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| Complete List of Authors: | Zia, Yasaman; Centers for Disease Control and Prevention, Division of Reproductive Health  
Wiener, Jeffrey; Centers for Disease Control and Prevention  
Snead, Margaret; Centers for Disease Control and Prevention, Division of Reproductive Health  
Papp, John; Centers for Disease Control and Prevention  
Phillips, Christi; Centers for Disease Control and Prevention, Division of STD Prevention  
Flowers, Lisa; Centers for Disease Control and Prevention, Division of Reproductive Health  
Medley-Singh, Natalie; Ministry of health, Epidemiology research training unit  
Costenbader, Elizabeth C.; FHI 360, Hylton-Kong, Tina; Ministry of Health  
Kourtis, Athena; Centers for Disease Control and Prevention, Division of Reproductive Health |
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ASSESSING CLINICAL DIAGNOSIS OF SEXUALLY TRANSMITTED INFECTIONS AMONG WOMEN INITIATING CONTRACEPTIVE IMPLANTS IN KINGSTON, JAMAICA

Yasaman Zia, MPH\(^{1,2}\); Jeffrey Wiener, PhD\(^1\); Margaret Christine Snead, PhD\(^1\); John Papp, PhD\(^3\); Christi Phillips, BS\(^3\); Lisa Flowers, MPA\(^1\); Natalie Medley-Singh, MBBS, DM\(^4\); Elizabeth Costenbader, PhD\(^5\); Tina Hylton-Kong, MBBS, MPH\(^6\); Athena P. Kourtis MD, PhD\(^1\)

\(^1\) Division of Reproductive Health, U.S. Centers for Disease Control and Disease Prevention (CDC), Atlanta, GA, USA
\(^2\) Association of Schools and Programs of Public Health (ASPPH), Washington, DC, USA
\(^3\) Division of Sexually Transmitted Disease Prevention, U.S. Centers for Disease Control and Disease Prevention (CDC), Atlanta, GA, USA
\(^4\) University Hospital of the West Indies, Kingston, Jamaica
\(^5\) Family Health International (FHI 360), Durham, NC, USA
\(^6\) Epidemiology Research and Training Unit, Ministry of Health, Kingston, Jamaica

Corresponding Author:
Yasaman Zia, Centers for Disease Control and Prevention, 4770 Buford HWY, MS-F-74, Atlanta, GA 30341, USA. Phone: 770-498-1704. Fax: 770-488-6391. E-mail: yzia@cdc.gov

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ABSTRACT

Objectives: To assess potentially missed STIs, we compared clinically-diagnosed STIs to laboratory-confirmed diagnoses of gonorrhea (GC), chlamydia (CT), and trichomonas (Tvag).

Setting: We used data and specimens previously collected for the Sino-Implant Study, a clinical trial in Kingston, Jamaica.

Participants: The Sino-Implant Study randomized 414 women to receive a levonorgestrel implant at either baseline or three months post-enrollment to evaluate unprotected sex after implant initiation. This analysis utilized 254 available vaginal swab samples.

Outcome Measures: Clinically-diagnosed STIs were determined from medical records by assessing clinical impressions and prescriptions. Laboratory-confirmed STIs included GC, CT, and Tvag tested by Aptima Combo 2 for CT/GC and Aptima Tvag assays (Hologic, San Diego, CA). Log-binomial regression models fit with generalized estimating equations were used to estimate associations of clinically-diagnosed STIs with laboratory-confirmed diagnoses and demographic and behavioral characteristics.

Results: Overall, 195 (76.8%) women had laboratory-confirmed STI (CT, GC or Tvag) while only 65 (25.6%) women had clinically-diagnosed cervicitis and/or vaginitis during the study period. Clinical diagnosis missed 79.7% of laboratory-confirmed STIs: 85% of GC (n= 17/20), 78.8% of CT (n= 141/179), and 80.0% of Tvag (n= 180/225). Hormonal contraceptive use in the month prior to the study visit was significantly associated with clinical diagnosis at any time point (Prevalence Ratio (PR): 1.65, 95% Confidence Interval (CI): 1.07, 2.54). As age...
increased, clinically missed infections significantly decreased (PR: 0.98 per year increase, CI: 0.97, 1.00).

**Conclusions:** The prevalence of laboratory-confirmed STIs was much higher than what was captured by clinical diagnosis. GC, CT, and Tvag were not accurately detected without lab confirmation. Missed diagnoses decreased with older age. Increased laboratory capacity and refinement of the syndromic approach are needed to protect the health of sexually-active Jamaican women.

**Trial Registration:** The Jamaica Sino-Implant Study was registered with clinicaltrials.gov (NCT01684358).

**Key Words:**

Sexually-transmitted infections, syndromic diagnosis, laboratory diagnosis, algorithms

**Strengths and Limitations:**

- This analysis provides updated data on the poor sensitivity of using only clinical signs and symptoms to guide diagnosis of STI among women in Jamaica.

- Our study is limited in that we did not assess if study clinicians were implementing risk score assessments to guide syndromic assessment of STI. Also, we were not able to examine the presence of bacterial vaginosis or STIs other than GC, CT, or Tvag by laboratory assays.
INTRODUCTION

Syndromic diagnosis and management of sexually transmitted infections (STI) is currently used in many resource-limited settings lacking laboratory infrastructure (1). While syndromic approaches are cost-effective and efficient in settings where laboratory testing is limited or unavailable, they may miss infections among asymptomatic or minimally symptomatic cases or, alternatively, may lead to unnecessary and costly treatment when the clinical presentation is non-specific (2, 3). For example, a meta-analysis evaluating the WHO syndromic approaches found that vaginal discharge flowchart perform effectively in detecting Trichomonas vaginalis (Tvag) and bacterial vaginosis (BV), but not Chlamydia trachomatis (CT) and Neisseria gonorrhoeae (GC) infections (2).

Overall, syndromic management may underestimate STI prevalence, due to the asymptomatic or non-specific presentation of many STIs (4). Cervical infections, such as CT and GC, are often asymptomatic, poorly correlated to vaginal discharge, and consequently difficult to assess using syndromic approaches (5-7). However, missed cervical infections may lead to serious complications such as pelvic inflammatory disease, infertility, ectopic pregnancy and other chronic issues among women of reproductive age (8).

