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Diagnosis and treatment of sexually transmitted infections in male partners of pregnant women in Brazil

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Abstract

Sexually transmitted infections (STIs) can adversely affect a woman's pregnancy and the health of the developing fetus. The source of these infections may be the male sexual partner who remains under-diagnosed and un-treated due to a combination of lack of symptoms, decreased access to health care, and poor health-seeking behaviors. From September 2018 to November 2019, we offered a cohort of pregnant women (gestational age range: 4.6–41 weeks) clinic-based STI testing for HIV and syphilis (via lateral flow assay rapid tests) and for *Neisseria (N.) gonorrhoeae*, *Chlamydia (C.) trachomatis*, and *Trichomonas (T.) vaginalis* (via PCR-based testing) at Santa Casa Hospital and 10 affiliated prenatal clinics in Porto Alegre, Brazil. 400 women between the ages of 18 and 46 years (mean age: 27 years) enrolled and 24% were diagnosed with an STI. Each woman enrolled agreed to invite their male partners to clinic for the same panel of STI testing, and 255 men (64%) between the ages of 18 and 64 years (mean age: 29 years) attended clinic and all accepted full intervention. In these male partners, 40 (16%) were diagnosed with an STI including 22 (8.7%) testing positive for *C. trachomatis*, 15 (6%) for treponemal antibody (syphilis), 7 (2.8%) for *T. vaginalis*, 3 (1.2%) for *N. gonorrhoeae*, and 1 (0.4%) for HIV antibody. In our multivariate analysis, having symptoms of an STI (AOR 4.5, 95% CI 1.3–15.2) and arguing about jealousy (AOR 3.1, 95% CI 1.2–8.2) remained significantly associated with male diagnosis of an STI. Sexually transmitted infections are common in sexual partners of pregnant women in Brazil and should be addressed to prevent reinfection of pregnant women.

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Declaration of conflicting interests

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Keywords

Partner testing; congenital syphilis; pregnancy; partner notification; STIs

Introduction

Behavioral factors including condom-less sex and sexual relationships outside of partnership can increase the likelihood of acquiring sexually transmitted infections (STIs) during pregnancy for both women and men.^{1,2} Although many of these infections are asymptomatic for pregnant women, maternal infection with *Chlamydia* (*C.*) *trachomatis*, *Neisseria* (*N.*) *gonorrhoeae*, and *Trichomonas* (*T.*) *vaginalis* have all been associated with premature rupture of membranes, preterm birth, and low birth weight.^{3–6} Maternal infection with *N. gonorrhea* and *C. trachomatis* at the time of vaginal delivery can result in directly infecting the infant's eyes and respiratory tract, causing neonatal conjunctivitis and pneumonia.⁷ Maternal infection with syphilis while pregnant can result in adverse pregnancy outcomes including miscarriages and stillbirth, low birth weight, and preterm birth. Congenital syphilis can also affect all organ systems including the skeletal system, the lungs, and the brain, resulting in high morbidity and mortality.^{8,9}

Porto Alegre, Brazil has the highest incidence rates of HIV infection in pregnant women in Brazil as well as one of the highest rates of HIV infection overall.^{10–12} In addition to HIV infection, Porto Alegre suffers from rising rates of syphilis with 10.5% of pregnant women having a positive treponemal antibody rapid test result during prenatal care.¹³ As a result, the incidence of congenital syphilis was 32/1000 live births in 2017, quadruple the incidence rates seen elsewhere in the country.¹⁴ Women are not regularly tested for *C. trachomatis*, *N. gonorrhea*, and *T. vaginalis* routinely and treatment is syndromic per World Health Organization guidelines,¹⁵ but in a published study of pregnant women in a relationship with a male partner at Santa Casa Hospital and ten associated primary health clinics, 9% of pregnant women tested positive for *C. trachomatis*, 5% for *T. vaginalis*, and 1% for *N. gonorrhoea*.¹⁶ As male partners are the source of these infections and treatment failures,¹⁰ many centers are seeking to proactively engage men in prenatal care, but uptake has been variable.

