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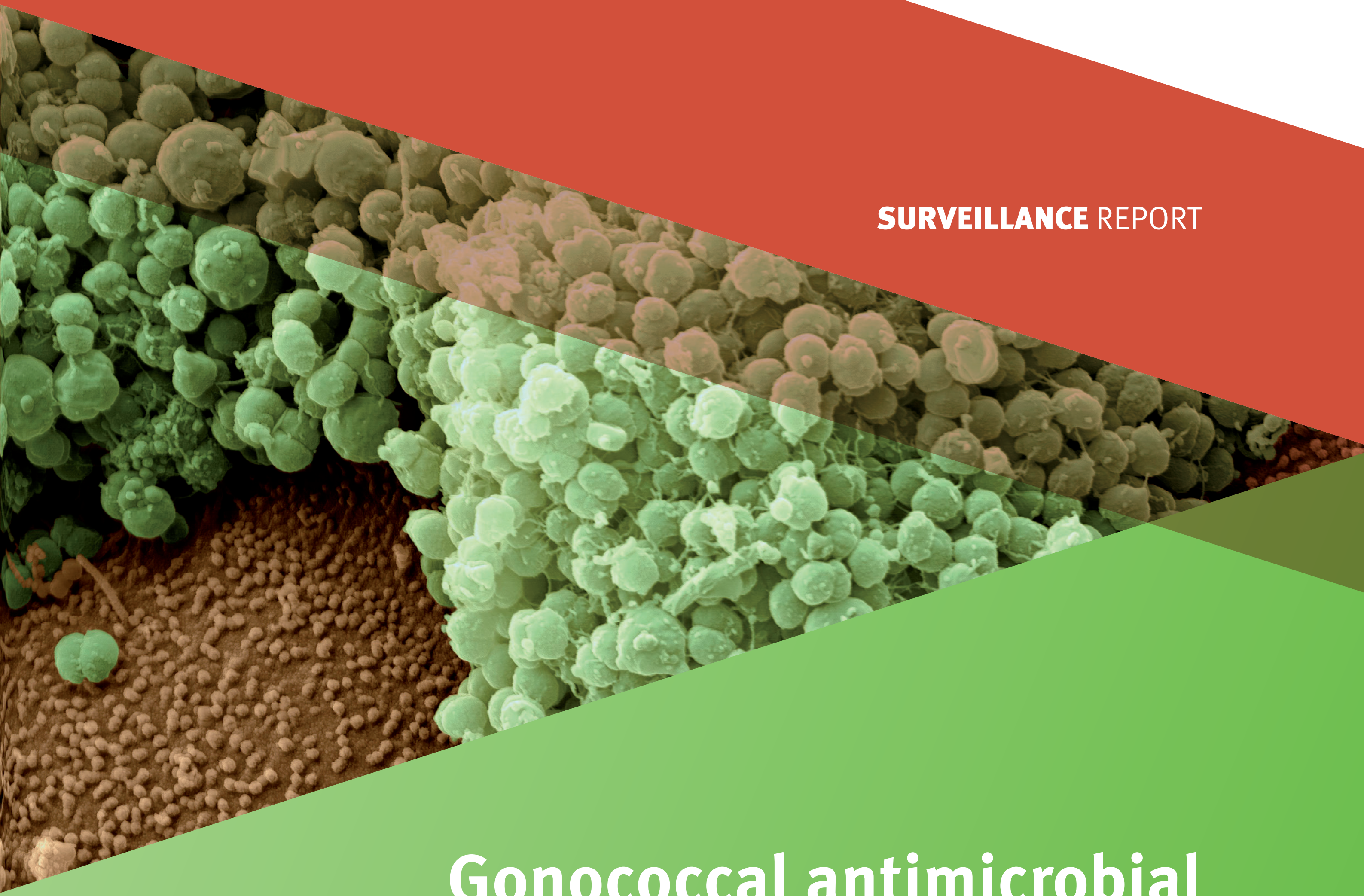

Gonococcal antimicrobial susceptibility surveillance in the European Union/ European Economic Area

Summary of results for 2020

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ECDC TECHNICAL REPORT

Gonococcal antimicrobial susceptibility surveillance in the Europe Union/European Economic Area

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This report was commissioned by the European Centre for Disease Prevention and Control (ECDC), coordinated by Benjamin Bluemel and Marieke J. van der Werf, and produced by the UK Health Security Agency, London, United Kingdom and Örebro University Hospital, Örebro, Sweden.

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Abbreviations

AMR	Antimicrobial resistance
CI	Confidence interval
ECDC	European Centre for Disease Prevention and Control
ECOFF	Epidemiological cut-off value
EEA	European Economic Area
EQA	External quality assessment
EU	European Union
EUCAST	European Committee on Antimicrobial Susceptibility Testing
Euro-GASP	European Gonococcal Antimicrobial Surveillance Programme
GC	Gonococcal
HIV	Human immunodeficiency virus
MDR	Multidrug-resistant
MGS	MIC gradient strip test
MIC	Minimum inhibitory concentration
MSM	Men who have sex with men
NAAT	Nucleic acid amplification test
OR	Odds ratio
STI	Sexually transmitted infection
TESSy	The European Surveillance System
UK	United Kingdom
UKHSA	UK Health Security Agency
WHO	World Health Organization
XDR	Extensively drug-resistant

Executive summary

The surveillance of *Neisseria gonorrhoeae* antimicrobial susceptibility in the European Union/European Economic Area (EU/EEA) is essential for detecting emerging and increasing antimicrobial resistance. Since 2009, this surveillance has been co-ordinated by the European Centre for Disease Prevention and Control (ECDC). The quality-assured data produced can be used to inform treatment guidelines.

During 2020, as in previous years, the European Gonococcal Antimicrobial Surveillance Programme (Euro-GASP) followed an annual decentralised and centralised testing model, requesting participating laboratories to collect gonococcal isolates during the period September–November. Susceptibility testing was performed on all isolates (MIC gradient strip test (mostly Etest) or agar dilution) for the following antimicrobials, where available: ceftriaxone, cefixime, azithromycin, ciprofloxacin, as well as testing for β-lactamase production to detect high-level penicillin resistance. Decentralised testing took place on the premises of the participating laboratories, fulfilling set quality criteria.

In 2020, 23 EU/EEA Member States participated in Euro-GASP, 19 via decentralised testing. In total, 3 291 isolates were tested, the majority of specimens were from male patients (84.4%), with patient age ranging from under one year to 79 years (median age 30 years). Overall, 25.8% of patients were under 25 years, and males were significantly older than females. The anatomical site of specimen collection was mainly genital (71.6%), followed by rectal (20.0%) and pharyngeal (6.0%). In 2020, as in 2019, data was captured on specific samples from blood (no cases reported), eye (0.3%) and joint fluid (0.1%) infection sites. Among cases with information on previous diagnosis of gonorrhoea (18.0%), 23.6% had previously been diagnosed with the infection. Of the 1 075 cases with information on concurrent sexually transmitted infections (STIs) (32.7%), 20.0% of the patients were concurrently diagnosed with a *Chlamydia trachomatis* (non-LGV) infection. Among cases with known sex and sexual orientation (55.0%), 28.1% were females, 25.1% were heterosexual males, and 46.8% were men who have sex with men (MSM). Among all cases, 12.3% were HIV-positive and 96.8% of those were MSM.

In 2020, only one isolate with resistance to ceftriaxone (MIC=0.25 mg/L) was detected, in Belgium. The isolate had an azithromycin MIC at the azithromycin epidemiological cut-off (ECOFF) (MIC=1 mg/L) and was ciprofloxacin resistant (MIC>32 mg/L). The Euro-GASP 2020 results revealed that in total 0.5% of gonococcal isolates were resistant to cefixime (MIC>0.125 mg/L), which was a significant decrease from the 0.9% of isolates recorded in 2019 (p=0.02). The number of countries reporting any resistant isolates also decreased from a previously stable fourteen to six.

Since January 2019, the European Committee on Antimicrobial Susceptibility Testing (EUCAST) clinical resistance breakpoint for azithromycin of MIC>0.5 mg/L has been replaced with an ECOFF value of MIC>1 mg/L. Following the significant increases in the proportion of isolates above azithromycin ECOFF in 2018 (7.6%) and 2019 (10.1%), the proportion remained stable at 11.0% in 2020. In 2020, 21 countries recorded at least one isolate with an MIC above the azithromycin ECOFF (MICs >1 mg/L) compared to 24 countries in 2019, 25 countries in 2018, 21 in 2017 and 20 countries in 2016, respectively. The proportion of isolates showing ciprofloxacin resistance remained at a level constant with that observed in 2019 (57.3%) – 57.7% in 2020.

Although dual azithromycin and ceftriaxone resistance is rare, over 10% of isolates had an azithromycin MIC above the ECOFF. Combined with the continued detection of ceftriaxone resistance, this remains a concern and may threaten the currently highly-effective dual-therapy regimen (ceftriaxone plus azithromycin) and high-dose ceftriaxone monotherapy adopted by some European countries. Even though the level of resistance to cefixime has significantly decreased, this needs to be monitored closely, particularly because gonococcal strains with resistance to both cefixime and ceftriaxone continue to be detected in and outside the EU/EEA. The continuation of quality-assured antimicrobial susceptibility surveillance activities, along with the development of alternative gonococcal regimens, is essential to ensure gonorrhoea remains a treatable infection.

1 Introduction

1.1 Background

The emergence and spread of antimicrobial resistance (AMR) in *Neisseria gonorrhoeae* is a serious threat to the treatment and control of gonorrhoea. The extended-spectrum cephalosporin ceftriaxone is the last remaining option for effective, empiric, first-line antimicrobial monotherapy and is the main therapeutic agent currently recommended in Europe [1]. Due to a decrease in susceptibility [2-6], the European treatment guideline recommends combination treatment with ceftriaxone plus azithromycin as first-line treatment, in an attempt to mitigate the development and/or spread of resistance to these antimicrobials. However, in some circumstances high-dose ceftriaxone monotherapy is also recommended [1]. Surveillance of susceptibility to these agents is essential in order to ensure effective patient management and monitor current and emerging trends in AMR [3].

