Neisseria gonorrhoeae: Unique antimicrobial susceptible lineages of *Neisseria gonorrhoeae* predominate in remote regions of Western Australia

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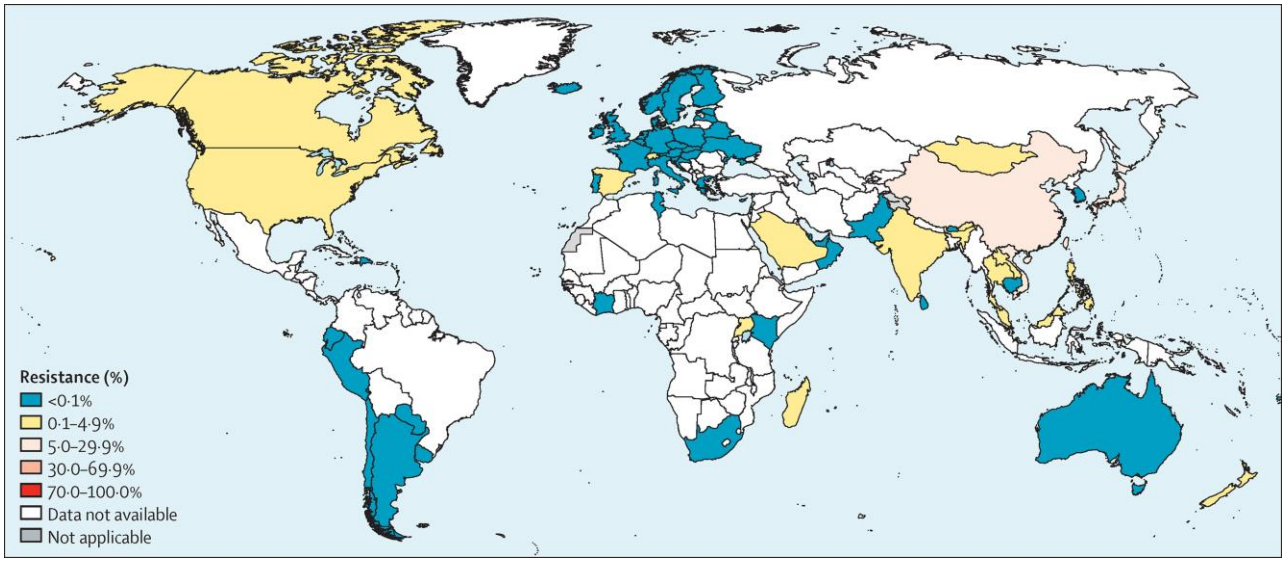
Acknowledgement of Country

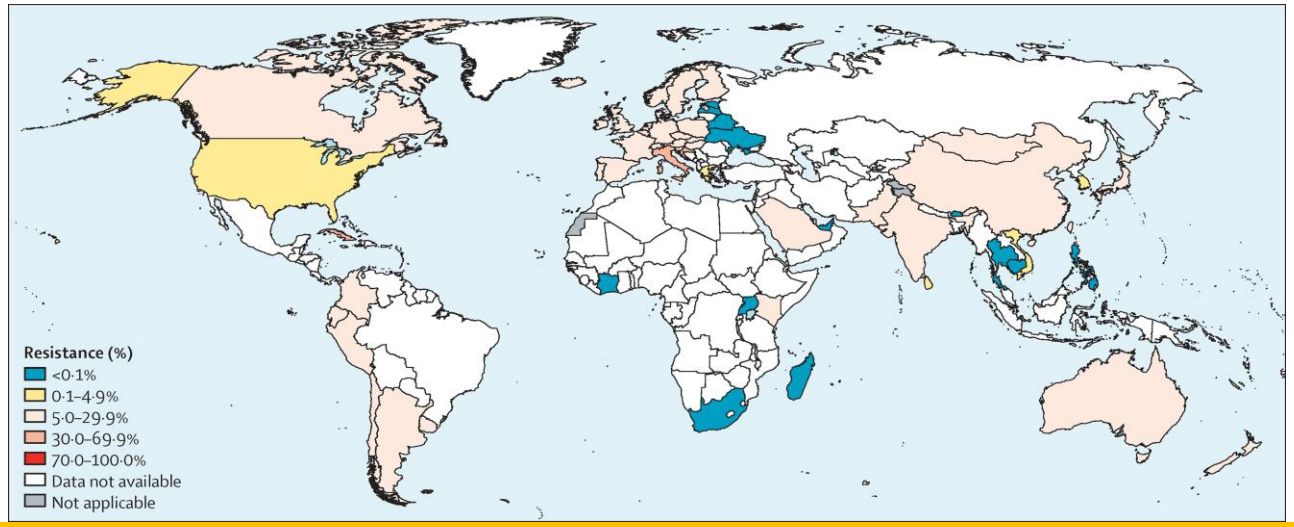
We acknowledge the
Traditional Owners
of the many lands and language groups
upon which this work was conducted and upon which we meet today.

We pay respects to their Elders past, present, and emerging.

