ashm

optimising care 2020

Optimising the care of people living with HIV: An update on management of comorbidities to improve patient health

GILEAD

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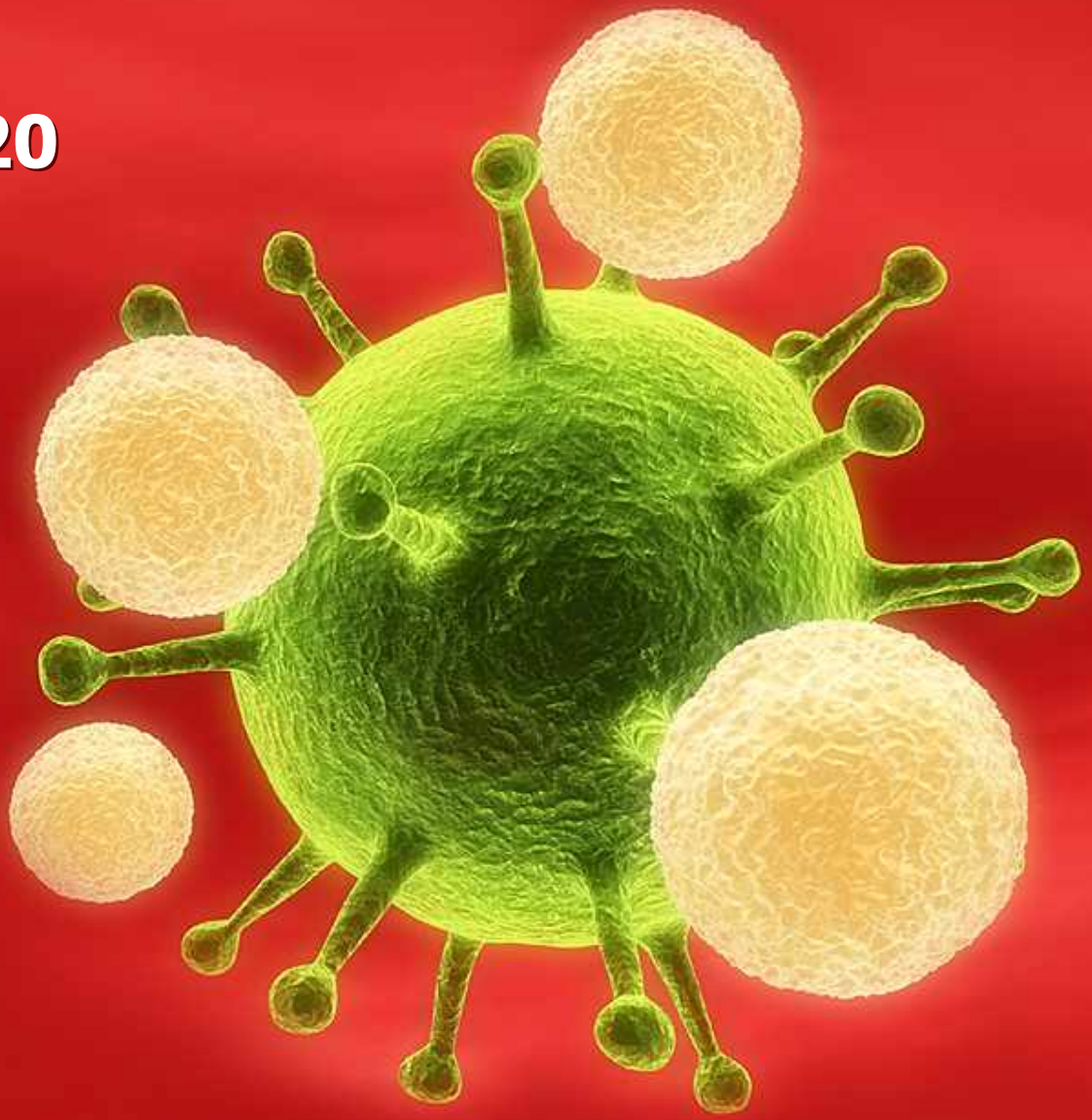
Sexual Health 2020

Dr Catriona Ooi



Sexual health in 2020

- Sex and covid 19
- Where are we now?
  - Epidemiology
- STI Guideline
- STI syndromes
- Sticky issues
  - MG
  - NG
  - STI Pre- exposure prophylaxis
  - Vaccines

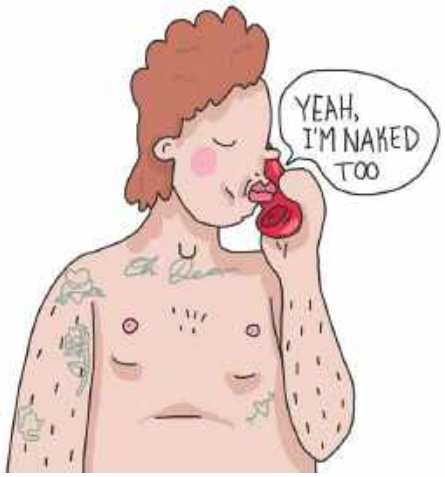
Sex and covid

"You are your safest sex partner."

- New York City Department of Health and Mental Hygiene

Sex and covid: what we know

- Covid 19 has been detected in saliva, faeces and semen
- Currently there is no evidence of transmission of covid 19 from exposure to semen/vaginal fluids or via faecal-oral route
- Risk associated with different types of sexual practices is unknown.

