

# **HPTN Regional Meeting**

## **Breakout Sessions**

### **Synergy in STI and HIV Research**

Moderators: Mitch Matoga & Joseph Makhema

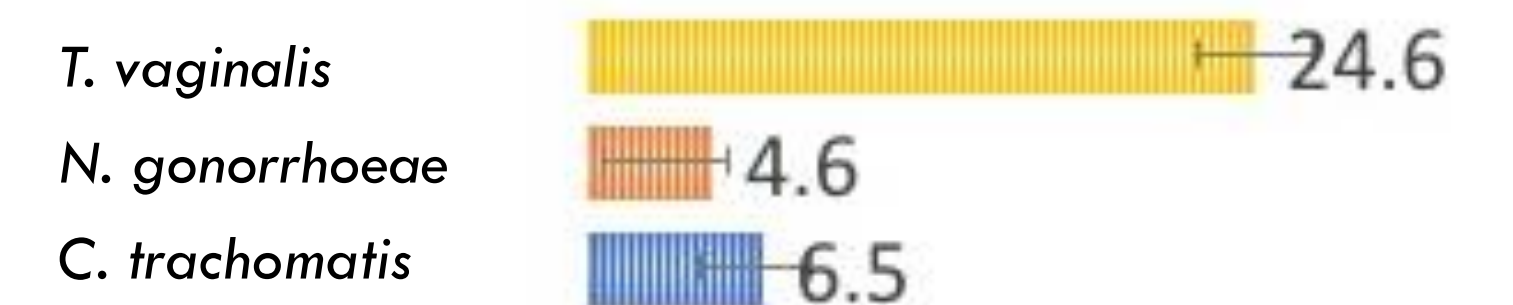
---

# Background

- *Chlamydia trachomatis* (CT), *Neisseria gonorrhoeae* (NG) and *Trichomonas Vaginalis* are common sexually transmitted infections (STIs)<sup>1</sup>
- STIs increase the risks for adverse health outcomes (particularly among women):
  - Pelvic inflammatory disease
  - Preterm birth (PTB) & low birth weight (LBW)<sup>2,3</sup>
  - Vertical transmission of CT/NG<sup>4</sup>
  - Increase risk of HIV acquisition and transmission<sup>4</sup>
- The majority of CT, NG, and TV infections are asymptomatic<sup>5</sup>
- Syndromic management, the standard of care in most African countries, misses asymptomatic infections (lacks sensitivity) and often overtreats (lacks specificity)<sup>5</sup>
- Without diagnostic testing, the true burden of STIs is unknown
  - Prior STI studies are outdated<sup>5</sup>

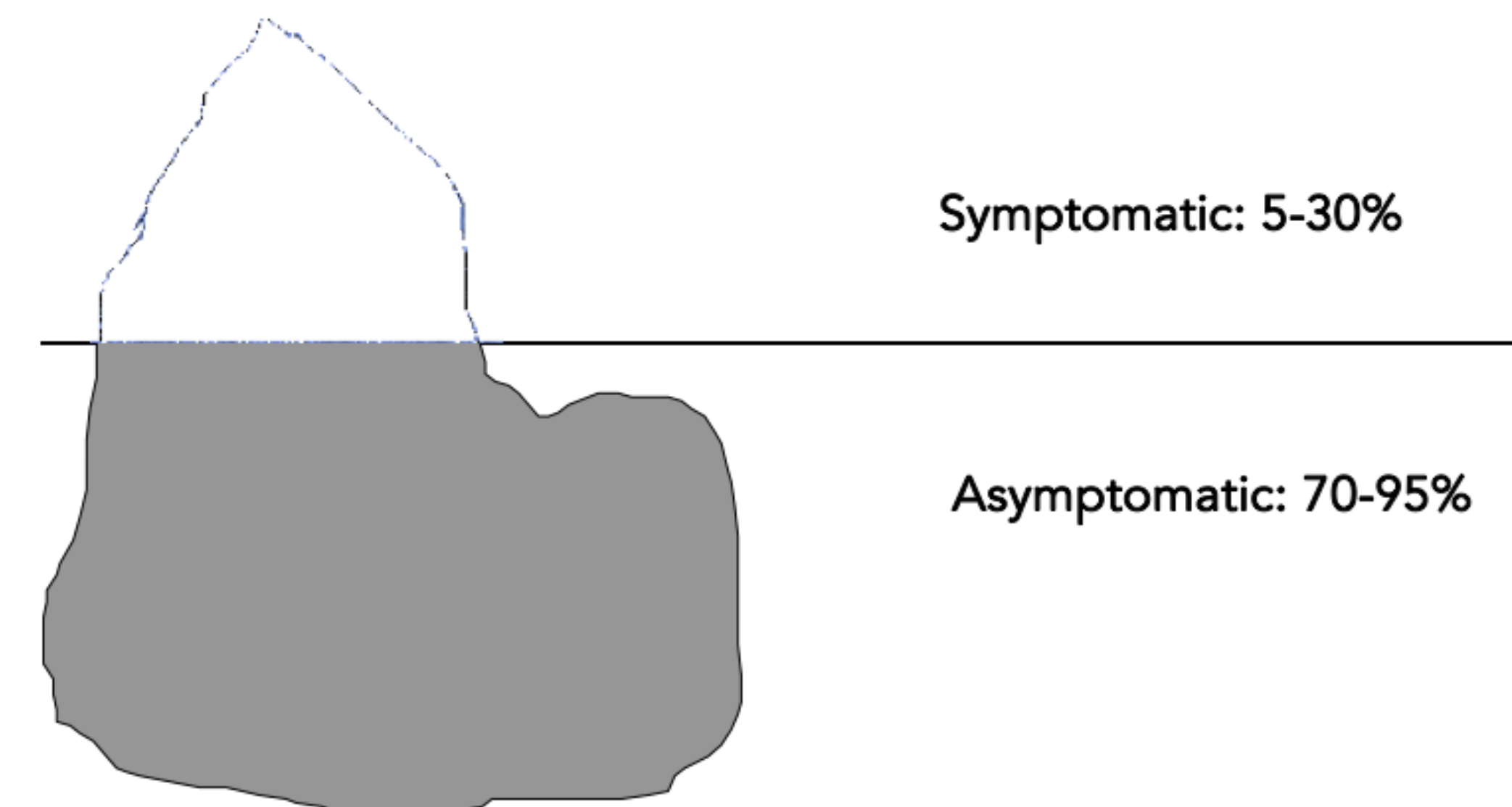
## STIs are common among pregnant women in Southern Africa