Global prevalence of antimicrobial resistance in *N. gonorrhoeae* is rising



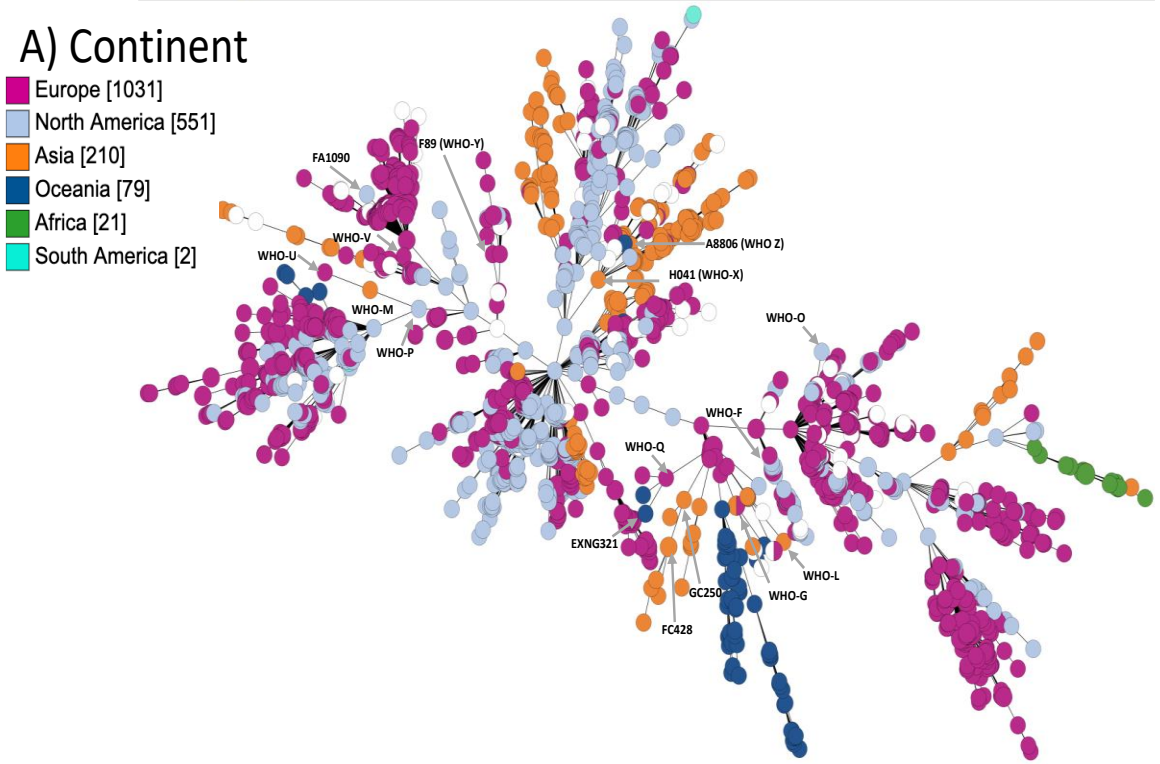
Ceftriaxone



Azithromycin

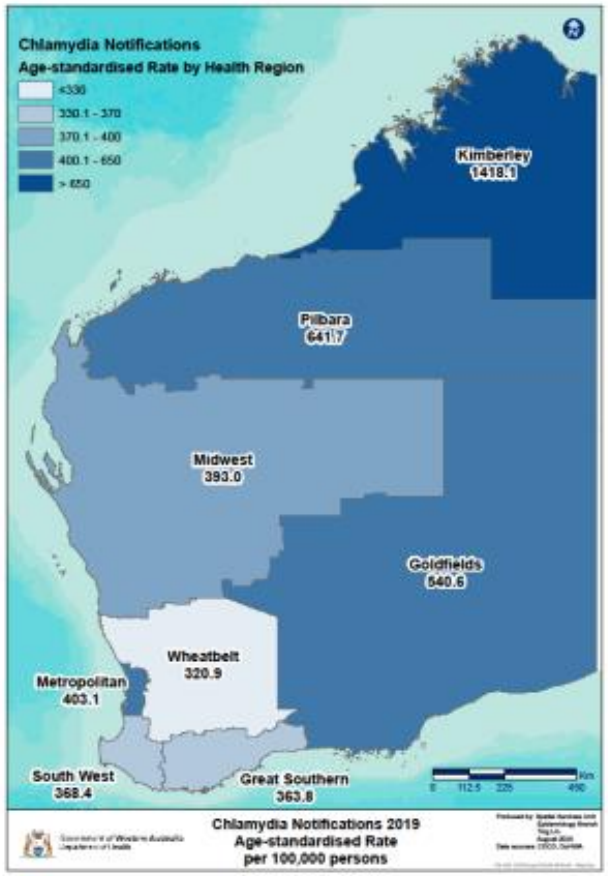
Unemo et al. (2021) *WHO global antimicrobial resistance surveillance for Neisseria gonorrhoeae 2017–18: a retrospective observational study* The Lancet Microbe 2(11): e627-636.