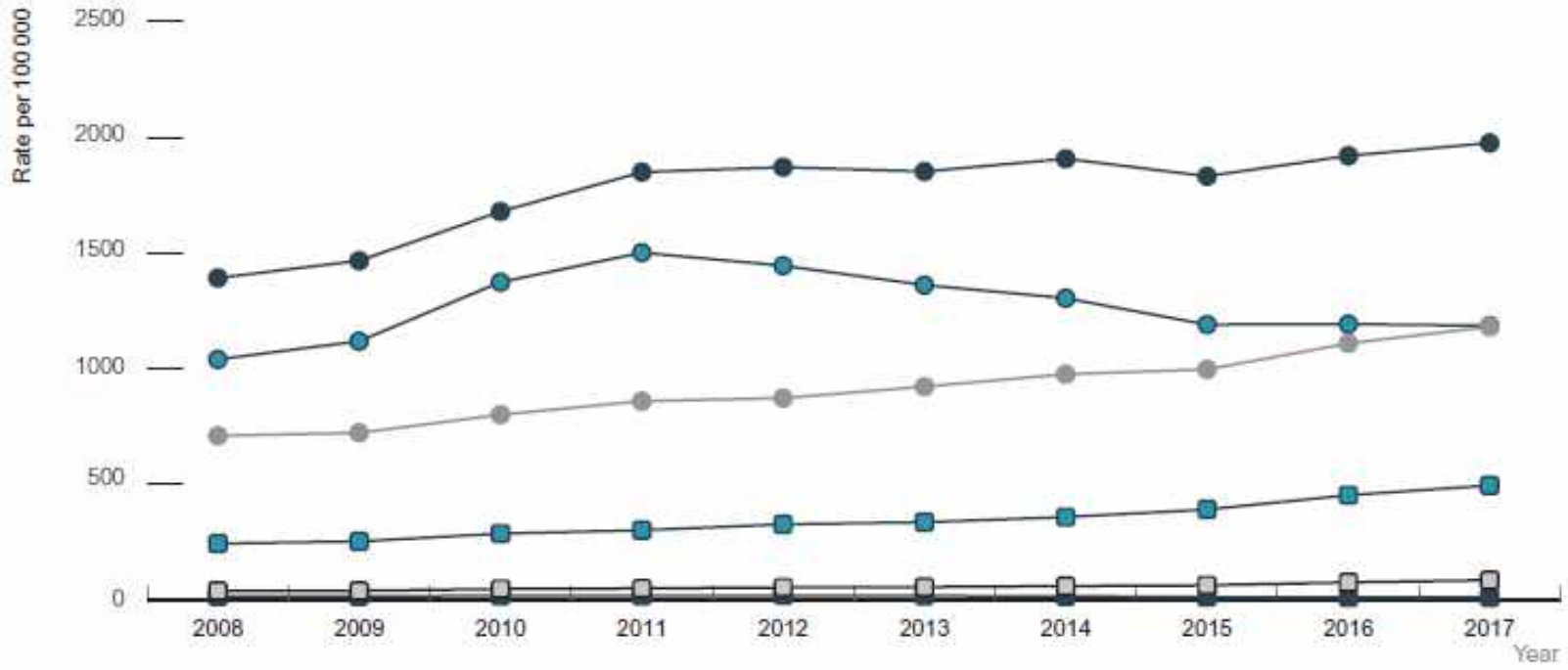


Sex and covid: minimizing the risk

- Wash before/after sex
- Avoiding face to face contact, wear a mask
- Avoid kissing, saliva exchange, close face-to-face contact, face touching
- Avoid sharing personal objects
- reduce contact with bodily secretions and faecal material (oral sex/rimming: use condoms and dental dams)
- Have online encounters
- Have short(er) encounters
- limit the number of sexual partners, avoid group sex, limit sex to small, trusted networks

Back to STIs……

Chlamydia notification rate per 100 000, 2008–2017, by year and age group



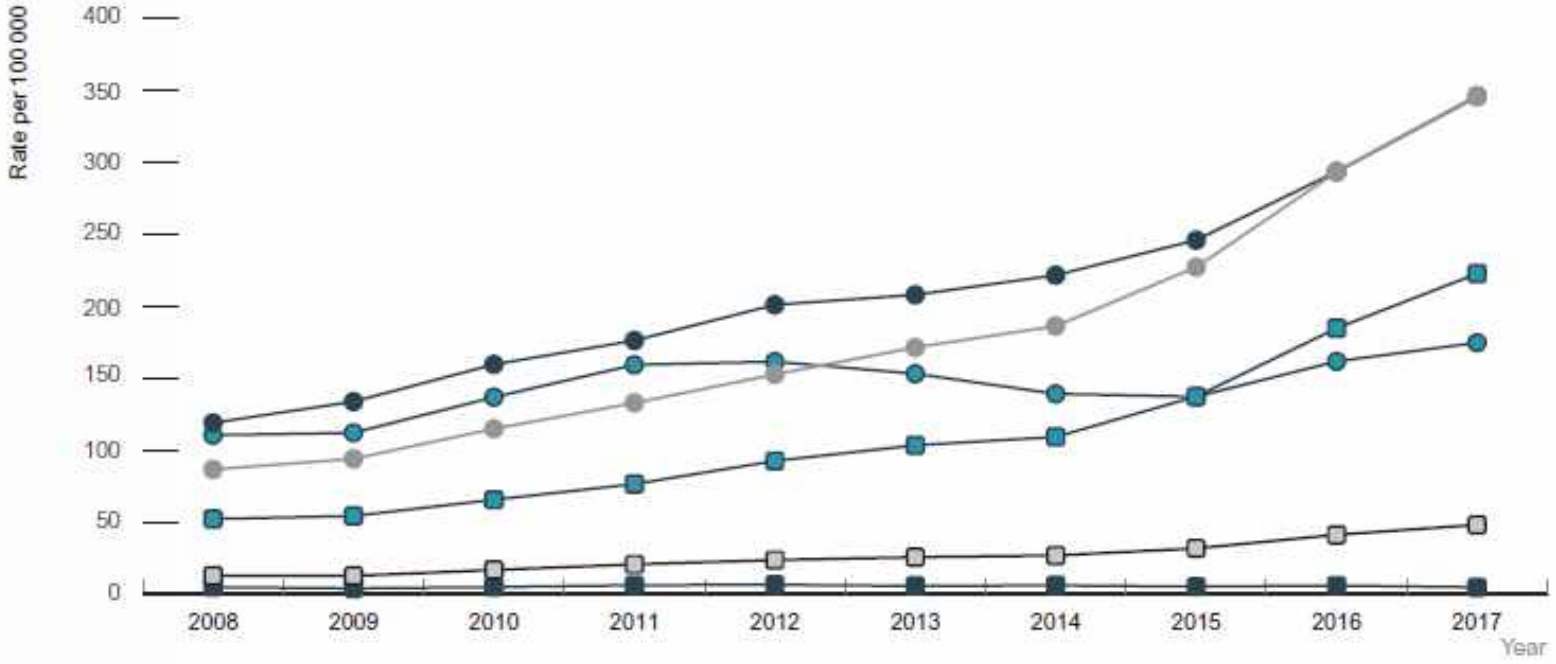
	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
0–14	14.2	14.5	17.5	17.7	18.2	16.6	15.4	11.3	11.0	9.8
15–19	1039.5	1118.1	1373.7	1501.0	1444.6	1361.1	1304.2	1189.8	1192.0	1185.3
20–24	1391.6	1466.2	1678.8	1849.4	1870.5	1851.9	1907.1	1831.6	1920.0	1975.4
25–29	709.1	721.9	800.2	859.1	872.0	921.7	975.6	996.2	1108.7	1180.9
30–39	243.0	252.4	286.2	300.5	326.2	335.4	357.5	390.3	452.3	494.2
40+	38.2	38.8	46.5	48.9	53.4	54.9	59.2	62.7	75.1	84.6

Source: Australian National Notifiable Diseases Surveillance System

Kirby Institute 2018

Back to STIs……

Gonorrhoea notification rate per 100 000 population, 2008–2017, by age group

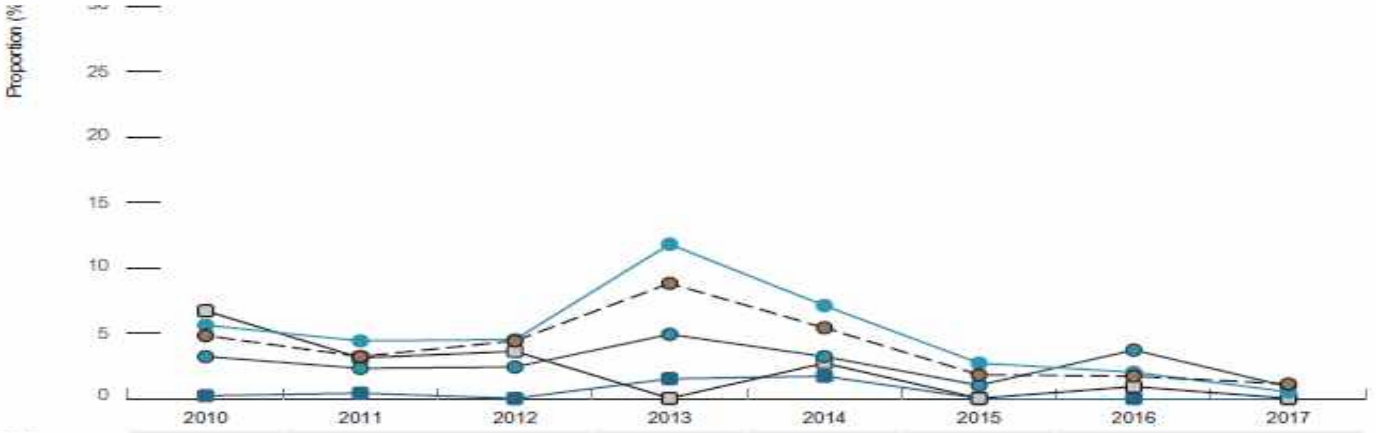


	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
0–14	4.5	3.6	4.5	5.8	6.1	5.3	5.7	4.8	5.6	4.3
15–19	110.2	111.9	136.7	159.2	161.4	153.0	139.0	137.0	161.6	174.6
20–24	118.8	133.6	159.5	176.1	201.0	207.9	221.6	246.0	293.7	346.3
25–29	86.4	93.8	114.7	132.7	152.5	171.3	186.2	227.2	293.5	345.6
30–39	51.9	54.0	65.3	76.2	92.3	103.2	109.0	137.2	184.7	222.7
40+	12.5	12.3	16.4	20.3	23.3	25.3	26.5	31.4	40.9	47.8

