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Australian Gonococcal Surveillance Programme Annual Report, 2020

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This document (last updated 15 September 2021) is a revised version of the AGSP 2020 Annual Report, which includes some data not received at the time of the first published version of this report (https://doi.org/10.33321/cdi.2021.45.24, published online 30 April 2021)

Annual report

Australian Gonococcal Surveillance Programme Annual Report, 2020

Monica M Lahra, Tiffany R Hogan, Masoud Shoushtari, Benjamin H Armstrong, for the National Neisseria Network, Australia

Abstract

The Australian Gonococcal Surveillance Programme (AGSP), established in 1981, has continuously monitored antimicrobial resistance in clinical isolates of *Neisseria gonorrhoeae* for more than 40 years. In 2020, a total of 7,222 clinical isolates of gonococci from patients in the public and private sectors, in all jurisdictions, were tested for *in vitro* antimicrobial susceptibility by standardised methods.

Current treatment recommendations for gonorrhoea, for the majority of Australia, continues to be dual therapy with ceftriaxone and azithromycin. In 2020, decreased susceptibility (DS) to ceftriaxone (minimum inhibitory concentration [MIC] value ≥ 0.06 mg/L) was found nationally in 0.9% of isolates. There was one isolate, reported from Victoria in 2020, that was resistant to ceftriaxone (MIC value ≥ 0.25 mg/L). Resistance to azithromycin (MIC value ≥ 1.0 mg/L) was found nationally in 3.9% of *N. gonorrhoeae* isolates, continuing a downward trend observed and reported since 2017. Isolates with high-level resistance to azithromycin (MIC value ≥ 256 mg/L) are identified sporadically in Australia; in 2020, there was one such isolate reported in Queensland.

In 2020, penicillin resistance was found in 27% of gonococcal isolates nationally, and ciprofloxacin resistance in 36%; however, there is considerable variation by jurisdiction. In some remote settings, penicillin resistance remains low, and this drug continues to be recommended as part of an empiric therapy strategy. In 2020, in remote Northern Territory, no penicillin resistance was reported, and in remote Western Australia 5/116 of gonococcal isolates (4.3%) were penicillin resistant. There was one ciprofloxacin-resistant isolate reported from remote Northern Territory, and ciprofloxacin resistance rates remain comparatively low in remote Western Australia (4/116; 3.4%).

Keywords: antimicrobial resistance; disease surveillance; gonococcal infection; *Neisseria gonorrhoeae*

Introduction

The National Neisseria Network (NNN) is a collaborative network, established in the late 1970s, of the jurisdictional *Neisseria* reference laboratories across Australia that perform testing of clinical isolates of the pathogenic *Neisseria* species: *Neisseria gonorrhoeae* (NG) and *N. meningitidis*. The Australian Gonococcal Surveillance Programme (AGSP) is a key activity of the NNN. The AGSP has been operational for more than 40 years,[1] and is the longest continually-running national surveillance system for gonococcal antimicrobial resistance (AMR). Over these decades, the AGSP has reported the emergence of resistance to all antibiotics used in the treatment of gonorrhoea, and has detected and reported multi- and extensively-drug-resistant gonococcal strains in recent years. In 2017, the first evidence of sustained spread of multi-drug-resistant gonorrhoea was reported,[2] followed in 2018 by coincident reports from Australia and the United Kingdom of the first extensively-drug-resistant *N. gonorrhoeae* isolates.[3–5] The emergence of NG AMR in Australia has long been influenced by the introduction of multi-resistant strains from overseas.[5,6] The importation and spread of ceftriaxone-resistant

gonococcal strains, and/or of new resistance developing, remains an ongoing concern for disease control strategies, and is a focus of the work of the NNN.

Whilst the background rate of isolates with decreased susceptibility to ceftriaxone (minimum inhibitory concentration [MIC] value ≥ 0.06 mg/L) in Australia has remained low, and relatively stable, since the introduction of dual therapy for gonorrhoea in 2014, vigilance is imperative in continuing culture-based surveillance to detect novel resistant strains. The increased proportion of gonococcal isolates with azithromycin resistance in recent years has also added to concerns about management strategies; however, after an increase nationally to 9.3% in 2017, this has consistently declined.

