Kirby Institute

HIGH CHLAMYDIA TREATMENT FAILURE RATES IN MEN WHO HAVE SEX WITH MEN

Smith KS[1], Guy R[1], Danielewski JA[2], Tabrizi SN[2,3,4], Chen M[5,6], Kaldor JM[1], Hocking JS[7] on behalf of REACT investigators

[1]The Kirby Institute, UNSW Australia, Sydney, Australia
[2]Department of Microbiology and Infectious Diseases, Royal Women's Hospital, Melbourne, Australia
[3]Department of Obstetrics and Gynaecology, University of Melbourne, Melbourne, Australia
[4]Murdoch Children's Research Institute, Melbourne, Australia
[5]Melbourne Sexual Health Centre, Melbourne, Australia
[6]Central Clinical School, Monash University, Melbourne, Australia
[7]Melbourne School of Population and Global Health, University of Melbourne, Melbourne, Australia

Chlamydia infections and reinfections

- Most frequently reported STI in most developed countries
- Notification rates have been increasing steadily
- ~86,000 chlamydia diagnoses in Australia in 2014 *(Kirby Institute 2014)*
- Greatest burden of infection among 15-24 year olds
- Chlamydia prevalence high in men who have sex with men (MSM) *(Vodstrcil, BMC infect Dis 2011; Annan, STI 2009)*
- Reinfections common (20-30%) *(Walker, PLoS ONE 2012; Harte, STI 2011)*
  - Increased risk of HIV *(Wasserheit, STI 1999; Bernstein, JAIDS 2010)*

Is treatment failure an issue?

Most repeat infections
- Due to reinfection from the same or a new partner
- Less commonly treatment failure *(Batteiger, J Infect Dis. 2010)*

Increasing concern about azithromycin treatment failure *(Golden, NEJM 2005; Handsfield, Sex Transm Dis 2011)*

Reported treatment failure rates:
- 5-14% in genital chlamydia infection;
- 6-21% in asymptomatic rectal infection *(Dukers-Muijrers, PLoS ONE 2013)*

Study design and methods

Aims:
- To compare repeat chlamydia infection rates between MSM and heterosexual men and women
- To compare treatment failure rates between MSM and heterosexual men and women

Study design:
- Prospective cohort in the context of a RCT *(Smith, Am J Prev Med 2015)*

Study sites:
- Melbourne and Sydney Sexual Health Centres

Participants:
- 600 people: 200 MSM, 200 women, 200 heterosexual men
- 16 years or above
- Diagnosed with chlamydia and treated with azithromycin

Cohort follow-up procedures

- Chlamydia retesting recommended at 3 months
- SMS reminder sent at 3 months
- Randomised to specimen collection at home or clinic
- Testing conducted by three diagnostic laboratories
- Positive specimens stored for further testing at reference laboratory

Cohort follow-up procedures

Survey
- SMS reminder at 4 months
- Demographics
- Treatment of the participant and their sexual partner/s
- Sexual behaviour since initial diagnosis:
  - Sexual intercourse
  - Condom use- always, inconsistent
  - Partner type - new partner/s, existing partner/s

Genovar and MLST testing

Quantitative real-time PCR (qPCR) assay

- Identify chlamydia positive samples
- Differentiate into 3 distinct phylogenetic clades based on the *ompA* gene:
  - B group (comprising B/Ba, D, E, L1, and L2)
  - C group (comprising A, C, H, I, J, K, and L3)
  - Intermediate (I) group (comprising F and G)

Multilocus sequence typing (MLST)

- Differentiate between identical genovars from the same individual

MLST analysis over 5 regions of the chlamydia genome

- *hctB,* CT682-*pbpB,* CT144, CT172, CT058

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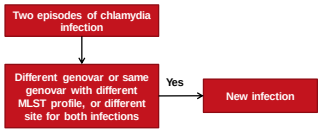
Classification of repeat positive cases

Repeat positive cases were differentiated according to an algorithm using:

