

Advances in Sexual Health

Dr. Suneeta Soni

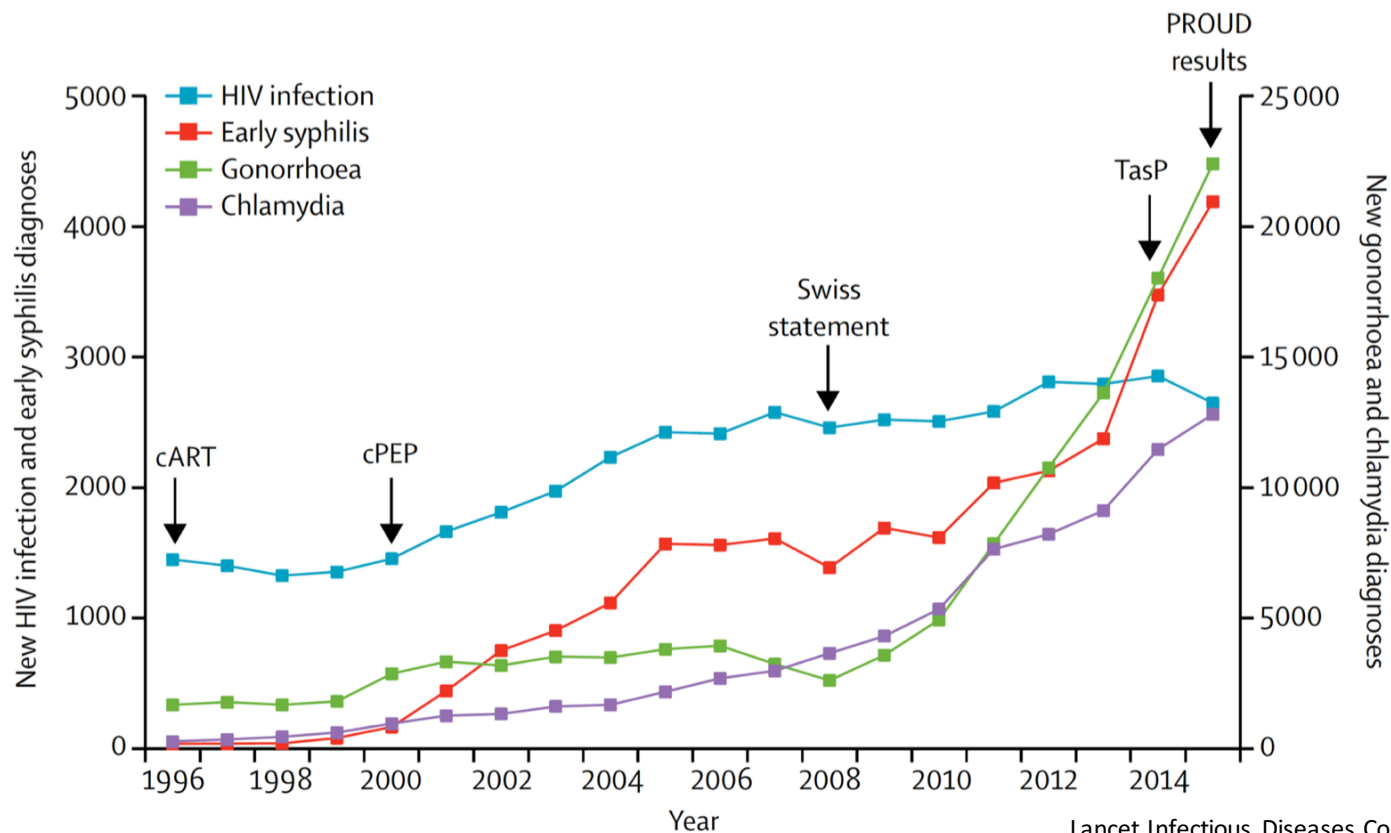
18 April 2018



Advances in STI

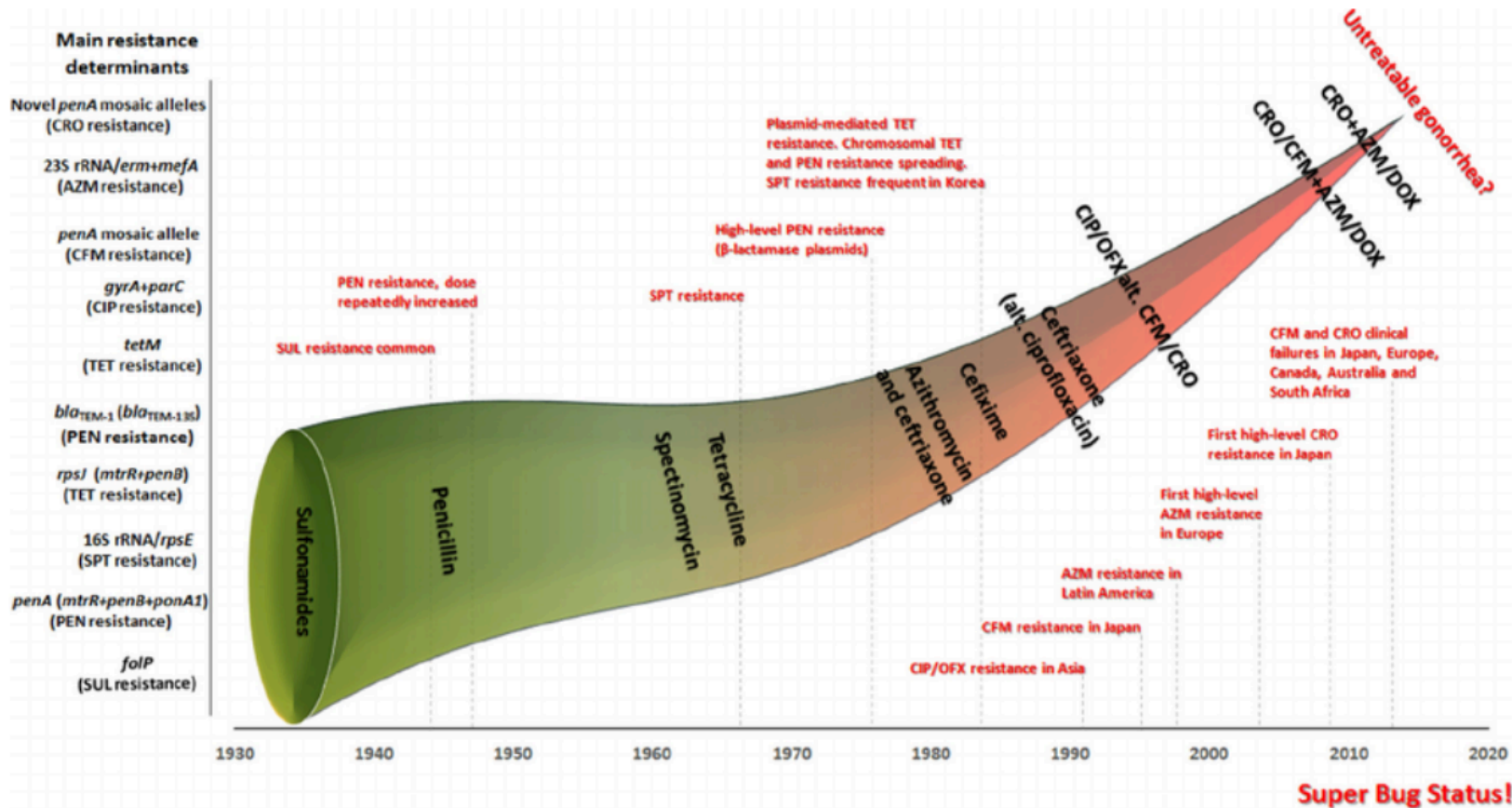
- Testing
- Treatment
- Prevention

New diagnoses of HIV, syphilis, gonorrhoea and chlamydia in MSM in England, 1996-2015

