table 1. The total prevalence of obesity (BMI >30), is in the text reported as 23.6, while in the table as 23.8 %.*

The prevalence in table 1 has been changed because of re-analysis (see Reviewer 1). Total prevalence of obesity (BMI>30) is now 23.5% in men in the text (page 7, Results; paragraph 1, line 4) and in table 1.

**Minor Essential Revision 4**

*Table 5, heading: “diabetic” should not be used as a noun; use for instance “diabetic patients”, “people with diabetes”; people should not be characterized by their disease.*

We agree with the reviewer 2 on this and changed the title of table 5 to “*Age- and sex-adjusted prevalence of screen-detected T2D, IGT, IFG and AGT by BMI and waist circumference categories. Excluding people with known diabetes from the calculations*”
Minor Essential Revision 5

Discussion, 5. paragraph, line 7: "those for central obesity between 1.9 and 2.6" should be rephrased to "-1.9 in women and 2.6 in men"

We have rephrased the text as suggested:

Page 9, Discussion, paragraph 4, line 6:
“The odds ratios in men and women with undiagnosed diabetes mellitus compared to non-diabetic subjects for obesity were 1.9 and those for central obesity -1.9 in women and 2.6 in men”.