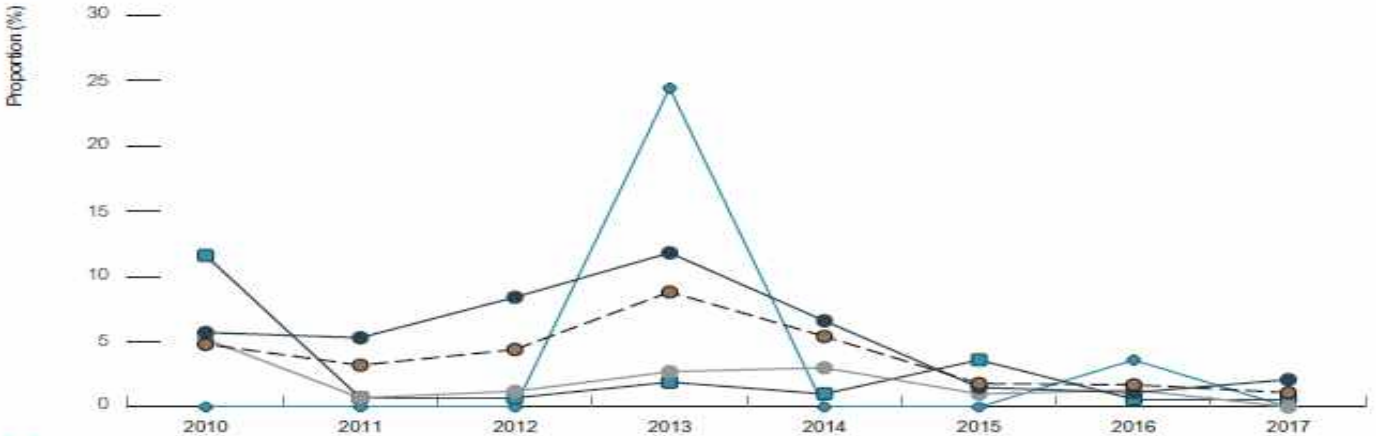
Source: Australian National Notifiable Diseases Surveillance System.

Kirby Institute 2018

Proportion of gonococcal isolates tested at the Australian Gonococcal Surveillance Programme with decreased susceptibility to ceftriaxone, 2010–2017, by state/territory



	2010	2011	2012	2013	2014	2015	2016	2017
ACT	6.7	3.1	3.6	0.0	2.7	0.0	0.9	0.0
NSW	5.6	4.4	4.5	11.8	7.1	2.7	2	0.5
NT	0.2	0.4	0	1.5	1.7	0.0	0	0.0
QLD	3.2	2.3	2.4	4.9	3.2	1.0	3.7	0.9
Australia	4.8	3.2	4.4	8.8	5.4	1.8	1.7	1.1

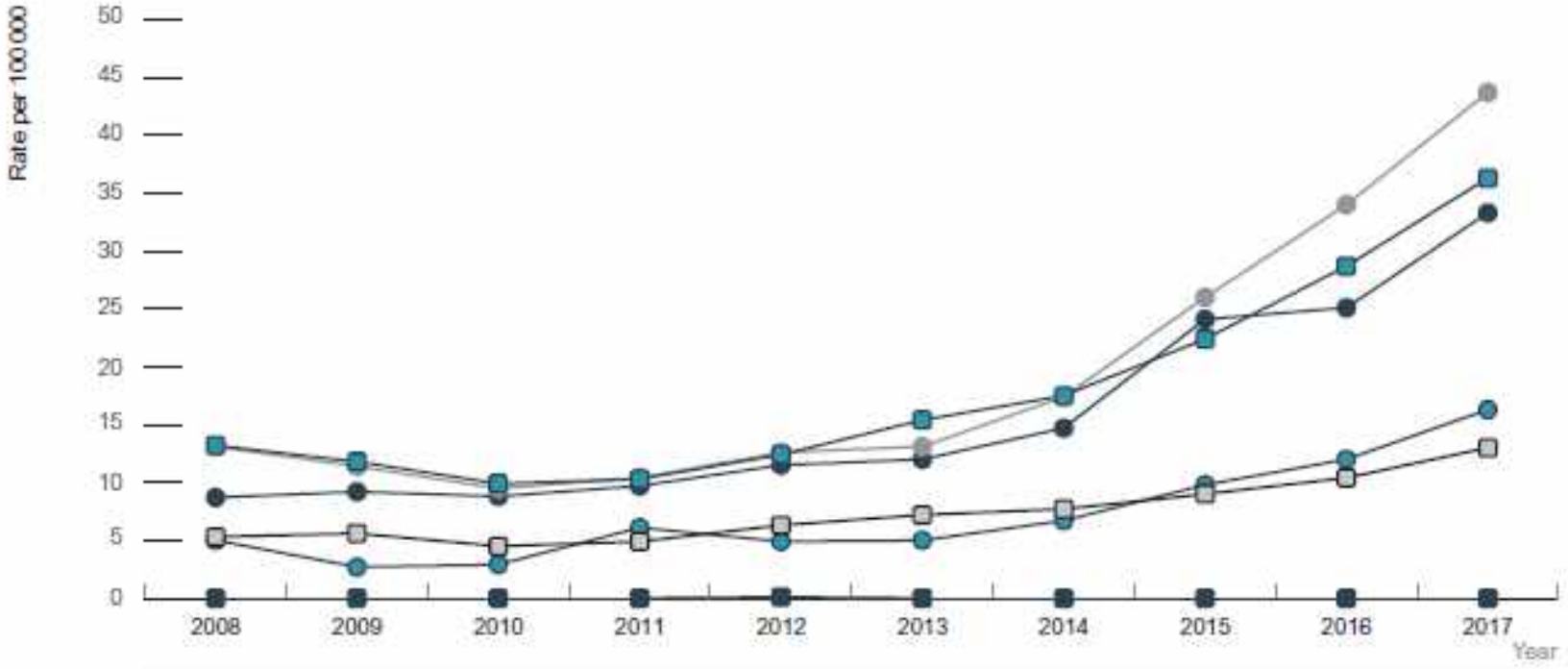


	2010	2011	2012	2013	2014	2015	2016	2017
SA	11.6	0.7	0.7	1.9	1	3.6	0.6	0.6
TAS	0	0	0	24.4	0	0.0	3.6	0.0
VIC	5.7	5.3	8.4	11.8	6.6	1.5	1.1	2.1
WA	5.2	0.7	1.2	2.7	3	1.0	1.3	0.0
Australia	4.8	3.2	4.4	8.8	5.4	1.8	1.7	1.1