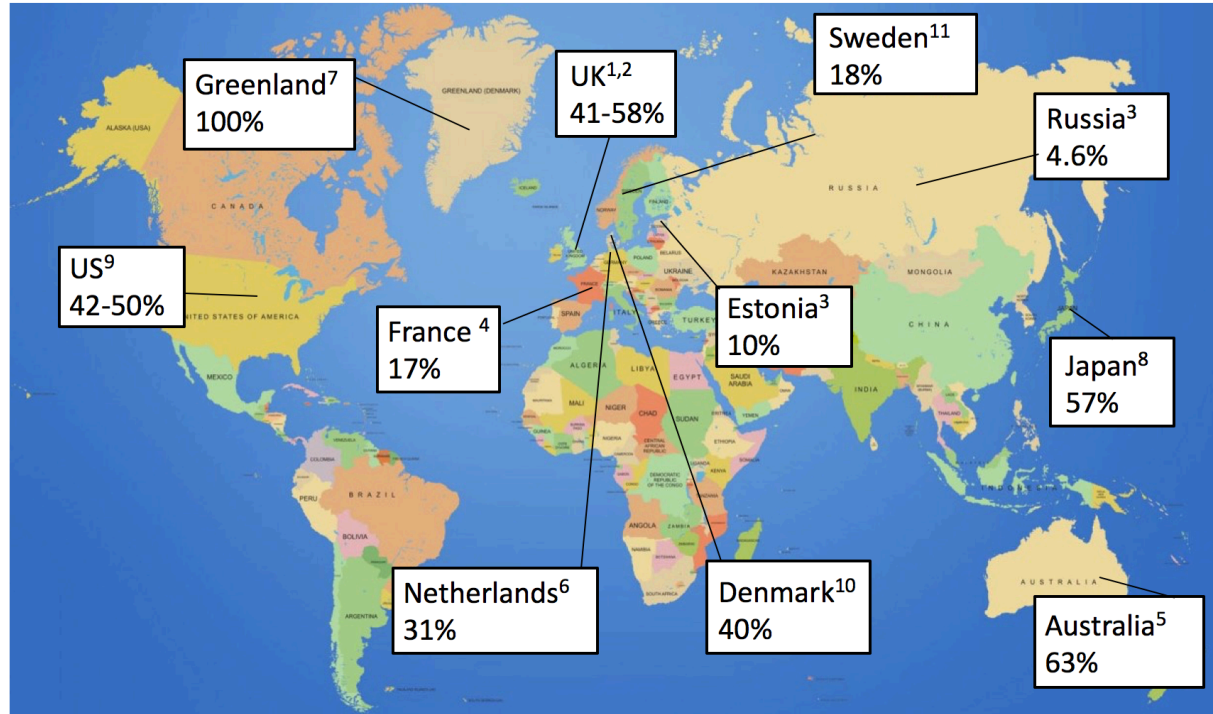


Current shortfalls

- Access to testing
 - Higher pressure on clinic, those with symptoms wait longer*
 - Online testing – patchy implementation, reaching enough people?
- Suboptimal diagnostics
 - Narrow repertoire of tests – poor coverage of TV and MG NAATs
 - Slow time to results
- Still managing STI syndromes rather than infections
 - Overuse of antibiotics
- Antimicrobial resistance



