

New STI Prevention Agents and Diagnostics

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Presentation Highlights

1. What is the main issue or question the presentation addresses?
 - To provide an overview of the STI landscape in context of HIV prevention in Southern Africa
2. What is the key finding or ‘takeaway message’?
 - Challenges remain with STI care, but there are new opportunities for research and implementation with new technologies and vaccines.
3. How does the research advance HIV prevention efforts?
 - Other STIs increase the risk of HIV acquisition, which means STI solutions are key to HIV prevention.

- The STI burden and Challenges of STI Care in Southern Africa
- Point-of-care Diagnostics to reduce Genital Inflammation and HIV Risk
- The STI Vaccine Pipeline
- The Story of DoxyPEP
- Way forward

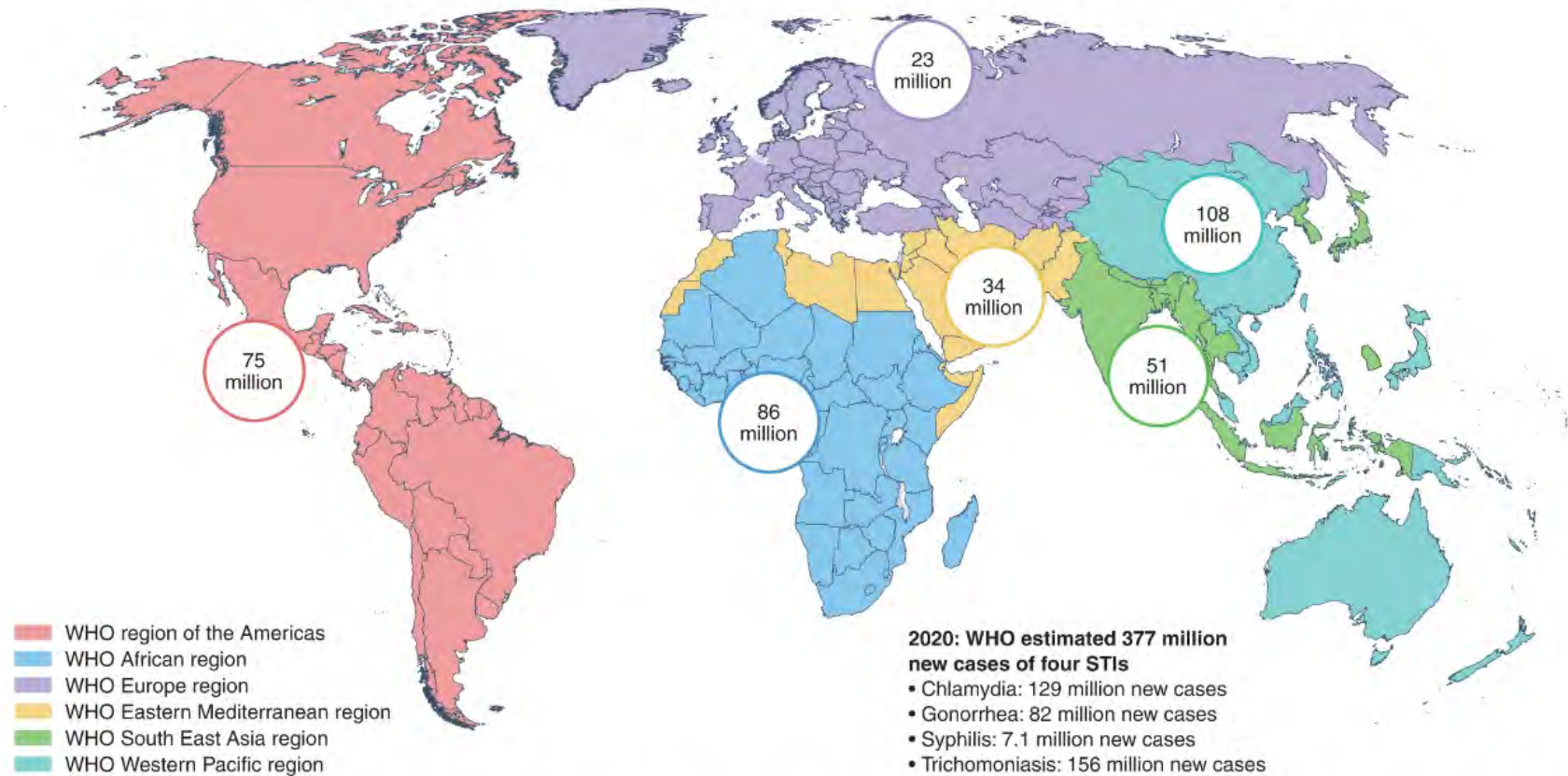
Most important STI News last Month

New director named at National Institute of Allergy and Infectious Diseases after Fauci's retirement



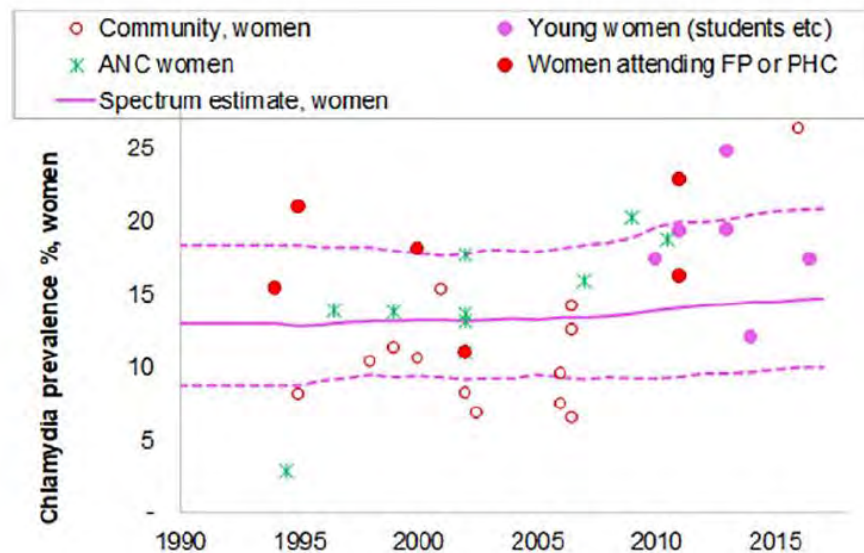
Global Burden of STIs, not just HIV

These numbers represent incident cases of chlamydia, gonorrhoea, trichomoniasis and syphilis in 2016.



WHO global regions and the incident cases of four STIs (chlamydia, gonorrhoea, trichomoniasis and syphilis) from 2016 estimates. The WHO estimates of new cases of these four STIs worldwide in 2020 are shown at the bottom right of the figure.

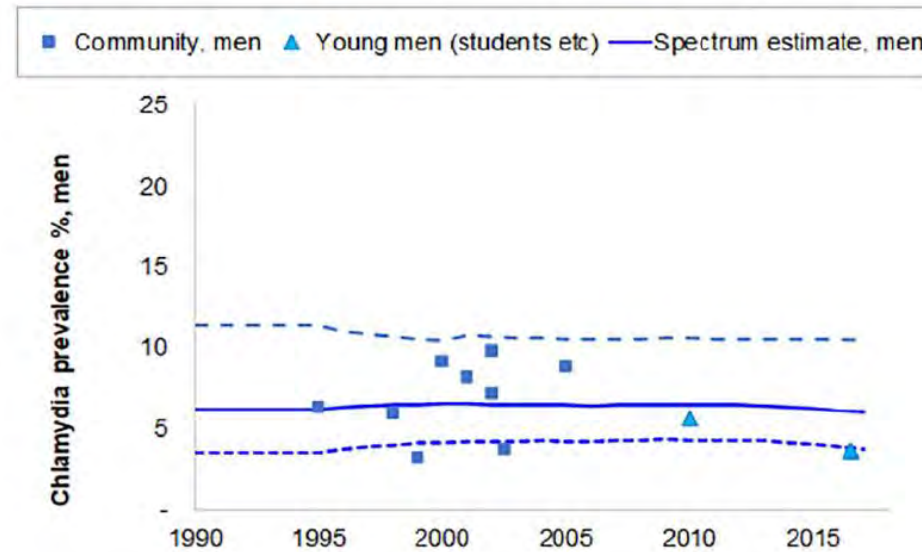
STI prevalence: continuously high



Women

Chlamydia: 14.7%

Gonorrhoea: 6.6%



Men

Chlamydia: 6.0%

Gonorrhoea: 3.5%

The Big Elephant in the Room

STI

Advancing STI care in low/middle-income countries: has STI syndromic management reached its use-by date?



