

Antimicrobial resistance in Neisseria gonorrhoeae, Ireland 2010-2023

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

Based on data from isolates submitted to EURO-GASP

October 2024

Gonorrhoea in Ireland



Trend in notification rate of gonorrhoea by gender, 2010-2023

There were **6,805** cases of gonorrhoea notified in 2023

Further information on epidemiology of gonorrhoea in 2023 can be found in the <u>Sexually Transmitted</u> <u>Infections (STIs) in Ireland:</u> <u>Trends to the end of 2023</u> report



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, 2020-2023= 2022 census

Between 2021 and 2022 free home Sexually Transmitted Infections (STI) sampling was introduced <u>www.sexualwellbeing.ie</u>

H Antimicrobial resistance (AMR) 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 <u>last remaining</u> option for first-line treatment
- The WHO <u>Bacterial Priority Pathogen List, 2024</u>, includes 15 families of antibiotic-resistant pathogens, grouped into critical, high and medium categories of priority for research and development and for public health measures. *N. gonorrhoeae*, of which multidrug-resistant strains have emerged, limiting treatment options has been listed in the high priority category

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 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



hpsc

- Participating since 2010
- Antimicrobial susceptibility testing performed by National Gonococcal Reference Laboratory (NGRL), St James's Hospital (2017-present), Department of Clinical Microbiology St James's Hospital (SJH) (2013-2016), and Public Health England (2010-2012)
- Linked epidemiological data is collated from isolate referral forms, enhanced surveillance forms and clinical notes (where available)
- Data source: All isolates received and tested in the NGRL over Euro-GASP survey period. Most recent data presented in this report are on 253 Irish isolates reported for 2023 (September-November): they represent 4% of total national gonorrhoea notifications and 23% of isolates tested at NGRL in 2023
- This report is based on data submitted to Euro-GASP and does not represent the total
 antimicrobial resistant profile nationally for 2023

F Epidemiological characteristics of individuals with isolates submitted to Euro-GASP by gender and mode of transmission, 2023

	Females	Heterosexual Males	~gbMSM	Other/unknown Males	Not reported	Total
Number of individuals	27	9	127	88	2	253
	n(% of N)	n(% of N)	n(% of N)	n(% of N)	n(% of N)	n(% of N)
Age Group Years						
15-19	7 (26%)	1 (11%)	2 (2%)	8 (9%)	0%	18 (7%)
20-24	13 (48%)	4 (44%)	16 (13%)	23 (26%)	0%	56 (22%)
25-29	3 (11%)	1 (11%)	30 (24%)	20 (23%)	0%	54 (21%)
30-34	2 (7%)	1 (11%)	39 (31%)	13 (15%)	1 (50%)	56 (22%)
35-39	2 (7%)	1 (11%)	23 (18%)	12 (14%)	0%	38 (15%)
40-44	0%	1 (11%)	9 (7%)	7 (8%)	1 (50%)	18 (7%)
45-49	0%	0%	3 (2%)	1 (1%)	0%	4 (2%)
50+	0%	0%	5 (4%)	4 (5%)	0%	9 (4%)
Unkown	0%	0%	0%	0%	0%	0%
Median age (Years)	22	23	37	28	37	29
Age range (Years)	17-37	19-41	18-71	17-63	33-41	17-71
Residence						
Dublin	19 (70%)	4 (44%)	104 (82%)	71 (81%)	1 (50%)	199 (79%)
Outside Dublin	8 (30%)	5 (56%)	23 (18%)	17 (19%)	1 (50%)	54 (21%)

Comparing 2022* and 2023 isolates:

- The proportion of isolates from females decreased from 17% in 2022 to 11% in 2023
- The age distribution of isolates remains relatively unchanged, the median age has increased slightly from 27 yrs in 2022 to 29 yrs in 2023
- In 2023, the proportion of isolates from people living in Dublin (79%) is similar to 2022 (77%)
 - The large proportion of isolates from the Dublin area is not unexpected. The NGRL test samples predominantly from STI clinics in Dublin

hpsc

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

*Antimicrobial resistance in Neisseria gonorrhoeae, Ireland 2010-2022

Epidemiological characteristics of individuals with isolates submitted to Euro-GASP by gender and mode of transmission, 2023