Neisseria gonorrhoeae has weakly clonal groups

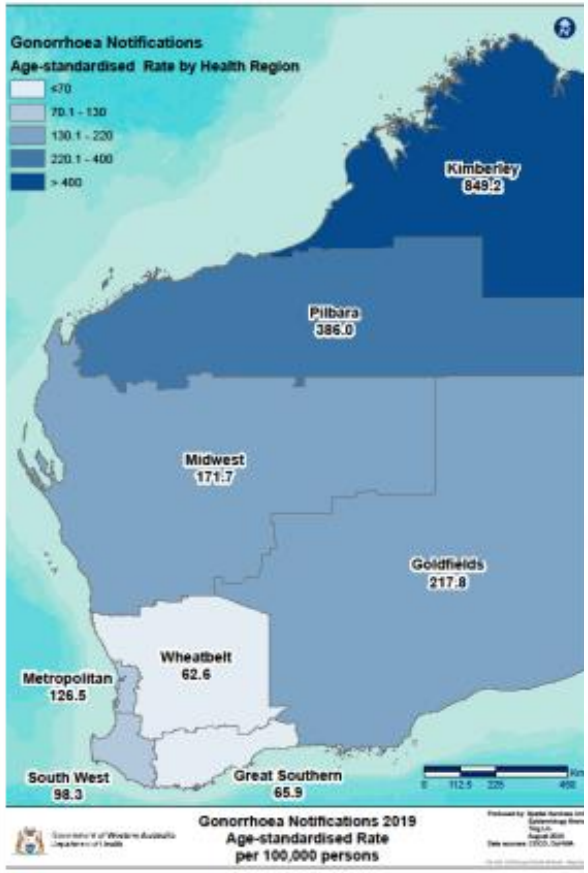


- With large genomic databases available:
  - *Neisseria gonorrhoeae* is weakly clonal
  - Genetic lineages emerge due to selective pressure of antimicrobial resistance – Once an isolate becomes resistant to antibiotics it moves around the globe through travel

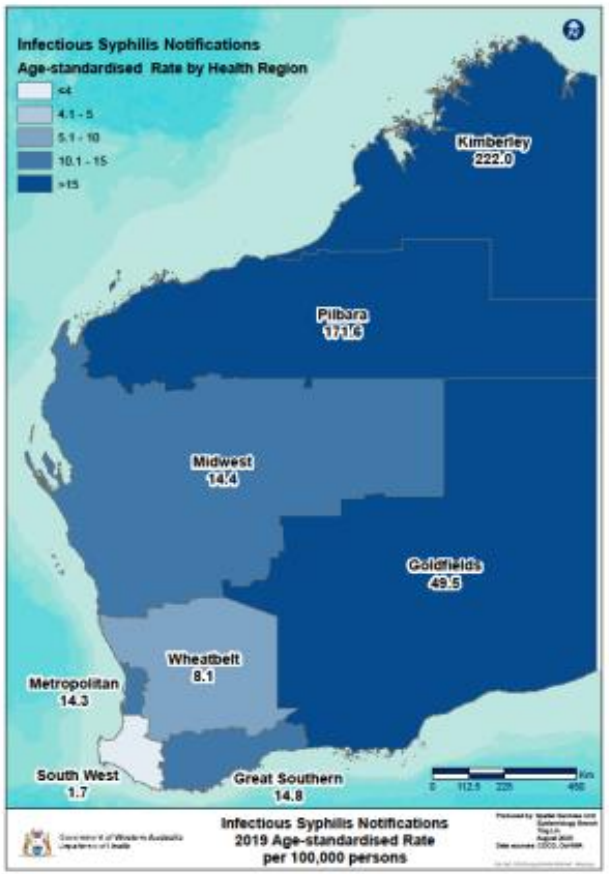
Epidemiology within Western Australia: the problem of remoteness



Chlamydia notifications by health region, WA, 2019



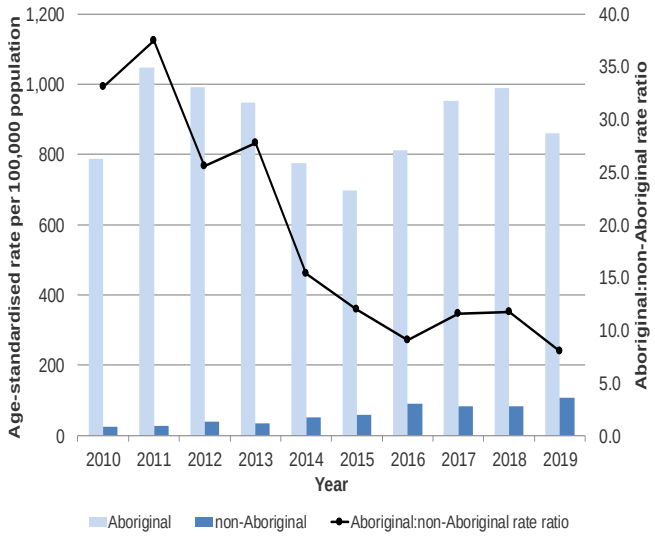
Gonorrhoea notifications by health region, WA, 2019



Syphilis notifications by health region, WA, 2019

The Epidemiology of Notifiable Sexually Transmitted Infections and Blood-Borne Viruses in Western Australia 2019. Gov of Western Australia. Department of Health

