PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	A systematic review and meta-analysis of diabetes mellitus, cardiovascular and respiratory condition epidemiology in sexual minority women.
AUTHORS	Meads, Catherine; Martin, Adam; Grierson, Jeffrey; Varney, Justin

VERSION 1 – REVIEW

REVIEWER	Michele Eliason San Francisco State University United States
REVIEW RETURNED	24-Nov-2017

GENERAL COMMENTS	I am satisfied with the revisions and think this paper has much to add to the current literature on SMW health

REVIEWER	Ellen McCreedy Brown University, School of Public Health, USA
REVIEW RETURNED	18-Dec-2017

GENERAL COMMENTS	This is much improved, but I still don't understand how the authors dealt with confounding by age. That is critical to interpreting their findings. 3.1.a. Thank you for including your search strings in this revision. 1. Why did you only use the acronym (wsw), and not the full phrase "women who have sex with women" in your keyword searches? 2. I'm not sure about limiting your search to "female." Gender identity is a different concept. I don't think that is part of your inclusion criteria. 3. You limit your searches to 2015 forward. I'm assuming this is the updated search? The original search was limited to 2010 forward, correct? You may want to show both. 3.1.b. I don't think this response was clear enough with respect to controlling for age. Given the relationship between age and development of chronic conditions, all the estimates used for the meta-analysis should be adjusted for age. "Where stated, these all adjust for age" is not the same as they are all adjusted for age. I would like some more details on how those estimates were adjusted for age before meta-analysis (which stratum were used for the M-H estimates). Alternatively, you could show me the meta-analyses for those less than 55 and those over 55 (or something like that). I'm happy to look at this again.

REVIEWER	Gilbert Gonzales Vanderbilt University School of Medicine, USA
REVIEW RETURNED	20-Dec-2017

GENERAL COMMENTS	Thank you for addressing my suggestions and comments. Here are a few minor suggestions that may help improve the manuscript: 1. Drop "inequalities" in the conclusions of the abstract. Just use "health estimates." 2. Please provide citations for "chronic disease risk factors" in the 2nd paragraph on page 4. 3. The authors describe previous systematic reviews of physical health on page 4, but are there other systematic reviews on health behaviors (e.g., tobacco use, alcohol consumption, obesity) and mental health that should be described here in the literature review? 4. Remove the extra period at the end of the "Methods" section on page 4. 5. Please be very specific on the words used to search "physical conditions" at the top of page 4. 6. Please remove the misplaced "and" at the top of page 6. 7. Please briefly describe or provide an overview of the results in Table 2 and Appendix Tables 3-5 mentioned on page 6. What should the reader take away from these tables, if anything? 8. Please make "sexual minoritypopulations" three words on page 10. 9. The new discussion about hormone levels in SMW is random on page 10. Some readers may also find this offensiveness, especially without credible sources or citations. 10. Please proofread this manuscript carefully prior to submission. Thank you for allowing me to review this manuscript.

VERSION 1 – AUTHOR RESPONSE

BMJ Open comment responses 2. 12 January 2018

Reviewer: 1
Reviewer Name: Michele Eliason
Institution and Country: San Francisco State University, United States Competing Interests: None declared

I am satisfied with the revisions and think this paper has much to add to the current literature on SMW health

Reviewer: 2
Reviewer Name: Ellen McCreedy
Institution and Country: Brown University, School of Public Health, USA Competing Interests: None Declared

This is much improved, but I still don’t understand how the authors dealt with confounding by age. That is critical to interpreting their findings.

3.1.a. Thank you for including your search strings in this revision.

1. Why did you only use the acronym (wsw), and not the full phrase “women who have sex with women” in your keyword searches?

Response: the search strings used the term ‘women’, which picks up ‘women who have sex with women’ so we did not add the longer term.

2. I’m not sure about limiting your search to “female.” Gender identity is a different concept. I don’t think that is part of your inclusion criteria.

Response: This project is on incidence of certain physical conditions in sexual minority women, so our inclusion criteria did specify women. This is why we limited the searches to female. We agree that gender identity is a different concept. We explained in the Appendix of our previous comment response that we would have included both cis and trans women in our systematic review. However, none of the included studies had sufficient samples of transwomen to give proportions of the conditions we were investigating. For example Boehmer 2014 states that ‘transgender identity was not ascertained; therefore data on transgender individuals was not available’. This limitation was also mentioned in Dilley 2010 and Mathews 2014, and Blosnich 2014 states that ‘information about transgender populations is extremely limited’.

