Strategies to achieve STI control in South Africa

Prof Remco Peters

4th South African HIV Clinicians Society Conference

27th of October 2018

PEPFAR USAID FROM THE AMERICAN PEOPLE ANOVA HEALTH INSTITUTE UNIVERSITEIT VAN PRETORIA UNIVERSITY OF PRETORIA YUNIBESITHI YA PRETORIA Maastricht UMC+

The spectrum of STIs

This presentation has been slightly amended to take some of the preliminary data and photographs shown in this talk. Please do not hesitate to contact me should you require further detail

Many thanks

Remco Peters

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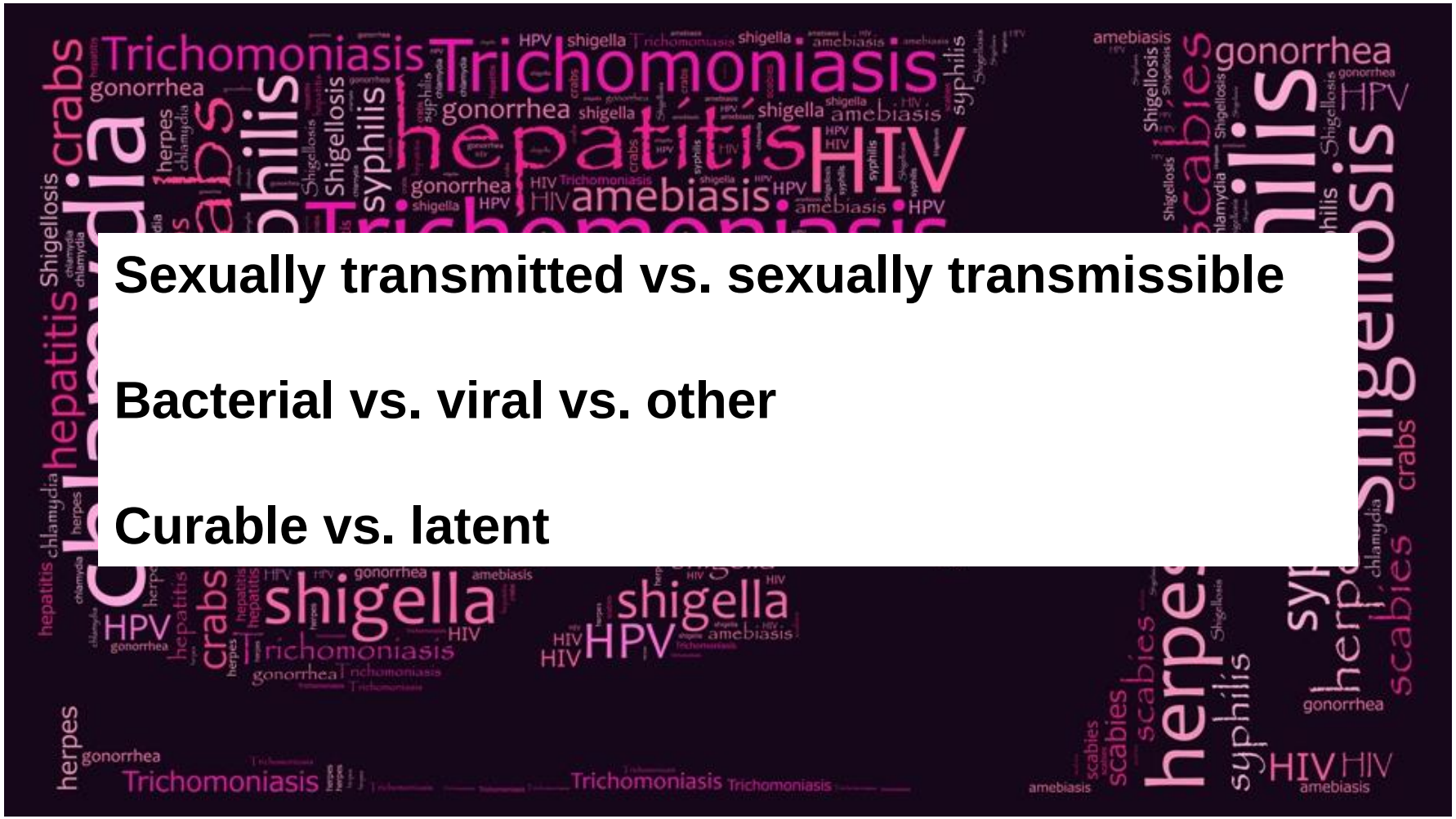
The spectrum of STIs



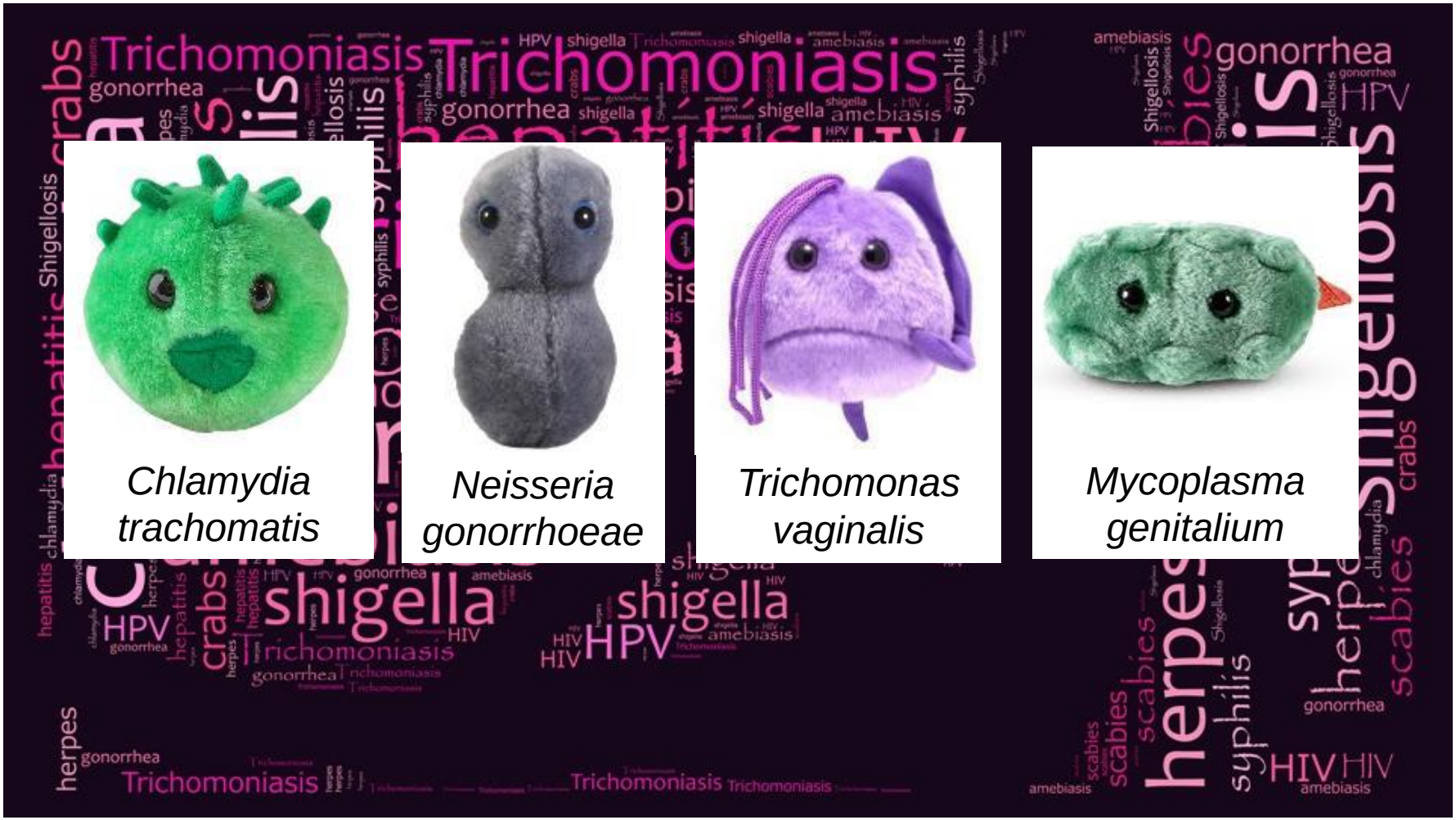
Sexually transmitted vs. sexually transmissible

