Health Protection Surveillance Centre & National Gonococcal Reference Laboratory, JSH.

Antimicrobial resistance in *Neisseria gonorrhoeae* in Ireland, 2010-2021

Based on data from isolates submitted to EURO-GASP

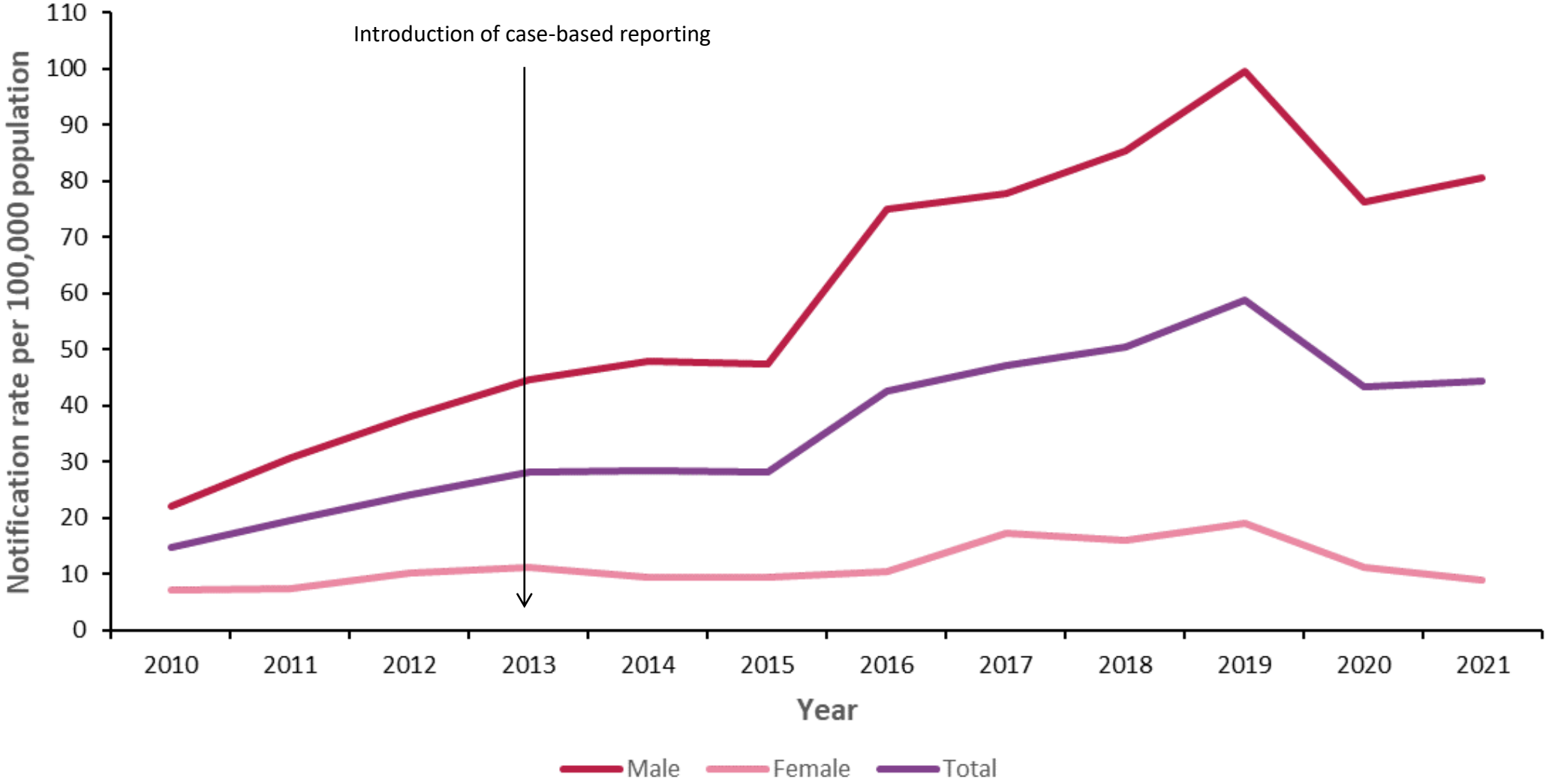
November 2022

Further information

Further information on gonorrhoea and gonorrhoea antimicrobial resistance (AMR) can be found on the HPSC website	https://www.hpsc.ie/a-z/sexuallytransmittedinfections/gonorrhoea/
National guidelines for the prevention and control of gonorrhoea and for managing the impact of antimicrobial resistance in *Neisseria gonorrhoeae*	https://www.hpsc.ie/a-z/sexuallytransmittedinfections/gonorrhoea/amrgonorrhoea/amrgonorrhoeaguidance/
ECDC response plan to control and manage the threat of multi-drug resistant (MDR) and extremely-drug resistant (XDR) gonorrhoea	https://www.ecdc.europa.eu/en/publications-data/response-plan-control-and-manage-threat-multi-and-extensively-drug-resistant
The National Gonococcal Reference Laboratory in SJH	https://www.stjames.ie/services/laboratorymedicinelabmed/nationalgonococcalreferencelaboratory/

Gonorrhoea in Ireland

Trend in notification rate of gonorrhoea by sex, 2010-2021



Antimicrobial resistance in *Neisseria gonorrhoeae*

World Health Organization priority

- Gonorrhoea infection is becoming increasingly difficult to treat due to the development of AMR to all major drug classes used to treat infection.
- The extended spectrum cephalosporin (ESC), ceftriaxone, is the current last remaining option for first-line treatment.
- The World Health Organization (WHO) has listed gonorrhoea resistance to ESCs as one of nine priority bacteria-antibacterial drug combinations of international concern for the development of antimicrobial resistance.

Euro-GASP

European Gonococcal Antimicrobial Surveillance Programme

- Monitors trends in gonococcal antimicrobial susceptibility to detect increasing and emerging AMR and provides quality-assured data to inform national and international treatment guidelines.

- Annual survey conducted over 3 month period (September-November).