Gonorrhoea incidence is increasing in the heterosexual population

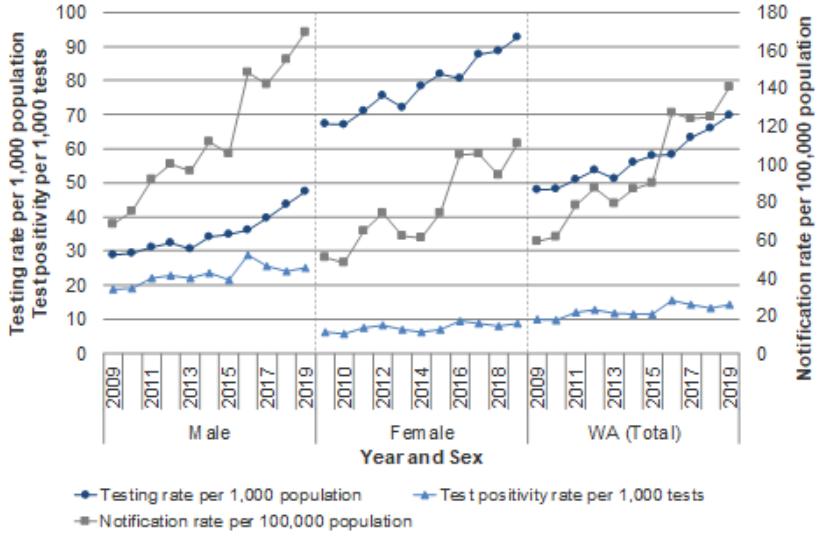


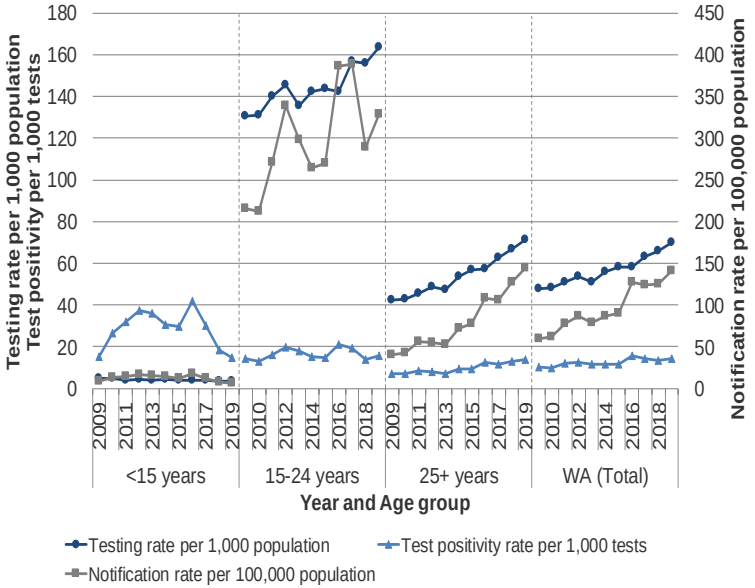
Ratio of disease is 8:1 in indigenous:non-indigenous

Equally distributed in indigenous men and women
In non-indigenous people, more men than women were positive

- 30% were same sex

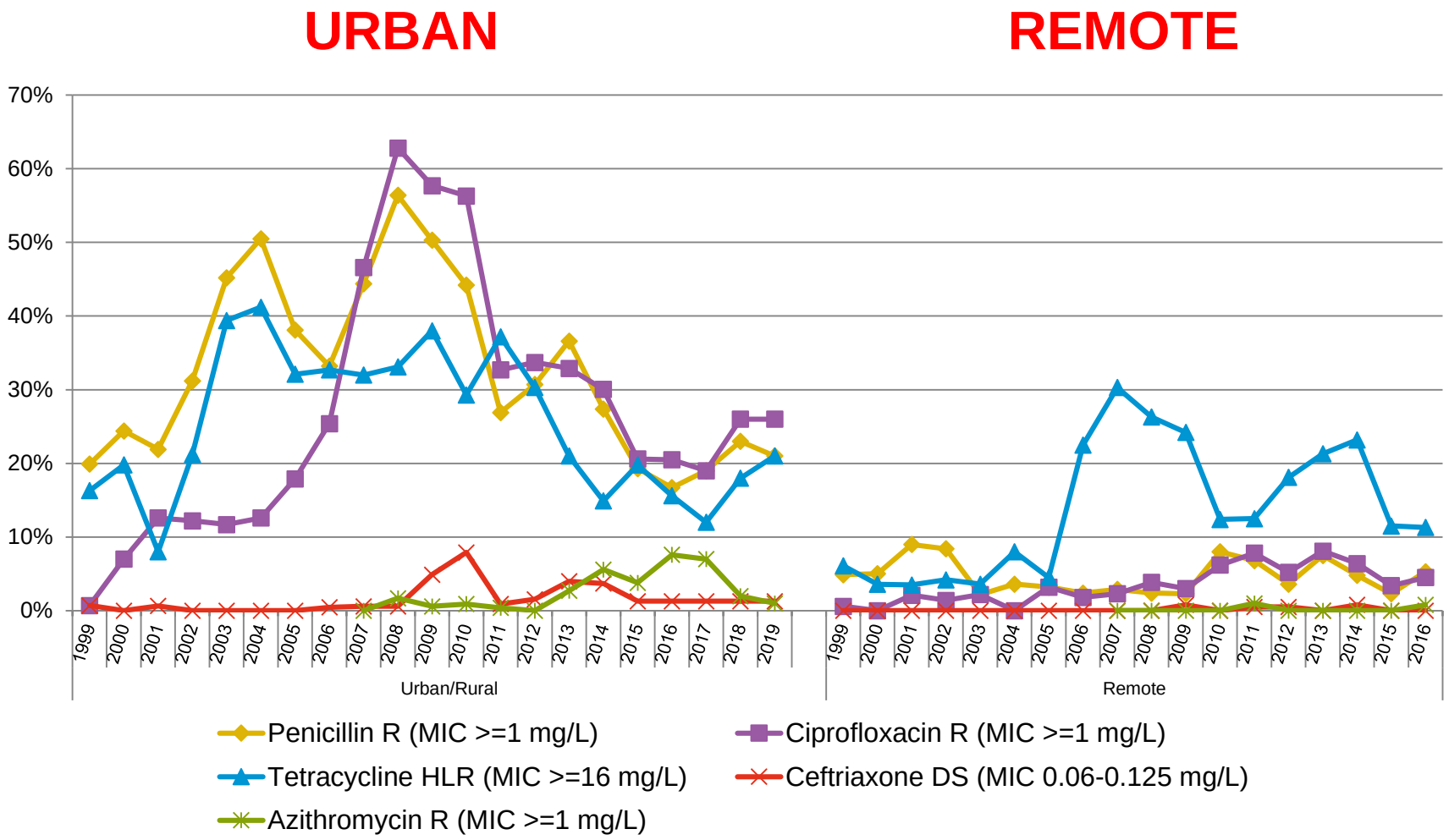
Most disease in WA is in the heterosexual population