Bacterial vs. viral vs. other

Curable vs. latent

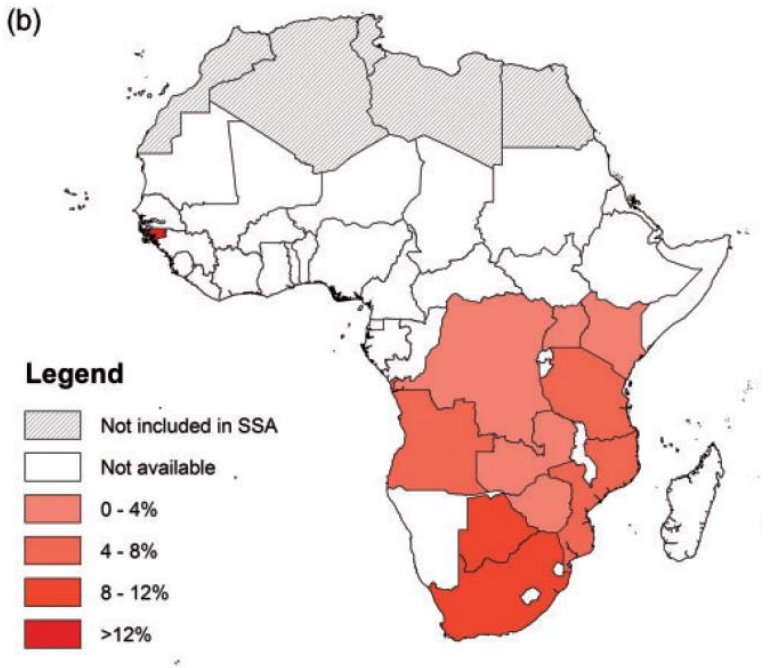
Source: thewellproject

The spectrum of STIs

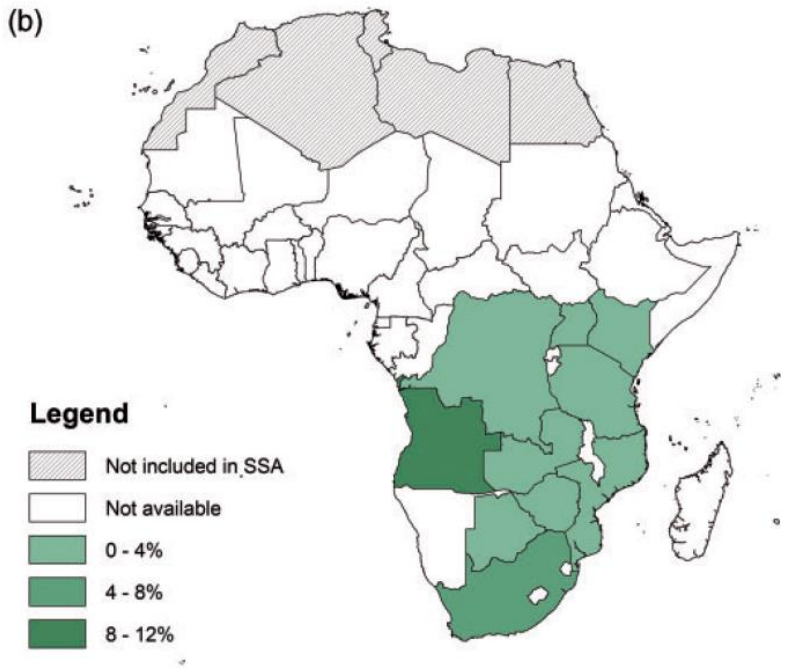


Source: thewellproject

Prevalence of STIs in women



Chlamydia trachomatis
6.0% (4.2% - 8.4%)

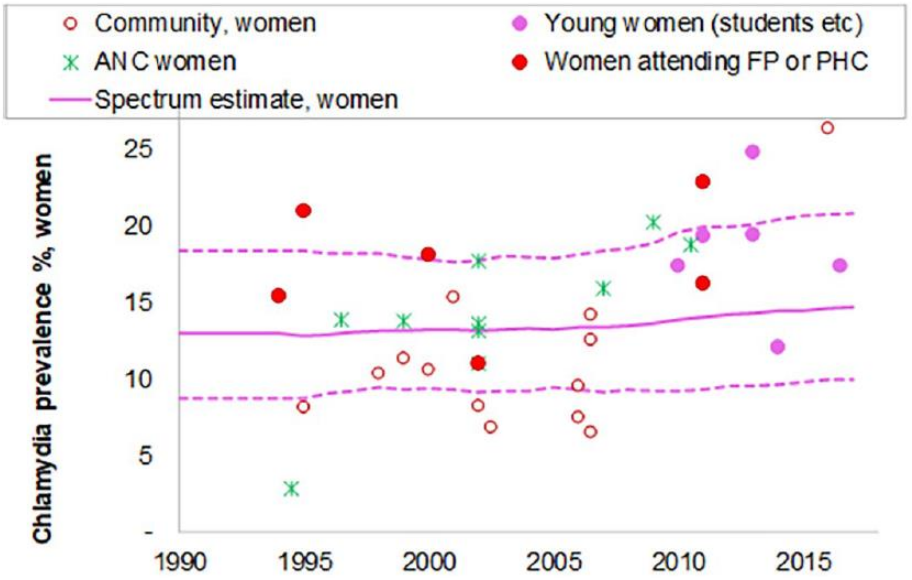


Neisseria gonorrhoeae
4.2% (3.2% - 5.6%)

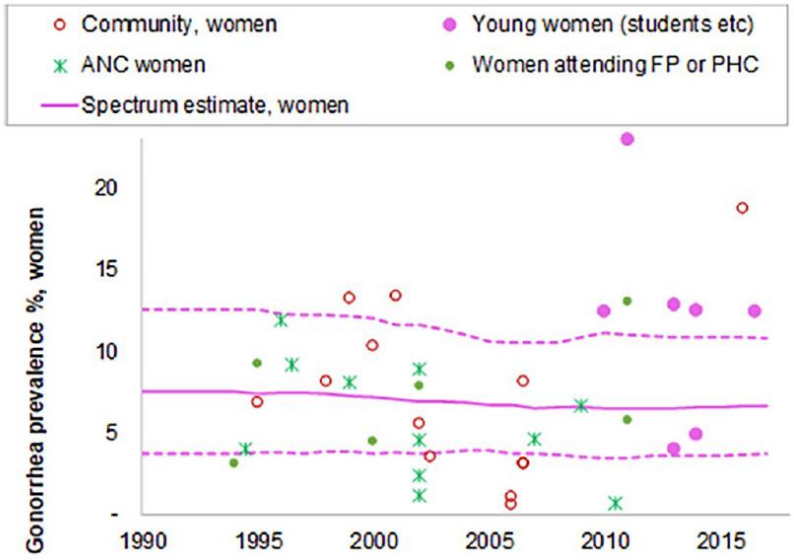
- Weighted prevalence in facility-based studies is high
- South Africa is among the highest..