Since 2009, the European Gonococcal Antimicrobial Surveillance Programme (Euro-GASP) has been coordinated by the European Centre for Disease Prevention and Control (ECDC), supported by an international network led by the UK Health Security Agency (UKHSA) (formerly Public Health England) (United Kingdom) and Örebro University Hospital (Sweden). Euro-GASP has identified decreasing susceptibility to extended-spectrum cephalosporins and treatment failures have been documented [3], prompting the creation of a European response plan to control and manage the threat of multidrug-resistant *N. gonorrhoeae* in the European Union (EU)/European Economic Area (EEA) in 2012 [4]. This response plan was reviewed and updated in 2019 [7], with indicators reviewed in 2020 [8].

1.2 Objectives

The overall aim of Euro-GASP is to strengthen the surveillance of gonococcal antimicrobial susceptibility in EU/EEA countries in order to provide quality-assured data to inform gonorrhoea treatment guidelines. The objectives are:

- to develop and implement sentinel surveillance of gonococcal susceptibility to a range of therapeutically relevant antimicrobials;
- to improve the timeliness of surveillance to allow more frequent monitoring of developments in gonococcal antimicrobial susceptibility across the EU/EEA;
- to link susceptibility data with epidemiological information to better understand the risk factors associated with emerging resistance patterns;
- to implement an external quality assessment (EQA) scheme for antimicrobial susceptibility testing across the EU/EEA;
- to provide training in gonococcal culture and antimicrobial susceptibility testing to facilitate enhanced gonococcal antimicrobial susceptibility surveillance, using a standardised methodology across the EU/EEA.

This report presents the results from the 2020 gonococcal antimicrobial susceptibility sentinel surveillance.

2 Methods

2.1 Participating laboratories and isolate collection

Twenty-three participating laboratories from 23 EU/EEA countries collected *N. gonorrhoeae* isolates from consecutive patients. This represents a decrease of three countries since 2019 - both Croatia and Latvia were unable to participate in 2020 due to the low numbers of isolates collected and the United Kingdom was no longer eligible to participate as it left the European Union on 31 January 2020. Although the official collection window was from September to November 2020, twenty-two countries collected outside of the collection window to attempt to reach the minimum 100 isolate target (seven of them collecting throughout the year). The COVID-19 pandemic had an impact on the isolates collected in 2020, with a survey of 98 STI testing services across the WHO European Region, with 95% of respondents reporting a decrease in testing volumes during March–May 2020 compared to the same period in 2019. In fact, 64% of these respondents reported more than a 50% decline in testing across all STIs [9]. Decreases in testing volumes were also reported during the period June–August 2020, compared to the period March–May 2019 [9].

The Euro-GASP collection criteria and methodology remained the same as in previous years [10-12]. Despite the COVID-19 pandemic, seven countries reported more than their target number of isolates, and all isolates reported were included in the analysis. Isolates from four (17.4%) countries were tested centrally at the UKHSA, UK or at Örebro University Hospital, Sweden, with the remaining 19 (82.6%) countries performing antimicrobial susceptibility testing in their own laboratories. All 23 Euro-GASP laboratories participated in an annual EQA programme [13-16] to ensure comparability of data. Countries that performed decentralised testing had fulfilled established quality criteria prior to commencing their testing, with the exception of Estonia which does not yet have a sufficient volume of data to be approved for decentralised testing, due to the low number of isolates collected annually. Nevertheless, Estonia has performed consistently well in the annual EQA and submitted its own susceptibility testing data for two isolates (below minimum number required for centralised testing) in 2020.

2.2 Antimicrobial susceptibility testing

Antimicrobial susceptibility testing was performed using MIC gradient strip tests (MGS; mainly Etest) or an agar dilution method (determination of MIC (mg/L) or breakpoint technique) for ceftriaxone, cefixime, azithromycin, and ciprofloxacin. Production of penicillinase resulting in high-level penicillin resistance was tested using nitrocefin, as previously described [10,11]. The results were interpreted using breakpoints from the European Committee on Antimicrobial Susceptibility Testing (EUCAST): cefixime/ceftriaxone resistance, MIC >0.125 mg/L; azithromycin epidemiological cut-off value (ECOFF), MIC >1 mg/L; and ciprofloxacin resistance, MIC >0.06 mg/L [14]. Gentamicin and spectinomycin were removed from the routine antimicrobial panel in 2014 as these antimicrobials are not in routine use. They are only tested in 'snapshot' studies every three years, with 2019 being the most recent 'snapshot' study year.

2.3 Data collection and analysis

The following data were collected for each isolate, where available: date specimen obtained; specimen site; sex; age; mode of transmission; previous gonorrhoea diagnosis; other sexual transmitted infections (STI) diagnosed during the current episode; place of residence; clinical service type; HIV status; probable country of infection; diagnostic test and treatment used. The combined variable 'sex and sexual orientation' was generated using the variables 'sex' and 'mode of transmission'. All susceptibility and epidemiological data were uploaded to TESSy by the Member States and then approved.

To evaluate the reporting completeness of epidemiological data for each country the number of nil responses and unknowns entered for each variable was subtracted from the total number of isolates received, and the result was used to calculate a percentage completeness value (number of responses/total isolates received x 100). An overall response rate for each country was then calculated by taking the average of the percentage completeness for all 13 epidemiological fields.

2.4 Statistical analysis

Statistical analysis was performed using Stata v15.1. The Z-test was used to determine the difference between epidemiological and AMR data collected in 2020 versus 2019, and a Mann-Whitney U test was used to test whether the differences in age distribution were statistically significant. Where datasets contained sufficient numbers, the odds ratios (OR) and 95% confidence intervals (CI) were calculated and Pearson's χ^2 test was used to measure if these odds ratios differed significantly from 1. For small cell numbers, Fisher's exact test was performed. Using a forward step-wise approach, the most significant and strongest associations from the univariate analysis were added to a multivariable logistic regression model sequentially. Statistical significance for all tests was assumed when $p<0.05$.

3 Results

In 2020, data from a total of 3 291 isolates provided by 23 countries were available for analysis. This represents a decrease of 875 isolates (21.0%) compared with 2019, partially due to the decreased number of countries participating in 2020 (including the non-participation of UK after its withdrawal from the EU), and probably also due to the impact of the COVID-19 pandemic. The number of isolates tested from each country varied from two (Cyprus and Estonia) to 450 (Norway).

3.1 Epidemiological data

Overall, the reporting completeness was 56.0%, compared to 56.4% in 2019, 62.1% in 2018, 58.2% in 2017 and 61.6% in 2016. The level of completeness was in line with previous years for the majority of variables with highest completeness for sex (99.7%) and age (99.4%) [10-12]. Following on from 2019's significant decrease ($p<0.05$) in reporting of all variables (with the exception of 'diagnostic test used'), there were further significant decreases in completeness for the variables 'treatment used' (20.2%, $p<0.01$) and 'previous gonorrhoea diagnosis' (18.0%, $p<0.01$). There were significant increases in completeness for the variables 'sex', 'age', 'site of infection', 'place of residence' and 'probable country of infection', while there was no significant change observed in the remaining variables. Further details on reporting completeness for 2020 data can be found in Annex 1.

As in previous years, the majority of gonococci (84.4%) were collected from men (Table 1). Information on the combined variable 'sex and sexual orientation' was available for 55.0% (n=1 811) of cases. The main anatomical site of specimen collection was similar to previous years, predominantly genital samples (71.6%), with an increase on 2019 (68.1%, $p<0.01$). The proportion of pharyngeal specimens decreased from 9.7% in 2019 to 6.0% in 2020 ($p<0.01$). Information on previous diagnosis of gonorrhoea was available for 18.0% of cases (n=592), 23.6% of which had a previous infection, which was comparable to the level observed in 2019 (24.7%). Information on other concurrent STIs was available for 32.7% (n=1 075) of cases: 20.0% had a concurrent chlamydia infection, 6.1% had another STI, and 73.9% had no concurrent STIs. Of 1 011 cases (30.7%) with known HIV status, 124 (12.3%) were HIV positive. Of HIV-positive cases with known mode of transmission (n=95), 96.8% were in MSM. The probable country of infection was available for 1 150 (34.9%) cases from 12 different countries. Overall, only 5.3% of these cases (n=61) were probably acquired in a country outside of the reporting country, representing a significant decrease on 2019 (10.2%, $p<0.01$).