Urban areas have higher levels of antimicrobial resistance (AMR) than remote jurisdictions

THE UNIVERSITY OF WESTERN AUSTRALIA



NOTE: Although AMR prevalence declined overall in 2017, overall disease incidence had increased in metropolitan areas

Hypothesis

Rationale

Increased incidence of gonorrhea in metropolitan areas 2015-2017 was associated with antimicrobial sensitive isolates.

Hypothesis

What is the origin of the antimicrobial sensitive isolates in metropolitan areas:

Bridging from remote regions?

International introduction?

Methodology

741 NG isolates WA

iPLEX

WA-genotypes

192 NG isolates WA

SPAdes/ BIGSdb

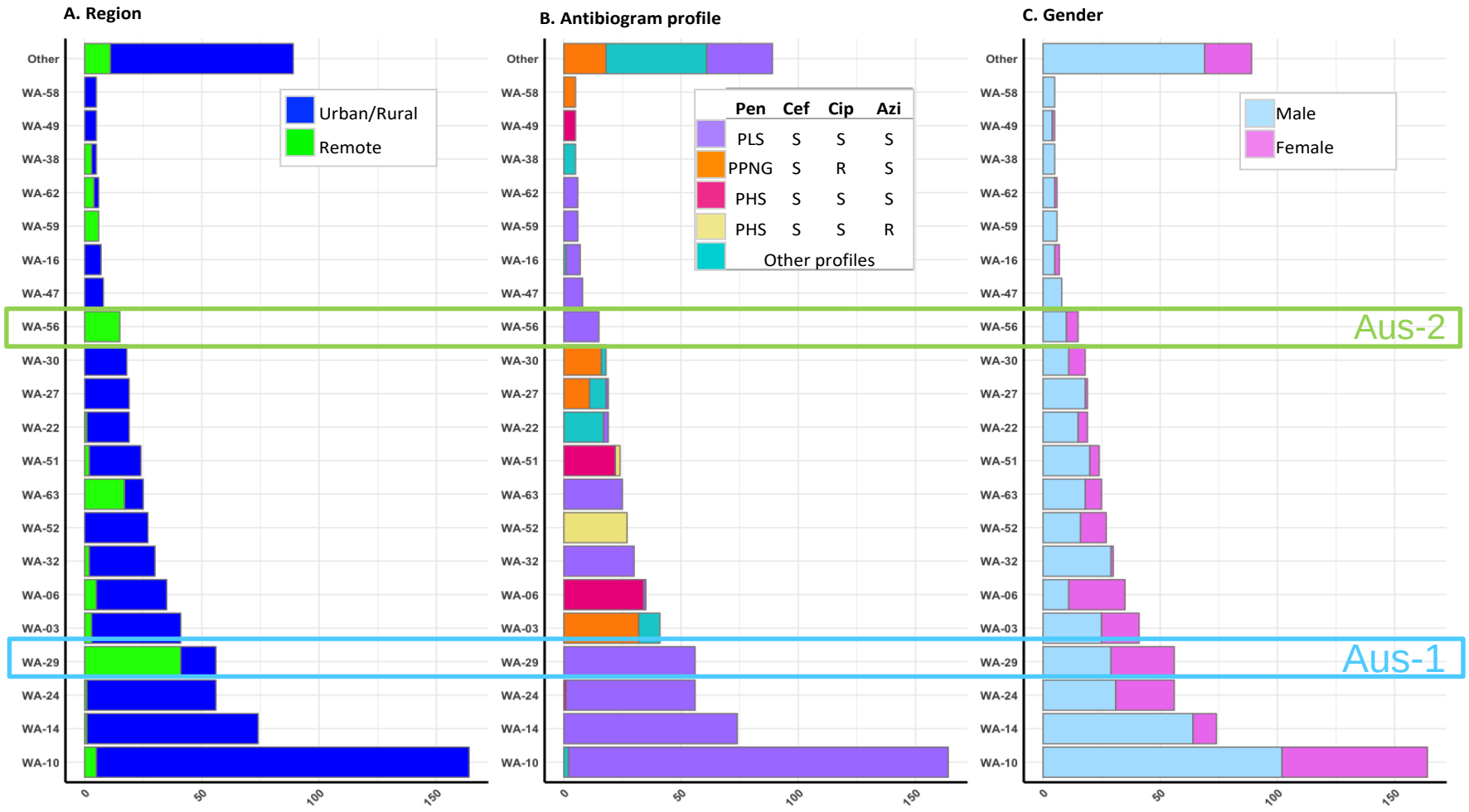
Core genome
cgMLST 970 genes
FastGear, BAPS
MLST
NG-MAST, NG-STAR

