





<u>Health Protection Surveillance Centre & National Gonococcal Reference Laboratory,</u> <u>SJH.</u>

Antimicrobial resistance in *Neisseria gonorrhoeae,* Ireland 2010-2022

Based on data from isolates submitted to EURO-GASP

November 2023

Gonorrhoea in Ireland

Trend in notification rate of gonorrhoea by gender, 2010-2022



Male includes cis male and trans male (where known) and female includes cis female and trans female (where known) Rates calculated: 2010-2013=2011 census, 2014-2019= 2016 census, 2020-2022= 2022 census Between 2021 and 2022 free home Sexually Transmitted Infections (STI) sampling was introduced <u>https://sh24.ie/</u>

HSE Health Protection Centre. Gonorrhoea in Ireland, 2022

Antimicrobial resistance in Neisseria gonorrhoeae



A World Health Organization priority

- Gonorrhoea infection is becoming increasingly difficult to treat due to the development of antimicrobial resistance 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

 Euro-GASP monitors trends in gonococcal antimicrobial susceptibility to detect increasing and emerging antimicrobial resistance and to provide quality-assured data to inform national and international treatment guidelines

European Gonococcal Antimicrobial Surveillance Programme (Euro-GASP) (europa.eu)

- Euro-GASP is a sentinel surveillance programme involving centralised or de-centralised antimicrobial susceptibility testing of *N. gonorrhoeae* isolates in participating countries
- EU/EEA Member States participate in Euro-GASP's annual survey conducted over 3-4 month period (September-December)
- 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 Euro-GASP



- Participating since 2010
- Antimicrobial susceptibility testing performed by Public Health England (2010-2012), Department of Clinical Microbiology St James's Hospital (SJH) (2013-2016), National Gonococcal Reference Laboratory (NGRL), St James's Hospital (2017-present)
- Linked epidemiological data collected from isolate referral forms, enhanced surveillance forms and clinical notes
- Data source: All isolates received and tested in the NGRL over Euro-GASP survey period. Most recent data presented in this report are on 294 Irish isolates reported for 2022 (September-December): they represent 7% of total national gonorrhoea notifications

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Not

Other/unknown

Epidemiological characteristics of individuals with isolates submitte to Euro-GASP by gender and mode transmission, 20

~ gbMSM: gay, bisexual and other m have sex with men

HSE Health Protection Centre. Gono

		Females	Heterosexual	~gbMSM	Other/unknown	Not	Total	
		remaies	Males	guivisivi	Males	reported		
	Number of individuals	49	9	154	81	1	294	
		n (% of N)	n (% of N)	n (% of N)	n (% of N)	n (% of N)	n (% of N)	
	Age Ggroup Years							
	15-19	15 (31%)	0%	6 (4%)	9 (11%)	0%	30 (10%)	
£	20-24	20 (41%)	9 (100%)	15 (10%)	15 (19%)	0%	59 (20%)	
of	25-29	8 (16%)	0%	41 (27%)	17 (21%)	0%	66 (22%)	
	30-34	1 (2%)	0%	41 (27%)	14 (17%)	0%	56 (19%)	
a d	35-39	1 (2%)	0%	15 (10%)	13 (16%)	0%	29 (10%)	
ed	40-44	0%	0%	16 (10%)	5 (6%)	1 (100%)	22 (7%)	
7	45-49	0%	0%	11 (7%)	3 (4%)	0%	14 (5%)	
C	50+	3 (6%)	0%	9 (6%)	4 (5%)	0%	16 (5%)	
e of	Unk	1 (2%)	0%	0%	1 (1%)	0%	2 (1%)	
22	Median Age	20	21	36	29	40	27	
	Age range	16-59	21-23	17-61	17-71	40	16-71	
	Residence							
	Dublin	36 (73%)	3 (33%)	128 (83%)	57 (70%)	1 (100%)	225 (77%)	
	Outside Dublin	13 (27%)	6 (67%)	26 (17%)	24 (30%)	0%	69 (23%)	
	Country of Birth							
men who	Ireland	6 (12%)	4 (44%)	51 (33%)	8 (10%)	0%	69 (23%)	
	Outside Ireland	2 (4%)	2 (22%)	32 (21%)	5 (6%)	0%	41 (14%)	
	Unknown	41 (84%)	3(33%)	71 (46%)	68 (84%)	1 (100%)	184 (63%)	
orrhoea in l	reland, 2022						6	