Table 1. Patient characteristics reported for Euro-GASP gonococcal isolates, 2011–2020

	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Total number of isolates	1 902	1 927	1 994	2 151	2 134	2 660	3 248	3 299	4 166	3 291
Sex										
Male	1 505 (82.4)	1 596 (83.7)	1 676 (84.7)	1 821 (85.1)	1 736 (81.8)	2 256 (85.1)^	2 737 (84.5)	2 795 (85.3)	3 389 (83.0)	2 762 (84.4)
Female	321 (17.6)	310 (16.3)	302 (15.3)	318 (14.9)	385 (18.2)	395 (14.9)	502 (15.5)	483 (14.7)	695 (17.0)	509 (15.6)
Unknown or other	76	21	16	11	13	9	9	21	82	20
Age (years)										
<25	572 (31.9)	617 (32.9)	554 (28.4)	605 (28.7)	617 (29.5)	720 (27.5)	898 (28.2)	925 (28.4)	1133 (28.4)	844 (25.8)
≥25	1 221 (68.10)	1 261 (67.1)	1 399 (71.6)	1 501 (71.3)	1 476 (70.5)	1 902 (72.5)	2 283 (71.8)	2 332 (71.6)	2 853 (71.6)	2 428 (74.2)
Unknown	109	49	41	44	41	38	67	42	180	19
Sex and sexual orientation										
Females	321 (27.1)	310 (28)	302 (25.7)	318 (22.7)	385 (26.4)	395 (22.9)	502 (22.6)	483 (21.3)	695 (29.5)	509 (28.1)
Heterosexual males	423 (35.6)	390 (35.2)	376 (32)	485 (34.7)	419 (28.7)	632 (36.7)	663 (29.9)	595 (26.3)	588 (24.9)	455 (25.1)
Men who have sex with men	442 (37.3)	408 (36.8)	496 (42.3)	594 (42.5)	657 (45.0)	696 (40.4)^	1 055 (47.5)*	1 186 (52.4)	1 074 (45.6)	847 (46.8)*
Unknown	716	819	820	754	673	937	1 028	1 035	1 809	1 480«
Site of infection										
Genital	1 466 (82.1)	1 537 (83)	1 531 (79)	1 549 (76.3)	1 517 (72.9)	1 943 (75.5)	2 166 (72.8)	2 155 (70.4)	2 578 (68.1)	2 175 (71.6)
Pharyngeal	79 (4.4)	92 (5)	122 (6.3)	154 (7.6)	180 (8.7)	165 (6.4)	254 (8.5)	259 (8.5)	368 (9.7)	182 (6.0)
Anorectal	216 (12.1)	188 (10.2)	255 (13.2)	192 (9.5)	280 (13.5)	366 (14.2)	435 (14.6)	570 (18.6)	743 (19.6)	608 (20.0)
Other	24 (1.3)	35 (1.9)	30 (1.5)	135 (6.6)	103 (5.0)	100 (3.9)	120 (4)	77 (2.5)	97± (2.6)	72 (2.4)¤
Unknown	117	75	56	121	54	86	273	238	380	254
Previous gonorrhoea										
Yes	146 (19)	130 (17.2)	142 (17.8)	163 (19.7)	157 (17.5)	171 (17.2)	235 (21.8)	264 (26.9)	251 (24.7)	140 (23.6)
No	621 (81)	627 (82.8)	654 (82.2)	663 (80.3)	739 (82.5)	824 (82.8)	845 (78.2)	718 (73.1)	767 (75.3)	452 (76.4)
Unknown	1 135	1 170	1 198	1 325	1 238	1 665	2 168	2 317	3 148	2 699
Concurrent STI										
Concurrent chlamydia infection	194 (22.2)	187†† (23.4)	183 (21.8)	170 (20)	153†† (19.0)	203 (23.9)˜	243 (23.6)≈	270†† (22.2)	288Ħ (21.7)	215 (20.0)›
Concurrent other STI (not HIV)	43 (4.9)	49ǂ (6.1)	55 (6.5)	41† (4.8)	48†† (6.0)	53 (6.2)††	67 (6.5)	90†† (7.4)	97 (7.3)	66 (6.1)
No concurrent STI	638 (72.9)	564 (70.6)	603 (71.7)	640 (75.2)	605 (75.1)	593 (69.9)	721 (69.9)	859 (70.7)	941 (71.0)	794 (73.9)
Unknown	1 027	1 127	1 153	1 300	1 328	1 811	2 217	2 084	2 840	2 216
HIV status										
Positive	141 (17.6)	104 (13.5)	144 (17.6)	172 (19.3)	132 (15.3)	156 (15.9)	188 (15.4)	224 (15.7)	179 (14.1)	124 (12.3)
Negative	661 (82.4)	668 (86.5)	675 (82.4)	720 (80.7)	733 (84.7)	823 (84.1)	1 029 (84.6)	1 204 (84.3)	1 088 (85.9)	887 (87.7)
Unknown	1 100	1 155	1 175	1 259	1 269	1 681	2 031	1 871	2 899	2 280
Probable country of infection										
Same as reporting country	700 (95.0)	790 (92.3)	764 (94.1)	552 (94.0)	800 (92.2)	614 (87.0)	795 (88.6)	1 155 (87.6)	1 167 (89.8)	1 089 (94.7)
Different from reporting country	37 (5.0)	66 (7.7)	48 (5.9)	35 (6.0)	68 (7.8)	92 (13.0)	102 (11.4)	163 (12.4)	133 (10.2)	61 (5.3)
Unknown	1 165	1 071	1 182	1 564	1 266	1 954	2 351	1 981	2 866	2 141

Percentages calculated from known values.
Cells shaded in blue indicate a significant difference compared to previous year (p<0.05)
† Includes two individuals with two concurrent STIs
†† Includes four individuals with two concurrent STIs
ǂ Includes six individuals with chlamydia and an additionally diagnosed STI.
Ħ Includes three individuals with chlamydia and an additionally diagnosed STI.
^ Includes one individual of unknown sex, but with mode of transmission reported as MSM.
˜ Includes nine individuals with chlamydia and an additionally diagnosed STI.
** Includes two individuals of unknown sex, but with mode of transmission reported as MSM*
≈ Includes thirteen individuals with chlamydia and an additionally diagnosed STI.
± Includes 1 blood, 3 eye and 4 joint fluid samples – included in other site for analysis due to low numbers
Ħ Includes three individuals with chlamydia and an additionally diagnosed STI.
** Includes one individual with mode of transmission reported as MSM and sex reported as other*
« Includes 11 individuals of unknown sex (three with mode of transmission reported as heterosexual), eight with sex reported as other (two with mode of transmission reported as mother-to-child), and nine males with transmission reported as other.
¤ Includes eight eye and three joint fluid infections.
› Includes two individuals with an additional concurrent STI.

The age of the patients ranged from <1 year to 79 years, with a median of 30 years. Males (median age 31 years) were significantly older than females (median age 25 years) (Mann-Whitney U p<0.01) (Table 2).

Table 2. Patient age distribution by sex and sexual orientation, 2020

Variable	N†	Age (years)		<25 years N (%)
		Range	Median	
All patients	3 272	0-79	30	844 (25.8)
Female	508	3-67	25	241 (47.4)
Male*	2 747	0-79	31	599 (21.8)
Heterosexual male	453	14-71	29	125 (27.6)
MSM	845	16-65	31	153 (18.1)

† Where information was available.
**Including all males, irrespective of sexual orientation.*

3.2 Antimicrobial susceptibility and resistance

Resistance to cefixime, ciprofloxacin and azithromycin (using breakpoints from the EUCAST for cefixime and ciprofloxacin and ECOFF for azithromycin) over time is summarised in Figure 1 and Table 3.

Figure 1. Percentage of resistant *Neisseria gonorrhoeae* by antimicrobial and year, Euro-GASP, 2011–2020

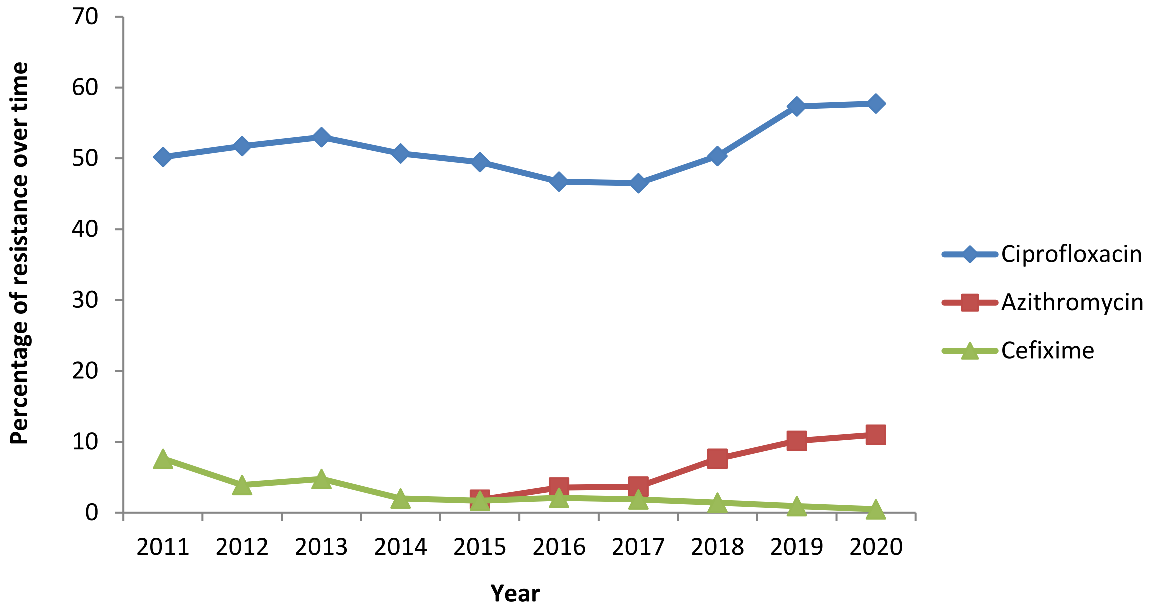


Table 3. Resistance to cefixime, ciprofloxacin and azithromycin (using resistance breakpoints from EUCAST for cefixime and ciprofloxacin and ECOFF for azithromycin) by country, Euro-GASP, 2020