Challenges with Syndromic Management

Poor accuracy of syndromic management

		Lab Diagnosis	
		+	-
Clinical Diagnosis	+	25	48
	-	179	723

Sensitivity = 12.3 % **7/8 remain undiagnosed.**

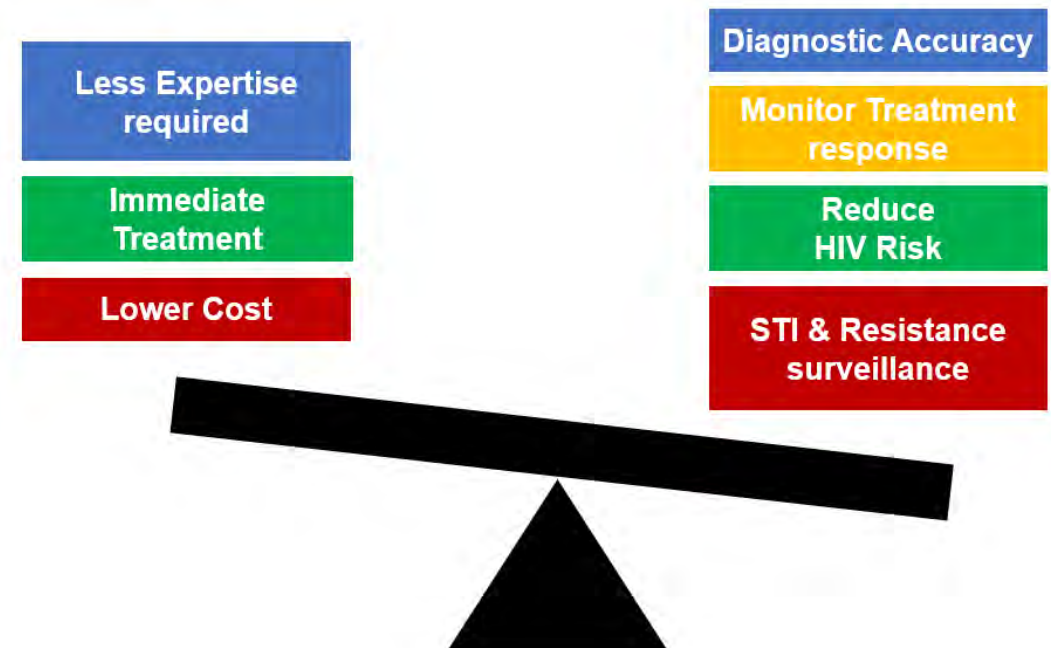
Specificity = 93.8%

PPV = 34.2%

2/3 are over-treated.

NPV = 80.2%

Syndromic vs diagnostic STI care



Mlisana, et al. Symptomatic vaginal discharge is a poor predictor of STIs and genital tract inflammation in high-risk women in South Africa, *J Infect Dis.* 2012 Jul 1;206(1):6-14

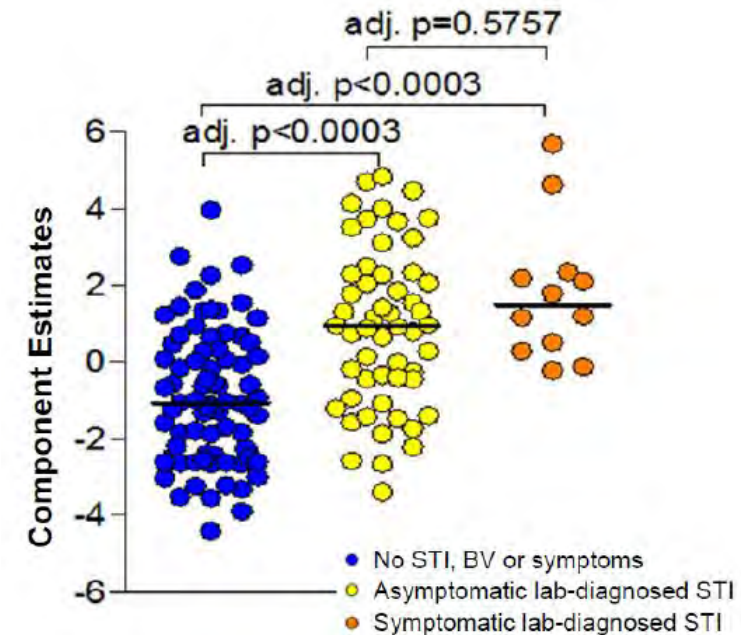
Why are STIs important for HIV prevention?

High burden of STIs in women at HIV acquisition

Infection	CAPRISA 002 (N=160)	
	Total %	Asymptomatic %
Chlamydia trachomatis	15.4	79
Neisseria gonorrhoeae	8.3	77
Mycoplasma genitalium	8.3	77
Trichomonas vaginalis	10.9	88
HSV-2 PCR	8.3	85
Syphilis	5.0	75
Bacterial vaginosis	62.6	78

