ARTICLE SUMMARY LINE

This first report of *Mycoplasma genitalium* in Papua New Guinea finds a high burden (12.5%) among 699 pregnant women. Additionally, more than one in two women were positive for a treatable reproductive tract infection associated with poor health outcomes.

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Mycoplasma genitalium in PNG

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High burden of *Mycoplasma genitalium* and other reproductive tract infections among pregnant women in Papua New Guinea

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ABSTRACT

There is a pressing need for detailed knowledge of the range of pathogens, extent of co-infection and clinical impact of reproductive tract infections (RTIs) among pregnant women. Here, we report on RTIs (*Mycoplasma genitalium, Chlamydia trachomatis, Neisseria gonorrhoeae, Trichomonas vaginalis, Treponema pallidum subspecies pallidum*, bacterial vaginosis and vulvovaginal candidiasis) and other sexual and reproductive health indicators among 699 pregnant women in Papua New Guinea (PNG). We found widespread *M. genitalium* infection (12.5% of women), the first time this pathogen has been reported in PNG, with no evidence of macrolide resistance. Most pregnant women (76.2%) had at least one RTI, most of which are treatable. Excluding syphilis, sexually-transmitted infections were detected in 37.8% women. Syndromic management of infections is greatly inadequate and there was remarkably little use of contraception; 98.4% report never having used barrier contraception. This work has implications for improving maternal and child health in PNG.

BACKGROUND

Reproductive Tract Infections (RTIs), including Sexually Transmitted Infections (STIs), are a preventable health burden. Of over 30 well recognised STIs, four are referred to as curable STIs: *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, *Trichomonas vaginalis* and *Treponema pallidum subspecies pallidum* (syphilis). An estimated 376.4 million new adult cases of these four infections occur annually and the World Health Organization (WHO) Western Pacific Region has the highest number of annual incident cases, estimated at 142 million(1-3). Other RTIs, such as bacterial vaginosis (BV) and *Candida* spp. causing vulvovaginal candidiasis (VVC) are common, but global estimates less available and challenged by differing diagnostic methodologies for BV(4) and that *Candida* spp can be pathogenic and commensal. Notwithstanding this, BV estimates range from 8% to 51% in pregnant women(5) and *Candida* spp. can be isolated from vaginal samples in 20-30% of asymptomatic women and 40% of symptomatic women (6). Women with RTIs can experience substantial pain and discomfort and may be subject to debilitating stigma(7). Complications can include pelvic inflammatory disease (PID), infertility, increased risk of acquisition and transmission of other STIs; and in pregnancy can result in miscarriage, stillbirth, preterm birth (PTB), neonatal death, and serious neonatal morbidities such as blindness, congenital malformations and lifelong disability(1, 8, 9).

The curable STI *Mycoplasma genitalium* has recently emerged as an important cause of poor sexual health, associated with PID, cervicitis, miscarriage and PTB(10, 11). Data on prevalence is more limited than for other curable STIs, available reports range from below 1% in the general adult population to 15.9% in high risk groups(12, 13), and in pregnancy from 0.7% in the United Kingdom(14) to 11.9% in the Solomon Islands(15). Importantly, there has been a marked decline in azithromycin cure over the past decade, with some areas reporting macrolide resistance as high as 68%(16-18). However, in many regions, the importance of *M. genitalium* is largely unrecognised due to a lack of data on prevalence and drug sensitivity.

Papua New Guinea (PNG) is a Pacific nation with more than 8.5 million people(19) and high rates of *C. trachomatis*, *N. gonorrhoeae* and *T. vaginalis* that exceed those seen in other high burden regions such as sub-Saharan Africa (1, 20). However, there are no reports on the prevalence of *M. genitalium*. In this study we evaluated the prevalence of *M. genitalium* and molecular markers of resistance, as well as rates of other RTIs and curable STIs, among pregnant women attending antenatal clinics in East New Britain Province (ENBP) of PNG. We investigated the relationships between different RTIs, factors associated with infection, and compared the performance of syndromic management to more accurate molecular and rapid test diagnostics.

METHODS

Study site and population

This study uses cross-sectional baseline data from 699 pregnant women attending their first antenatal clinic (ANC1) who were enrolled into a prospective cohort study "Healthy Mothers Healthy Babies" (HMHB) undertaken across five health facilities in ENBP, PNG. Enrolment occurred between March 2015 and June 2017. Women aged 16 years or older, living in the facilities' catchment area and attending clinic for the first time in the current pregnancy regardless of gestation, were eligible to participate. At each site women were randomly selected and invited to participate. After eligibility screening and informed consent, a questionnaire was administered by a trained research officer. We collected socio-demographic and clinical information, after which biological samples were obtained, including self-collected vaginal swabs, urine, capillary finger prick and venous blood samples. All abnormal results available at the point-of-care (urine dipstick, syphilis, malaria, haemoglobin) were communicated directly to the participant, the health care provider and documented in the individual client-held health record book, at the time of interview, to enable treatment by the health care provider.

Study procedures

Routine antenatal care was provided by the health facility staff in line with PNG national guidelines (Supplemental methods)(21, 22). As per national STI syndromic management guidelines, women reporting current abnormal vaginal discharge receive: intravaginal nystatin pessaries (100,000 units, twice daily for 7 days) or a clotrimazole pessary once followed by intravaginal clotrimazole cream for 7 days; amoxycillin 2g orally (PO); probenecid 1g PO; augmentin 2 tablets PO, and azithromycin 1g PO.