3. You limit your searches to 2015 forward. I’m assuming this is the updated search? The original search was limited to 2010 forward, correct? You may want to show both.

Response: The searches detailed in the Web Appendix are indeed the 2016 searches. We have now added the search terms used in the OVID Medline 2015 searches. It can be seen that they were very similar but for the 2016 searches we omitted the less useful 2015 terms.

3.1.b. I don’t think this response was clear enough with respect to controlling for age. Given the relationship between age and development of chronic conditions, all the estimates used for the meta-analysis should be adjusted for age. “Where stated, these all adjust for age” is not the same as they are all adjusted for age. I would like some more details on how those estimates were adjusted for age before meta-analysis (which stratum were used for the M-H estimates). Alternatively, you could show me the meta-analyses for those less than 55 and those over 55 (or something like that).

Response: We are very sorry that our previous response was insufficiently clear. On Web Table 1 we list the weightings mentioned in the study reports for the prevalence estimates and for the adjusted odds ratios. It can be seen that most of the studies state that they adjust for age. Some do not state the adjustment factors. Few of them are explicit as to exactly how they adjusted for age.
For example, Blosnich 2014 states that ‘while adjusting for age, race/ethnicity …’ but does not give how this was done, whereas Boehmer 2014 states that age was considered the main independent variable and was categorised into three age groupings – 20-39, 40-59 and 60+. In Everett 2013, age was coded as a continuous variable ranging from 24 to 34 years. Farmer 2013 calculated vascular age using the Framingham algorithm. Fredriksen-Goldsen 2013 only investigated people aged 50+. Garland-Forshee 2014 coded people into three age groups – 18-34, 35-54 and 55+. Jackson 2016 coded people into 2 age groups – 18-30 and 31-85+ years. Kann 2016 investigated schoolchildren aged 15-18. All of the participants in McNair were aged 25-30 years. None of the other included studies described how they adjusted for age. Some of them do not give mean and ranges for the ages of participants in the sample (see Web Table 1). So we are very sorry but there is insufficient data to conduct stratified analyses. We do present meta-analysis of adjusted odds ratios and this are much more likely to give more accurate results than the percentages, as AORs are adjusted and almost of them specify that age was adjusted for. We discuss the difficulties around adjusting for age in the strengths and weaknesses section. We would be happy to add more if you consider it appropriate.

One of the difficulties with systematic reviewing is that you can only use the data as presented in the included studies. We agree that the included studies' reporting on age adjustment is less than ideal. The way to do this much better would be to do an individual patient meta-analysis, but this would involve all of the studies sending their patient data in to a central review team and the systematic reviewers re-analysing by age. This would be very useful but beyond the resources of the current project.

Reviewer: 3
Reviewer Name: Gilbert Gonzales
Institution and Country: Vanderbilt University School of Medicine, USA Competing Interests: None declared.

Thank you for addressing my suggestions and comments. Here are a few minor suggestions that may help improve the manuscript:

1. Drop "inequalities" in the conclusions of the abstract. Just use "health estimates."

Response: done

2. Please provide citations for "chronic disease risk factors" in the 2nd paragraph on page 4.

Response: done

3. The authors describe previous systematic reviews of physical health on page 4, but are there other systematic reviews on health behaviors (e.g., tobacco use, alcohol consumption, obesity) and mental health that should be described here in the literature review?

Response: The already used citations listed below investigated health behaviours and mental health in the LGB community:
*Committee on Lesbian, Gay, Bisexual and Transgender Health Issues and Research Gaps and Opportunities. The health of lesbian, gay, bisexual and transgender (LGBT) people: building a foundation for better understanding; Board on the Health of Select Populations; Institute of Medicine, The National Academy of Science. Washington DC, 2011.
* Hudson-Sharp N, Metcalf H. Inequality among lesbian, gay bisexual and transgender groups in the UK: a review of evidence. National Institute of Economic and Social Research, London 2016
*Edmondson D, Hodges R, Williams H. The lesbian, gay, bisexual and trans public health outcomes framework companion document, 2016 update. National LGB&T Partnership, 2016
*Blondeel K, Say L, Chou D, Toskin R, Khosla R, Scolaro E, et al. Evidence and knowledge gaps on the disease burden in sexual and gender minorities: a review of systematic reviews. International Journal for Equity in Health 2016;15:16
We agree that there are a number of other systematic reviews in these areas but are not sure that additional citations would add more to the journal article.