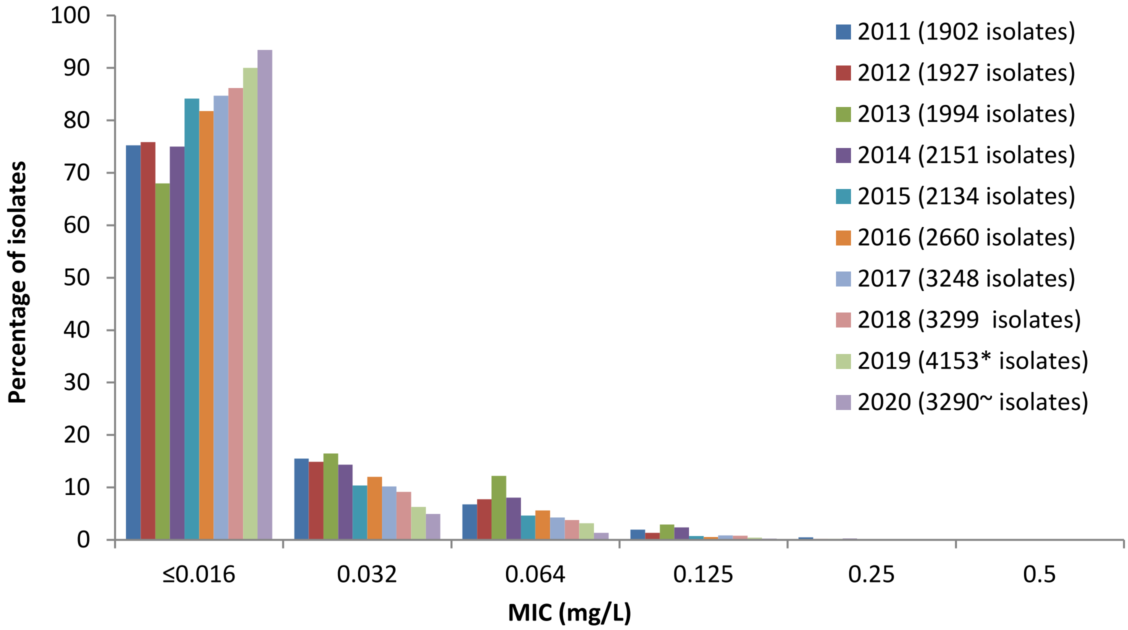
Country	Number of isolates 2020	Number of isolates 2011-2020	Resistance									Method of testing
			Cefixime			Azithromycin			Ciprofloxacin			
			No.	%	% 2011-2020	No.	%	% 2015-2020	No.	%	% 2011-2020	
Austria	245		0	0.0		33	13.5		143	58.4		Decentralised – MGS
Belgium	159		3	1.9		28	17.6		86	54.1		Decentralised – MGS/MIC
Cyprus	2		1	50.0		1	50.0		1	50.0		Decentralised – MGS
Czech Republic	116		0	0.0		6	5.2		31	26.7		Centralised – MGS
Denmark	110		0	0.0		2	1.8		53	48.2		Decentralised – MGS
Estonia	2		0	0.0		0	0.0		2	100.0		Decentralised – MGS
Finland	203		0	0.0		8	3.9		107	52.7		Decentralised – MGS
France	200		0	0.0		19	9.5		119	59.5		Decentralised – MGS
Germany	200		0	0.0		32	16.0		115	57.5		Decentralised – MGS
Greece	100		1	1.0		3	3.0		86	86.0		Decentralised – MGS
Hungary	80		1	1.3		19	23.8		53	66.3		Centralised – MGS
Iceland	42		0	0.0		5	11.9		17	40.5		Decentralised – MGS/MIC
Ireland	104		0	0.0		2	1.9		63	60.6		Decentralised – MGS
Italy	100		0	0.0		4	4.0		67	67.0		Decentralised – MGS
Malta	5		0	0.0		0	0.0		3	60.0		Decentralised – MGS
Netherlands	332		0	0.0		49	14.8		187	56.3		Decentralised – MGS
Norway	450		5	1.1		34	7.6		243	54.0		Decentralised – MGS
Poland	23		0	0.0		8	34.8		11	47.8		Centralised – MGS
Portugal	110		0	0.0		17	15.5		69	62.7		Decentralised – MGS
Slovakia	108		0	0.0		3	2.8		53	49.1		Centralised – MGS
Slovenia	168		0	0.0		24	14.3		143	85.1		Decentralised – MGS
Spain	232		0	0.0		21	9.1		125	53.9		Decentralised – MGS
Sweden	200		5	2.5		44	22.0		123	61.5		Decentralised – MGS
Total:	3291											
Cefixime	3290		16	0.5								
Ciprofloxacin	3291								1900	57.7		
Azithromycin	3291					362	11.0					
95% CI				0.3-0.8			10.0-12.1			56.0-59.4		

MGS: MIC gradient strip test; MIC: MIC by agar dilution. Proportion with MICs above ECOFF displayed from 2015 to 2020 due to earlier use of breakpoint plates.

Only one isolate displayed ceftriaxone resistance in 2020, a decrease on the three isolates observed in 2019 and three in 2018 (and compared to zero in both 2017 and 2016) (Figure 2). The ceftriaxone-resistant (MIC=0.25 mg/L) isolate was detected in Belgium with azithromycin MIC=1 mg/L and ciprofloxacin MIC>32 mg/L. This was a genital isolate from a female patient born in Belgium. The country of infection and the treatment used were unknown. The isolate was also resistant to cefixime.

The MIC distribution for ceftriaxone in 2020 changed significantly compared to 2019, with a further increase in highly susceptible isolates (MIC≤0.016 mg/L) ($p<0.01$), a decrease in isolates with an MIC of 0.032 mg/L ($p=0.01$) and a decrease in isolates with an MIC of 0.064 mg/L ($p<0.01$). The proportion of samples with MICs just below the breakpoint (MIC of 0.125 mg/L) remained constant with that observed in 2019 ($p=0.25$).

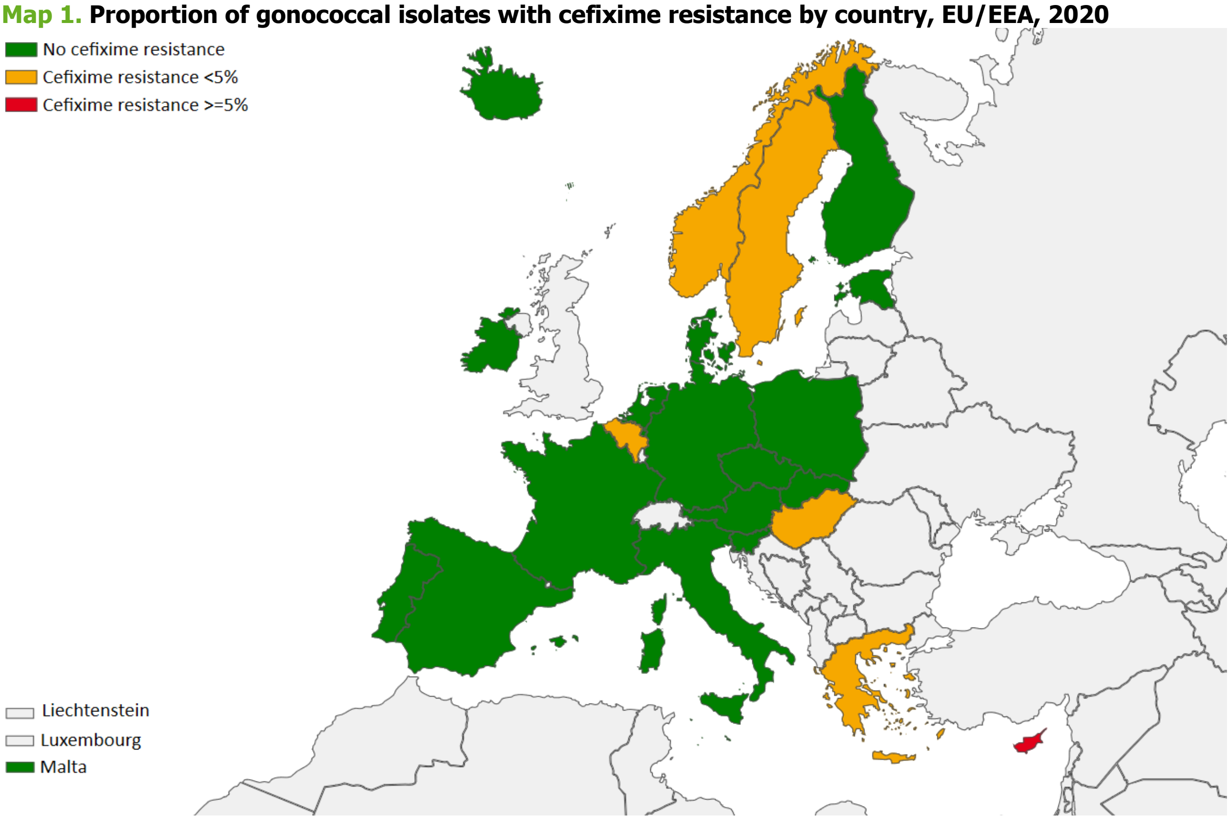
Figure 2. Distribution of MIC for ceftriaxone in Euro-GASP, 2011–2020



** In 2019, 4 166 isolates were tested, 13 isolates had MIC ≤0.125 mg/L. These isolates were excluded from the MIC distribution analysis as they did not fit into one discrete category.*
~ In 2020, 3 291 isolates were tested and one had an MIC <=0.032 mg/L. This isolate was excluded from the MIC distribution analysis as it did not fit into one discrete category.

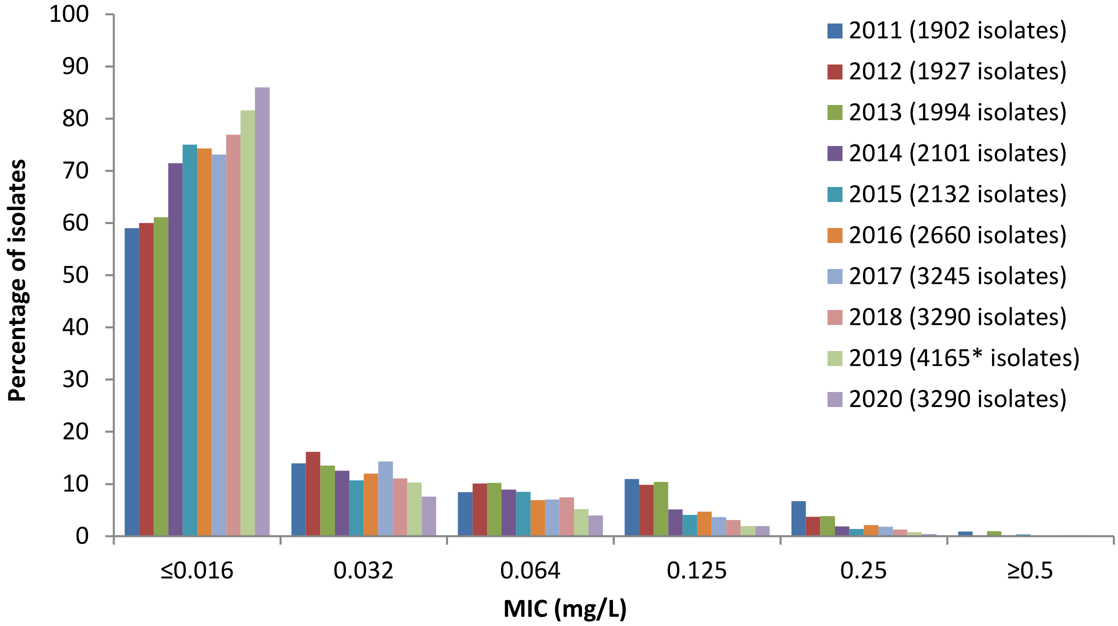
A total of 16 isolates (0.5%) were cefixime-resistant compared to 39 (0.9%) in 2019 (Figures 1 and 3, Table 3) and this represents a significant decrease (p=0.02). There has been a further significant increase in the number of isolates with a cefixime MIC ≤0.016 mg/L (86.0%) on that recorded between 2018 and 2019 (77.0% in 2018, 81.6% in 2019, p<0.01) as well as significant decreases in isolates with MICs in the 0.032–0.064 mg/L range (p=0.01) (Figure 3). Percentages of cefixime-resistant isolates in 2020 by country are shown in Map 1.