Dubbink JH *et al*. Int J STD AIDS 2018

Prevalence of STIs in South Africa



Chlamydia trachomatis

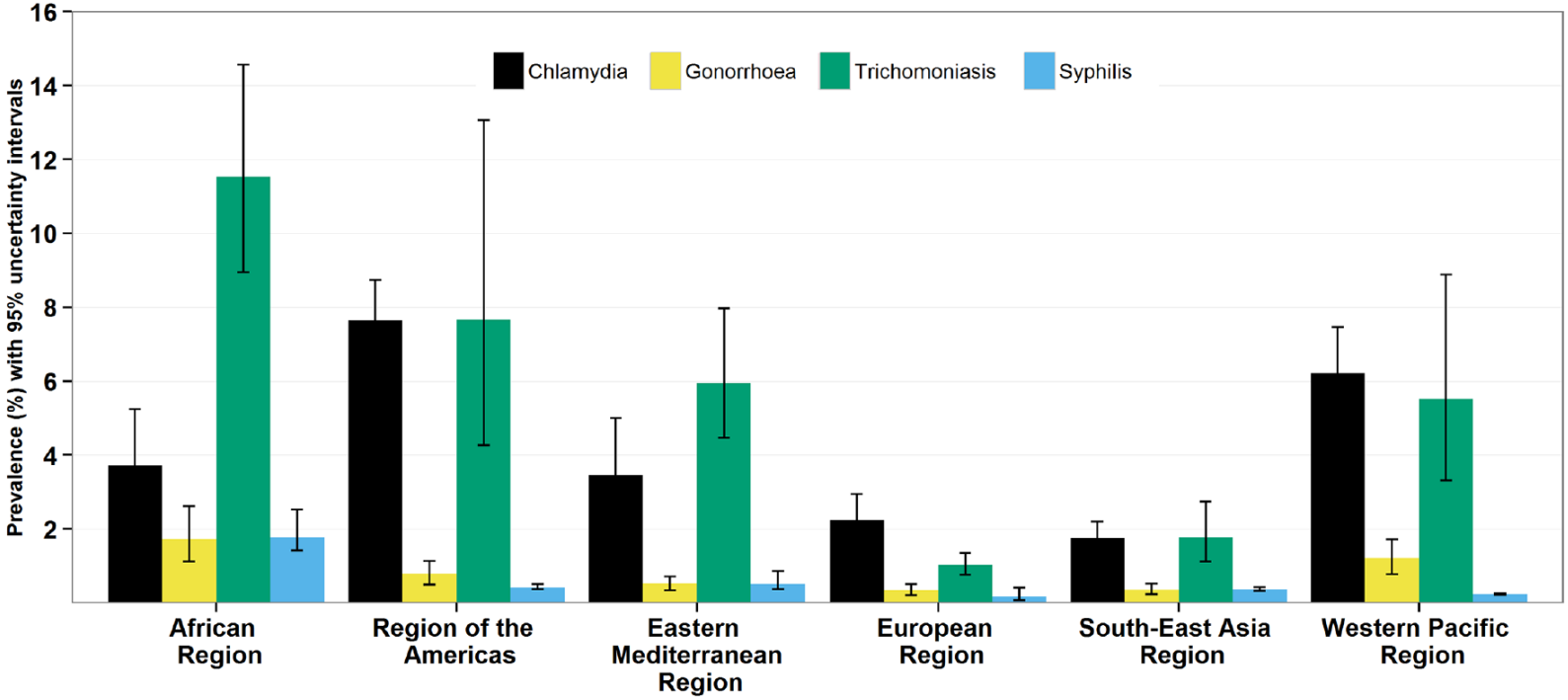


Neisseria gonorrhoeae

- Spectrum-STI model shows a high prevalence of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* over time
- Similar trend at slightly lower prevalence in men

Kularatne RS et al. PLOS One 2018

Prevalence of STIs in South Africa



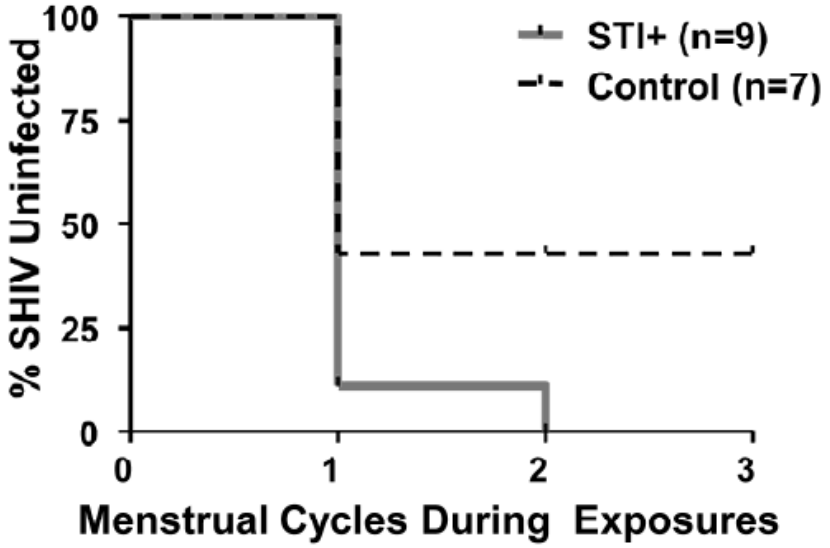
- *Trichomonas vaginalis* the most prevalent STI globally
- *Mycoplasma genitalium* prevalence generally in a fairly similar range to that of *Chlamydia trachomatis*

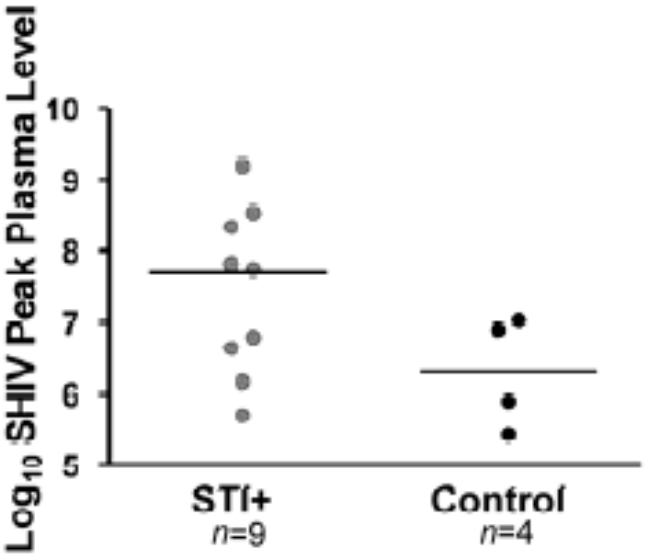
Newman L *et al*. PLOS One 2015

Why is STI control essential?

- Reproductive tract complications (PID, EUG)
- Tubal factor infertility
- Adverse pregnancy outcomes
- Neonatal infections
- Facilitation of HIV acquisition and transmission
- Affect sexual health and pleasure
- Psychosocial effects

STIs & HIV acquisition

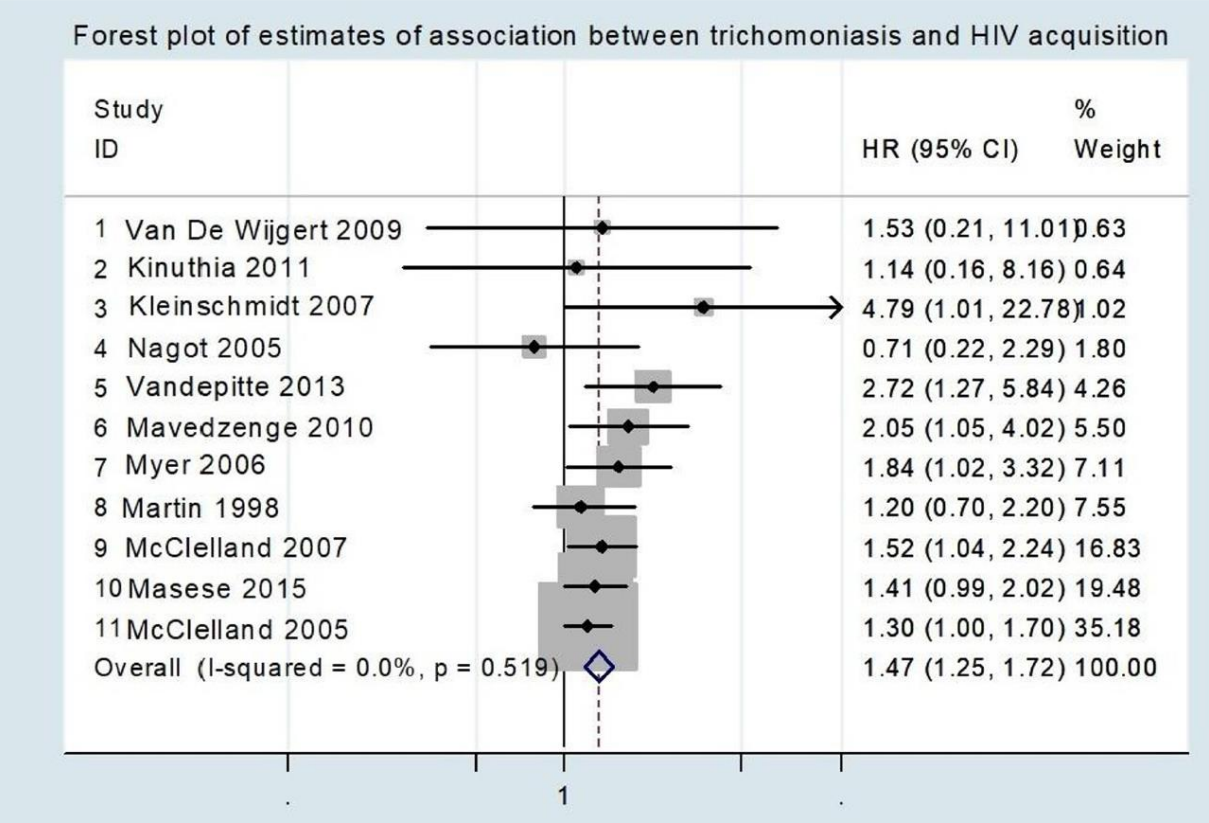




- Biologically plausible effect in pigtail macaques of coinfection by *C. trachomatis* with *T. vaginalis* on HIV acquisition and SHIV load