Mlisana, et al. *J Infect Dis.* 2012 Jul 1;206(1):6-14

Genital inflammation caused by STIs associated with HIV acquisition

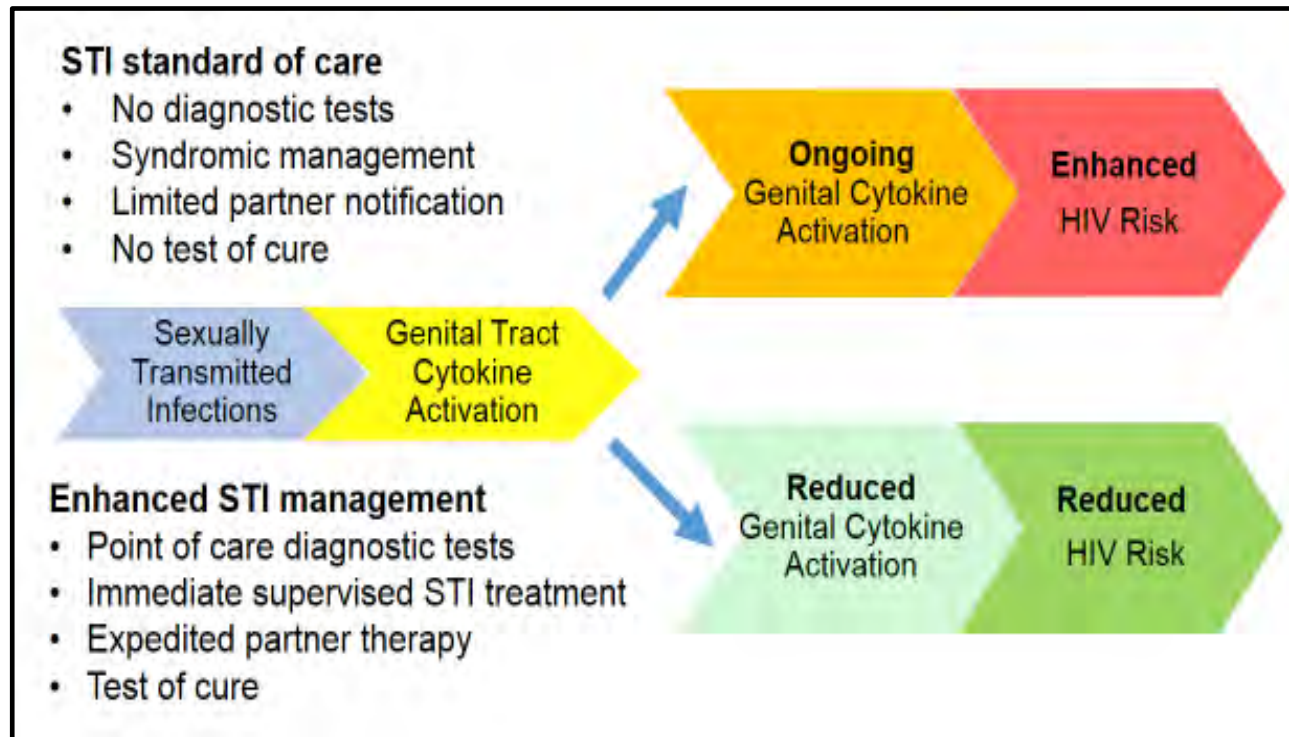


Masson L, et al. *Clin Infect Dis.* 2015 Jul 15;61(2):260-9

Increased HIV susceptibility due to disruption of epithelial barrier and increase in HIV target cells.

Aim of CAPRISA 083 study

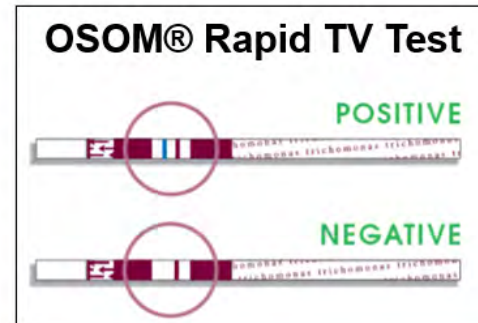
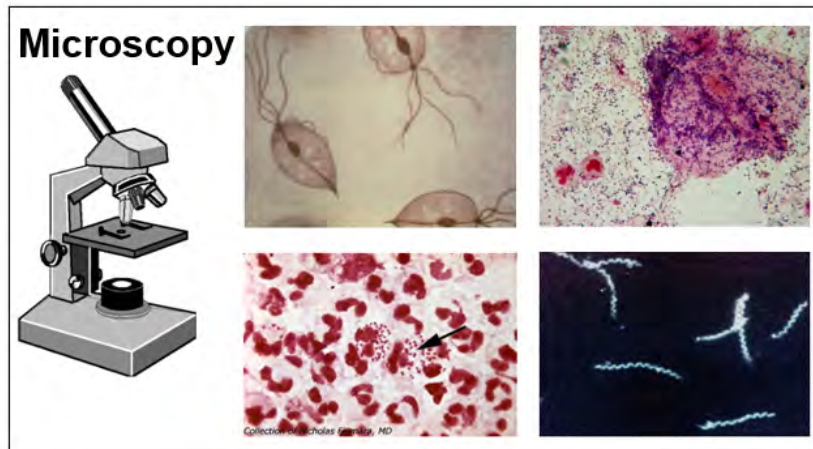
To evaluate a model of enhanced STI care to reduce genital inflammation & HIV risk among young women in SA



Recommended reading: Golden, et al. Effect of expedited treatment of sex partners on recurrent or persistent gonorrhea or chlamydial infection. *N Engl J Med.* 2005 Feb 17;352(7):676-85

An alternative STI care approach for young women in South Africa

Point-of-care testing, Immediate Treatment and Expedited partner therapy



Garrett, et al. Beyond syndromic management: Opportunities for diagnosis-based treatment of sexually transmitted infections in low- and middle-income countries. *Plos One*. 2018

Good performance of POC assays

Table 1 Evaluation of the Xpert CT/NG and OSOM TV against the Anyplex II STI-7 Detection and FTD STD9 assays (n=247)

POC assay		Anyplex II STI-7 Detection +/- FTD STD9		Accuracy with 95% CI
		Positive	Negative	
Xpert CT	Positive	37	5	Sensitivity=100% (100% to 100%) Specificity=97.6% (95.6% to 99.7%) PPV=88.1% (78.3% to 97.9%) NPV=100% (100% to 100%)
	Negative	0	205	
Xpert NG	Positive	12	0	Sensitivity=100% (100% to 100%) Specificity=100% (100% to 100%) PPV=100% (100% to 100%) NPV=100% (100% to 100%)
	Negative	0	235	
OSOM TV	Positive	6	0	Sensitivity=75.0% (45.0% to 100%) Specificity=100% (100% to 100%) PPV=100% (100% to 100%) NPV=99.2% (98.0% to 100%)
	Negative	2	239	

FTD, Fast Track Diagnostics; NG, Neisseria gonorrhoeae; POC, Point-of-care; TV, Trichomonas vaginalis.

Garrett, et al. Diagnostic accuracy of the Xpert CT/NG and OSOM Trichomonas Rapid assays for point-of-care STI testing among young women in South Africa: a cross-sectional study. *BMJ Open*. 2019

Effective STI clearance after POC testing, immediate treatment and EPT

High STI and BV prevalence at baseline

Infection	Percentage
Chlamydia trachomatis	18.4*
Neisseria gonorrhoeae	5.2#
Trichomonas vaginalis	3.0
BV or intermediate microbiota	69.3
Candida	18.0

Effective STI clearance

Pathogen (N=77)*	Baseline N (%)	Week 6 N (%)	Week 12 N (%)	p-value
C. trachomatis	35 (45.5)	4 (5.2)	2 (2.6)	<0.001
N. gonorrhoeae	10 (13.0)	0 (0)	1 (1.3)	0.041
T. vaginalis	5 (6.5)	2 (2.6)	0 (0)	0.013
Any of CT, NG or TV	46 (59.7)	6 (7.8)	3 (3.9)	<0.001
Bacterial vaginosis	40 (52.0)	26 (33.8)	19 (24.7)	<0.001
Candidiasis	14 (18.2)	7 (9.1)	12 (15.6)	0.668

*Total enrolled 101, but 24 missed either week 6 or month 3 visit

STI treatment was strongly associated with reduced concentrations of pro-inflammatory cytokines IL-6, IL-1 β , TNF- α .

High Uptake of Expedited Partner Therapy

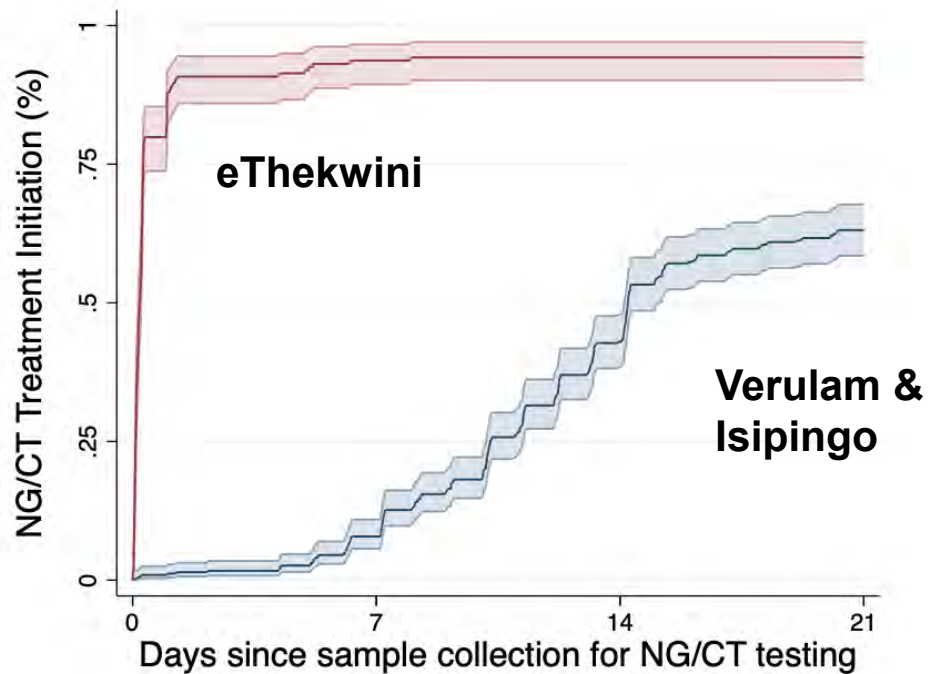
- 87% accepted EPT, mainly for one partner.
- 89% stated successful EPT, i.e. partner took treatment.
- 17% of women and 6% of partners experienced mild side effects consistent with antibiotic profiles.
- No allergic reactions or social harms reported.

