PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (**http://bmjopen.bmj.com/site/about/resources/checklist.pdf**) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	A prospective, observational study investigating the use of carbon monoxide screening to identify maternal smoking in a large university hospital in Ireland.
AUTHORS	Reynolds, Ciara; Egan, Brendan; Kennedy, Rachel; O'Malley, Eimer; Sheehan, Sharon; Turner, Michael

VERSION 1 – REVIEW

REVIEWER	Jamie Bryant University of Newcastle, Australia
REVIEW RETURNED	15-Feb-2018

GENERAL COMMENTS	"Similar rates were found in other developed countries"- this statement needs supporting references "However, younger women have consistently higher smoking rates, regardless of pregnancy status." What is the relevance of this statement? This paper does not focus on younger women Introduction needs to include a discussion of previous research that has used BCO testing with pregnant women- this is not the first study to do this. What this study is therefore adding to the literature also needs to be more clearly emphasized. There is no consideration of previous research which has looked at rates of deception in reporting of smoking status amongst pregnant women. Currently the need for the study and what information it is adding is not clearly articulated. Im unsure whether the purpose of the paper is to provide data about rates of deception in reporting of smoking status amongst pregnant women at their first antenatal visit, to establish an optimal cut point for CO testing, or both? Methods section is lacking detail in reporting of procedures used. What does "recruited via convenience sampling" mean? More detailed required here- i am unsure how the authors recruited their sample Who were women recruited by- their healthcare provider or a research assistant? This is important information as it may have impacted consent rates What was the rationale for offering "any individual in attendance with the woman at the first visit" participation in the study? Presumably this person was not pregnant, and the aim of the study is to "evaluate the use of BCO screening to detect cigarette smoking in women presenting to a maternity hospital for antenatal care". Suggest the authors remove this data from the manuscript, or refine

	their paper to include an aim related to this data "Due to large variations in the cut8off criteria used previously to distinguish between smokers and non smokers" This statement needs supporting references. More detail is needed about the self-report information collected from participants. Much of the information in the discussion could be moved into the introduction to better contextualise the research. E.g the paragraph 'A challenge of BCO testing is the half8life of CO" provides background information.

REVIEWER	Katarzyna Campbell, Research Fellow University of Nottingham, UK
REVIEW RETURNED	28-Feb-2018

GENERAL COMMENTS	Thank you for the opportunity to read and review this interesting manuscript. The issue of identification of smokers early in pregnancy is an important one and there is an ongoing need to perfect the methodology and tools used for this purpose. I didn't think the use of CO for identification of smokers in pregnancy is a particularly novel subject, however I have not seen a study conducted in Ireland, and perhaps making this more context specific could add value to the findings. I have found a few issues that I would like to highlight: Methods: Could the Authors consider that the data collected in this study were presented as a figure/list (I refer the Authors to Bauld, Hackshaw, Ferguson et al., 2012, doi:10.1111/j.1360-0443.2012.04086.x for an example). It could help to see, at a glance, what type of data was collected at which point and by whom. Describing the contents of the questionnaire in more detail would also be helpful. The fact that the BCO smoking status was not verified using other biomarkers, such as cotinine levels, as well as self-report is a limitation of the study. I agree with the Authors that using saliva/urine samples may not be practical or cost effective in general practice, however considering the aims of the paper and the fact that the sample was relatively small, perhaps the Authors could provide the rationale for not using other biomarkers to verify smoking status. Page 7, line 49 – Based on previous work – please reference. Has this study received ethical approval? If yes, please consider reporting this, if not – please explain why this was unnecessary. Results: Please could the Authors review the way results are presented in text and tables. For example, Page 9, Lines 9 – 21, in the text there are some analyses presented (not for all variables), but these findings don't appear in the table – please could you explain if only

