

## 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

<b>TITLE (PROVISIONAL)</b>	Trends in HIV testing in the UK Primary Care setting: A 15 year retrospective cohort study 2000 to 2015
<b>AUTHORS</b>	Gompels, Mark; Michael, Skevi; Davies, Charlotte; Jones, Tim; Macleod, John; May, Margaret

### VERSION 1 – REVIEW

<b>REVIEWER</b>	J.E.A.M van Bergen Amsterdam UMC / Soa Aids Nederland Amsterdam, The Netherlands
<b>REVIEW RETURNED</b>	06-Dec-2018

<b>GENERAL COMMENTS</b>	<p>Interesting and well-written manuscript with relevant research question about the contribution of primary care in addressing the hiv epidemic in UK. Trends in hiv testing in primary care 2000-2010-2015.</p> <p>My questions and comments for the authors and editors are listed below:</p> <ol style="list-style-type: none"><li>1. Graph 1 is missing a legenda (eg figure 2)</li><li>2. the denominator that is used is persons 'all ages' ( which is I presume all ages above 16), and stratified in 16-44 and &gt; 45. I have 2 questions: a considerable amount of annual new diagnosis relates to people 45-59. Is this cut-off point 44 yr standard for the UK?. Moreover the NICE quidelines refer to the population aged 15-59 yr if I am correct. These denominators also reflect to the area of high prevalence (2/1000) and very high prevalence (5/1000). Is this difference in denominators taken into consideration comparing the diffent databases?</li><li>3. There is a duplicating time period in your manuscript compared to the Evans publication in 2009. If I compare your rates in 2005 with the rates published in 2009 ( Seks Transm Inf hiv testing primary care 1995-2005), I see that there is a small difference in testing rates in 2005 ( eg Evans women:61,20) compared to data in suppl table 2 in your manuscript (women: 77.0/1000.000). It is the same database although.. any explanation?</li><li>4. On pag 9 r 40 you mention that "there is no evidence of better targetting". But on p 11 line 46 you mention that testing has increased in groups and areas with high deprivation in london..." suggesting better targetting.</li><li>5. Some questions and reflections on your discussion and conclusion: p 12 line 43. " it is clear that many patients will be diagnosed in other health care settings ". It would be interesting to know what part of the total annual new hiv diagnoses are made by testing in general practice. Does the database allows you to see how often the diagnose of hiv is within the READ system but not related to testing by the GP?. I wonder if comparing surveillance</li></ol>
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	<p>data will address sufficiently this question. I do agree there must be some degree of underreporting, but as a GP it would be strange NOT to know the hiv status of your patient and NOT to have this information in your file.</p> <p>6. I do not share completely your conclusion p12 line 55 that increased testing "must" have occurred in other settings because of 'no increase /decrease in testing in primary care and still a decline in rate of late diagnosis'. If testing is targetted better in primary care, still those people that get tested, will get tested earlier . In fact we expect lower positivity rates because of better testing and declining incidence. So even stable positiviy rates may mean better testing in primary care. Having said this, I do agree that accelerated testing in primary care is an important and challenging issue that needs better attention. An pos rates in PC that are higher than in Sexual Health Centres indicate the need for more proactive testing.</p> <p>7. It was very interesting to see that your data show ( counterintuitively) that there is less hiv testing in 2015 compared to 2010, although the quidelines advised already several years the need for more proactive screening. We see similar (counterintuitive) trend in the Netherlands 2010-2015 , also after the new GP quideline in 2013 on proactive hiv testing in primary care.</p> <p>8. In the list of references I missed the papers of hiv testing and late presentation in Primary Care in the Netherlands (Joore et al), although the conclusions that these papers cover are quite similar to the topics that are well addressed in the text in your manuscript.</p>
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<b>REVIEWER</b>	Ann Avery MetroHealth Medical Center USA
<b>REVIEW RETURNED</b>	13-Dec-2018