Two self-collected vaginal swabs were provided by each participant; one was used to prepare a vaginal smear for microscopy, and each swab was then placed into a DNA preserving transport

medium tube, stored in a chilled cooler and returned to the laboratory at the end of each day. Urine samples were collected in a sterile container, placed on ice and later stored at -20 degrees Celsius. Swabs were tested in ENB for *C. trachomatis, N. gonorrhoea* and *T. vaginalis;* other samples were shipped to Burnet Institute Melbourne, Australia in batches. In cases where testing was delayed, specimens were stored at 2-7°C or at -20°C if an extended delay was anticipated. Molecular testing usually occurred within seven days with results communicated back to participants and treatment advised for themselves and their partner.

Laboratory methods

The GeneXpert molecular platform (Cepheid, Sunnyvale CA, USA) was used to test vaginal and urine specimens at the Burnet / PNG Institute of Medical Research (PNG IMR) laboratory, Vunapope Hospital Kokopo for *C. trachomatis, N. gonorrhoea and T. vaginalis*. Lifetime exposure to *T. pallidum* (syphilis) was determined to be positive if women tested positive by Alere Determine™ Syphilis TP (Abbott, Illinois, USA). This was initially performed at health facilities in line with national guidelines; however, inconsistency in test availability at different sites meant the research team supplied rapid tests for study women.

Shipped vaginal specimens were stored at the Burnet Institute Melbourne at -20 or -80°C until all samples had been received. After thawing, genomic DNA was extracted using the QIAamp® BiOstic® Bacteremia DNA kit (QIAGEN N.V, Venlo, The Netherlands). To optimise this protocol for vaginal specimens rather than cultured blood, the total volume of sample required was adjusted to 450µl. Extracted DNA was tested for *M. genitalium* using the *ResistancePlus*® MG kit (SpeeDx, Sydney, Australia) which uses the PlexPCR® and PlexPrime® technologies (SpeeDx) for concurrent amplification of *M. genitalium* and detection of five *M. genitalium* point mutations (A2058G, A2058C, A2058T, A2059G, and A2059C) within the macrolide resistance-determining region (MRDR) of the 23S rRNA gene(17). The *ResistancePlus*® MG kit is commercially available, approved by Therapeutic Goods Administration Australia, and has a sensitivity and specificity of

98% and 100% for *M. genitalium* and 96% and 100% for macrolide resistance mutations(23-25). Gram-stained vaginal smears were read by an experienced microscopist at Melbourne Sexual Health Centre. BV diagnosis was based on Nugent scoring (BV, Nugent score 7 to 10) and presumptive diagnosis of candidiasis was based on observation of pseudohyphae and or budding yeasts. Because the diagnosis of *M. genitalium*, BV and VVC was on stored samples many months after collection it was not possible to specifically treat those women who tested positive beyond any syndromic management they would have received as part of national guidelines.

Data management and statistical analysis

Questionnaire responses were entered by research officers directly into an electronic tablet (e-tablet) using a study specific questionnaire on the platform Mobile Data Studio 7.3 (MDS, CreativityCorp Pty Ltd, Perth, Australia), and stringent data management protocols were in place (supplemental methods).

Exposures of interest included clinic details (enrolment clinic; rural or urban); participant characteristics at enrolment and relevant obstetric history (see supplemental methods for a full list of variables and definitions). Outcomes measured were *M. genitalium, C. trachomatis, N.gonorrhoea, T. vaginalis, T. pallidum* (syphilis), BV and VVC. The association between exposures and *C. trachomatis, N. gonorrhoea, T. vaginalis, M. genitalium* and syphilis were assessed using logistic regression. All variables of interest were included in univariable analyses and variables associated with the outcome at $p<0.10$ in univariable analyses were included in a multivariable model along with the pre-specified variable of enrolment clinic site.

Ethical considerations and informed consent procedures

All participants provided individual written, informed consent. Ethical approval was provided from the Medical Research Advisory Committee of the PNG National Department of Health (No. 14.27), the PNG IMR Institutional Review Board (No. 1114) and the Human Research Ethics

166 Committee of the Alfred Hospital (No. 348/14) in Australia. Provincial approval was obtained from
167 the East New Britain Province (ENBP) Executive Committee, participating facilities and a series of
168 community engagement meetings provided broader community support and assent for the study.
169

RESULTS

A total of 699 pregnant women were enrolled at five antenatal clinics in East New Britain Province (ENBP). Median maternal age was 26 years (interquartile range, IQR 22-30), a quarter of women were primigravida (177/699, 25.4%), the majority were married / co-habiting (663/697, 95.1%) and 46.5% had only completed primary school (325/698) (Table 1).

Current abnormal vaginal discharge was reported by 14.0% (98/697), an additional 37 women reported abnormal vaginal discharge at some point in this pregnancy prior to clinic attendance (total symptomatic discharge in pregnancy 19.3%, 135/698). Most women (82.5%, 569/690) had never used a modern method of contraception, with only 11 women (1.6%, 11/690) reporting having ever used either a male or female condom.

