

BMJ Open 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

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ABSTRACT

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

Design Secondary analysis of a randomised controlled trial.

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

Participants The Sino-Implant Study randomised 414 women to receive a levonorgestrel implant at either baseline or 3 months post-enrolment to evaluate unprotected sex after implant initiation. This analysis used 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, California, USA). Log-binomial regression models fit with generalised estimating equations were used to estimate associations of clinically diagnosed STIs with laboratory-confirmed diagnoses and demographic and behavioural 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% CI 1.07 to 2.54). As age increased, clinically missed infections significantly decreased (PR: 0.98 per year increase, 95% CI 0.97 to 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

Strengths and limitations of this study

- This analysis provides updated data on the poor sensitivity of using only clinical signs and symptoms to guide diagnosis of sexually transmitted infection (STI) among women in Jamaica.
- A strength of the study is that this is a secondary analysis from a randomised 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 gonorrhoea, chlamydia or trichomonas by laboratory assays.

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 number NCT01684358.

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 randomised 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 was a randomised controlled clinical trial that assigned 414 women to receive a levonorgestrel implant at either baseline or 3 months post-enrolment, with follow-up at 1 month and 3 months post-enrolment, 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 enrolment. 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 χ^2 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, California, USA), 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, California, USA) and further quality assurance testing was confirmed at the CDC using the quantitative total PSA assay (Abbott Diagnostics, Abbott Park, Illinois, USA).^{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 3 months). 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 aetiological 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 IQRs and those of categorical variables using frequencies and percentages. Comparisons of baseline characteristics by clinical STI status were made using χ^2 tests for categorical variables and Wilcoxon ranked sum test for continuous variables.

Log-binomial regression models fit with generalised 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 behaviour 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 10% 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 postrandomisation study visits. All analyses were conducted using SAS V.9.3 (SAS, Cary, North Carolina, USA).

RESULTS

The baseline characteristics, sexual behaviours, 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

Table 1 Characteristics of Sino-Implant Study participants tested for STIs at one or more study visits (n=254) by syndromic cervicitis/vaginitis status at any time point

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

*Missing baseline STI lab results, n=246 for Overall, n=62 for STI+ and n=184 for STI-.

†Missing values from eight participants.

PSA, prostate-specific antigen; STI, sexually transmitted infection.

participants who had clinically diagnosed cervicitis or vaginitis (p=0.03) at any point during the study period compared with 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 categorised 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