Henning T *et al*. J Infect Dis 2014

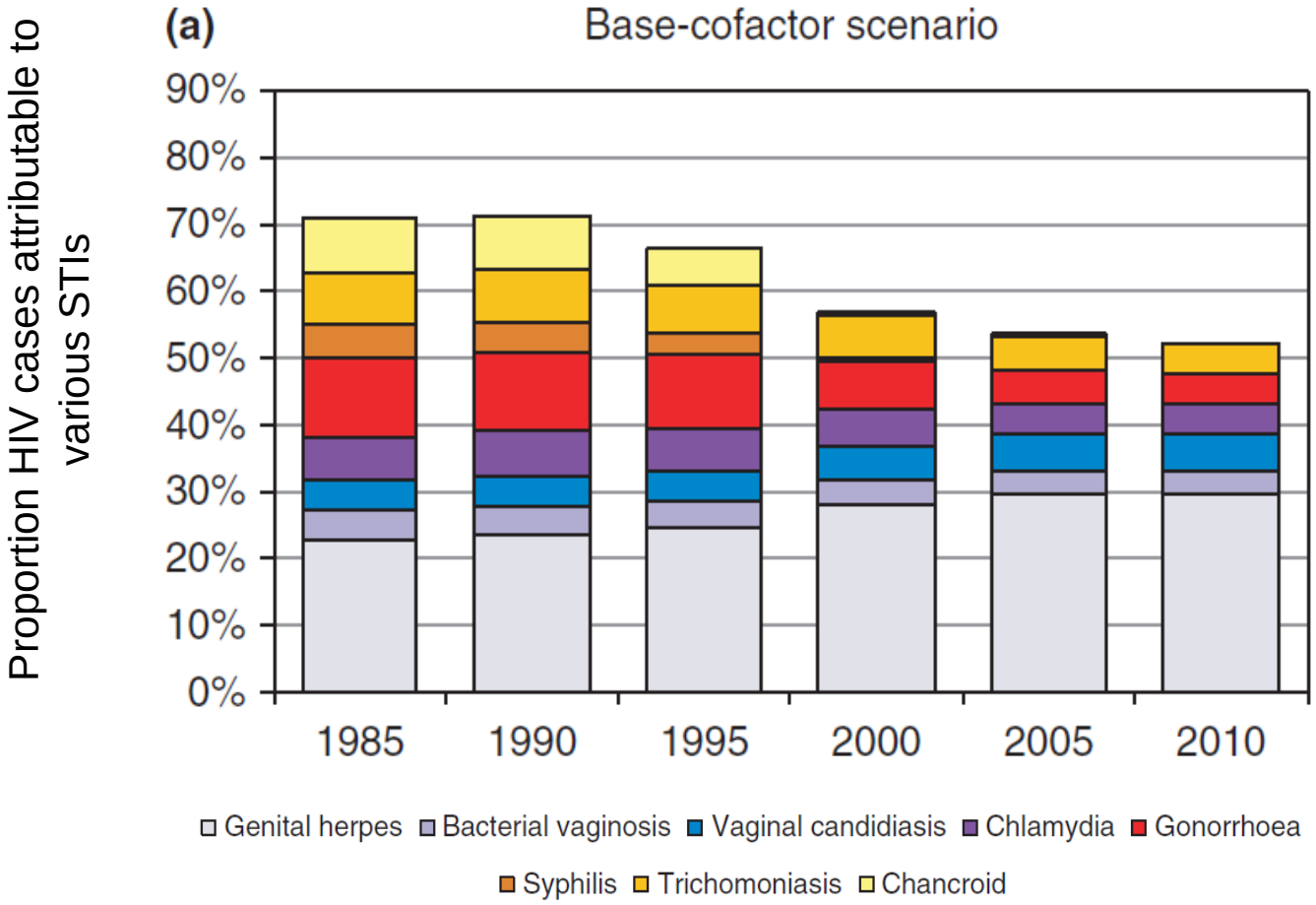
STIs & HIV acquisition



- *Trichomonas vaginalis* infection: 1.5 times more likely to acquire HIV

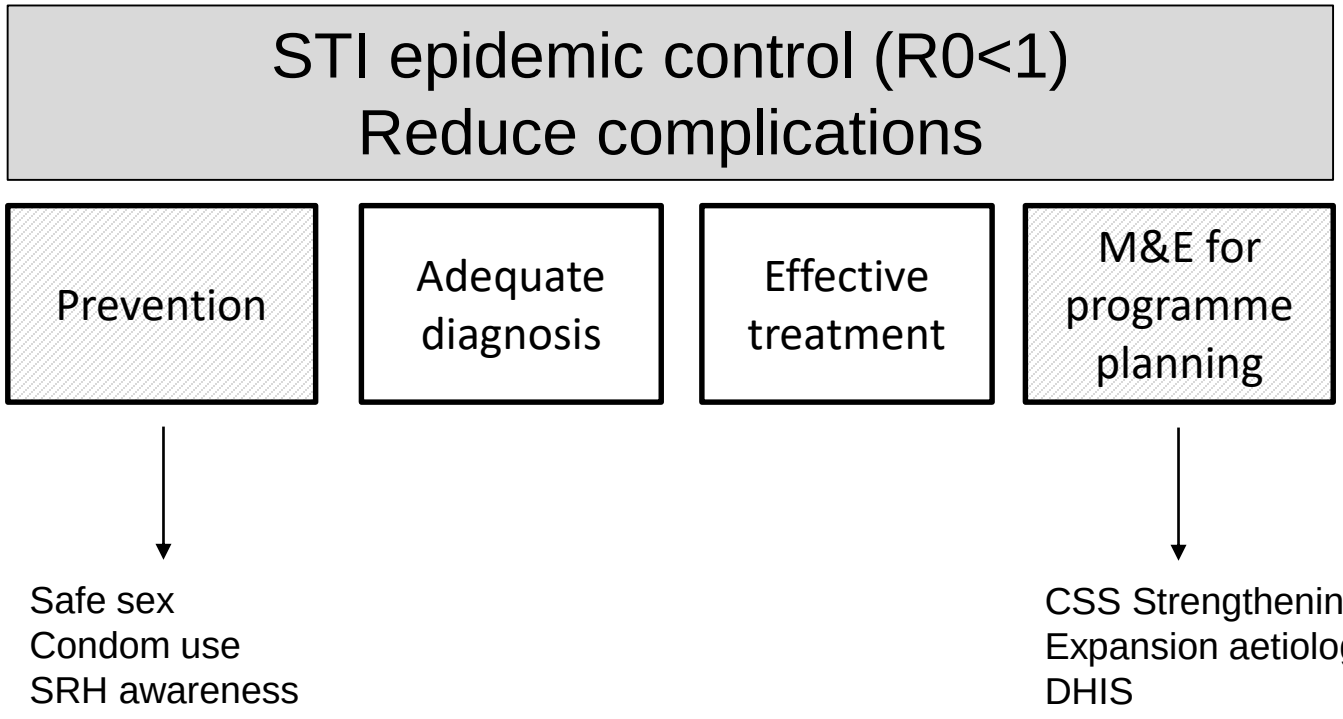
Masha CS *et al*. Sex Transm Infect 2018

STIs & HIV acquisition

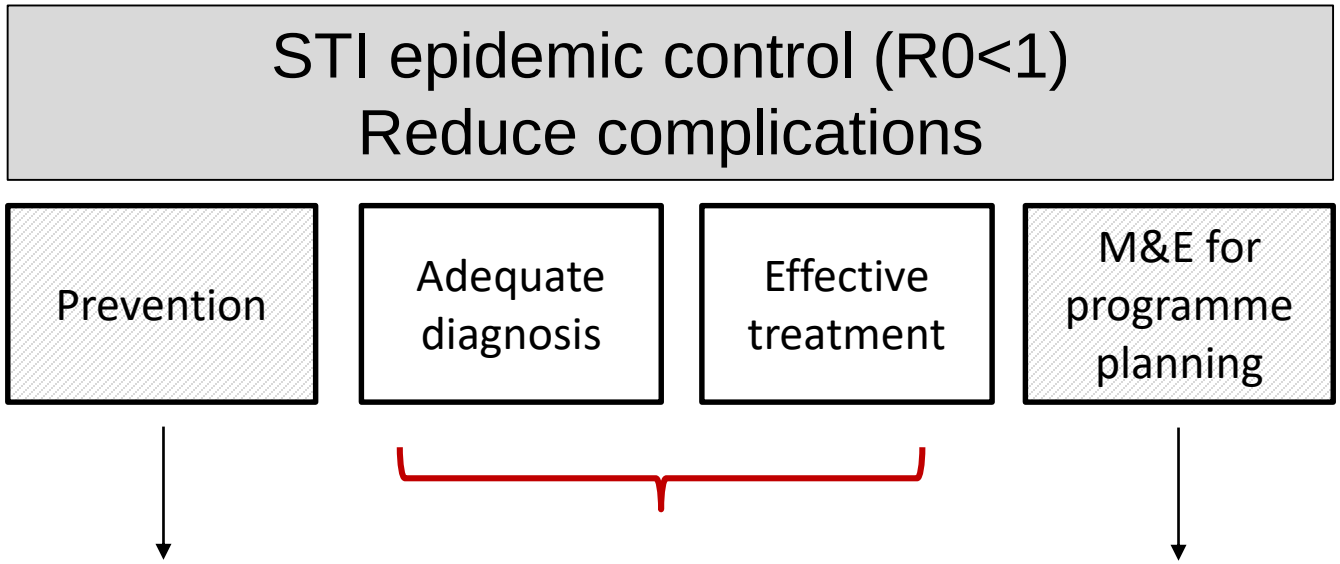


Johnson LF *et al*. Trop Med Int Health 2012

Components of STI control



Components of STI control



Safe sex
Condom use
SRH awareness

"Getting the basics right"