iPLEX: informative SNPs
in 6 MLST genes
and 12 AMR alleles

Prof David Whiley (UQ)

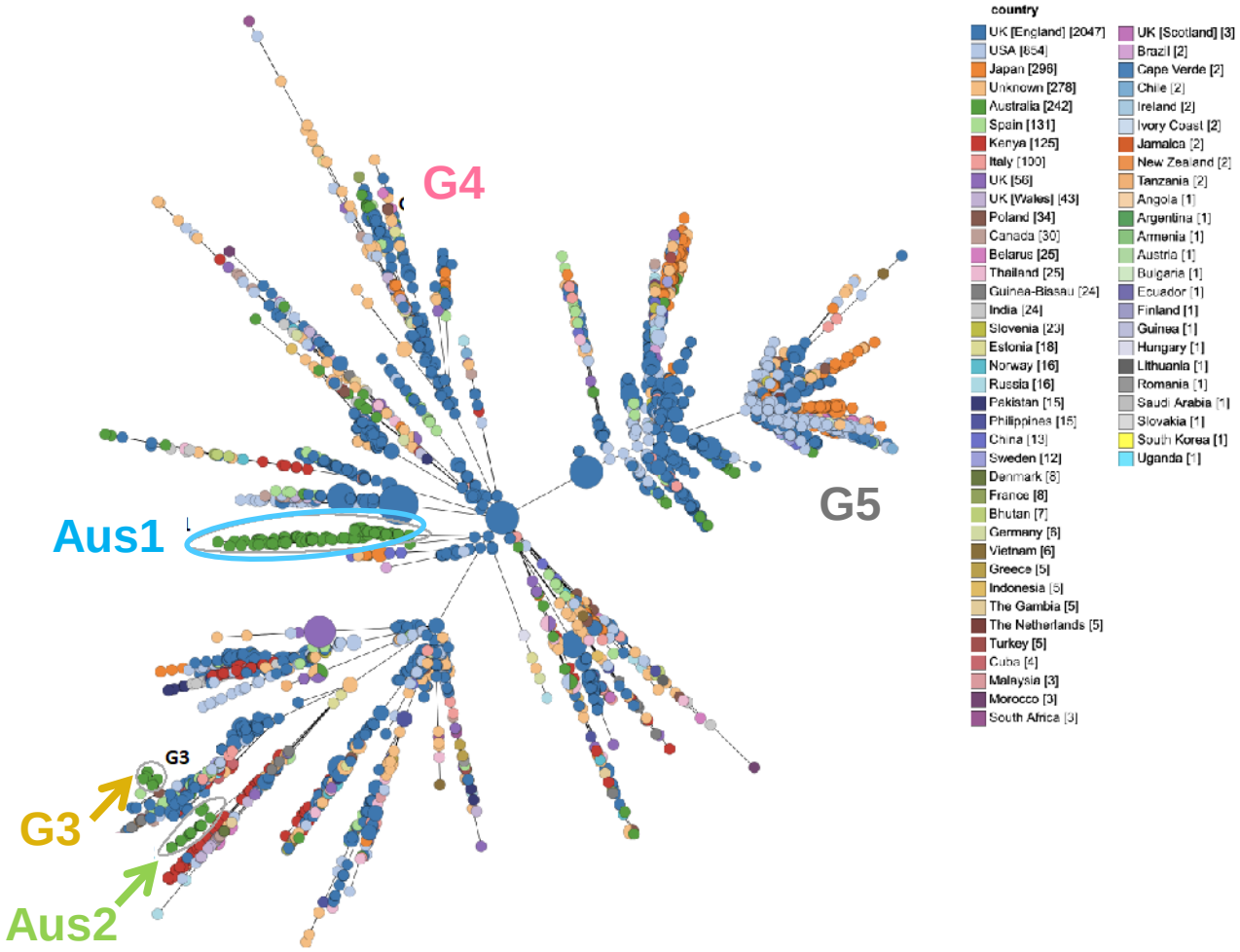
Trembizki, Ella, et al. (2014) High-throughput informative single nucleotide polymorphism-based typing of Neisseria gonorrhoeae using the Sequenom MassARRAY iPLEX platform. J antimicrob chemotherapy. 69(6):1526-32

