Single-dose azithromycin may be effective for genital *Chlamydia trachomatis* biovar-L infection in South African women

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Faculty of
Health Sciences

Fakulteit Gesondheidswetenskappe
Lefapha la Disaense tša Maphelo

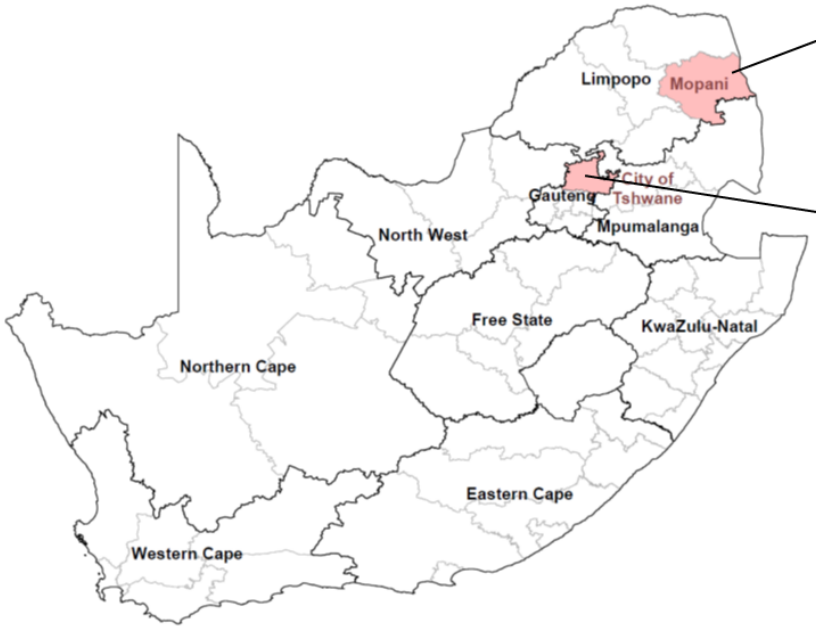
28th of June 2018
IUSTI Dublin 2018
Remco Peters

Make today matter

Background – lymphogranuloma venereum

- Geographic variation in epidemiology:
- EU/USA
  - Outbreak largely restricted to MSM (proctocolitis, urethritis)
  - Sporadic cases of genital infection in women
  - Sporadic cases of lymphatic LGV
- Africa & other tropical areas
  - Lymphatic LGV is endemic (“Tropical bubo”)
  - Occurrence of genital infection is unknown

Biovar-L *Chlamydia trachomatis* in women



0/43 rectal *Chlamydia trachomatis* infections in women

0/52 cervical *Chlamydia trachomatis* infections

7/30 (23%) positive in women visiting an academic hospital (O&G, STI or HIV clinic

Peters RP *et al*. Emerg Infect Dis 2017
Peters RP *et al*. Sex Transm Dis 2014
Hoffman CM *et al*. Submitted

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Presentation of genital LGV in women

- Retrospective analysis of existing cohorts
  - Clinical presentation?
  - Impact on syndromic management?

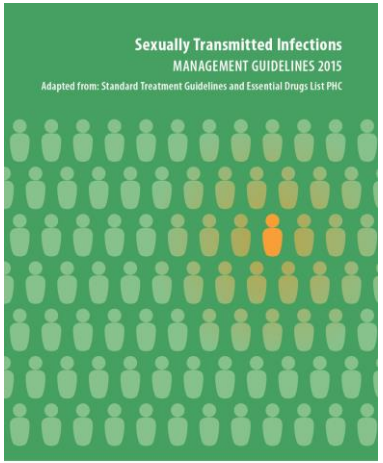
Table 1. Characteristics of 7 women with vaginal discharge and a positive PCR result for *Chlamydia trachomatis* biovar L, Pretoria, South Africa, 2012–2016*