- Countries should aim to report AMR and linked epidemiological data for 100 cases (or 10%) of total national notifications and up to 200 cases for countries with a higher number of national notifications.

Irish participation in Euro-GASP

- Participating since 2010
- Antimicrobial susceptibility testing performed in National Gonococcal Reference Laboratory SJH (2017-present),Department of Clinical Microbiology SJH (2013-2016)PHE (2010-2012).
- Linked epidemiological data collected from isolate referral forms, enhanced surveillance forms and clinical notes. Due to the impact of the COVID-19 pandemic, limited enhanced surveillance data are available for 2020-2021.
- Data source: Isolates tested in NGRL(local isolates and isolates referred from other laboratories) submitted to the European Gonococcal Antimicrobial Surveillance Programme (Euro-GASP) over survey period. 119 Irish isolates reported to Euro-GASP in 2021: 6% of total national notifications.

Limitations

- Interpretation of the data presented in the following slides should be considered in light of the COVID-19 pandemic, which impacted in several ways, including long periods of national lockdown, social and physical distancing measures, reduced sexual health and GP services and reduced testing opportunities.

Of note,

- The number of gonorrhoea isolates tested during the Euro-GASP survey period (September to December) was significantly lower during 2020 and 2021 compared to previous years.

- The collection and reporting of enhanced data variables, such as mode of transmission was reduced in 2020 and 2021. Initiatives to improve data quality are underway.

Antimicrobial resistance definitions

Breakpoints from the European Committee on Antimicrobial Susceptibility Testing (EUCAST):

Antimicrobial	Guideline	MIC Breakpoint (mg/L)
		Resistant
Azithromycin ^	EUCAST	> 1.0
Cefixime	EUCAST	> 0.125
Ceftriaxone	EUCAST	> 0.125
Ciprofloxacin	EUCAST	> 0.064
Penicillinase positive	EUCAST	> 1.0

^Until 2018, EUCAST set a breakpoint of MIC 0.5 mg/L for *N. gonorrhoeae* azithromycin resistance. This has since been replaced with an 'epidemiological cut-off' of 1.0 mg/L .