Adjusted mean prevalences of *T. vaginalis*, *N. gonorrhoeae*, and *C. trachomatis* among pregnant women in Southern Africa



Source: Joseph Davey et al. 2016

## Syndromic Management misses asymptomatic CT, NG, & TV infections

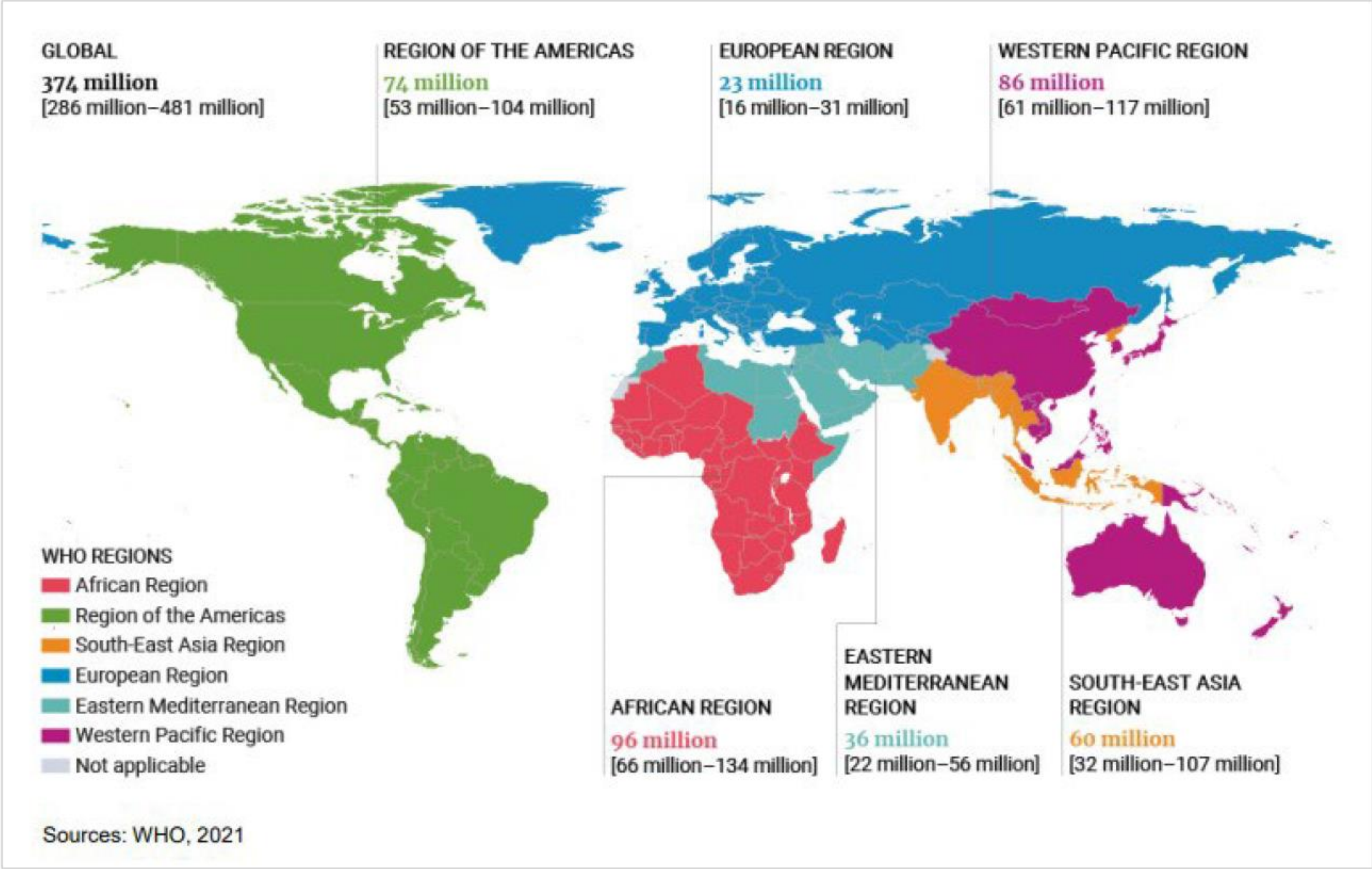


- Highlights need for a testing strategy &
- Affordable diagnostic tests for STIs

