Reviewer’s report

Title: Influence of smoking and diet on glycated haemoglobin and 'pre-diabetes' categorisation: a cross-sectional analysis.

Version: 2 Date: 9 September 2013

Reviewer: Amir Amir Shafat

Reviewer's report:

As a reviewer, I did not have access to previous comments made on this manuscript.

This manuscript presents a retrospective analysis of the Scottish Health Survey 2003-2010. It seeks to find an association between 1. Smoking and glycated HbA1c 2. Fruit/vegetable consumption and glycated HbA1c. The results demonstrate increased HBA1c in the smokers group both in the diabetic range and the pre-diabetic range of HBA1c. Consumption of extra vegetable portion was associated with a small but statistically significant reduction in HbA1c. The authors conclude that this manuscript adds evidence for a link between oxidative stress and protein glycation.

The manuscript is well written, figures are clear and tables neat.

1. The research question is timely and important. The possible association between smoking and diabetes is a valuable one. However, throughout the manuscript, it is not clear if smoking affects diabetic control and so suggestive of a causal role for smoking, or, that smoking increases the glycation of HbA1c, and is therefore a source of bias in the measurement of HbA1c. This distinction should be made explicit.

2. The methods are appropriate and described clearly.

3. The data demonstrate a very small effect – for example for the 0.01% decrease in HbA1c per 80g vegetable portion consumed. Some of the associations may well be the result of correction for 8 different confounders (e.g XYZ)

Discretionary Revisions

L126 consider replacing “variables” with “participants”
L181 Consider changing “approaching 3” to “more than 2 fold” for 2.63 OR
L249 consider re-wording “secure”
L251 consider rephrasing “7% higher” for HbA1c (%)
L316 consider replacing “only” with “only, or even the main”

Minor Essential Revisions

L39 please add a p value to all comparisons made in the abstract
L39 “Smokers twice as likely” – is this data after correction for age, BMI etc.
Please clarify

Blood glucose fluctuations are assumed to be minimal (L82) in non-diabetic participants. However, Wainer (2008, Chance, vol 21 no.4 56-71) illustrate the importance of variability in diabetes.

L162-164 There are 10 adjuster described here Please comment on the possibility that small errors in some adjusters explains the significant differences observed.

L170-171 The data in table 1 appears to be no different between the groups (5.3±0.4 non-smokers vs 5.4±0.4 smokers (% HbA1c). Is there a way to present this data that illustrates the differences?

L287-290 The effect of vegetables is extrapolated here to mean antioxidants. This generalisation is not trivial and would need to be substantiated.

To comply with data deposition standards of publication, please add a link to the data deposition and the experimental design deposition (e.g. www.clinicaltrials.gov)

Major Compulsory Revisions
1. Clarify if the hypothesis is that smoking causes diabetes or biases the HbA1c measurements.
2. L44-46 The conclusion that “this study adds evidence to the neglected link between oxidative stress and protein glycation” is overreaching. No evidence is presented to support the “neglected” link. Furthermore, the generalisation to oxidative stress and protein glycation is not warranted by epidemiological retrospective study.
3. The assumption that glucose levels do not differ among non-diabetic participants needs to be substantiated. It forms the basis of the conclusion that smoking affects HbA1c glycation, but no evidence is presented. In my experience, there is substantial difference both in fasting and postprandial glycaemia within the non-diabetic range. Indeed, the progressive nature of the disease suggests that would be the case (Tabak et al 2012 Lancet 397 2279-90).

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**
I declare that I have no competing interests