Mycoplasma genitalium: global macrolide resistance



With permission Katie Ovens

1) Pond MJ, Nori AV, Witney AA, Lopeman RC, Butcher PD, Sadiq ST. High prevalence of antibiotic-resistant *Mycoplasma genitalium* in nongonococcal urethritis: the need for routine testing and the inadequacy of current treatment options. *Clin Infect Dis*. 2014 Mar;58(5):631-72. Dean G, Whetham J, Soni S, Pitt R, Alexander S. *Mycoplasma genitalium* and macrolide resistance in pelvic inflammatory disease (PID) presented at the Annual Conference for the British Association for Sexual Health and HIV, Oxford, England, July 10-12, 2016. 3. Elena Shipitsyna et al. Prevalence of macrolide and fluoroquinolone resistance-mediating mutations in *Mycoplasma genitalium* in five cities in Russia and Estonia. *PLoS One*. 2017; 12(4): e0175763. 4. Chloé Le Roy, Nadège Hélin, Sabine Pereyre, and Cécile Bébear. Fluoroquinolone-Resistant *Mycoplasma genitalium*, Southwestern France. *Emerg Infect Dis*. 2016 Sep; 22(9): 1677-1679. 5. Tabrizi SN, Su J, Bradshaw S, Fairley CK, Walker S, Tan LY, Mokany E, Garland SM. Prospective evaluation of ResistancePlus™ MG, a new multiplex qPCR assay 2 for the detection of *Mycoplasma genitalium* and macrolide resistance. *J. Clin. Microbiology* 2017 April 6. RH Nijhuis et al. High Levels of Macrolide Resistance-Associated Mutations in *Mycoplasma Genitalium* Warrant Antibiotic Susceptibility-Guided Treatment. *J Antimicrob Chemother* 70 (9), 2515-2518. 2015 May 2017. Gesink DC, Mulvad G, Montgomery-Andersen R, et al. *Mycoplasma genitalium* presence, resistance and epidemiology in Greenland. *Int J Circumpolar Health* 2012; 71:1-8. 8. Shimada Y, Deguchi T, Nakane K, et al. Macrolide resistance-associated 23S rRNA mutation in *Mycoplasma genitalium*, Japan. *Emerg Infect Dis* 2011; 17:1148-50. 11. Damon Getman, Alice Jiang, Meghan O'Donnell and Seth Cohen: *Mycoplasma genitalium* Prevalence, Coinfection, and Macrolide Antibiotic Resistance Frequency in a Multicenter Clinical Study Cohort in the United States. *J. Clin. Microbiol.* Sept 2016 ; 54 (9): 2278-2283. Kirsten Salado-Rasmussen and Jørgen Skov Jensen. *Mycoplasma genitalium* Testing Pattern and Macrolide Resistance: A Danish Nationwide Retrospective Survey. *Clin Infect Dis*. 2014 Jul 1; 59(1): 24-30. 11. E. Bjornelius, C Magnusson, JS Jensen. *Mycoplasma Genitalium* Macrolide Resistance in Stockholm, Sweden. *Sex Transm Infect* Published Online First: 08 August 2016. doi: 10.1136/sextrans-2016-052688

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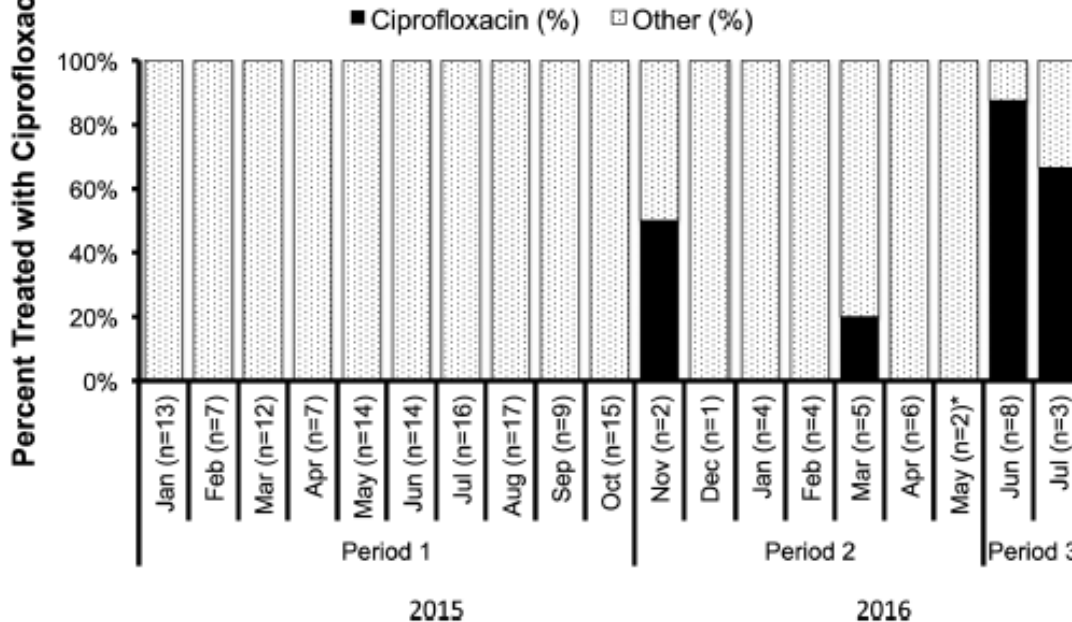
Macrolide resistance testing in *M. genitalium*

- Simultaneous detection of MG and mutations in the 23sRNA gene
A2058G, A2058T, A2059G, A2059T
- proportion of treatment failures can be reduced from 40% to around 3%
(Bradshaw - unpublished work)
- Quinolone resistance assay in development

