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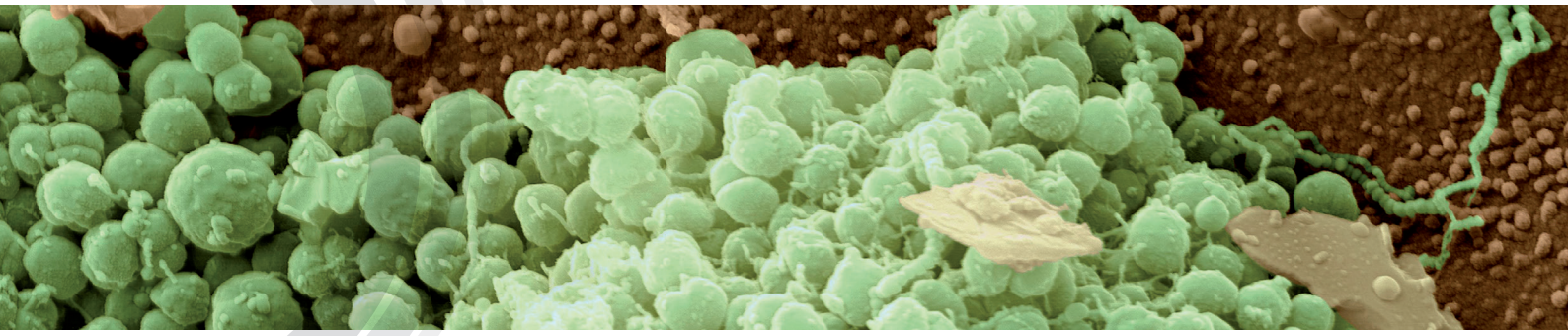

Gonococcal antimicrobial susceptibility surveillance in Europe

2016

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Abbreviations

AMR	Antimicrobial resistance
CI	Confidence interval
CT	*Chlamydia trachomatis*
DV	Dermatology-venereology
EEA	European Economic Area
EQA	External quality assessment
ESCs	Extended-spectrum cephalosporins
ESSTI	European Surveillance of Sexually Transmitted Infections project
EU	European Union
Euro-GASP	European Gonococcal Antimicrobial Surveillance Programme
GC	Gonococcal
GONOAMR	Gonococcal antimicrobial resistance
GP	General practitioner
GRASP	Gonococcal Resistance to Antimicrobials Surveillance Programme
GUM	Genitourinary medicine
HIV	Human immunodeficiency virus
IQC	Internal quality control
MIC	Minimum inhibitory concentration
MSM	Men who have sex with men
NAAT	Nucleic acid amplification test
NG-MAST	*Neisseria gonorrhoeae* multi-antigen sequence typing
OR	Odds ratio
PHE	Public Health England
PPNG	Penicillinase-producing *Neisseria gonorrhoeae*
QC	Quality control
STI	Sexually transmitted infection
TESSy	The European Surveillance System at ECDC
WHO	World Health Organization

Executive summary

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

In 2016, 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 (Etest or agar dilution) for the following antimicrobials: cefixime, ceftriaxone, ciprofloxacin, gentamicin, spectinomycin and azithromycin, as well as testing for β-lactamase production (nitrocefin test) for detection of high-level penicillin resistance. Decentralised testing took place on the premises of participating laboratories fulfilling set quality criteria.

In 2016, 25 EU/EEA Member States participated in Euro-GASP, 17 via decentralised testing. A total of 2660 isolates were collected and tested, covering 4% of the gonorrhoea cases captured by routine surveillance. The majority of gonococcal isolates (85.1%) were collected from male patients. The age of the patients ranged from under one year to 93 years, with a median age of 30 years. Overall, 27.5% of patients were under 25 years, and males were significantly older than women. The anatomical site of specimen collection was mainly genital (75.5%), followed by rectal (14.2%) and pharyngeal (6.4%). Among cases with information on previous diagnosis of gonorrhoea, 17.2% had previously been diagnosed with the disease. Twenty-four percent of the patients were concurrently diagnosed with *Chlamydia trachomatis* infection. Among cases with known sexual orientation and gender, 59.6% were heterosexual men or women, and 40.4% were men who have sex with men (MSM). Among all cases, 15.9% were HIV-positive and 94.9% of those were MSM.