Note: Decreased susceptibility was defined as having an MIC (minimum inhibitory concentration) between 0.06 and 0.125 mg/L.
Source: Australian Gonococcal Surveillance Programme.[41]

Kirby Institute 2018

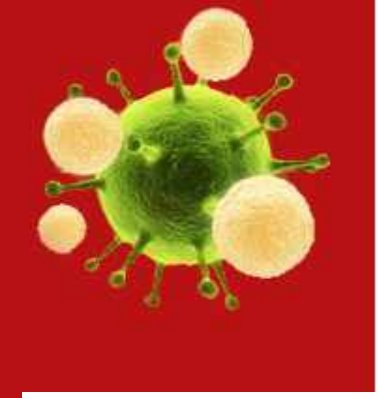
Infectious syphilis notification rate per 100 000, 2008–2017, by year and age group



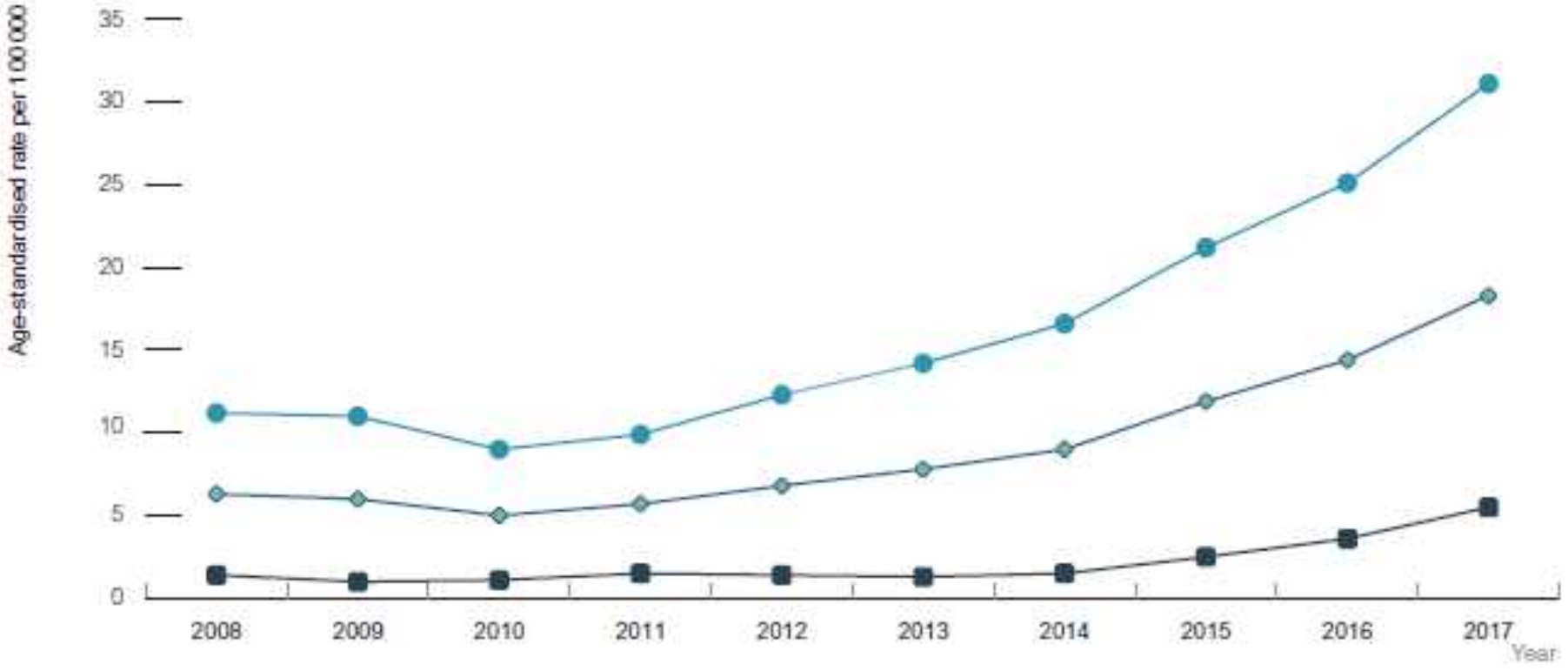
	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
0–14	0.2	0.1	0.0	0.3	0.1	0.2	0.2	0.4	0.4	0.5
15–19	5.0	2.7	2.9	6.1	4.9	5.0	6.7	9.8	12.0	16.3
20–24	8.7	9.2	8.8	9.7	11.5	12.0	14.7	24.1	25.1	33.3
25–29	13.1	11.4	9.5	10.4	12.6	13.1	17.4	26.0	34.0	43.7
30–39	13.2	11.8	9.9	10.3	12.4	15.4	17.5	22.4	28.7	36.3
40+	5.3	5.6	4.5	4.9	6.3	7.2	7.7	9.0	10.4	13.0

Source: Australian National Notifiable Diseases Surveillance System.

Kirby Institute 2018



Infectious syphilis notification rate per 100 000 population, 2008–2017, by sex

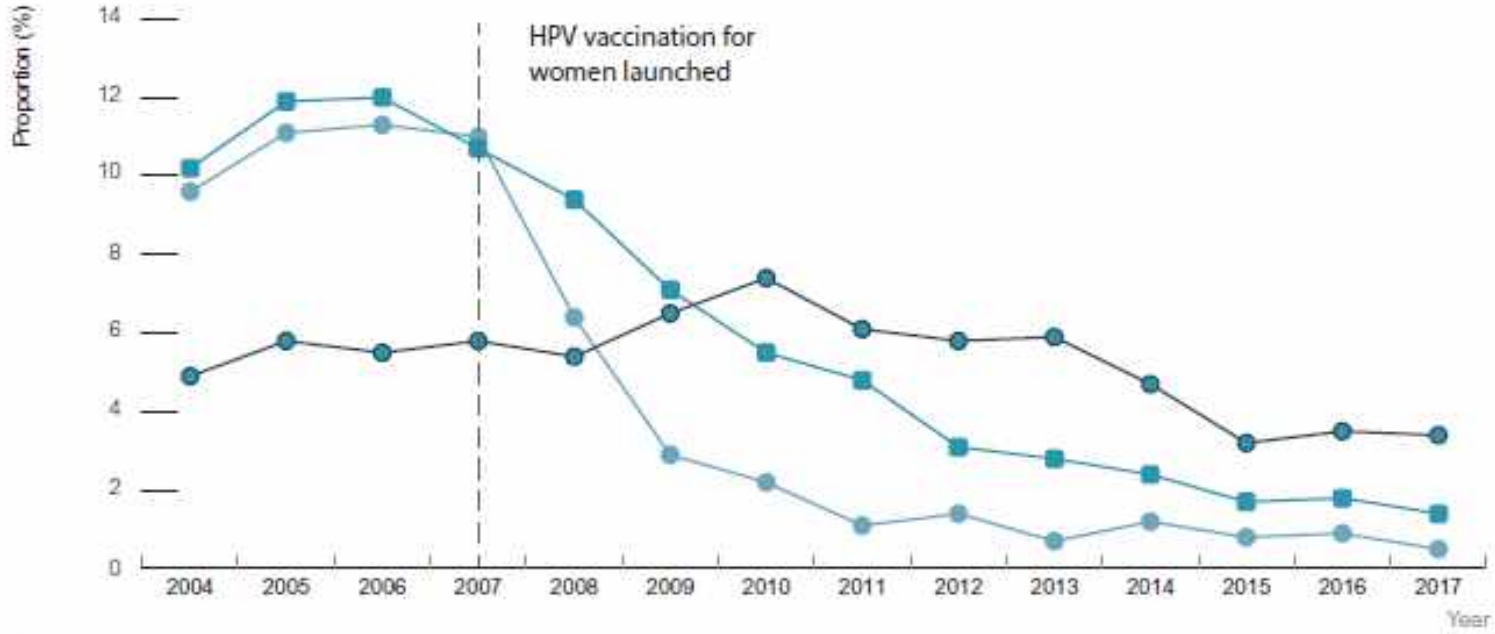


	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Male	11.2	11.0	9.0	9.9	12.3	14.2	16.6	21.2	25.1	31.1
Female	1.4	1.0	1.1	1.5	1.4	1.3	1.5	2.5	3.6	5.5
Total	6.3	6.0	5.0	5.7	6.8	7.8	9.0	11.9	14.4	18.3

Source: Australian National Notifiable Diseases Surveillance System.

