

## PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form ([see an example](#)) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below. Some articles will have been accepted based in part or entirely on reviews undertaken for other BMJ Group journals. These will be reproduced where possible.

### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Prevalence of Prediabetes in England from 2003-2011: Population Based, Cross Sectional Study
<b>AUTHORS</b>	Mainous III, Arch; Tanner, Rebecca; Baker, Richard; Zayas, Cilia; Harle, Christopher

### VERSION 1 - REVIEW

<b>REVIEWER</b>	King, Dana West Virginia University, USA
<b>REVIEW RETURNED</b>	18-Mar-2014

<b>GENERAL COMMENTS</b>	<p>Excellent paper, well written, clear rationale, excellent references, and the methods and variables are well described. the limitations are discussed adequately. The results and conclusions are startling. A few questions and suggestions for the authors are below.</p> <p>Is overweight defined as a BMI over 25, or 25-29.9? it is somewhat unclear in the paper.</p> <p>The Table 2 could be improved by putting darker bars between the study years 2003, 2006, etc. As it is now, the table runs together too much.</p> <p>The results are repeated a lot between the text and the tables. The results would be less redundant if only a few select results that need emphasis appeared in the text.</p>
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<b>REVIEWER</b>	<p>Sonia Saxena Imperial College London United Kingdom</p> <p>I have previously co authored reports with Professor Mainous and Professor Baker but was not involved in this work in any way</p>
<b>REVIEW RETURNED</b>	28-Mar-2014

<b>GENERAL COMMENTS</b>	<p>This study carries a simple but important and alarming message showing the dramatic rise in pre diabetes in England despite an endemicity of obesity</p> <p>Its strengths are that it is internally valid , being based on a combination of anthropometric measures from well conducted standardised surveys</p> <p>The manuscript is well argued, referenced and very clearly presented</p> <p>Increased ascertainment as a result of screening activity -health checks programme has been mentioned as an alternative or additional explanation for the increase in prediabetes across the study time frame. The 2003 data predate the introduction of the pay for performance scheme in the UK and I wonder to what extent</p>
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	<p>would the addition of these targets to manage existing diabetes have impacted on the results? e.g some of those who were picked up as a result may have already had a diagnosis and made a lifestyle change or taken up treatment that would reduce their HbA1c level</p> <p>The study has a major implication for both clinicians to target and identify those at risk and counselling them to make lifestyle changes. There are also higher level implications fro policy makers about resource, cost and possible intervention through legislation that are equally important.</p>
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<b>REVIEWER</b>	Naomi Holman University of Glasgow, UK
<b>REVIEW RETURNED</b>	01-Apr-2014

<b>GENERAL COMMENTS</b>	<p>This paper provides estimates of pre-diabetes in England using the Health Survey for England for 2003 to 2011. It is a novel analysis that presents important data. I have some specific comments below.</p> <p>Page 4, para 1 – the authors indicate that pre-diabetes is associated with a greater risk of vascular and renal complications. However the evidence suggests that the additional risk of macro-vascular disease associated with hyperglycaemia becomes evident at a HbA1c of about 7% whilst the risk for micro-vascular disease rises at about a HbA1c of 6.5%. Both of these levels are in the diabetic rather than pre-diabetic range. I suggest this paragraph needs to be reworded.</p> <p>Page 5, line 5 – the authors refer to ‘minorities’. I think they are referring to ethnic minorities but this should be clarified.</p> <p>Page 7, para 2 – Please refer to which version of the Indices of Multiple Deprivation used and whether it is the same version for all years analysed.</p> <p>Results section – please provide confidence intervals for all percentages reported. Given the size of the samples in this analysis the confidence intervals for many of the values reported will be large and this should be made explicit. If Table 3 is redesigned slightly (also see point below) it would be possible to reduce the reporting of percentages in the text and concentrate on highlighting the pertinent results with appropriate references to the table. This would make the paper easier to read.</p> <p>Table 1 – Please define high blood pressure and high cholesterol level</p> <p>Table 2 – The columns for ‘no pre-diabetes’ are not needed as they can be calculated simply from the data on people with pre-diabetes. This table should also include confidence intervals.</p> <p>Page 15 – the first section of this page appears to be a repeat of earlier text.</p> <p>Table 3/regression model – Age has been divided into two groups but this will still hide potentially significant variations in the risk of prediabetes. I would suggest either including age as a continuous variable or using more detailed breakdown. I would also suggest a more detailed breakdown of BMI might be appropriate.</p> <p>The paper would be further enhanced by including an estimate of the proportion of the increase in prediabetes that can be attributed to the aging population and how much to other factors such as obesity and inactivity.</p>
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## VERSION 1 – AUTHOR RESPONSE

REVIEWER 1

COMMENT:

Is overweight defined as a BMI over 25, or 25-29.9? it is somewhat unclear in the paper.

RESPONSE:

We have modified the manuscript to indicate that in some instances overweight is a BMI of 25-29.9 and obese is a BMI of 30 or higher. In the previous version we had some analyses which classified the population as 25 or higher. We have attempted to be clear about these classifications by indicating to the reader the actual operationalization of the variable.

COMMENT:

The Table 2 could be improved by putting darker bars between the study years 2003, 2006, etc. As it is now, the table runs together too much.

RESPONSE:

We have modified the table in line with this suggestion

COMMENT:

The results are repeated a lot between the text and the tables. The results would be less redundant if only a few select results that need emphasis appeared in the text.