Heterosexual

Epidemiological characteristics of individuals with isolates submitted to Euro-GASP by gender and mode of transmission, 2022

† Not all individuals are tested for gonorrhoea at each site, and individuals can be infected at more than one site

^ Concurrent STI: another STI diagnosed within 4 weeks of the positive gonorrhoea notification

* Yes- known to have previous infection, No- known not to have had previous infection, Unk – could not be determined if previously infected

~ gbMSM: gay, bisexual and other men who have sex with men

	Females Heterosexual Males		~gbMSM	Other/unknown Males	Not reported	Total
Number of individuals	49	9	154	81	1	294
	n (% of N)	n (% of N)	n (% of N)	n (% of N)	n (% of N)	n (% of N)
HIV Status						
Negative	7 (14%)	0%	90 (58%)	27 (33%)	0%	124 (24%)
Positive	0%	1 (11%)	21 (14%)	3 (4%)	0%	25 (9%)
Not reported	42 (86%)	8 (89%)	43 (28%)	51 (63%)	1 (100%)	145 (49%)
Site of Infection +						
Genital	41 (84%)	8 (89%)	53 (34%)	41 (51%)	0%	143 (49%)
Rectal	1 (2%)	1 (11%)	70 (45%)	17 (21%)	0%	89 (30%)
Pharyngeal	5 (10%)	0%	29 (19%)	17 (21%)	1 (100%)	52 (18%)
Other Site	2 (4%)	0%	2 (1%)	6 (7%)	0%	10 (3%)
Concurrent STI^						
Chlamydia	9 (18%)	1 (11%)	35 (23%)	8 (10%)	0%	53 (18%)
Herpes Type 2 (HSV-2)	0%	0%	1 (1%)	0%	0%	1 (0.3%)
Syphilis	1 (2%)	0%	17 (11%)	5 (6%)	0%	23 (8%)
No concurrent infection	1 (2%)	0%	20 (13%)	14 (17%)	0%	35 (12%)
Unk	39 (80%)	8 (89%)	86 (56%)	55 (68%)	1(100%)	189 (64%)
Previous gonorrhoea infec	ction*					
Yes	0%	1 (11%)	50 (32%)	8 (10%)	0%	59 (20%)
No	0%	0%	19 (12%)	0%	0%	19 (6%)
Unk	49 (100%)	8 (89%)	85 (55%)	73 (90%)	1 (100%)	216 (73%)

Epidemiological antimicrobial resistance definitions



To allow for European comparison, results from antimicrobial susceptibility testing were interpreted in line with Euro-GASP analysis, using breakpoints from the European Committee on Antimicrobial Susceptibility Testing (EUCAST):

- cefixime resistance, MIC >0.125 mg/L
- ceftriaxone resistance, MIC >0.125 mg/L
- tetracycline resistance, MIC> 0.5mg/L
- ciprofloxacin resistance, MIC >0.064 mg/L
- β-lactamase production for detection of high-level penicillin resistance, penicillinase positive
- azithromycin epidemiological cut-off value (ECOFF), MIC >1 mg/L[^]

^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' (ECOFF) of >1.0 mg/L

European Committee on Antimicrobial Susceptibility Testing (EUCAST). 'Breakpoint tables for interpretation of MICs and zone diameters, version 13.1' <u>EUCAST</u>

Trends in gonorrhoea antimicrobial resistance in Ireland* (Euro-GASP, 2010-2022)



- *EUCAST guidelines, version 13.1' <u>EUCAST</u> **Azithromycin MIC above ECOFF (>1 mg/L)
- ^1 cefixime resistant isolate in 2022 (0.03%)
- HSE Health Protection Centre. Gonorrhoea in Ireland, 2022