The 2016 antimicrobial susceptibility data revealed stable cefixime and azithromycin resistance (2.1% and 7.5%, respectively) compared with 2015 (1.7% and 7.1%) although there were more countries reporting resistant isolates for both antimicrobials in 2016 compared with 2015. Specifically, there were 14 countries with cefixime resistant isolates in 2016 (2015: 9), and 21 countries with azithromycin resistant isolates in 2016 (2015: 18). A slightly lower proportion of tested isolates showed ciprofloxacin resistance: 46.5% compared with 49.4% in 2015. No isolates with resistance to ceftriaxone were detected compared with one in 2015, five in 2014 and seven in 2013, however the MIC distribution for ceftriaxone in 2016, compared with 2015, showed a slightly lower proportion of more susceptible gonococcal isolates (MIC≤0.016 mg/L) along with an increased proportion of isolates with higher MICs (from 0.032 mg/L to 0.125 mg/L).

The absence of ceftriaxone resistance is encouraging and most probably in part due to the current highly effective dual-therapy regimen (ceftriaxone plus azithromycin). However, the level of resistance to azithromycin (7.5%) is a concern and threatens the effectiveness of this regimen. Even though the rise in cefixime resistance was not significant, the situation needs to be followed closely, particularly due to the recent spread of cefixime resistance across Europe. Novel antimicrobials and/or new dual antimicrobial therapy regimens and continuing surveillance are essential to ensure that gonorrhoea remains treatable.

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 therapeutic agents currently recommended in Europe [1], extended-spectrum cephalosporins (ESCs), are the last remaining options for effective empiric first-line antimicrobial monotherapy. Susceptibility to these antimicrobials has decreased in the past [2], which is why the current European treatment guidelines recommend combination treatment with ESCs plus azithromycin in an attempt to mitigate the development and/or spread of resistance to these antimicrobials [1]. Surveillance of the susceptibility to these agents is therefore essential in order to ensure effective patient management and monitor current and emerging trends in AMR [3].

In 2009, the European Centre for Disease Prevention and Control (ECDC) took over the coordination of the European Gonococcal Antimicrobial Surveillance Programme (Euro-GASP), supported by an international network led by Public Health England (United Kingdom) and Örebro University Hospital (Sweden).

Over the years, Euro-GASP has identified decreasing susceptibility to ESCs and treatment failures were documented [3], eventually prompting the creation of a European response plan to control and manage the threat of multidrug-resistant *N. gonorrhoeae* in Europe [4].

In 2015, Euro-GASP ran sentinel surveillance programmes in 24 EU/EEA countries. Major findings can be summarised as follows [5,6]:

- Cefixime resistance was observed in 1.7% of tested isolates. This is a 0.3% decrease compared with 2014, continuing the decreasing trend that began in 2010 and was interrupted only once in 2013 by a slight increase.
- Euro-GASP 2015 detected one isolate resistant to ceftriaxone, compared with five in 2014.
- The overall rate of ciprofloxacin resistance in 2015 (49.4%) was similar to the rate in 2014 (50.7%) and remained very high.
- Azithromycin resistance decreased slightly from 7.9% in 2014 to 7.1% in 2015.

1.2 Objectives

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

- Develop and implement sentinel surveillance of gonococcal susceptibility to a range of therapeutically relevant antimicrobials.
- Improve the timeliness of surveillance to allow more frequent monitoring of developments in gonococcal antimicrobial susceptibility across Europe.
- Link susceptibility data with epidemiological information to better understand the risk factors associated with emerging resistance patterns.
- Implement an EQA scheme for antimicrobial susceptibility testing across Europe.
- Provide training in gonococcal culture and antimicrobial susceptibility testing to facilitate enhanced gonococcal antimicrobial susceptibility surveillance, using a standardised methodology across Europe.