European Committee on Antimicrobial Susceptibility Testing (EUCAST). 'Breakpoint tables for interpretation of MICs and zone diameters, version 11.0' EUCAST

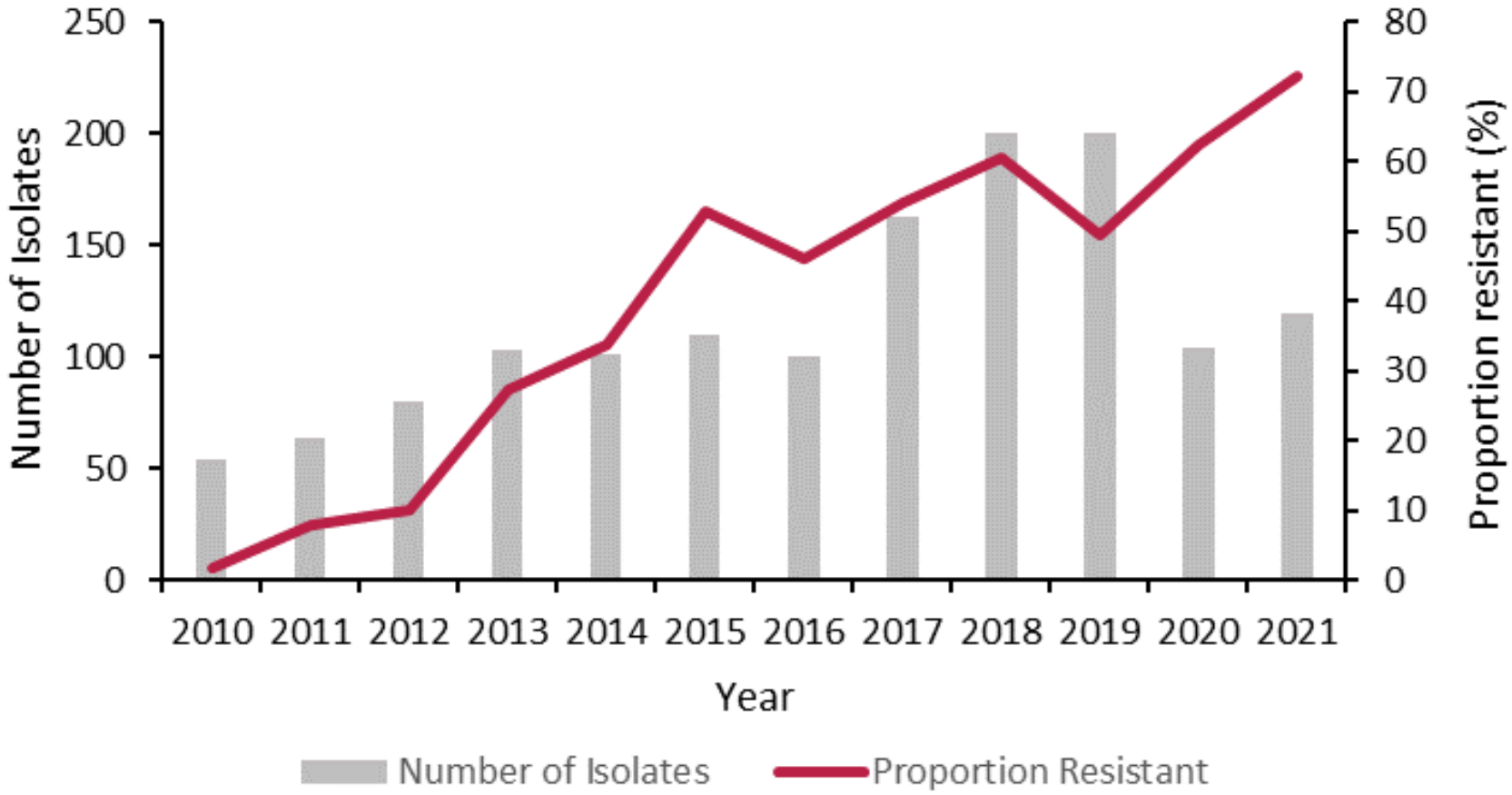
Epidemiology of isolates submitted to Euro-GASP, 2021

Of the 119 isolates submitted to Euro-GASP:

- 97% were male and 3% were female
- Among males median age was 34 years (age range 19-66 years)
- Among females median age was 32 years (age range 21-56 years)
- 87% reported Dublin as their place of residence
- Mode of transmission was available for 24%; where known:
  - gbMSM: 90%
  - Heterosexual: 10%
- Where information on concurrent STI was available, 12% were concurrently infected with another STI. 87% of concurrent infections were chlamydia