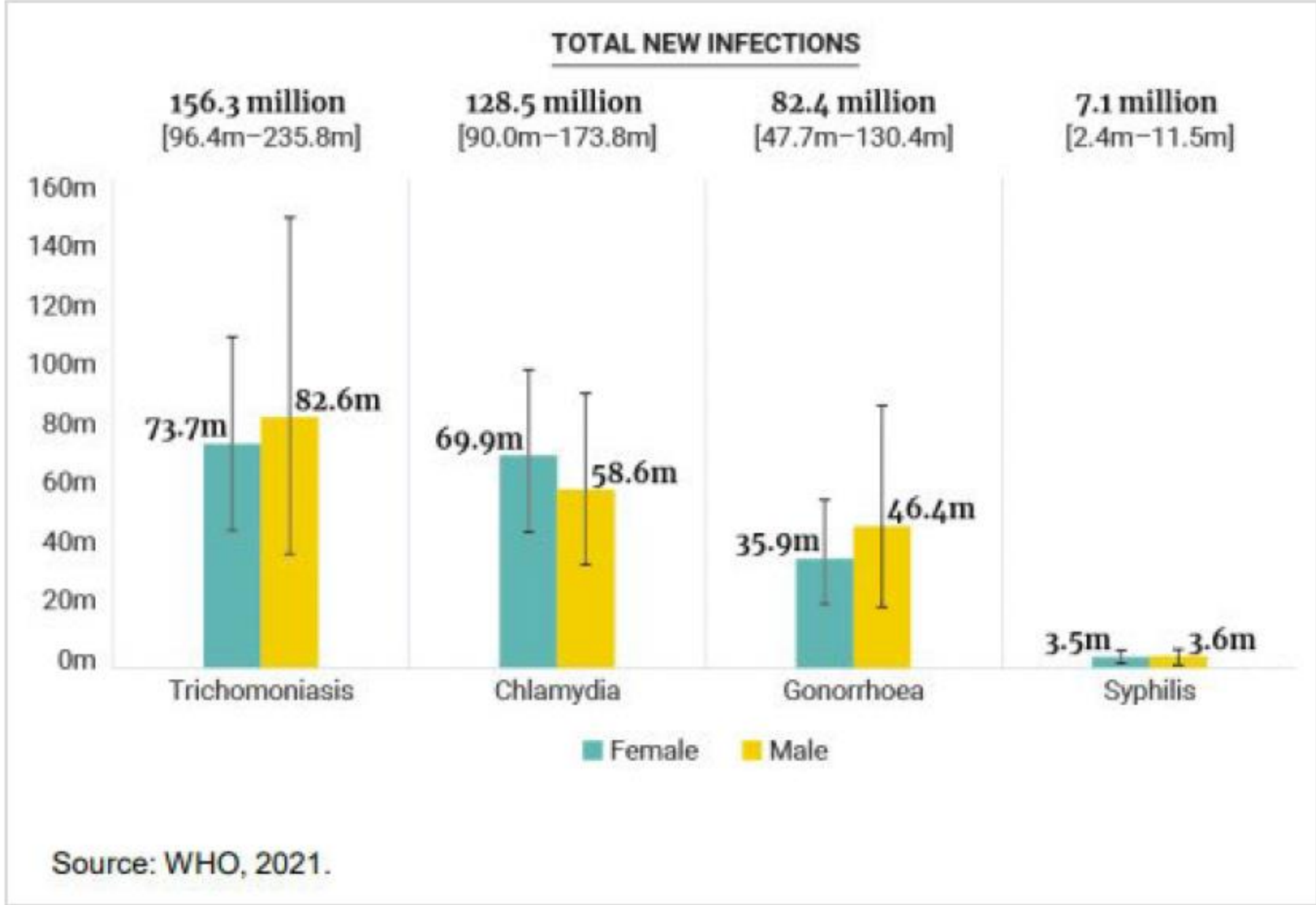
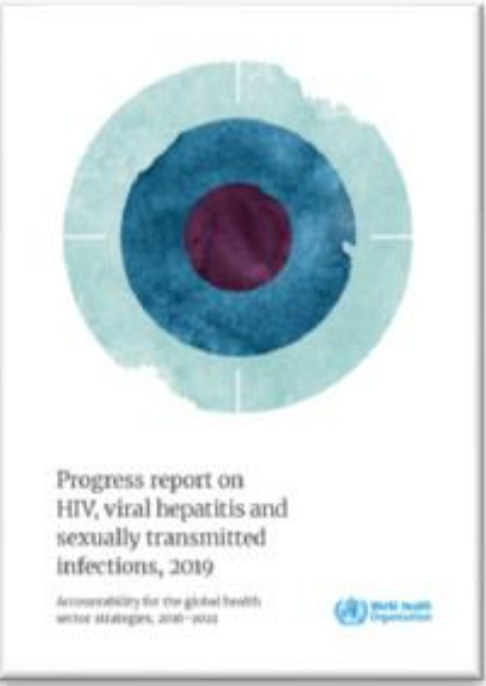
Source: Farley 2003;  
Korenromp 2002; Ndowa 2016

# Background

## Incident cases of four curable STIs among adults (15 to 49 years old), 2020



- 374 million new infections in 2020
- Over one million new infections a day



# High STI burden among people on HIV PrEP

## Global STI pooled prevalence of people prior to start PrEP and on PrEP by anatomical site of detection (2019)<sup>1</sup>

Pathogen	Pooled prevalence at baseline (95% CI)	Pooled incidence per 100 PY (95% CI)
<i>C. trachomatis</i> (any site)	10.8% (6.4-16.1)	21.5 (17.9-25.8)
<i>N. gonorrhoeae</i> (any site)	11.6% (7.6-16.2)	37.1 (18.3-25.5)
<i>T. pallidum</i> (active infection)	5.0% (3.1-7.4)	11.6 (9.2-14.6)
<i>M. genitalium</i>	17.2% (12.2-23.2)	-
<i>Trichomonas vaginalis</i>	5.9% (4.7-7.2)	0
Any <i>C. trachomatis</i> , <i>N. gonorrhoeae</i> or <i>T. pallidum</i>	23.9% (18.6-29.6)	72.2 (60.5-86.2)