Syndromic vs. aetiological approach

CSS Strengthening
Expansion aetiological surveillance
DHIS

Access to services

- Provision of routine (to all patients) STI services in a mobile clinic in rural Mopani District, Limpopo

Hoffman C *et al*. In press

Access to services

Table 2. Microbiological detection of sexually transmitted infections in women visiting the Mobile Clinic in Mopani district, South Africa

	Total no. of women (%) (n = 251)	No. of symptomatic* women (%) (n = 81)	No. of asymptomatic women (%) (n = 170)
Sexually transmitted infection	133 (53)	49 (60)	84 (49)
Chlamydia trachomatis	52 (21)	19 (24)	33 (19)
Neisseria gonorrhoeae	39 (16)	12 (15)	27 (16)
Trichomonas vaginalis	81 (32)	31 (38)	50 (29)
Mycoplasma genitalium	21 (8)	11 (14)	10 (6)
Other reproductive tract infection	38 (15)	38 (47)	-
Bacterial vaginosis	34 (14)	34 (42)	-
Candida albicans	6 (2)	6 (7)	-
No reproductive tract infection detected	106 (42)	20 (25)	86 (51)

*Vaginal discharge, dysuria and/or genital itch, according to the vaginal discharge syndrome management guidelines of South Africa.

- More than half of all women diagnosed with STI

Hoffman C *et al*. In press

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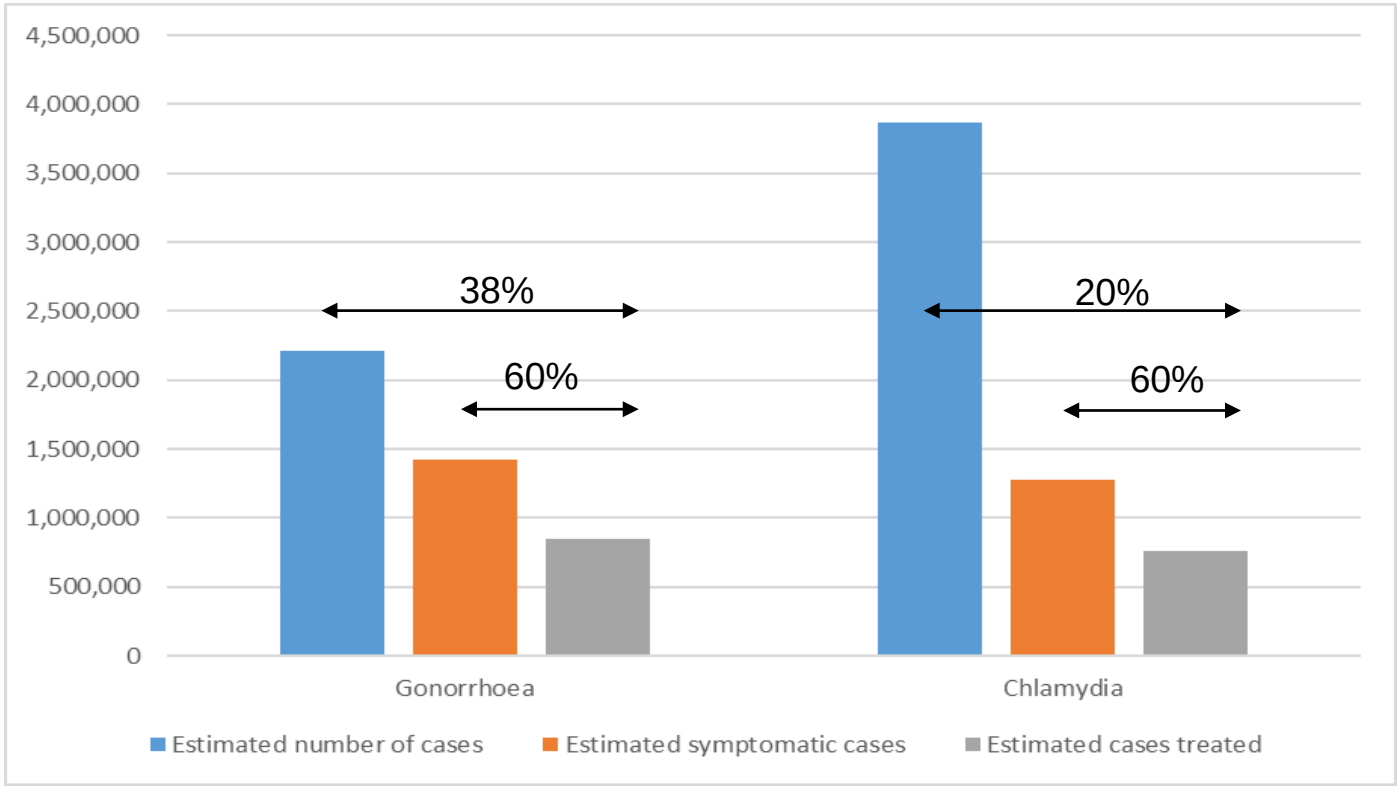
- One-third of all women symptomatic, but untreated
- Even 50% of asymptomatic women has an STI

Hoffman C *et al*. In press

Access to services



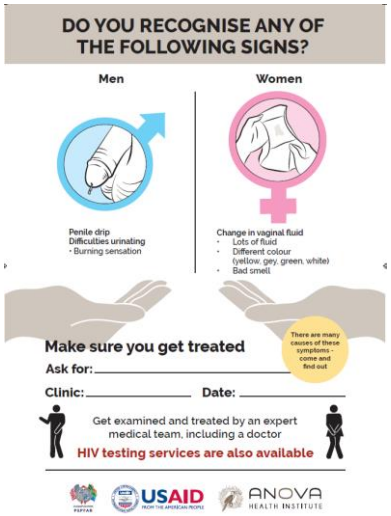
- Spectrum-STI model also suggests large unmet need: less than half of the cases is treated

Modified from Kularatne *et al*. PLOS One 2018

Community mobilisation for STI care

- Mobilising the unmet need in four villages and two townships in rural Mopani District

	Women	Men
Population reached	36,614	27,786
Number of individuals mobilised	134	43
Proportion with untreated symptoms	0,37%	0,15%
	1:275	1:650



Hoffman C *et al*. In preparation

Access to services

	Women (n = 134)	Men (n = 43)	*p*-value
Patient knowledge & beliefs	64 (49)	16 (37)	0.29
Not aware of symptoms	50 (37)	10 (23)	
Clinic is too far / no money to visit	2 (2)	2 (5)	
Embarrassed or afraid of reaction clinic staff	10 (8)	1 (3)	
Traditional beliefs	0 (0)	3 (7)	
Partner does not allow	2 (2)	0 (0)	
Healthcare service-related	14 (11)	14 (33)	**<0.01**
Disappointed with health services previously	14 (10)	4 (9)	
Lack of male healthcare workers	0	9 (21)	
Do not trust clinic staff	0 (0)	1 (2)	
Disappointed with effect of previous treatment	54 (41)	13 (30)	0.28
Persistent symptoms after treatment	35 (26)	6 (14)	
Recurrent symptoms after treatment	19 (14)	7 (16)	

Hoffman C *et al*. In preparation

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Quality of STI services

- 195 Standard Patient (SP) visits at 50 Clinical Sentinel Surveillance sites in South Africa
- How about other facilities? And the private sector?