<b>GENERAL COMMENTS</b>	<p>This article shows important trends in HIV testing using an extensive sample size over 15 years, however, there are a few major issues that need to be addressed. The first issue is the purpose of the study is not clear. The introduction touches upon many facts around HIV testing and care but does not mention what the point of the study at hand is. This made it difficult to tell throughout the methods if the study was looking at number of tests administered by general practitioners or the benefit of early testing.</p> <p>The importance of testing for HIV earlier is mentioned both in the introduction and conclusion but there is not a strong connection of this to the methods of the study. The methods of the study appear to look at rates of HIV testing, not at any missed testing opportunities. While the importance of early testing is a great point, this should be tied more strongly to the findings of the study. A large portion of the discussion section is about early testing and its benefits, but the methods of the study do not mention anything about when patients were tested and if they could have been diagnosed earlier.</p> <p>The methods section should also be made clearer. It was difficult to tell at first what was being taken from CPRD versus PHE. It was also unclear until the discussion and conclusion section why the study only looked at general practitioners. It may be worth mentioning the reasoning behind looking at general practitioners in the methods section.</p>
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	<p>The authors mention annual screening in high-risk areas or if a patient presents with an indicator condition, but the data does not separate out high risk clinics or the presence of a high-risk condition (though it seems like data on indicator conditions was available). They do mention an increase in the most deprived areas but it is unclear what defines a deprived area or if this correlates to high risk areas. Also, given the large amount of data over 15 years, it is surprising that the authors did not investigate or incorporate prior testing status in their analyses.</p> <p>Lastly, under statistical methods, the patients were divided into two age groups: 16-44 and 45+. There is no reasoning stated for this grouping making it seem arbitrary. Youth is typically seen as being ages 15 through about 30 so by making the first group 16 through 44 you are including both youths and adults in the same group. It is known that healthcare trends are different between youths and adults, so it might be better to group these separately. If not, then give an explanation for choosing to create these two age groups.</p> <p>Other comments, the article is way too long and wordy. I don't think that including the STROBE guidelines as supplementary material is appropriate and personally, don't find the inclusion of appendix 1,2 or 3 useful.</p> <p>A successful testing program will eventually observe a decrease in HIV testing in general so understanding repeat testing or need for testing is important.</p> <p>I have no idea what Figure 1 means- needs a legend</p>
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### VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: J.E.A.M van Bergen

Institution and Country: Amsterdam UMC / Soa Aids Nederland, Amsterdam, The Netherlands

Interesting and well-written manuscript with relevant research question about the contribution of primary care in addressing the HIV epidemic in UK. Trends in HIV testing in primary care 2000-2010-2015.

Response: Thanks for your positive assessment of our paper.

My questions and comments for the authors and editors are listed below:

1. Graph 1 is missing a legend (eg figure 2)

Response: we have added legend to graphs at end of manuscript.

2. the denominator that is used is persons 'all ages' (which is I presume all ages above 16) and stratified in 16-44 and > 45. I have 2 questions: a considerable amount of annual new diagnosis relates to people 45-59. Is this cut-off point 44 yr standard for the UK? Moreover, the NICE guidelines refer to the population aged 15-59 yr if I am correct. These denominators also reflect to the area of high prevalence (2/1000) and very high prevalence (5/1000). Is this difference in denominators taken into consideration comparing the different databases?

Response: Yes, all ages is 16 years and above – we have changed abstract to reflect this “adults aged ≥ 16 years”. We used the same age group strata previously used in the Evans paper so that our results would be comparable with the earlier time trends reported. We allowed for different denominators in the comparison with PHE and NICE figures. There will be little difference in defining

adult from age 15 or 16 and comparisons with surveillance data were done across all ages above that.

3. There is a duplicating time period in your manuscript compared to the Evans publication in 2009. If I compare your rates in 2005 with the rates published in 2009 (Sexs Transm Inf hiv testing primary care 1995-2005), I see that there is a small difference in testing rates in 2005 ( eg Evans women:61,20) compared to data in suppl table 2 in your manuscript (women: 77.0/1000.000). It is the same database although. Any explanation?

Response: Yes, the GPRD and the CPRD are essentially the same database. However, additional practices have joined CPRD in more recent years and they would have contributed retrospective data collected on their local GP system. Therefore, there maybe some discrepancies in the figures due to different data being included. Most of the figures in our paper approximately match those by Evans et al, there may be some discrepancies due to the additional data from practices. We are unable to explain why these figures are out of line but we have checked our calculations and are confident our figure is correct.

4. On pag 9 r 40 you mention that "there is no evidence of better targeting". But on p 11 line 46 you mention that testing has increased in groups and areas with high deprivation in london..." suggesting better targeting.

Response: We found evidence of increased testing in older or more deprived groups in later years showing targeting, but there was no evidence of better targeting of individuals because the positivity rate did not increase. We have clarified that P9 refers to individuals "The percentage of tests that were positive peaked around 2003 and have fallen sharply since 2010, indicating that there is no evidence of better targeting of testing to individuals in later years."

5. Some questions and reflections on your discussion and conclusion: p 12 line 43. " it is clear that many patients will be diagnosed in other health care settings ". It would be interesting to know what part of the total annual new hiv diagnoses are made by testing in general practice. Does the database allow you to see how often the diagnose of hiv is within the READ system but not related to testing by the GP? I wonder if comparing surveillance data will address sufficiently this question. I do agree there must be some degree of underreporting, but as a GP it would be strange NOT to know the hiv status of your patient and NOT to have this information in your file.