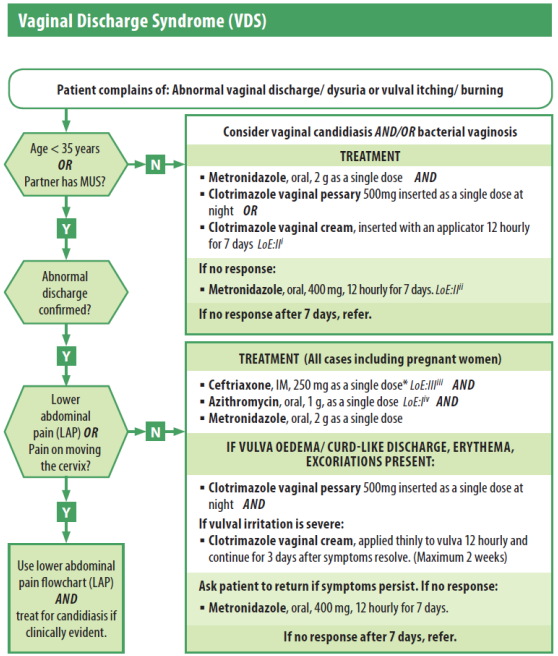
Patient ID	Healthcare setting	HIV status	Co-infection	*C. trachomatis* WGS result	Mean read depth	Genome coverage, %
1	ART clinic	Positive	*Trichomonas vaginalis*	L2 confirmed	41	99.5
2	ART clinic	Positive	*T. vaginalis*	L2 confirmed	12	98.3
3	ART clinic	Positive	*Mycoplasma genitalium*	L2 confirmed	21	98.6
4	ART clinic	Positive	*M.a genitalium*	L2 confirmed	72	99
5	ART clinic	Positive	*T. vaginalis*	Insufficient WGS read coverage	0.5	29
6	STI clinic	Unknown	*Neisseria gonorrhoeae*	Insufficient clinical material	ND	ND
7	STI clinic	Unknown	*N. gonorrhoeae*	Insufficient clinical material	ND	ND

*ART, antiretroviral therapy; ID, identification; ND, not determined; STI, sexually transmitted infection; WGS, whole-genome sequencing.

Peters RP *et al*. Emerg Infect Dis 2017

Genital LGV and syndromic management

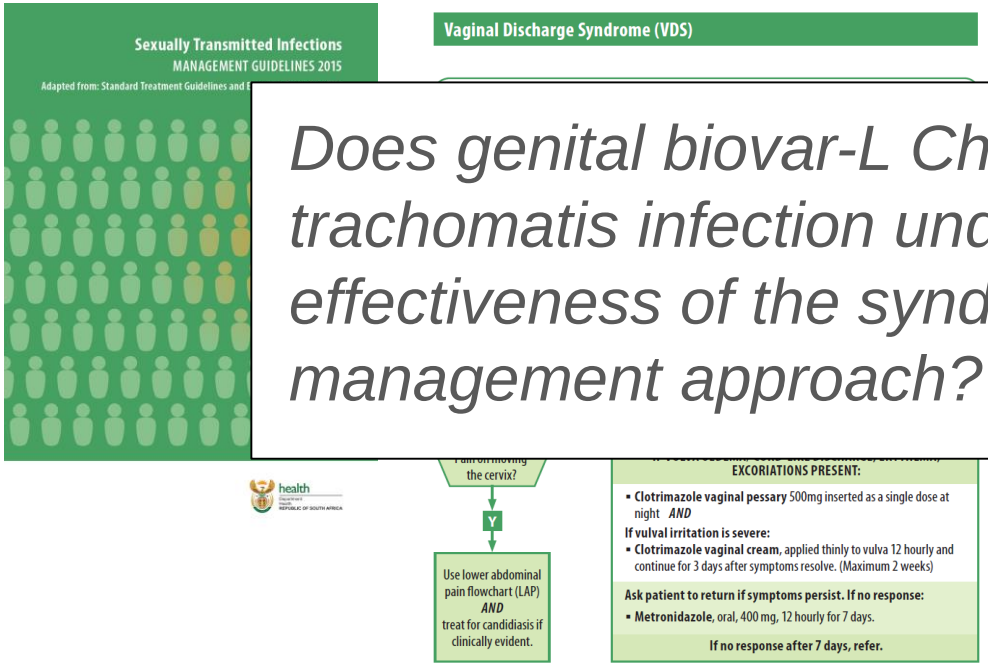




- Empirical treatment with azithromycin, ceftriaxone & metronidazole if <35 years
- Asymptomatic infections remain untreated
- No place for doxycycline in the current syndromic approach