Syndromic algorithms for the management of STIs are currently the recommended practice in Jamaica (1), but to our knowledge, there is a lack of recent data on how clinical diagnosis of STI compares to the “gold standard” of laboratory testing among Jamaican women (9, 10). This is despite the fact that the clinical burden of STI in Jamaica is high, particularly among young women (11). In order to address this question, we compared syndromic approaches with the laboratory detection of CT, GC, and Tvag infections among sexually active women who participated in a randomized trial of a progestin implant initiation in
Jamaica (11, 12). We also assessed characteristics associated with a clinical diagnosis as well as with a clinically missed STI among these women.

**MATERIALS AND METHODS**

The Sino-Implant Study (SIS) was a randomized controlled clinical trial that assigned 414 women to receive a levonorgestrel implant at either baseline or three months post-enrollment, with follow-up at 1-month and 3-months post-enrollment, in order to evaluate whether contraceptive initiation was associated with changes in frequency of condomless sex after implant initiation. The study was conducted in public family planning clinics in Kingston, Jamaica from September 2012 to January 2014. The results of this study have been reported previously (12).

This analysis included 254 (61% of the 414 total) participants with available clinician-collected vaginal swabs from at least one study visit for laboratory STI testing. Participants’ characteristics from the baseline visit were compared between those with and without specimens available for STI testing (using chi-squared tests and t-tests) in order to ensure that the lack of specimen availability did not introduce bias into the analysis (11). Vaginal swabs for laboratory testing of STIs and prostate-specific antigen (PSA) were collected at baseline, 1-month and 3-month follow-up visits. Available vaginal swab samples (N=254) were tested for CT, GC by Aptima Combo 2 assay for CT/GC and Tvag by Aptima *Trichomonas vaginalis* assay with the Panther system (Hologic, San Diego, CA), at the US Centers for Disease Control and Prevention (CDC). Assessment for exposure to semen was conducted onsite via PSA testing using the ABAcard 30 (Abacus Diagnostics, West Hills, CA) and further quality
assurance testing was confirmed at the CDC using the quantitative total PSA assay (Abbott Diagnostics, Abbott Park, IL) (11, 12).

Clinical STI diagnoses were determined from medical records by assessing clinical notes and antibiotic prescriptions for STI for each participant that had an available swab by study visit (baseline, 1 month and three month). As the laboratory testing included CT, GC, and Tvag, we only included for comparison corresponding clinical diagnoses of cervicitis (which included presumed CT, GC, and unspecified cervicitis), and vaginitis (which included presumed Tvag, BV, and unspecified vaginitis). Clinical diagnoses of yeast infections, human papilloma virus (HPV), herpes simplex virus (HSV) infections, and other unspecified STIs were excluded, to correspond with the etiologic agents included in the laboratory testing.

Cases were considered “missed” if they were clinically-diagnosed as “healthy” but had a laboratory-detected STI. Cases were considered “unmatched” when the clinically diagnosed STI code for cervicitis or vaginitis was incorrectly identified in accordance with the lab results of GC, CT and/or Tvag or when the clinical STI code indicated yeast infection, HSV/HPV, or other undetermined STI.

Statistical Methods

Distributions of continuous variables were described using medians and interquartile ranges, and those of categorical variables using frequencies and percentages. Comparisons of baseline characteristics by clinical STI status were made using chi-squared tests for categorical variables and Wilcoxon ranked sum test for continuous variables.

Log-binomial regression models fit with generalized estimating equations to account for multiple study visits were used to estimate associations of clinically diagnosed STI or missed STI with laboratory-confirmed diagnoses and with demographic and sexual behavior characteristics, adjusting for study arm. Additional adjustment for baseline laboratory STI
status was determined with a change in estimate approach for variables that resulted in a ten percent change in the point estimate. The association of study arm with clinically-diagnosed STIs was assessed using a similar model, adjusting for baseline STI outcome and restricting to the two post-randomization study visits. All analyses were conducted using SAS 9.3 (SAS Institute, Cary, NC).

Ethical Review

The study protocol was approved by the ethical review boards of the Jamaican Ministry of Health, the University of West Indies, and the U.S. Centers for Disease Control and Prevention; the SIS trial was registered with clinicalTrials.gov (NCT01684358).

RESULTS

The baseline characteristics, sexual behaviors, and laboratory results are described in Table 1. There were no observed differences in baseline characteristics by clinical diagnosis of an STI (Table 1). However, there were more laboratory-detected STIs at baseline among participants who had clinically-diagnosed cervicitis or vaginitis (p-value=0.03) at any point during the study period compared to participants who never had clinically-diagnosed cervicitis or vaginitis.

Overall, 65 of 254 women (25.6%) had at least one clinical diagnosis of cervicitis or vaginitis, and a total of 84 such clinical instances during the study period. Most (89.3%) clinical cases were categorized as vaginitis (n=75 cases). There were 62 cases of other genital infections, of which 54 were yeast infections, 2 were HPV or HSV, and 6 were undetermined/other STIs. In comparison, 195 (76.8%) women had at least one laboratory-detected CT, GC, or Tvag, and a total of 424 such cases of laboratory-detected STI during the study period (Figure 1). Most laboratory detections were of Tvag (n=225) and CT (n=179)
(Figure 1); in 88 cases two pathogens were simultaneously detected and in 4 instances all three. Additionally, there were 67 participants with infections at adjacent visits as detected by laboratory test, 65 of which were missed clinically. Twenty nine of these women had the same infection across three study visits. In total, clinical diagnosis missed 79.7% of all laboratory-detected STI (424 cases): GC (n= 17 cases, 85.0%), CT (n= 141 cases, 78.8%), and Tvag (n= 180 cases, 80.0%) (Figure 1). The clinical assessments did not match the laboratory-detected STI in 61 instances.

When assessing associations of participant characteristics and sexual behaviors with clinically-diagnosed STI outcomes using a model that accounts for repeated observations per subject, use of hormonal contraception in the month prior to the study visit was significantly associated with clinical cervicitis and/or vaginitis, adjusting for study arm (Prevalence Ratio (PR): 1.65, 95% Confidence Interval (CI): 1.07, 2.54) (Table 2). Increasing age was significantly associated with reduced prevalence of missed infections (PR: 0.98 per year increase, CI: 0.97, 1.00), adjusting for study arm. Study arm was not significantly associated with clinically diagnosed cervicitis and/or vaginitis (PR: 0.71, CI: 0.43, 1.17), adjusting for baseline STI and restricting to the two post-randomization visits.