Response: We have added the requested information from PHE HIV Testing in England: 2017 report to discussion on P12 "PHE estimated that in England during 2016 5.9% and 7.3% of new diagnoses in men and women, respectively, were made in Primary Care." The database does not allow you to see how often the diagnosis of HIV is made within the READ system that is not related to the GP. We have clarified that comparing to PHE surveillance data gives an approximate figure to the under-reporting of HIV prevalence in general practice. Many of those with HIV do not appear to consult a GP at all and hence will not appear in CPRD. "We estimated the prevalence of diagnosed HIV recorded in CPRD and compared this with estimated prevalence from national surveillance data collected by PHE using SOPHID and HARS to determine the proportion of all HIV diagnoses that were recorded in CPRD."

6. I do not share completely your conclusion p12 line 55 that increased testing "must" have occurred in other settings because of 'no increase /decrease in testing in primary care and still a decline in rate of late diagnosis'. If testing is targetted better in primary care, still those people that get tested, will get tested earlier. In fact we expect lower positivity rates because of better testing and declining incidence. So even stable positivity rates may mean better testing in primary care. Having said this, I do agree that accelerated testing in primary care is an important and challenging issue that needs better attention. Any pos rates in PC that are higher than in Sexual Health Centres indicate the need for more proactive testing.

Response: We have reworded to “likely occurred in other settings”. During the period of the study incidence was declining only very slowly, although it has accelerated in the past 2 years with advent of PreP so there is still considerable need to focus on testing in Primary Care. We have added P13 “If testing has become better targeted in Primary Care and incidence is decreasing in the consulting population then even without an increase in testing, those who get tested may be tested earlier in the course of HIV infection leading to reduced rates of late diagnoses.”

7. It was very interesting to see that your data show (counterintuitively) that there is less hiv testing in 2015 compared to 2010, although the guidelines advised already several years the need for more proactive screening. We see similar (counterintuitive) trend in the Netherlands 2010-2015 , also after the new GP guideline in 2013 on proactive hiv testing in primary care.

Response: We have added to discussion on P13 “HIV testing in Primary Care in the Netherlands also decreased between 2010-2015 despite similar guidelines encouraging more pro-active screening for HIV.” Ref Joore et al. BMC Fam Pract. 2018; 19: 36. doi: 10.1186/s12875-018-0723-8 Development and evaluation of a blended educational programme for general practitioners’ trainers to stimulate proactive HIV testing.

8. In the list of references I missed the papers of hiv testing and late presentation in Primary Care in the Netherlands (Joore et al), although the conclusions that these papers cover are quite similar to the topics that are well addressed in the text in your manuscript.

Response: We added references to the work by Joore and colleagues on P5 Introduction and P14 discussion (and in 7 above):

Joore et al. BMJ Open. 2016 Jan 21;6(1):e009194. doi: 10.1136/bmjopen-2015-009194. Missed opportunities to offer HIV tests to high-risk groups during general practitioners’ STI-related consultations: an observational study.

Joore et al. Sex Transm Infect. 2015 Nov;91(7):467-72. doi: 10.1136/sextrans-2015-052073. Epub 2015 Jun 30. HIV indicator condition-guided testing to reduce the number of undiagnosed patients and prevent late presentation in a high-prevalence area: a case-control study in primary care.

Joore et al. BMC Fam Pract. 2016 Nov 17;17(1):161. The need to scale up HIV indicator condition-guided testing for early case-finding: a case-control study in primary care.

Reviewer: 2

Reviewer Name: Ann Avery

Institution and Country: MetroHealth Medical Center, USA

1. This article shows important trends in HIV testing using an extensive sample size over 15 years, however, there are a few major issues that need to be addressed. The first issue is the purpose of the study is not clear. The introduction touches upon many facts around HIV testing and care but does not mention what the point of the study at hand is. This made it difficult to tell throughout the methods if the study was looking at number of tests administered by general practitioners or the benefit of early testing.

Response: This study focusses on trends in testing rates in Primary Care as clearly stated in the title “Trends in HIV testing in the UK Primary Care setting: A 15 year retrospective cohort study 2000 to 2015”. However, the motivation behind guidelines to test for HIV in Primary Care is to decrease late diagnosis of HIV which often occurs in hospitals when patients are very sick. Therefore we think it justifiable to discuss the issue of decreasing late diagnosis and the benefits of early testing to give context to our study. We have clarified the focus on HIV testing in Primary Care in the introduction, first sentence “HIV testing in Primary Care is an important component of the strategy to diagnose HIV

earlier and reduce transmission of HIV” and last sentence of paragraph 3 “However, no recent evidence is available to know if HIV testing in Primary Care has been increasing and guidelines have been implemented over the country and not just in high risk areas”.