	significant differences between groups are presented? I would like to see all analyses (or at least the significance levels) in the table, to allow the reader to make their own comparison. Page 9, Lines 23 – 31: is this data in Table 3? If so, it appears before Table 2 is described. Please ensure all tables contain all relevant information that is being discussed, describe all tables in sufficient detail and correct order, making sure each table is referenced in the text. I am not sure what is the significance of the partners smoking levels is within this study (Page 9, lines 33 – 53) – this is not part of the aims and these findings are not discussed. Discussion: I found that some important papers on the subject of using CO for identification of smokers have been omitted. Particularly, in the aforementioned study by Bauld et al. the authors conducted similar ROC analysis. (This could be mentioned on Page 12, Line 5 – 7) They estimated the cut-off point at 4ppm. Considering that non-disclosers in the current study had significantly lower CO than disclosers and "tend to have more similar characteristics to non-smokers than smokers" (Page 12, Line 53), could the Authors discuss their findings in light of Bauld et al., particularly commenting on the benefits vs risks of lowering CO cut-off point, and the effects this may have on false positive results. Other studies (e.g. Campbell, Cooper, Fahy et al., 2017; Campbell, Bowker, Naughton, et al., 2016) also used 4ppm cut of point and described the difference between self-reported smoking rates and CO-verified rates as well as discussed the impact of the false positive results on the women who do not smoke and health professionals. Finally, there are some issues with the writing style. I suggest the Authors proofread the manuscript, as there are some mistakes; just to give a couple examples: Page 5, line 9: "Smoking cessation either pregnancy or in the first half of pregnancy" – Should this read "either before pregnancy or in the first half…"? Page 5, line 33: from urine, saliva or urinary samples – "blood samples"? The Discussion is a bit hard to read, as the examples don't always match the statement before, the linking words are sometimes used inappropriately and on occasion I felt the sentence finished before the Authors got to the point, for example: Page 13, Line 7: I wonder if the Authors meant "therefore" instead of

	"for example" Page 13, lines 9 – 18: This needs more careful consideration and more discussion of your findings in light of other studies. I found it difficult to follow as it is.

REVIEWER	Van Tong CDC, USA
REVIEW RETURNED	18-Mar-2018

GENERAL COMMENTS	The authors conducted used a prospective observational study to evaluate the use of carbon monoxide (CO) screening to detect cigarette smoking in women presenting to a maternal hospital for antenatal care. One overarching concern of using biochemical measures is that pregnant women who don't disclose smoking may not want cessation assistance. Authors should discuss the implication of this type of screening if resistance is seen in women, and how it may or may not be patient-centered. A few comments are provided for the authors' consideration. • Abstract, line 32. It appears there is a typo. • From methods page 6, line 45. It is unclear what was the self-reported question of smoking at the antenatal visit and in the research questionnaire. There are number of studies that have found asking a simple yes no question ascertains less smoking than other questions that allow women to report a number of different smoking patterns. This would help to better assess the quality of the self-reported measure. • Page 7, line 46. Please verify one call out of the references, as it says "new reference 1" • Given that SHS and other smoke exposure could explain possible false positives, the authors note in the discussion that others sources of smoke did not change the cut-offs. However, this was not detailed in methods or results. • Page 13, para 2. It is not clear what the authors mean in the paragraph. Do you mean that the antenatal care screening is interview administered and research questionnaire is self-administers? The authors should also add more detail in the methods if this will be included as a discussion point. • In general, the authors compare their findings with other studies, but the discussion lacks clarity and focus in what overarching messages they are trying to convey. Improvements in the discussion are needed.

VERSION 1 – AUTHOR RESPONSE

Reviewer 1 comments:

"Similar rates were found in other developed countries"- this statement needs supporting references.

The references Reynolds et al. 2017 and Reitan and Callinan 2017 have been added to this statement.

"However, younger women have consistently higher smoking rates, regardless of pregnancy status." What is the relevance of this statement? This paper does not focus on younger women.

This statement has been removed from the manuscript.

Introduction needs to include a discussion of previous research that has used BCO testing with pregnant women- this is not the first study to do this. What this study is therefore adding to the literature also needs to be more clearly emphasized. There is no consideration of previous research which has looked at rates of deception in reporting of smoking status amongst pregnant women.

Many thanks for this helpful feedback. The following has been added to the second paragraph of the introduction 'As many as three quarters of women may not disclose their smoking status when they present to the maternity services, however, there are large discrepancies in the literature regarding rates of non-disclosure and none to date have been reported for Ireland.'