Multiple barriers to male partner involvement in prenatal care have been identified, including poor communication within couples,^{17–19} unstable relationships,^{17,18,20} harmful gender norms,^{21,22} lack of male-friendly services,^{18,19,22} scheduling conflicts due to work,^{19,21} and long wait times.¹⁸ As a result, many men remained untested, undiagnosed, and unlinked to appropriate care and treatment. Although expedited partner therapy (EPT) can be used for treatment of sexual partners who refuse testing with some STIs (eg, oral treatment for *C. trachomatis*), it is poorly suited for others (eg, parenteral treatment for syphilis) and may result in overtreatment as partner concordance of STIs can be variable. Our group hypothesized that a clinic-based intervention offering STI testing and treatment as well as immunizations to all male partners of pregnant women could be acceptable to a majority of men and could improve the health of the entire family unit including the father, mother, and infant.

Methods

Design

From September 2018 until November 2019, in a prospective cohort study, we offered enrollment for STI etiological screening to a convenience sample of 400 women and their partners seeking prenatal care at Santa Casa Hospital and 10 affiliated primary clinics in Porto Alegre, Brazil. Enrollment was initiated in a hospital-based clinic and then extended to primary health clinics in the surrounding communities after the pilot phase of 50 participants based on feedback from male partner patients and our qualitative work.²³ Details of our intervention recruiting and testing pregnant women are described in a previous publication.¹⁶ In order to participate, women had to be 18 years of age or older, have a stable male partner who was 18 years of age and older for at least 3 months, and be able to give informed consent. Women were excluded if they did not meet inclusion criteria or endorsed a history of intimate partner violence. As part of this protocol, each woman then received couple-oriented counseling to invite their male partners to either the current prenatal care visit (if male partner was in waiting room) or to present male partner with a written invitation/work excuse to attend clinic independently or at future prenatal clinic visits. The couple-oriented counseling guide used to interview women enrolled in this study was adapted from Prenahtest ANRS 12127 Protocol, which has been validated to encourage male partner participation in HIV testing during prenatal care.^{24,25} This strategy uses counseling, education, and role-play to identify the partner, describe the relationship, predict barriers, and role-play possible solutions to empower women to discuss sexual issues with their male partners. We modified the existing guidance using motivators and barriers to prenatal care attendance identified in previous qualitative and quantitative work with male partners living in Porto Alegre for the purposes of this study.^{23,26} For example, optimizing infant health was a large motivator for men to participate and this was emphasized in our counseling. Enrollment to partners was available until the time of women's delivery as maternal infection and/or reinfection up until the time of delivery could cause complications for infant's perinatal health.^{27,28}

Male partners

Male partners were invited to attend clinic for testing either at initial women intake or afterward on their own if deemed more acceptable. Men who attended clinic receive STI testing, confirmatory testing, and evaluations as described below. Partners also answered an audio computer-assisted survey instrument interview about the general demographics, pregnancy, substance use, sexual behaviors, and acceptability of intervention. Alcohol use and abuse was assessed using the AUDIT-C 3 item alcohol screen.²⁹ All men enrolled in the primary health clinics were offered immunizations for influenza (during influenza season), tetanus, measles, hepatitis B, and yellow fever, which were administered in the primary health clinics during visit as an additional strategy to improve the health of participants and to decrease exposure of the newborn to these infections during early infancy. Of note, immunizations were found to be highly acceptable in previous surveys of male partners.²⁶ The vaccines offered as part of this intervention are recommended for all residents in Brazil but have variable uptake due to poor health-seeking behavior and access.