Trends in gonorrhoea antimicrobial resistance in Ireland, 2010-2021

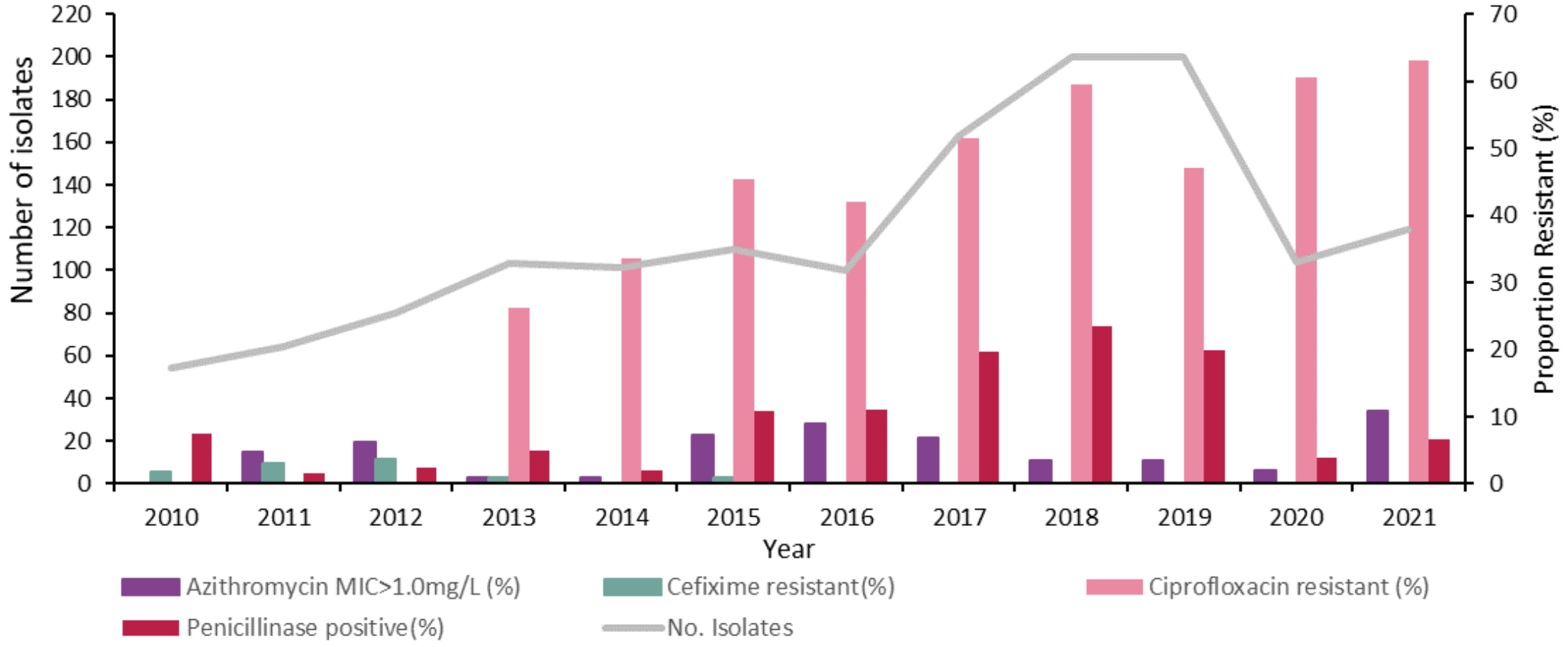
There is an increasing trend in the proportion* of isolates resistant to one or more antimicrobial



*Based on an isolate being resistant to one or more of the following: Azithromycin, Cefixime, Ciprofloxacin, and Ceftriaxone.

Trends in gonorrhoea antimicrobial resistance in Ireland, 2010-2021

Resistance to cefixime, ciprofloxacin, azithromycin, and penicillinase (using EUCAST breakpoints for cefixime, ciprofloxacin, and penicillinase and ECOFF for azithromycin).