## STI rates among sexually active African women (18-25 years old) in three PrEP cohorts (2020)<sup>2</sup>

	Chlamydia trachomatis	Neisseria gonorrhoeae
MTN-020/ASPIRE (n= 2692) (phase III microbicide trial) S. Africa, Zimbabwe, Zambia, Malawi and Uganda	Prevalence = 12% Incidence = 27% per 100 person-years	Prevalence = 4% Incidence = 11% per 100 person-years
HPTN 082 (n=434) (PrEP demonstration project) S. Africa and Zimbabwe	Prevalence = 29% Incidence = 33% per 100 person-years	Prevalence = 8% Incidence = 14% per 100 person-years
POWER (n=284) (PrEP implementation project) S. Africa and Kenya	Prevalence = 26% Incidence = 53% per 100 person-years	Prevalence = 10% Incidence = 20% per 100 person-years

AFRICA REGION PREVALENCE	NG	CT
Women (15-49 years)	1.6% (range 1.1-2.2)	5.5 (range 4.3-7.0)
Men (15-49 years)	0.7% (range 0.3-1.1)	



- Ong JJ, Baggaley RC, WI TE, et al. Global Epidemiologic Characteristics of Sexually Transmitted Infections Among Individuals Using Preexposure Prophylaxis for the Prevention of HIV Infection: A Systematic Review and Meta-analysis. *JAMA Netw Open*. 2019;2(12):e1917134. doi:10.1001/jamanetworkopen.2019.17134
- Stewart J, Bukusi E, Celum C, Delany-Moretlwe S, Baeten JM. Sexually transmitted infections among African women: an opportunity for combination sexually transmitted infection/HIV prevention. *AIDS*. 2020;34(5):651-658.
- Global progress report on HIV, viral hepatitis and sexually transmitted infections, 2021. Accountability for the global health sector strategies 2016–2021: actions for impact. Geneva: World Health Organization; 2021

# STI and HIV integration: HPTN STUDIES

- HPTN 094 : an integrated package of HIV prevention & treatment with STI treatment for PWID.
- HPTN 111 : Uptake of HIV Self-testing and Linkage to Prevention and Care among Heterosexual Men attending Barbershops in Uganda: A Cluster Randomized Trial. (in dev)
- HPTN112 Improving HIV prevention among heterosexual men seeking STI services in sub-Saharan Africa: examining the feasibility, acceptability, and associated costs of a systems-navigator-delivered integrated prevention package ( in dev)
- HPTN 113: Double Prevention: A Vanguard Study of an Integrated Strategy of HIV PrEP and STI PEP for Young Latino Sexual Minority Men (SMM) in the Americas. Doxy PEP for STIs becoming important area in field.