Testing protocol

Once consent was obtained, enrolled women and men received testing for HIV (BIOCLIN-HIV), syphilis (Alere TP), hepatitis B (VIKIA-HBsAg), and hepatitis C (Alere HCV) via fingerprick rapid tests platform provided by the Brazilian government, as well as immunizations. As part of study protocol, two vaginal swabs were collected from each woman, one for *C. trachomatis*/*N. gonorrhoeae* and one for *T. vaginalis* PCR testing via the Gene Xpert platforms (Cepheid, Sunnyvale, CA). Male participants provided urine samples per Gene Xpert instructions. Three men had inconclusive results with *C. trachomatis*/*N. gonorrhoeae* urine specimens and repeat samples were not able to be collected despite outreach to participants, but the remainder had either positive or negative results.

Confirmation and treatment

Urine, vaginal, and endocervical swabs were placed in transport reagent and then moved to the Gene Xpert machine located in the research office. Once office visits were completed, all samples were transferred to cartridges and testing was conducted that evening. Results were recorded and patients were notified of their results either that evening or the next morning by phone. Treatment was prescribed as described below. Individuals with reactive HIV rapid tests had a second confirmatory rapid test performed. If both rapid tests were positive, the subject was classified as HIV-positive in our analysis. All individuals with any positive rapid test had viral loads performed and were immediately referred to specific clinics for HIV-positive pregnant women and men for appropriate staging, treatment and prevention of mother to child transmission services. Men diagnosed with syphilis were treated immediately with penicillin G benzathine 2.4 million units via intra-muscular injection if they had a positive treponemal rapid test and if they had no previous history of treated syphilis in their medical records. For men who had a history of syphilis, VDRL was obtained, and if there was an increase in VDRL titers concerning for relapse or indicative of a new infection, they received treatment at clinic site. Individuals infected with chlamydia received a prescription for azithromycin 1 g by mouth x 1. Individuals infected with gonorrhea were given a prescription for cefixime 400 mg by mouth x 1. Individuals infected with *Trichomonas* were given a single dose of metronidazole 2 g x 1 per CDC guidelines.²⁸ Although immediate directly observed therapy by the clinician was preferred, several clinics did not stock these medications and participants were asked to obtain them from the appropriate pharmacy with follow-up phone calls 1 week after to ascertain treatment uptake.

Statistical analysis

Two-sample T-test and Pearson chi-square statistics were used to analyze continuous and categorical outcomes, respectively, and were used to describe men's sociodemo-graphic factors (age, race, gender, parity, schooling, employment, and need for outside financial support), sexual risk factors (recent sexual activity including type of contact—oral, vaginal, receptive, and insertive anal, age of sexual debut, number of previous sexual partners, and condom use), and other behavioral factors associated with STIs including alcohol, marijuana, cocaine, amphetamines, solvents, and heroin use during partner's pregnancy. Marital status was not included as a question in our survey as common law marriage is

recognized under the Brazilian civil code, and formal marriage is uncommon, but length of relationship was recorded. Univariate and multivariate logistic regression was performed to assess predictors associated with (1) male partner involvement, (2) a positive STI result, (3) a positive treponemal antibody result, and (4) a positive chlamydia PCR result. All computations were done using SAS version 9.4 Institutional Review Board approval was obtained at both UCLA, at Santa Casa Local Ethics Committee and the Porto Alegre Health Municipal Department IRB as well as from the Brazilian National Ethics Committee. Missing data were censored unless >5% of total sample size.

Results

Four hundred women with stable male partners (>3 months) consented to participate in this study and 255 (64%) of their partners attended clinic. All men who attended clinic accepted the full interventions described above including providing blood sample and urine samples, and accepting offered vaccinations. As seen in Table 1, the average age of partners who attended was 29 years of age. Forty-nine percent self-identified as white, 25.5% as black, and 21.6% as mixed race. Although 76% of participants stated they were employed, 53% stated that they had to ask their family for money to meet expenses in the past month. Over 80% of men stated they were in their current relationship for longer than one year, and 57% stated they planned the pregnancy with their partner. Most men were sexually active during their partner's pregnancy with 87.8% having vaginal sex, 29.4% having anal sex, and 60.8% having oral sex with current pregnant partner and with 13.3% stating they had outside sexual relationships during their partner's pregnancy. Only 8.6% admitted to always using condoms. There were relatively high rates of substance use with 27% meeting criteria for alcohol abuse, and 28% admitting to illicit drug use. Sixteen percent of men stated they were likely to have an STI, and 8.6% stated they had symptoms of STI (defined as abnormal urethral discharge or ulcers) during their partner's pregnancy.