Map 1. Proportion of gonococcal isolates with cefixime resistance by country, EU/EEA, 2020



Please note; only two isolates were reported from Cyprus in 2020, percentage resistance should therefore be interpreted with caution.

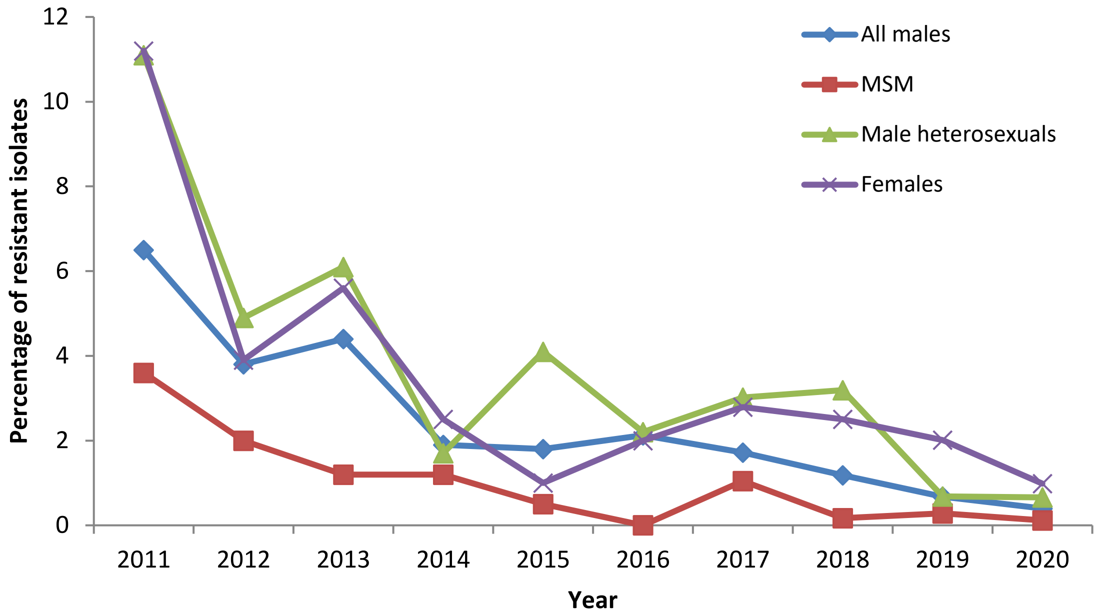
Figure 3. Distribution of MIC for cefixime in Euro-GASP, 2011–2020



** In 2019, 4 166 isolates were tested and one isolate had MIC ≤0.125 MIC. This isolate was excluded from the MIC distribution analysis as it did not fit into one discrete category.*

Cefixime resistance in isolates from both male and female patients was stable (no significant differences) in 2020 compared to 2019 (Figure 4). As in 2019, cefixime resistance was higher in isolates from females than in heterosexual males and MSM, although there were no significant associations identified (Annex 2).

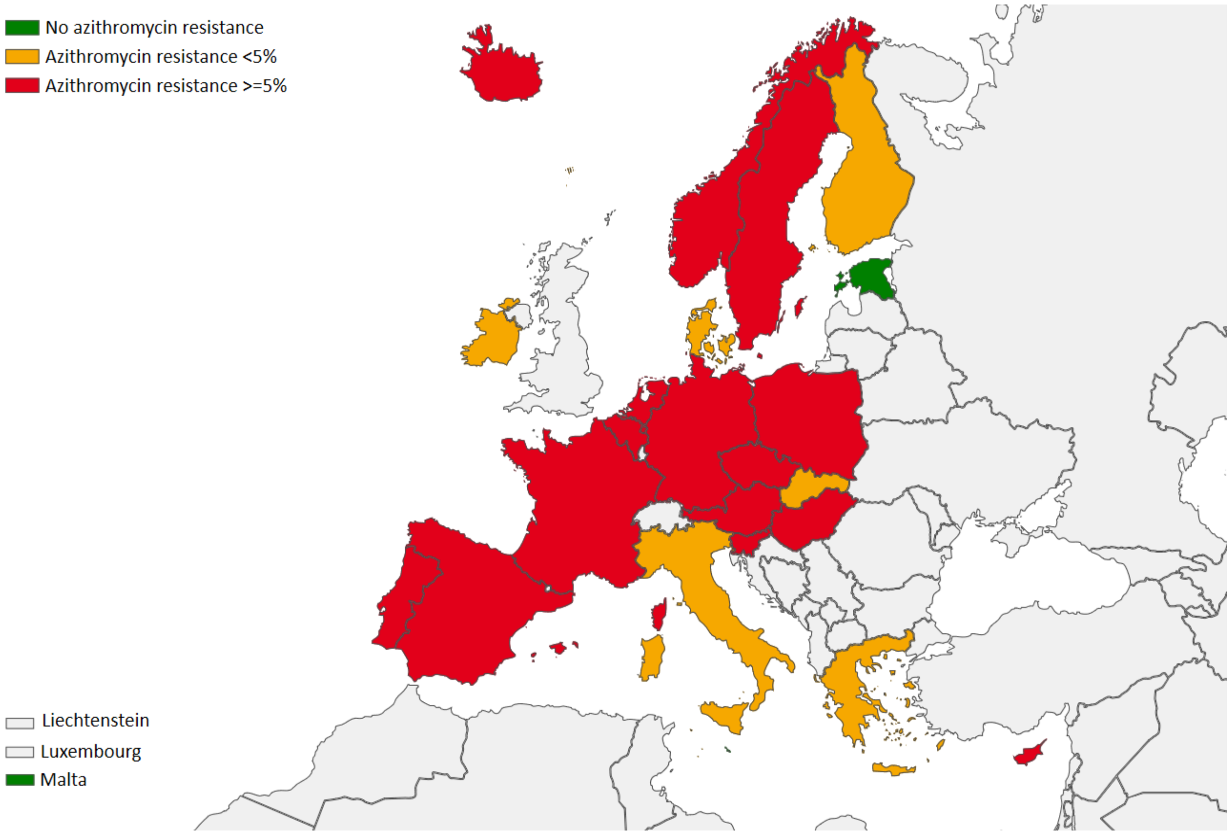
Figure 4. Percentage of isolates with cefixime resistance by sex and male sexual orientation, Euro-GASP, 2011–2020



A total of 362 isolates (11.0%) had an MIC of >1 mg/L (EUCAST ECOFF) to azithromycin which is similar to the level observed in 2019 (421 isolates, 10.1%) (Figure 1; Table 3). Fifteen isolates displayed 'high-level azithromycin resistance' (MICs of ≥256 mg/L) compared to 15 in 2019, five in 2018, eight in 2017 and seven in 2016. These 15 isolates consisted of eight isolates from Norway, three from Sweden, two from Austria, one from France and one from Spain. During the collection period, Norway identified a 'high-level azithromycin resistant' isolate for both 2019 and 2020 consecutively. All 15 isolates were susceptible to all other antimicrobials tested except ciprofloxacin, to which two were resistant (MIC >32 mg/L).