High burden of reproductive tract infections in pregnancy

Of the 699 women enrolled, prevalence of *M. genitalium* was 12.5% (78/625; 95% CI 10.0-15.4), with no evidence of macrolide resistant mutations (Table 2). Other RTIs were: *C. trachomatis* 19.1% (122/640; 95% CI 16.1-22.4), *N. gonorrhoeae* 5.5% (35/640; 95% CI 3.9-7.6), *T. vaginalis* 20.2% (117/581; 95% CI 17.0-23.7) and prevalence of lifetime exposure to syphilis was extremely high at 18.1% (79/437; 95% CI 14.6-22.1). Of the 503 vaginal smears available for microscopy, BV prevalence was 25.7% (129/503; 95% CI 21.9-29.7) and 39.4% (198/503; 95% CI 35.1-43.8) had presumptive candidiasis detected on microscopy (VVC).

The majority of women (76.2%, 272/357), had at least one current RTI (BV, VVC, *M. genitalium, C. trachomatis, N. gonorrhoea* or *T. vaginalis)*, with at least one current STI present in 37.8% (183/485, *M. genitalium, C. trachomatis, N. gonorrhoea* or *T. vaginalis*). One in three women (32.1%, 175/546) had a current STI diagnosed using GeneXpert (*C. trachomatis, N. gonorrhoea* or *T. vaginalis)*, 11.4% (75/661) had at least two co-existing STIs, 15 women (2.8%, 15/536) had at least three infections and one woman had all four STIs.

Relationships between infections

Of the 78 women with *M. genitalium*, 28 women (35.9%) had a concurrent STI detected: 20 (25.6%) had co-infection with *C. trachomatis*, 13 (16.7%) had co-infection with *T. vaginalis* and 6 (7.7%) had *N. gonorrhoeae* (Figure 1 and Table S2). Co-infections were most frequent in women positive for *N. gonorrhoea* (80%, 28/35), with the majority of these women having a co-infection with *C. trachomatis* (71.4%, 25/35) followed by *T. vaginalis* (22.8%, 8/35) and *M. genitalium* (17.1%, 6/35). Syphilis was not included in estimates of co-infections as it was not known if their exposure represented current or previous infection.

Of 129 women with bacterial vaginosis, 37.2% (48/129) had a co-infection, the most common of which was *C. trachomatis* 22.5% (29/129), followed by *T. vaginalis* (12.4%, 16/129), *M. genitalium* (11.6%, 15/129) and *N. gonorrhoea* (7.7%, 10/129) (Table S3).

Relationship between abnormal vaginal discharge and infection

We compared clinical symptoms used in PNG national treatment guidelines (current abnormal vaginal discharge) with an alternative question of abnormal vaginal discharge currently or at any time in pregnancy up to their first antenatal clinic visit (ANC1) (Table 3). A total of 98 women (14.1%, 98/697) had current symptoms that would have prompted treatment as per PNG national guidelines. An additional 37 women experienced abnormal vaginal discharge earlier in the pregnancy, but no current symptoms, and therefore would not normally receive treatment.

Most current STIs were asymptomatic. Neither the standard question used in national guidelines nor the alternative question performed well as a marker of infection. Of those women with an STI detected, no current symptoms were reported by 84.1% (154/183), and even with the more inclusive alternative question, 77.0% (141/183) reported no history of symptoms either currently or at any time earlier in the pregnancy. Of the women with *M. genitalium*, 78.2% (61/78) had no

symptoms either currently or at any time in the pregnancy up to ANC1, and only 12 women (15.4%, 12/78) would have been treated using current syndromic management.

Asking if women had any symptoms in pregnancy up to and including the current time (the alternative question) was consistently more sensitive for any individual infection or group of infections compared the standard question (Figure 2); despite this, sensitivity remained below 30%. The alternative question did perform better to distinguish those women with *T. vaginalis* infection (p=0.005) (Table S4), and VVC (p=0.007) compared to the current question.

Factors associated with curable STI infection

There was no factor in either univariable (Table S5) or multivariable (Table 4) analysis found to be associated with an increased odds of *M. genitalium* infection. Given first pregnancy and younger women had a collinear relationship, only pregnancy number was included in the multivariable analysis. Those in their first pregnancy, employment, those who were single or separated and those with abnormal vaginal discharge at any time in the pregnancy up to and including ANC1 were all identified as risk factors for different STIs to varying degrees of statistical significance. Not having used a modern method of contraception appeared to be an important risk factor for a number of STIs in univariable analyses; however this association weakened in multivariable analysis. Risk of exposure to syphilis appeared to vary depending on clinic site.

DISCUSSION

We report the first data on *M. genitalium* in PNG, finding that pregnant women in PNG have one of the highest infections rates globally, with a striking absence of macrolide resistance despite resistance rates of up to 68%(18) in neighbouring regions such as Australia. The high prevalence of *M. genitalium* (12.5%) among pregnant women shown here equates to an estimated 13,000 prevalent cases (95% CI 10,342 to 15,823) of *M. genitalium* among women of reproductive age (15 to 49 years) in the province (Supplemental methods). Additionally, these are the first data on RTIs to be reported from the New Guinea Islands region of PNG in over twenty years and provides a more complete understanding of the burden of RTIs in pregnancy(26). This study indicates that more than one in two women (55.2%) have a treatable RTI (BV and or current STI) that causes harmful sexual and reproductive health outcomes and is not detected by current antenatal screening in PNG. Given that PNG has one of the largest populations among Pacific islands, these findings have major public health and regional significance.