4. Remove the extra period at the end of the "Methods" section on page 4.

Response: done

5. Please be very specific on the words used to search "physical conditions" at the top of page 4.

Response: We didn't use search terms to search for these conditions (CVD, hypertension, diabetes mellitus and respiratory conditions). In the Prisma diagram you will see that we looked through 692

full texts. We were looking for any includable studies reporting relevant physical conditions. We did this because searching via the databases would have yielded fewer studies because most the titles and abstracts of the included studies did not mention the conditions we were looking for. We now make this explicit in the text.

6. Please remove the misplaced "and" at the top of page 6.

Response: we're very sorry but we can't find a misplaced 'and'

7. Please briefly describe or provide an overview of the results in Table 2 and Appendix Tables 3-5 mentioned on page 6. What should the reader take away from these tables, if anything?

Response: we have added a short paragraph about this.

8. Please make "sexual minoritypopulations" three words on page 10.

Response: done

9. The new discussion about hormone levels in SMW is random on page 10. Some readers may also find this offensiveness, especially without credible sources or citations.

Response: We are currently completing the systematic review of hormone levels so cannot cite it as yet, so have deleted this sentence.

10. Please proofread this manuscript carefully prior to submission.

Response: done

IN ADDITION
In response to the Editorial Office request, I have combined figures 1 and 2 into one subgroup meta-analysis, which also includes the results for SMW now so improves this aspect of reporting of the results. The text in the main document has been altered to match. Previous correspondence with the Editorial Office discussed the fact that Revman files can only be saved in a limited number of formats, and that you indicated that the .png format was the best one to use, so I have uploaded the forest plot in that format and hope that it has a resolution of at least 300 dpi. Also as requested I have uploaded the supplementary file as a pdf.
In response to the second editorial request, I have included a reference to the Web Figure 1 in the main text. Regarding the Forest plot, please note that this was done in the Revman package which is an industry standard for systematic reviews. Therefore you must have had numerous Forest plots submitted to BMJ Open drawn in this package. As you already know, I have previously had correspondence with you about the available formats for saving Forest plots in this package. Therefore I have uploaded a pdf of my email correspondence with Faye Paraiso - one of your production assistants about this, where she accepted that .jpg and .tiff were not available so asked me to submit in .png instead. This I have done. If you have changed your mind about which version you would like from the six available, please let me know.
Further to this, I have had yet another email from you asking me yet again to upload a version of the Forest plot, but not specifying which type you want. So I have now uploaded all six types so you can choose.

VERSION 2 – REVIEW

REVIEWER	Ellen McCreedy Brown University, School of Public Health, USA
REVIEW RETURNED	01-Feb-2018

GENERAL COMMENTS	1. Why did you only use the acronym (wsw), and not the full phrase "women who have sex with women" in your keyword searches? Response: the search strings used the term 'women', which picks up 'women who have sex with women' so we did not add the longer term. **Looking at Web Supplement 1, I don't see where your search strings include the term "women."** **2.** I'm not sure about limiting your search to "female." Gender identity is a different concept. I don't think that is part of your inclusion criteria. Response: This project is on incidence of certain physical conditions in sexual minority women, so our inclusion criteria did specify women. This is why we limited the searches to female. We agree that gender identity is a different concept. We explained in the Appendix of our previous comment response that we would have included both cis and trans women in our systematic review. However, none of the included studies had sufficient samples of transwomen to give proportions of the conditions we were investigating. For example Boehmer 2014 states that 'transgender identity was not ascertained; therefore data on transgender individuals was not available'. This limitation was also mentioned in Dilley 2010 and Mathews 2014, and Blosnich 2014 states that 'information about transgender populations is extremely limited'. **Okay, thanks.** **3.** You limit your searches to 2015 forward. I'm assuming this is the updated search? The original search was limited to 2010 forward, correct? You may want to show both. Response: The searches detailed in the Web Appendix are indeed the 2016 searches. We have now added the search terms used in the OVID Medline 2015 searches. It can be seen that they were very similar but for the 2016 searches we omitted the less useful 2015 terms. **Okay, thanks.**