# STI burden among people MSM in Africa

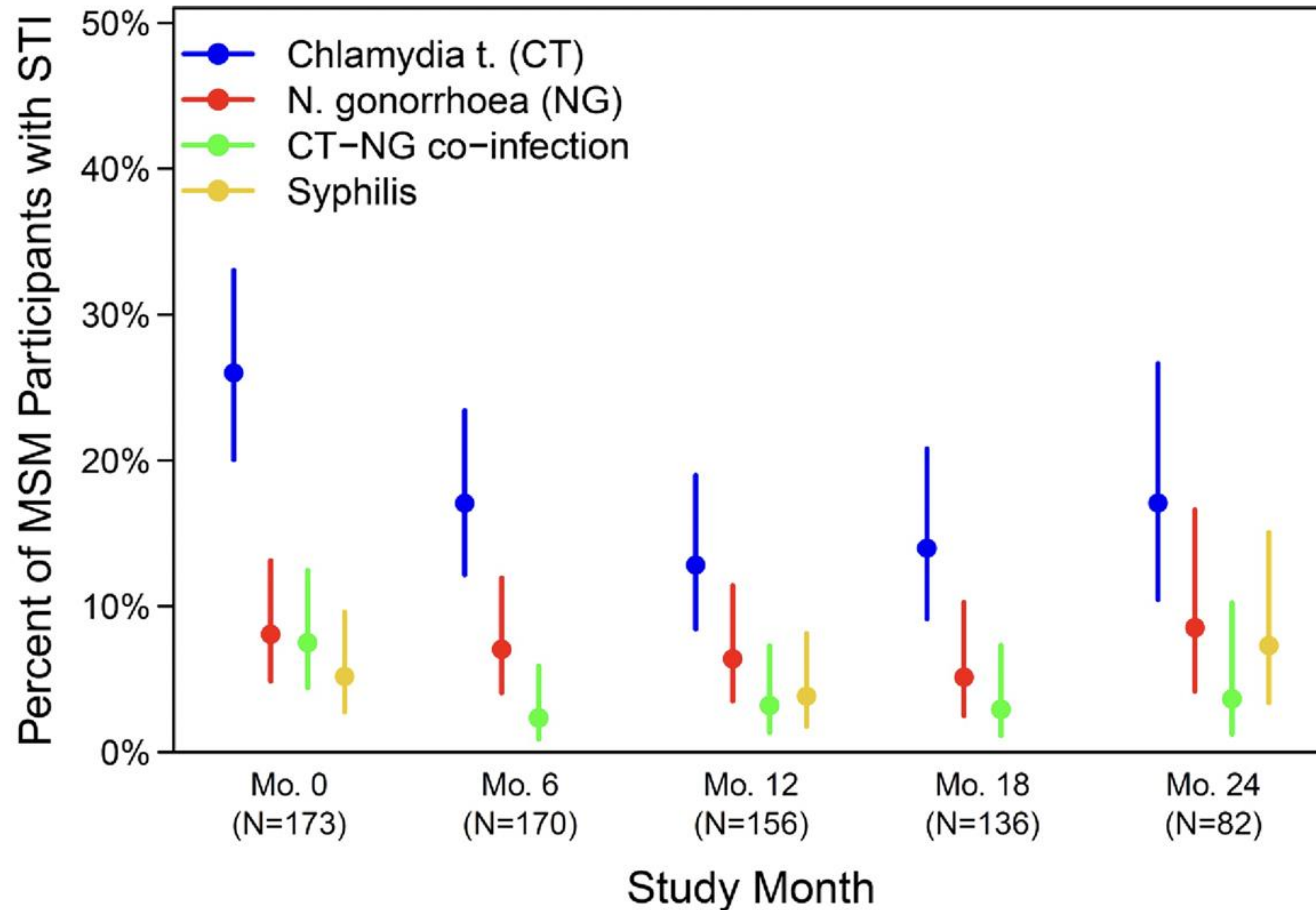


Fig 1. Estimated STI prevalence and 95% CIs over time among MSMs with STI testing data available in HVTN 702.

<https://doi.org/10.1371/journal.pgph.0001782.g001>

Source: Mashingaidze et al, PLOS Glob Public Health, 2023

Table 1. Incident and persistent STDs at follow-up in a cohort of high-risk men who have sex with men in Johannesburg, South Africa.

Type	Age	Baseline symptoms	Baseline STD		Follow-up STD	
			Urethral	Rectal	Urethral	Rectal
<b>Incident infection</b>						
	26	Urethral	NG	CT, NG	TV	-
	31	Urethral	NG, TV	TV	-	CT
	27	Urethral	NG, TV	TV	MG	-
	21	Urethral	-	NG	NG	-
	25	Urethral	NG	-	-	CT
	40	Urethral	-	-	-	TV
	32	Rectal	NG	-	-	NG
	28	Rectal	-	NG	NG	-
	32	Rectal	-	-	CT	-
	23	Rectal	-	-	NG	-
	27	Rectal	-	-	NG	-
	29	Both	-	NG	TV	TV
<b>Persistent positivity</b>						
	27	Urethral	NG	-	NG <sup>2</sup>	-
	43	Urethral	-	NG	-	NG
	24	Urethral	-	CT, NG	-	NG
	39	Urethral	NG	-	NG	-
	29	Urethral	NG	NG	-	NG
	35	Urethral	CT	NG	-	NG
<b>Incident infection and persistent positivity</b>						
	30	Urethral	CT, NG	-	NG, TV <sup>2</sup>	-
	36	Urethral	NG	NG	NG, TV, MG	NG, TV
	*	Urethral	CT, NG	-	CT, NG	CT, NG
	32	Rectal	NG	-	NG, TV, MG	TV

<sup>1</sup> The proportion positive for any STD at follow up was comparable between HIV positive and HIV negative MSM (P=0.79), and comparable between MSM on ART and MSM not on ART (P=0.52). <sup>2</sup> Patient reported urethral discharge at follow up. \*data is missing. - no STD detected.

We did not observe differences in the proportion baseline STD, follow-up STD, incident infection and persistent positivity between the clinics (P=0.43, P=0.77, P=0.35, P=0.87, respectively).

Abbreviations: NG *Neisseria gonorrhoeae*, CT *Chlamydia trachomatis*, TV *Trichomonas vaginalis* and MG *Mycoplasma genitalium*.

Source: Van Liere et al, University of Pretoria

# STI Vaccines

- Several vaccine candidates undergoing preclinical trials
- **HPTN 107/DMID 19-0004** is evaluating the Bexsero meningococcal vaccine for prevention of gonococcal infection in collaboration with IDCRC (US and possibly Malawi).

# STI Diagnosis and Management

- Management of STIs largely syndromic in Africa
- Limited rapid or point-of-care diagnostics
- High cost of diagnostics



# How much does STI testing and treatment cost compared to syndromic management?

**An important barrier to expanding diagnostic STI testing is cost**

## Methods

- Modelled a hypothetical population of 50,000 pregnant women to compare one-year costs and outcomes associated with three antenatal STI testing strategies
  - 1) point-of-care
  - 2) centralized laboratory hubs
  - 3) a mixed approach (point-of-care at high-volume sites, and hubs elsewhere)
  - syndromic management

## Results

- Syndromic management
  - Lowest delivery cost
  - Most infections at delivery, uninfected women overtreated, CT/NG-related low birth weight infants, disability adjusted life years (DALYs), and LBW hospitalization costs
- Point-of-care CT/NG testing
  - Highest costs
  - Treat and cure the most infections, avert the most infections at delivery, low birth weight infants and DALYs
- The mixed scenario had the most favorable cost per woman treated and cured.
- Incremental cost-effectiveness ratio of \$953 per DALY averted (mixed compared to syndromic management)

### Modeled delivery costs of point-of-care, laboratory, mixed, and syndromic management for antenatal CT/NG testing and treatment in Gaborone

	Point-of-Care	Laboratory	Mixed	Syndromic
<b>Cost per test/assessment</b>	\$57 (\$45-69)	\$27 (\$20-35)	\$26 (\$19-35)	\$18 (\$4-51)

# Is STI testing & treatment acceptable & feasible?

PMH ANC clinic, July 2015 and May 2016

- Uptake of CT/NG/TV testing using self-collected vaginal swabs was high: 86% (400/466)
- Feasibility was high
  - 99% received results (61% in person, same-day)
  - 98% were treated (77% on the same day)
  - 70% received test of cure