In 2020, physical distancing and travel restrictions imposed as public health measures in response to the COVID-19 pandemic had an impact on many communicable diseases in Australia, including gonorrhoea.[7] There were 29,516 gonorrhoea disease notifications in 2020, down from 34,244 in 2019, a decrease of 14%. This is on a background of increasing gonococcal disease notifications in this country from 68.1 per 100,000 in 2014 to 135.1 per 100,000 in 2019, an overall increase of 98%.[8] Gonococcal disease rates in the Aboriginal and Torres Strait Islander population remain markedly higher than in the non-Indigenous population (135.9 per 100,000 versus 95.6 per 100,000), and are highest in remote and very remote areas (832.2 per 100,000; i.e., 30 times greater than the non-Indigenous population).[9] Whilst gonococcal disease rates are highest in Australia in remote and very remote areas, in contrast, NG AMR in remote regions remains low, in locally-acquired infections. In some remote regions the recommended therapeutic strategy, based on surveillance data, remains centred on oral penicillin.[10]

Heightened global awareness of AMR, and increasing gonococcal disease rates reported in Australia and elsewhere,[9,11–14] have coincided with increased uptake of nucleic acid amplification testing (NAAT) for diagnosis, replacing bacterial culture and antimicrobial susceptibility testing (AST). The corollary of this is a reduction in gonococcal isolates available for AST surveillance: whilst AST is able to be readily performed when diagnosis is made by bacterial culture, NAAT is limited in their use for AST. NAAT is able to detect some genetic mutations already known to be associated with resistance; however, it cannot detect resistance via novel mutations. Uniquely, in some remote regions of Australia, NAAT is used to detect penicillin resistance in NAAT-positive samples for NG,[15,16] the first documented use of routine molecular testing for NG AMR detection and surveillance.[17,18] These data inform local treatment guidelines.[18]

Strategies for treatment and control of gonorrhoea are based on regimens effecting cure in a minimum of 95% of cases. Surveillance data of antibiotics in clinical use are critical to monitor AMR; to detect imported or novel resistance; and to inform treatment guidelines.[15] The World Health Organization (WHO) has called for enhanced surveillance as a fundamental component of its Global Action Plan to control the spread and impact of gonococcal AMR.[16]

Methods

All confirmed cases of gonorrhoea in Australia are notifiable to the National Notifiable Diseases Surveillance System (NNDSS) under legislation. The NG isolates tested by the NNN, and reported by the AGSP, therefore represent a proportion of the total number of notified cases. The NNN laboratories test gonococcal isolates for susceptibility to ceftriaxone; azithromycin; penicillin; ciprofloxacin; spectinomycin; and tetracycline. In recent years many NNN laboratories are also testing gentamicin, and these data are reported in the AGSP Annual Report for the first time in 2020. Testing for AMR is performed using previously-described standardised methodology to determine the minimum inhibitory concentration (MIC) values.[19] The MIC value is the lowest antibiotic concentration that inhibits *in vitro* growth under defined conditions. The AGSP conducts a programme-specific quality assurance program.[20]

Gonococcal AST data from each jurisdiction are submitted quarterly to the World Health Organization Collaborating Centre for Sexually Transmitted Infection and Antimicrobial Resistance (WHO CC, Sydney), the coordinating laboratory for the NNN. Where available, the AGSP collects data on the sex of the patient; the country of acquisition of infection; and the site of isolation of gonococcal isolates. Data collected across jurisdictions are predominantly from urban centres. Data from the Northern Territory and Western Australia are further divided into non-remote and remote regions determined at the jurisdictional level, based on antibiograms, and therapeutic recommendations consequently differ.

Results

Proportion of gonococcal infections with antimicrobial susceptibility testing

In 2020, there were 29,516 gonococcal infections notified in Australia; the NNN laboratories received and tested 7,222 clinical isolates. Overall, 24% of gonococcal infections notified had AST undertaken at NNN laboratories (Table 1). Gonococcal notifications and clinical gonococcal isolates were reduced in number, correlating with the COVID-19 pandemic. This is reflected in Figure 1, which plots notifications of diagnosis made by culture (AGSP data) against all notifications of diagnosis that includes both the AGSP and culture-independent diagnosis. What is evident is the downturn in both notifications and isolates for culture in 2020, on a background of increasing gonococcal disease notifications in recent years.