Kirby Institute 2018

Proportion of Australian-born non-Indigenous females diagnosed with genital warts at first visit at sexual health clinics, 2004–2017, by age group



	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
<21 years (%)	9.6	11.1	11.3	11.0	6.4	2.9	2.2	1.1	1.4	0.7	1.2	0.8	0.9	0.5
21–30 years (%)	10.2	11.9	12.0	10.7	9.4	7.1	5.5	4.8	3.1	2.8	2.4	1.7	1.8	1.4
>30 years (%)	4.9	5.8	5.5	5.8	5.4	6.5	7.4	6.1	5.8	5.9	4.7	3.2	3.5	3.4

Note: Excludes Aboriginal and Torres Strait Islander females.
Source: Genital Wart Surveillance Network.

Kirby Institute 2018

STIs in the era of PrEP

- greater STI risk: younger; use of PrEP and PEP prior to enrolment; rectal NG or CT or TP prior to enrolment; more oral sex partners; more anal sex partners; inconsistent/no condom use with casual partners; group sex
- STI incidence increased from 69.5 / 100 pys prior to enrolment to 98.4 per 100 pys during follow-up (IRR, 1.41 [95% CI, 1.29-1.56]).
- after adjusting for testing frequency, the change in incidence of any STI from pre to post enrolment among PrEP participants was not significant

Traeger, et al. *JAMA* 2019

Snapshot:
STI guidelines: ch-ch-changes

- ✓ Urethritis: *doxycycline* first line
- ✓ Cervicitis: *doxycycline* first line
- ✓ pharyngeal NG: ceftriaxone + *2gm* azithromycin
- ✓ screening in men: *include NG urine PCR*
- ✓ PID treatment: Ceftriaxone + Metronidazole + Doxycycline 100mg PO, BD 14/7 *(no azithromycin)*
- ✓ Chlamydia: *doxycycline* or *azithromycin*

Syndromes: proctitis

- Common STIs: NG, CT (incl LGV) and HSV
- EXAMINE (with proctoscope)
- TEST:
  - **All sites of risk**
  - **Swab Tests : CT PCR, NG PCR + culture, HVS PCR +/- TP PCR**
  - **Serology: HIV, syphilis**
- TREAT:
  - **ceftriaxone stat, doxy (21/7), antiviral 5-10/7**
- ?MG testing: Consider if MG contact or other tests negative, however insufficient evidence to suggest that *M. genitalium* is a cause of proctitis.

Syndromes: PID

- Polymicrobial: STI and vaginal anaerobes
- Most common STIs: NG, CT, MG
- EXAMINE (with speculum)
- TEST:
  - **All sites of risk**
  - **Swab Tests : CT PCR, NG PCR + culture, MG PCR**
  - **Serology: HIV, syphilis**
- TREAT:
  - **ceftriaxone stat, doxy (14/7), metronidazole 14/7**

Around the country

- NSW: new strain of MDR shigella in MSM
- Vic: HAV in PWID and homeless people; increase in syphilis and congenital syphilis; MDR shigella
- WA: Syphilis outbreak

MDR SHIGELLOSIS ALERT

Please distribute this information to all medical staff

NSW GOVERNMENT Health

Key Points:

1. **Several different multidrug resistant (MDR) *Shigella* strains are circulating among men who have sex with men (MSM) in NSW**
2. **Request full sensitivities including azithromycin on stool specimens for MSM with diarrhoea**
3. **Consider referral for IV antibiotics for patients who require immediate treatment**
4. **Discuss the risk of MDR shigellosis and prevention with all MSM patients**

- Identified in MSM sexual contact.
- resistant to ceftriaxone, cotrimoxazole, ampicillin/amoxicillin AND azithromycin, but is SUSCEPTIBLE to ciprofloxacin.
  - **(the most common Shigella strain which is RESISTANT to ciprofloxacin, cotrimoxazole, ampicillin/amoxicillin AND azithromycin)**

Sticky issues: MG

- What we still don't know
  - **Clinical relevance in asymptomatic people**
  - **Natural history**
  - **Disease spectrum: preterm birth? Spontaneous abortion?, HIV transmission cofactor?**

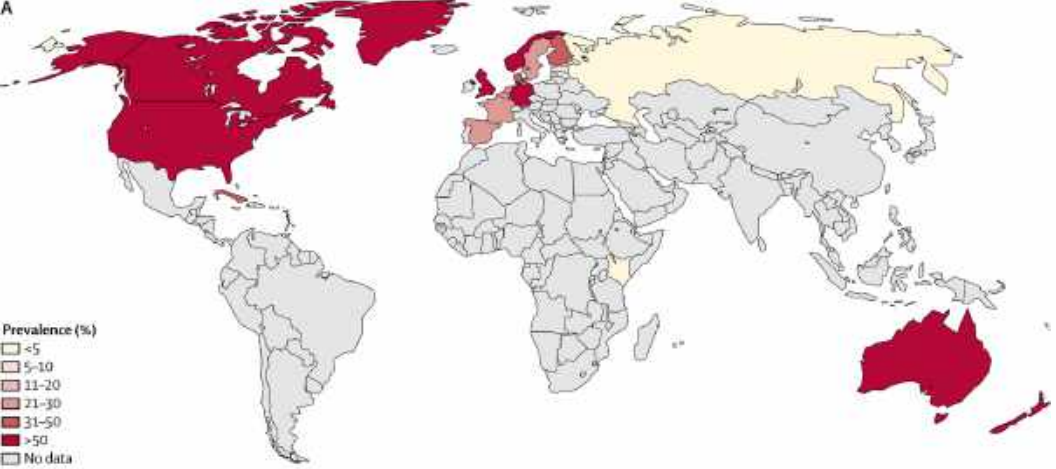
- What are the issues?
  - **Resistance**
  - **Surveillance**
  - **Access to testing**
  - **Syndromic management**

