

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)	ASSESSING PREVALENCE OF MISSED LABORATORY-CONFIRMED SEXUALLY TRANSMITTED INFECTIONS AMONG WOMEN IN KINGSTON, JAMAICA: RESULTS FROM A SECONDARY ANALYSIS OF THE SINO-IMPLANT CLINICAL TRIAL.
AUTHORS	Zia, Yasaman; Wiener, Jeffrey; Snead, Margaret; Papp, John; Phillips, Christi; Flowers, Lisa; Medley-Singh, Natalie; Costenbader, Elizabeth C.; Hylton-Kong, Tina; Kourtis, Athena

VERSION 1 – REVIEW

REVIEWER	Giuseppe Benagiano University la Sapienza, Rome, Italy
REVIEW RETURNED	13-Oct-2017

GENERAL COMMENTS	<p>This is a secondary analysis of a study on the use of a long-acting contraceptive subcutaneous implant in Jamaica.</p> <p>My main concern refers to the methodology used to quantify the different accuracy between "clinical" and "laboratory" diagnoses of a sexually transmitted disease (STI). Authors mention (without actually describing them) the syndromic approach, algorithms, risk evaluation scores, while admitting that they do not know whether and to what extent physicians utilized them.</p> <p>They carry out sophisticated statistical evaluations of their data, but the statistical validity of data depends first and foremost on the quality of data collection.</p> <p>In this case, the value of the information collected seems to be in doubt.</p> <p>In addition, the fact that clinical diagnosis of STIs is of limited value is well-known. As reported by the Authors even in Jamaica there have been studies on this issue.</p> <p>Therefore, in my opinion, this investigation has value only if it can add precision to the existing view that clinical diagnosis is inferior to the laboratory one.</p> <p>For this reason, before this article can be accepted a substantial clarification of this point is required.</p>
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REVIEWER	Michael Marks London School of Hygiene & Tropical Medicine, UK
REVIEW RETURNED	27-Dec-2017

GENERAL COMMENTS	1) The authors do not appear to have performed an assessment of
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	<p>factors associated with lab diagnosed STIs (I am aware that they have looked at factors associated with 'missed STIs which includes a large % of the lab diagnosed cases). This might be of value. As women were presumably not treated based on these results at the time, I think I might consider an association analysis restricted to the first lab diagnosed STI (because repeat diagnosis at a second visit is unsurprising in the absence of treatment) but an overall association with lab based STIs would also be fine.</p> <p>2) Is any data available on the actual symptoms women did/did not have? For example were women with a missed STI actually asymptomatic or did they have symptoms but not meet diagnostics criteria for clinical diagnosis?</p> <p>3) Are the associations shown in Table 2 adjusted or unadjusted prevalence ratios? Please make this clear both in the methods and the table.</p> <p>4) The same applies to the presentation of association data in Lins 181-189.</p> <p>5) Line 168 - I think a word is missing (probably 'occurred) in the sentence: and a total of 84 such clinical instances during the study period</p>
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VERSION 1 – AUTHOR RESPONSE

Dear Dr. Sucksmith,

Thank you for your review of our manuscript. We have carefully considered the requested revisions and made the necessary changes in text. Please see below for our responses to each comment raised by the editor and reviewers, in bold. . We thank the reviewers and the editors for their time and efforts regarding this manuscript.

Editorial Requests:

- Please revise your title so that it includes your study design. This is the preferred format for the journal.
- The title has been updated, as requested.
- Please expand the 'Strengths and Limitations' section on page 4. Please include one or two strengths relating to the study's design and methods.
- Strengths have been updated regarding the study design and methods (Page 4)
- Please add a statement to the methods confirming that you obtained written informed consent from participants.
- Methods have been updated with informed consent (Line 114-115)
- Along with your revised manuscript, please provide a completed copy of the STROBE checklist (<http://www.strobe-statement.org/>).
- STROBE checklist has been provided (Supplementary File)

Reviewer: 1

Reviewer Name: Giuseppe Benagiano

Institution and Country: University la Sapienza, Rome, Italy Competing Interests: no competing interests

Please leave your comments for the authors below This is a secondary analysis of a study on the use of a long-acting contraceptive subcutaneous implant in Jamaica.