	4. I don't think this response was clear enough with respect to controlling for age. Given the relationship between age and development of chronic conditions, all the estimates used for the meta-analysis should be adjusted for age. "Where stated, these all adjust for age" is not the same as they are all adjusted for age. I would like some more details on how those estimates were adjusted for age before meta-analysis (which stratum were used for the M-H estimates). Alternatively, you could show me the meta-analyses for those less than 55 and those over 55 (or something like that) Response: We are very sorry that our previous response was insufficiently clear. On Web Table 1 we list the weightings mentioned in the study reports for the prevalence estimates and for the adjusted odds ratios. It can be seen that most of the studies state that they adjust for age. Some do not state the adjustment factors. Few of them are explicit as to exactly how they adjusted for age. For example, Blosnich 2014 states that 'while adjusting for age, race/ethnicity …' but does not give how this was done, whereas Boehmer 2014 states that age was considered the main independent variable and was categorised into three age groupings – 20-39, 40-59 and 60+. In Everett 2013, age was coded as a continuous variable ranging from 24 to 34 years. Farmer 2013 calculated vascular age using the Framingham algorithm. Fredriksen-Goldsen 2013 only investigated people aged 50+. Garland-Forshee 2014 coded people into three age groups – 18-34, 35-54 and 55+. Jackson 2016 coded people into 2 age groups – 18-30 and 31-85+ years. Kann 2016 investigated schoolchildren aged 15-18. All of the participants in McNair were aged 25-30 years. None of the other included studies described how they adjusted for age. Some of them do not give mean and ranges for the ages of participants in the sample (see Web Table 1). So we are very sorry but there is insufficient data to conduct stratified analyses. We do present meta-analysis of adjusted odds ratios and this are much more likely to give more accurate results than the percentages, as AORs are adjusted and almost of them specify that age was adjusted for. We discuss the difficulties around adjusting for age in the strengths and weaknesses section. We would be happy to add more if you consider it appropriate. One of the difficulties with systematic reviewing is that you can only use the data as presented in the included studies. We agree that the included studies' reporting on age adjustment is less than ideal. The way to do this much better would be to do an individual patient meta-analysis, but this would involve all of the studies sending their patient data in to a central review team and the systematic reviewers re-analysing by age. This would be very useful but beyond the

	resources of the current project. **Thank you, please only include studies with low or medium risk of bias that adjust for age in your meta-analyses.**

VERSION 2 – AUTHOR RESPONSE

Thank you for your continued interest in our article. The remaining comments are:

The literature search is quite old now (more than 12 months ago), so some recent studies may have been missed. Are you able to update your search? At the very least we would be grateful if you could include this as a limitation in the discussion section.

RESPONSE:

I have included this as a limitation in the discussion section. I have done this rather than redo the searches for two reasons - firstly, its unlikely that the main finding of the paper of higher rates of asthma in lesbians and bisexual women will be overturned by new papers. A scoping search found, for example:

Patterson JG; Jabson JM; Sexual orientation measurement and chronic disease disparities: National Health and Nutrition Examination Survey, 2009-2014. Annals Of Epidemiology 2018;28 (2):72-85. which showed higher rates of asthma in lesbians and bisexual women. So redoing the searches would find more papers but the main messages of our systematic review would be the same.

Secondly, BMJ 'lost' my paper for 3 months which is why publication has been delayed.

Looking at Web Supplement 1, I don’t see where your search strings include the term “women.”

RESPONSE: The term 'women' was used in either the search term 'bisexual women' or 'women who have sex with women' in all of the searches up to 2016. NB It wasn't in the Medline April 2015 search, which may have been the one you were looking at?

Also, the key thing in the searches is whether we missed any studies published up to December 2016. We don't think we have but if you have any extra please let us know.

Thank you, please only include studies with low or medium risk of bias that adjust for age in your meta-analyses.

RESPONSE: All of the AOR meta-analyses only use the studies that adjusted for age. This is now mentioned in the results section and the discussion. The quality assessment results (in Web Table 2) show that the studies contributing to the AOR meta-analyses were all similar in quality.

ALSO

It has been bounced back by an editorial assistant YET AGAIN because of the Revman Forest Plot. Will you PLEASE negotiate with Cochrane to fix this problem - as you know Revman is a standard package for meta-analysis and I should not be having this problem.

ALSO As requested I have now added a statement in the methods section about PPI.