RESPONSE:

We have removed several sentences from the text of the results to eliminate redundancy. We also removed some of the subgroup analyses presented in the text of the results to focus on the most important findings.

REVIEWER 2

COMMENT:

The 2003 data predate the introduction of the pay for performance scheme in the UK and I wonder to what extent would the addition of these targets to manage existing diabetes have impacted on the results? e.g some of those who were picked up as a result may have already had a diagnosis and made a lifestyle change or taken up treatment that would reduce their HbA1c level

RESPONSE:

The reviewer makes an important point. This may be true for people with diabetes, but for those without a diagnosis the numbers of people on Quality Outcomes Framework (QOF) registers are much less than expected. The number of patients on QOF obesity registers are much less than expected. Practices are not being successful in identifying most obese people. This may be explained to some extent by the pressure on time and resources.

REVIEWER 3

COMMENT:

Page 4, para 1 – the authors indicate that pre-diabetes is associated with a greater risk of vascular and renal complications. However the evidence suggests that the additional risk of macro-vascular disease associated with hyperglycaemia becomes evident at a HbA1c of about 7% whilst the risk for micro-vascular disease rises at about a HbA1c of 6.5%. Both of these levels are in the diabetic rather than pre-diabetic range. I suggest this paragraph needs to be reworded.

**RESPONSE:**

The reviewer makes an important point about the relationship between hyperglycaemia and micro and macro-vascular complications. Although presence of disease is clearly more common at the level consistent with diabetes, our reading of the literature is that there is presence of disease at the prediabetes level. Cheng et al (2009), which we had previously cited, showed that evidence of retinopathy begins at HbA1c levels of 5.5%. Further, Plantinga et al (2010), a new article which we have added to our citations, shows 17.7% of adults with prediabetes have indications of chronic kidney disease which is significantly higher than those with no diabetes (11.8%). Moreover, the systematic review/meta-analysis by Ford et al (2010), which we had previously cited, does indicate a modest statistically significant increase in cardiovascular disease at the prediabetic level. We have modified the language to indicate that although disease is more prevalent at the level consistent with diabetes there is evidence that disease is present at prediabetic levels.

**COMMENT:**

Page 5, line 5 – the authors refer to ‘minorities’. I think they are referring to ethnic minorities but this should be clarified.

**RESPONSE:**

The reviewer is correct. We have modified the manuscript accordingly.

**COMMENT:**

Page 7, para 2 – Please refer to which version of the Indices of Multiple Deprivation used and whether it is the same version for all years analysed.

**RESPONSE:**

We have modified the manuscript to indicate that the Indices of Multiple Deprivation are those included in the HSE. The versions used in each of the analyzed HSEs are indicated in the text of the methods.

**COMMENT:**

Results section – please provide confidence intervals for all percentages reported. Given the size of the samples in this analysis the confidence intervals for many of the values reported will be large and this should be made explicit. If Table 3 is redesigned slightly (also see point below) it would be possible to reduce the reporting of percentages in the text and concentrate on highlighting the pertinent results with appropriate references to the table. This would make the paper easier to read.

**RESPONSE:**

We have added confidence intervals. As with our response to the comment from Reviewer 1 we have removed some of the subgroup analyses presented in the text of the results to focus on the most important findings.

**COMMENT:**

Table 1 – Please define high blood pressure and high cholesterol level

**RESPONSE:**

We have revised the manuscript in line with this suggestion and added more language in the text indicating that these variables are reports by the subject as to whether he/she has previously been diagnosed by a doctor with high blood pressure or high cholesterol. They are not clinical levels. We have also added more language to the tables to indicate that these are reports of previous diagnosis.

**COMMENT:**

Table 2 – The columns for ‘no pre-diabetes’ are not needed as they can be calculated simply from the

data on people with pre-diabetes. This table should also include confidence intervals.

**RESPONSE:**

We have removed the residual category as requested. We have also added confidence intervals as requested.

**COMMENT:**

Page 15 – the first section of this page appears to be a repeat of earlier text.

**RESPONSE:**

We have removed this text in line with the suggestion.

**COMMENT:**

Table 3/regression model – Age has been divided into two groups but this will still hide potentially significant variations in the risk of prediabetes. I would suggest either including age as a continuous variable or using more detailed breakdown. I would also suggest a more detailed breakdown of BMI might be appropriate.

**RESPONSE:**

As was previously indicated in the Methods we defined age in this way to be consistent with the NHS Health Check. We feel that this provides significant meaningful information by linking to the screening recommendations of the Health Check. In terms of the classification of BMI we have split BMI into normal, overweight and obese for analyses. This splitting of BMI is also relevant in light of the Department of Health's Chief Medical Officers annual surveillance report discussing obesity. We have cited that report in our revised manuscript.

**COMMENT:**

The paper would be further enhanced by including an estimate of the proportion of the increase in prediabetes that can be attributed to the aging population and how much to other factors such as obesity and inactivity.

**RESPONSE:**

The reviewer makes an important point and obesity and sedentary lifestyle may have had a lagged effect on the prevalence of prediabetes. The population based results in Table 1 show that from 2003-2011 the proportion of the population aged 40 years or older showed only a slight increase (58.2%-59.5%) and the proportion of the population with a BMI of 30 or higher also exhibited a slight increase (21.2%-22.8%). At the same time the prevalence of prediabetes increased from 11.6% to 35.3%. It may be that obesity and age, variables we know are associated with hyperglycaemia, have a lagged effect on the population prevalence of prediabetes but not a clear positive correlation with similar increases over time.