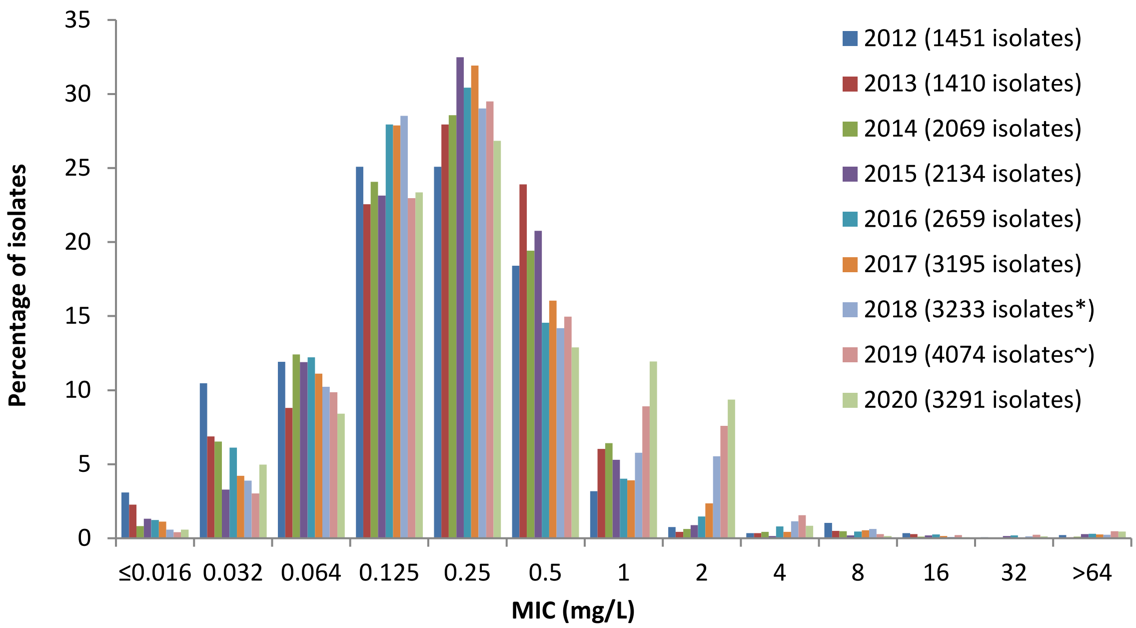
The MIC distribution for azithromycin in 2020 was different to the 2019 distribution, with a significant increase in the number of isolates with an MIC=0.032 mg/L (p<0.01) after the decrease observed in 2019. There was a further increase in isolates with MIC=1 mg/L (p<0.01) and MIC=2 mg/L (p=0.01) on top of the increase observed in 2019. In a change to the distribution in 2019 there was a significant decrease in isolates with MIC=0.064 mg/L (p=0.03), MIC=0.25 mg/L (p=0.01), MIC=0.5 mg/L (p=0.01), and MIC=4 mg/L (p<0.01). Eighty-five percent of isolates above the ECOFF had an MIC of 2 mg/L and the modal MIC continued to be 0.25 mg/L in 2020 (Figure 5). In 2020, as in 2019, the proportion of isolates with an azithromycin MIC above the azithromycin ECOFF (>1 mg/L) was highest in males (11.6%) with a significant increase in MSM (15.0% in 2020, 8.4% in 2019 p<0.01), followed by stable levels of 8.1% in females and 6.2% in heterosexual males (Figure 6). In multivariate analysis, azithromycin MICs above the ECOFF (>1 mg/L) were significantly associated with isolates from MSM patients (OR 2.01, CI 1.39-2.92, p<0.01) compared to females (findings of the univariate analyses in Annex 2).

Map 2. Proportion of gonococcal isolates above azithromycin ECOFF (>1 mg/L) by country, EU/EEA, 2020



Please note; only two isolates were reported from Cyprus in 2020, percentage resistance should therefore be interpreted with caution.

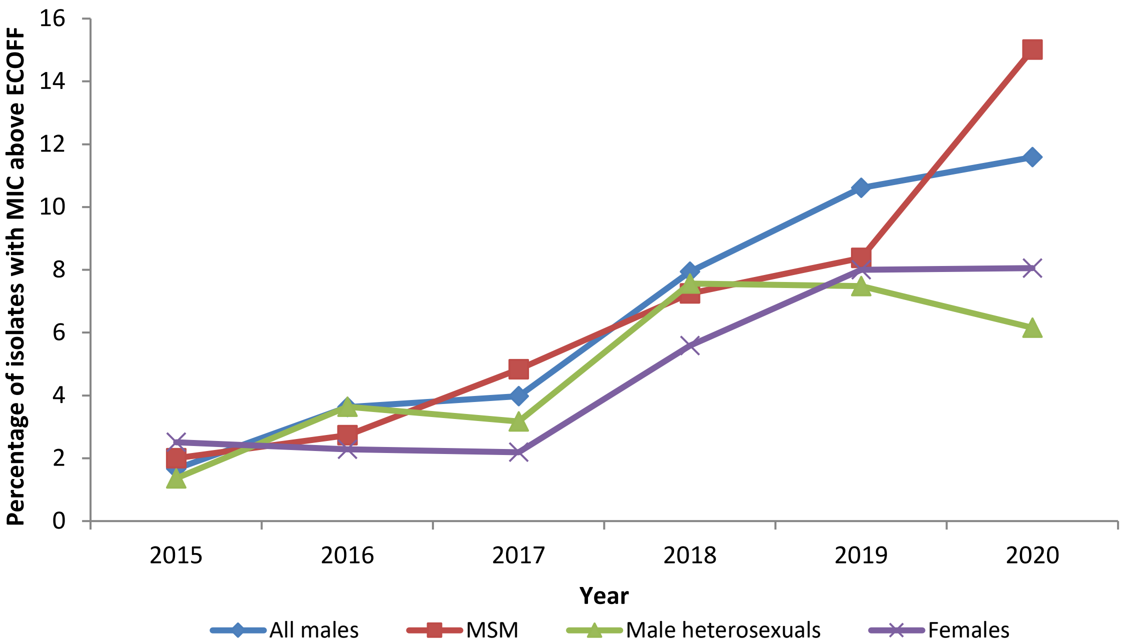
Figure 5. Distribution of MIC for azithromycin in Euro-GASP, 2011–2020



** In 2018, of 3 299 isolates were tested, 66 had an MIC ≤0.06 mg/L. These isolates were excluded from the MIC distribution analysis as they did not fit into one discrete category.*

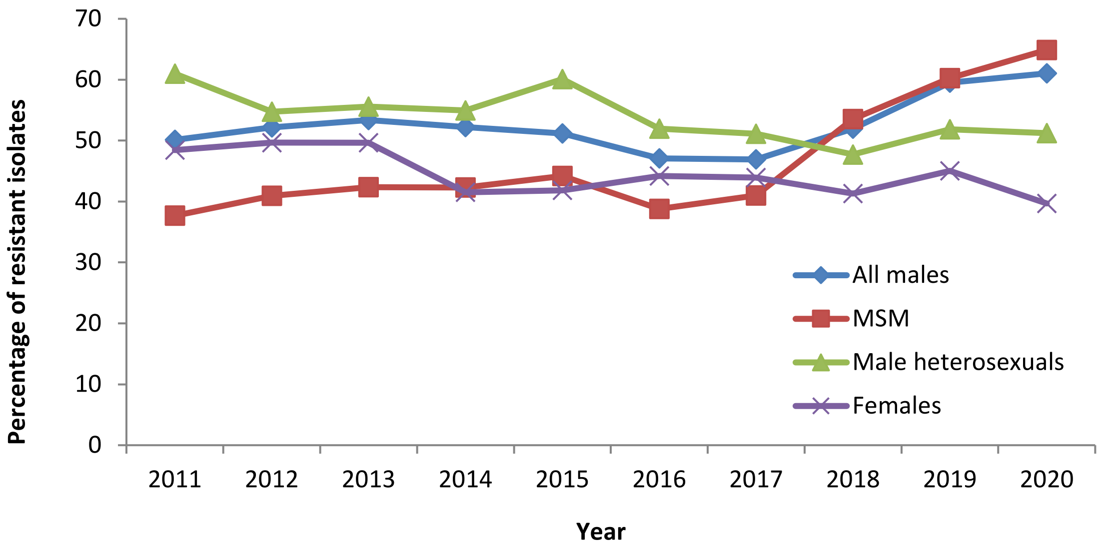
~ In 2019, 4 151 isolates were susceptibility tested with azithromycin and 77 isolates had MIC ≤0.06 mg/L. These isolates were excluded from the MIC distribution analysis as they did not fit into one discrete category.

Figure 6. Percentage of isolates with azithromycin MIC above ECOFF (>1 mg/L) by sex and male sexual orientation, Euro-GASP, 2015–2020



Overall, ciprofloxacin resistance levels in 2020 (57.7%; 1 900/3 291) remained at a constant level after the significant increase observed in 2019 (57.3% in 2019, 50.4% in 2018) (Figure 1). As observed in previous years, resistance was highest among MSM at 64.9%, representing a significant increase on 2019 (60.2%, p=0.04), and lowest in females at 39.7%. In the multivariable analysis, ciprofloxacin resistance remained associated with isolates from MSM (OR 2.53, CI 2.00–3.19, p<0.01) and heterosexual males (OR 1.49, CI 1.15-1.93, P<0.01) compared to females, and with the age group 25 years and over (OR 1.49 CI 1.20-1.85, p<0.01) compared to the under-25 age group (findings of the univariate analyses in Annex 2).

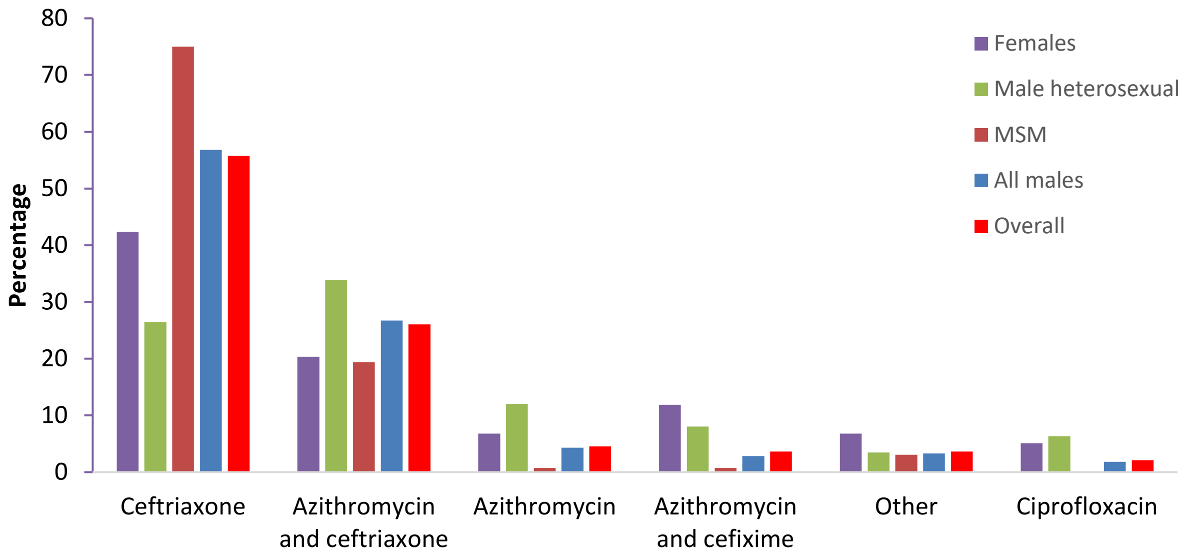
Figure 7. Percentage of isolates with ciprofloxacin resistance by sex and male sexual orientation, Euro-GASP, 2011–2020