Across jurisdictions, the proportion of notifications that were made by culture vary, as shown in Table 1, ranging from 20% to 26% (with the exception of the Northern Territory, where bacterial cultures are less often performed in patients from remote and very remote communities where disease rates are high).[8] The proportion is higher from the Australian Capital Territory; however, the number of notifications is small.

Gonococcal isolates, Australia, 2020, by sex, site and jurisdiction tested

There were 5,598 isolates from males (77.5%) and 1,580 (21.9%) from females tested in 2020 (Table 2). There were 44 isolates (0.6%) from patients whose gender was recorded as other, or was unknown. The proportion of gonococcal isolates from males and females has remained stable over recent years (2009–2019), ranging between 17% and 22% for females and 78% and 83% for males. The infected site was reported as 'other' or not specified for 111 isolates from males and 45 isolates from females (Table 2). Isolates from urine samples were regarded as genital tract isolates.

Antimicrobial resistance profile of Neisseria gonorrhoeae

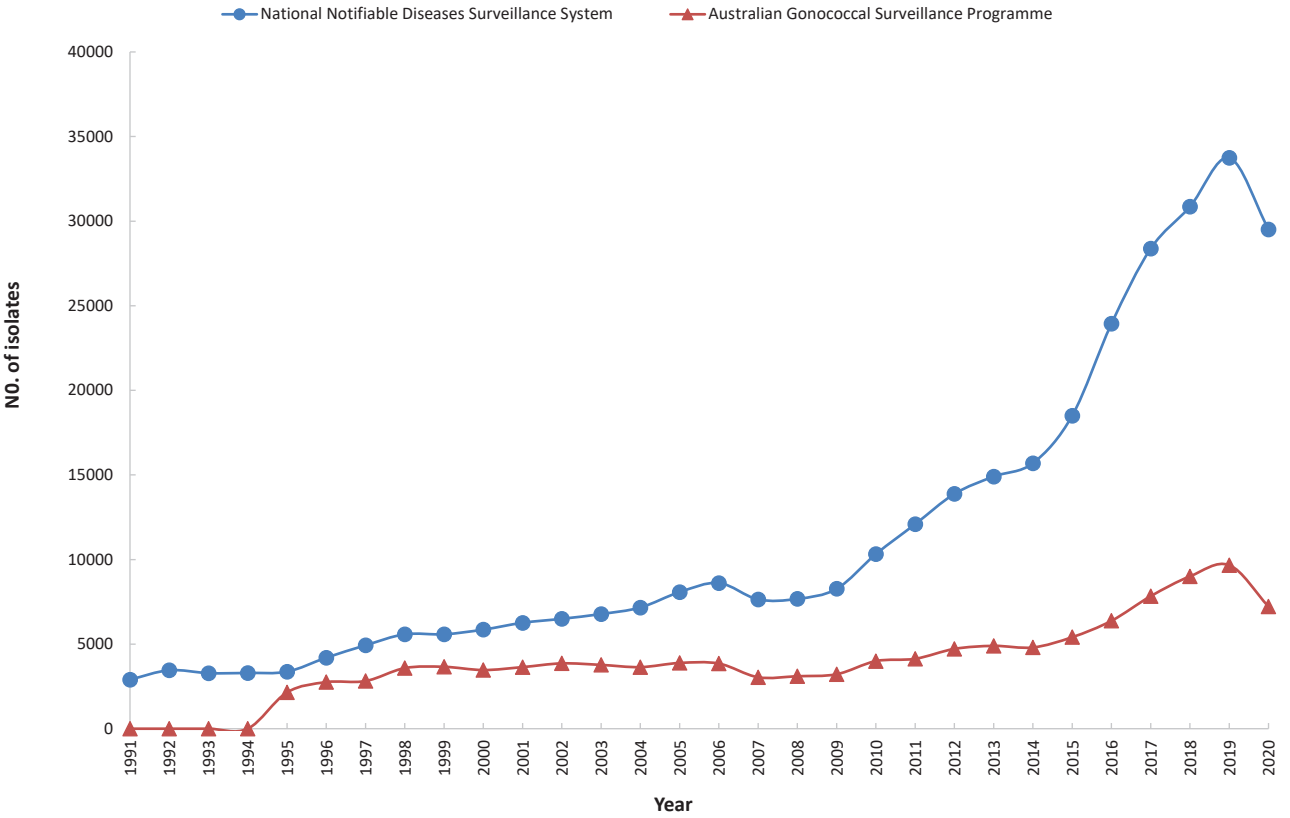
For 2020, the numbers and proportions of gonococcal isolates resistant to azithromycin, penicillin and ciprofloxacin, and with decreased susceptibility to ceftriaxone, are shown in Table 3. There continues to be variation across jurisdictions, as well as in remote settings when compared to non-remote settings.

