PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	A population-based observational study of diabetes during pregnancy in Victoria, Australia, 1999-2008
AUTHORS	Abouzeid, Marian; Versace, Vincent; Janus, Edward; Davey, Mary-Ann; Philpot, Ben; Oats, Jeremy; Dunbar, James

VERSION 1 - REVIEW

REVIEWER	Maximilian de Courten Centre for Chronic Disease Prevention and Management, Victoria University
REVIEW RETURNED	25-May-2014

GENERAL COMMENTS	The manuscript by Abouzeid et al on secular trends in prevalence of diabetes in pregnancy in Victoria, Australia during the past decade has to be characterised as: 'as good as it gets'. Meaning: the topic is researched and presented in a very professional and satisfactorily manner - but the limitations of the data set are so significant that there are only very limited conclusions to be drawn from the findings. The working title and listed objectives of the manuscript aim to characterise and explore drivers of the secular trend in prevalence of diabetes in pregnancy, but - as pointed out by the authors - key drivers such as maternal BMI and diabetes screening practices are not available to them. Hence the focus of the work/manuscript is limited to maternal age and country of birth of the pregnant women - and all conclusions reduced to their relevance. Therefore, albeit a very well researched and written paper, its relevance to a larger audience will remain limited. Given the limitations of the paper, the overall length (especially of the discussion) might be reduced and some of the tables offered as a web-based appendix.

REVIEWER	Denice S Feig Associate Professor, University of Toronto Department of Medicine, Division of Endocrinology and Metabolism Canada
REVIEW RETURNED	26-Aug-2014

GENERAL COMMENTS	This is an interesting study of trends in prevalence of GDM and pre-existing DM in Victoria, Australia. Trends in different ethnic groups according to birth place is also assessed. 1. Page 4, line 54. A more recent large population-based study outlines the trends in GDM and pre-existing DM in Ontario, Canada:

	Feig DS, Hwee J, Shah BR, Booth GL, Bierman AS, Lipscombe LL. Trends in Incidence of Diabetes in Pregnancy and Serious Perinatal Outcomes: A Large Population-Based Study in Ontario, Canada 1996-2010. Diabetes Care 2014;37(6):1590-6. 2. Page 8 it states “As the assumption of independence that underlies tests for linear trend was not fulfilled, such analyses were not performed on the full dataset,” Can you please explain this more fully? Which dataset was used then? Which pregnancies were eliminated? 3. There seems to be an increase in prevalence of GDM after 2004 according to the figures. Can this be explained by changes in diagnostic criteria? Screening? 4. The authors state: “GDM prevalence increased at a greater rate amongst Australian-born non-Indigenous women than among migrant women”. Any possible explanation for this? 5. I assume that all increases in prevalence were statistically significant but the authors have not included p values. Please include somewhere in document. What model was used to assess the trends? 6. Another limitation is that ethnicity is based on place of birth. There may be women of different ethnic groups that are born in Australia that are counted in the non-indigenous group. If they have increased in number then this may explain in part the increase in GDM prevalence in that group. Are they a very small group?

REVIEWER	Signe Foghsgaard Center for Diabetes Research, Department of Medicine, Gentofte Hospital, Copenhagen, Denmark
REVIEW RETURNED	27-Aug-2014

GENERAL COMMENTS	I find the methodological issues discussed in this paper very interesting and highly appropriate to be addressed. The paper is well written and figures easy to understand. Sadly, I do not have extensive knowledge within epidemiological statistics and would not be the right person to judge if the tecnicalities in the analysis are appropriate - but certainly they are described fully.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Reviewer Name Maximilian de Courten
Institution and Country Centre for Chronic Disease Prevention and Management,
Victoria University
Australia
Please state any competing interests or state ‘None declared’: None declared

The manuscript by Abouzeid et al on secular trends in prevalence of diabetes in pregnancy in Victoria, Australia during the past decade has to be characterised as: 'as good as it gets'.
Meaning: the topic is researched and presented in a very professional and satisfactorily manner - but the limitations of the data set are so significant that there are only very limited conclusions to be drawn from the findings.
The working title and listed objectives of the manuscript aim to characterise and explore drivers of the secular trend in prevalence of diabetes in pregnancy, but - as pointed out by the authors - key drivers such as maternal BMI and diabetes screening practices are not available to them. Hence the focus of

the work/manuscript is limited to maternal age and country of birth of the pregnant women - and all conclusions reduced to their relevance.
Therefore, albeit a very well researched and written paper, its relevance to a larger audience will remain limited.

Given the limitations of the paper, the overall length (especially of the discussion) might be reduced and some of the tables offered as a web-based appendix.

We note the reviewer's comments with thanks. We have considered the suggestion that some of the tables be moved to the supplementary appendix. However, we feel it is important to retain the demographic information (table 1) and the prevalence rates (table 2) in the main manuscript.

The manuscript by Abouzeid et al reports on secular trends in prevalence of diabetes in pregnancy in Victoria, Australia during the past decade.
Although the topic is researched and presented in a very professional and satisfactorily manner - the limitations of the data set available to the researchers are so significant that there are only very limited conclusions to be drawn from the findings.

The working title and listed objectives of the manuscript aim to characterise and explore drivers of the secular trend in prevalence of diabetes in pregnancy, but - as fully pointed out by the authors - key drivers such as maternal BMI and diabetes screening practices were not available to them. Hence the focus of the work/manuscript is limited to maternal age and country of birth of the pregnant women - and all conclusions reduced to their relevance.
The reviewer wonders whether the deduction that maternal age is not the only driver of increased diabetes prevalence in pregnancy could also be statistically tested (by multiple regression models against a dummy or unknown variable (= residual drivers) rather than by deduction from the graphs as they authors seem to have done.