Table 3 Weighted proportions of SP actors reporting receipt of STI services in South African public health facilities, 2014

Services provided to SP actors	Total % (95% CI)	Men % (95% CI)	Women % (95% CI)
Delivery of STI services			
Offered a physical genital exam	50.2 (36.2 to 64.3)	43.4 (27.6 to 60.8)	56.9 (41.1 to 71.3)
Treatment consistent with national guidelines*	60.7 (49.1 to 71.3)	70.7 (54.8 to 82.8)	50.9 (38.7 to 63.0)
Received ≥1 condom*	31.4 (21.3 to 43.8)	37.2 (23.0 to 54.0)	25.8 (16.0 to 38.9)
Partner notification slip or counselling*	70.2 (61.5 to 77.6)	79.9 (69.0 to 87.7)	60.6 (48.1 to 71.9)
Provided counselling about safer sex	62.5 (49.4 to 74.0)	70.9 (54.7 to 83.1)	54.2 (37.9 to 69.7)

Kohler PK *et al*. Sex Transm Dis 2017

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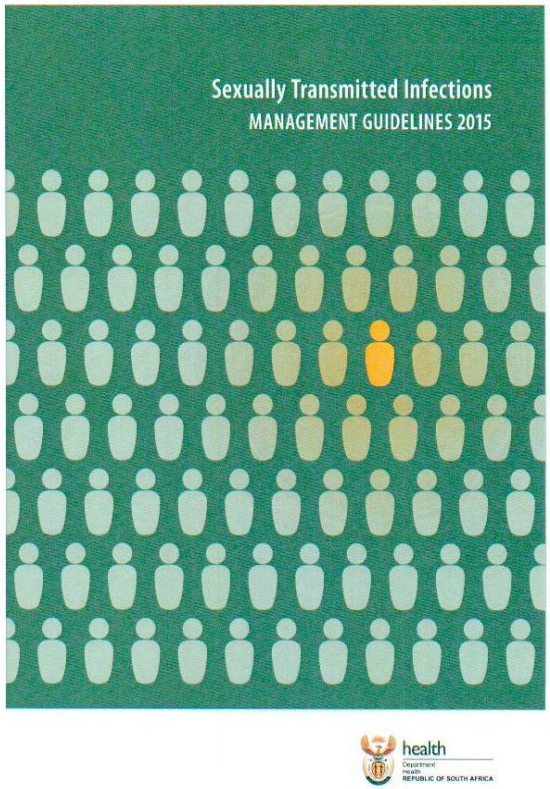
Provided counselling about safer sex	62.5 (49.4 to 74.0)	70.9 (54.7 to 83.1)	54.2 (37.9 to 69.7)

Kohler PK *et al*. Sex Transm Dis 2017

Syndromic management



Vaginal discharge syndrome

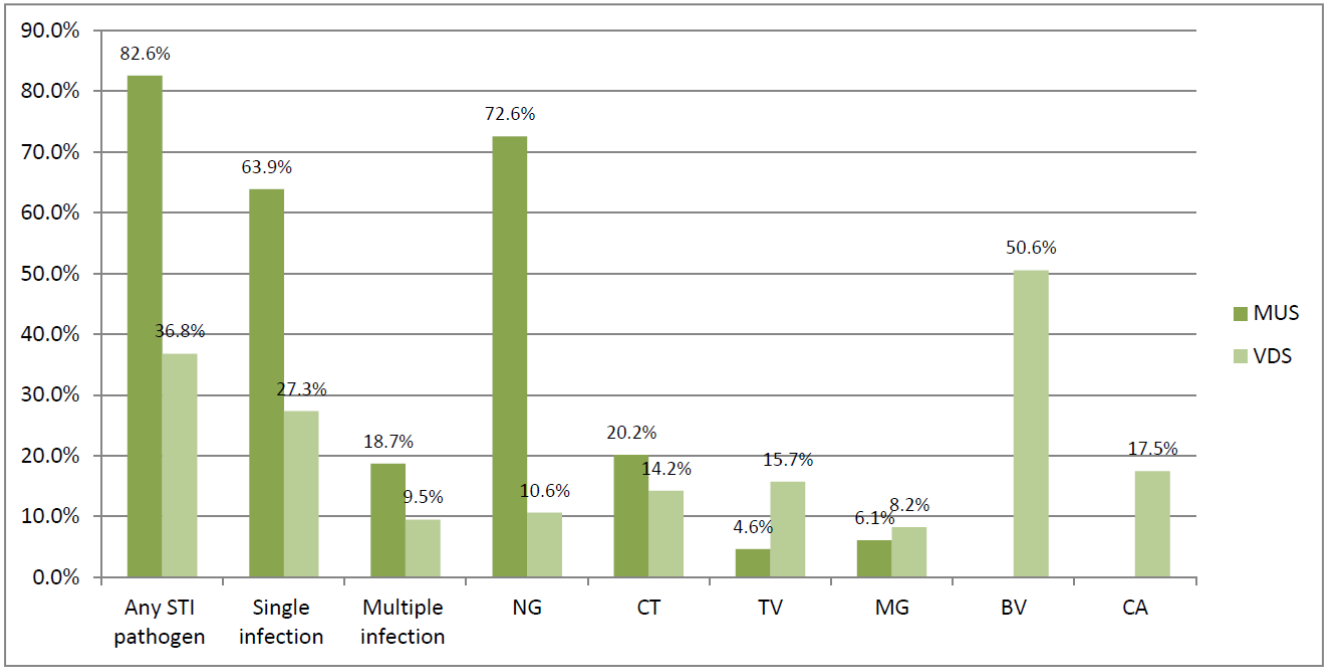
Male urethritis syndrome

These are reproductive tract diseases!

Limitations of syndromic management

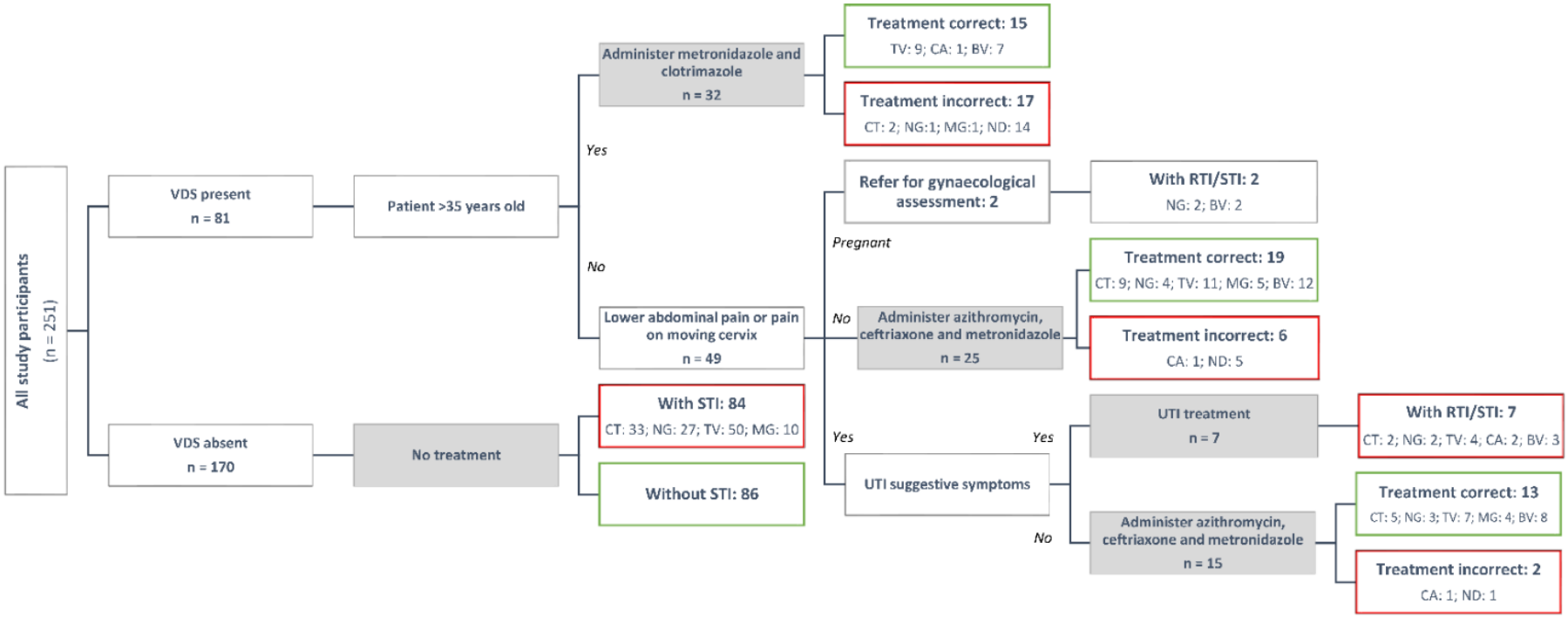
- Incorrect treatment for aetiology of discharge
  - Undertreatment: persistent/recurrent infection
  - Overtreatment: unnecessary antibiotics

Figure 1: Distribution of aetiological pathogens among participants with MUS and VDS (N=540)



NICD, Sentinel surveillance 2014 - 2015

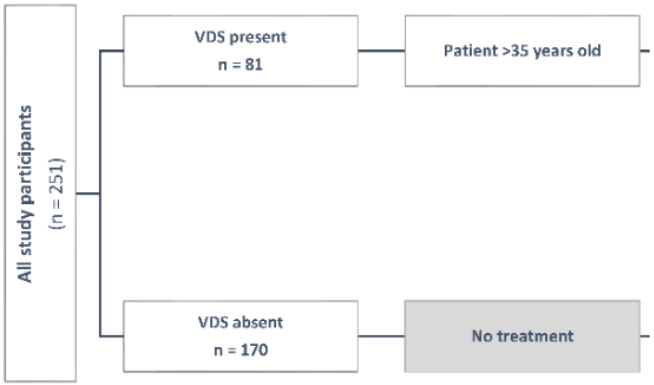
Limitations of syndromic management



- Limited treatment accuracy of syndromic management for STIs resulting in over- and undertreatment