Currently the need for the study and what information it is adding is not clearly articulated. I'm unsure whether the purpose of the paper is to provide data about rates of deception in reporting of smoking status amongst pregnant women at their first antenatal visit, to establish an optimal cut point for CO testing, or both?

We agree the aim and novelty of the study was lacking clarity and so the following aims have been added to the final paragraph of the introduction section 'The purpose of this study was to evaluate the use of BCO screening in detecting cigarette smoking in women presenting to an Irish maternity hospital for antenatal care as well as characterise the difference between disclosers and non-disclosers of smoking status. We also investigated if other extrinsic factors affected the women's' BCO levels in pregnancy.'

We have also outlined the gaps in current literature on carbon monoxide screening that this study is addressing such as 'there are large discrepancies in the literature regarding rates of non-disclosure and none to date have been reported for Ireland' and 'there is a dearth of knowledge of the degree to which these extrinsic factors, as well as partners smoking habits and BCO levels can affect routine CO screening.'

Methods section is lacking detail in reporting of procedures used. What does "recruited via convenience sampling" mean? More detailed required here- i am unsure how the authors recruited their sample.

This statement has been removed and a clearer explanation of recruitment has been added to the second and third paragraph of the methods section. A flow diagram of recruitment and data collection has also been created for further clarity (Figure 1.).'

Who were women recruited by- their healthcare provider or a research assistant? This is important information as it may have impacted consent rates.
A single researcher (C.R.) recruited all women to the study. This information has also been added to the methods section in the second and third paragraph.

What was the rationale for offering "any individual in attendance with the woman at the first visit" participation in the study? Presumably this person was not pregnant, and the aim of the study is to "evaluate the use of BCO screening to detect cigarette smoking in women presenting to a maternity hospital for antenatal care". Suggest the authors remove this data from the manuscript, or refine their paper to include an aim related to this data

The rationale of asking partners of the women to also take to BCO test was to assess if partners' BCO had any effect on maternal BCO levels.

Introduction paragraph five now states the rationale 'there is a dearth of knowledge of the degree to which these extrinsic factors, as well as partners smoking habits and BCO levels can affect routine CO screening.'

The final paragraph of the introduction now contains the related aim 'We also investigated if other extrinsic factors affected the women's' BCO levels in pregnancy.'

"Due to large variations in the cut-off criteria used previously to distinguish between smokers and non smokers" This statement needs supporting references.

Supporting references (West et al. 2005;Campbell et al. 2001; Bauld et al 2012, Nice 2010; Campbell et al. 2016, Campbell et al. 2017) have now been added to the above statement.

More detail is needed about the self-report information collected from participants

The self-reported data and when it was collected is explained in more detail in the new figure created (Figure 1; see the end page of this document).

Much of the information in the discussion could be moved into the introduction to better contextualise the research. E.g the paragraph 'A challenge of BCO testing is the half8life of CO" provides background information.

The introduction now contains the paragraph 'A challenge of BCO testing is the half-life of CO.'

Paragraphs three and four have been amended and added to in an effort to better contextualise the research.

Reviewer 2 comments: Attached file

I have not seen a study conducted in Ireland, and perhaps making this more context specific could add value to the findings.

Thank you for this helpful comment the following has been added to the second paragraph of the introduction in light of this feedback 'however there are large discrepancies in the literature regarding rates of non-disclosure and none to date have been reported for Ireland'

Could the Authors consider that the data collected in this study were presented as a figure/list (I refer the Authors to Bauld, Hackshaw, Ferguson et al., 2012, doi:10.1111/j.1360-0443.2012.04086.x for an

example). It could help to see, at a glance, what type of data was collected at which point and by whom. Describing the contents of the questionnaire in more detail would also be helpful.

Figure 1 has been created, with assistant from the reference Bauld et al 2012. This figure contains the type of data collected, by whom and gives insights into the contents of the questionnaire. The figure has been attached to the final page of this document.

The fact that the BCO smoking status was not verified using other biomarkers, such as cotinine levels, as well as self-report is a limitation of the study. I agree with the Authors that using saliva/urine samples may not be practical or cost effective in general practice, however considering the aims of the paper and the fact that the sample was relatively small, perhaps the Authors could provide the rationale for not using other biomarkers to verify smoking status.