This report presents the results from the 2016 gonococcal antimicrobial susceptibility sentinel surveillance.

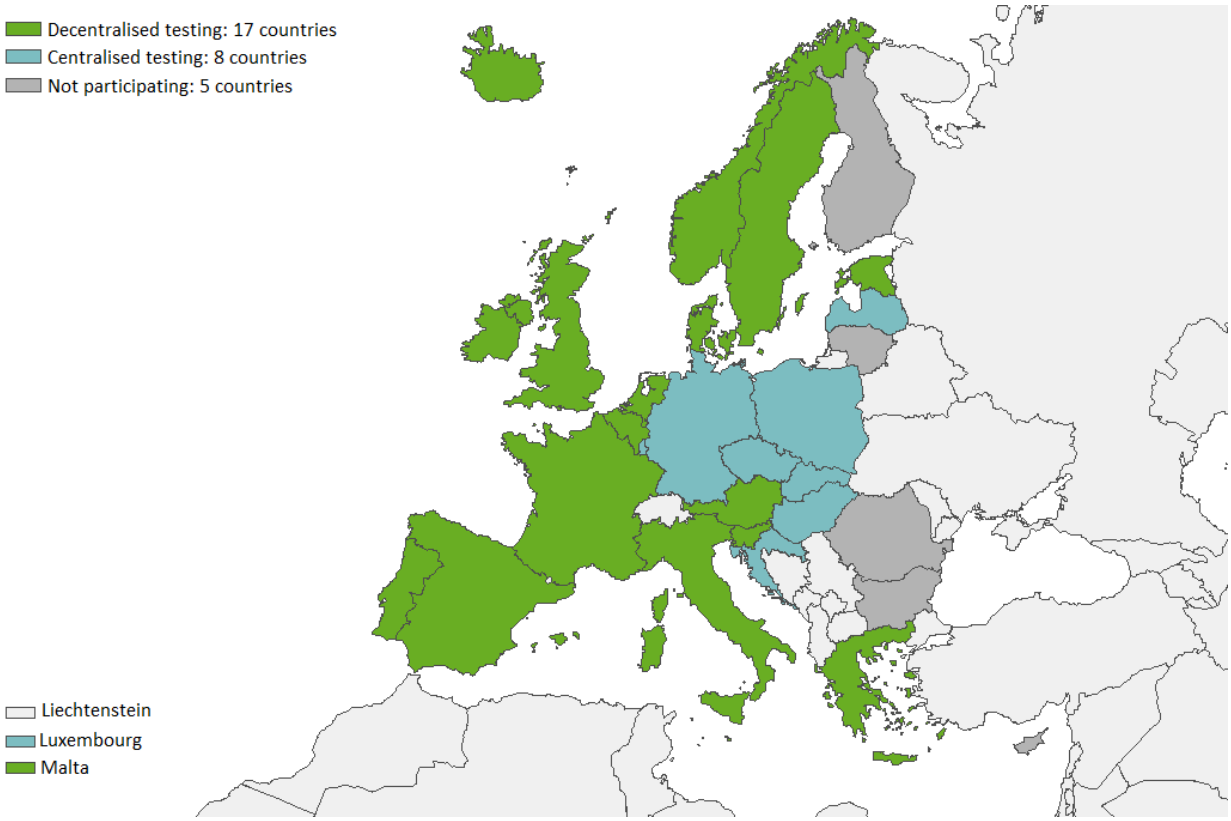
2 Methods

Participating laboratories were requested to collect gonococcal isolates between September and November 2016. The centralised and decentralised testing model continued to be used: for decentralised testing, participating laboratories fulfilling set quality criteria performed their own susceptibility testing; all other participating countries followed the centralised testing model, where susceptibility testing was performed at Public Health England (London) or at Örebro University Hospital (Örebro) using the same methodology (see Section 2.4 on antimicrobial susceptibility testing). Countries were asked to upload their results to The European Surveillance System (TESSy). Full details on the framework for Euro-GASP and the criteria for decentralised testing can be found in Annex 1.