Of the 255 partners who attended prenatal care, 40 (16%) had positive results for an STI: 34 (13%) had one STI, 4 (1.5%) had two STIs, and 2 (0.8%) had three STIs. Twenty-two (8.7%) tested positive for *C. trachomatis* and 17 reported they received treatment. Fifteen (6%) had positive treponemal antibody and 13 received treatment, 7 (2.8%) tested positive for *T. vaginalis* and all reported they received treatment, 3 (1.2%) for *N. gonorrhea* and 2 reported they received treated, and 1 (0.4%) for HIV antibody and was appropriately referred. None had positive results for hepatitis B sAg or hepatitis C antibody. Figure 1 displays the concordance between infected women and their partners. STI partnership concordance was 25% for HIV, 32% for syphilis, 47% for *T. vaginalis*, 50% for *N. gonorrhoeae*, and 68% for *C. trachomatis*. Of the 94 women who tested positive for STIs, only 60 (68%) of their male partners participated and the rest were offered EPT.

Table 2 evaluated individual and partnership factors associated with a diagnosis of an STI in men. In the univariate analysis, older age (OR 0.9, 95% CI 0.9–1), being recruited in the hospital site (OR 0.3, 95% CI 0.08–1), having an older age of sexual debut (OR 0.9, 95% CI 0.9–1), and arguing about finances (OR 0.1, 95% CI 0.02–1) were protective against having an STI, whereas having symptoms of an STI (OR 4.5 95% CI 1.8–11.4) and stating they had argued with their pregnant partner about “jealousy” (OR 3.1, 95% CI 1.2–8.2) were strongly

associated with a diagnosis of an STI. Both having symptoms of an STI and “arguing about jealousy” remained significantly associated with male diagnosis of an STI in the multivariate model. In an exploratory analysis looking at factors associated with each STI, we found that younger age as a continuous variable (OR 1.2, 95% CI 1.1–1.3), arguing about jealousy (OR 5.2, 95% CI 1.7–15.8) and having symptoms of STIs (OR 3.7, 95% CI 1.2–11.2) were significant factors associated with being diagnosed with chlamydia, even in a multivariate model. None of the factors were found to be highly associated with diagnosis of other single STIs.

Finally, we evaluated pregnant women’s characteristics that were associated with male partners’ involvement in prenatal care as all men who attended clinic accepted the full intervention. In the univariate relationship, shorter length of relationship (OR 0.6, 95% CI 0.4–0.9), fighting about jealousy (OR 0.5, 95% CI 0.3–0.9), maternal alcohol use (OR 0.6, 95% CI 0.4–0.9), and women admitting to outside sexual partnerships (OR 0.3 95% CI 0.14–0.9) were associated with men not attending prenatal care. In contrast, being sexually active during the pregnancy (OR 1.9, 95% CI 1.1–3.4 for vaginal sex, OR 1.8, 95% CI 1.2–2.7 for oral sex) was associated with higher odds of male partner involvement. None of these factors reached statistical significance in the multivariate model.

Discussion

Our research collaboration has focused on encouraging male partner involvement in prenatal care in Porto Alegre, consistent with WHO and Brazilian Ministry of health guidelines.^{30,31} We have performed qualitative and quantitative investigations,^{23,26} and have found individual, partnership, and systemic factors can facilitate men’s decision to attend prenatal care and once men navigate these factors to attend prenatal care, they would be willing to receive STI testing, treatment, and immunizations. In Figure 2, we adapted a conceptual framework³² that suggests individual and partner characteristics influence partnership dynamics, which in turn influence risk behaviors such as concurrency and condom use, and which are all ultimately associated with risk of HIV and other STIs. Based on our univariate analysis, women who described more tumultuous relationship dynamics (shorter in duration, endorsing outside sexual relationships, and arguing about jealousy) were less likely to have their partner involved, versus those in more stable partnerships. Convincing men to participate in prenatal care who are perhaps less invested in the partnership can be a difficult obstacle to overcome, and creative approaches should be considered. Our counseling was focused on the health of the newborn, as fatherhood was an important role to most men in our preliminary studies, but perhaps, this can be re-emphasized. Fortunately, once men attended clinic, all received testing and a majority did receive appropriate treatment. For men who were not directly contacted for diagnosis and treatment despite multiple attempts, we provided EPT where the woman was given a prescription to deliver to their partner.