Pathogen	Overall (N=51)	EPT (N=46)	No EPT (N=5)	p-value
	% (n/N)	% (n/N)	% (n/N)	
C. trachomatis	3.9 (2/51)	2.2 (1/46)	20.0 (1/5)	0.188
T. vaginalis	2.0 (1/51)	0	20.0 (1/5)	0.098
CT or TV*	5.9 (3/51)	2.2 (1/46)	40.0 (2/5)	0.023

*No *N. gonorrhoeae* cases were detected at 6-week follow-up.

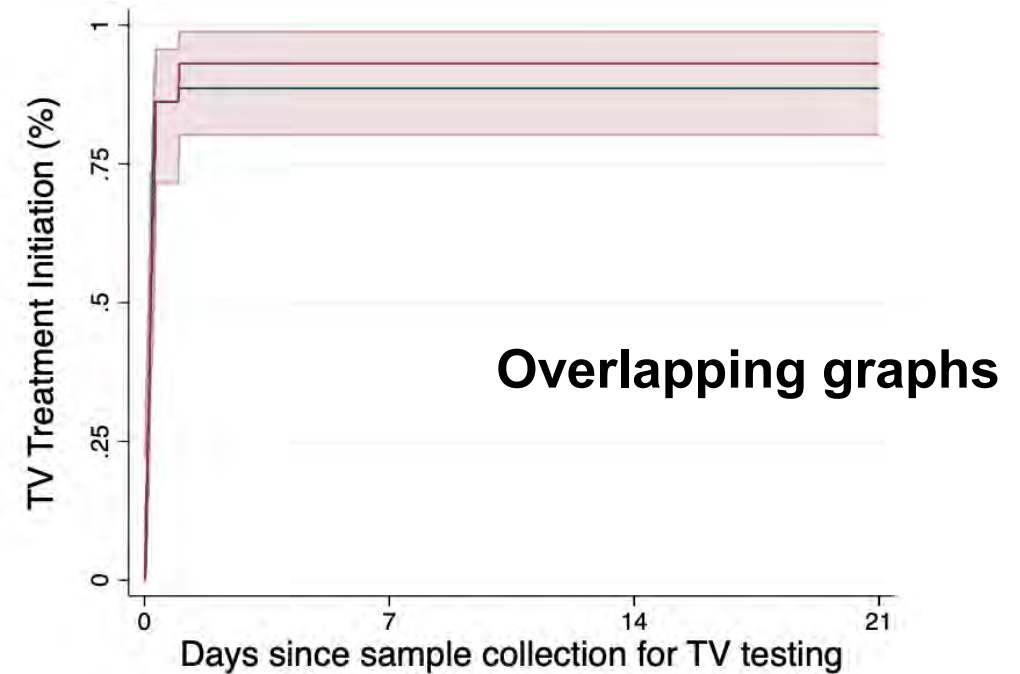
Impact of POC Testing vs Lab-based Testing on STI Management in a large HIV Vaccine Trial

NG/CT Treatment initiation: eThekwini clinic used POC testing



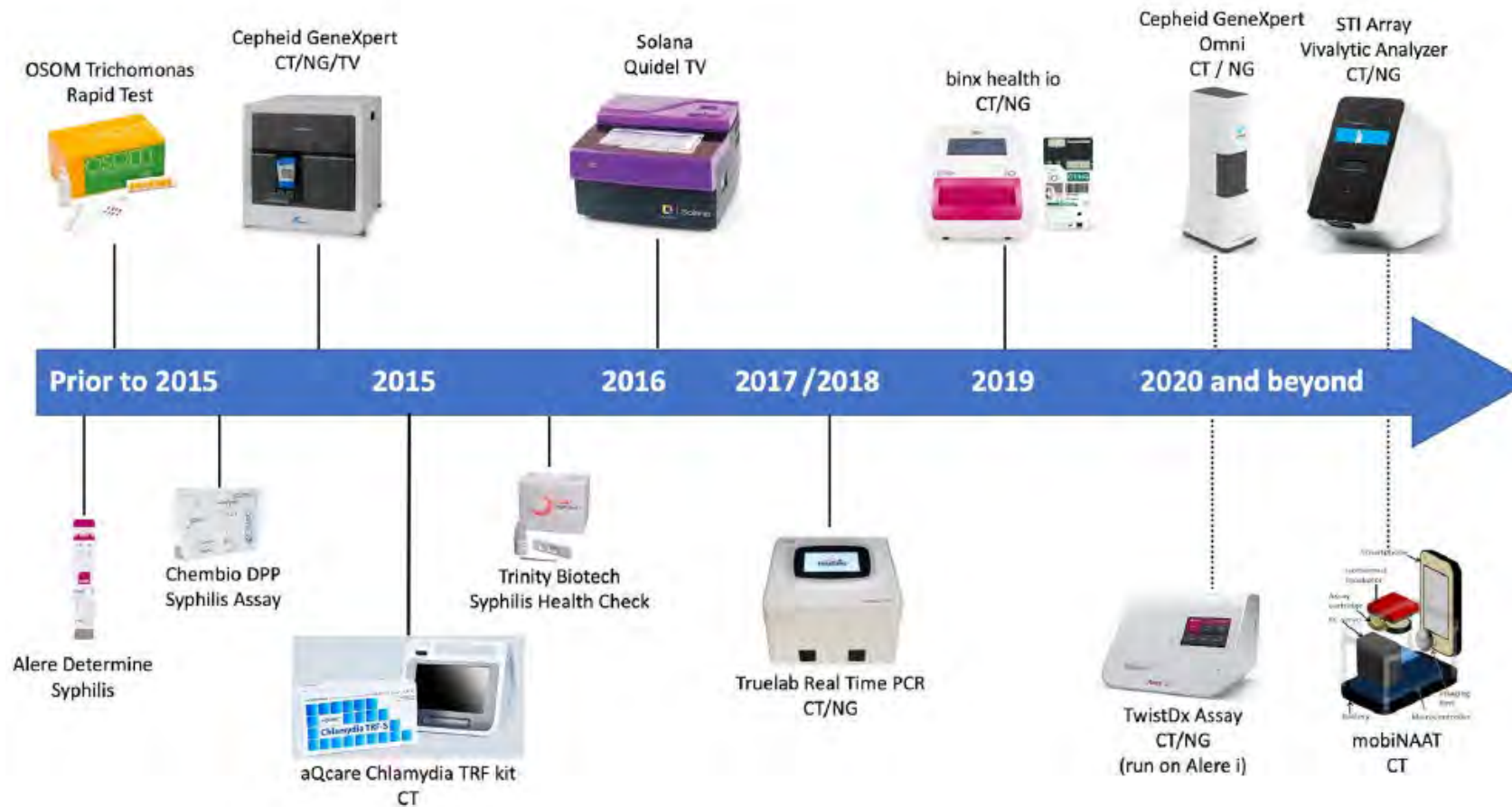
**39 times faster NG/CT Treatment initiation
at eThekwini vs Verulam-Isipingo aHR = 39.6, p < 0.001**