This limitation has not been addressed in the manuscript in the fourth paragraph of the discussion section and also provides rationale for not using other biomarkers to verify smoking 'A limitation of our study is that we did not collect cotinine samples for verification of smoking status; however, our aim was not to compare screening methods, but to report the levels of non-disclosures in Ireland using current guidelines (NICE 2010). Furthermore, our lower cut-off point provided high sensitivity values and has been supported by previous research that also identified this value as optimal when identification of smoking abstinence with a high degree of certainty is of high importance (Javours et al.2005).'

Page 7, line 49 – Based on previous work – please reference

This line has now been referenced with Tong et al. 2015.

Has this study received ethical approval? If yes, please consider reporting this, if not – please explain why this was unnecessary.

This study has received ethical approval and the following statement has been added to the first paragraph of the methods section: 'The study was approved by the Hospital Research Ethics Committee (17-2015).'

Please could the Authors review the way results are presented in text and tables. For example, Page 9, Lines 9 – 21, in the text there are some analyses presented (not for all variables), but these findings don't appear in the table – please could you explain if only significant differences between groups are presented? I would like to see all analyses (or at least the significance levels) in the table, to allow the reader to make their own comparison.
The significance levels have now been added to Table 1 and an extra supplementary table has been added to show results not previously presented within the manuscript due to table number restrictions.

Page 9, Lines 23 – 31: is this data in Table 3? If so, it appears before Table 2 is described. Please ensure all tables contain all relevant information that is being discussed, describe all tables in sufficient detail and correct order, making sure each table is referenced in the text.
This data has now been included in Table 2 in the supplementary file as the restriction on the numbers of table in the main document did not allow for further additions.

I am not sure what is the significance of the partners smoking levels is within this study (Page 9, lines 33 – 53) – this is not part of the aims and these findings are not discussed.

An aim regarding partners BCO and smoking levels has been added 'We also investigated if other extrinsic factors affected the women's' BCO levels in pregnancy.' These have now been discussed in the discussion paragraph 3 beginning 'There is a dearth of knowledge on what factors other than active smoking can effect BCO levels and SSS often find difficult to explain high results in non-smokers (Campbell et al.2016)…….'

I found that some important papers on the subject of using CO for identification of smokers have been omitted. Particularly, in the aforementioned study by Bauld et al. the authors conducted similar ROC analysis. (This could be mentioned on Page 12, Line 5 – 7) They estimated the cut-off point at 4ppm. Considering that non-disclosers in the current study had significantly lower CO than disclosers and "tend to have more similar characteristics to non-smokers than smokers" (Page 12, Line 53), could the Authors discuss their findings in light of Bauld et al., particularly commenting on the benefits vs risks of lowering CO cut-off point, and the effects this may have on false positive results. Other studies (e.g. Campbell, Cooper, Fahy et al., 2017; Campbell, Bowker, Naughton, et al., 2016) also used 4ppm cut of point and described the difference between selfreported smoking rates and CO-verified rates as well as discussed the impact of the false positive results on the women who do not smoke and health professionals.

Many thanks for this very helpful comment and useful references. All aforementioned references have now been added and discussed in the manuscript. Paragraphs six, seven and eight discuss our results in light of Bauld et al. as well as the potential reasons the non-disclosures 'have more similar characteristics to non-smokers than smokers'. We have discussed the implications of increasing or maintaining the cut-off point, as well as offering a solution to the concerns healthcare staff have in relation to false positive results reported in Campbell et al. 2016. Paragraph 11 also discusses our 'self-reported smoking rates' in relation to Campbell et al. 2017 and Bauld et al. 2012 who used the higher cut-off point.

Page 5, line 9: "Smoking cessation either pregnancy or in the first half of pregnancy" –
Should this read "either before pregnancy or in the first half…"?
This line now reads: 'smoking cessation either pre-pregnancy or in the first half of pregnancy'. Many thanks for this observation.

Page 5, line 33: from urine, saliva or urinary samples – “blood samples”?
‘Urinary samples’ has now been replaced with ‘blood samples’.