2.1 Participating laboratories

In 2016, nominated contact points for STI surveillance from 25 EU/EEA countries participated in Euro-GASP (Map 1), one more country than in 2015; two new countries joined (the Czech Republic and Luxembourg). Cyprus did not participate in 2016.

Map 1. EU/EEA Member States participating in Euro-GASP, 2016



2.2 National protocol

Each country submitting gonococcal isolates or susceptibility data was requested to provide additional information on the implementation of Euro-GASP at the national level (Annex 2). This information is critical for interpreting data and ensuring accurate linkage of laboratory and epidemiological data.

2.3 Isolate collection

Each country was asked to contribute 100 isolates per year (110 from countries which followed the centralised-testing model, with the aim of retrieving and testing 100 isolates). Countries where 100 isolates represent substantially less than 10% of the total number of reported gonorrhoea cases (the Netherlands, Spain and the United Kingdom) were requested to collect 200 isolates. The aim was to collect all isolates between September and November. Countries with a low number of collected isolates were allowed to include isolates collected throughout the year. In the United Kingdom, the collection of samples for England and Wales took place between July and September to coincide with the collection period for the national Gonococcal Resistance to Antimicrobials Surveillance Programme (GRASP).

When multiple anatomical sites were infected in one patient, laboratories were requested to only collect one isolate in the following order of preference:

- Males: pharyngeal, rectal, urethral, other
- Females: pharyngeal, cervical, other anogenital (high vaginal swab/rectal/urethral), other.

For centralised testing, pure cultures (18–24 hours old) were saved on Microbank beads and stored at -70°C or below. The isolates were then sent frozen on dry ice to Public Health England, London, or Örebro University Hospital, Örebro, for susceptibility testing.

2.4 Antimicrobial susceptibility testing

Centralised susceptibility testing

Centralised susceptibility testing was performed using either an agar dilution breakpoint technique that allows for isolates to be categorised as susceptible or resistant (including intermediate resistance, where applicable), or gradient strips to determine the MIC and monitor drift in susceptibility. The results were interpreted using the Euro-GASP (EUCAST) standard breakpoints (Annex 3).

The antimicrobials that were tested included those currently recommended for treatment (ceftriaxone and azithromycin, and cefixime, which is recommended when ceftriaxone is not available or an injection is refused) and those previously used for treatment (ciprofloxacin and penicillin G, enzyme-mediated high-level resistance only). Gentamicin and spectinomycin were removed from the routine antimicrobial panel in 2014 as these antimicrobials are either not in routine use or are difficult to acquire and are only tested in snapshot studies every three years. The first snapshot study was performed in 2016, and results are included in this report.

The following methods were used to determine susceptibility:

- Breakpoint (ciprofloxacin and spectinomycin)
- Agar dilution (gentamicin)
- Gradient strips (azithromycin, cefixime, ceftriaxone, gentamicin, ciprofloxacin and spectinomycin)
- Penicillinase production by nitrocefin.

Further details on the testing methodology and breakpoints can be found in Annex 3.

Decentralised susceptibility testing

Laboratories participating in decentralised testing performed susceptibility testing in their own laboratories (Annex 1); results were interpreted using EUCAST breakpoints (Annex 3). In 2016, Estonia, France and the Netherlands did not test for penicillinase production, while Iceland tested one of their 35 isolates for penicillinase production. Malta, the Netherlands, Ireland, Greece, Norway, France, the UK, Iceland and Austria did not test for gentamicin susceptibility. Estonia, Iceland, Ireland, France and the Netherlands did not test for susceptibility to spectinomycin.