My main concern refers to the methodology used to quantify the different accuracy between "clinical" and "laboratory" diagnoses of a sexually transmitted disease (STI). Authors mention (without actually describing them) the syndromic approach, algorithms, risk evaluation scores, while admitting that they do not know whether and to what extent physicians utilized them.

They carry out sophisticated statistical evaluations of their data, but the statistical validity of data depends first and foremost on the quality of data collection.

In this case, the value of the information collected seems to be in doubt.

In addition, the fact that clinical diagnosis of STIs is of limited value is well-known. As reported by the Authors even in Jamaica there have been studies on this issue.

Therefore, in my opinion, this investigation has value only if it can add precision to the the existing view that clinical diagnosis is inferior to the laboratory one.

For this reason, before this article can be accepted a substantial clarification of this point is required.

We thank the reviewer for the opportunity to clarify this point. During the study visits, information was collected from the participants about the presence of any clinical symptoms that could be indicative of an STI, and the clinical providers performed an examination and documented any clinical signs that were present. All this information was documented, along with the clinical impression of the provider and any antibiotic prescriptions given, in the medical charts. The data were collected systematically and comprehensively, and the study clinics were some of the busiest and most versed in STI care clinical sites in Kingston, Jamaica. However, as noted, it is not possible to know whether providers actually used risk evaluation scores or only clinical symptoms to guide their impression and management. This is an issue that applies to clinical practice widely, and as such, reflects the reality of syndromic approaches in STI diagnosis in Jamaica, as well as other settings. We believe that our analysis adds valuable information, as recent data on the value of clinical diagnosis of STI in Jamaica was lacking, it adds precision by indicating that the extent of clinically missed STIs seems to be at the upper bound of previous estimates, and as such, makes a compelling case for the need to introduce laboratory approaches for STI diagnosis in Jamaica.

Reviewer: 2

Reviewer Name: Michael Marks

Institution and Country: London School of Hygiene & Tropical Medicine, UK Competing Interests: None

1) The authors do not appear to have performed an assessment of factors associated with lab diagnosed STIs (I am aware that they have looked at factors associated with 'missed STIs which includes a large % of the lab diagnosed cases). This might be of value. As women were presumably not treated based on these results at the time, I think I might consider an association analysis restricted to the first lab diagnosed STI (because repeat diagnosis at a second visit is unsurprising in the absence of treatment) but an overall association with lab based STIs would also be fine.

• We thank the reviewer for this comment. Indeed, we assessed factors associated with laboratory-diagnosed STIs in a previously published manuscript (reference 11). We have now added a statement to mention this and highlight the lack of significant associations of individual participant characteristics with laboratory-confirmed STIs, other than younger age (Discussion section, page 11).

2) Is any data available on the actual symptoms women did/did not have? For example were women with a missed STI actually asymptomatic or did they have symptoms but not meet diagnostics criteria for clinical diagnosis?

- Data on clinical symptoms that could be indicative of an STI were collected during study visits (now clarified in lines 132-133), and the clinical provider documented any relevant clinical signs in the study visit notes. Women with a missed STI did not have any reported symptoms documented in their medical chart.

3) Are the associations shown in Table 2 adjusted or unadjusted prevalence ratios? Please make this clear both in the methods and the table.

- They were adjusted. This has now been clarified in the text of methods, results, and in Table 2.

4) The same applies to the presentation of association data in Lines 181-189.

- Further clarification that these are adjusted analyses has now been provided in the prevalence ratios presented in the text (aPR instead of PR).

5) Line 168 - I think a word is missing (probably 'occurred') in the sentence: and a total of 84 such clinical instances during the study period

- Thank you. We have now added the word "occurred" on line 168.

We hope that the above have satisfactorily addressed the reviewers' comments. If you need any further information, please do not hesitate to ask. Thank you again for your valuable review of this manuscript.

Kindly,
Yasaman Zia, MPH

VERSION 2 – REVIEW

REVIEWER	Michael Marks London School of Hygiene & Tropical Medicine, UK
REVIEW RETURNED	12-Jan-2018

GENERAL COMMENTS	I am satisfied that the authors have responded appropriately to comments from the reviewers.
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REVIEWER	Giuseppe Benagiano Sapienza University of Rome, Rome, Italy
REVIEW RETURNED	20-Jan-2018

GENERAL COMMENTS	I believe that the revised text can be published. I have no additional comments
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