3.3 Treatments used

Data on treatment used were recorded for 664 cases from nine different countries, with the majority of data originating from the Netherlands (50%) (data summarised in Figure 8). The most commonly reported treatment for patients overall was ceftriaxone monotherapy (55.7%), with the highest levels among MSM (75%) and the lowest among heterosexual males (26.4%). Among heterosexual males, ceftriaxone and azithromycin dual therapy was the most commonly reported treatment (33.9%) and the second most commonly reported treatment for other patient groups (females 20.3%, MSM 19.4%). A noticeable change on 2019, is the decrease in the use of ceftriaxone and doxycycline dual therapy from 6.5% to 0.6% in 2020 (in 2019 data were available from 1 010 patients from 12 countries, the majority from the Netherlands (36.0%) and the UK (21.2%)). Apart from the loss of ceftriaxone and doxycycline from the most common treatments used in 2020, the overall order of treatments used remained consistent with that recorded in 2019. However, there were significant changes between the two years: a reduction in overall use of ceftriaxone, with or without an additional antimicrobial, from 87.6% in 2019 to 82.5% in 2020 ($p<0.01$) and an increase in overall use of azithromycin with ceftriaxone, with or without an additional antimicrobial, from 21.2% in 2019 to 26.2% in 2020 ($p<0.01$). Data on the completeness of reporting for treatment type is presented by country in Table A1 (Annex 1).

Figure 8. Percentage of known treatments by sex and transmission type for the most frequently used therapies, 2020



Note: Nineteen different combinations of antimicrobials were recorded in 2020, and only treatments with ≥2.5% in any sex/ transmission group are shown (differences in concentration of antimicrobials prescribed have been grouped for analysis). The chart presents data for the 664 patients with a recorded treatment type. Treatment used was reported by nine countries (Table A.1). In total, 78.9% of the data presented was reported by just three countries; the Netherlands (50.0%), the Czech Republic (15.4%) and Greece (13.6%). Slovakia (9.6%), Italy (3.9%), Poland (3.5%), Belgium (3.2%), Malta (0.8%) and Cyprus (0.2%) contributed the remaining 21.1%.

4 Conclusions

Trends in susceptibility for the antimicrobials tested in Euro-GASP were similar to previous years. Encouragingly, in 2020, the proportion of isolates that were highly susceptible to ceftriaxone continued to increase. However, it is of concern that one isolate (0.03%) from Belgium displayed ceftriaxone resistance in 2020. The antibiogram of this isolate does not suggest clonality with the ceftriaxone-resistant isolate identified in Belgium in 2019. In both 2019 and 2018, there were three ceftriaxone-resistant isolates (0.1%) detected, compared to none in 2017 and 2016. The countries in which these isolates were detected in 2019 were different to those in 2018 and none of gonococci, including the isolate identified in 2020, were extensively-drug resistant, as all isolates had an MIC at or below the ECOFF for azithromycin. In 2020, a continuing decreasing trend was observed in levels of cefixime resistance within Euro-GASP: 0.5% compared to 0.9% in 2019, 1.4% in 2018 compared to the previously stable level of 1.7−2.1% in 2014 to 2017. Cefixime-resistant isolates were detected in only six (26.1%) of the 23 countries reporting in 2020, representing a decrease from the 14/26 (53.8%) countries reporting resistant isolates in 2019. Cefixime resistance continued to be lowest among MSM (0.1%), with resistance in both females (1.0%) and all males (0.4%) at a constant level compared with 2019. Genomic surveillance of gonococcal isolates from Euro-GASP showed that susceptibility to ceftriaxone and cefixime is increasing as the lineage associated with decreased susceptibility and resistance to extended-spectrum cephalosporins (NG-MAST G1407) has been progressively disappearing since 2009–10 in EU/EEA countries [17]. Where treatment was reported, 82.5% of patients were administered ceftriaxone with or without an additional antimicrobial, which is a significant decrease on the level observed in 2019 (87.6%, p<0.01). Although some changes in treatments were observed in 2020, this is probably an artefact of the countries reporting treatment used since the number of countries reporting these variables decreased from 12 in 2019 to nine in 2020. In 2019, the Netherlands and the UK data combined contributed 57.2% of the total treatment data. With the exclusion of UK data in 2020 (since the country is no longer part of the EU), the Netherlands (which recommends ceftriaxone monotherapy for treatment of gonorrhoea) contributed 50.0% of the data alone. Data on antimicrobial consumption in EU/EEA countries is collected within the European Surveillance of Antimicrobial Consumption Network (ESAC-Net) and is available as an annual report [18].

It is more difficult to compare data from 2020 on reported treatment used with that for previous years due to the fact that data from the UK, a consistently strong contributor, is no longer included, and also due to the impact of the COVID-19 pandemic. Not only were STI testing services drastically reduced in 2020 due to testing site closures, but testing capacity was also reduced due to the limited number of staff and appointments available and the reduction in referrals [9]. Similarly, limitations on travel and local/national lockdowns restricting transmission pathways had a further impact. The effect of restricted travel can be seen in the significant increase in probable country of infection being the same as the reporting country - from 89.9% in 2019 to 94.7% in 2020.

Despite the differences in datasets between 2019 and 2020, the proportion of isolates above the azithromycin ECOFF (>1 mg/L) remained constant at 11.0% (10.1% in 2019). The reported use of azithromycin monotherapy remained stable at 4.5% in 2020 and 3.1% in 2019. It should be noted that the majority of isolates with an azithromycin >1 mg/L (EUCAST ECOFF) are just above the ECOFF (85.1% had an MIC of 2 mg/L) and 52.1% of isolates previously classified as resistant (>0.5 mg/L) had MICs of 1 mg/L. In 2020, ciprofloxacin resistance remained constant at 57.7% following the significant increase observed between 2018 and 2019 (from 50.4% to 57.3%). Neither azithromycin nor ciprofloxacin are recommended for monotherapy, unless the isolates are first shown to be susceptible. In 2020, six ciprofloxacin-resistant isolates were recorded as being treated with ciprofloxacin monotherapy and one azithromycin-resistant isolate with azithromycin monotherapy. With regard to multidrug- or extensive drug-resistance (MDR and XDR, respectively), in 2020 one isolate was detected with an azithromycin MIC=2 mg/L and both cefixime and ciprofloxacin resistance in a national of Cyprus, with an unknown country of infection. In both 2019 and 2018, one isolate with an azithromycin MIC >16 mg/L and both cefixime and ciprofloxacin resistance were also detected. In 2019, the isolate was detected in a Dutch national with the probable country of infection unknown and in 2018, the isolate came from a Spanish resident with the probable country of infection recorded as Spain. The continued presence of extensively-resistant isolates is of concern, although it is encouraging that numbers have not increased.

In a change from previous years, MSM had the highest levels of resistance to both azithromycin (15.0%) and ciprofloxacin (64.9%), with significant increases observed in both resistance proportions (from 8.4%, p<0.01 and 60.2%, p=0.04 respectively in 2019). This may be linked to fluctuations in MSM case numbers reported from different countries. In 2020, there were no UK or Latvian data included and decreases in data were reported for MSM in 8/23 countries, most notably from Ireland with a decrease of 137 isolates on 2019. Both azithromycin and ciprofloxacin resistance were associated with both MSM and anorectal infection sites by univariate analysis, and with MSM in the multivariate analysis. In contrast, MSM continued to have the lowest incidence of cefixime resistance in 2020 - only 0.1% in MSM compared to 0.7% in heterosexual males and 1% in females.

Given the continued increase of azithromycin MICs above the ECOFF and detection of ceftriaxone resistance, it is important that Member States continue to adhere to the European response plan to control the threat of multidrug-resistant *N. gonorrhoeae* in Europe [7] to enhance the surveillance of gonococcal antimicrobial susceptibility and help identify and report treatment failures to ensure that gonorrhoea remains a treatable infection. Euro-GASP plays a major role in fulfilling the objectives of the response plan, set out below.

- Strengthening surveillance of gonococcal antimicrobial susceptibility in the EU/EEA countries by providing sufficient epidemiological information to inform national treatment guidelines and public health interventions. In 2020, the overall completeness of variables (56.0%) remained at a level similar to 2019 (56.4%). Significant improvements in reporting are urgently required for many variables if statistical analysis of the linked antimicrobial susceptibility and patient data is to be robust.
- Ensuring that appropriate capacity for culture and antimicrobial susceptibility testing in EU/EEA Member States is available or further developed. Training in STI diagnostics and antimicrobial susceptibility testing is provided and experts (or relevant staff) are encouraged to participate, and eventually move towards decentralised testing. Unfortunately, the AMR training scheduled for 2020 had to be postponed due to the COVID-19 pandemic.
- Effectively disseminating results from AMR surveillance in order to increase awareness and inform authorities, professional societies, clinicians, healthcare workers and others exposed to the threat of multidrug-resistant (MDR) and extensively drug-resistant (XDR) *N. gonorrhoeae*. The Euro-GASP AMR surveillance data is freely accessible online via ECDC's Atlas [19], which is updated annually prior to the publication of the annual surveillance data report. Data from the project is frequently published in peer-reviewed journals and presented at international conferences.
- Introducing strategies to reduce the burden of gonorrhoea, such as implementation of appropriate gonorrhoea management, prevention, control and AMR policies/guidelines, including enhanced focus on high-risk groups, as well as mandatory reporting of gonorrhoea. The use of recommended therapies to treat gonorrhoea is advocated by the Euro-GASP project and it was encouraging to see the continued use of the highly-effective ceftriaxone, with or without azithromycin. Nevertheless, it is of major concern that some patients continue to be inappropriately treated (e.g. with ciprofloxacin), particularly those who harbour ciprofloxacin-resistant strains (of fourteen patients treated with ciprofloxacin, six carried a ciprofloxacin-resistant strain in 2020).