There is currently no global *M. genitalium* surveillance, limiting our understanding of its epidemiology. High-income countries report rates of *M. genitalium* infection ranging from 0.3 to 3.3%(11, 13, 27) in the general population, with higher estimates in certain risk groups(28, 29). Fewer data are available from low- and middle- income countries (LMICs) but it appears prevalence may be higher ranging from 3% in the general population in Tanzania(13) to 8-9% in Honduras and South Africa(13, 30). The highest burden has been reported amongst those who sell sex, 16% in Kenya(31) and 26% in Uganda(32). Data specific to pregnancy remains limited despite the association with adverse pregnancy outcomes(28); in the United Kingdom and France prevalence among pregnant women is low (0.7-0.8%(14, 33)) with higher rates reported from Guinea-Bissau (6.2%)(34) and the Solomon Islands (11.9%)(15). Clearly more data on the burden of *M. genitalium* in pregnancy, and its consequences, are needed.

Recent data from the Solomon Islands examined the impact of mass drug administration (MDA) of 1g of azithromycin orally for the elimination of ocular *C. trachomatis* on *M. genitalium* and reported a pre-MDA *M. genitalium* prevalence of 11.9% (95% CI 8.3 – 16.6%; n=236) among women attending antenatal clinics. Post MDA *M. genitalium* prevalence remained high at 10.9% with no evidence of macrolide resistance in either pre- or post-MDA groups; however this is not surprising given only 5 of the 28 women positive for *M. genitalium* in the post-MDA group reported receiving azithromycin(15). The lack of macrolide resistance in *M. genitalium* infections in PNG found in this study was striking and warrants further exploration in other populations in PNG. While it may reflect a lack of exposure to macrolides in this population, macrolides are available and used widely in PNG, and their use has repeatedly been associated with an increase in macrolide resistant isolates in other settings.

The burden of curable STIs observed among pregnant women reported here is substantially greater than most settings included in the 2018 global estimates of curable STIs(3). The 32.1% observed prevalence of at least one current STI diagnosable by GeneXpert is lower than the 42.7% reported in a study of antenatal clinics from Eastern Highlands, Hela and Central Provinces of PNG in 2014(20), but similar to that reported in Madang Province in 2012 (33.7%)(35). *C. trachomatis* prevalence (19.1%) is consistent with recent reports from other provinces (Vallely 2016 (22.9%), Badman 2016 (20.0%)) and neighbouring Solomon Islands (20.3%)(36). These latter three studies were the highest reported rates from any study in the global prevalence estimates(3). Similarly for *N. gonorrhoea* in pregnancy, PNG and Solomon Islands have the highest reported rates globally (5.1% to 14.2%)(35-38), although two studies from South Africa also report very high rates at 10.1% in a primary care setting(39) and 6.4% among pregnant women(40). Regarding *T. vaginalis*, recent PNG estimates among pregnant women are generally higher than the 20.2% reported in this study (21.3-37.6%.(35, 37, 38, 41)).

Risk factors for STIs identified in this study (primigravida, employed, single/separated or having abnormal vaginal discharge at some point in the pregnancy up to ANC1) could have a number of explanations. Younger women in their first pregnancy may have had less interaction with reproductive health services, and employed women may be more mobile with an associated increase risk of STI acquisition through unprotected sex. Interestingly, no risk factors were identified for *M. genitalium*. Risk factors for STIs in pregnancy reported elsewhere in PNG include more than one lifetime sexual partner, level of education of the woman or her partner, rurality, previous miscarriage or stillbirth, and socioeconomic status(20, 35).

This study also provides important data regarding BV and VVC, with 58.3% of women having at least one of these infections. VVC is readily treatable(42) and can cause extreme discomfort in addition to increasing a woman's risk of post-partum breast candidiasis with potential impact on breastfeeding. The prevalence reported here (39.4%) is higher than the only previous report from PNG in 1991 (23%)(43), comparisons with other LMICs are difficult as data is limited and not contemporary(42, 44). The prevalence of one in four women with BV reported here is higher than previous reports in PNG (17.6%)(41) but in keeping with recent global estimates of 23-29%(5). However, our results may underestimate the true burden of disease as diagnosis was limited to those with a Nugent's score of seven to ten.

Syndromic management of RTIs is a pragmatic approach in the absence of definitive diagnosis. However, as has been reported in PNG and elsewhere(30, 37), we found this approach performed poorly, missing 78.2% of *M. genitalium* infections and three quarters of any RTI. Symptoms were associated with a higher odds of *T. vaginalis* infection; however, sensitivity remained low. It is clear that syndromic management is an inadequate tool to effectively treat RTIs, even for those infections more commonly associated with vaginal discharge. Improved access to affordable, accurate point-of-care diagnostics may be transformative. There is an urgent need for

alternative approaches to more effectively detect and treat asymptomatic RTIs and reduce prevalence in a cost-effective and feasible manner in resource-limited settings.

The main limitation of this study is the facility-based recruitment of participants; results may not represent women who do not attend any antenatal clinic. Routinely collected provincial data for the study years estimated 73% to 85% of pregnant women attended clinic at least once during their pregnancy(45). A limitation of the syphilis data is that it represents lifetime exposure to *Treponema* species, and as such does not differentiate between active or latent infection, nor are we able to exclude exposure to yaws. Yaws is endemic in PNG(46), however prevalence estimates vary widely by region and precise estimates are not known for ENB. A population wide survey on an island in neighbouring New Ireland Province estimated a population prevalence of 1.8% for active yaws(47). Additionally, coverage with syphilis rapid tests was affected by supply interruptions.