Sticky issues: MG

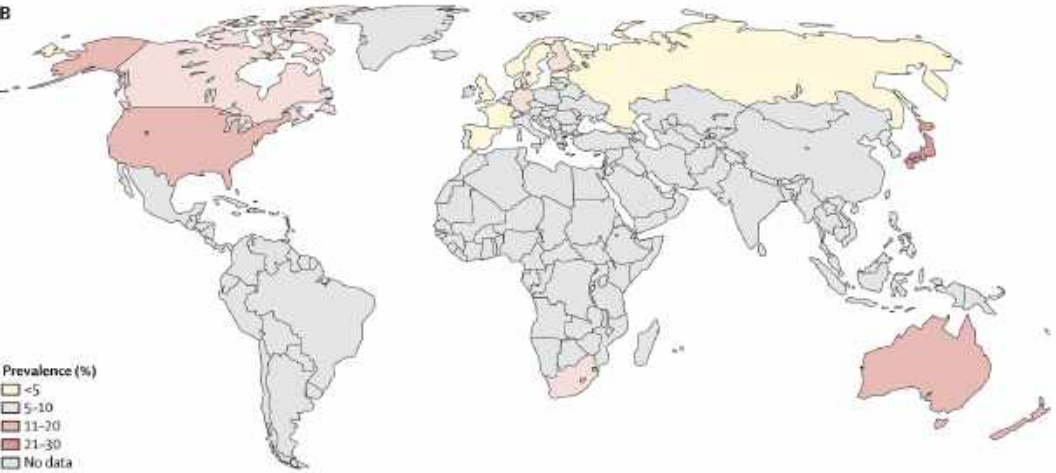
Background

- ✓ no cell wall, therefore resistant to β-lactam antibiotics.
- ✓ Treatment with antimicrobials that disrupt protein synthesis (e.g. tetracyclines, macrolides, streptogramins) or DNA replication (e.g. fluoroquinolones).
- ✓ Rapid resistance: broad predictors: geographical region (& country), sex, and population sampled
- ✓ In Australia, significant rates of asymptomatic carriage highest: MSM, taking PrEP, attending sexual health clinics, HIV+

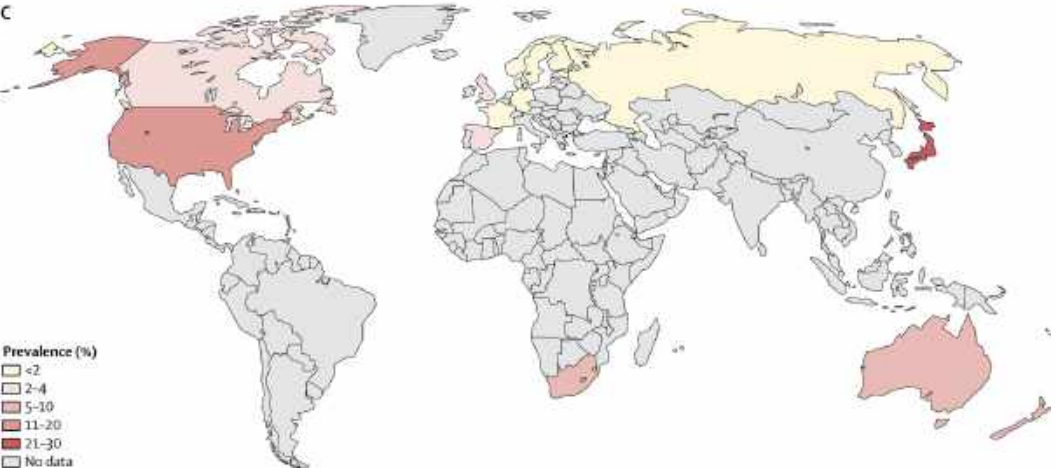
prevalence of single-nucleotide polymorphisms



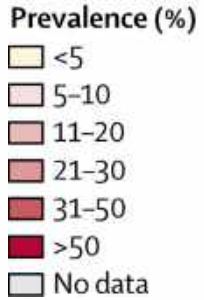
A. macrolide resistance
23S ribosomal RNA gene



B. fluoroquinolone resistance
parC and gyrA genes



C. dual macrolide and fluoroquinolone resistance



Machalek et al, Lancet Infect Dis 2020

Treatment options

a. **macrolide-susceptible:** doxycycline 100mg bd, 7 days, followed by azithromycin 1g stat, then 500mg daily for another three days (2.5g total)

b. **macrolide resistant:** doxycycline 100mg bd, 7 days, followed by moxifloxacin 400mg daily for seven days

c. **Pristinamycin and Minocycline:** Pristinamycin 1g tds combined with doxycycline 100mg bd for 10 days or minocycline at a dose of 100mg daily for 14 days

Pristinamycin + doxycycline cured 75% (95% CI, 64%–85%), and minocycline cured 71% (95% CI, 54%–85%) of cases. Read et al. *Emerg Infect Dis*. 2018 and Doyle et al *Open Forum Infect Dis*. 2020

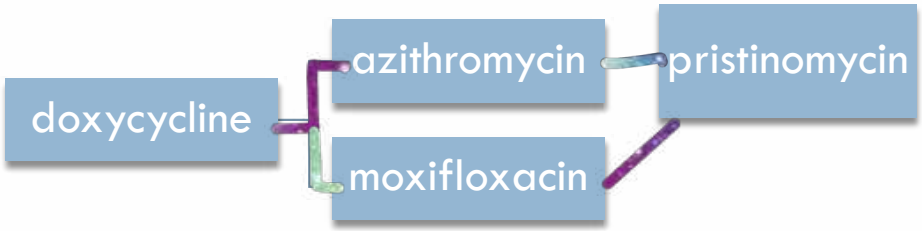
d. **Sitafloxacin:** sitafloxacin 100mg twice daily in combination with doxycycline 100mg twice daily for 7 days. test of cure 3 weeks after completing therapy

cured 11/12 infections that had failed prior regimens with moxifloxacin and pristinamycin. Durukan D, et al. *Emerg Infect Dis*. 2020

Resistance guided sequential treatment

resistance guided, sequential treatment is now standard

- **Improves cure rates of susceptible infections**
- **Reduces selection of macrolide resistance**



- Josamycin (macrolide)
- Solithromycin (fluoroketolide)
- Lefamulin (pleuomutalin)
- **Sitafloxacin (fluoroquinolone)**
- Zoliflodacin (spiropyrimidinetrione)
- Spectinomycin (aminoglycoside)

– **Ongoing issues:**

– **Different treatment regimens, availability of testing, time to results of resistance assays, treatment options**

What are we doing?

- Test only symptomatic people: urethritis, cervicitis, PID
- Resistance profiling and resistance guided treatment are key success
- TOC essential
- contact tracing?- current partners only

Sticky issues: NG

The World's First Confirmed Gonococcal Isolate Resistant to Ceftriaxone (XDR-NG)

Is *Neisseria gonorrhoeae* Initiating a Future Era of Untreatable Gonorrhea?: Detailed Characterization of the First Strain with High-Level Resistance to Ceftriaxone

Makoto Ohnishi, Daniel Golparian, Ken Shimuta, Takeshi Saika, Shinji Hoshina, Kazuhiro Iwasaku, Shu-ichi Nakayama, Jo Kitawaki, and Magnus Unemo

Recently, the first *Neisseria gonorrhoeae* strain (H041) that is highly resistant to the extended-spectrum cephalosporin (ESC) ceftriaxone, the last remaining option for empirical first-line treatment, was isolated. We performed a detailed characterization of H041, phenotypically and genetically, to confirm the finding, examine its antimicrobial resistance (AMR), and elucidate the resistance mechanisms. H041 was examined using seven species-confirmatory tests, antibiograms (30 antimicrobials), *penA* sequencing, *N. gonorrhoeae* multiantigen sequence typing (NG-MAST), multilocus sequence typing (MLST), and sequencing of ESC resistance determinants (*penA*, *mtrR*, *porB*, *ponA*, and *pilQ*). Transformation, using appropriate recipient strains, was performed to confirm the ESC resistance determinants. H041 was assigned to serovar IB-prot, MLST sequence type (ST) ST7362, and the new NG-MAST ST4220. H041 proved highly resistant to ceftriaxone (2 to 4 μg/ml, which is 4- to 8-fold higher than any previously described isolate) and all other cephalosporins, as well as most other antimicrobials tested. A new *penA* mosaic allele caused the ceftriaxone resistance. In conclusion, *N. gonorrhoeae* has now shown its ability to also develop ceftriaxone resistance. Although the biological fitness of ceftriaxone resistance in *N. gonorrhoeae* remains unknown, *N. gonorrhoeae* may soon become a true superbug, causing untreatable gonorrhea. A reduction in the global gonorrhea burden by enhanced disease control activities, combined with wider strategies for general AMR control and enhanced understanding of the mechanisms of emergence and spread of AMR, which need to be monitored globally, and public health response plans for global (and national) perspectives are important. Ultimately, the development of new drugs for efficacious gonorrhea treatment is necessary.