TV Treatment initiation: all clinics used POC testing



**Fast TV Treatment initiation at all clinics
AHR = 0.9, p = 0.770**

Pipeline of Point-of-care STI assays



Key features:

- Accurate
- Fast turnaround time
- Simple to operate
- Affordable

New STI Guidelines and NSP STI Policy

Southern African Journal of HIV Medicine
ISSN: (Online) 2078-6751, (Print) 1608-9693

Page 1 of 12 | Guideline

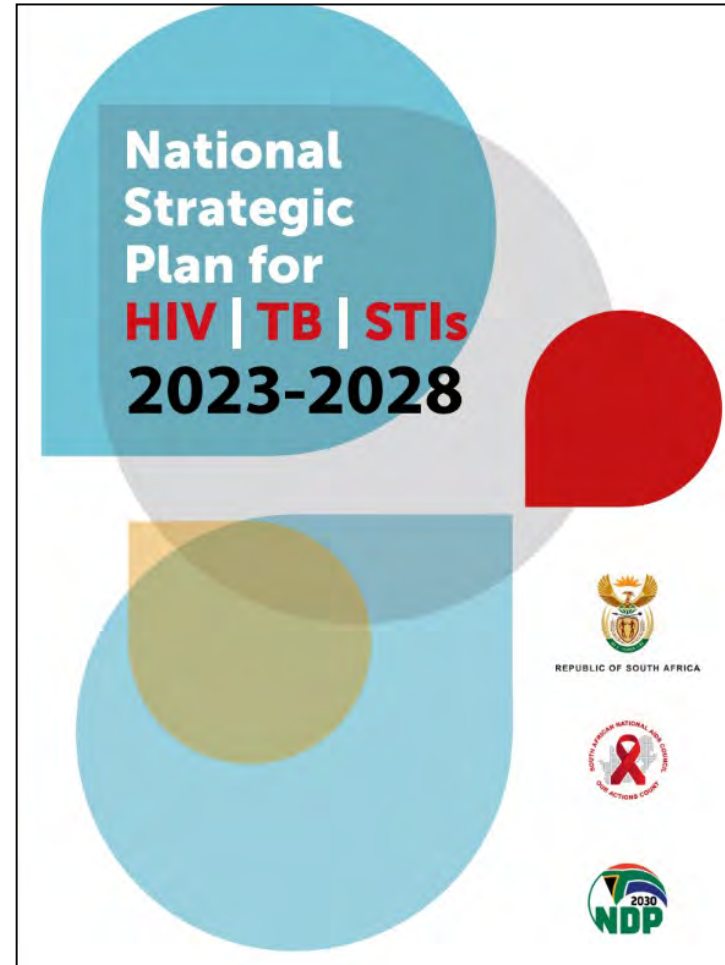
Southern African HIV Clinicians Society 2022 guideline for the management of sexually transmitted infections: Moving towards best practice

Authors:
 Ramona K.H. Peters^{1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22,23,24,25,26,27,28,29,30,31,32,33,34,35,36,37,38,39,40,41,42,43,44,45,46,47,48,49,50,51,52,53,54,55,56,57,58,59,60,61,62,63,64,65,66,67,68,69,70,71,72,73,74,75,76,77,78,79,80,81,82,83,84,85,86,87,88,89,90,91,92,93,94,95,96,97,98,99,100}
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<http://www.sajhivmed.org.za> | Open Access



- HIV Clinicians Society New STI guidelines
- NSP now includes specific objectives and targets for:
 - common STIs
 - HPV prevention and treatment
 - Hepatitis B and C prevention and treatment

WHO STI Vaccine Roadmap

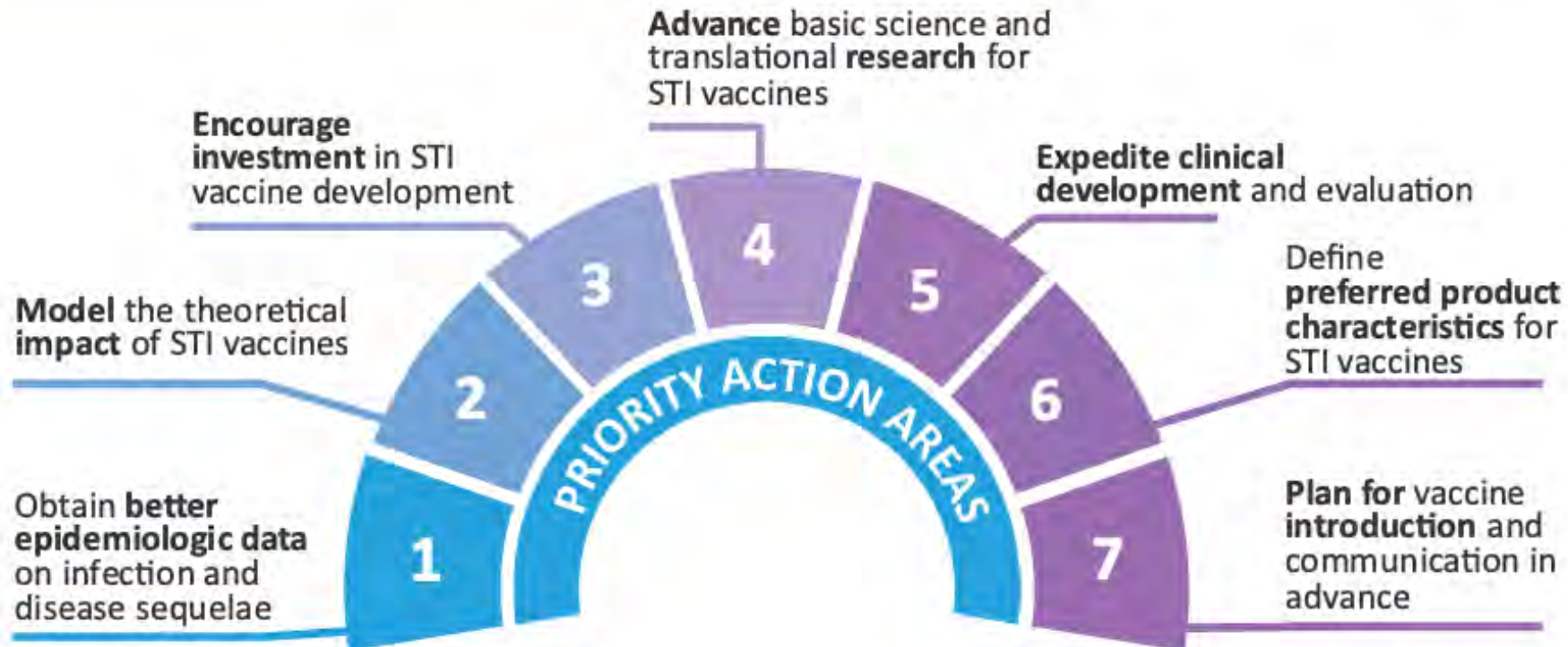
STI Vaccine Roadmap: Priority Action Areas