This study provides the first data on *M. genitalium* prevalence and drug resistance markers in PNG, revealing a high burden of infection that is currently unrecognised, and provides valuable new data to understand the burden of this infection among pregnant women globally. STIs in pregnancy were alarmingly common, with 37.8% of pregnant women having at least one current STI. This study also highlights the high burden of bacterial vaginosis and VCC and clearly shows that current antenatal screening with syndromic management is inadequate in detecting reproductive tract infections. Such a high burden of disease with associated impacts on poor sexual and reproductive health demands urgent action towards ensuring access to affordable prevention, diagnostics and treatment for communities in PNG and similar settings. This will be crucial for achieving progress towards the sustainable development goals and improving reproductive health outcomes.

NOTES

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Authors contribution statement.

Study design: led by JGB, BSC, FJIF, CM, MJLS with input from WP, SL, EK, PMS, LJR, AV, SGB, AJU. Data collection: MJLS, PM, EP, RF. Vaginal smears read by GF. Data analysis, interpretation and manuscript led by MJLS with input from all authors. All authors read and approved the final manuscript.

Conflict of interest

The authors declare they have no competing interests.

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513 **TABLE 1:** Socio-demographic characteristics and obstetric history of women at first antenatal clinic

514 visit in East New Britain, PNG.

	Total at ANC1 n (%) N=699 unless specified
Sociodemographic details for enrolled women	
Enrolment Clinic	
Vunapope	184 (26.3)
Nonga	83 (11.9)
Keravat	125 (17.9)
Napapar	158 (22.6)
Paparatava	149 (21.3)
Clinic administration	
Government	208 (29.8)
Catholic Health	491 (70.2)
Location	
Urban	342 (48.9)
Rural	357 (51.1)
Age, years[a]	26 {22 – 30}, 16 - 49
Highest level of education completed[b]	
Primary (Grade 8 or less)	325 (46.5)
High school (grade 9,10)	177 (25.4)
Secondary / Vocational / Tertiary	196 (28.1)

Employment status	
Not employed	531 (76.0)
Employed in paid work or student	168 (24.0)
Province of birth	
East New Britain	578 (82.7)
Other Province	121 (17.3)
Religion[b]	
Catholic	345 (49.4)
Other	353 (50.5)
Marital status[c]	
Married or cohabiting	663 (95.1)
Single, seperated or widowed	34 (4.9)
Poligamy[d]	
One wife	583 (88.1)
More than one wife	79 (11.9)
Household monthly expenditure in Kina[e]	150 {50-300}
Cost of ANC in Kina[f]	4 {2-20}
Family Planning	
Method used[a]	
Never used modern FP method	569 (82.5)
Has used modern FP method	121 (17.5)
Maternal Health Parameters at 1st Antenatal Clinic	

Gravidity	
Primigravidae	177 (25.3)
Multigravidae (2-4)	384 (54.9)
Grandmulti (≥5)	138 (19.7)
Abnormal vaginal discharge	
Abnormal discharge at any time in preg[b]	135 (19.3)
Current symptoms[c]	98 (14.0)
Smoking[c]	
Never smoked	427 (61.3)
Stopped when pregnant	241 (34.6)
Current smoker	29 (4.2)
Previous pregnancy outcomes	
Age at first pregnancy[g]	21 {19-24}
History pregnancy loss (in multiparous)	n=522
History of miscarriage	46 (8.8)
History of abortion	1 (0.2)
History of stillbirth	16 (3.1)
Partner details	
Partner's employment status	
Not employed	269 (39.6)
Employed in paid work	411 (60.4)
Partner attending ANC1	

No	571 (82.3)
Yes	123 (17.7)

Data are mean [SD], range; or median {IQR}, range; or n (%)

Missing Data n(%): [a] 9 (1.3), [b] 1 (0.1), [c] 2(0.3), [d] 37 (5.3), [e] 36 (5.1), [f] 17 (2.4), [g] 7(1)

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517 **TABLE 2.** Prevalence of reproductive tract infections among pregnant women in ENB PNG

Reproductive Tract Infection	Obs	Freq	Prevalence % (95% CI)
Mycoplasma genitalium	625	78	12.5 (10.0 - 15.4)
Chlamydia trachomatis	640	122	19.1 (16.1 - 22.4)
Neisseria gonorrhoeae	640	35	5.5 (3.9 - 7.6)
Trichomonas vaginalis	581	117	20.2 (17.0 - 23.7)
Syphilis (Alere Determine)	437	79	18.1 (14.6 - 22.1)
Bacterial Vaginosis	503	129	25.7 (21.9 - 29.7)
Vulvovaginal candidiasis	503	198	39.4 (35.1 - 43.8)
At least 1 of a group of RTIs^			
At least 1 current RTI[a]	357	272	76.2 (71.5 - 80.6)
At least 1 current STI[b]	485	183	37.8 (33.5 - 42.3)
At least 1 of MG, CT, NG, TV or Syphilis	302	144	47.7 (42.0 - 53.5)
At least 1 of MG, CT, NG, TV or BV	357	197	55.2 (49.9 - 60.5)
At least 1 GeneXpert diagnosed infection[c]	546	175	32.1 (28.2 - 36.2)
At least 1 vaginal infection[d]	409	281	68.8 (64.0 - 73.2)
At least 1 of BV or VVC	503	293	58.3 (53.9 - 62.6)
Multiple current STIs			
Any 2 current STIs	661	75	11.4 (9.1 - 14.1)
Any 3 current STIs	536	15	2.8 (1.6 - 4.6)