Jealousy was a significant point of discussion in many of our qualitative interviews with male partners, and in this study, jealousy is an important factor in both decreasing partner involvement and in partners being diagnosed with STIs. Given the relatively high rates of outside partnerships, jealousy may also be a marker for the fragile state of the partnership,

but in our analysis, arguing about jealousy was not indicative of having an outside sexual relationship. An exploratory analysis looking at the interactions between arguing about jealousy and having outside relationships did not reveal a significant association between these two ($p = 0.99$); however, there was an association between arguing about jealousy and having a duration of relationship less than 1 year ($p = 0.021$). Jealousy and alcohol use are both associated with intimate partner violence,³³ and in this study, jealousy is associated with STIs, especially chlamydia infection in men. Future interventions should focus on exploring jealousy in relationships during pregnant patient's evaluations and if present, performing more intensive counseling around male partner involvement and STI testing

We found higher rates of STIs in pregnant women than in men, with 24% of pregnant women having an STI and only 16% of men, although we may be underestimating rates in men as we only tested men who chose to attend prenatal care. Whereas we did not note an association between symptoms and etiological evidence of an STI in pregnant women, men's symptoms of abnormal urethral discharge or ulcers were strongly associated with having an STI, and in particular, chlamydia. So although broad screening for pregnant women should be considered, for men, a screening algorithm focused on behavioral risk factors and symptoms could be created and validated.

Concordance in partners varied by each STI and because this was a cross-sectional study, we did not evaluate direction of transmission over time. Studies of concordance of STIs in partners during pregnancy are, limited, but range from syphilis concordance rates were 3.5%,³⁴ 33% for chlamydia,³⁵ and 23% of *T. vaginalis*.³⁶ Another limitation to our study is that we did not evaluate for treatment failure with repeat testing per CDC guidelines²⁸ to see if male partner involvement was associated with decreased treatment failure. Future studies should include this important step, especially in the era of increasing resistance to available antimicrobials. However, our study did have strengths as we recruited from both hospital-based and primary care clinics spread throughout the city, which may make our results more generalizable to other prenatal care clinics in Porto Alegre.

In planning this intervention, our focus was on minimizing external barriers by performing the intervention in the neighborhood primary clinics and allowing flexible times. We also rendered written and oral invitations and excuses from work. Despite this, we only had 64% participation overall and 68% participation among partners of pregnant women with an STI, suggesting that clinic-based interventions may be limited in achieving 100% participation. Home-based interventions should be considered in optimizing male partner participation in prenatal care for those men who refuse in person attendance, and could include virtual visits between providers and male partners, and testing conducted using partner delivered testing kits/treatment. Of those who attended, all received the recommended evaluations for HIV, STIs and also received immunizations against hepatitis B, measles, yellow fever, influenza, and tetanus. Given the high rates of under-diagnosed and un-treated infections in both pregnant women and their male partners and concerns for treatment failure and/or reinfection during pregnancy, testing and treatment of male partners for STIs, if widely implemented, could significantly improve the health of families.

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Key Messages

- Of 400 pregnant women enrolled, 255 (64%) of their male partners attended prenatal care for STI testing and immunizations.
- All of the men who attended prenatal care accepted STI testing and immunizations, and 40 (16%) were diagnosed with an STI.
- STI concordance in partnerships ranged from 25% to 68%. Of women diagnosed with STI, 68% of their partners attended prenatal care.
- Clinic-based male partner involvement can be successful, but remains imperfect for capturing all men who need diagnosis and treatment.