Ceftriaxone

Gonococcal isolates with decreased susceptibility to ceftriaxone (MIC values ≥ 0.06 mg/L) have been detected in Australia since 2001. The proportion reported increased to 4.4% in 2012, before doubling to 8.8% in 2013. However, from 2014, coincident with the introduction of dual ceftriaxone and azithromycin therapy, there has been an overall declining trend in the proportion of gonococcal isolates with decreased susceptibility to ceftriaxone in Australia, as shown in Table 4 and Table 5.

From 2016 to 2018, the proportion of isolates with MIC values of ≥ 0.125 mg/L for ceftriaxone remained stable in the range 0.04–0.06%; however, in 2019, this increased to 0.11% (Table 5). In 2019, there were five gonococcal clinical isolates with ceftriaxone MIC values ≥ 0.25 mg/L (three from Victoria, one from non-remote Western

Figure 1: Number of gonococcal disease cases reported to the National Notifiable Diseases Surveillance System compared with Neisseria gonorrhoeae isolates available for laboratory testing by the Australian Gonococcal Surveillance Programme, Australia, 1991–2020[a]



a These data were extracted from the NNDSS on 18 March 2021.

Australia and one from New South Wales). All had the *penA*60 allele, thus were resistant to penicillin, as well as ciprofloxacin, but were susceptible to azithromycin. In 2020, there was one such isolate reported from Victoria.

Azithromycin

Nationally, in 2020, 3.9% of isolates exhibited azithromycin resistance (MIC value ≥ 1.0 mg/L) (Table 3), a decrease from 4.6% in 2019. Since 2012, rates of azithromycin resistance increased from 1.3% to a peak of 9.3% in 2017, then declined to 3.9% in 2020 (Table 6). Rates of azithromycin-resistant NG were highest in New South Wales (7.0%), the Australian Capital Territory (4.1%) and non-remote Northern Territory (3.9%) (Tables 3 and 6). In 2020, there was one isolate from Queensland exhibiting high-level resistance to azithromycin (MIC ≥ 256 mg/L).

Penicillin

Resistance in NG to the penicillin group of antibiotics (penicillin, ampicillin, and amoxicillin with or without clavulanic acid) results from ß-lactamase production (i.e., penicillinase) and/or the aggregation of chromosomally-controlled resistance mechanisms. These are denoted respectively as penicillinase-producing *N. gonorrhoeae* (PPNG) and chromosomally-mediated resistance to penicillin (CMRP). Chromosomally-mediated resistance is defined as a penicillin MIC ≥ 1 mg/L.

In 2020, in Australia, 1,920 (26.6%) isolates were penicillin resistant (Table 3), which was an increase from 2019 (22.1%). The proportion of penicillin-resistant isolates fluctuated in the range 22.5% to 44.0% between 2008 and 2018. In 2020, 387 (5.4%) isolates had CMRP and 1,533 (21.2%) were PPNG; 79.8% of penicillin-resistant isolates were PPNG.

Table 1: Number of Australian Gonococcal Surveillance Programme gonococcal isolates tested as a proportion of National Notifiable Diseases Surveillance System (NNDSS) gonorrhoea notifications, Australia, 2020, by state or territory

State or territory	Number of isolates tested	Number of cases notified	Number of isolates tested/ Number of cases notified (%)
Australian Capital Territory	148	284	52%
New South Wales	2,585	9,875	26%
Northern Territory	151	1,340	11%
Queensland	1,504	6,346	24%
South Australia	334	1,660	20%
Tasmania	38	150	25%
Victoria	1,665	6,288	26%
Western Australia	797	3,573	22%
Australia	**7,222**	**29,516**	**24%**

Penicillin resistance in remote Australia

In 2020, there were 151 isolates tested from the Northern Territory, with 100 derived from remote areas (including Alice Springs, Katherine, Tennant Creek, and Arnhem Land region) and 51 from Darwin and surrounding urban areas (non-remote). In 2020, there were 797 isolates tested from Western Australia, with 116 obtained from remote regions and 681 from urban and suburban Perth (non-remote).