National Department of Health, South Africa, 2015

Genital LGV and syndromic management



Does genital biovar-L Chlamydia trachomatis infection undermine the effectiveness of the syndromic management approach?

- Empirical treatment with
  , ceftriaxone &
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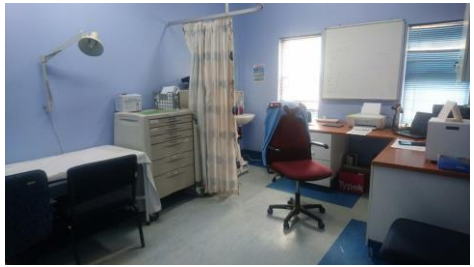
- doxycycline in
  the current syndromic
  approach

National Department of Health, South Africa, 2015

Methods – study design

- Analysis of *Chlamydia trachomatis*-positive specimens collected in a cohort study of HIV-infected pregnant women in Pretoria[1]
- Vaginal swab for on-site Xpert® CT/NG and TV testing; second swab obtained for other microbiological tests
- Standard treatment provided; follow-up test after 1 month for women with an STI detected



[1]Mudau M *et al*. Int J STD AIDS 2018

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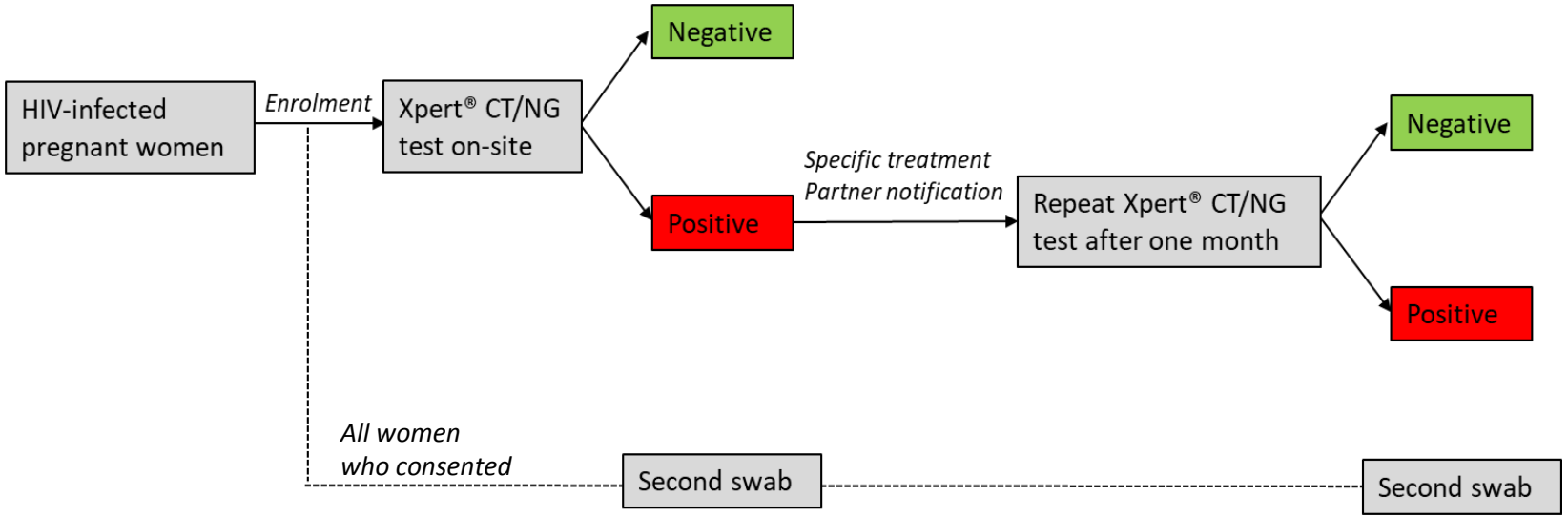