Trends in gonorrhoea antimicrobial resistance in Ireland, 2010-2021

Antimicrobial resistance to key antibiotics (numbers and proportions that are resistant) 2010-2021

Year	Isolates tested	AZM-R	%AZM-R	CFM-R	%CFM-R	CIP-R	%CIP-R	PPNG	% PPNG
2010	54	0	0%	1	2%	0	0%	4	7%
2011	64	3	5%	2	3%	0	0%	1	2%
2012	80	5	6%	3	4%	0	0%	2	2.50%
2013	103	1	1%	1	1%	27	26%	5	5%
2014	101	1	1%	0	0%	34	34%	2	2%
2015	110	8	7%	1	1%	50	45%	12	11%
2016	100	9	9%	0	0%	42	42%	11	11%
2017	163	11	7%	0	0%	84	52%	32	20%
2018	200	7	4%	0	0%	119	60%	47	24%
2019	200	7	4%	0	0%	94	47%	40	20%
2020	104	2	2%	0	0%	63	61%	4	4%
2021	119	13	11%	0	0%	75	63%	8	7%

AZM-R, azithromycin resistant; CFM-R, cefixime- resistant; CIP-R, ciprofloxacin-resistant; PPNG, penicillinase-producing N. gonorrhoeae.

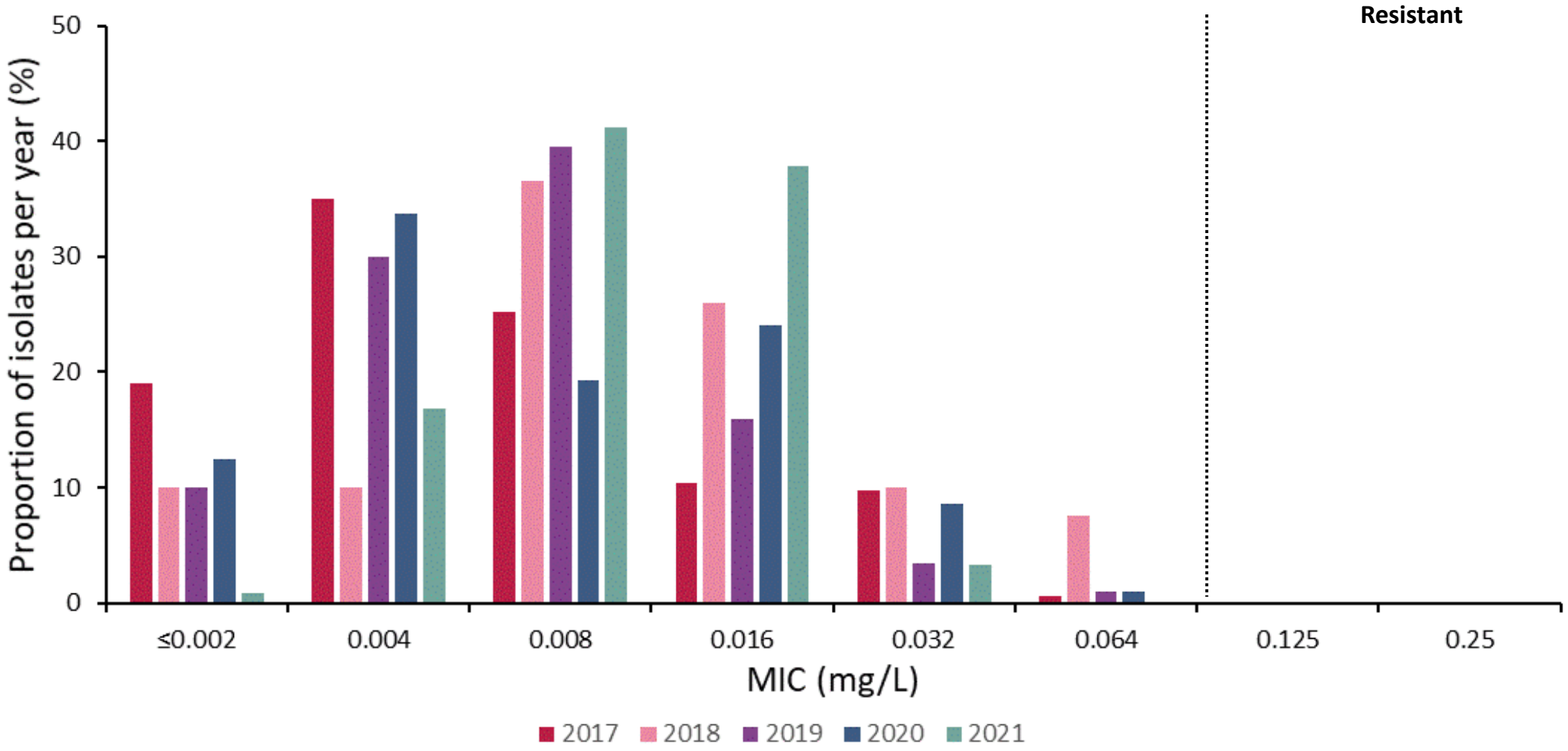
Cephalosporins (ceftriaxone and cefixime)