- Sexual behaviour data
- Chlamydia genotyping

8 Batteiger, J Infect Dis 2010; Walker, PLoS One 2012

New infection



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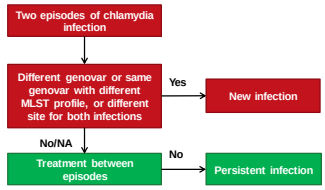
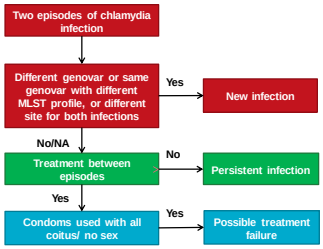
Persistent infection



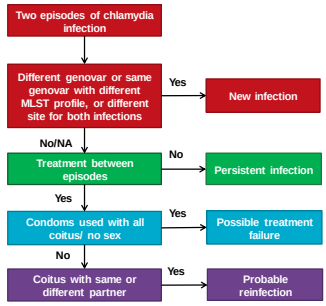
10 NA=not available

Possible treatment failure



11 NA=not available

Probable reinfection



12 NA=not available

Results: Sample characteristics at baseline n=290

Variable	Heterosexual men and women	MSM	P-value
Total	189	101	
Age (median) (IQR)	26 (22-29)	30 (27-37)	<0.01
Born in Australia %	40.9	58.8	<0.01
Used condoms consistently in last 3 months %	6.3	37.6	<0.01
>5 partners in last 3 months %	7.4	39.6	<0.01
Anal/ urogenital symptoms %	48.7	43.6	0.41
Previous chlamydia diagnosis %	8.5	18.8	0.01
Site of infection %	NA	Rectal = 57.4 Urethral = 35.6 Both = 6.9	

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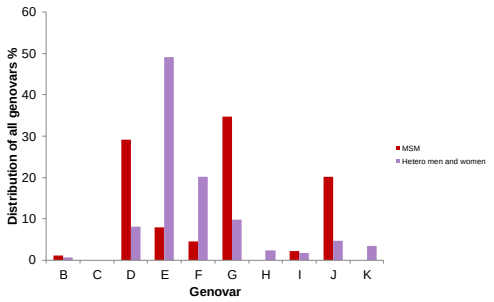
Genovar distribution at baseline



Note: there were no L genovar strains

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Genovar and MLST results

Of those with repeat infection (n=43):

- Paired genovar data available for 31 individuals
- 4 (13%) had a different genovar
- 27 (87%) had the same genovar
  - Of these 27, MLST further identified 2 new infections

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Treatment outcomes 1-4 months

Classification	Details	Heterosexuals n % (95%CI)	MSM n (%) (95%CI)	P value
Retested		189	101	
Repeat infections		22 11.6% (7.4-17.1)	21 20.8% (13.4-30.0)	0.04
New infection	Different genovar or same genovar with different MLST or different site	3 1.6% (0.3-4.6)	6 5.9% (2.2-12.5)	0.04
Persistent infection	Same genovar/ MLST, no treatment	1 0.5% (0.1-2.9)	0 0.0% (0-3.6)	0.46
Possible treatment failure	Same genovar/MLST and/or always used condoms/no sex	5 2.6% (0.9-6.1)	9 8.9% (4.2-16.2)	0.02
Probable reinfection	Same genovar/ MLST and/or inconsistent condom use	11 5.8% (2.9-10.2)	6 5.9% (2.2-12.5)	0.97

All rectal infections at baseline

16 Note: two heterosexuals could not be classified

New infection

	Details	Heterosexual men and women	MSM
New infection	Different genovar	2	2
	Same genovar, different MLST	1	1
	Different site	0	3
	Total	3	6

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Limitations

- Small sample
- Self-reported sexual behaviour
- Possible misclassifications in those who reported always using condoms *(Jin, STI 2007)*
- Not all specimens were available for genotyping
- If an individual has two episodes of chlamydia infection with the same genovar and the same MLST profile, we cannot differentiate between reinfection and treatment failure

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Conclusions

- Repeat positivity was highest among MSM
- Different circulating genovars among MSM – consistent with literature *(Herrmann, JCM 2015)*
- Applying genotyping and behavioural data allowed us to further classify repeat infections
- Treatment failure appears to be more common in MSM with rectal chlamydia
- High repeat infection rates, particularly among MSM, highlight the importance of retesting around 3 months following treatment

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