^Participants result included only if they had all tests done for each of the infections within group of RTIs

[a] current RTI includes at least 1 of MG, CT, NG, TV, BC or VVC (syphilis not included)

[b] current STI includes at least 1 of MG, CT, NG, TV (syphilis not included)

[c] GeneXpert diagnosed infections include any 1 of CT, NG or TV

[d] vaginal infections includes at least 1 of BV, TV or VVC

RTI (reproductive tract infection), STI (Sexually transmitted infection), MG (Mycoplasma genitalium), CT (Chlamydia trachomatis), NG (Neisseria gonorrhoea), TV (Trichomonas vaginalis), BV (Bacterial Vaginosis), VVC (Vulvovaginal candidiasis)

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FIGURE 1: Relationships between current STIs: *Mycoplasma genitalium* (MG), *Chlamydia trachomatis* (CT), *Neisseria gonorrhoea* (NG) *and Trichomonas vaginalis* (TV). Each line connecting two or more infections represents one participant. Mono infections are represented by the space under each STI with no lines.

FIGURE 2: Sensitivity of syndromic management using the standard question as per PNG national guidelines "Do you currently have any abnormal vaginal discharge?", or an alternative question "Have you experienced any abnormal vaginal discharge earlier in the pregnancy or now?".

531 **TABLE 3:** Number of women with a Reproductive Tract Infection and symptoms (abnormal vaginal
532 discharge)

	Question as per syndromic management			**Alternative question**		
	Do you currently have any abnormal vaginal discharge?			Have you experienced any abnormal vaginal discharge earlier in the pregnancy or now?^		
	No n(%)	Yes n(%)	Total	No n(%)	Yes n(%)	Total
	599 (85.9)	98 (14.1)	697	563 (80.7)	135 (19.3)	698
Reproductive Tract Infection						
Mycoplasma genitalium	66 (84.6)	12 (15.4)	78	61 (78.2)	17 (21.8)	78
Chlamydia trachomatis	98 (80.3)	24 (19.7)	122	90 (73.8)	32 (26.2)	122
Neisseria gonorrhoeae	28 (80.0)	7 (20.0)	35	26 (74.3)	9 (25.7)	35
Trichomonas vaginalis	94 (80.3)	23 (19.7)	117	83 (70.9)	34 (29.1)	117
Syphilis (Alere Determine)	68 (86.1)	11 (13.9)	79	65 (82.3)	14 (17.7)	79
Bacterial Vaginosis	109 (84.5)	20 (15.5)	129	101 (78.3)	28 (21.7)	129
Vulvovaginal candidiasis	160 (80.8)	38 (19.2)	198	146 (73.7)	52 (26.3)	198
At least 1 of a group of RTIs						
At least 1 current RTI[a]	224 (82.3)	48 (17.6)	272	204 (75.0)	68 (25.0)	272
At least 1 current STI[b]	154 (84.1)	29 (15.8)	183	141 (77.0)	42 (22.9)	183
At least 1 GeneXpert diagnosed infection[c]	141 (80.6)	34 (19.4)	175	127 (72.6)	48 (27.4)	175
At least 1 vaginal infection[d]	228 (81.1)	53 (18.9)	281	207 (73.7)	74 (26.3)	281
At least 1 of BV or VVC	242 (82.6)	51 (17.4)	293	222 (75.8)	71 (24.2)	293

Multiple current STIs						
Any 2 current STIs	58 (77.3)	17 (22.7)	75	53 (70.7)	22 (29.3)	75

^1 woman who responded yes to the second question had a missing response to the first question

[a] active RTI includes at least 1 of MG, CT, NG, TV, BC or VVC (syphilis not included)

[b] active STI includes at least 1 of MG, CT, NG, TV (syphilis not included)

[c] GeneXpert diagnosed infections include any 1 of CT, NG or TV

[d] vaginal infections includes at least 1 of BV, TV or VVC

MG (Mycoplasma genitalium), CT (Chlamydia trachomatis), NG (Neisseria gonorrhoea), TV (Trichomonas vaginalis), BV (Bacterial Vaginosis), VVC (Vulvovaginal candidiasis)

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535 **TABLE 4:** Multivariable analysis of factors associated with curable Sexually Transmitted Infections.