Frequency of most common iPLEX types (>5 isolates)



Total iPLEX types = WA-1 to WA-78 (21 types had >5 isolates)

Aus-1 and Aus-2 form distinct lineages in Australia



Aus-1 (WA-29) – unique

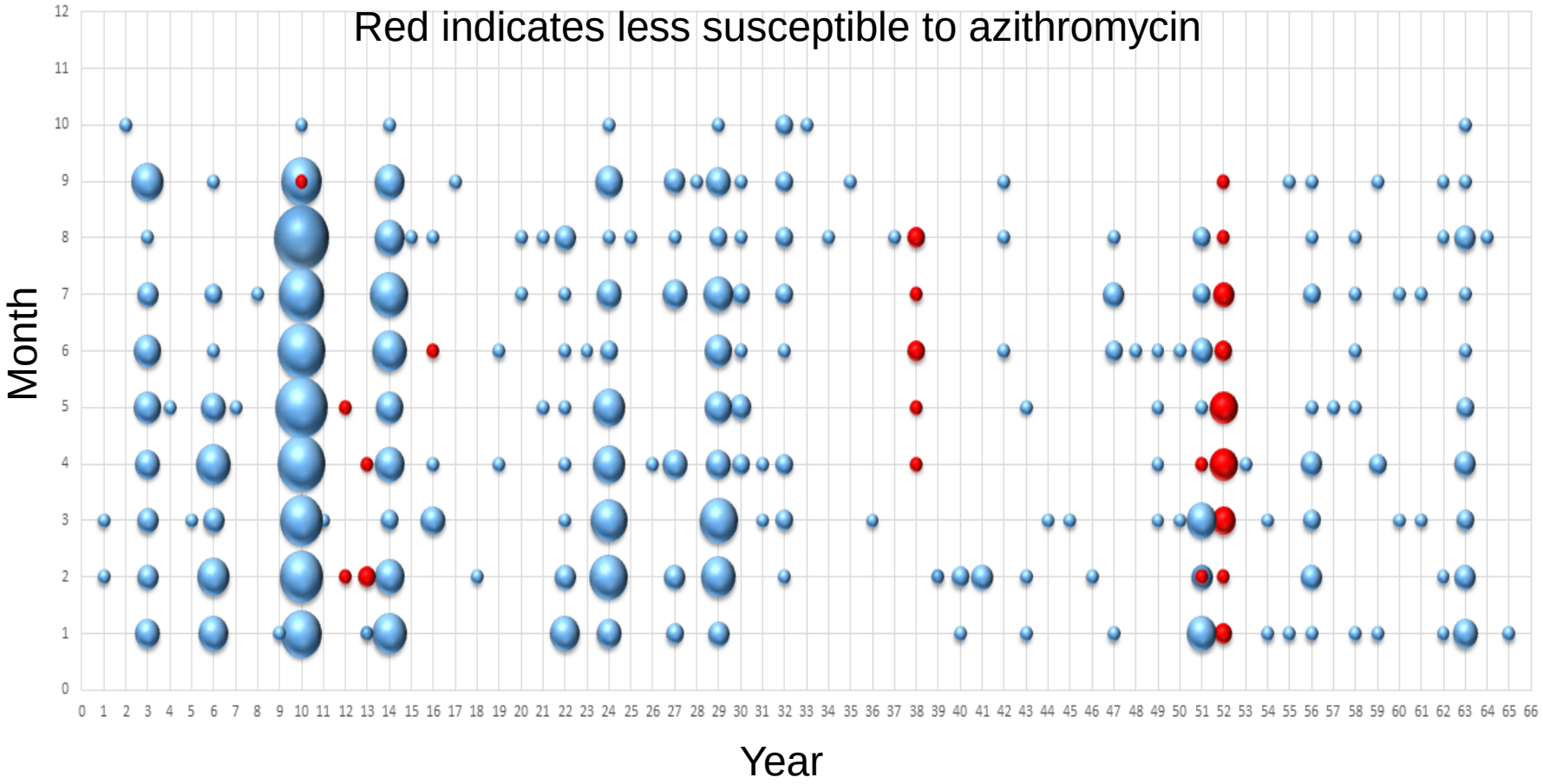
Aus-2 (WA-56) - historical link to international group

G3 closely related to a UK lineage

G4 and G5 cluster of international isolates collected globally (1960-2019)

Minimum-spanning tree of 4,569 *Neisseria gonorrhoeae* isolates based on allelic profiles generated from the core genome MLST of 1,658 genes determined by GrapeTree analysis tool implemented in the PubMLST database. Nodes are coloured based on country and size of the node is proportional to the number of isolates.

WA-iPLEX types distribution plotted by month of 2017.