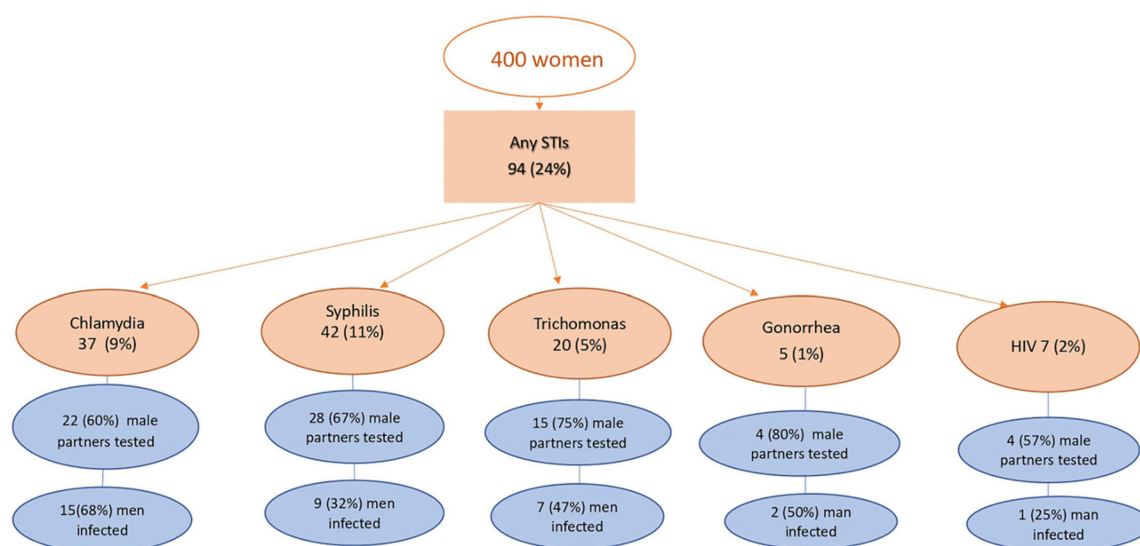


Figure 1. Flowchart of the frequency of STIs in pregnant women and their partners in Porto Alegre, Brazil. Of 94 women, 5 women had three STIs and 7 women had two STIs. Of 40 men, 2 partners had three STIs and 4 had two STIs.

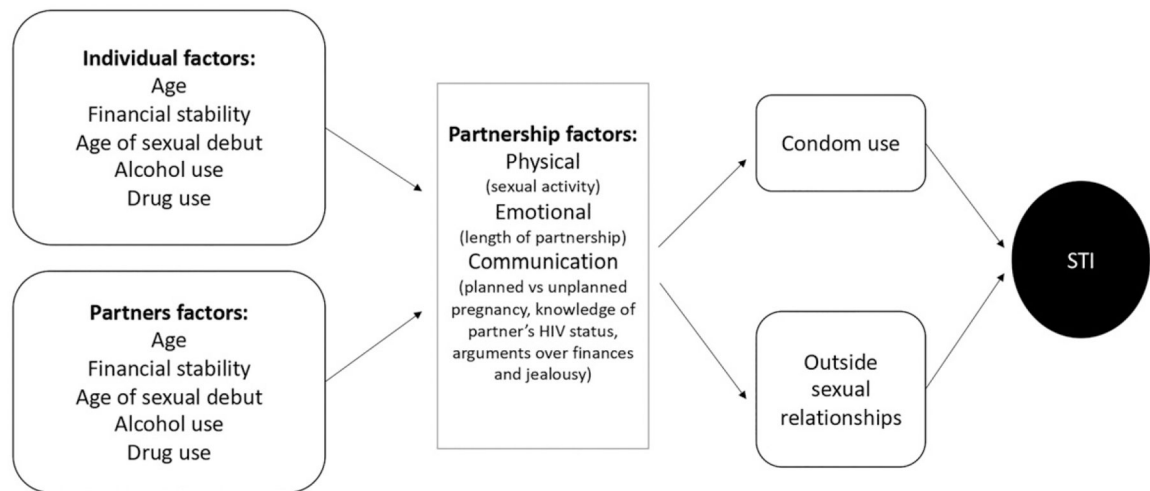


Figure 2.
Conceptual framework of individual and partnership dynamics associated with risk of STIs in male partners of pregnant women.