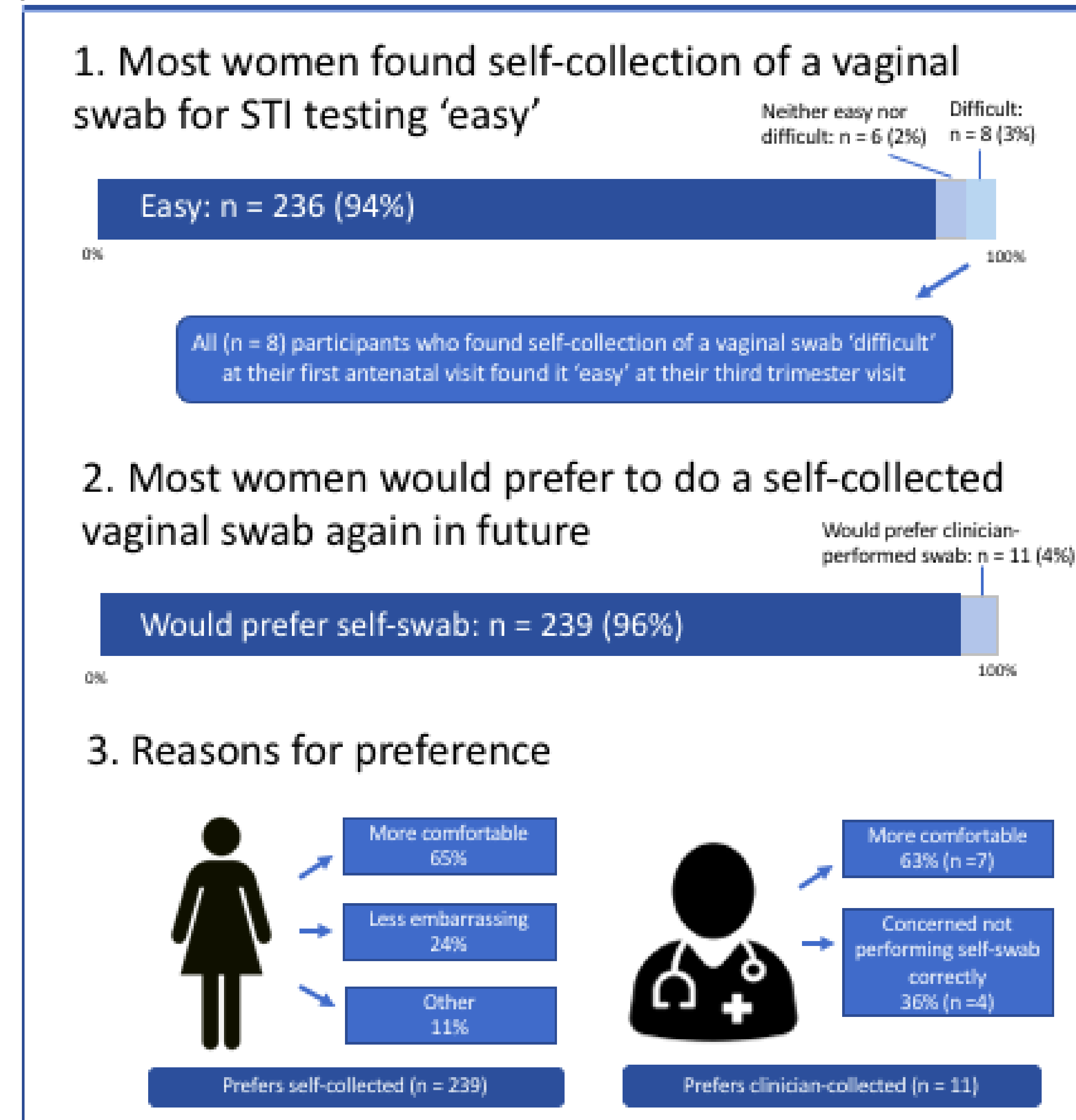
## PLWH at PMH IDCC Clinic

- 65% of those approached were interested (older population)
- Almost all reported sample collection was easy
- **High feasibility:** 91% received same-day results

**Maduo Study (NIH R21):** Old Naledi, Lesirane, Maflitlagkosi, Tlokweng;

- Self-collected vaginal swabs are acceptable (Figure 1)
- CT/NG testing and treatment is feasible
  - 100% (58/58) of women who tested positive received results
  - 98% (57/58) were treated prior to delivery
  - 100% (52/52) were cured at test of cure