Hoffman C *et al*. Sex Transm Dis 2018

Limitations of syndromic management



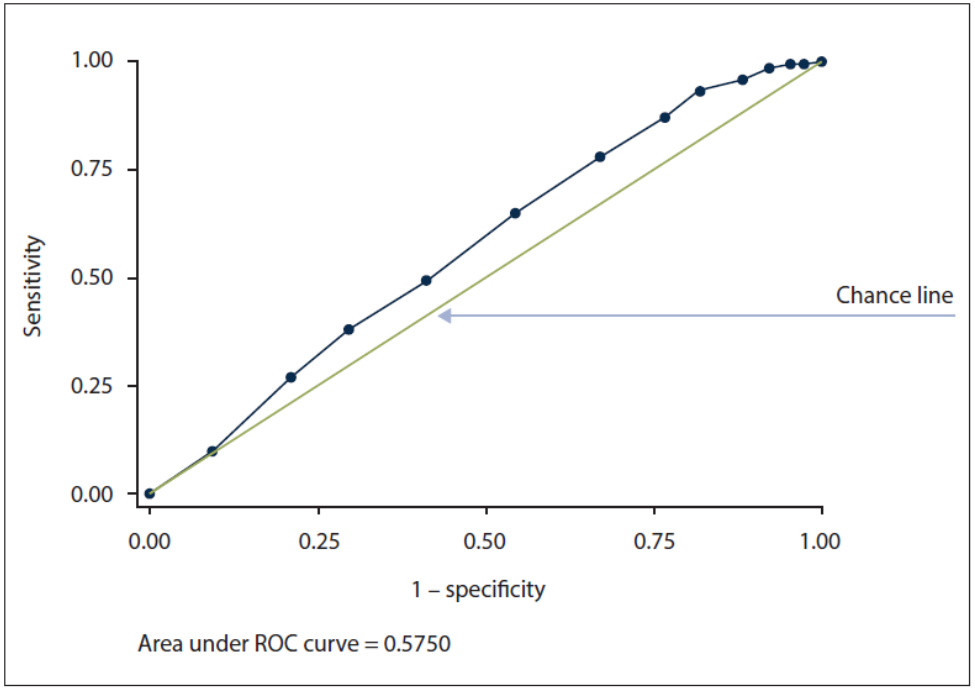


Fig. 1. ROC for performance of age in predicting presence of Neisseria gonorrhoeae, Chlamydia trachomatis *or* Mycoplasma genitalium. *(ROC = receiver operator curve.)*

- The ‘age step’ in the algorithm is problematic

Kufa T *et al*. SAMJ 2018

Limitations of syndromic management

- Incorrect treatment for aetiology of discharge
  - Undertreatment: persistent/recurrent infection
  - Overtreatment: unnecessary antibiotics
  - Drug-resistant infection (NG, MG)

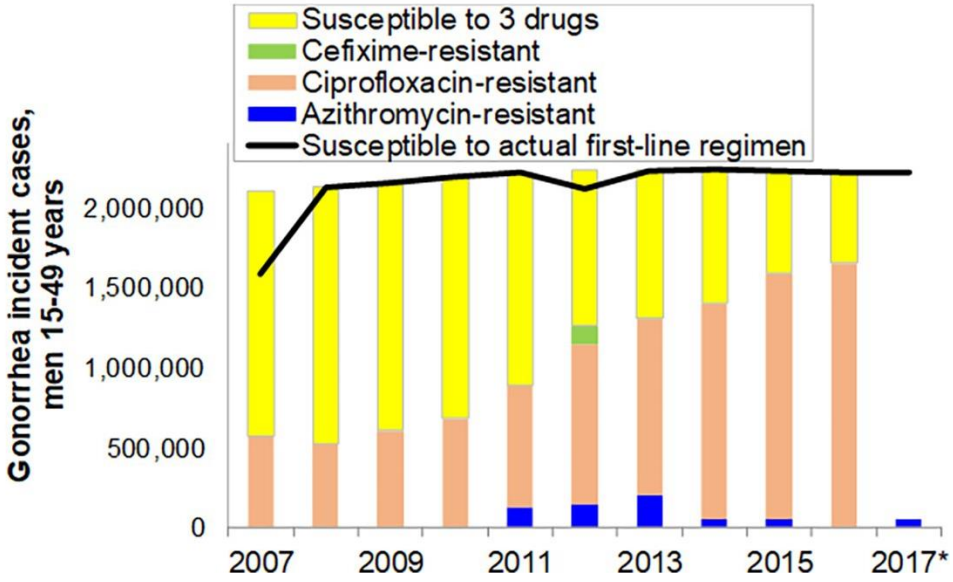


Table 1. Mutations associated with macrolide and quinolone resistance in *Mycoplasma genitalium* infection in a patient failing management of male urethritis syndrome in South Africa

Drug resistance associated alterations in *Mycoplasma genitalium*		
23S rRNA gene[a]	***par*C gene**[a]	***gyr*A gene**
A2071G	C234T (Pro-62→Ser)[b]	Wild type

Kularatne RS *et al*. PLOS One 2018
Maduna L *et al*. Submitted

Limitations of syndromic management

- Incorrect treatment for aetiology of discharge
  - Undertreatment: persistent infection
  - Overtreatment: unnecessary antibiotics
  - Drug-resistant infection

- Lack of capacity to manage complicated cases
  - Guidelines and aetiological knowledge (new EDL)
  - Skills development programme required
  - Access to aetiological and drug resistance testing

Diagnostic approach to STIs

RESEARCH ARTICLE

Beyond syndromic management: Opportunities for diagnosis-based treatment of sexually transmitted infections in low- and middle-income countries

(Young) HIV-negative women (CAPRISA 083)

Nigel J. Garrett[1,2]*, Farzana Osn
Andrew Gibbs[3], Emily Norman[1,
Nireshni Mitchev[6], Ravesh Singl
Koleka Mlisana[6,7], Anne Rompal

High prevalence of asymptomatic sexually transmitted infections among human immunodeficiency virus-infected pregnant women in a low-income South African community

HIV-positive pregnant women

Maanda Mudau[1], Remco P Peters[2,3], Lindsey De Vos[1], Dawie H Olivier[1], Dvora J Davey[4,5,6], Edwin S Mkwanazi[1], James A McIntyre[2,7], Jeffrey D Klausner[5,6] and Andrew Medina-Marino[1]

Chlamydia and Gonorrhea in HIV-Infected Pregnant Women and Infant HIV Transmission

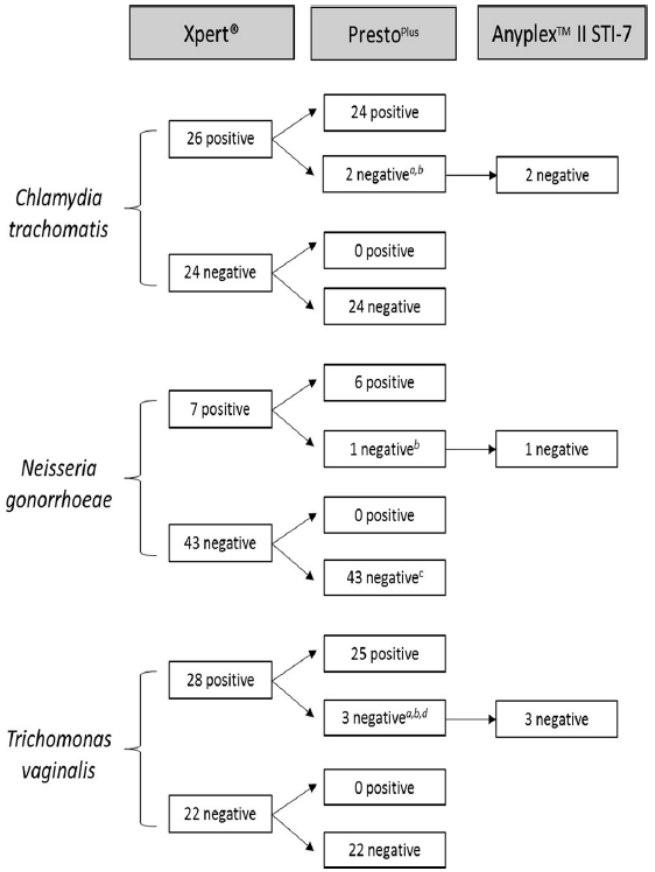
HIV-positive pregnant women in Botswana

Kristina Adachi, MD, Jeffrey D. Klausner, MD, MPH,* Claire C. Bristow, MSc,† Jiahong Xu, MS, MPH,‡ Bonnie Ank, BA,* Mariza G. Morgado, PhD,§ D. Heather Watts, MD,¶ Fred Weir, PhD,|| David Persing, MD, PhD,|| Lynne M. Mofenson, MD,** Valdilea G. Veloso, MD,§ Jose Henrique Pilotto, MD,†† Esau Joao, MD,‡‡ Karin Nielsen-Saines, MD, MPH* for the NICHD HPTN 040 Study Team*

Diagnostic approach is feasible

Laboratory Validation of Xpert *Chlamydia trachomatis/Neisseria gonorrhoeae* and *Trichomonas vaginalis* Testing as Performed by Nurses at Three Primary Health Care Facilities in South Africa

Remco P. H. Peters,[a,b,c] Lindsey de Vos,[d] Liteboho Maduna,[a] Maanda Mudau,[d] Jeffrey D. Klausner,[e,f] Marleen M. Kock,[a,g] Andrew Medina-Marino[d]



Peters RP *et al*. J Clin Microbiol 2017

But how to roll-out diagnostic approach?