- Ceftriaxone is the only recommended empirical monotherapy for treatment of gonorrhoea at present (for treatment guidelines, see Gonorrhoea - HSE.ie)

- Ireland has not reported a ceftriaxone resistant isolate to the Euro-GASP programme.
  - One ceftriaxone resistant isolate was reported in Ireland in 2018 (outside Euro-GASP survey period): http://ndsc.newsweaver.ie/epiinsight/bv8rkspoij310gkzp9yxn5?a=1&p=53827183&t=17517774

- There have been no cefixime resistant isolates reported to Euro-GASP since 2015.

Ceftriaxone MICs among gonococcal isolates in Ireland, 2017-2021



Azithromycin

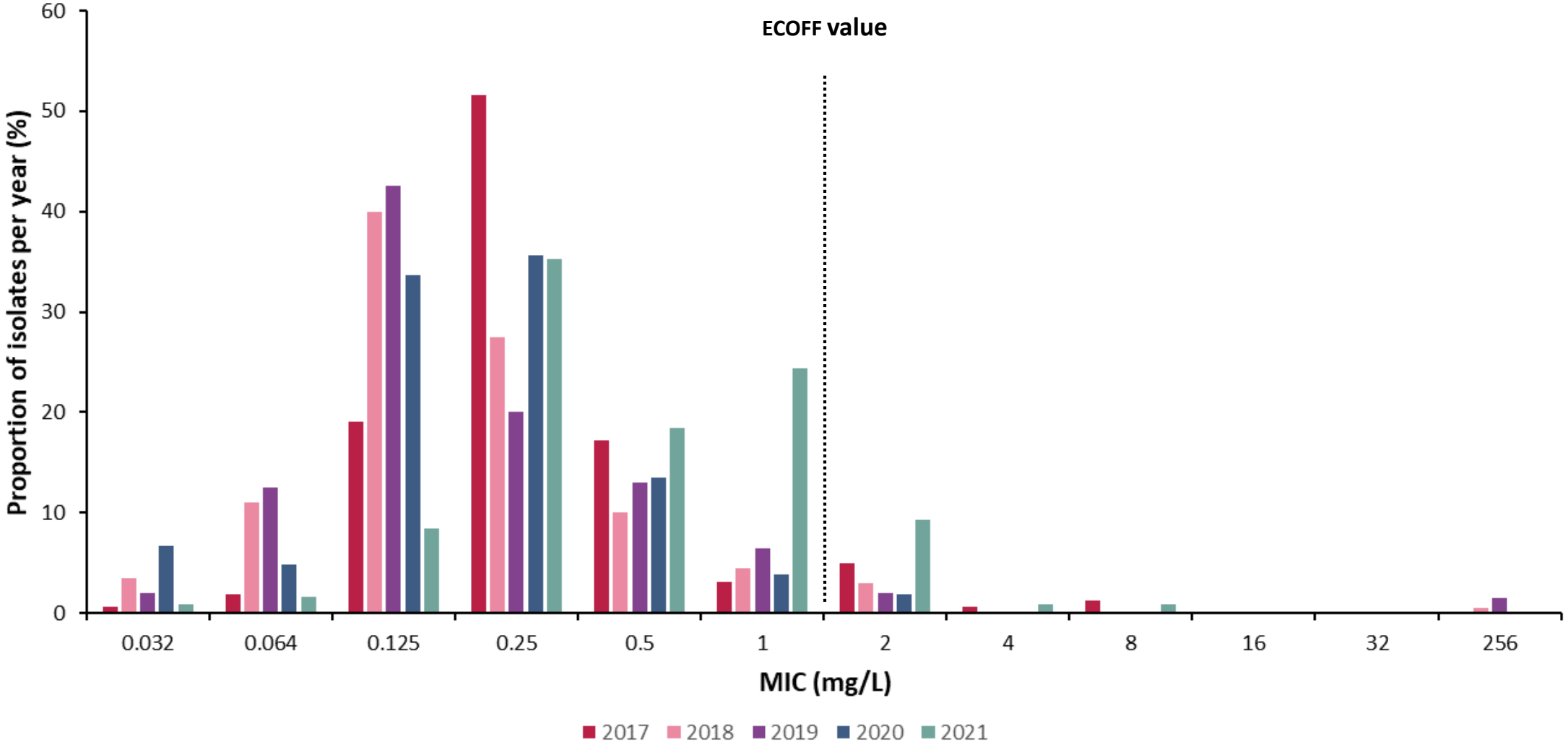
- Dual therapy including azithromycin is no longer recommended as first-line treatment for gonorrhoea -for treatment guidelines, see Gonorrhoea - HSE.ie