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Trends in gonorrhoea antimicrobial resistance in Ireland* (Euro-GASP, 2010-2022)



Year	Isolates tested	AZM- MIC>1.0	%AZM- MIC>1.0	CFM-R	%CFM-R	CIP-R	%CIP-R	PPNG	% PPNG	Isolates tested	TET-R	%TET-R
		mg/L	mg/L							(TET)		
2010	54	0	0%	1	2%	0	0%	4	7%	0		
2011	64	3	5%	2	3%	0	0%	1	2%	0		
2012	80	5	6%	3	4%	0	0%	2	3%	0		
2013	103	1	1%	1	1%	27	26%	5	5%	0		
2014	101	1	1%	0	0%	34	34%	2	2%	0		
2015	110	8	7%	1	1%	50	45%	12	11%	0		
2016	100	9	9%	0	0%	42	42%	11	11%	0		
2017	163	11	7%	0	0%	84	52%	32	20%	9	0	0%
2018	200	7	4%	0	0%	119	60%	47	24%	25	9	36%
2019	200	7	4%	0	0%	94	47%	40	20%	4	3	75%
2020	104	2	2%	0	0%	63	61%	4	4%	15	1	7%
2021	119	13	11%	0	0%	75	63%	8	7%	23	3	13%
2022	294	138	47%	1	0%	175	60%	20	7%	247	113	46%

AZM- MIC>1.0mg/L – above ECOFF; CFM-R, cefixime- resistant; CIP-R, ciprofloxacin-resistant; PPNG, penicillinase positive, TET-R, tetracycline resistance

*EUCAST guidelines, version 13.1' EUCAST

HSE Health Protection Centre. Gonorrhoea in Ireland, 2022.

Ceftriaxone



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

Ireland has not yet 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 <u>&t=17517774</u>

Ceftriaxone minimum inhibitory concentration (MIC)(mg/L) among gonococcal isolates in Ireland, (Euro-GASP, 2010-2022)



The line indicates the threshold for antimicrobial resistance according to EUCAST guidelines.

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Azithromycin



- Dual therapy including azithromycin is <u>no longer</u> recommended as first-line treatment for gonorrhoea -for treatment guidelines, see <u>Gonorrhoea - HSE.ie</u>
- 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
- The proportion of isolates exhibiting MICs above the ECOFF increased to **47%** in 2022.
 - Compared with 11% in 2021, 2% in 2020 and 4% in 2019
 - This may reflect use of azithromycin for other genital infections and for non-genital infections
- Isolates with MICs above the ECOFF by sex and mode of transmission in 2022
 - Males
 - 46% overall
 - 64% gbMSM
 - 4% heterosexual males
 - 32% males where mode of transmission not known
 - Females
 - 53%

Azithromycin minimum inhibitory concentration (MIC)(mg/L) among gonococcal isolates in Ireland (Euro-GASP, 2010-2022)



■ 2017 ■ 2018 ■ 2019 ■ 2020 ■ 2021 ■ 2022

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Tetracycline resistance MICs among gonococcal isolates in Ireland, 2017-2022



The European Committee on Antimicrobial Susceptibility Testing (EUCAST) updated the resistance breakpoint to > 0.5mg/L for tetracycline treatment of gonorrhoea in 2023 Interpretation using the new breakpoint was retrospectively applied for analysis of trends in tetracycline resistance

		MIC (mg/L)										
		Susceptible				Resistant						
Year	Number of Isolates	Isolates tested (TET)	0.064	0.125	0.25	0.5	1	2	4	8	16	32
2017	100	9	11%	56%	0%	33%	0%	0%	0%	0%	0%	0%
2018	200	25	8%	12%	16%	28%	20%	0%	4%	0%	12%	0%
2019	76	4	0%	0%	0%	25%	50%	25%	0%	0%	0%	0%
2020	104	15	7%	7%	60%	20%	7%	0%	0%	0%	0%	0%
2021	119	23	0%	0%	30%	57%	13%	0%	0%	0%	0%	0%
2022	294	247	0%	2%	6%	46%	38%	2%	0%	0%	3%	2%