2. The importance of testing for HIV earlier is mentioned both in the introduction and conclusion but there is not a strong connection of this to the methods of the study. The methods of the study appear to look at rates of HIV testing, not at any missed testing opportunities. While the importance of early testing is a great point, this should be tied more strongly to the findings of the study. A large portion of the discussion section is about early testing and its benefits, but the methods of the study do not mention anything about when patients were tested and if they could have been diagnosed earlier.  
Response: We have cut some of the material about early testing in the introduction and discussion and emphasised that the paper is about testing rates in Primary Care.

3. The methods section should also be made clearer. It was difficult to tell at first what was being taken from CPRD versus PHE. It was also unclear until the discussion and conclusion section why the study only looked at general practitioners. It may be worth mentioning the reasoning behind looking at general practitioners in the methods section.

Response: We state the sources of all data on P6-7 and have clarified that the HARS and SOPHID data were supplied by PHE. “Data on HIV prevalence were derived from the HIV and AIDS Reporting System (HARS) and for earlier years the Survey of Prevalent HIV Infections Diagnosed (SOPHID) available from PHE.” We have also made the methods clearer P8 “To validate our estimates of HIV testing rates recorded in CPRD, we compared them with those from national surveillance data collected by PHE for 2015. Finally, we estimated the prevalence of diagnosed HIV recorded in CPRD and compared this with estimated prevalence from national surveillance data collected by PHE using SOPHID and HARS to determine the proportion of all HIV diagnoses that were recorded in CPRD.” We have also made it clearer that study is about Primary Care (see answer to point 1 above).

4. The authors mention annual screening in high-risk areas or if a patient presents with an indicator condition, but the data does not separate out high risk clinics or the presence of a high-risk condition (though it seems like data on indicator conditions was available). They do mention an increase in the most deprived areas but it is unclear what defines a deprived area or if this correlates to high risk areas.

Response: We were unable to separate out General Practices with high HIV risk patients but assumed that the stratification on London and urban corresponded to a stratification by HIV prevalence since HIV is much higher in London than elsewhere in the UK and also is higher in the large conurbations. We say on P6 methods “We used individual level quintiles of the Index of Multiple Deprivation, 2015”. We say in discussion P11 that “Testing ... has increased in the groups and areas of high deprivation within London. This is reassuring as it also reflects the higher prevalence of HIV in these areas” which implies correlation. We have added the following reference for the English indices of deprivation, so it is clear what defines a deprived area:  
(<https://www.gov.uk/government/statistics/english-indices-of-deprivation-2015>)

5. Also, given the large amount of data over 15 years, it is surprising that the authors did not investigate or incorporate prior testing status in their analyses.

Response: In methods on P7 we say that we excluded those who had previously tested positive from subsequent years. We did not look at repeat testing per se but included repeat tests (all negative tests up to first positive test).

6. Lastly, under statistical methods, the patients were divided into two age groups: 16-44 and 45+. There is no reasoning stated for this grouping making it seem arbitrary. Youth is typically seen as being ages 15 through about 30 so by making the first group 16 through 44 you are including both youths and adults in the same group. It is known that healthcare trends are different between youths

and adults, so it might be better to group these separately. If not, then give an explanation for choosing to create these two age groups.

Response: We used the same age group strata previously used in the Evans paper so that our results would be comparable with the earlier time trends reported. We added to methods P7 “grouped by age (16-44, ≥ 45 years chosen to match study by Evans et al.)”

7. Other comments, the article is way too long and wordy. I don’t think that including the STROBE guidelines as supplementary material is appropriate and personally, don’t find the inclusion of appendix 1,2 or 3 useful.

Response: We have cut the introduction and discussion to make shorter. We understood that the BMJ required STROBE guidelines to be adhered to and thought it useful to include checklist – this may be omitted. We included the web appendices so that the methods would be transparent and reproducible by researchers who might want to look at time trends in HIV testing in the future. We think it is important to publish these data.

8. A successful testing program will eventually observe a decrease in HIV testing in general so understanding repeat testing or need for testing is important.

Response: We agree with this point and studies of repeat testing have been done in sexual health clinic setting, particularly the need for testing and understanding repeat testing in MSM, but repeat testing in Primary Care is much less frequent and so we did not study this.

9. I have no idea what Figure 1 means- needs a legend

Response: Have added figure legend.