DISCUSSION

Among this population of sexually active women in Jamaica initiating long acting contraception in public clinics, the prevalence of laboratory-detected STI was much higher than what was captured by clinical diagnosis. GC, CT and Tvag infections were not accurately detected by clinical impressions, and this varied by age. Previous studies have also shown that syndromic approaches tend to underestimate the prevalence of STIs (4, 6, 13-15). In our study, clinical impressions missed the majority (80%) of laboratory-detected STIs, which indicates quite low
sensitivity of clinical approaches to identifying cervico-vaginal infections. This is probably due
to the asymptomatic, minimally symptomatic or non-specific manifestations of many STIs in
women. Another study in South Africa similarly found that only 12.3% of laboratory-confirmed
STIs had clinically evident symptoms (6).

Previous research among women attending STI clinics in Jamaica indicated the
sensitivity and specificity of clinical assessment in detecting GC, CT, and Tvag to range from
72.8%-84.7% and 37.9%-55.5%, respectively (9). Adding risk assessment (a risk score) to the
syndromic algorithm improved sensitivity to 84.9%-84.5% and reduced specificity to 25.5%-40.0% (9). Syndromic approaches also resulted in poor diagnostic value and comparatively
worse sensitivity (11.1%-66.7%) among pregnant women in Jamaica who were presumably at
lower risk of STI than in higher prevalence settings (10). The lower sensitivity of the clinical
approach to diagnosis in our study, compared with the estimated sensitivity above, may be due
to the fact that clinicians may not have used the recommended algorithm that includes risk
assessment, and may rely only on complaints and physical findings. The utility of adding
uniform criteria (such as age <21 years, more than one and/or new partner in the last three
months, partner with symptoms of urethral discharge syndrome and/or not living with a steady
partner) of STI risk to the algorithm’s assessment becomes apparent from the fact that it is not
easy to differentiate risk level based on individual characteristics; most participant risk
characteristics examined in this study were not associated with clinical symptoms or signs.

Our study provides updated data on the poor sensitivity of using only clinical signs and
symptoms to guide diagnosis of STI among women in Jamaica. These results point to the
need for continuous education of clinical providers on the use of syndromic algorithms that
incorporate risk assessment to diagnose STI. To our knowledge, data on comparisons of
clinical and laboratory diagnosis of STI among high risk women in Jamaica have not been
published in several years (9). While this comparison was not a primary objective of the
original study, this study provided a rare opportunity to utilize available medical charts and specimens. However, our study has also several limitations. We did not assess if study clinicians were implementing risk score assessments to guide syndromic assessment of STI. Therefore, our analysis likely represents an assessment of clinical impressions, rather than an assessment of the recommended syndromic algorithm for cervico-vaginal discharge, against the gold standard of laboratory detection. We were not able to examine the presence of bacterial vaginosis, yeast infections, HPV/HSV, or other STI considering the lack of laboratory testing for these etiologies. Tvag can occasionally be a cause of non-specific cervicitis, and not just vaginitis. The generalizability of our findings may be limited given that recruitment from particular public sector clinics in the study may not be representative of all Jamaican women and Jamaican clinicians.

Laboratory detection of STI represents the gold standard and development and availability of point-of-care laboratory tests may make this a feasible goal for resource-limited settings. Our study findings certainly point to the need for wider availability of such laboratory diagnostic means in Jamaica, given the high prevalence, often asymptomatic nature of STI, and the potentially devastating consequences for a woman’s future health and fertility. Continuing education of health care providers on the optimal use of STI diagnostic algorithms remains important in this regard as well.
Table 1. Characteristics of Sino-Implant Study participants tested for sexually transmitted infections at one or more study visits (N=254) by syndromic cervicitis/vaginitis status at any time point

<table>
<thead>
<tr>
<th>Baseline characteristics</th>
<th>Overall (N=254)</th>
<th>Syndromic STI + (N=65)</th>
<th>Syndromic STI - (N=189)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immediate implant study arm</td>
<td>123 (48.4%)</td>
<td>32 (49.2%)</td>
<td>91 (48.2%)</td>
<td>0.88</td>
</tr>
<tr>
<td>Single vs. cohabiting, married, divorced</td>
<td>177 (69.7%)</td>
<td>46 (70.8%)</td>
<td>131 (69.3%)</td>
<td>0.83</td>
</tr>
<tr>
<td>Did not complete high school</td>
<td>74 (29.1%)</td>
<td>21 (32.3%)</td>
<td>53 (28.0%)</td>
<td>0.51</td>
</tr>
<tr>
<td>Four or more alcoholic drinks</td>
<td>9 (3.5%)</td>
<td>4 (6.2%)</td>
<td>5 (2.7%)</td>
<td>0.19</td>
</tr>
<tr>
<td>Positive PSA test</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline positive STI lab result*</td>
<td>99 (40.2%)</td>
<td>32 (51.6%)</td>
<td>67 (36.4%)</td>
<td>0.03</td>
</tr>
<tr>
<td>Unprotected sex in 2 days</td>
<td>40 (15.8%)</td>
<td>13 (20.0%)</td>
<td>27 (14.3%)</td>
<td>0.28</td>
</tr>
<tr>
<td>Ever received money or gifts in exchange for sex</td>
<td>14 (5.5%)</td>
<td>3 (4.6%)</td>
<td>11 (6.5%)</td>
<td>0.71</td>
</tr>
<tr>
<td>Hormonal contraception in past month</td>
<td>66 (25.6%)</td>
<td>11 (16.9%)</td>
<td>54 (28.6%)</td>
<td>0.06</td>
</tr>
<tr>
<td>More than 1 partner in past month</td>
<td>15 (5.5%)</td>
<td>3 (4.6%)</td>
<td>12 (6.4%)</td>
<td>0.61</td>
</tr>
<tr>
<td>Age</td>
<td>25 (21-30)</td>
<td>24 (21-29)</td>
<td>25 (21-30)</td>
<td>0.61</td>
</tr>
<tr>
<td>Parity**</td>
<td>2 (1-3)</td>
<td>2 (1-3)</td>
<td>2 (1-3)</td>
<td>0.84</td>
</tr>
</tbody>
</table>

*Missing baseline STI lab results, N=246 for Overall, N= 62 for STI+, and N=184 for STI-
**Missing values from 8 participants

![Figure 1. Total and Missed Laboratory Detected Cases and Clinical Diagnoses, for Overall Total and by Study Visit](image-url)

*Laboratory-detected cases include unmatched cases, defined as cases where the expected clinical STI code was identified in accordance with the lab results of GC, CT and/or Tvag or when the clinical STI code indicated yeast infection, HSV/HPV, or other undetermined STI. There were 61 total unmatched cases, of which 3 were GC, 31 CT, and 21 Tvag.