- Europe/USA: targeted access. RSA: included for asymptomatic infections in national strategy
- Could possibly utilise the existing Xpert® platforms
  - Sufficient capacity to add on another test(s)?
  - Cost Xpert® CT/NG higher than MTB/Rif
- Whom to prioritise for access to diagnostics?

Key populations
Adolescents and young adults
Pregnant women

Aetiological approach ≠ STI control

Preliminary data

- Cohort of HIV-infected pregnant women
- Repeat Xpert® CT/NG or TV test at four weeks after treatment
- Active partner notification system including packs

Courtesy of Maanda Mudau, Foundation for Professional Development

Aetiological approach ≠ STI control

Preliminary data

- Cohort of HIV-infected pregnant women
- Repeat Xpert® CT/NG or TV test at four weeks after treatment
- Active partner notification system including packs
- Various reasons for repeat Xpert test positivity, but that may undermine effectiveness

Courtesy of Maanda Mudau, Foundation for Professional Development

Aetiological approach ≠ STI control

Preliminary data

- Cohort of HIV-infected pregnant women
- Tested at first ANC visit and post-natal visit

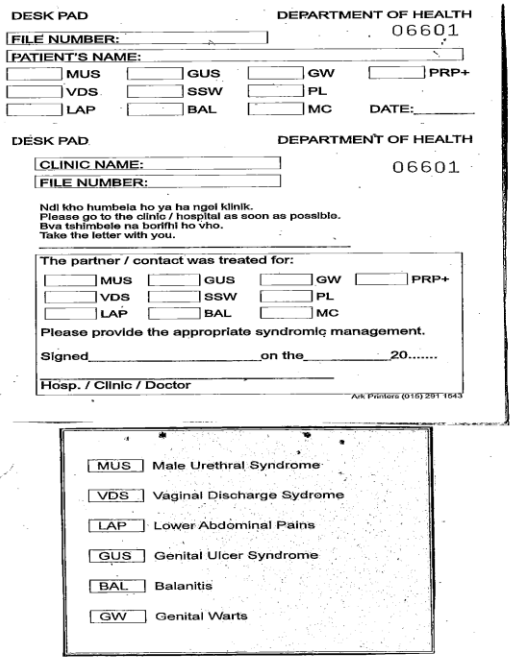
- High incidence may undermine effectiveness of aetiological management of STIs

Courtesy of Maanda Mudau, Foundation for Professional Development

Expedited partner therapy

Table 3. Comparison of STI detection rates among 51 women with STIs, 6 weeks after an EPT intervention.

Pathogen	Overall (N = 51) % (n/N)	EPT issued (N = 46) % (n/N)	No EPT issued (N = 5) % (n/N)	p-value
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
C. trachomatis or *T. vaginalis* [a]	5.9 (3/51)	2.2 (1/46)	40.0 (2/5)	0.023


DESK PAD DEPARTMENT OF HEALTH
06601
FILE NUMBER:
PATIENT'S NAME:
MUS GUS GW PRP+
VDS SSW PL
LAP BAL MC DATE:

DESK PAD DEPARTMENT OF HEALTH
06601
CLINIC NAME:
FILE NUMBER:

Ndi kho humbela ho ya ha ngeli klinik.
Please go to the clinic / hospital as soon as possible.
Bva tshimbele na bofhi ho vho.
Take the letter with you.

The partner / contact was treated for:
MUS GUS GW PRP+
VDS SSW PL
LAP BAL MC

Please provide the appropriate syndromic management.

Signed_____on the_____20.....

Hosp. / Clinic / Doctor

Ark Printers (015) 291 1643

MUS Male Urethral Syndrome
VDS Vaginal Discharge Sydrome
LAP Lower Abdominal Pains
GUS Genital Ulcer Syndrome
BAL Balanitis
GW Genital Warts

Garrett NJ *et al*. PLOS One 2018
Ferreira A *et al*. Cochrane 2013

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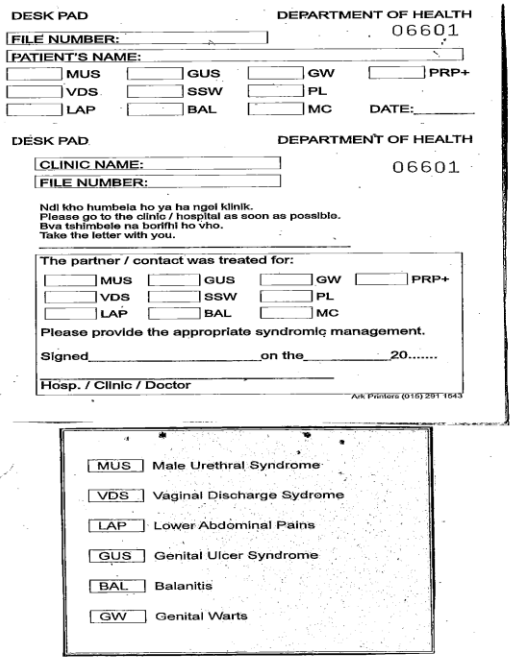
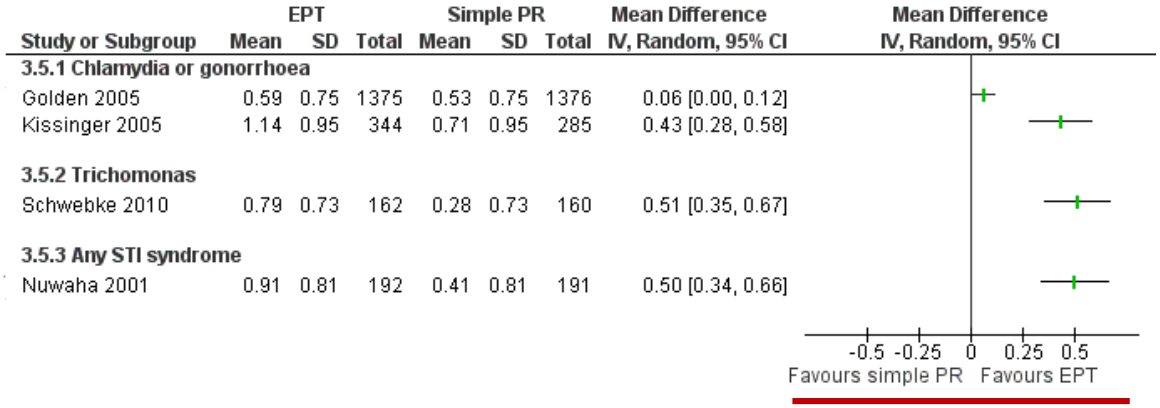
Pathogen	Overall (N = 51) % (n/N)	EPT issued (N = 46) % (n/N)	No EPT issued (N = 5) % (n/N)	p-value
C. trachomatis	3.9 (2/51)	2.2 (1/46)	20.0 (1/5)	0.188
T. vaginalis	2.0 (1/51)	0	20.0 (1/5)	0.098
C. trachomatis or *T. vaginalis* [a]	5.9 (3/51)	2.2 (1/46)	40.0 (2/5)	0.023





Garrett NJ *et al*. PLOS One 2018
Ferreira A *et al*. Cochrane 2013

In conclusion

- Large burden of STIs in South Africa with large unmet need for care and occurrence of complications
- Strengthening basics of care provision is required
  - Patient awareness
  - Communication with patients
  - Make sexual healthcare ‘sexy’
  - Implementation of guidelines
  - Partner notification
- Skills building and referral networks for 2nd line
- Targeted introduction of diagnostics for specific groups and in specific settings

Thank you!

All staff, MSc and PhD students and collaborators!

Please contact me

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