Table 1.
Demographic characteristics and behaviors reported by male partners attending prenatal care.

	Male partners (N = 255)
Median age in years (range)	29 (18–64)
Ethnicity	
White, <i>n</i> (%)	125 (49%)
Black, <i>n</i> (%)	65 (25.5%)
Mixed race, <i>n</i> (%)	55 (21.6%)
Length of relationship	
<1 year	49 (19.2%)
≥ 1 year	206 (81%)
School	
Elementary or less	101 (39.6%)
>Elementary	154 (60.4%)
Employed (yes)	193 (76%)
Need to ask extended family for financial support in the last month (yes)	135 (53%)
First child	60 (23.5%)
Planned pregnancy	145 (57%)
Drank alcohol during pregnancy (yes)	167 (65.5%)
Alcohol abuse per AUDIT-C (yes)	70 (27%)
Drugs in past 6 months	71 (28%)
Marijuana	59 (23%)
Cocaine	25 (9.8%)
Heroin	2 (0.8%)
Sex during pregnancy	
Vaginal	224 (87.8%)
Oral	255 (60.8%)
Anal	75 (29.4%)
Condom use (always)	22 (8.6%)
Sexual relationship outside of partnership (yes)	34 (13.3%)
Argument with partner in past week (yes)	137 (53.7%)

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Male partners (N = 255)	
Has your partner been tested for HIV (yes)	240 (60%)
Do you know your partner's HIV results (yes)	190 (74%)
Same sex relationships (yes)	3 (1%)
Self-reported likelihood of having STI (very likely/likely)	40 (15.7%)
Self-reported STI symptoms during women's pregnancy (yes)	22 (8.6%)

STI: sexually transmitted infections.

Table 2.
Factors associated with diagnosing any sexually transmitted infections (STIs) in male partners.

	Any STI	
	OR (95% CI)	AOR (95% CI)
Age (years)	0.9 (0.9–0.98)*	0.96 (0.9–1)
Ethnicity (non-white)	1.5 (0.8–3)	1 (0.4–2.7)
Education (completed elementary versus more)	1.3 (0.7–2.6)	
Employed	1.1 (0.5–2.5)	
Did not receive medical care due to cost	0.6 (0.2–1.5)	
Location of clinic (hospital versus primary clinic)	0.3 (0.08–1)*	0.6 (0.1–3.2)
Planned pregnancy	0.9 (0.5–1.8)	
Length of relationship (≤ 1 year)	2 (1–4.4)	
Argue with partner in last week	1.8 (0.9–3.6)	
Argue about jealousy	3.1 (1.2–8.2)*	3.1 (1.2–8.2)*
Argue about finances	0.1 (0.02–1)*	
Drug use in past 6 months	1.1 (0.5–2.4)	
Alcohol use	1.3 (0.6–2.7)	
Age of sexual debut	0.9 (0.8–0.1)*	0.9 (0.8–1.1)
Vaginal sex during pregnancy	0.5 (0.2–1.2)	
Anal sex	0.7 (0.3–1.3)	
Oral sex	0.9 (0.4–1.9)	
Self-reported condom use during pregnancy (always)	2 (0.8–5.7)	
Relationships outside partnership (yes)	0.9 (0.3–2.5)	
Self-assessed likelihood of having STI? (likely or very likely)	1.6 (0.5–5.1)	
Have any symptoms of STI?	4.5 (1.8–11.4)*	4.5 (1.3–15.2)*

STI: sexually transmitted infections.

* denotes $p < 0.05$.