World Health
Organization



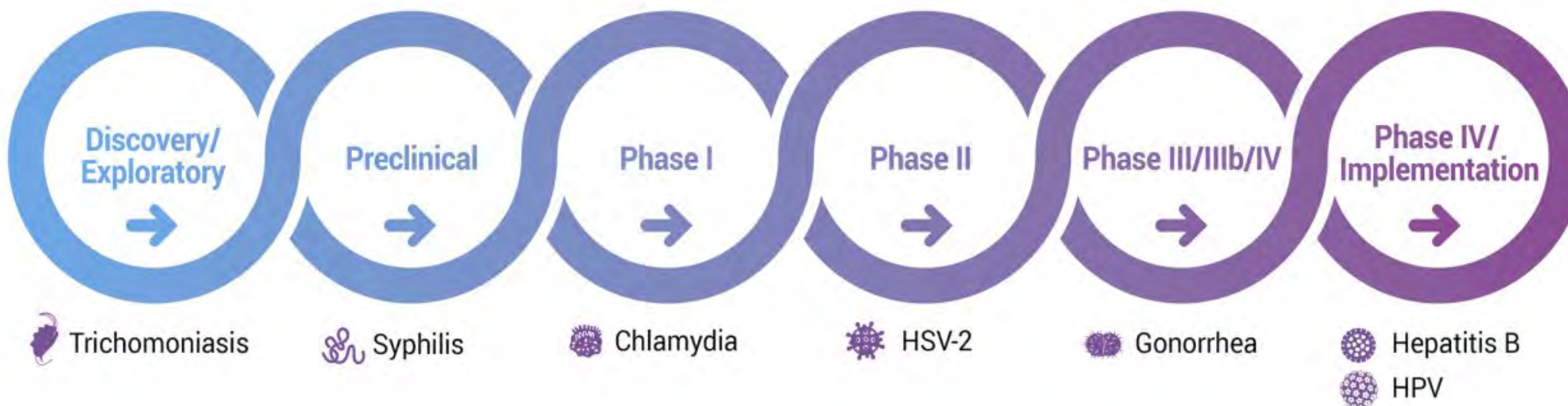
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STI Vaccine Development Pipeline

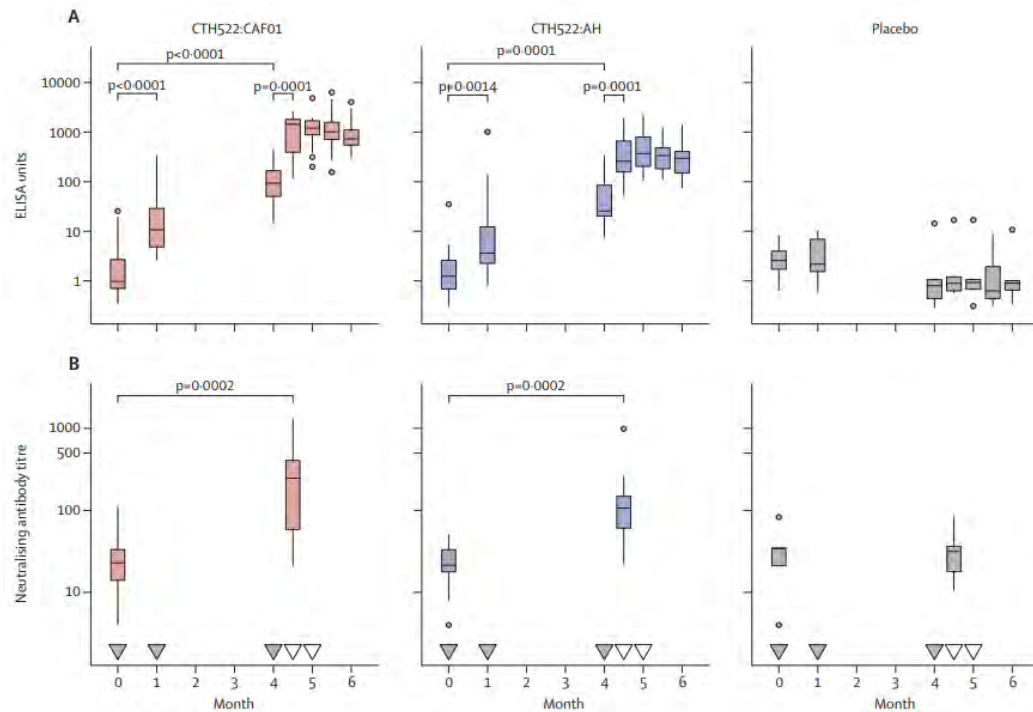
Current Status of Vaccine Development



Chlamydia Vaccine Development

Safety and immunogenicity of the chlamydia vaccine candidate CTH522 adjuvanted with CAF01 liposomes or aluminium hydroxide: a first-in-human, randomised, double-blind, placebo-controlled, phase 1 trial

Sonya Abraham*, Helene B Juel*, Peter Bang, Hannah M Cheeseman, Rebecca B Dohn, Tom Cole, Max P Kristiansen, Karen S Korsholm, David Lewis, Anja W Olsen, Leon R McFarlane, Suzanne Day, Sara Knudsen, Kjersti Moen, Morten Ruhwald, Ingrid Kromann, Peter Andersen, Robin J Shattock, Frank Follmann



Vaccines induced anti-CTH522 IgG antibodies in all participants after 5 immunisations

Imperial College London
First vaccine for chlamydia shows promise in early trials
CHLAMYDIA VACCINE HOPE - The first ever early clinical trial for a vaccine for genital chlamydia has shown it to be safe and effective at...
Aug 12, 2019

SN Science News
The first chlamydia vaccine has passed a major test
A clinical trial for a vaccine against the sexually transmitted disease found that the product provoked an immune response.
Aug 15, 2019

People
Chlamydia Vaccine Trial Proves to Be an Early Success: 'The Findings Are Encouraging'
The British and Danish scientists who conducted the study are hoping a vaccine for Chlamydia will become as prevalent as the one for HPV.
Aug 13, 2019

The Guardian
Chlamydia vaccine moves a step closer
Pioneering clinical trial raises hopes of cure for 'hidden' sexually transmitted infection.
Aug 12, 2019

Potential Impact of a Chlamydia Vaccine

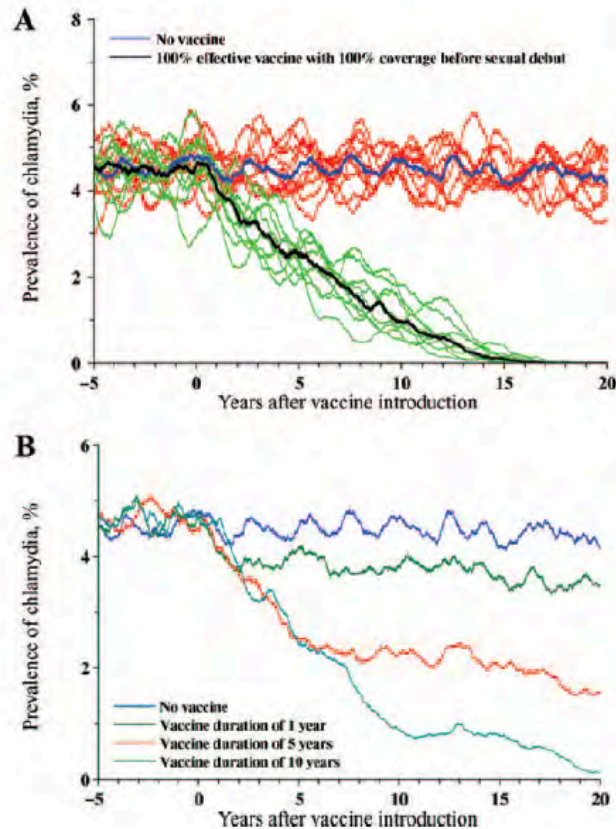


Figure 1. A, Prevalence of chlamydia infection in a heterosexual population as a function of time, indicating the impact of a 100% protective vaccine. All model simulations are shown for 100% vaccine coverage before sexual debut (green with median in black), compared with the baseline scenario of no vaccine (red with median in blue). B, Prevalence of chlamydia infection as a function of time for vaccines that wane after a finite duration of 1, 5, or 10 years.