**Defined as cases that were clinically diagnosed as healthy but had a laboratory-confirmed ST

*Cervicitis includes diagnoses of chlamydia, gonorrhea, and unspecified cervicitis

^Vaginitis includes diagnoses of bacterial vaginosis, trichomonas, and unspecified vaginitis
Table 2. Associations between participant characteristics and clinically-diagnosed or missed STIs

<table>
<thead>
<tr>
<th>Clinically-Diagnosed Vaginitis and/or Cervicitis</th>
<th>PR</th>
<th>95% CI</th>
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<tr>
<td>Any Positive Lab Result*</td>
<td>1.07</td>
<td>0.61 1.90</td>
</tr>
<tr>
<td>Positive PSA test</td>
<td>1.42</td>
<td>0.91 2.20</td>
</tr>
<tr>
<td>Unprotected sex in 2 days*</td>
<td>0.96</td>
<td>0.52 1.77</td>
</tr>
<tr>
<td>Age (increase 1 year)</td>
<td>0.98</td>
<td>0.94 1.01</td>
</tr>
<tr>
<td>Parity (increase of 1)</td>
<td>0.98</td>
<td>0.83 1.17</td>
</tr>
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<td>Single, vs. cohabiting, married, divorced</td>
<td>0.99</td>
<td>0.59 1.67</td>
</tr>
<tr>
<td>Did not complete high school</td>
<td>1.19</td>
<td>0.73 1.93</td>
</tr>
<tr>
<td>Four or more alcoholic drinks*</td>
<td>1.60</td>
<td>0.68 3.80</td>
</tr>
<tr>
<td>Ever received money or gifts in exchange for sex</td>
<td>1.09</td>
<td>0.37 3.21</td>
</tr>
<tr>
<td>Hormonal contraception in past month</td>
<td>1.65</td>
<td>1.07 2.54</td>
</tr>
<tr>
<td>More than 1 partner in past month*</td>
<td>1.18</td>
<td>0.50 2.77</td>
</tr>
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<table>
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<tr>
<th>Missed Cases of Lab-Confirmed Gonorrhea, Chlamydia, Trichomonas *</th>
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<tbody>
<tr>
<td>Positive PSA test</td>
</tr>
<tr>
<td>Unprotected sex in 2 days</td>
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<td>More than 1 partner in past month*</td>
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PR= Prevalence Ratio. 95% CI= 95% Confidence Interval

* Analyzed with generalized estimating equations for repeated measures, adjusting for study arm
* Additionally adjusting for baseline STI status
* Defined as cases that were clinically diagnosed as healthy but had a laboratory-confirmed STI
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Competing Interests: The authors report no conflicts of interest.

Data Sharing: For data sharing inquiries, please contact AKourtis@cdc.gov.

Ethics Approval: The study protocol was approved by the Jamaican Ministry of Health, the Centers for Disease Control, and the University of West Indies ethical review boards and this study was registered with clinicaltrials.gov (NCT01684358).

Contributorship Statement: All authors participated in the interpretation of the study and drafting of the manuscript. All authors have seen and approved the final version. YZ, JW, MCS, APK were involved in the design of the study, data analysis and interpretation, and writing of the manuscript. TH-K, NM-S, and BC were involved in overall study design and conduct, and provided input for the manuscript. MCS, JP, LF, and CB were involved in data acquisition and lab analyses. YZ and JW performed the statistical analyses.

Collaborators: The authors thank the Jamaica Sino-Implant Study team for their assistance with study coordination, data collection, and patient care, as well as the study participants for their contributions.
REFERENCES


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\textsuperscript{1} Division of Reproductive Health, U.S. Centers for Disease Control and Disease Prevention (CDC), Atlanta, GA, USA
\textsuperscript{2} Association of Schools and Programs of Public Health (ASPPH), Washington, DC, USA
\textsuperscript{3} Division of Sexually Transmitted Disease Prevention, U.S. Centers for Disease Control and Disease Prevention (CDC), Atlanta, GA, USA
\textsuperscript{4} University Hospital of the West Indies, Kingston, Jamaica
\textsuperscript{5} Family Health International (FHI 360), Durham, NC, USA
\textsuperscript{6} Epidemiology Research and Training Unit, Ministry of Health, Kingston, Jamaica

Corresponding Author:
Yasaman Zia, Centers for Disease Control and Prevention, 4770 Buford HWY, MS-F-74, Atlanta, GA 30341, USA. Phone: 770-498-1704. Fax: 770-488-6391. E-mail: yzia@cdc.gov

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Disclosures: The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention or the Association of Schools and Programs of Public Health.
ABSTRACT

Objectives: To assess potentially missed STIs, we compared clinically-diagnosed STIs to laboratory-confirmed diagnoses of gonorrhea (GC), chlamydia (CT), and trichomonas (Tvag).

Design: Secondary analysis of a randomized controlled trial.

Setting: We used data and specimens previously collected for the Sino-Implant Study in Kingston, Jamaica.

Participants: The Sino-Implant Study randomized 414 women to receive a levonorgestrel implant at either baseline or three months post-enrollment to evaluate unprotected sex after implant initiation. This analysis utilized 254 available vaginal swab samples.

Outcome Measures: Clinically-diagnosed STIs were determined from medical records by assessing clinical impressions and prescriptions. Laboratory-confirmed STIs included GC, CT, and Tvag tested by Aptima Combo 2 for CT/GC and Aptima Tvag assays (Hologic, San Diego, CA). Log-binomial regression models fit with generalized estimating equations were used to estimate associations of clinically-diagnosed STIs with laboratory-confirmed diagnoses and demographic and behavioral characteristics.