Even though Euro-GASP detected a continued decreasing trend in levels of cefixime resistance in 2020, the persistent rise in ciprofloxacin resistance and continuously high azithromycin MICs, along with the detection of one ceftriaxone-resistant isolate are all cause for concern. Ceftriaxone treatment failures have been documented [20,21], along with sustained transmission of high-level azithromycin-resistant (HLAziR, MIC >256 mg/L) strains [20], and gonococcal strains with resistance to ceftriaxone have been detected internationally [17,20-27]. Therefore, continuous implementation of quality-assured antimicrobial surveillance activities and adherence to the recently updated and refined response plan is essential. In addition, the development of alternative therapy regimens is urgently needed to ensure gonorrhoea remains a treatable infection.

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Annex 1. Percentage completeness of epidemiological variables

Table A1. Completeness of epidemiological variable reporting, 2020

Country	Number of isolates	Sex	Age	Mode of transmission	Site of infection	Diagnostic test	Treatment	Previous gonorrhoea	Concurrent STI	Place of residence	Clinical service type	Country of birth	Probable country of infection	HIV status	Overall Percentage response rate
Austria	245	99.6	99.6	0.0	95.5	100.0	0.0	6.9	4.9	58.4	93.9	0.0	0.0	4.1	**43.3**
Belgium	159	100.0	99.4	38.4	99.4	100.0	13.2	37.1	38.4	100.0	22.6	57.2	20.8	35.8	**58.6**
Cyprus	2	100.0	50.0	0.0	100.0	100.0	50.0	0.0	0.0	100.0	50.0	50.0	0.0	0.0	**46.2**
Czech Republic	116	100.0	100.0	87.9	89.7	100.0	87.9	87.1	79.3	100.0	100.0	87.9	100.0	85.3	**92.7**
Denmark	110	98.2	100.0	83.6	94.5	100.0	0.0	0.0	0.0	89.1	100.0	88.2	82.7	63.6	**69.2**
Estonia	2	100.0	100.0	100.0	100.0	100.0	0.0	100.0	100.0	100.0	100.0	0.0	50.0	0.0	**73.1**
Finland	203	100.0	100.0	89.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	96.6	83.7	0.0	**36.1**
France	200	100.0	100.0	48.5	99.0	100.0	0.0	0.0	84.5	90.5	98.5	52.0	56.5	67.0	**69.0**
Germany	200	97.5	99.0	0.0	97.5	100.0	0.0	0.0	0.0	100.0	77.0	0.0	0.0	0.0	**43.9**
Greece	100	100.0	90.0	84.0	99.0	100.0	90.0	67.0	7.0	73.0	100.0	87.0	86.0	2.0	**75.8**
Hungary	80	100.0	100.0	0.0	98.8	100.0	0.0	0.0	0.0	0.0	100.0	0.0	0.0	0.0	**38.4**
Iceland	42	100.0	100.0	57.1	100.0	100.0	0.0	92.9	100.0	92.9	100.0	92.9	0.0	2.4	**72.2**
Ireland	104	100.0	100.0	11.5	99.0	6.7	0.0	25.0	94.2	94.2	100.0	16.3	0.0	56.7	**54.1**
Italy	100	99.0	99.0	33.0	100.0	100.0	26.0	32.0	27.0	42.0	100.0	41.0	27.0	26.0	**57.8**
Malta	5	100.0	100.0	100.0	100.0	100.0	100.0	100.0	80.0	100.0	100.0	100.0	100.0	80.0	**96.9**
Netherlands	332	100.0	100.0	98.5	100.0	100.0	100.0	0.0	100.0	99.4	100.0	99.7	0.0	96.4	**84.2**
Norway	450	100.0	100.0	0.0	97.6	100.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	**30.6**
Poland	23	100.0	100.0	34.8	100.0	100.0	100.0	0.0	0.0	0.0	100.0	0.0	0.0	0.0	**48.8**
Portugal	110	100.0	100.0	11.8	100.0	100.0	0.0	0.0	0.0	100.0	34.5	5.5	0.0	0.0	**42.4**
Slovakia	108	100.0	98.1	68.5	100.0	0.0	59.3	100.0	85.2	100.0	100.0	97.2	71.3	81.5	**81.6**
Slovenia	168	100.0	100.0	35.1	100.0	100.0	0.0	81.0	81.0	99.4	96.4	82.1	0.0	82.1	**73.6**
Spain	232	100.0	99.6	87.5	100.0	100.0	0.0	0.0	0.4	100.0	100.0	0.0	100.0	1.3	**60.7**
Sweden	200	99.0	100.0	99.5	100.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	99.5	0.0	**38.3**
Grand total	**3 291**	**99.7**	**99.4**	**47.9**	**92.3**	**81.5**	**20.2**	**18.0**	**32.7**	**64.0**	**66.0**	**41.3**	**34.9**	**30.7**	**56.0**

Annex 2. Statistical tables

Table A2. Univariate association of cefixime resistance/susceptibility and patient characteristics, Euro-GASP, 2020

	Cefixime resistance N (%, 95% CI)	Odds ratio	95% CI	P value
Site of infection (n=3036)				
Genital (2174)	13 (0.6, 0.3-1.0)			0.38*
Anorectal (608)	2 (0.3, 0.1-1.1)			
Pharyngeal (182)	0 (0.0, 0.0-2.1)			
Other (72)	1 (1.4, 0.2-7.5)			
Sex and sexual orientation (n=1810)				
MSM (847)	1 (0.1, 0.0-0.7)			0.05*
Heterosexual male (455)	3 (0.7, 0.2-1.9)			
Female (508)	5 (1.0, 0.4-2.3)			
Previous GC (n=591)				
Yes (140)	0 (0.0, 0.0-2.7)			1.00*
No (451)	2 (0.4, 0.1-1.6)			
Concurrent chlamydia (n=1074)				
Yes (215)	0 (0.0, 0.0-1.8)			#
No (859)	0 (0.0, 0.0-0.4)			
HIV status (n=1011)				
Positive (124)	0 (0.0, 0.0-3.0)			#
Negative (887)	0 (0.0, 0.0-0.4)			
Age (n=3271)				
<25 years (844)	5 (0.6, 0.3-1.4)	1		0.50
≥25 years (2427)	10 (0.4, 0.2-0.8)	0.69	2.04	

*Note: *Expected value for one cell < 5, so Fisher's Exact test performed.*

 # Not possible to test as both variables are zero.

Table A3. Univariate association of azithromycin MICs above/below ECOFF (>1 mg/L) and patient characteristics, Euro-GASP, 2020

	Azithromycin resistance N (%, 95% CI)	Odds ratio	95% CI	P value
Site of infection (n=3037)				
Genital (2175)	238 (10.9, 9.7-12.3)	1		
Anorectal (608)	89 (14.6, 12.1-17.7)	1.4	1.07-1.81	**0.01**
Pharyngeal (182)	17 (9.3, 5.9-14.4)	0.84	0.50-1.41	0.50
Other (72)	8 (11.1, 5.7-20.4)	1.02	0.48-2.15	0.96
Sex and sexual orientation (n=1811)				
MSM (847)	127 (15.0, 12.7-17.6)	2.01	1.39-2.92	**<0.01**
Heterosexual male (455)	28 (6.2, 4.3-8.8)	0.75	0.45-1.23	0.25
Female (509)	41 (8.1, 6.0-10.7)	1		
Previous GC (n=592)				
Yes (140)	12 (8.6, 4.7-9.3)	1.32	0.66-2.65	0.44
No (452)	30 (6.6, 5.0-14.4)	1		
Concurrent chlamydia (n=1075)				
Yes (215)	18 (8.4, 5.4-12.8)	0.74	0.44-1.26	0.27
No (860)	94 (10.9, 9.0-13.2)	1		
HIV status (n=1011)				
Positive (124)	13 (10.5, 6.2-17.1)	1.06	0.57-1.97	0.84
Negative (887)	88 (9.9, 8.1-12.1)	1		
Age (n=3272)				
<25 years (844)	82 (9.7, 7.9-11.9)	1		
≥25 years (2428)	278 (11.5, 10.2-12.8)	1.2	0.93-1.56	0.17

Table A4. **Univariate association of ciprofloxacin resistance/susceptibility and patient characteristics, Euro-GASP, 2020**

	Ciprofloxacin resistance N (%, 95% CI)	Odds ratio	95% CI	P value
Site of infection (n=3037)				
Genital (2175)	1 233 (56.7, 54.6-58.8)	1		
Anorectal (608)	390 (64.1, 60.3-67.9)	1.37	1.13-1.65	**<0.01**
Pharyngeal (182)	102 (56.0, 48.8-63.1)	0.97	0.72-1.32	0.87
Other (72)	42 (58.1, 46.8-69.0)	1.07	0.66-1.72	0.78
Sex and sexual orientation (n=1811)				
MSM (847)	550 (64.9, 61.7-68.1)	2.8	2.23-3.56	**<0.01**
Heterosexual male (455)	233 (51.2, 46.6-55.8)	1.6	1.23-2.06	**<0.01**
Female (509)	202 (39.7, 35.5-44.0)	1		
Previous GC (n=592)				
Yes (140)	93 (66.4, 58.3-73.7)	1.3	0.87-1.93	0.20
No (452)	273 (60.4, 55.8-64.8)	1		
Concurrent chlamydia (n=1075)				
Yes (215)	102 (47.4, 40.9-54.1)	1		
No (860)	520 (60.5, 57.2-63.7)	1.69	1.25-2.29	**<0.01**
HIV status (n=1011)				
Positive (124)	81 (65.3, 56.6-73.1)	1.4	0.96-2.11	0.08
Negative (887)	505 (56.9, 53.7-60.2)	1		
Age (n=3272)				
<25 years (844)	402 (47.6, 44.3-51.0)	1		
≥25 years (2428)	1 482 (61.0, 59.1-63.0)	1.7	1.47-2.02	**<0.01**

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