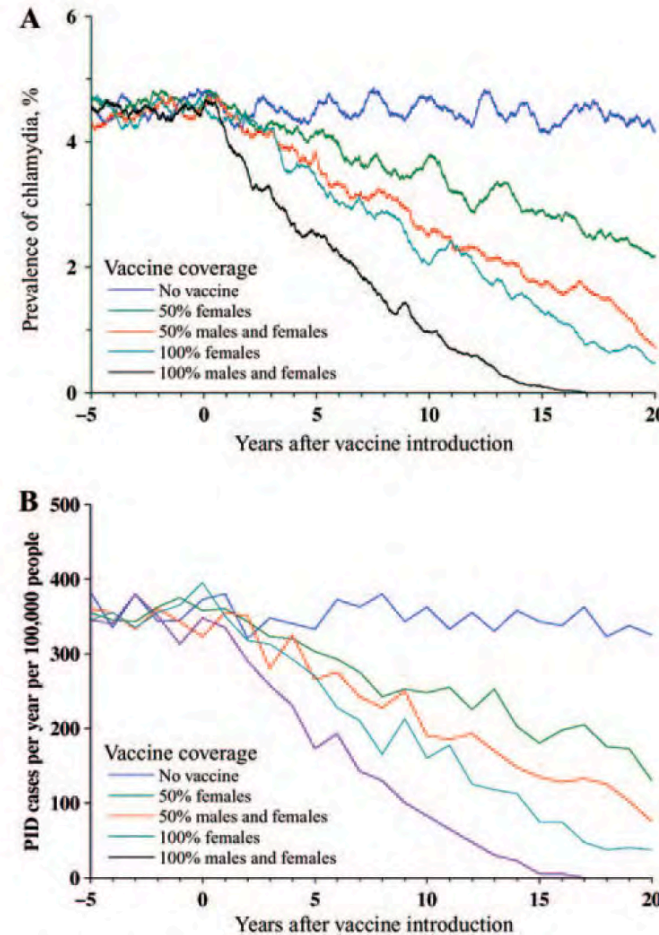


Figure 2. Effects of different male and female coverage rates before sexual debut on the prevalence of chlamydia infection (A) and the incidence of pelvic inflammatory disease (PID) (B) for a 100% protective vaccine. Results are median values for 10 model simulations. The results for 100% coverage of males and females are the same as in figure 1.

Modeling the Impact of Potential Vaccines on Epidemics of Sexually Transmitted *Chlamydia trachomatis* Infection

Richard T. Gray,¹ Kenneth W. Beagley,² Peter Timms,² and David P. Wilson¹

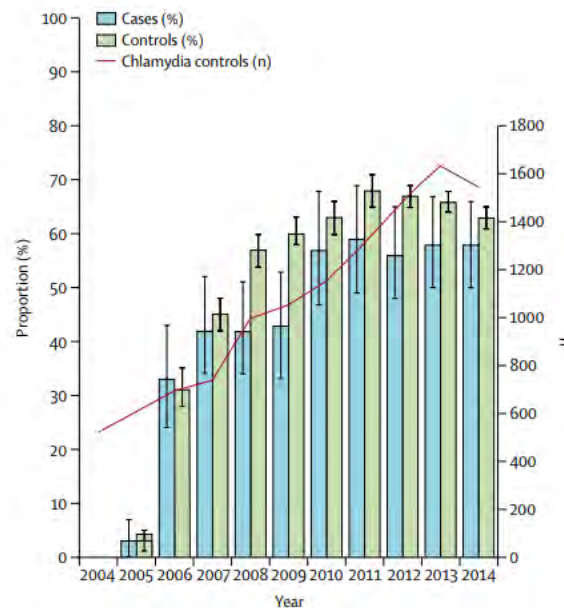
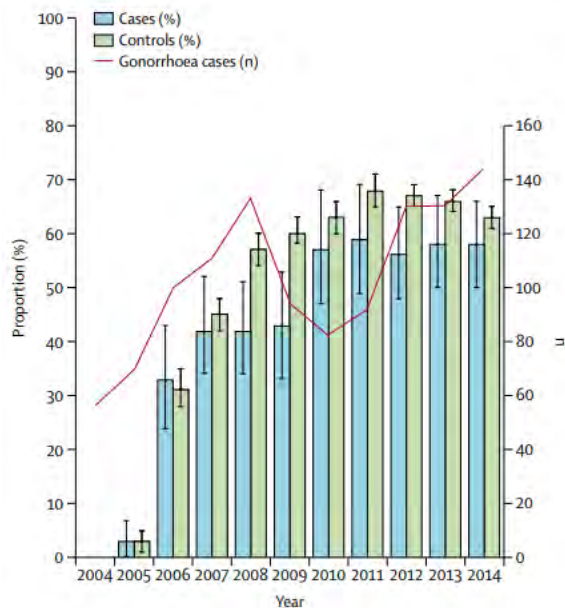
¹National Centre in HIV Epidemiology and Clinical Research, Faculty of Medicine, University of New South Wales, Sydney, and ²Institute of Health and Biomedical Innovation, Queensland University of Technology, Kelvin Grove, Brisbane, Australia

Gray RT, et al. *J Infect Dis.* 2009 Jun 1;199(11):1680-8

Meningococcal B Vaccine and Gonorrhoea

Effectiveness of a group B outer membrane vesicle meningococcal vaccine against gonorrhoea in New Zealand: a retrospective case-control study

Helen Petousis-Harris, Janine Paynter, Jane Morgan, Peter Saxton, Barbara McArdle, Felicity Goodyear-Smith, Steven Black



Helen Petousis-Harris, et al. *Lancet*. 2017 Sep 30;390(10102):1603-1610

News

Meningitis vaccine could protect against gonorrhoea, studies find

BMJ 2022 ; 377 doi: <https://doi.org/10.1136/bmj.o997> (Published 19 April 2022)

Cite this as: *BMJ* 2022;377:o997

JOURNAL ARTICLE

Prevention of *Neisseria gonorrhoeae* With Meningococcal B Vaccine: A Matched Cohort Study in Southern California

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Katia J Bruxvoort ✉, Joseph A Lewnard, Lie H Chen, Hung Fu Tseng, Jennifer Chang, Jennifer Veltman, Jeanne Mrazek, Lei Qian

Clinical Infectious Diseases, Volume 76, Issue 3, 1 February 2023, Pages e1341–e1349,

<https://doi.org/10.1093/cid/ciac436>

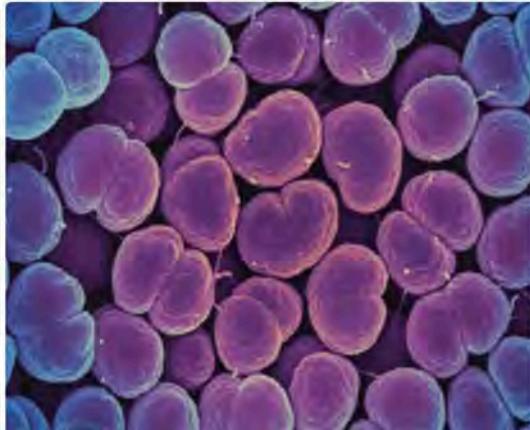
Published: 01 June 2022 [Article history](#) ▼

NIH Awards Will Advance Development of Vaccines for Sexually Transmitted Infections

NIAID Announces Four New Cooperative Research Centers

May 9, 2019

The National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health, today announced awards to establish four Cooperative Research Centers (CRCs) focused on developing vaccines to prevent sexually transmitted infections (STIs). The grants, totaling \$41.6 million over five years, will support collaborative, multidisciplinary research on the bacteria that cause syphilis, gonorrhea and chlamydia. At the end of the program, each center is expected to identify at least one candidate vaccine ready for testing in clinical trials.



[1 U19 AI144177-01](#) 

Awardee Organization: University of Connecticut School of Medicine, Farmington, Connecticut

Principal Investigator: Justin Radolf, M.D.