- Gonococcal strain H041 was isolated from the pharynx of a female sex worker in Kyoto, Japan
- MIC to ceftriaxone 2-4 mg/l and to cefixime 8 mg/l
- Resistant to most beta-lactams including piperacillin/tazobactam, fluoroquinolones, macrolides, tetracycline, co-trimoxazole, chloramphenicol and nitrofurantoin
- Susceptible to spectinomycin, imipenem and rifampicin

Ohnishi M *et al.,* Emerg. Infect. Dis. 2011;**17**:148-149 Ohnishi M *et al*. , Antimicrob. Agents Chemother. 2011;**55**:3538-3545

Australian Government
Department of Health

Professor Brendon Murphy
Commonwealth Chief Medical Officer

MEDIA STATEMENT

17 April 2018

Multi-drug resistant gonorrhoea

GONORRHOEA – antimicrobial resistance

Information for NSW clinicians

NSW GOVERNMENT Health

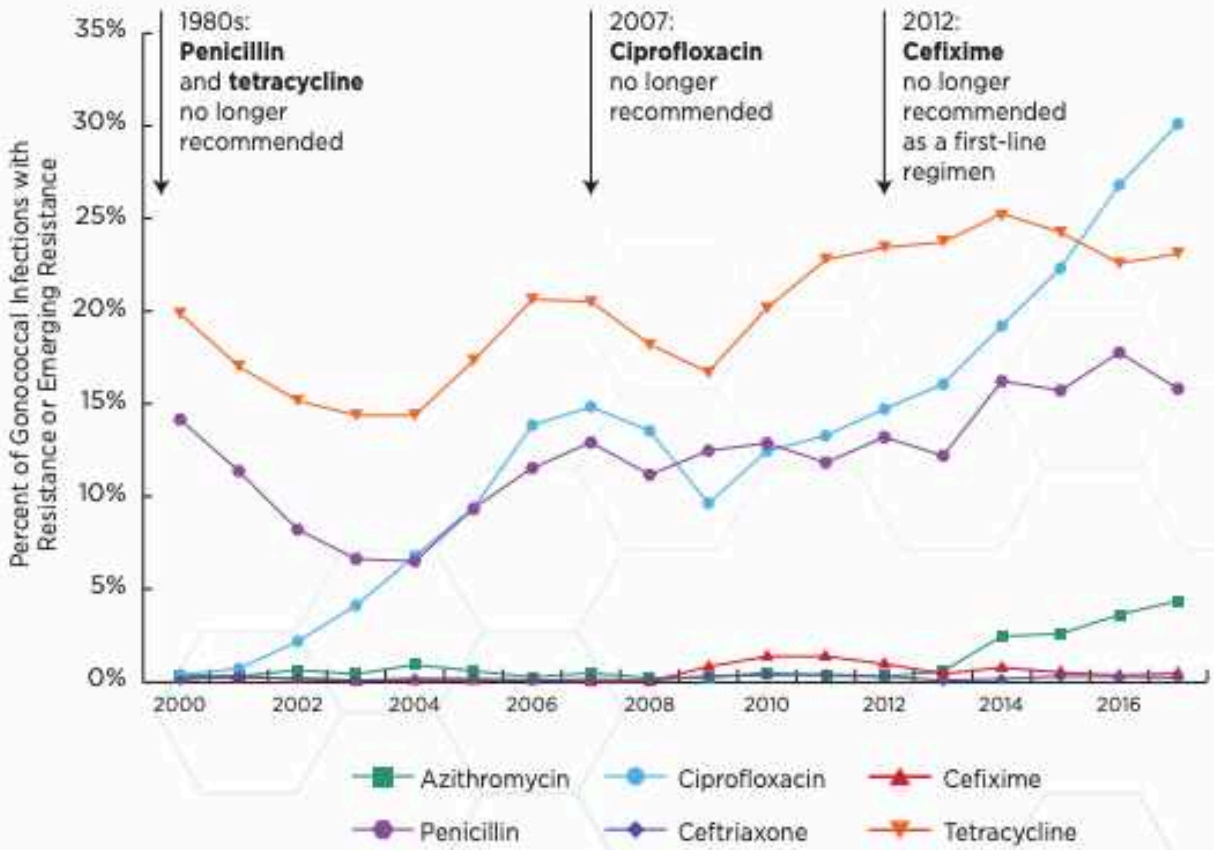
1. **Two cases of gonorrhoea highly resistant to antibiotics detected in Australia**
2. **Take swabs for culture and antimicrobial resistance testing**
3. **Treat gonorrhoea with ceftriaxone 500 mg IM plus azithromycin 1 g orally**
4. **Perform a NAAT test of cure 2 weeks after treatment**

Multi-drug resistant gonorrhoea in Australia

- Two cases of gonorrhoea with high level resistance to ceftriaxone, azithromycin, ciprofloxacin, penicillin and tetracycline were diagnosed in Australia in February and March 2018
- One case had recent sex in Southeast Asia; the other case had no recent overseas travel
- It's likely that there are undetected cases
- Emergence of this gonococcal strain in Australia is of concern, as treatment is complex
- Gonorrhoea has increased in heterosexual women and men, and in men who have sex with men in all states and territories

EMERGING ANTIBIOTIC RESISTANCE

Gonorrhea rapidly develops resistance to antibiotics—ceftriaxone is the last recommended treatment.



CDC 2019 Antibiotic Resistance Threats Report.

NG resistance in Australia

2019 report The Australian Gonococcal Surveillance Programme (AGSP).

- Decreased susceptibility (DS) to ceftriaxone (MIC ≥ 0.06 mg/L) was found nationally in 1.3% of isolates.
- 5 isolates ceft-resist (MIC ≥ 0.25 mg/L), and also resistant to penicillin; all were resistant to cipro but susceptible to azith (Vicx3, non-remote WAx1, NSW x1).
- Resistance to azith (MIC ≥ 1.0 mg/L) in 4.6% of isolates (downward trend since 2017)
- Isolates with high-level resistance to azith (MIC ≥ 256 mg/L) continue to be reported sporadically in Australia, with 8 in 2019: 2xNSW, 2x QLD, 2x Vic, 1xTAS, 1x non-remote WA.
- 2,136 isolates (22.1%) were penicillin resistant (considerable variation by jurisdiction, and in some remote settings there is little resistance and this drug is recommended empiric therapy) I
- Remote NT no penicillin resistance was reported, but remote WA 6/85 (7.1%) were penicillin resistant. There was no ciprofloxacin resistance reported from isolates tested from remote regions of the Northern Territory, and ciprofloxacin resistance rates remain comparatively low (7/85; 8.2%) in remote Western Australia.