Figure 1: Results from Maduo Study



# Are partners notified and treated for STIs?

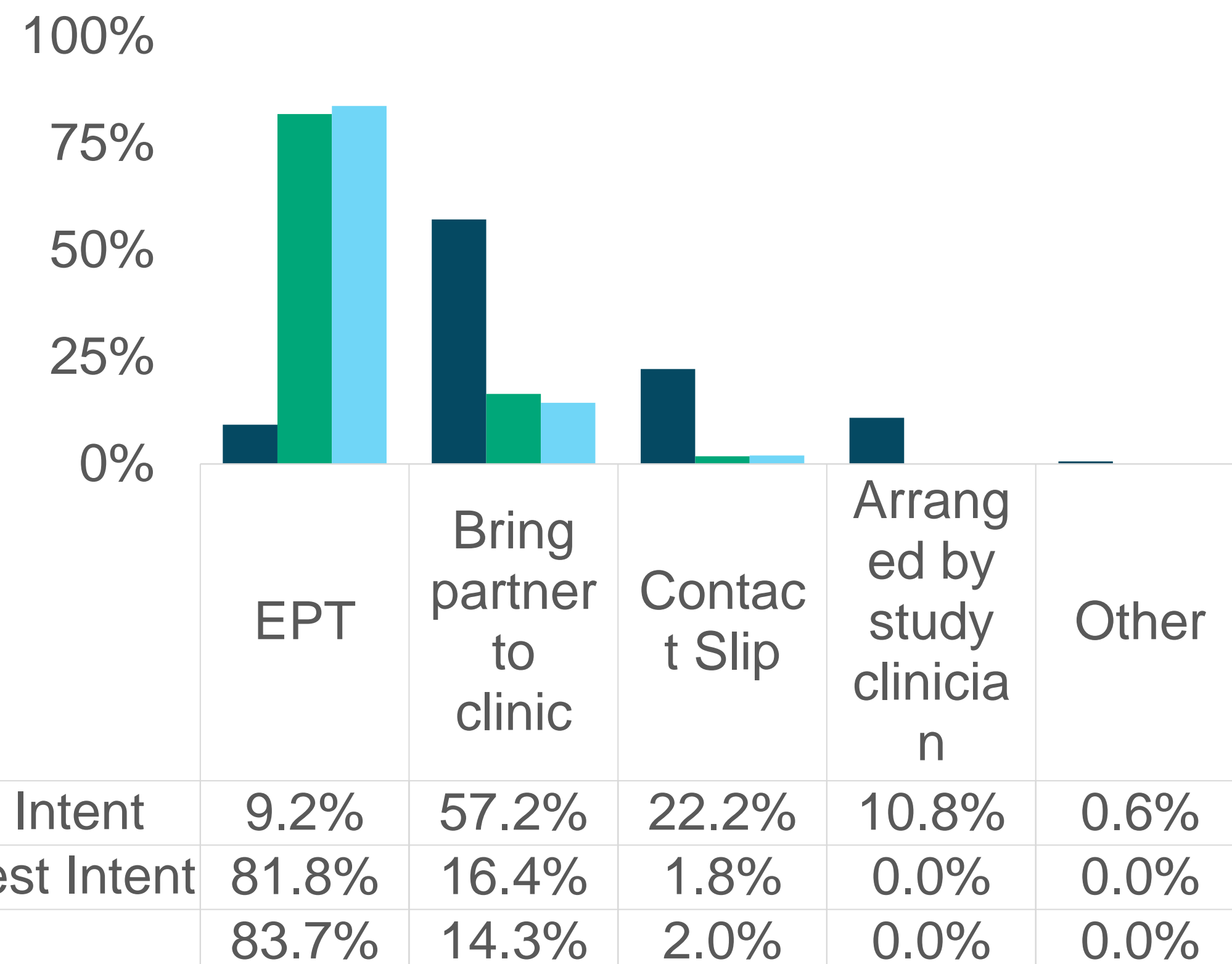
## Pregnant women at PMH

- 84% reported they notified partners
- 63% reported that their partners were treated
- Among the 4 women who tested positive at the test of cure, 3 said their partners were not treated

## Maduo Study

- Self-reported partner notification and treatment
- Most chose EPT despite low interest in prior study

Figure 2. Maduo Study Partner Treatment Methods



## Partner notification and treatment experiences among pregnant women at PMH ANC, August 2016-February 2017 (n=15)

Theme	Quote
Partners were notified in person	<i>I didn't go around in circles, I got in and said, "I was in [the clinic] and there were people testing for STDs so I also tested, but came back positive...now you can read these papers and see what kind of disease it is."</i>
Few partners reacted badly	<i>Now he is shouting at me... "What did you check for?" saying "you like testing yourself for so many things!" .."So you think I sleep around with girls, am I sick?" Right then we had sex again because he was shouting right... I was calming him down.</i>
Many women need more information for partners	<i>"no when you get to the hospital, there's no evidence that I can give you, when you get to the hospital you tell them my partner was tested and she was found with STI's."</i>
Women preferred to accompany partners to clinic	<i>But if you give me the paper [contact slip] I'm going to need to go with him because if I don't he won't do it [get treated].</i>
Women did not prefer expedited partner therapy	<i>Ah, it wasn't going to be good. He was going to refuse... He was going to ask himself what pills I was giving to him that he hasn't been told about.</i>

# Conclusions

- Testing for curable STIs is acceptable and feasible
  - High uptake of testing and treatment
  - High cure rate
- Women self-report high levels of partner notification and prefer expedited partner treatment
- Syndromic management is missing many infections
- CT and NG infection testing is more costly, but identifies more infections, treats more infections (including partners), reduces overtreatment, and may reduce adverse pregnancy and birth outcomes and antimicrobial resistance

# Questions

- STI drug resistance is an increasing concern in people with and without HIV ? How do we address it
- STI diagnosis and management often lack data ( syndromic approaches probably both over and undertreat)
- Do we have High Quality pregnancy safety for drugs used to treat STI's in pregnancy
- Doxy PEP for STIs becoming important area in field.
  - Can DoxyPEP reduce both STI and HIV incidence among high-risk populations such as PWUD, MSM, transgender women and sex workers?
  - How do we roll it out?
  - Lessons from 083 AND 084, Do we undertake similar but concurrent HPTN PEP and DoxyPEP studies uptake in MSM & in Hetero-sexuals
- Will the benefits of DoxyPEP in terms of reductions in STI/HIV incidence be offset by increased rates of antimicrobial resistance?
- Will PrEP for HIV and STIs (e.g. DoxyPrEP) offered simultaneously reduce HIV and STI prevalence among high risk populations (e.g., MSM, PWUD, at risk adolescents, sex workers) compared to offering these medications alone.
- How do we leverage HIV Diagnosis/treatment infrastructure to diagnose /treat other STIs

# Questions

- Does screening and treatment for curable STIs reduce the risk of adverse birth outcomes, such as preterm birth and low birth weight?
- Are there sub-groups where screening is more effective at reducing adverse birth outcomes?
  - Women living with HIV
  - Younger women or those with higher risks (new or multiple partners)
  - Nulliparous women
- Can we integrate point-of-care STI screening into routine antenatal care?
  - What is the cost and where do costs need to be in order to be affordable?
  - Do providers have the capacity to offer STI screening beyond HIV and syphilis?
  - Can STI screening, HIV testing and prevention, and sexual health care be integrated during antenatal care?
- How can we optimize partner notification and treatment for STIs?
  - What are the most effective strategies to ensure partners are treated to reduce reinfection?
  - Can we engage male partners in sexual health via STI screening, including HIV testing and linkage?