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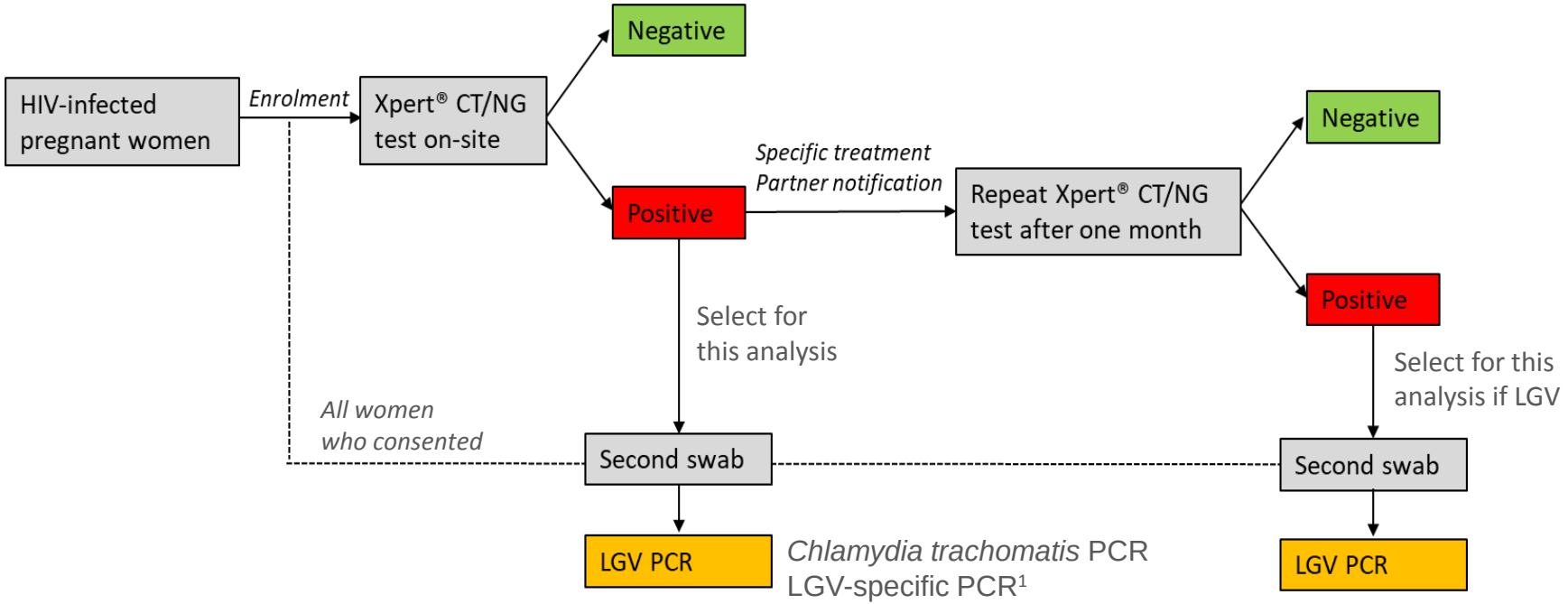

[1]Verweij SP *et al*. Clin Microbiol Infect 2011

Results – Study population

- We selected specimens of 85 HIV-infected pregnant women with *Chlamydia trachomatis* infection in this analysis

Characteristic	Number (%)
Number of participants	85
Age (years, mean (sd))	30 (5.6)
Employed	29 (35)
Pregnancy stage	
1st trimester	14 (17)
2nd trimester	55 (67)
3rd trimester	13 (16)
Relationship status	
Married	8 (9.5)
Stable, living together	28 (33)
Stable, not living together	45 (54)
No relationship	3 (3.6)
Concurrent partners	13 (15)
Condom use last sex act	23 (27)