Multivariable analysis	**Mycoplasma Genitalium**	**Chlamydia**	**Gonorrhoea**	**Trichomonas**	**Syphilis (Alere Determine)**
	aOR (95% CI) ; p value	aOR (95% CI) ; p value	aOR (95% CI) ; p value	aOR (95% CI) ; p value	aOR (95% CI) ; p value
Enrolment Clinic					
Vunapope(REF)	REF	REF	REF	REF	REF
Nonga	0.67 (0.29-1.59) ; 0.363	0.86 (0.43 - 1.73) ; 0.662	2.25 (0.73 - 6.96) ; 0.16	0.82 (0.39 - 1.74) ; 0.591	0.3 (0.12 - 0.71) ; 0.006
Keravat	0.93 (0.45-1.93) ; 0.839	0.59 (0.3 - 1.14) ; 0.112	1.04 (0.31 - 3.48) ; 0.96	0.8 (0.4 - 1.62) ; 0.532	0.62 (0.3 - 1.26) ; 0.18
Napapar	0.73 (0.36-1.49) ; 0.379	0.95 (0.54 - 1.67) ; 0.835	1.12 (0.37 - 3.4) ; 0.844	1.08 (0.61 - 1.93) ; 0.798	0.44 (0.22 - 0.89) ; 0.022
Paparatava	0.88 (0.45-1.74) ; 0.707	0.83 (0.46 - 1.51) ; 0.532	1.93 (0.67 - 5.57) ; 0.227	0.99 (0.54 - 1.78) ; 0.948	0.29 (0.14 - 0.64) ; 0.002
Gravidity					
Multigravida (REF)	REF	REF	REF	REF	REF
Primigravid	1.06 (0.6-1.85) ; 0.863	2.73 (1.74 - 4.28) ; <0.001	5.90 (2.69 - 12.96) ; <0.001	1.47 (0.91 - 2.37) ; 0.121	1.41 (0.8 - 2.52) ; 0.243
Marital status					
Married/Cohabiting (REF)	REF	REF	REF	REF	REF
Single or separated	1.10 (0.36-3.37) ; 0.875	1.42 (0.62 - 3.27) ; 0.419	0.48 (0.10 - 2.31) ; 0.356	3.87 (1.69 - 8.86) ; 0.001	0.45 (0.1 - 2.08) ; 0.301

Vaginal discharge					
No symptoms (REF)	REF	REF	REF	REF	REF
Abnormal discharge prior to ANC1 or currently	1.17 (0.64-2.13) ; 0.623	1.35 (0.83 - 2.2) ; 0.24	1.54 (0.67 - 3.56) ; 0.314	1.70 (1.04 - 2.78) ; 0.036	0.94 (0.48 - 1.82) ; 0.833
Contraception use					
Has used a modern method FP (REF)	REF	REF	REF	REF	REF
Never used modern method FP	1.89 (0.85-4.18) ; 0.12	1.1 (0.6 - 2.03) ; 0.77	0.82 (0.25 - 2.69) ; 0.74	1.35 (0.72 - 2.55) ; 0.36	1.84 (0.84 - 4.05) ; 0.13
Employment status					
Not employed(REF)	REF	REF	REF	REF	REF
Employed	0.88 (0.49-1.57) ; 0.642	1.27 (0.8 - 2.03) ; 0.318	2.45 (1.17 - 5.17) ; 0.019	0.96 (0.58 - 1.58) ; 0.843	0.74 (0.39 - 1.41) ; 0.351