# Peer Reviewed Publications

1. Wynn A, Ramogola-Masire D, Gaolebale P, Moshashane N, Agatha Offorjebe O, Arena K, Klausner JD, Morroni C. Acceptability and Feasibility of Sexually Transmitted Infection Testing and Treatment among Pregnant Women in Gaborone, Botswana, 2015. *Biomed Res Int.* 2016; PMC4826911.
2. Offorjebe OA, Wynn A, Moshashane N, Joseph Davey D, Arena K, Ramogola-Masire D, Gaolebale P, Morroni C, Klausner JD. Partner notification and treatment for sexually transmitted infections among pregnant women in Gaborone, Botswana. *Int J STD AIDS.* 2017 Oct;28(12):1184-1189. PMID: PMC5810551.
3. Wynn A, Ramogola-Masire D, Gaolebale P, Moshashane N, Sickboy O, Duque S, Williams E, Doherty K, Klausner JD, Morroni C. Prevalence and treatment outcomes of routine Chlamydia trachomatis, Neisseria gonorrhoeae and Trichomonas vaginalis testing during antenatal care, Gaborone, Botswana. *Sex Transm Infect.* 2018 May;94(3):230-235. PMID: PMC6117829.
4. Hansoti B, Kalbarczyk A, Hosseinipour MC, Prabhakaran D, Tucker JD, Nachega J, Wallis L, Stiles JK, Wynn A, Morroni C. Global Health Mentoring Toolkits: A Scoping Review Relevant for Low- and Middle-Income Country Institutions. *Am J Trop Med Hyg.* 2019 Jan;100(1\_Suppl):48-53. PMID: PMC6329353.
5. Wynn A, Moucheraud C, Moshashane N, Offorjebe OA, Ramogola-Masire D, Klausner JD, Morroni C. Using partner notification to address curable sexually transmitted infections in a high HIV prevalence context: a qualitative study about partner notification in Botswana. *BMC Public Health.* 2019 May 29;19(Suppl 1):606. PubMed Central PMID: PMC6538557.
6. Wynn A, Moucheraud C, Morroni C, Ramogola-Masire D, Klausner JD, Leibowitz A. Scaling up diagnostic-driven management of sexually transmitted infections in pregnancy. *Lancet Infect Dis.* 2019 Aug;19(8):809-810. PubMed PMID: 31345453.
7. Elliott T, Kohler RE, Monare B, Moshashane N, Ramontshonyana K, Muthoga C, Wynn A, Howett R, Luckett R, Morroni C, Ramogola-Masire D. Performance of vaginal self-sampling for human papillomavirus testing among women living with HIV in Botswana. *Int J STD AIDS.* 2019 Sep 27; PubMed PMID: 31558129.
8. Maan I, Lawrence DS, Tlhako N, Ramontshonyana K, Mussa A, Wynn A, Marks M, Ramogola-Masire D, Morroni C. Using a dual antibody point-of-care test with visual and digital reads to diagnose syphilis among people living with HIV in Botswana. *Int J STD AIDS.* 2021 Apr;32(5):453-461. PubMed Central PMID: PMC8008391.
9. Carveth-Johnson T, Dunin De Skrzyzynno S, Wynn A, Moshashane N, Ramontshonyana K, Lebelonyane R, Mussa A, Ramogola-Masire D, Klausner J, Morroni C. Integrating STI testing and treatment with routine HIV care in Gaborone, Botswana. *Sex Transm Dis.* 2021 Jun 26 [Epub ahead of print] PubMed PMID: 34174039.
10. Wynn A, Moucheraud C, Martin NK, Morroni C, Ramogola-Masire D, Klausner JD, Leibowitz A. Bridging the gap between pilot and scale-up: A model of antenatal testing for curable sexually transmitted infections from Botswana. *Sexually Transm Dis.* 2021 Aug 26.
11. Grant JS, Chico RM, Lee AC, Low N, Medina-Marino A, Molina RL, Morroni C, Ramogola-Masire D, Stafylis C, Tang W, Vallely AJ, Wynn A, Yeganeh N, Klausner JD. Sexually transmitted infections in pregnancy: a narrative review of the global research gaps, challenges, and opportunities. *Sex Transm Dis.* 2020 Jan; 47(1): 5-11.
12. Hansman E, Wynn A, Moshashane N, Ramontshonyana K, Mompe A, Mussa A, Ryan R, Ramogola-Masire D, Klausner JD, Morroni C. Experiences and preferences with sexually transmitted infection care and partner notification in Gaborone, Botswana. *Int J STD AIDS.* 2021 Jul 25;9564624211033231.
13. Wynn A, Mussa A, Ryan R, Hansman E, Simon S, Bame B, Moreri-Ntshabele B, Ramogola-Masire D, Klausner JD, Morroni C. Evaluating the diagnosis and treatment of Chlamydia trachomatis and Neisseria gonorrhoeae in pregnant women to prevent adverse neonatal consequences in Gaborone, Botswana: protocol for the Maduo study. *BMC Infect Dis.* 2022 Mar 7;22(1):229.
14. Babalola CM, Siebert JC, Kallapur SG, Maecker HT, Rosenberg-Hasson Y, Hansman E, Wynn A, Mussa A, Ryan R, Simon S, Morroni C, Klausner JD. Discrete Plasma Cytokine Profiles among Pregnant Women in Botswana by Chlamydia trachomatis infection, HIV status, and Gestational age. *J Infect Dis.* 2022 Jul 25;jiac302.