Of the 100 isolates from remote Northern Territory, none were penicillin resistant, while two isolates (3.9%) from Darwin and surrounding urban areas were penicillin resistant. One of these isolates (2.0%) was PPNG, a marked decrease from 18% in 2019. Of the 116 isolates from remote Western Australia, five (4.3%) were penicillin resistant, with all being PPNG.

Ciprofloxacin

Ciprofloxacin resistance is defined as MIC ≥ 1 mg/L. In 2020, ciprofloxacin resistance was seen in 2,625 isolates (36.4%), an increase from 28.4% in 2019 (Table 3). Ciprofloxacin has not been recommended in Australia as first-line therapy for gonococcal infections since the late 1990s, and the rate of ciprofloxacin resistance has progressively declined in Australia since 2008, when 54% of isolates tested were resistant.

Tetracyclines

To optimise reporting tetracycline resistance in *N. gonorrhoeae*, from 2018 NNN reference laboratories have performed tetracycline MIC testing where possible. This replaces historical breakpoint testing for high-level tetracycline-resistant *N. gonorrhoeae* (TRNG) (MIC ≥ 16 mg/L) that was previously reported as an epidemiological marker for plasmid-mediated resistance.

Tetracycline resistance is defined as MIC ≥ 2 mg/L. Whilst tetracycline antibiotics are not a recommended treatment for gonorrhoea, and are rarely, if ever, used for treatment of gonorrhoea in Australia, there has been recent interest in the proportion of tetracycline resistance in NG, due to its use as a potential agent for prophylaxis of chlamydia and syphilis infections in high-risk populations.[21,22] This practice has already experienced some uptake in Australia.[23] Nationally in 2020, thirty-six percent of isolates (2,630/7,222) were tested, and 30% (780/2,630)

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Table 2: Gonococcal isolates, Australia, 2020, by sex, site and jurisdiction tested

Gender	Site	ACT	NSW	NT	Qld	SA	Vic.	Tas.	WA	Australia
Male	Genital	49	1,182	101	679	151	689	8	409	3,266
	Rectal	42	589	4	190	56	464	6	90	1,441
	Pharynx	25	333	2	116	15	225	3	49	768
	DGI[a]	0	3	0	4	1	0	0	1	9
	Other/NS[b]	2	31	4	18	26	23	4	4	111
	Total	**118**	**2,138**	**111**	**1,007**	**249**	**1,401**	**21**	**553**	**5,598**
Female	Genital	23	345	38	443	72	209	15	227	1,372
	Rectal	0	12	0	8	5	3	0	3	31
	Pharynx	6	58	0	28	2	22	0	9	125
	DGI	0	0	1	2	1	1	0	2	7
	Other/NS	1	10	1	16	4	8	2	3	45
	Total	**30**	**425**	**40**	**497**	**84**	**243**	**17**	**244**	**1,580**
Other	Genital	0	12	0	0	0	6	0	0	18
	Rectal	0	1	0	0	0	4	0	0	5
	Pharynx	0	0	0	0	0	5	0	0	5
	DGI	0	0	0	0	0	0	0	0	0
	Other/NS	0	0	0	0	1	0	0	0	1
	Total	**0**	**13**	**0**	**0**	**1**	**15**	**0**	**0**	**29**
Unknown	Genital	0	6	0	0	0	5	0	0	11
	Rectal	0	1	0	0	0	1	0	0	2
	Pharynx	0	2	0	0	0	0	0	0	2
	DGI	0	0	0	0	0	0	0	0	0
	Other/NS	0	0	0	0	0	0	0	0	0
	Total	**0**	**9**	**0**	**0**	**0**	**6**	**0**	**0**	**15**
Total		**148**	**2,585**	**151**	**1,504**	**334**	**1,665**	**38**	**797**	**7,222**

a DGI: Disseminated gonococcal infection.
b NS: not specified.