Other antimicrobials



- Ciprofloxacin may be recommended for treatment of gonorrhoea in cases of cephalosporin allergy if the isolate is known to be quinolone sensitive
- **60%** of isolates were resistant to ciprofloxacin in 2022
- Isolates resistant to ciprofloxacin by sex and mode of transmission in 2022
 - Males
 - 61% overall
 - 66% gbMSM
 - 4% heterosexual males
 - 30% males where mode of transmission not known

– Females

- 55%
- Production of β -lactamase confers high level resistance to penicillin
- **7%** of isolates produced β -lactamase (i.e. penicillinase positive) in 2022
 - Since 2020 decreasing proportions compared to earlier years

Key points summary

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

- Gonorrhoea notifications have risen by 45% from 2019 (n=2805) to 2022 (n=4,062)
- Data submitted to Euro-GASP covered 6% of all 2022 gonorrhoea notifications
- 2022 data shows a trend towards increasing antimicrobial resistance
- Azithromycin ECOFF above (MIC >1 mg/L) in **47%** of isolates
- Ciprofloxacin resistance (MIC >0.06 mg/L) in **60%** of isolates
- Tetracycline resistance (MIC >0.5 mg/L) in **46%** of isolates
- β -lactamase (i.e. penicillinase positive) in **7%** of isolates
- Cefixime resistance (MIC >0.125 mg/L) in **one** isolate
- No ceftriaxone resistance



Public health implications and key recommendations for Public Health



- Support the development of comprehensive sexual health services that are appropriately funded and resourced to meet sexual health needs.
- 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 <u>national</u> <u>guidelines</u>
- 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
- Isolates suspected of resistance should be submitted to the NGRL 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
- Possible cases of treatment failure should be reported to the HPSC. The <u>treatment failure form</u>, enhanced <u>Euro-GASP Surveillance form</u> and the <u>protocol for surveillance of ceftriaxone resistant gonorrhoea</u> can be found on the HPSC website

Further information

Further information on gonorrhoea and gonorrhoea antimicrobial resistance can be found on the HPSC website

National Gonococcal Reference Laboratory, SJH

National guidelines for the prevention and control of gonorrhoea and for managing the impact of antimicrobial resistance in *Neisseria gonorrhoeae*

National framework for sexual health and wellbeing

ECDC response plan to control and manage the threat of MDR and XDR gonorrhoea

The Man2Man campaign for gbMSM aged 18+

The HSE Sexual Health Crisis Pregnancy Programme (SHCPP)

https://www.hpsc.ie/a-z/sexuallytransmittedinfections/gonorrhoea/

National Gonococcal Reference Laboratory | St James's Hospital

https://www.hpsc.ie/az/sexuallytransmittedinfections/gonorrhoea/amrgonorrhoea/amrg onorrhoeaguidance/

https://www.gov.ie/en/policy-information/8feae9-national-sexualhealth-strategy/?referrer=/wpcontent/uploads/2015/10/national-sexual-health-strategy.pdf/

https://www.ecdc.europa.eu/en/publications-data/response-plancontrol-and-manage-threat-multi-and-extensively-drug-resistant

Man2Man.ie

Sexualwellbeing.ie



Technical notes



Slide 2: Gonorrhoea in Ireland

- Please note that the information from previous years is updated on an ongoing basis in the Computerised Infectious Disease Reporting (CIDR) system, and so information on previous years represents our current understanding and most up to date data as of 1st October 2023, and may not correspond exactly with what was reported in previous annual reports. Similarly, data for 2022 may be updated further in due course and will be reported on in subsequent annual reports.
- While efforts are made to remove duplicate records from these data, it is not always
 possible to link and remove all duplicate records and some patients or disease events may
 be counted more than once.

Abbreviations

- gbMSM: gay, bisexual and other men who have sex with men
- Trans female: Assigned sex at birth is male and gender identity is female
- Trans male: Assigned sex at birth is female and gender identity is male

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