The Discussion is a bit hard to read, as the examples don’t always match the statement before, the linking words are sometimes used inappropriately and on occasion I felt the sentence finished before the Authors got to the point, for example:
Page 13, Line 7: I wonder if the Authors meant “therefore” instead of “for example”
Correct this line should have read ‘therefore’ instead of ‘for example’ and has now been amended.
Overall, the discussion has been heavily edited and redrafted in sections in light of all reviewers helpful comments and suggestions.

Page 13, lines 9 – 18: This needs more careful consideration and more discussion of your findings in light of other studies. I found it difficult to follow as it is.
These lines have now been removed and replaced with discussions relating to studies the reviewer mentioned that used a higher cut-off point to verify smoking status. This can be read in paragraph number six of the Discussion section.

Reviewer 3 comments:
The authors conducted used a prospective observational study to evaluate the use of carbon monoxide (CO) screening to detect cigarette smoking in women presenting to a maternal hospital for antenatal care. One overarching concern of using biochemical measures is that pregnant women who don’t disclose smoking may not want cessation assistance. Authors should discuss the implication of this type of screening if resistance is seen in women, and how it may or may not be patient-centered.

Many thanks for this helpful comment. This has been discussed in relation to the ‘opt-out’ referral system recommended by NICE 2010. ‘A further concern is that women who may smoke but did not report doing so at their first appointment may not wish to receive cessation advice. However, guidelines recommend an opt-out referral system whereby women who are identified as smokers in early pregnancy and those who do not specifically object are referred to smoking cessation services (NICE 2010). Thus this non-mandatory referral system is centred on the patient’s best interests and it does not overrule personal choice.’

Abstract, line 32. It appears there is a typo.

This typo ‘when’ has been fixed to ‘women’, many thanks for this observation.

From methods page 6, line 45. It is unclear what was the self-reported question of smoking at the antenatal visit and in the research questionnaire. There are number of studies that have found asking a simple yes no question ascertains less smoking than other questions that allow women to report a number of different smoking patterns. This would help to better assess the quality of the self-reported measure.

Thank you for this helpful feedback. Further information on the self-reported data collected at each time point has been included in a new figure created to clarify all data collection methods. Please see Figure 1 included on the last page of this document.

Page 7, line 46. Please verify one call out of the references, as it says “new reference 1”

Many thanks for this observation; this ‘reference 1’ has been replaced with the reference ‘Middleton et al. 2000’.

Given that SHS and other smoke exposure could explain possible false positives, the authors note in the discussion that others sources of smoke did not change the cut-offs. However, this was not detailed in methods or results.

Details on the extrinsic carbon monoxide exposure collected as part of the study is now detailed in the methods section (paragraphs 4 and 5), Figure 1 and in the results section (paragraphs 4-6).

Page 13, para 2. It is not clear what the authors mean in the paragraph. Do you mean that the antenatal care screening is interview administered and research questionnaire is self-administers? The authors should also add more detail in the methods if this will be included as a discussion point.

We agree that this discussion point, on reflection, was unclear and has since been removed given the large amount of discussion added due to other reviewer comments.

In general, the authors compare their findings with other studies, but the discussion lacks clarity and focus in what overarching messages they are trying to convey. Improvements in the discussion are needed

Overall, the discussion has been heavily edited and redrafted in sections in light of all reviewers helpful comments and suggestions.

VERSION 2 – REVIEW

REVIEWER	Katarzyna Campbell University of Nottingham, UK
REVIEW RETURNED	18-Apr-2018

GENERAL COMMENTS	I found the revised manuscript to be much improved in content and clarity. I have no further comments. Thank you.

VERSION 2 – AUTHOR RESPONSE

Thank you for your helpful feedback. All of the feedback has been addressed and changes within the manuscript are highlighted in red text.

1. As part of the rational for carrying out your study is that this research question has not been examined previously in Ireland please modify the 'setting' section of your Abstract to include the country.

The country has been added to the 'setting' section of the manuscript. The setting section now reads 'A university obstetric hospital in an urban setting in Ireland.'

2. We recommend that you thoroughly proofread your revised article before submission to improve the quality of the English. For example, we noted several places in the revised text where duplicate words interrupt the flow of the text.

The article has been thoroughly read and many changes have been made to improve the quality of English including the deletion of duplicate words.