2.5 Data collection and analysis

The following data were collected for each isolate, where available: date specimen obtained, specimen site, gender, age, sexual orientation, previous gonorrhoea diagnosis, other STI diagnosed during the current episode, place of residence, clinical service type, HIV status, probable country of infection, diagnostic test and treatment used. The full variable list and variable codes are described in Annex 4.

To aid the clinical service type analysis, the 14 coded variables were merged into six groups (Table 1).

Data generated by centralised testing were sent to the national contacts, complemented with available epidemiological data, uploaded to TESSy by each Member State, and then approved. Data from centres performing decentralised testing were uploaded to TESSy in the same manner. Percentages shown are for known data.

Where available, graphs display data between 2007 and 2016 for ceftriaxone, and 2009 to 2016 for all other graphs other than for the azithromycin MIC distribution graph, where data from 2011 to 2016 are displayed due to the high proportion of breakpoint plates (i.e. no MIC data available) prior to 2011. Note that no data collection was organised in 2005.

Table 1. Description of clinical service type coding and subsequent grouping

Grouping	Coded value	Description
Antenatal care clinic	ANC	ANC
Outpatient clinic	ED	Hospital emergency department
Outpatient clinic	GYN	Gynaecology clinic
Outpatient clinic	ID	Infectious disease clinic
Outpatient clinic	URO	Urology
Other	O	Other
Primary care	GP	General practitioner
Primary care	OPC	Other primary care
STI and sexual health clinics	COMB	Combined service
STI and sexual health clinics	DV	Dermatology-venereology clinic
STI and sexual health clinics	FPC	Family planning clinic
STI and sexual health clinics	STI	Dedicated STI clinic
STI and sexual health clinics	YTH	Youth clinics
Unknown	UNK	Unknown

2.6 Statistical analysis

Statistical analysis was performed using Stata v13.1. The Z-test was used to determine the difference between epidemiological and AMR data collected in 2016 versus 2015, and a Mann-Whitney 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 the Pearson's $\chi 2$ 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

3.1 Completeness of data

Overall, reporting completeness was comparable to previous years for the majority of variables in 2016 (Table 2). Completeness of data remained high for 'gender', 'age' and 'site of infection' (over 96%) and improved for 'diagnostic test', 'treatment' and 'clinical service type'. There were slight decreases in reporting for 'mode of transmission', 'previous gonorrhoea', 'HIV status', and 'concurrent STI', with larger decreases for 'country of birth' and 'probable country of infection'.

Table 2. Completeness of reporting, Euro-GASP, 2016

Variables	2010 (n=1766)		2011 (n=1902)		2012 (n=1927)		2013 (n=1994)		2014 (n=2151)		2015 (n=2134)		2016 (n=2660)	
	No	%	No	%	No	%	No	%	No	%	No	%	No	%
Gender	1749	99.0	1826	96.0	1906	98.9	1978	99.2	2140	99.5	2121	99.4	2651	99.7
Age	1740	98.5	1793	94.3	1878	97.5	1953	97.9	2106	97.9	2093	98.1	2622	98.6
Mode of transmission	1001	56.7	1061	55.8	987	51.2	1044	52.4	1260	58.6	1301	61.0	1552	58.3
Site of infection	1683	95.3	1785	93.8	1852	96.1	1938	97.2	2030	94.4	2080	97.5	2574	96.8
Diagnostic test	NI	NI	NI	NI	NI	NI	NI	NI	1455	67.6	1644	77.0	2125	79.9
Treatment	NI	NI	NI	NI	NI	NI	NI	NI	400	18.6	779	36.5	991	37.3
Previous gonorrhoea	691	39.1	767	40.3	757	39.3	796	39.9	826	38.4	896	42.0	995	37.4
Concurrent STI	779	44.1	875	46.0	800	41.5	841	42.2	851	39.6	806	37.8	849	31.9
Place of residence*	720	83.1	1437	75.6	1541	80.0	1436	72.0	1596	74.2	1579	74.0	1835	69.0
Clinical service type*	610	70.4	1544	81.2	1476	76.6	1535	77.0	1619	75.3	1708	80.0	2148	80.8
Country of birth*	392	45.3	861	45.3	988	51.3	1029	51.6	879	40.9	1132	53.0	1244	46.8
Probable country of infection*	263	30.4	737	38.7	856	44.4	812	40.7	588	27.3	878	41.1	723	27.2
HIV status*	310	35.8	802	42.2	772	40.1	819	41.1	892	41.5	865	40.5	979	36.8