Results: Overall, 195 (76.8%) women had laboratory-confirmed STI (CT, GC or Tvag) while only 65 (25.6%) women had clinically-diagnosed cervicitis and/or vaginitis during the study period. Clinical diagnosis missed 79.7% of laboratory-confirmed STIs: 85% of GC (n= 17/20), 78.8% of CT (n= 141/179), and 80.0% of Tvag (n= 180/225). Hormonal contraceptive use in the month prior to the study visit was significantly associated with clinical diagnosis at any time.
point (Prevalence Ratio (PR): 1.65, 95% Confidence Interval (CI): 1.07, 2.54). As age increased, clinically missed infections significantly decreased (PR: 0.98 per year increase, CI: 0.97, 1.00).

Conclusions: The prevalence of laboratory-confirmed STIs was much higher than what was captured by clinical diagnosis. GC, CT, and Tvag were not accurately detected without lab confirmation. Missed diagnoses decreased with older age. Increased laboratory capacity and refinement of the syndromic approach are needed to protect the health of sexually-active Jamaican women.

Trial Registration: The Jamaica Sino-Implant Study was registered with clinicaltrials.gov (NCT01684358).

Key Words: Sexually-transmitted infections, syndromic diagnosis, laboratory diagnosis, algorithms

Strengths and Limitations:

- This analysis provides updated data on the poor sensitivity of using only clinical signs and symptoms to guide diagnosis of STI among women in Jamaica.

- A strength of the study is that this is a secondary analysis from a randomized controlled clinical trial, with systematic collection of data on clinical signs/symptoms and on antibiotic prescriptions, as well as laboratory detection of STI for comparison.
• Our study is limited in that we did not assess if study clinicians were implementing risk score assessments to guide syndromic assessment of STI. Also, we were not able to examine the presence of bacterial vaginosis or STIs other than GC, CT, or Tvag by laboratory assays.
INTRODUCTION

Syndromic diagnosis and management of sexually transmitted infections (STI) is currently used in many resource-limited settings lacking laboratory infrastructure (1). While syndromic approaches are cost-effective and efficient in settings where laboratory testing is limited or unavailable, they may miss infections among asymptomatic or minimally symptomatic cases or, alternatively, may lead to unnecessary and costly treatment when the clinical presentation is non-specific (2, 3). For example, a meta-analysis evaluating the WHO syndromic approaches found that vaginal discharge flowchart perform effectively in detecting *Trichomonas vaginalis* (Tvag) and bacterial vaginosis (BV), but not *Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (GC) infections (2).

Overall, syndromic management may underestimate STI prevalence, due to the asymptomatic or non-specific presentation of many STIs (4). Cervical infections, such as CT and GC, are often asymptomatic, poorly correlated to vaginal discharge, and consequently difficult to assess using syndromic approaches (5-7). However, missed cervical infections may lead to serious complications such as pelvic inflammatory disease, infertility, ectopic pregnancy and other chronic issues among women of reproductive age (8).

Syndromic algorithms for the management of STIs are currently the recommended practice in Jamaica (1), but to our knowledge, there is a lack of recent data on how clinical diagnosis of STI compares to the “gold standard” of laboratory testing among Jamaican women (9, 10). This is despite the fact that the clinical burden of STI in Jamaica is high, particularly among young women (11). In order to address this question, we compared syndromic approaches with the laboratory detection of CT, GC, and Tvag infections among sexually active women who participated in a randomized trial of a progestin implant initiation in
Jamaica (11, 12). We also assessed characteristics associated with a clinical diagnosis as well as with a clinically missed STI among these women.

**MATERIALS AND METHODS**

The Sino-Implant Study (SIS) was a randomized controlled clinical trial that assigned 414 women to receive a levonorgestrel implant at either baseline or three months post-enrollment, with follow-up at 1-month and 3-months post-enrollment, in order to evaluate whether contraceptive initiation was associated with changes in frequency of condomless sex after implant initiation. The study was conducted in public family planning clinics in Kingston, Jamaica from September 2012 to January 2014. Written informed consent was obtained from study participants at enrollment. The results of this study have been reported previously (12, 13).

This analysis included 254 (61% of the 414 total) participants with available clinician-collected vaginal swabs from at least one study visit for laboratory STI testing. Participants’ characteristics from the baseline visit were compared between those with and without specimens available for STI testing (using chi-squared tests and t-tests) in order to ensure that the lack of specimen availability did not introduce bias into the analysis (11). Vaginal swabs for laboratory testing of STIs and prostate-specific antigen (PSA) were collected at baseline, 1-month and 3-month follow-up visits. Available vaginal swab samples (N=254) were tested for CT, GC by Aptima Combo 2 assay for CT/GC and Tvag by Aptima *Trichomonas vaginalis* assay with the Panther system (Hologic, San Diego, CA), at the US Centers for Disease Control and Prevention (CDC). Assessment for exposure to semen was conducted onsite via PSA testing using the ABAcard 30 (Abacus Diagnostics, West Hills, CA) and further quality
assurance testing was confirmed at the CDC using the quantitative total PSA assay (Abbott Diagnostics, Abbott Park, IL) (11, 12).

Clinical STI diagnoses were determined from medical records by assessing clinical notes for signs and symptoms consistent with an STI and for antibiotic prescriptions for STI for each participant that had an available swab by study visit (baseline, 1 month and three month). As the laboratory testing included CT, GC, and Tvag, we only included for comparison corresponding clinical diagnoses of cervicitis (which included presumed CT, GC, and unspecified cervicitis), and vaginitis (which included presumed Tvag, BV, and unspecified vaginitis). Clinical diagnoses of yeast infections, human papilloma virus (HPV), herpes simplex virus (HSV) infections, and other unspecified STIs were excluded, to correspond with the etiologic agents included in the laboratory testing.

Cases were considered “missed” if they were clinically-diagnosed as “healthy” but had a laboratory-detected STI. Cases were considered “unmatched” when the clinically diagnosed STI code for cervicitis or vaginitis was incorrectly identified in accordance with the lab results of GC, CT and/or Tvag or when the clinical STI code indicated yeast infection, HSV/HPV, or other undetermined STI.

**Statistical Methods**

Distributions of continuous variables were described using medians and interquartile ranges, and those of categorical variables using frequencies and percentages. Comparisons of baseline characteristics by clinical STI status were made using chi-squared tests for categorical variables and Wilcoxon ranked sum test for continuous variables.