Abbreviations: OR, odds ratio; CI, confidence interval; FP, family planning

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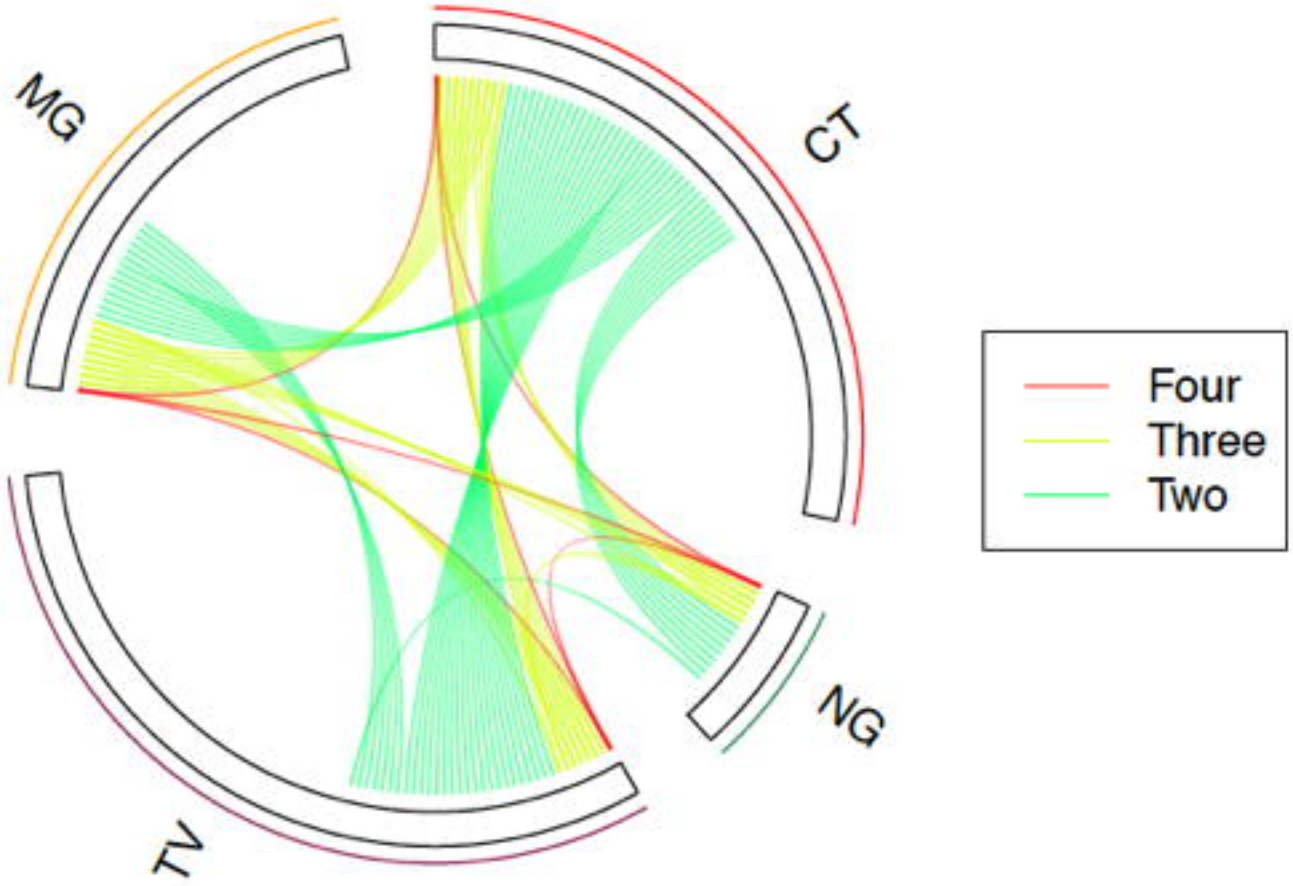
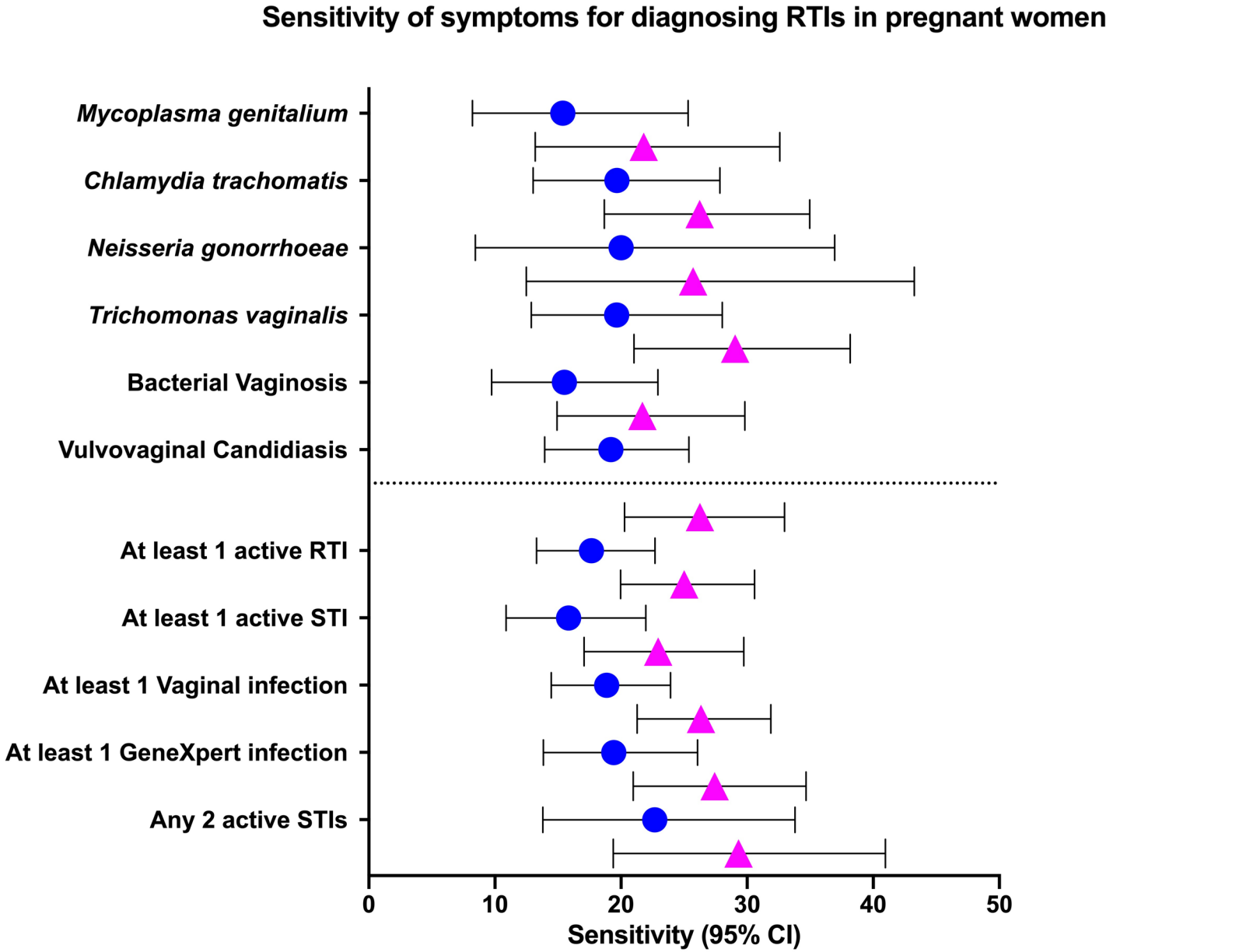

MG
CT
NG
TV
Four
Three
Two


Sensitivity of symptoms for diagnosing RTIs in pregnant women
Mycoplasma genitalium
Chlamydia trachomatis
Neisseria gonorrhoeae
Trichomonas vaginalis
Bacterial Vaginosis
Vulvovaginal Candidiasis
At least 1 active RTI
At least 1 active STI
At least 1 Vaginal infection
At least 1 GeneXpert infection
Any 2 active STIs
0
10
20
30
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50
Sensitivity (95% CI)
Standard syndromic management: Do you currently have any abnormal vaginal discharge?
Alternative question: Have you experienced any abnormal vaginal discharge earlier in the pregnancy or now?