### VERSION 2 – REVIEW

<b>REVIEWER</b>	Ann Avery MetroHealth Medical Center USA
<b>REVIEW RETURNED</b>	22-Feb-2019

<b>GENERAL COMMENTS</b>	<p>Overall, the paper is improved however, I think there are major issues with the conceptual framework.</p> <p>The authors state that their objective to be “To estimate trends in HIV testing, positivity and prevalence in UK Primary Care for 2000-2015 as part of a wider investigation into reasons for late diagnosis of HIV.” They achieve this objective though the paper remains far too long for this purpose.</p> <p>I cannot find a response to reviewers in the submission or a copy of the reviewers’ notes which makes re-review a bit tedious.</p> <p>The edits they made under statistical methods helped clear up the confusion on how CRPD and PHE were being used and they also added an explanation for the age grouping of 16-44 and 45+ (to match another study they referenced, although I still think it would make more sense to separate young adults as they tend to have different trends). I think they made a lot of strong claims in their first draft without much support which were changed in this draft. They also fixed the legends for their figures.</p> <p>The introduction lacks a clear purpose of the study in the introduction. They removed a lot of the facts from the introduction which did help it flow better but they didn’t add anything to help</p>
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	<p>explain what they are trying to accomplish with their review is which I think would better help to understand the methods.</p> <p>My general concern is they seem reference the NICE guidelines incorrectly. In reviewing the NICE guidelines, there is not a recommendation to test all new patients in primary care unless the clinic is in an area of high prevalence or the patient comes from an area of high prevalence or has an indicator condition. None of these characteristics are evaluated to determine if testing is occurring appropriately or if the changes match the NICE recommendations. They talk about areas of deprivation but do not define what that means, why not use areas of high HIV prevalence? (often similar). They are reviewing all sorts of read codes but not for indicator conditions (or if they did, it was buried). There is way too much detail about the read codes with respect to prenatal testing and nothing about using it for identifying visits for indicator conditions.</p> <p>As a result, it is impossible to draw conclusions on the state of testing in primary care other than overall it increased until 2010 and decreasing since.</p> <p>Grammatically- this is a fragment Line 41-42 This may be presenting to general practice or hospital care, but without a high degree of clinical suspicion, the diagnosis is often missed.</p> <p>Way too much description of information in Figure 1 Figure 2 is too confusing, no need for all the subgroups- summarize and highlight</p>
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## VERSION 2 – AUTHOR RESPONSE

Reviewer: 2

Reviewer Name: Ann Avery

Institution and Country: MetroHealth Medical Center USA

1. Overall, the paper is improved however, I think there are major issues with the conceptual framework.

The authors state that their objective to be “To estimate trends in HIV testing, positivity and prevalence in UK Primary Care for 2000-2015 as part of a wider investigation into reasons for late diagnosis of HIV.” They achieve this objective though the paper remains far too long for this purpose. I cannot find a response to reviewers in the submission or a copy of the reviewers’ notes which makes re-review a bit tedious.

Response: Thankyou for your constructive comments we agree that the paper is improved since the previous draft and that we achieved the objective of the paper. We also agree that the word count could be reduced. We have therefore deleted the following sentences/ paragraphs from the discussion section to reduce article length and to make this section more concise.

Discussion section wording deleted: page 13, lines 8 to 12

“showing that delaying therapy was detrimental to individual health and the beneficial effects of treatment as prevention (TasP). Therefore, in recent years the majority of new infections will have



been transmitted by those who were undiagnosed<sup>39</sup> because most patients who are diagnosed are treated with effective ART and unlikely to transmit HIV.<sup>9,40,41</sup> “

Discussion section wording deleted: page 13, lines 18 to 22

“Each prevented infection saves an estimated £300,000 in lifetime treatment costs.<sup>43,44</sup> According to PHE surveillance, in 2016, HIV test positivity rates in Primary Care in high (0.5%) and extremely high (0.4%) diagnosed HIV prevalence areas exceeded those seen in sexual health services, indicating that more testing should be carried out in primary care<sup>34</sup>.“

Discussion section wording deleted : page 13 Lines 30 to 31

“HCPs in the UK have opportunities to initiate HIV testing in at-risk individuals and reduce the proportion of undiagnosed infection.<sup>12,14</sup> “

The ‘Responses to reviewers comments’ were included in two separate documents with the previous submission entitled “Reviewer responses CPRD HIV testing\_submitted “ and at the bottom of the letter to the editor document entitled “Letter to Editor\_18.01.19” -these two documents were resubmitted to BMJ open with the track changes made to the paper.