Log-binomial regression models fit with generalized estimating equations to account for multiple study visits were used to estimate associations of clinically diagnosed STI or missed STI with laboratory-confirmed diagnoses and with demographic and sexual behavior.
characteristics, adjusting for study arm. Additional adjustment for baseline laboratory STI status was determined with a change in estimate approach for variables that resulted in a ten percent change in the point estimate. The association of study arm with clinically-diagnosed STIs was assessed using a similar model, adjusting for baseline STI outcome and restricting to the two post-randomization study visits. All analyses were conducted using SAS 9.3 (SAS Institute, Cary, NC).

**Ethical Review**

The study protocol was approved by the ethical review boards of the Jamaican Ministry of Health, the University of West Indies, and the U.S. Centers for Disease Control and Prevention; the SIS trial was registered with clinicalTrials.gov (NCT01684358).

**RESULTS**

The baseline characteristics, sexual behaviors, and laboratory results are described in Table 1. There were no observed differences in baseline characteristics by clinical diagnosis of an STI (Table 1). However, there were more laboratory-detected STIs at baseline among participants who had clinically-diagnosed cervicitis or vaginitis (p-value=0.03) at any point during the study period compared to participants who never had clinically-diagnosed cervicitis or vaginitis.

Overall, 65 of 254 women (25.6%) had at least one clinical diagnosis of cervicitis or vaginitis, and a total of 84 such clinical instances occurred during the study period. Most (89.3%) clinical cases were categorized as vaginitis (n=75 cases). There were 62 cases of other genital infections, of which 54 were yeast infections, 2 were HPV or HSV, and 6 were undetermined/other STIs. In comparison, 195 (76.8%) women had at least one laboratory-detected CT, GC, or Tvag, and a total of 424 such cases of laboratory-detected STI during the
study period (Figure 1). Most laboratory detections were of Tvag (n=225) and CT (n=179)
(Figure 1); in 88 cases two pathogens were simultaneously detected and in 4 instances all
three. Additionally, there were 67 participants with infections at adjacent visits as detected by
laboratory test, 65 of which were missed clinically. Twenty nine of these women had the same
infection across three study visits. In total, clinical diagnosis missed 79.7% of all laboratory-
detected STI (424 cases): GC (n= 17 cases, 85.0%), CT (n= 141 cases, 78.8%), and Tvag (n=
180 cases, 80.0%) (Figure 1). The clinical assessments did not match the laboratory-detected
STI in 61 instances.

When assessing associations of participant characteristics and sexual behaviors with
clinically-diagnosed STI outcomes using a model that accounts for repeated observations per
subject, use of hormonal contraception in the month prior to the study visit was significantly
associated with clinical cervicitis and/or vaginitis, adjusting for study arm (Adjusted Prevalence
Ratio (aPR): 1.65, 95% Confidence Interval (CI): 1.07, 2.54) (Table 2). Increasing age was
significantly associated with reduced prevalence of missed infections (aPR: 0.98 per year
increase, CI: 0.97, 1.00), adjusting for study arm. Study arm was not significantly associated
with clinically diagnosed cervicitis and/or vaginitis (aPR: 0.71, CI: 0.43, 1.17), adjusting for
baseline STI and restricting to the two post-randomization visits.

**DISCUSSION**

Among this population of sexually active women in Jamaica initiating long acting contraception
in public clinics, the prevalence of laboratory-detected STI was much higher than what was
captured by clinical diagnosis. GC, CT and Tvag infections were not accurately detected by
clinical impressions, and this varied by age. Previous studies have also shown that syndromic
approaches tend to underestimate the prevalence of STIs (4, 6, 14-16). In our study, clinical
impressions missed the majority (80%) of laboratory-detected STIs, which indicates quite low sensitivity of clinical approaches to identifying cervico-vaginal infections. This is probably due to the asymptomatic, minimally symptomatic or non-specific manifestations of many STIs in women. Another study in South Africa similarly found that only 12.3% of laboratory-confirmed STIs had clinically evident symptoms (6).

Previous research among women attending STI clinics in Jamaica indicated the sensitivity and specificity of clinical assessment in detecting GC, CT, and Tvag to range from 72.8%-84.7% and 37.9%-55.5%, respectively (9). Adding risk assessment (a risk score) to the syndromic algorithm improved sensitivity to 84.9%-84.5% and reduced specificity to 25.5%-40.0% (9). Syndromic approaches also resulted in poor diagnostic value and comparatively worse sensitivity (11.1%-66.7%) among pregnant women in Jamaica who were presumably at lower risk of STI than in higher prevalence settings (10). The lower sensitivity of the clinical approach to diagnosis in our study, compared with the estimated sensitivity above, may be due to the fact that clinicians may not have used the recommended algorithm that includes risk assessment, and may rely only on complaints and physical findings. The utility of adding uniform criteria (such as age <21 years, more than one and/or new partner in the last three months, partner with symptoms of urethral discharge syndrome and/or not living with a steady partner) of STI risk to the algorithm’s assessment becomes apparent from the fact that it is not easy to differentiate risk level based on individual characteristics; most participant risk characteristics examined in this study were not associated with clinical symptoms or signs. Further, in a previous analysis of factors associated with laboratory detection of an STI in this
study, no individual characteristic other than younger age was associated with a laboratory-confirmed STI (11).

Our study provides updated data on the poor sensitivity of using only clinical signs and symptoms to guide diagnosis of STI among women in Jamaica. These results point to the need for continuous education of clinical providers on the use of syndromic algorithms that incorporate risk assessment to diagnose STI. To our knowledge, data on comparisons of clinical and laboratory diagnosis of STI among high risk women in Jamaica have not been published in several years (9). While this comparison was not a primary objective of the original study, this study provided a rare opportunity to utilize available medical charts and specimens. However, our study has also several limitations. We did not assess if study clinicians were implementing risk score assessments to guide syndromic assessment of STI. Therefore, our analysis likely represents an assessment of clinical impressions, rather than an assessment of the recommended syndromic algorithm for cervico-vaginal discharge, against the gold standard of laboratory detection. We were not able to examine the presence of bacterial vaginosis, yeast infections, HPV/HSV, or other STI considering the lack of laboratory
testing for these etiologies. Tvag can occasionally be a cause of non-specific cervicitis, and not
just vaginitis. The generalizability of our findings may be limited given that recruitment from
particular public sector clinics in the study may not be representative of all Jamaican women
and Jamaican clinicians.