Table 3: Number and proportion (%) of gonococcal isolates with resistance to azithromycin, penicillin and ciprofloxacin and decreased susceptibility to ceftriaxone reported, Australia, 2020, by state or territory

State or territory	Number of isolates tested	Decreased susceptibility		Resistance					
	2020	Ceftriaxone MIC ≥ 0.06 mg/L		Azithromycin MIC ≥ 1.0 mg/L		Ciprofloxacin MIC ≥ 1.0 mg/L		Penicillin MIC ≥ 1.0 mg/L incl. PPNG	
		n	%	n	%	n	%	n	%
Australian Capital Territory	148	0	0.0	9	6.1	59	40.7	25	17.2
New South Wales	2,585	30	1.2	181	7.0	1,138	44.0	909	35.2
Queensland	1,504	17	1.1	43	2.9	482	32.0	327	21.7
South Australia	334	0	0.0	1	0.3	57	17.1	23	6.9
Tasmania	38	0	0.0	0	0.0	9	23.7	4	10.5
Victoria	1,665	18	1.1	29	1.7	648	38.9	427	25.6
Northern Territory non-remote	51	0	0	2	3.9	8	15.7	2	3.9
Northern Territory remote	100	0	0	0	0.0	1	1.0	0	0.0
Western Australia non-remote	681	3	0.4	18	2.6	219	32.2	198	29.1
Western Australia remote	116	0	0.0	1	0.9	4	3.4	5	4.3
Australia	**7,222**	**68**	**0.9**	**284**	**3.9**	**2,625**	**36.4**	**1,920**	**26.6**

were tetracycline resistant. Tetracycline resistance data are presented by jurisdiction and aggregated for Australia as shown in Table 7.

Spectinomycin

In 2020, all isolates tested (n = 7222) were susceptible to spectinomycin.

Gentamicin

In 2020 gentamicin susceptibility testing data was available for 1,635 isolates originating from New South Wales, Tasmania, Western Australia and the Northern Territory. The median MIC value was 4 mg/L and no isolate was resistant to gentamicin.

Discussion

The World Health Organization (WHO) recommends that treatment regimens for gonorrhoea are based on epidemiological surveillance of the distribution and extent of AMR, and that a resistance rate of 5% or more is the nominal threshold for change of treatment recommendations.[15,25,26]

In 2020, the NNN examined 7,222 clinical isolates for susceptibility testing to ceftriaxone; azithromycin; ciprofloxacin; penicillin; tetracycline; and, for the first time, gentamicin. The isolates tested were from urban and remote settings in the public and private health sectors, constituting a comprehensive sample of about one-quarter of all notifications nationally.[11] The remote populations of Western Australia and the Northern Territory have the highest rates of gonococcal disease, but the lowest of diagnosis by culture (n = 216), as a function of laboratory access. Possibly secondary to reduced ingress of NG, as a function of their remoteness, these communities have low rates of AMR in NG. Consequently, these regions require continued vigilance with monitoring of AMR in NG, using both culture- and molecular-based surveillance strategies.

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Table 4: Number and proportion (%) of gonococcal isolates with decreased susceptibility to ceftriaxone (MIC ≥ 0.06mg/L), Australia, 2014 to 2020, by state or territory

State or territory	Decreased susceptibility to ceftriaxone													
	2014		2015		2016		2017		2018		2019		2020	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Australian Capital Territory	2	2.7	0	0.0	1	0.9	0	0	4	1.9	1	0.5	0	0.0
New South Wales	119	7.1	52	2.7	45	2.0	13	0.5	30	0.8	44	1.2	30	1.2
Queensland	21	3.2	7	1.0	32	3.7	11	0.9	18	1.3	16	1.0	17	1.1
South Australia	2	1.0	9	3.6	2	0.6	2	0.6	3	1.3	9	1.6	0	0.0
Tasmania	0	0	0	0	1	3.6	0	0	4	7.3	1	2.1	0	0.0
Victoria	95	6.6	25	1.5	19	1.1	48	2.1	83	3.2	42	1.6	18	1.1
Northern Territory non-remote	3	3.0	0	0	0	0	0	0	0	0	0	0	0	0.0
Northern Territory remote	1	0.8	0	0	0	0	0	0	0	0	0	0	0	0.0
Western Australia non-remote	14	3.6	5	1.3	9	1.3	9	1.4	14	2.1	11	1.5	3	0.4
Western Australia remote	1	0.9	0	0	0	0	0	0	0	0	2	2.4	0	0.0
Australia	**258**	**5.4**	**98**	**1.8**	**109**	**1.7**	**83**	**1.1**	**156**	**1.7**	**127**	**1.3**	**68**	**0.9**