treatment

- Recycling: cipro, gentamycin
- Existing drugs
- newer antimicrobial agents such as solithromycin, zoliflodacin and gepotidacin

Sticky issues: doxycycline PrEP

- A new concept? Historical examples
  - **BMJ 1886**
  - **Boston medical and surgical journal 1904**
- Response to outbreaks and epidemics
  - **Fresno county, California, 1976**
  - **MSM in LA correctional facility 2000**
  - **Vancouver 2000**

Data thus far…

Key Characteristics of Completed Studies on Doxycycline Prophylaxis for Sexually Transmitted Infections

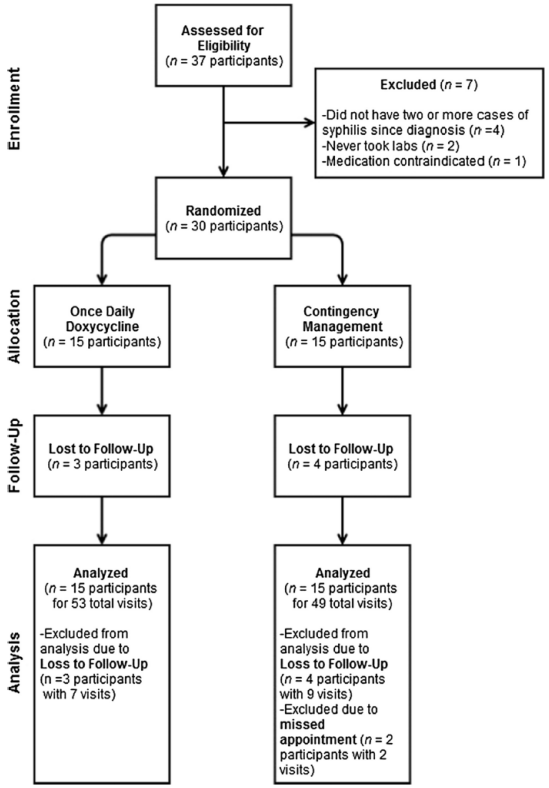
Study, First Author [Reference]	Design	Sample Size	Intervention	Study Population and Inclusion Criteria	Duration	Findings
Bolan [16]	Open-label RCT; patients randomized 1:1 to intervention and standard of care	30	Daily doxycycline hyclate, 100 mg tablet	MSM living with HIV infection; 2 or more treated syphilis diagnoses since HIV diagnosis	48 weeks	Diagnosis of any bacterial STI at any site: odds ratio 0.27 (0.09–0.83), P = .02; no significant differences in sex behaviors at baseline or follow-up. One patient discontinued doxycycline due to GERD.
ANRS IPERGAY Doxy PEP study, Molina [17]	Open-label RCT; patients randomized 1:1 to intervention and no prophylaxis	232	Doxycycline hyclate, 200 mg tablet, single dose within 24–72 hours post–condomless sexual encounter; maximum 3/week	MSM and transgender women without HIV on HIV PrEP having condomless sex with men	Median follow-up, 8.7 months	Diagnosis of any bacterial STI at any site: hazard ratio = 0.57 (0.13–0.62), P = .014. No substantive difference in sexual behaviors at baseline or during study; 32 patients discontinued doxycycline, 8 for gastrointestinal side effects. Remainder discontinued for multiple reasons with no discernable pattern.
Wilson [18]	Model of sexual behavior	NA	Daily doxycycline, 100 mg	MSM	NA	Assuming 50% adoption and 70% efficacy, ~50% reduction in syphilis after 12 months and 85% reduction after 10 years. Similar effect seen if only MSM with >10 partners in 6 months receiving intervention.
Wilson [18]	Survey and focus groups using respondent-driven and convenience sampling	2095	NA	MSM	NA	52.7% (95% confidence interval, 50.6–54.8%) very/slightly likely to use doxycycline to prevent syphilis in themselves; 75.8% (74.0–77.6%) very/slightly likely to use doxycycline to help control syphilis in MSM community. Survey findings supported by focus groups.

Abbreviations: ANRS IPERGAY, France Recherche Nord & sud SIDA-HIV hépatites Intervention Préventive de l'Exposition aux Risques avec et pour les Gays; Doxy, doxycycline; GERD, gastroesophageal reflux disease; HIV, human immunodeficiency virus; MSM, men who have sex with men; NA, not applicable; PEP, postexposure prophylaxis; PrEP, pre-exposure prophylaxis for HIV; RCT, randomized controlled trial; STI, sexually transmitted infection.

Grant et al, *Clin Infect Dis*, 2020

More recently

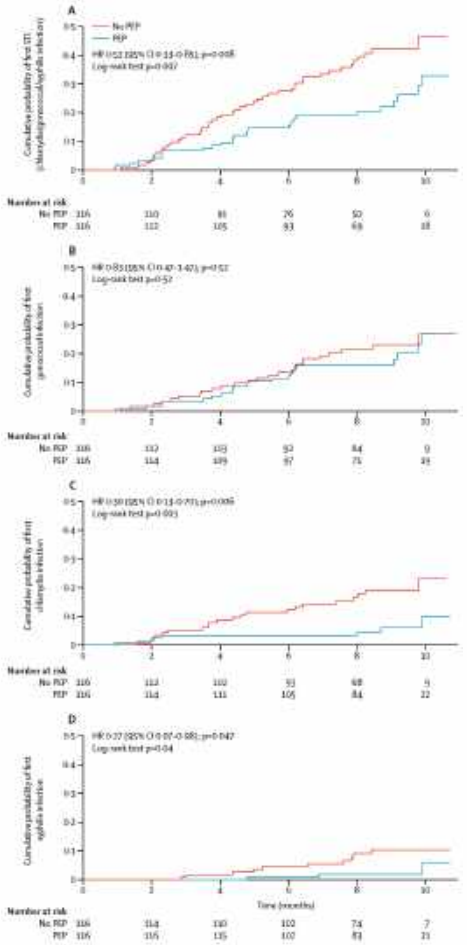
- Small pilot study of daily doxy
- High risk MSM; tested NG, CT, STS
- Review weeks 12, 24, 36 & 48
- Doxy arm sig < for any bacterial STI during follow-up (OR: 0.27) compared to CM arm
- There were no sig self-reported behaviour differences



[1]Bolan RK, et al. *Sex Transm Dis* 2015;42:98-103.

In the PrEP era

- Substudy of the ANRS IPERGAY trial[1]
- Single dose 200 mg doxy within 24 h post sex
- 232 MSM, 10 months
- Occurrence PEP vs no PEP
  - **1st STI HR 0.53 p=0.008**
  - **1st CT HR 0.30 p=0.006**
  - **1st STS HR 0.27 p=0.047**
  - **1st NG HR 0.83 p=0.52**



[1]Molina JM, et al. *Lancet Infect Dis* 2018;18:308-17.

In Australia

- Is it happening?

Pros and cons

- What do we need to know?
  - efficacy; target population; community acceptability; behavioural risk compensation; dose, regimen, and formulation; long-term safety; antimicrobial resistance; cost-effectiveness; and risk–benefit.
- Microbiome of gut
- Consider the goals; serious outcomes mostly assoc. with female genital tract and the foetus
- NNT to prevent infection, to prevent serious adverse outcome
- Cost? Inconvenience? Side effects? Safety? Other infections?

What else is on the table?

- Mouthwash
  - **OMEGA and PReGo**

vaccines

- CT
- TP
- NG

ashm

optimising care 2020

Optimising the care of people living with HIV: An update on management of comorbidities to improve patient health

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