** Inclusion from the 2010 second collection period only; NI – not included*

3.2 Isolate and patient data

Information on the source of the data, as described by the 'Protocol implementing Euro-GASP at the national level' (Annex 2), and/or the data source variable in TESSy is set out in Table 3.

Table 3. Characteristics of national protocols for implementing Euro-GASP, 2016

Country	Coverage	Specimen source	Comprehensiveness	Sampling method
Austria	Mainly capital area and some national	GPs, gynaecologists, urologists and sex worker monitoring	Other	Consecutively
Belgium	National	GPs, hospitals, STI clinics, gynaecologists	Comprehensive	Consecutively
Croatia	National	STI clinics, DV clinics, GPs, hospitals	Sentinel	Consecutively
Czech Republic	Regional	DV clinic	Sentinel	Consecutively
Denmark	National	STI clinics, DV clinics, GPs, hospitals	Comprehensive	Consecutively
Estonia	National	All	Other	Consecutively
France	National	GPs, STI clinics and hospitals	Sentinel	Consecutively
Germany	National	Medical practices, out-patients, hospital laboratories, public health departments and STI ambulances.	Other	Consecutively
Greece	National	STI clinics and general hospitals	Other	Consecutively
Hungary	Regional/capital area	STI clinics	Sentinel	Selectively
Iceland	National	STI clinics, DV clinics, GPs, hospitals, private practitioners	Comprehensive	Consecutively
Ireland	National	STI clinic and GPs	Other	Consecutively
Italy	Regional	STI clinics, hospitals, university/hospital microbiology units, DV clinics	Comprehensive	Consecutively
Latvia	National	STI clinics	Other	Consecutively
Luxembourg	National	GPs, hospitals, urology and family planning clinics	Other	Consecutive
Malta	National	STI clinic. GPs and hospitals	Comprehensive	Selectively
Netherlands	Regional/Amsterdam	STI clinic	Sentinel	Consecutively
Norway	National	STI clinics, GPs	Unknown	Consecutively
Poland	Regional/capital and surrounding area	STI clinic	Other	Consecutively
Portugal	National	STI clinics, DV clinics, GPs, hospitals, urology and gynaecology clinics	Other	Consecutively
Slovakia	Regional	DV, urology and gynaecology practices	Comprehensive	Consecutively
Slovenia	Regional	DV and STI clinics	Other	Consecutively
Spain	National	STI clinics and hospitals	Sentinel	Consecutively
Sweden	National	STI clinics	Comprehensive	Consecutively
United Kingdom	National	GUM/STI clinics, GPs and out-patients	Sentinel	Consecutively

DV: dermatology-venereology, GUM: genitourinary medicine, GP: general practitioner

Comprehensive: reporting is based on cases occurring within the whole population of the geographical area where the surveillance system is set up (national, regional, etc.).

Sentinel: reporting is based on a selected group of physicians/hospitals/laboratories or other institutions with notifications and/or cases occurring within a selected population group defined by age, gender, exposure or other selection criteria.

Other: reporting is based on an unspecified part of the population or group of physicians (or other institutions) – for example reporting by some laboratories with no selection criteria.