2. The edits they made under statistical methods helped clear up the confusion on how CRPD and PHE were being used and they also added an explanation for the age grouping of 16-44 and 45+ (to match another study they referenced, although I still think it would make more sense to separate young adults as they tend to have different trends). I think they made a lot of strong claims in their first draft without much support which were changed in this draft. They also fixed the legends for their figures.

Response: We are pleased that our further explanations included in the document helped clarify our reasoning behind the methods that we used.

3. The introduction lacks a clear purpose of the study in the introduction. They removed a lot of the facts from the introduction which did help it flow better but they didn’t add anything to help explain what they are trying to accomplish with their review is which I think would better help to understand the methods.

Response: Yes we agree, we removed a lot of facts from the introduction which now makes this section flow better . We have also re-worded the last paragraph of the introduction to make our objectives clearer.

The last paragraph of the Introduction has been reworded (below): Page 6 , Lines 5 to 7

“Our main objective was to analyse data from the same source collected between the years 2000 to 2015 to study if HIV testing trends continued to increase in primary care over this extended time period. In addition we investigated differences in HIV testing rates and HIV diagnosis by demographic characteristics and estimated the prevalence of HIV recorded in primary care and compared it with estimates from national surveillance”.

4. My general concern is they seem reference the NICE guidelines incorrectly. In reviewing the NICE guidelines, there is not a recommendation to test all new patients in primary care unless the clinic is in an area of high prevalence or the patient comes from an area of high prevalence or has an indicator condition. None of these characteristics are evaluated to determine if testing is occurring appropriately or if the changes match the NICE recommendations.

Response: Thankyou for your comment we have reworded a paragraph in the Introduction and Discussion sections to add clarification , it was beyond the scope of this study to determine if testing was occurring appropriately

We have deleted the 3rd paragraph of the introduction , page 5

“Expanding HIV testing is a national health priority<sup>18</sup> with 2016 NICE guidelines offering evidence

based advice on the practicalities of how to do this in the UK and how to integrate HIV testing into usual clinical care.<sup>11</sup> Regardless of local HIV prevalence, a test should be routinely offered to patients in Primary Care when presenting with any HIV indicator condition and/or if patients are from a high risk group, for example, someone reporting an HIV positive partner or a history of injecting drug use or chemsex.<sup>11</sup> “

We have added a sentence to the Introduction section, page 5 lines 20 and 21

“Given the increase in HIV prevalence over time we would expect that there would be an increase in GP testing for HIV”

We have added wording to the Discussion section, page 11, line 10

“....given the NICE recommendations on testing, which would increase with increased prevalence 31, 32”

5. They talk about areas of deprivation but do not define what that means, why not use areas of high HIV prevalence? (often similar). They are reviewing all sorts of read codes but not for indicator conditions (or if they did, it was buried).

Response: Since the reviewer was not able to see our previous responses (as mentioned in comment 1) we have copied our original response again here:

We were unable to separate out General Practices with high HIV risk patients but assumed that the stratification on London and urban corresponded to a stratification by HIV prevalence since HIV is much higher in London than elsewhere in the UK and also is higher in the large conurbations. We say on P6 methods “We used individual level quintiles of the Index of Multiple Deprivation, 2015”. We say in discussion P11 that “Testing ... has increased in the groups and areas of high deprivation within London. This is reassuring as it also reflects the higher prevalence of HIV in these areas” which implies correlation. We have added the following reference (in Method section page 6, line 12) for the English indices of deprivation, so it is clear to the reader what defines a deprived area :

(<https://www.gov.uk/government/statistics/english-indices-of-deprivation-2015>)

Regarding the comment for the read codes we didn't review read codes for indicator conditions as this was beyond the scope of the study as we were just looking at HIV testing trends and not the reason for testing/or reason testing was requested by the GP. We just focused on the antenatal read codes because of the huge impact of antenatal HIV testing to the overall testing rates and we also wanted to compare testing rates by gender. However, we agree it is certainly an area for future work.

6. There is way too much detail about the read codes with respect to prenatal testing and nothing about using it for identifying visits for indicator conditions.

As a result, it is impossible to draw conclusions on the state of testing in primary care other than overall it increased until 2010 and decreasing since.

Response: We included detailed information of pre-natal read codes (as well as read codes for HIV diagnosis and testing) so that the methods would be transparent and reproducible by researchers who might want to look at time trends in HIV testing in the future. Regarding comment on indicator conditions please see our response to comment 5 above.

In our concluding paragraph we have removed our reference to HIV testing guidelines to make our assumptions less strong

In Conclusion section, page 14, line 3

“Adherence to HIV testing guidelines 15, 31, 32 would likely increase the number of positive tests....” was deleted and replaced with “Increased testing would likely increase the number of positive tests .....