Characteristic	Number (%)
HIV infection	85 (100)
On ART	85 (100)
STI-associated symptoms	
No	64 (75)
Yes	21 (25)
Vaginal discharge reported	17 (20)
Vaginal discharge observed	23 (27)
Dysuria	5 (5.9)
Vaginal bleeding	1 (1.2)
Coinfections present	
Neisseria gonorrhoeae	10 (12)
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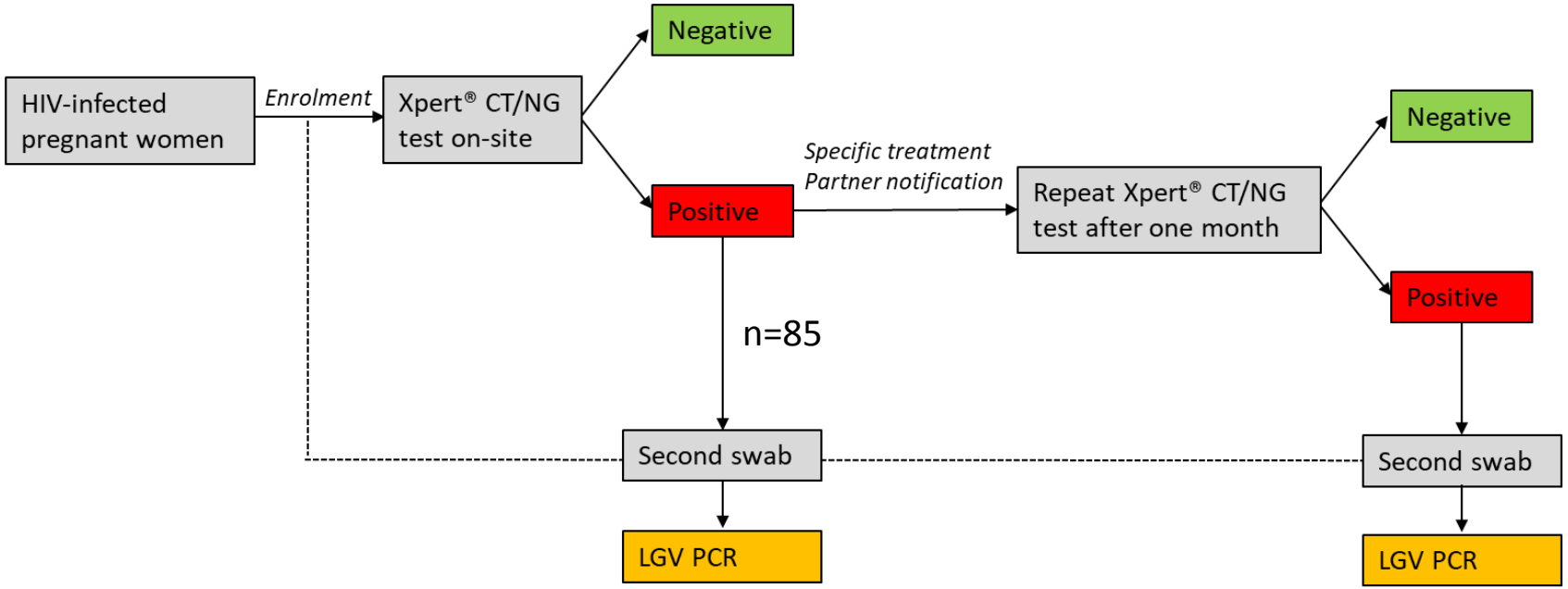
Detection of biovar-L *C. trachomatis* infection