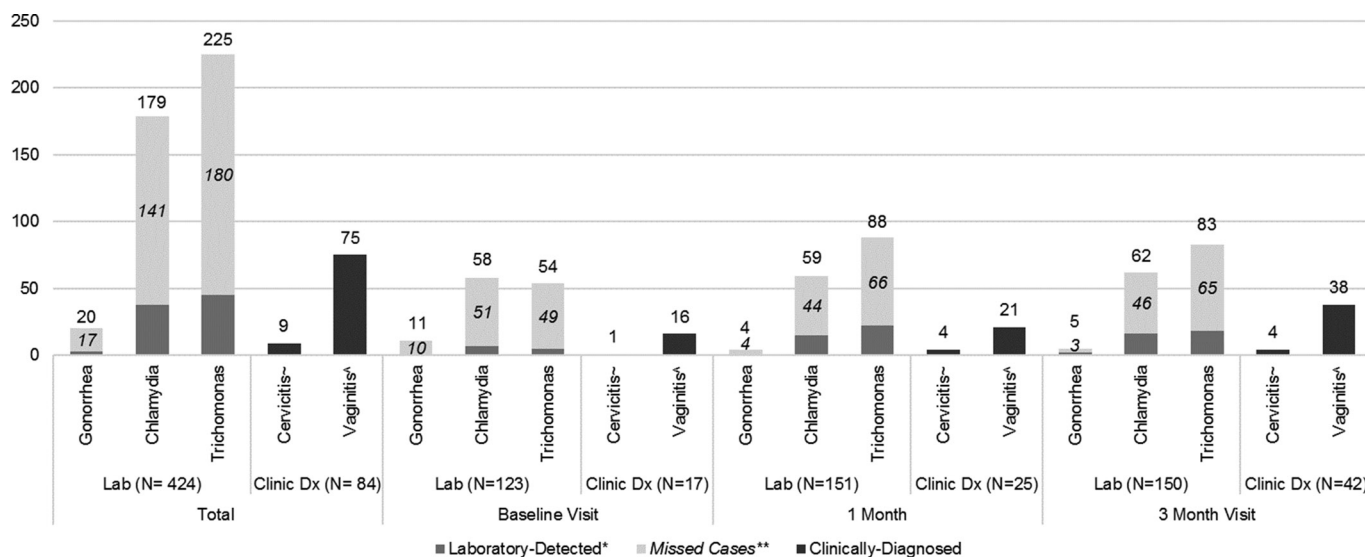


Figure 1 Total and missed laboratory detected cases and clinical diagnoses, by overall total and by study visit. *Laboratory-detected cases include unmatched cases, defined as cases where the expected clinical STI code was identified in accordance with the lab results of GC, CT and/or Tvag or when the 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 STI. ~Cervicitis includes diagnoses of CT, GC and unspecified cervicitis. ^ Vaginitis includes diagnoses of bacterial vaginosis, Tvag and unspecified vaginitis. CT, chlamydia; GC, gonorrhoea; HPV, human papilloma virus; HSV, herpes simplex virus; STI, sexually transmitted infection; Tvag, trichomonas.

Table 2 Associations between participant characteristics and clinically diagnosed or missed STIs*

	aPR	95% CI
Clinically diagnosed vaginitis and/or cervicitis		
Any positive lab result†	1.07	0.61 to 1.90
Positive PSA test	1.42	0.91 to 2.20
Unprotected sex in 2 days‡	0.96	0.52 to 1.77
Age (increase 1 year)	0.98	0.94 to 1.01
Parity (increase of 1)	0.98	0.83 to 1.17
Single vs cohabiting, married, divorced	0.99	0.59 to 1.67
Did not complete high school	1.19	0.73 to 1.93
Four or more alcoholic drinks‡	1.60	0.68 to 3.80
Ever received money or gifts in exchange for sex	1.09	0.37 to 3.21
Hormonal contraception in past month	1.65	1.07 to 2.54
More than one partner in past month‡	1.18	0.50 to 2.77
Missed cases of laboratory-confirmed gonorrhoea, chlamydia, trichomonas‡		
Positive PSA test	0.94	0.75 to 1.18
Unprotected sex in 2 days	1.14	0.90 to 1.46
Age (increase 1 year)	0.98	0.97 to 1.00
Parity (increase of 1)†	1.03	0.96 to 1.09
Single vs cohabiting, married, divorced‡	0.97	0.82 to 1.15
Did not complete high school	1.17	0.94 to 1.45
Four or more alcoholic drinks	0.91	0.54 to 1.55
Ever received money or gifts in exchange for sex‡	0.88	0.61 to 1.23
Hormonal contraception in past month	1.18	0.95 to 1.46
More than one partner in past month	1.22	0.87 to 1.70

*Analysed with generalised 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.

aPR, adjusted prevalence ratio; PSA, prostate-specific antigen; STI, sexually transmitted infection.

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 behaviours 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% CI 1.07 to 2.54) (Table 2). Increasing age was significantly associated with reduced prevalence of missed infections (aPR: 0.98 per year increase, CI: 0.97 to 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 postrandomisation 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% to 84.7% and 37.9% to 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 3 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 use 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 BV, yeast infections, HPV/HSV or other STI considering the lack of laboratory testing for these aetiologies. Tvag can occasionally be a cause of non-specific cervicitis and not just vaginitis. The generalisability 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 healthcare providers on the optimal use of STI diagnostic algorithms remains important in this regard as well.

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Contributors 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 and 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.

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Competing interests None declared.

Patient consent Obtained.

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).

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