Focus: Syphilis

[1 U19 AI144180-01](#) 

Awardee Organization: Henry M. Jackson Foundation for the Advancement of Military Medicine, Bethesda, Maryland

Principal Investigator: Ann Jerse, Ph.D.

Focus: Gonorrhea

[1 U19 AI144182-01](#) 

Awardee Organization: Georgia State University, Atlanta, Georgia

Principal Investigator: Cynthia Nau Cornelissen, Ph.D.

Focus: Gonorrhea

[1 U19 AI144181-01](#) 

Awardee Organization: University of North Carolina Chapel Hill, Chapel Hill, North Carolina

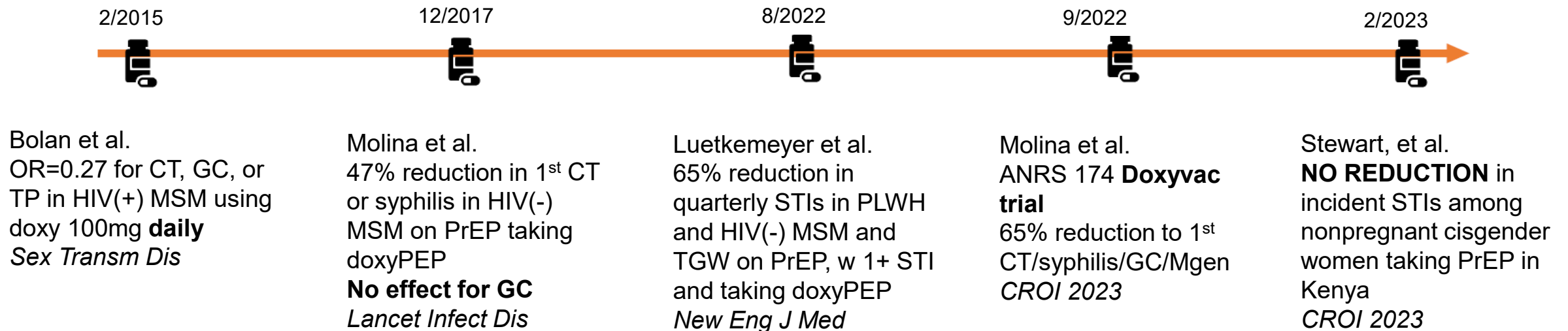
Principal Investigator: Toni Darville, M.D.

Focus: Chlamydia

Use of doxycycline as prophylaxis against bacterial STIs

Two options studied:

DoxyPrEP	DoxyPEP
Doxycycline as pre -exposure prophylaxis for bacterial STIs	Doxycycline as post -exposure prophylaxis for bacterial STIs 24–72 hours after condomless sex



The case for and against DoxyPEP

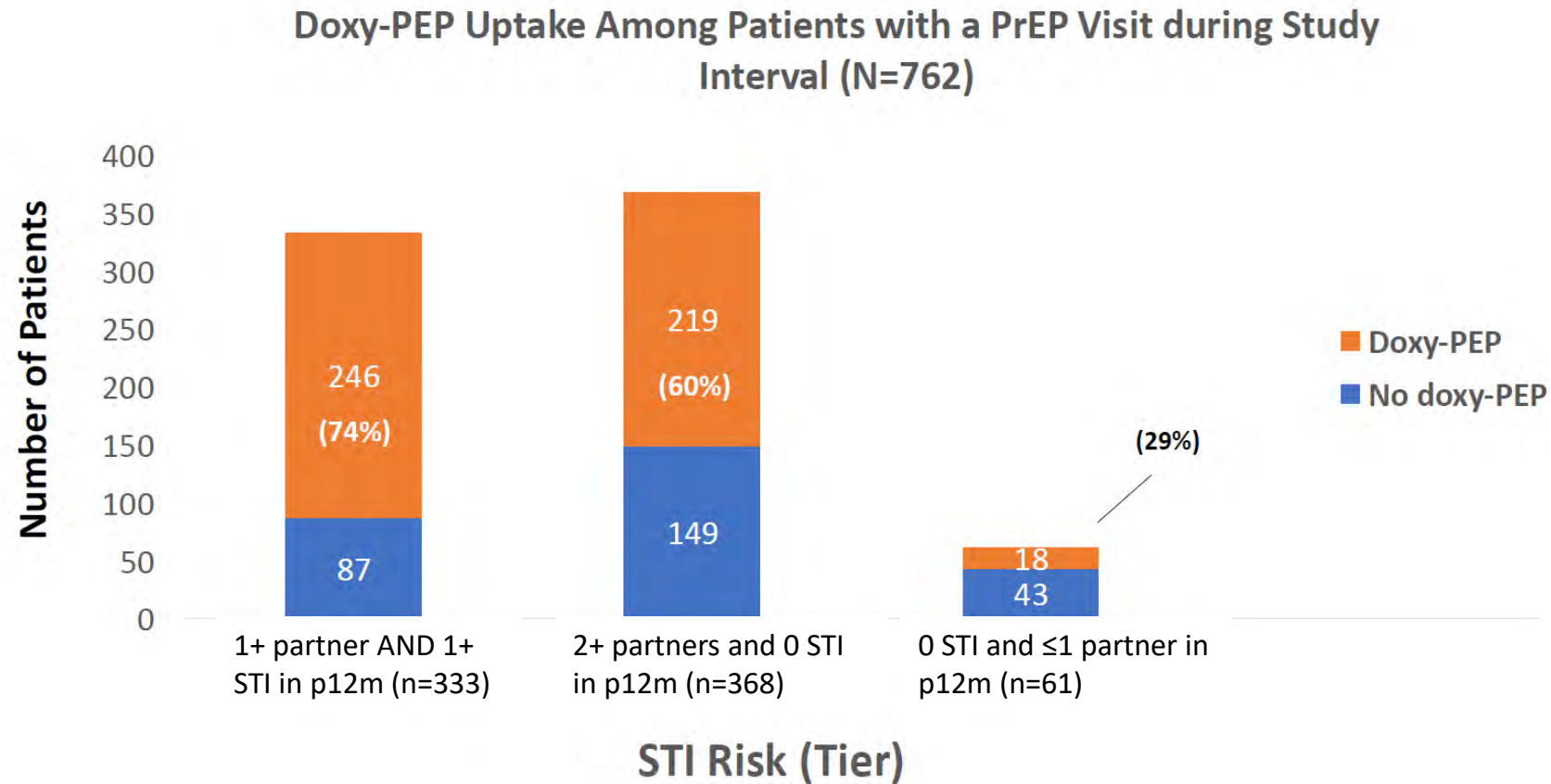
For

- Effective in studies with **MSM populations**
- Doxycycline generally **well tolerated**
- **High rates of STIs among persons on HIV PrEP** = opportunity for targeted intervention
- Persons on HIV PrEP want **access** to doxyPEP

Against

- **? Not effective among cisgender women** (?anatomy, resistance, adherence)
- Could promote **antimicrobial resistance**
- **Limited data** available from RCTs
- If bundled with HIV PrEP use, **low use among heterosexual men and women** may limit potential impact

Real-world doxyPEP uptake – San Francisco



Bacon et al., STI & HIV 2023 World Congress, Chicago, IL, USA, July 2023

- Unacceptably high burden of STIs – urgent need for low-cost diagnostic care solutions in Southern Africa
- Drive development of POC technology for faster, accurate and affordable solutions
- Rapidly evaluate STI vaccine products – if effective against STIs, these trials could have HIV incidence endpoints
- Urgently assess reasons for DoxyPEP limitations among cisgender women
- Engage stakeholders and communities to re-energize STI research and implement solutions

Acknowledgement

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- Anne Rompalo, Adrian Mindel and the CAPRISA 083 participants and study team
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- Many others