- The European Committee on Antimicrobial Susceptibility Testing (EUCAST) removed the clinical resistance breakpoint of 0.5mg/L for azithromycin treatment of gonorrhoea
  - Use of the Epidemiological Cut-Off Value (ECOFF) of 1.0mg/L is now recommended

- Interpretation using the ECOFF was retrospectively applied for analysis of trends in azithromycin susceptibility

- Azithromycin MICs are shifting towards MICs above the azithromycin ECOFF (EURO-GASP, 2019): in 2021 the proportion of isolates exhibiting MICs above the ECOFF increased to 11%.
  - Compared with 2% in 2020 and 4% in 2019; the highest proportion since 2016 at 9%

Azithromycin MICs among gonococcal isolates in Ireland, 2017-2021



Other antimicrobials

- Ciprofloxacin may be recommended for treatment of gonorrhoea in cases of cephalosporin allergy if the isolate is known to be quinolone sensitive
- 63% of isolates were resistant to ciprofloxacin in 2021
  - Increased from 61% in 2020 and 47% in 2019

- Production of penicillinase confers high level resistance to penicillin
- 7% of isolates produced penicillinase in 2021
  - 2021 & 2020 isolates show a decrease in the proportion that produce penicillinase compared to earlier years.

Key points

These data have important implications for the clinical management of gonorrhoea in Ireland:

- Euro-GASP data covered 6% of all gonorrhoea notifications in 2021.
- 72% of isolates reported were resistant to one or more antibiotic tested: Increased from 63% in 2020 and 50% in 2019.
- There were no ceftriaxone resistant isolates in the 2021 Euro-GASP submission
- Azithromycin MICs are shifting towards MICs above the azithromycin ECOFF (EURO-GASP, 2019): in 2021 the proportion of isolates exhibiting MICs above the ECOFF increased to 11%.
- Ciprofloxacin resistance has increased from 26% in 2013 to 63% in 2021.
- Due to the impact of the COVID-19 pandemic, there is limited epidemiological data available on the 2021 Euro-GASP isolates. This limits our understanding of the key population groups who are most affected. HPSC will continue to work with clinical services and Departments of Public Health to improve the quality and completeness of the data.

Key recommendations

- Clinicians should ensure that all cases of gonorrhoea are managed according to national guidelines and that samples for culture and antimicrobial susceptibility testing are taken as recommended in the national guidelines: https://www.hpsc.ie/a-z/sexuallytransmittedinfections/gonorrhoea/amrgonorrhoea/amrgonorrhoeaguidance/
- Laboratories should ensure isolates are tested for susceptibility to ceftriaxone and azithromycin, the recommended antimicrobials for first and second-line use in the treatment of gonorrhoea infection respectively.
- Isolates suspected of resistance should be submitted to the GCRL for confirmation, determination of antibiogram and molecular analysis.
- A focus on prevention of gonorrhoea should be maintained through promotion of public health messages on safer sex and regular testing for STIs.

Acknowledgements

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https://www.stjames.ie/services/laboratorymedicinelabmed/nationalgonococcalreferencelaboratory/

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