Table 5: Proportion (%) of gonococcal isolates tested in Australia with ceftriaxone MIC values at 0.06 mg/L and ≥ 0.125 mg/L, 2010–2020

Ceftriaxone MIC mg/L	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
0.06	4.80%	3.20%	4.10%	8.20%	4.80%	1.70%	1.65%	1.02%	1.67%	1.19%	0.87%
≥ 0.125	0.10%	0.10%	0.30%	0.60%	0.60%	0.10%	0.05%	0.04%	0.06%	0.11%	0.07%
Total decreased susceptibility	**4.90%**	**3.30%**	**4.40%**	**8.80%**	**5.40%**	**1.80%**	**1.70%**	**1.06%**	**1.73%**	**1.30%**	**0.94%**

Table 6: Number and proportion (%) of gonococcal isolates with resistance to azithromycin (MIC ≥ 1.0 mg/L), Australia, 2012 to 2020, by state or territory

State or territory	Azithromycin resistance																	
	2012		2013		2014		2015		2016		2017		2018		2019		2020	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Australian Capital Territory	0	0	1	2.2	7	9.3	0	0	8	7.1	3	2.1	18	8.7	14	7.1	9	6.1
New South Wales	9	0.5	14	0.9	33	2.0	43	2.3	82	3.6	261	9.3	230	6.5	215	6.0	181	7.0
Queensland	15	2.1	38	5.7	23	3.5	42	5.8	10	1.2	61	4.9	68	4.9	32	1.9	43	2.9
South Australia	1	0.7	6	2.8	1	0.5	7	2.8	68	19.5	46	12.8	7	3.0	11	2.0	1	0.3
Tasmania	0	0	0	0	1	3.3	1	4.3	4	14.3	5	9	3	6	1	2.0	0	0.0
Victoria	34	2.7	35	2.3	33	2.3	30	1.8	93	5.4	304	13.5	217	8.3	161	6.2	29	1.7
Northern Territory non-remote	0	0	1	1.0	0	0	0	0	1	1.9	1	1.7	1	1.5	1	1.8	2	3.9
Northern Territory remote	0	0	0	0	0	0	0	0	0	0	1	0.6	0	0.0	0	0.0	0	0.0
Western Australia non-remote	3	0.6	9	1.9	21	5.3	15	3.8	51	7.6	40	6.4	16	2.5	12	1.6	18	2.6
Western Australia remote	0	0	0	0	0	0	0	0	1	0.8	4	3.4	1	0.9	1	1.2	1	0.9
Australia	**62**	**1.3**	**104**	**2.1**	**119**	**2.5**	**138**	**2.6**	**318**	**5.0**	**726**	**9.3**	**561**	**6.2**	**448**	**4.6**	**284**	**3.9**

Table 7: Number and proportion (%) of gonococcal isolates with resistance to tetracycline (MIC ≥ 2 mg/L), Australia, 2020, by state or territory

State or territory	Number of isolates tested	Resistance MIC ≥ 2 mg/L	
	2020	Tetracycline	
		n	%
Australian Capital Territory	121	30	24.8
New South Wales	NT[a]	–	–
Queensland	NT[a]	–	–
South Australia	2	2	100
Tasmania	38	6	15.8
Victoria	1,642	535	32.6
Northern Territory non-remote	1	0	0.0
Northern Territory remote	30	1	3.3
Western Australia non-remote	680	202	29.7
Western Australia remote	116	4	3.4
Australia	**2,630**	**780**	**29.7**

a NT: not tested.