	Females	Heterosexual Males	~gbMSM	Other/unknown Males	Not reported	Total
Number of individuals	27	9	127	88	2	253
	n (% of N)	n (% of N)	n (% of N)	n (% of N)	n (% of N)	n (% of N)
Country of Birth						
Ireland	4 (15%)	8 (89%)	37 (29%)	7 (8%)	1 (50%)	57 (23%)
Outside Ireland	1 (4%)	0%	55 (43%)	3 (3%)	1 (50%)	60 (24%)
Unknown	22 (81%)	1 (11%)	35 (28%)	78 (89%)	0%	136 (54%)
HIV Status						
Negative	13 (48%)	0%	90 (71%)	61 (69%)	0%	164 (65%)
Positive	0%	0%	19 (15%)	4 (5%)	1 (50%)	24 (9%)
Not reported	14 (52%)	9 (100%)	18 (14%)	23 (26%)	1 (50%)	65 (26%)
Site of Infection +						
Genital	21 (78%)	9 (100%)	31 (24%)	46 (52%)	1 (50%)	108 (43%)
Rectal	1 (4%)	0%	58 (46%)	13 (15%)	0%	72 (28%)
Pharyngeal	4 (15%)	0%	38 (30%)	28 (32%)	1 (50%)	71 (28%)
Other Site	1 (4%)	0%	0%	1 (1%)	0%	2 (1%)
Concurrent STI^						
Chlamydia	3 (11%)	2 (22%)	28 (22%)	12 (14%)	0%	45 (18%)
Syphilis	0%	0%	4 (4%)	1 (1%)	0%	5 (2%)
Mycoplasma genitalium	1 (4%)	0%	0%	0%	0%	1 (<1%)
No concurrent infection	10 (37%)	0%	23 (18%)	35 (40%)	1 (50%)	69 (27%)
Unknown	13 (48%)	7 (78%)	72 (57%)	40 (45%)	1 (50%)	133 (53%)
Previous gonorrhoea infe	ection*					
Yes	2 (7%)	0%	56 (44%)	13 (15%)	0%	71 (28%)
No	0%	0%	12 (9%)	0%	1 (50%)	13 (5%)
Unknown	25 (93%)	9 (100%)	59 (46%)	75 (85%)	1 (50%)	169 (67%)

Note: Direct comparison with previous years is not advised due to lack of completeness in enhanced data

From the available enhanced data:

- 9% of isolates are from individuals who are living with HIV
- 43% of isolates were obtained from genital swabs
- 18% of individuals were co infected with chlamydia
- 28% of individuals had a previous gonorrhoea infection

+ 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

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



H 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[^]

*MIC: Minimum Inhibitory Concentration

^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>

H Trends in gonorrhoea antimicrobial resistance in Ireland* (Euro-GASP, 2010-2023)



*EUCAST guidelines, version 13.1' EUCAST

**Azithromycin MIC above ECOFF (>1 mg/L)

^1 cefixime resistant isolate in 2022

hpsc

F Trends in gonorrhoea antimicrobial resistance in Ireland* (Euro-GASP, 2010-2023)

hpsc

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%	13	2	15%
2018	200	7	4%	0	0%	119	60%	47	24%	25	9	36%
2019	200	7	4%	0	0%	94	47%	40	20%	26	8	31%
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	<1%	175	60%	20	7%	248	114	46%
2023	253	105	42%	0	0%	127	50%	27	11%	253	95	38%

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





Cefixime

• No cefixime resistance isolate reported in the study period (Sept-Nov 2023)

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
- <u>One ceftriaxone resistant</u> isolate was reported in Ireland in 2018 (outside Euro-GASP survey period): http://ndsc.newsweaver.ie/epiinsight/bv8rkspoij310gkzp9yxn5?a=1&p=53827183&t=17517774

Ceftriaxone MIC (mg/L) among gonococcal isolates in Ireland, (Euro-GASP, 2018-2023)

hpsc



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

HE 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 decreased to 42% in 2023
 - Compared with 47% in 2022, 11% in 2021, 2% in 2020 and 4% in 2019
 - Although there has been a decrease in proportion of isolates exhibiting MICs above the ECOFF in 2023, the increase above 2020 levels may reflect use of azithromycin for non-genital infections
- Isolates with MICs above the ECOFF by sex and mode of transmission in 2023

Male	
Total Male	42%
gbMSM	60%
Heterosexual males	4%
Males where mode of transmission not known	35%
Female	
Total Female	41%

H Azithromycin MIC (mg/L) among gonococcal isolates in (Ireland (Euro-GASP, 2018-2023)

hpsc



■ 2018 ■ 2019 ■ 2020 ■ 2021 ■ 2022 ■ 2023

H Tetracycline resistance MICs among gonococcal isolates in Ireland, 2018-2023



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



■ 2018 ■ 2019 ■ 2020 ■ 2021 ■ 2022 ■ 2023

	2018	2019	2020	2021	2022	2023
Number of Isolates	200	200	104	219	294	253
Number of Isolates tested for Tetracycline Resistance	25	26	15	23	248	253