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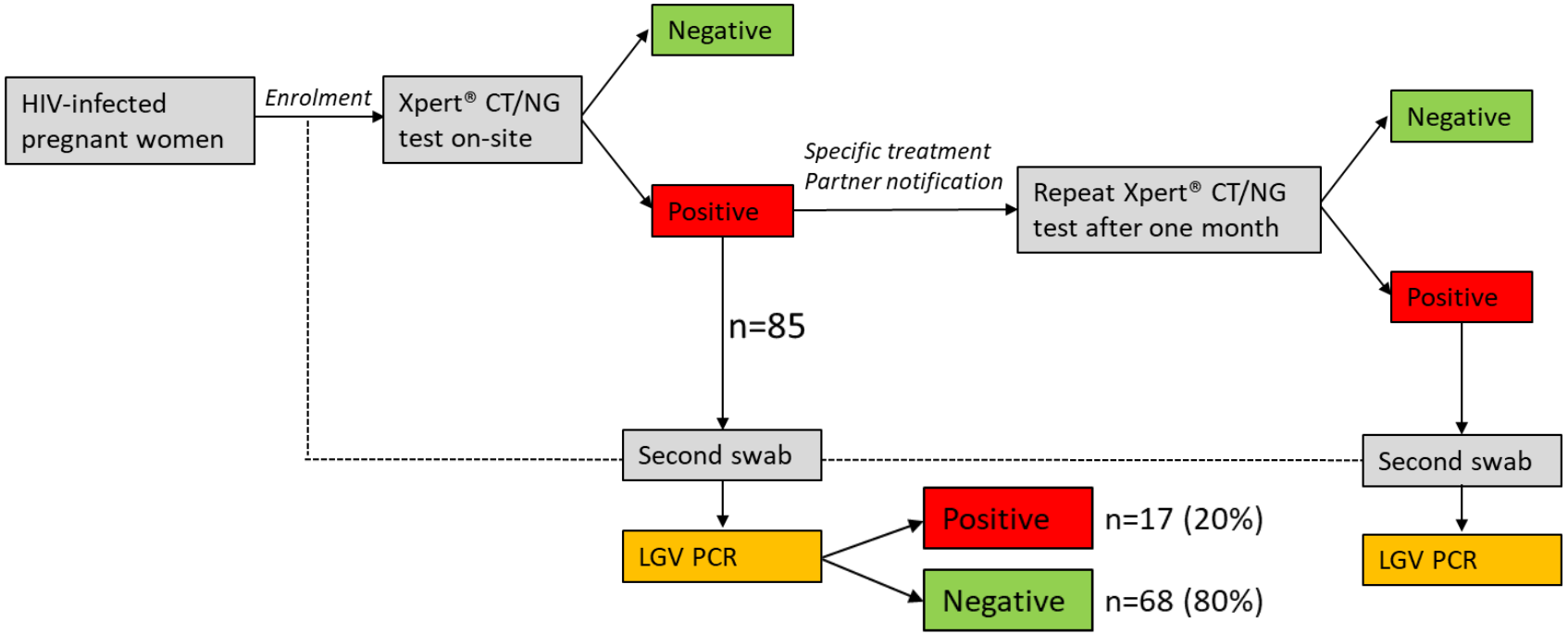

Clinical presentation of genital LGV

Characteristic	Number (%)
HIV-infected	17 (100)
On ART	17 (100)
Symptomatic	8 (47)
Vaginal discharge reported	5 (29)
Dysuria reported	2 (12)
Vaginal discharge observed	6 (35)
Coinfections	6 (35)
Neisseria gonorrhoeae	3 (18)
Trichomonas vaginalis	6 (35)
Mycoplasma genitalium	0

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- Symptomatic and asymptomatic infections