For the majority of gonococcal surveillance programmes around the world, the monitoring of ceftriaxone and azithromycin MIC values is the primary focus. For the AGSP, ceftriaxone MIC values of ≥ 0.06 mg/L have been reported historically to have decreased susceptibility. In Australia, the proportion of isolates with decreased susceptibility to ceftriaxone has steadily and substantially declined since 2013, from 8.80% to 0.94% in 2020 (Table 5). The travel restrictions of 2020 will have a likely impact on circulating strains and resistance; however, in recent years multiple and extensively drug resistant strains have been reported from Asia, Europe and Australia.[25-28] It is known that continued importation of resistant N. gonorrhoeae strains is the first step to establishment of resistance. [6,29]

In 2013, high-level resistance (HLR; MIC ≥ 256 mg/L) to azithromycin in gonococci was reported for the first time in Australia in four strains, two with suspected contact in China.[30] Since then there have been only sporadic reports of HLR to azithromycin in Australia annually, and there was one isolate in 2020. Continued close observation is ongoing as evidence of co-evolving cephalosporin and azithromycin resistance is being observed outside Australia and is of significant concern.[31] Azithromycin resistance has been reported by the AGSP since 2007. Following introduction of dual therapy in 2014, resistance to azithromycin in all jurisdictions of Australia has been observed (Table 6), increasing from 2016, and peaking at 9.3% in 2017, proportional resistance to azithromycin fell to 3.9% in 2020 nationally (Table 6). Importantly, in South Australia there was a rapid increase in azithromycin resistance from 2.8% in 2015 to 19.5% in 2016), however azithromycin resistance rates have now fallen and stabilised (Table 6).[27] In 2020, azithromycin resistance was highest in New South Wales (7%), the Australian Capital Territory (6.1%) and non-remote Northern Territory (3.9%). Globally there have been increasing reports of azithromycin resistance.[29]

In 2020, the AGSP report includes data on gentamicin for the first time. Gentamicin is recommended by both the most recent WHO and Australian guidelines for management of

resistant gonococcal infections.[32,33] Although there is a paucity of clinical data relative to other anti-gonococcal therapies, recent clinical studies have demonstrated efficacy for gentamicin treatment of urethral gonorrhoea, but with reduced rates of oropharyngeal clearance compared to current standard therapy; data on rectal and other body site infections are limited.[34,35] A recent large-scale laboratory-based evaluation of gentamicin susceptibility in 2,768 clinical *N. gonorrhoeae* isolates from New South Wales demonstrated no *in vitro* resistance to gentamicin, and no detectable gentamicin MIC creep, over the years 2015–2020.[36] With the addition of a further 943 isolates from other states and territories, this report is reassuring for the broader applicability of this New South Wales study to other jurisdictions of Australia, demonstrating comparable gentamicin MICs across all isolates tested, and no gentamicin resistance detected in any isolate. The addition of gentamicin as an indicator for ongoing surveillance by the AGSP is in line with the developing surveillance strategies of the WHO Global Antimicrobial Resistance Surveillance System (GLASS).

The recent reports of international spread of NG with resistance to ceftriaxone,[4] and the emergence of azithromycin resistance, heighten concerns about the future treatment strategies for NG AMR.[37] As developed nations continue to transition to widespread pharmacological prevention of HIV infection (e.g. pre-exposure prophylaxis, treatment as prevention) in high-risk populations, a return to, and reinvigoration of, public health strategies promoting primary prevention (e.g. condoms) of gonorrhoea and other sexually transmissible infections is urgently required.[38,39] Additionally, NG vaccine development is a research priority and may be key in the control of this disease. As Australian clinicians become increasingly dependent on NAAT for diagnosis of NG, and with 76% of diagnoses in 2020 made with NAAT alone, health care provider education regarding the continued importance of bacterial culture and AST is paramount. Whilst advances in molecular detection of AMR have great promise, this report underscores the ongoing importance of bacterial culture and AST of NG for clinical management, detection of resistance and novel resistant strains, AMR surveillance, and test of cure. Given its strong history and association with NG AMR in Australia, treating clinicians should pay particular note to patient travel history, as for imported cases of NG, the benefit of bacterial culture and susceptibility testing is critical.

The WHO Global Action Plan states that disease control strategies and the understanding of the global scope of AMR need to continue to be informed by surveillance programs of AMR, nationally and internationally.[16] The ongoing need for close and enhanced monitoring of gonococcal AMR can be supported, but not replaced, by molecular-based assays, and strain-specific assays can be used for routine and sentinel site surveillance in high-risk populations. The data are critically important to inform therapeutic strategies; to monitor for the presence and spread of resistance; and to detect instances of treatment failure.

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