- WA-13, 12, 16 = Ng_cgc100_867 group reported from Europe in 2014
- WA-38 = ST1584 from Poland in 2010 (Formed BPG-3), very clonal
- WA- 51 and 52 = ST1596 local national lineage

Summary

- 78 iPLEX types were identified but 50% belonged to four genotypes
    - WA-10 = ST11428 – first isolation UK in 2011
    - WA-14 = ST11864 – associated with MSM communities on the east coast of Australia from 2012
    - WA-24 = ST7359 – associated with heterosexual communities of east coast from 2012, original Brighton UK
    - WA-38- AziR ST1584 – associated with an outbreak in Poland in 2010 (BPG-3)
    - Multiple strains in BPG-4/5 – all international AMR lineages, mostly from Europe

    •Aus-1 = WA-29 = ST7363
    - associated with heterosexual indigenous communities of east coast, major genetic lineage in Aus-1 – but unique to Australia

    •Aus 2 = WA-56 = ST12042
    - unique to Australia

- Over the 6 yrs
    - Aus-1 and Aus-2 persisted in remote communities with minimal bridging into urban areas (8.5 cases per 1000 population annually), completely antimicrobial susceptible (AMS)
    - Rise in cases in 2017- was due to introduction of AMS lineages from interstate/overseas into urban areas

What are the options for remote healthcare in WA?

Sex Health. 2015 Jun;12(3):181-2. doi: 10.1071/SH15036.

Early presentation of symptomatic individuals is critical in controlling sexually transmissible infections

Christopher K Fairley [1], Eric P F Chow [1], Jane S Hocking [2]

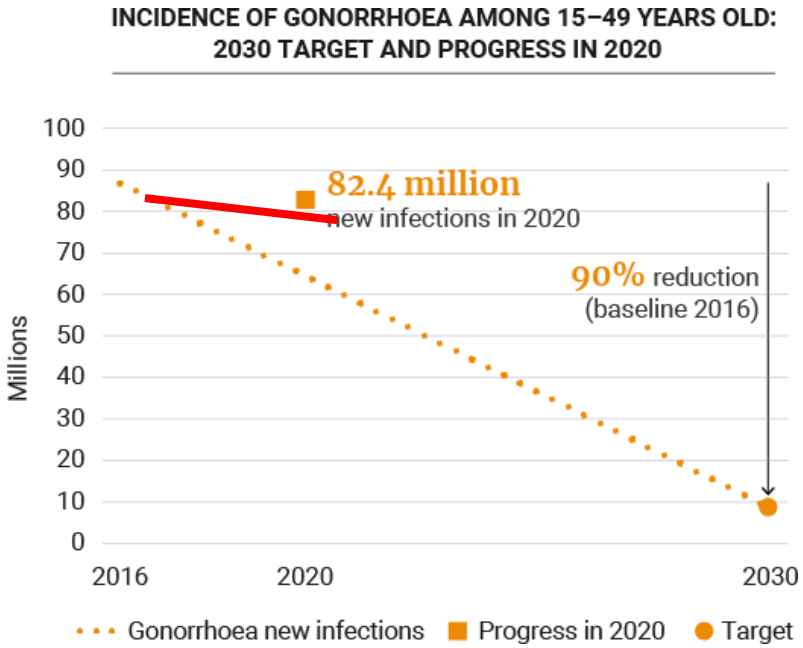
Affiliations + expand

PMID: 26053954 DOI: 10.1071/SH15036

Abstract

Two papers in this issue by Williams et al. and Scott et al. describe the sexual risks and health-seeking behaviour of young Indigenous Australians. Their sexual risks and health-seeking behaviours are similar to the general Australian population, yet their risk of past sexually transmissible infections (STIs) is higher. These findings are consistent with previous findings and suggest that access to health care, and not sexual risk, remain critical to STI control in remote Indigenous communities.

"Screening, even of everyone, every year can only reduce the duration of infection from 180 days to 120 days; early presentation is therefore the key."



Source: WHO, 2021.

WHO Summary: 7 yrs of testing/treatment has not made an appreciable impact on disease rates globally

Two community-based approaches under development

Vaccination

Meningococcal vaccine 4CmenB is made of a mixture of proteins

This protein vaccine raises a cross-protective response that reduces hospitalisation due to pelvic inflammatory disease

Efficacy is below 35%[1,2,3,4,5]

Could this be widely implemented OR can an improved vaccine be made?

Many candidates in Phase I and II trials.

Pre/post exposure prophylaxis (PEP)

Vaginal silicone rings impregnated with anti-HIV drug has been approved for clinical use in women to reduce HIV transmission in South Africa.[6]

WHO and International partnerships for Microbiocides (https://www.ipmglobal.org/) has reignited interest in the development of narrow spectrum drugs for continuous use in gels or implants.

Mostly still in early phases of development

1. Petousis-Harris H *et al. Lancet* 2017;390:1603–1610 2. Paynter J *et al. Vaccines (Basel)* 2019;7:5 3. Longtin J *et al. Open Forum Infect Dis* 2017;4:S734–S735 4. Abara W *et al. Sex Transm Dis* 2020;47(Suppl 2):S46–S47 and Erratum. *Sex Transm Dis* 2021;48:e34 5. Deceuninck G *et al. Vaccine* 2019;37:4243–4245
6. https://www.who.int/news/item/26-01-2021-who-recommends-the-dapivirine-vaginal-ring-as-a-new-choice-for-hiv-prevention-for-women-at-substantial-risk-of-hiv-infection

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