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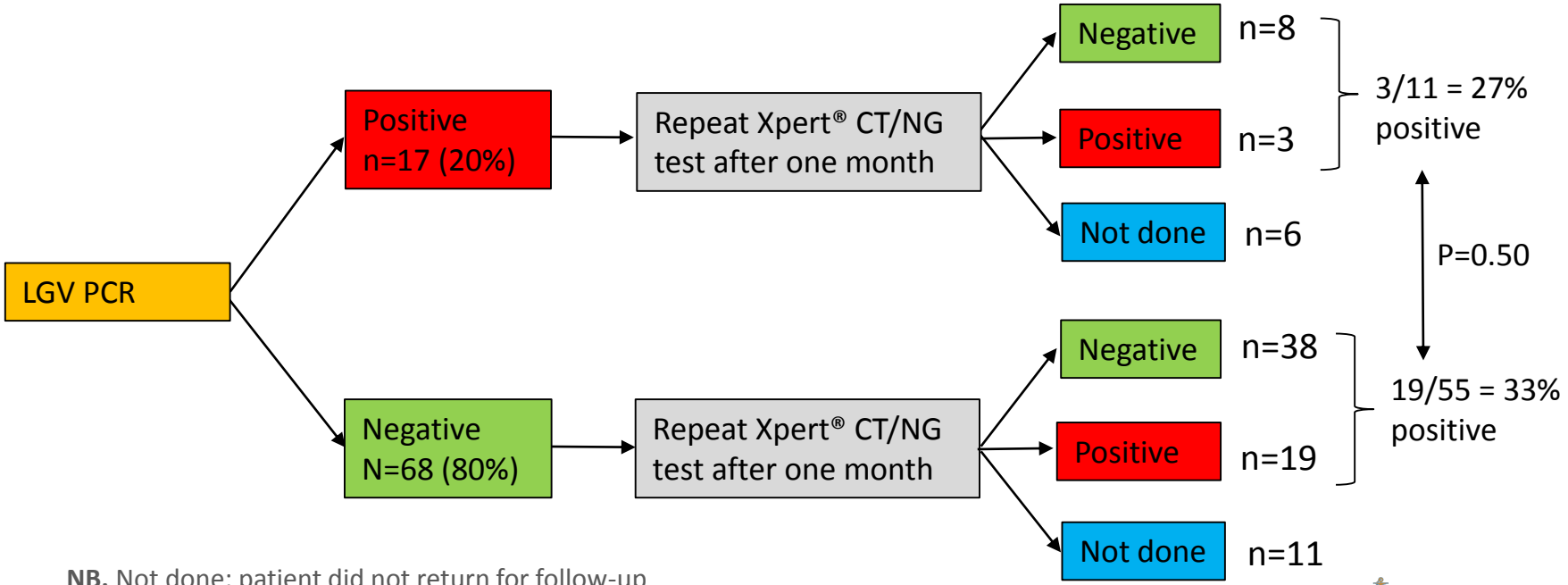
- Symptomatic and asymptomatic infections
- One-third had coinfection
- No association of biovar-L vs. non-L biovar infection for various demographic, behavioural or clinical factors

One-month cure rate is similar for biovar-L and non-L biovar *C. trachomatis* infection



NB. Not done: patient did not return for follow-up

Effectiveness of singe-dose azithromycin

- 8/11 women had negative Xpert® CT/NG test at one-month after treatment with single-dose azithromycin
- 3/11 cases had a positive Xpert® CT/NG test at one-month follow-up, however:
  - All three follow-up specimens tested negative for LGV
  - The possibility of incident *C. trachomatis* infection is supported by participant's history
  - All three patients tested negative for *C. trachomatis* at the second follow-up visit, after repeat treatment with single-dose azithromycin

Discussion

- These data confirm high prevalence of biovar-L genital *C. trachomatis* infection in women living in Pretoria
  - How about men?
  - How about distribution of other biovars?
- Clinical spectrum is diverse and coinfections occur – similar to rectal infection in MSM
- No clear demographic, behavioural or clinical factors associated with LGV for risk stratification

Discussion

- Good effectiveness of single-dose azithromycin for genital LGV in South African women: high cure rate observed
  - Larger sample size required to confirm
  - Incident vs. persistent infections?
  - Follow-up period?
- There is no indication that effectiveness of syndromic management is undermined by genital biovar-L infections

Acknowledgments

Local support

Study participants
Department of Health
Study team

Investigators

Jeff Klausner
Andrew Medina-Marino
Maanda Mudau
Lindsey de Vos
James McIntyre
Liteboho Maduna
Marleen Kock

National Institutes of Health
Turning Discovery Into Health

Grant/award Number: 1R21HD084274-01A1

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