7. Grammatically- this is a fragment Line 41-42 . This may be presenting to general practice or hospital care, but without a high degree of clinical suspicion, the diagnosis is often missed.

Response: Thankyou for pointing this out , we have changed the wording in this sentence to make it

grammatically correct.

Page 5, Line 16 to 17

“This may be presenting to general practice or hospital care. But without a high degree of clinical suspicion, the diagnosis is often missed”.

8. Way too much description of information in Figure 1 Figure 2 is too confusing, no need for all the subgroups- summarize and highlight

Response: We think Figure 2 is useful as it stands as it can be compared to the similar figure used in the Evans et al paper . We agree regarding description of information in Figure 1 and have deleted some of the wording to make this description less verbose, therefore wording has been deleted under the heading ‘Trends in HIV testing rates 2000-2015 in Primary Care’ in the Result section.

Sentence re-worded in result section page 8 , line 31

“....,which are lower than rates for females even when antenatal tests are excluded.”

Wording deleted from result section page 9 , lines 4 to 6

“ in 2000, 2010 and 2015, respectively. For the whole period, HIV testing rates were higher in females than males (figure 1). This was true even when HIV tests carried out as part of antenatal screening were excluded.

Wording deleted from Result section page 9, lines 11 to 12

“ HIV testing rates with 95% confidence intervals (CI) are listed for all years from 2000-2015 for males, females and females excluding antenatal tests”

### VERSION 3 – REVIEW

<b>REVIEWER</b>	Ann Avery, MD MetroHealth Medical Center Cleveland, OH USA
<b>REVIEW RETURNED</b>	24-Jun-2019

<b>GENERAL COMMENTS</b>	BMJ open This revised version is much better, just a few comments 1. Can the authors comment briefly on who does not contribute to CPRD and why? What percentage of clinics/ pts are represented?  2. Enhanced HIV testing is considered to be cost-effective in areas with a local diagnosed HIV prevalence that exceeds 2 per 1000 in adults aged 15-59 years. <sup>2,10</sup> In these high HIV prevalence areas recommendations are an HIV test should be routinely offered to all new GP registrations, those undergoing tests for other sexually transmitted infections or having blood tests for any reason, and all new hospital medical admissions. The authors do not seem to account for new registrants or STI testing despite pulling massive amounts of data and read codes. This at least should be acknowledged as a limitation  3. national surveillance data for 2015 estimated that General Practices in extremely
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	<p>high prevalence areas defined as greater than 5/1000 population (comparable with “London” in our CPRD study) carried out the highest number of tests per practice population, 860 per 100 000 person years. This was nearly double the coverage rate of General Practices in high diagnosed prevalence areas defined as greater than 2/1000 population (440/100 000), and ten times the coverage rate among General Practices in low diagnosed prevalence areas (90/100 000).—it’s unclear that the number in parentheses are for testing. Suggest defining the prevalence in parentheses and then reporting the rate in the sentence</p> <p>4. The estimates from surveillance were higher than our estimates from CPRD (table 2 and table 3). The proportion of positive tests among those tested in Primary Care estimated from SSBBV surveillance data was 0.4%-- clarify estimates of what</p> <p>Prevalence of recorded HIV in CPRD and comparison with national surveillance estimates-Suggest deleting this section, doesn’t add much and there are numerous gaps or flaws in logic</p>
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### VERSION 3 – AUTHOR RESPONSE

Reviewer: 2

Reviewer Name: Ann Avery

Institution and Country: MetroHealth Medical Center USA

This revised version is much better, just a few comments

1. Can the authors comment briefly on who does not contribute to CPRD and why? What percentage of clinics/ pts are represented?

Response to comment 1: Thankyou for your constructive comments we agree that the paper is much improved since the previous version. To address comment 1 we have added the following sentences to the Method section of the paper (shown underlined below) to explain that only practices with particular compatible software will contribute to CPRD and we have included the percentage of practices in the UK that this represents.

Methods section – the following wording has been inserted : page 6 , lines 12 to 16

“The CPRD database contains information from GP practices in the UK using the Vision software system (roughly 9% of UK practices) who consent to data collection; the sample is broadly representative of the adult UK population<sup>26</sup>. Only GP practices in England are eligible for linkage to other datasets such as hospital admissions, and practices can opt out of linkage. CPRD provided anonymised Primary Care records and linked secondary care and mortality records on patients registered between 2000 and 2015 in 404 primary care practices in England”.