- Ciprofloxacin may be recommended for treatment of gonorrhoea in cases of cephalosporin allergy if the isolate is known to be quinolone sensitive
- **50%** of isolates were resistant to ciprofloxacin in 2023, a <u>reduction</u> of 10% from 2022
- Isolates resistant to ciprofloxacin by sex and mode of transmission in 2023

Male	
Total Male	52%
gbMSM	59%
Heterosexual males	3%
Males where mode of transmission not known	38%
Female	
Total Female	33%

- Production of β-lactamase confers high level resistance to penicillin
- **11%** of isolates produced β -lactamase (i.e. penicillinase positive) in 2023
 - Increased proportion from 7% in 2022

H Key points summary

hpsc

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

- Gonorrhoea notifications have risen by 143% from 2019 (n=2805) to 2023 (n=6,805)
- Data submitted to Euro-GASP covered 4% of all 2023 gonorrhoea notifications
- No cefixime resistance isolate reported in the study period (Sept-Nov)
- No ceftriaxone resistance reported in 2023
- Azithromycin ECOFF above (MIC >1 mg/L) in **42%** of isolates, a <u>reduction</u> of 5% from 2022
- Ciprofloxacin resistance (MIC >0.06 mg/L) in **50%** of isolates, a <u>reduction</u> of 10% from 2022
- Tetracycline resistance (MIC >0.5 mg/L) in **36%** of isolates, a <u>reduction</u> of 8% from 2022
- β-lactamase (i.e. penicillinase positive) in **11%** of isolates, an <u>increase</u> of 4% from 2022

H Public health implications and key recommendations for Public Health



- Surveillance of AMR in *N. gonorrhoeae* is crucial for monitoring national and international trends in antimicrobial resistance. Strengthening *N. gonorrhoeae* and *N. gonorrhoeae* AMR surveillance should be a priority to safeguard existing antimicrobial drugs and deliver effective public health measures
- Current submissions to EuroGASP only include isolates tested at the NGRL during Sept-Nov annually, expansion of surveillance to include regional laboratories and year round surveillance would increase understanding of AMR in N. gonorrhoeae at a national level
- Lack of complete data on *N. gonorrhoeae* notifications make it difficult to interpret data trends and effectively monitor disease transmission dynamics
- It is important to monitor tetracycline resistance in *N. gonorrhoeae* in light of the evolving role and use of doxycycline as post-exposure prophylaxis for STIs (DoxyPEP)
- Initiatives to improve data collection and completeness:
 - HPSC are currently undertaking an evaluation of *N. gonorrhoeae* surveillance
 - HPSC along with colleagues in Public Health and the Gay Men's Health Service (GMHS) are participating in a European Centre for Disease Prevention and Control (ECDC) project designed to improve national surveillance systems for STIs through using electronic health records (EHR) (EHR-STI). The aim is to identify a data flow process that will improve the timeliness, and completeness for enhanced data on STI notifications

F Public health implications and key recommendations for Public Health Cont.



- 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 national guidelines
- All 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 STI
- Possible cases of treatment failure should be reported to the HPSC. The <u>treatment failure form</u>, enhanced <u>Euro-GASP</u> <u>Surveillance form</u> and the <u>protocol for surveillance of ceftriaxone resistant gonorrhoea</u> and <u>Surveillance of High Level</u> <u>Azithromycin Resistant (HL-AziR) Gonorrhoea</u> can be found on the HPSC website



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 Programme (SHP)

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=/wp-content/uploads/2015/10/nationalsexual-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







This report is based on data submitted to Euro-GASP and does not represent the total antimicrobial resistant profile nationally for 2023

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 2024 and may not correspond exactly with what was reported in previous annual reports. Similarly, data for 2023 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





Laboratory data were provided by Public Health England, Brendan Crowley, Antoinette Power, Sinéad Saab, Candice Principe, Lisa Rose and members of the Central Pathology Laboratory, SJH and the National Gonococcal Reference Laboratory, SJH

Surveillance data were provided by GUIDE, Gay Men's Health Service, STI/GUM clinicians, GPs and personnel in Departments of Public Health

We would sincerely like to thank all who provided data for this report; the National Gonococcal Reference Laboratory in SJH, other hospital microbiology laboratories, personnel within the Departments of Public Health, Consultants in Infectious Disease/Genitourinary Medicine, personnel within STI clinics and GPs.

These slides may be copied and reproduced, provided HPSC is acknowledged. Suggested citation: HSE-Health Protection Surveillance Centre. Antimicrobial resistance in *Neisseria gonorrhoeae*, Ireland 2010-2023. Dublin: HPSC; October 2024.