ResistancePlus™ MG
Go Beyond Detection



Percent Treated with Ciprofloxacin



Implemented a Gyr A genotypic assay

Text reminders that cipro
could be used

Increased use of cipro from:
Period 1 0%
Period 2 12.5% (3/24)
Period 3 81.8% (9/11)

Rapid diagnostics

Cepheid
90 minutes



Atlas Genetics io
30 minutes



TwistDx
15 minutes




Test and wait

- Do all partners need treating?
- *N. gonorrhoeae* guidelines 2018 - if contact was >2 weeks ago, test and wait for results
- Needs to be weighed up against the risk of re-infection
- Decision should be based on a clinical risk assessment and in partnership with the patient.
- *M. genitalium* guidelines 2018 – test current partner only

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Future possibilities for treatment of GC

- Use less ceftriaxone, use other sensitive agents
 - New drugs
 - Solithromycin – Phase 3 SOLITAIRE-U non-inferior to cef/azith
 - Zoliflodacin, Gepotidacin
 - Recycling of older antibiotics – spectinomycin, gentamicin, fosfomycin
- 
- Poor activity against
non-genital gonorrhoea

Kissing kids to blame for gonorrhoea spike, 'evidence out of Melbourne' suggests

1. Gonorrhoea in saliva – implications for transmission without direct inoculation of pharynx

2. Saliva used as lubricant for anal receptive practices

3. RCT - Listerine against pharyngeal GC

- Gargled Listerine or saline for 1 min
- Less likely to be culture positive on after listerine ($p=0.013$)
- Look out for OMEGA study – daily mouthwash



Dequalinium intravaginal tablet for treatment of bacterial vaginosis

- 6 days pv tablet compared with clindamycin
- Cure rate 81.5% cf 78.4% clindamycin
- Non-inferiority demonstrated
- Only short term follow up



Arch Gynecol Obstet (2016) 293:469–484

- Well tolerated
- Cost – slightly more than metronidazole
- No interactions
- 2018 - NIHR have commissioned a BV study with dequalinium

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Vaccines – MeNZB (Bexsero)

- No GC vaccines so far. *N. meningitidis* and *N. gonorrhoea* are similar
- Mass vaccination programme of <20 year olds in NZ
- Retrospective case control study of young people attending GUM clinics
- Those vaccinated significantly less likely to have GC
- Vaccine effectiveness 31%



PEP with doxycycline 200mg <24hours for MSM taking PrEP

232 MSM

Molina JM *et al Lancet Infect Dis*
2018 Mar;18(3):308-317

Overall reduction in incident STIs 47%

70% decrease in CT diagnoses, 73% decrease in syphilis diagnoses



Public Health
England



Position Statement on Doxycycline as Post-Exposure Prophylaxis for Sexually Transmitted Infections



CART
\$0.00



**EXPRESS DELIVERY: TENVIR
EM (U.K. & N-IRELAND)**

\$72.00 – \$140.00



Product not as displayed

**Kamagra 100 (U.K. &
N-IRELAND)**

\$26.00 – \$88.00



Product not as displayed

**Doxycycline (U.K. &
N-IRELAND)**

\$33.00 – \$67.00

Doxycycline PEP - more evidence needed

- Larger clinical trials – how long before resistance detected?

ClinicalTrials.gov Identifier: NCT02864550

Official Title: A Randomized, Placebo-controlled Trial of Oral Doxycycline for the Prevention of Syphilis in Men Who Have Sex With Men (MSM)

- Observational data from clinics
 - “Have you taken any antibiotics since your last visit?”
 - How are they taking it? Daily? Event based?
 - Tolerability
 - Incident infections
- UK sales data from Dynamix

Summary

- Decoupling of incident HIV and bacterial STI
- Syndromic management is still routine for certain STI presentations
- Faster and more novel tests in pipeline
- Threat of AMR – two almost untreatable STI

Top tips

1. Use less antibiotics (test and wait)
2. Use the right antibiotic (reflex resistance testing, known antimicrobial sensitivities)
3. In future consider using a non-antibiotic
4. Find out if your patients are taking doxycycline