Laboratory detection of STI represents the gold standard and development and
availability of point-of-care laboratory tests may make this a feasible goal for resource-limited
settings. Our study findings certainly point to the need for wider availability of such laboratory
diagnostic means in Jamaica, given the high prevalence, often asymptomatic nature of STI,
and the potentially devastating consequences for a woman’s future health and fertility.

Continuing education of health care providers on the optimal use of STI diagnostic algorithms
remains important in this regard as well.

**Figure:** Total and Missed Laboratory Detected Cases and Clinical Diagnoses, for Overall Total
and by Study Visit
Table 1. Characteristics of Sino-Implant Study participants tested for sexually transmitted infections at one or more study visits (N=254) by syndromic cervicitis/vaginitis status at any time point

<table>
<thead>
<tr>
<th>Baseline characteristics</th>
<th>Overall (N=254)</th>
<th>Syndromic STI + (N=65)</th>
<th>Syndromic STI - (N=189)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immediate implant study arm</td>
<td>123 48.4%</td>
<td>32 49.2%</td>
<td>91 48.2%</td>
<td>0.88</td>
</tr>
<tr>
<td>Single vs. cohabiting, married, divorced</td>
<td>177 69.7%</td>
<td>46 70.8%</td>
<td>131 69.3%</td>
<td>0.83</td>
</tr>
<tr>
<td>Did not complete high school</td>
<td>74 29.1%</td>
<td>21 32.3%</td>
<td>53 28.0%</td>
<td>0.51</td>
</tr>
<tr>
<td>Four or more alcoholic drinks</td>
<td>9 3.5%</td>
<td>4 6.2%</td>
<td>5 2.7%</td>
<td>0.19</td>
</tr>
<tr>
<td>Positive PSA test</td>
<td>64 25.2%</td>
<td>21 32.3%</td>
<td>43 22.8%</td>
<td>0.13</td>
</tr>
<tr>
<td>Baseline positive STI lab result*</td>
<td>99 40.2%</td>
<td>32 51.6%</td>
<td>67 36.4%</td>
<td><strong>0.03</strong></td>
</tr>
<tr>
<td>Unprotected sex in 2 days</td>
<td>40 15.8%</td>
<td>13 20.0%</td>
<td>27 14.3%</td>
<td>0.28</td>
</tr>
<tr>
<td>Ever received money or gifts in exchange for sex</td>
<td>14 5.5%</td>
<td>3 4.6%</td>
<td>11 5.8%</td>
<td>0.71</td>
</tr>
<tr>
<td>Hormonal contraception in past month</td>
<td>65 25.6%</td>
<td>11 16.9%</td>
<td>54 28.6%</td>
<td>0.06</td>
</tr>
<tr>
<td>More than 1 partner in past month</td>
<td>15 5.9%</td>
<td>3 4.6%</td>
<td>12 6.4%</td>
<td>0.61</td>
</tr>
<tr>
<td><strong>Median (IQR)</strong></td>
<td><strong>Median (IQR)</strong></td>
<td><strong>Median (IQR)</strong></td>
<td>Wilcoxon</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>25 21-30</td>
<td>24 21-29</td>
<td>25 21-30</td>
<td>0.61</td>
</tr>
<tr>
<td>Parity**</td>
<td>2 1-3</td>
<td>2 1-3</td>
<td>2 1-3</td>
<td>0.84</td>
</tr>
</tbody>
</table>

*Missing baseline STI lab results, N=246 for Overall, N=62 for STI+, and N=184 for STI-
**Missing values from 8 participants

Figure 1. Total and Missed Laboratory Detected Cases and Clinical Diagnoses, by Overall Total and by Study Visit

*Laboratory-detected cases include unmatched cases, defined as cases where the expected clinical STI code was identified in accordance with the lab results of GC, CT and/or Tvag or when the clinical STI code indicated yeast infection, HSV/HPV, or other undetermined STI. There were 61 total unmatched cases, of which 3 were GC, 31 CT, and 21 Tvag.

**Defined as cases that were clinically diagnosed as healthy but had a laboratory-confirmed ST
~Cervicitis includes diagnoses of chlamydia, gonorrhea, and unspecified cervicitis
^Vaginitis includes diagnoses of bacterial vaginosis, trichomonas, and unspecified vaginitis
Table 2. Associations between participant characteristics and clinically-diagnosed or missed STIs

<table>
<thead>
<tr>
<th>Clinical-Diagnosed Vaginitis and/or Cervicitis</th>
<th>aPR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any Positive Lab Result*</td>
<td>1.07</td>
<td>0.61</td>
</tr>
<tr>
<td>Positive PSA test</td>
<td>1.42</td>
<td>0.91</td>
</tr>
<tr>
<td>Unprotected sex in 2 days*</td>
<td>0.96</td>
<td>0.52</td>
</tr>
<tr>
<td>Age (increase 1 year)</td>
<td>0.98</td>
<td>0.94</td>
</tr>
<tr>
<td>Parity (increase of 1)</td>
<td>0.98</td>
<td>0.83</td>
</tr>
<tr>
<td>Single, vs. cohabiting, married, divorced</td>
<td>0.99</td>
<td>0.59</td>
</tr>
<tr>
<td>Did not complete high school</td>
<td>1.19</td>
<td>0.73</td>
</tr>
<tr>
<td>Four or more alcoholic drinks*</td>
<td>1.60</td>
<td>0.68</td>
</tr>
<tr>
<td>Ever received money or gifts in exchange for sex</td>
<td>1.09</td>
<td>0.37</td>
</tr>
<tr>
<td>Hormonal contraception in past month</td>
<td>1.65</td>
<td>1.07</td>
</tr>
<tr>
<td>More than 1 partner in past month*</td>
<td>1.18</td>
<td>0.50</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Missed Cases of Lab-Confirmed Gonorrhea, Chlamydia, Trichomonas a</th>
<th>aPR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive PSA test</td>
<td>0.94</td>
<td>0.75</td>
</tr>
<tr>
<td>Unprotected sex in 2 days</td>
<td>1.14</td>
<td>0.90</td>
</tr>
<tr>
<td>Age (increase 1 year)</td>
<td>0.98</td>
<td>0.97</td>
</tr>
<tr>
<td>Parity (increase of 1)*</td>
<td>1.03</td>
<td>0.96</td>
</tr>
<tr>
<td>Single, vs. cohabiting, married, divorced *</td>
<td>0.97</td>
<td>0.82</td>
</tr>
<tr>
<td>Did not complete high school</td>
<td>1.17</td>
<td>0.94</td>
</tr>
<tr>
<td>Four or more alcoholic drinks</td>
<td>0.91</td>
<td>0.54</td>
</tr>
<tr>
<td>Ever received money or gifts in exchange for sex*</td>
<td>0.88</td>
<td>0.61</td>
</tr>
<tr>
<td>Hormonal contraception in past month</td>
<td>1.18</td>
<td>0.95</td>
</tr>
<tr>
<td>More than 1 partner in past month</td>
<td>1.22</td>
<td>0.87</td>
</tr>
</tbody>
</table>