In 2016, a total of 2 660 isolates were tested. This represents an increase of 526 isolates (24.6%) compared with 2015. The number of isolates tested from each country varied from two (Estonia) to 365 (Spain) (Table 4). Isolates from Northern Ireland are now included in the United Kingdom submission.

The coverage (number of isolates tested compared to the number of reported cases as part of the enhanced epidemiological surveillance of STI in 2016 [5]) ranged from 1% (United Kingdom and France) to 75% (Croatia). Luxembourg and Slovenia had coverage of over 100% as the number of isolates received exceeded the number of reported cases. As in previous years, the Netherlands and the United Kingdom had less than 5% coverage, along with Belgium, Estonia and France for the first time. Latvia and Poland reported on significantly less than the required 100 isolates although there were sufficient numbers of cases reported to achieve the aim of 100 isolates. Reaching this target, however, is not always possible if cases are mainly diagnosed through nucleic acid amplification test (NAAT). The percentage of isolates tested in Euro-GASP compared to cases reported showed an increase from 3% in 2014 and 2015 to 4% in 2016, which is encouraging given the increase in the number of cases reported through epidemiological surveillance and the likely increased number of cases diagnosed with NAAT during this period.

Table 4. Number of *N. gonorrhoeae* isolates tested in Euro-GASP, gonorrhoea patients reported in 2016, and percentage of isolates tested compared with reported cases, by country, EU/EEA, 2009–2016

Country	Number of isolates tested 2016	Number of cases reported 2016 [5]	% isolates tested*							
			2016	2015	2014	2013	2012	2011	2010	2009
Austria	192	NR	N/A	N/A	N/A	9	27	23	32	77
Belgium**	99	1997	5	7	13	11	12	13	15	15
Croatia	9	12	75	44	NP	NP	NP	NP	NP	NP
Czech Republic	90	1437	6	NP	NP	NP	NP	NP	NP	NP
Denmark	111	2007	6	4	10	13	17	25	20	20
Estonia	2	94	2	16	10	NP	NP	NP	NP	NP
France**	99	7757	1	6	8	8	12	18	24	32
Germany***	109	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Greece	100	N/A†	N/A	42	NR	34	29	26	31	67
Hungary**	94	1176	8	5	5	6	5	1	1	NP
Iceland	35	95	37	31	32	26	NP	NP	NP	NP
Ireland	100	1951	5	9	8	8	7	8	14	NP
Italy	100	760	13	15	N/A	N/A	35	24	42	48
Latvia	8	166	5	3	6	7	6	5	6	3
Luxembourg	20	9	222*	NP	NP	NP	NP	NP	NP	NP
Malta	25	74	34	44	41	51	55	28	62	92
Netherlands**	255	6129	4	4	2	3	4	6	8	5
Norway	111	1096	10	13	16	22	25	21	11	54
Poland	77	437	18	11	9	NP	NP	NP	NP	NP
Portugal	110	273	40	26	55	95	92	91	81	75
Slovakia	110	277	40	30	26	29	38	58	70	13
Slovenia	106	81	131*	149	134	118	104	76	64	80
Spain	365	6816	5	3	3	4	3	4	5	5
Sweden	100	1774	6	6	7	9	10	11	10	18
United Kingdom	233	40166	1	1	1	1	1	1	1	1
Total (number or % isolates tested)	**2660**	**74584**	**4**	**3**	**3**	**4**	**4**	**5**	**6**	**6**

** Percentages above 100% suggest under-reporting of cases in epidemiological surveillance*

*** Sentinel epidemiological surveillance data*

**** There is no epidemiological surveillance for gonorrhoea in Germany*

† Greece have data reporting issues and are currently unable to provide data for 2016

NR = not reported; NP = not participating; N/A = Not applicable.