2. Enhanced HIV testing is considered to be cost-effective in areas with a local diagnosed HIV prevalence that exceeds 2 per 1000 in adults aged 15-59 years. In these high HIV prevalence areas recommendations are an HIV test should be routinely offered to all new GP registrations, those undergoing tests for other sexually transmitted infections or having blood tests for any reason, and all new hospital medical admissions.

The authors do not seem to account for new registrants or STI testing despite pulling massive amounts of data and read codes. This at least should be acknowledged as a limitation

Response to comment 2: Thankyou for highlighting this we have added a sentence to the section titled 'Strengths and weaknesses' to explain that we were not able to decipher from the CPRD data the reason why the HIV test was requested/undertaken (i.e if being tested as a newly registered patient) by the GP practice.

'Strengths and weaknesses' section- the following sentences has been added to acknowledge this limitation (page 12, lines 23 to 24 )

"This study can only show the composite rates of testing in Primary Care. We were not able to categorise the different indications for an HIV test".

3. national surveillance data for 2015 estimated that General Practices in extremely high prevalence areas defined as greater than 5/1000 population (comparable with "London" in our CPRD study) carried out the highest number of tests per practice population, 860 per 100 000 person years. This was nearly double the coverage rate of General Practices in high diagnosed prevalence areas defined as greater than 2/1000 population (440/100 000), and ten times the coverage rate among General Practices in low diagnosed prevalence areas (90/100 000).—it's unclear that the number in parentheses are for testing. Suggest defining the prevalence in parentheses and then reporting the rate in the sentence

Response to comment 3 : Thankyou for your comment we have now included the rates as part of the sentence and removed the parentheses and have now put the prevalence in parentheses

Result section : page 10, lines 14 to 16

"areas (defined as greater than 2/1000 population), which was estimated at 440 per 100 000 per person years, and ten times the coverage rate among General Practices in low diagnosed prevalence areas, which was estimated at 90 per 100 000 person years".

4. a) The estimates from surveillance were higher than our estimates from CPRD (table 2 and table 3). The proportion of positive tests among those tested in Primary Care estimated from SSBBV surveillance data was 0.4%-- clarify estimates of what

b) Prevalence of recorded HIV in CPRD and comparison with national surveillance estimates-Suggest deleting this section, doesn't add much and there are numerous gaps or flaws in logic

Response to comment 4a: We agree with your comments and we have clarified that the estimates are for HIV testing rates (underlined below)

Results section, under sub heading 'HIV testing rates and positivity according to national surveillance data' : page 10 , lines 7 and 8

"The estimates of HIV testing rates from surveillance were higher than our estimates from CPRD (table 2 and table 3)".

Response to comment 4b: Regarding the second part of comment 4 we acknowledge why the reviewer has highlighted this section. We are keen to keep part of this section in as it was one of the objectives of the study and we think it is important to calculate the prevalences within the various groups over the 15 year time period. However we agree that in our efforts to explain the differences

with the surveillance data we may have included unnecessary assumptions -making this section a little confusing. Therefore we have removed a number of sentences and shortened this section and now briefly refer to why we thought there were differences in the estimations.

Result section : page 10 and 11 ( sentences underlined below have been deleted from this section)

Prevalence of recorded HIV in CPRD and comparison with national surveillance estimates

In 2015 the prevalence of diagnosed HIV recorded in CPRD was 2.8 per 1000 adult patients in London practices and 0.8 per 1000 in the rest of the UK (table 4). According to PHE surveillance, in 2015 HIV prevalence in UK was estimated to be 1.6 per 1000, and excluding undiagnosed HIV was 1.3 per 1000 population.<sup>2</sup> The HIV prevalence in London was estimated to be 4.7 per 1000, substantially higher than the rest of the UK at 1.1 per 1000. The corresponding observed prevalence, that is, excluding undiagnosed cases of HIV, was 4.2 and 0.9 per 1000 population in London and the rest of the UK, respectively.<sup>2</sup> Therefore, only two-thirds of PLWHIV in London were likely known to General Practice whereas in the rest of the UK this increased to nearly 90%. However, these percentages are likely to be over-estimated as children aged <16 years were not included in the CPRD calculations of prevalence but were included in PHE data. If we assume that 20% of the UK population are aged <16 years old and that only 1000 children are living with HIV, then the prevalence of diagnosed HIV among adults could be as high as 5.1 and 1.2 per 1000 in London and outside London, respectively. The estimated percentage of HIV diagnoses among adults recorded in CPRD may be as low as 55% and 67% in London and the rest of the UK, respectively. In General Practices in London, prevalence of HIV recorded in CPRD was higher for males, older individuals, Black African ethnicity and most deprived quintile (table 4) with a similar pattern in practices outside London except that prevalence did not vary by age.