aPR= Adjusted Prevalence Ratio, 95% CI= 95% Confidence Interval
~Analyzed with generalized estimating equations for repeated measures, adjusting for study arm
* Additionally adjusting for baseline STI status
a Defined as cases that were clinically diagnosed as healthy but had a laboratory-confirmed STI
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**Competing Interests:** The authors report no conflicts of interest.

**Data Sharing:** For data sharing inquiries, please contact Akourtis@cdc.gov.

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**Ethics Approval:** The study protocol was approved by the Jamaican Ministry of Health, the Centers for Disease Control, and the University of West Indies ethical review boards and this study was registered with clinicaltrials.gov (NCT01684358).

**Contributorship Statement:** All authors participated in the interpretation of the study and drafting of the manuscript. All authors have seen and approved the final version. YZ, JW, MCS, APK were involved in the design of the study, data analysis and interpretation, and writing of the manuscript. TH-K, NM-S, and ECC were involved in overall study design and conduct, and provided input for the manuscript. MCS, JP, LF, and CP were involved in data acquisition and lab analyses. YZ and JW performed the statistical analyses.
Collaborators: The authors thank the Jamaica Sino-Implant Study team for their assistance with study coordination, data collection, and patient care, as well as the study participants for their contributions.
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15. Otieno FO, Ndivo R, Oswago S, Ondiek J, Pals S, McLellan-Lemal E, Chen RT, Chege W, Gray KM. Evaluation of syndromic management of sexually transmitted infections within the Kisumu Incidence Cohort
Figure 1. Total and Missed Laboratory Detected Cases and Clinical Diagnoses, by Overall Total and by Study Visit

Figure 1. Total and Missed Laboratory Detected Cases and Clinical Diagnoses, by Overall Total and by Study Visit
STROBE Statement—Checklist of items that should be included in reports of *cohort studies*

<table>
<thead>
<tr>
<th>Item No</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Title and abstract</strong></td>
<td>1 <em>(a)</em> Indicate the study’s design with a commonly used term in the title or the abstract [Page 1] <em>(b)</em> Provide in the abstract an informative and balanced summary of what was done and what was found [Page 3-4]</td>
</tr>
<tr>
<td><strong>Introduction</strong></td>
<td>2 Explain the scientific background and rationale for the investigation being reported [Page 6]</td>
</tr>
<tr>
<td><strong>Objectives</strong></td>
<td>3 State specific objectives, including any prespecified hypotheses [Page 6-7]</td>
</tr>
<tr>
<td><strong>Methods</strong></td>
<td>4 Present key elements of study design early in the paper [Page 7]</td>
</tr>
<tr>
<td><strong>Study design</strong></td>
<td>5 Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection [Page 7]</td>
</tr>
<tr>
<td><strong>Setting</strong></td>
<td>6 <em>(a)</em> Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up [Page 7] <em>(b)</em> For matched studies, give matching criteria and number of exposed and unexposed [N/A]</td>
</tr>
<tr>
<td><strong>Participants</strong></td>
<td>7 Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable [Page 7-8]</td>
</tr>
<tr>
<td><strong>Variables</strong></td>
<td>8* For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group [Page 7-8]</td>
</tr>
<tr>
<td><strong>Data sources/ measurement</strong></td>
<td>9 Describe any efforts to address potential sources of bias [Page 9]</td>
</tr>
<tr>
<td><strong>Bias</strong></td>
<td>10 Explain how the study size was arrived at [Page 7]</td>
</tr>
<tr>
<td><strong>Study size</strong></td>
<td>11 Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why [Page 8-9]</td>
</tr>
<tr>
<td><strong>Quantitative variables</strong></td>
<td>12 <em>(a)</em> Describe all statistical methods, including those used to control for confounding [Page 8-9] <em>(b)</em> Describe any methods used to examine subgroups and interactions [N/A] <em>(c)</em> Explain how missing data were addressed [N/A- secondary analysis, limited to those with outcome of interest] <em>(d)</em> If applicable, explain how loss to follow-up was addressed [N/A] <em>(e)</em> Describe any sensitivity analyses [Page 8-9]</td>
</tr>
<tr>
<td><strong>Statistical methods</strong></td>
<td>13* <em>(a)</em> Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed [N/A- secondary analysis, original study methods cited in previous manuscript included as supplementary material] <em>(b)</em> Give reasons for non-participation at each stage[N/A- secondary analysis, original study methods cited in previous manuscript included as supplementary material] <em>(c)</em> Consider use of a flow diagram[N/A- secondary analysis, original study methods cited in previous manuscript included as supplementary material]</td>
</tr>
<tr>
<td><strong>Participants</strong></td>
<td>14* <em>(a)</em> Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders [Page 9] <em>(b)</em> Indicate number of participants with missing data for each variable of interest [N/A- secondary analysis, limited to those with outcome of interest]</td>
</tr>
</tbody>
</table>
(c) Summarise follow-up time (eg, average and total amount) [Figure 1, Page 13]

Outcome data 15* Report numbers of outcome events or summary measures over time [Figure 1, Page 13]

Main results 16

(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included [Page 10]

(b) Report category boundaries when continuous variables were categorized [N/A]

(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period [N/A]

Other analyses 17 Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses [N/A]

Discussion

Key results 18 Summarise key results with reference to study objectives [Page 10-11]

Limitations 19 Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias [Page 12]

Interpretation 20 Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence [Page 11-12]

Generalisability 21 Discuss the generalisability (external validity) of the study results [Page 12]

Other information

Funding 22 Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based [Page 15]

*Give information separately for exposed and unexposed groups.