We appreciate the reviewer's suggestion to attempt to determine any statistically significant residual drivers that may be present. Whilst it may be possible to undertake the analysis suggested we feel it would not add to the substance of this paper, particularly noting the previous comment about the length of the paper. Based on the existing analyses, we have concluded that factors other than those considered in this study likely largely explain our trend results; essentially, that there is residual confounding by unmeasured variables. If regression analysis proved to be significant, ultimately this same conclusion would be reached. As noted in the comment below, future comparable studies post-2009 data will be able to incorporate BMI. Further to this, the authors currently have under review a paper exploring associations of GDM with socio-economic status.

Given the severe limitations posed by the dataset, the reviewer suggests to include into the text a strong recommendation of obtaining BMI information on pregnant women plus some indication of whether they have been previously screened for diabetes.
A statement has been inserted into the text noting that maternal height and weight have been recorded in the data set since 2009, and that further research is warranted when sufficient BMI trend data become available.

In the section on study limitations, we have noted that it is not possible to identify unscreened pregnancies from the available data. As per the reviewer's suggestion, we have inserted a recommendation that information on diabetes testing status be captured in birth report forms.

Reviewer: 2
Reviewer Name Denice S Feig
Institution and Country Associate Professor, University of Toronto

Department of Medicine, Division of Endocrinology and Metabolism
Canada
Please state any competing interests or state ‘None declared’: None declared

This is an interesting study of trends in prevalence of GDM and pre-existing DM in Victoria, Australia. Trends in different ethnic groups according to birth place is also assessed.

1. Page 4, line 54. A more recent large population-based study outlines the trends in GDM and pre-existing DM in Ontario, Canada: Feig DS, Hwee J, Shah BR, Booth GL, Bierman AS, Lipscombe LL. Trends in Incidence of Diabetes in Pregnancy and Serious Perinatal Outcomes: A Large Population-Based Study in Ontario, Canada 1996-2010. Diabetes Care 2014;37(6):1590-6.

Reference 11 has been replaced with this more recent study.

2. Page 8 it states “As the assumption of independence that underlies tests for linear trend was not fulfilled, such analyses were not performed on the full dataset,” Can you please explain this more fully? Which dataset was used then? Which pregnancies were eliminated?

We apologise for the ambiguity of this statement. Tests for linear trend were not performed on the full dataset in which the same woman could be represented multiple times. Rather, tests for linear trend were only performed as part of the sensitivity analysis on the subgroup of women in their first pregnancy. This has been clarified in the text.

3. There seems to be an increase in prevalence of GDM after 2004 according to the figures. Can this be explained by changes in diagnostic criteria? Screening?

Recommendations for screening and diagnostic criteria were consistent over the study period. As noted in the text, it is possible that screening practice may have changed over time. However, unscreened pregnancies cannot be identified from the available data. We have inserted a recommendation that birth report forms collect information on maternal diabetes screening status.

4. The authors state: “GDM prevalence increased at a greater rate amongst Australian-born non-Indigenous women than among migrant women”. Any possible explanation for this?

From the available data, it is not possible to elucidate the underlying cause. As noted in the text, it is possible that risk factor distribution or screening uptake changed more over time for some groups than others, or that there is a difference in the proportion of diagnosed to undiagnosed diabetes between migrants and locally-born women.

5. I assume that all increases in prevalence were statistically significant but the authors have not included p values. Please include somewhere in document. What model was used to assess the trends?

We have opted in this manuscript to provide the reader with confidence intervals as opposed to large numbers of p-values. We believe this allows the reader to interrogate Table 2 and draw their conclusions about the prevalence of GDM over time (1999 to 2008) using different denominators. We feel this presentation coupled with the accompanying text strikes the right balance.
With reference to the final sentence in first paragraph under subheading ‘Prevalence of GDM’ we have inserted the word ‘linear’ to define the type of trend we are discussing. This sentence now reads:

‘Analysis of data from women in their first pregnancy who did not have pre-existing diabetes revealed a significant positive linear trend in the prevalence of the crude ($p<0.001$) and age-standardised

($p<0.001$) rates of GDM over the study period.'

With reference to the figures 1a, 1b and 1c, the data used to generate these includes women with multiple pregnancies during the study window – this precludes the use of a linear regression as the assumption of non-independence is violated. The intention of these figures is descriptive as they present administrative data for the reader.

6. Another limitation is that ethnicity is based on place of birth. There may be women of different ethnic groups that are born in Australia that are counted in the non-indigenous group. If they have increased in number then this may explain in part the increase in GDM prevalence in that group. Are they a very small group?

We agree with the reviewer that women may have been born in Australia and therefore included in the Australian non-Indigenous group but be of various ethnic backgrounds and have the behavioural and biological risk profile of their ethnicities of origin. As ethnicity is not captured in the dataset, it is not possible to ascertain the extent to which this is the case. We have included this point in the limitations section of the discussion.

Reviewer: 3
Reviewer Name Signe Foghsgaard
Institution and Country Center for Diabetes Research, Department of Medicine, Gentofte Hospital, Copenhagen, Denmark
Please state any competing interests or state 'None declared': none declared

I find the methodological issues discussed in this paper very interesting and highly appropriate to be addressed. The paper is well written and figures easy to understand.
Sadly, I do not have extensive knowledge within epidemiological statistics and would not be the right person to judge if the technicalities in the analysis are appropriate - but certainly they are described fully.

We note the reviewer comments with thanks.

VERSION 2 – REVIEW

REVIEWER	Denice S Feig University of Toronto, Canada
REVIEW RETURNED	03-Oct-2014

GENERAL COMMENTS	The authors have addressed the comments satisfactorily.