As in previous years, the majority of gonococci (85.1%) were collected from men. Gender was reported as unknown for nine cases (Table 5). The age of the patients ranged from <1 year to 93 years, with a median of 30 years, an interquartile range of 24 to 38 years, and 27.5% of patients under 25 years (Table 6). Males (mode age 28 years) were significantly older (Mann-Whitney p<0.0001) than females (mode age 20 years), with the highest and lowest percentage of <25-year-olds in the female (51.5%) and MSM patient groups (20.1%), respectively (Table 6).

The anatomical site of specimen collection was mainly genital (75.5%); it was reported as unknown for 86 cases (Table 5).

Information on previous diagnosis of gonorrhoea was available for 995 cases (37.4%), 17.2% of which had had a previous infection. Information on concurrent STI was available for 849 cases (31.9%); 23.9% had a concurrent chlamydia infection, 6.2% had another STI, and 69.9% did not have any concurrent STIs. Of 979 cases (36.8%) with known HIV status, 156 (15.9%) were HIV positive (Table 5). Of these 156 HIV-positive cases, 94.9% were MSM.

Information on sexual orientation and gender was available for 64.8% (1723) of the cases. In these cases, 59.6% of the *N. gonorrhoeae* infections were reported as heterosexually acquired (38.5% females and 61.5% males) and 40.4% were from MSM. An additional 928 males with unknown or other mode of transmission had *N. gonorrhoeae* isolated from the pharynx (n=36), anorectal region (n=84), genital region (n=659), other site (82) or unknown (67).

The distribution of some of the epidemiological data has changed over the years (Table 5). The proportion of isolates obtained from men increased from 2011 (82.4%) to 2016 (85.1%), with a significant increase in males from 2015 to 2016 (p<0.01) although this follows a significant decrease from 85.1% in 2014 to 81.8% in 2015 (p<0.01). The

increase of isolates from men was mirrored by a concomitant significant decrease in the proportion of isolates from females from 17.6% in 2011 to 14.9% in 2016 (p<0.01). Between 2009 and 2015, the proportion of isolates from MSM increased from 32% to 45%, there was, however, a significant decrease from 45% in 2015 to 40.4% in 2016 (p<0.01). The decrease in proportion of MSM was likely caused by the higher number of isolates received from Spain (n=365), combined with a lower proportion of MSM reported (n=53) compared with previous years. If data from Spain were excluded, the proportion of MSM in 2016 would rise to 47.3%.

Isolates from heterosexual males decreased from 40.1% in 2009 to 28.7% in 2015, with a significant increase to 36.7% in 2016 (p<0.01). In 2016, there was no significant change in the proportion of patients under 25 years and the proportion of HIV-positive patients when compared with 2015. The decrease in the proportion of genital isolates seems to have come to a stop (from 86.5% in 2009 to 72.9% in 2015 to 75.5% in 2016), as has the increase in the proportion of pharyngeal isolates, which have significantly decreased from 8.7% in 2015 to 6.4% in 2016 (p<0.01).

The trend of increasing proportions of anorectal isolates and decreasing proportions of isolates from other sites observed between 2014 and 2015 continued into 2016 although the changes were not significant. The proportion of isolates from patients with concurrent chlamydia infection significantly increased from 19.0% in 2015 to 23.9% in 2016 (p=0.01), with a concomitant decrease in the proportion of isolates from patients with no concurrent STI (from 75.1% in 2015 to 69.9% in 2016, p=0.02).

Table 5. Patient characteristics reported for Euro-GASP gonococcal isolates, 2009–2016

	2009 N (%)	2010 N (%)	2011 N (%)	2012 N (%)	2013 N (%)	2014 N (%)	2015 N (%)	2016 N (%)
Total number of isolates	1366	1766	1902	1927	1994	2151	2134	2660
Gender								
Male	1123 (83.7)	1441 (82.4)	1505 (82.4)	1596 (83.7)	1676 (84.7)	1821 (85.1)	1736 (81.8)‡	2256 (85.1)^ ‡
Female	219 (16.3)	308 (17.6)	321 (17.6)	310 (16.3)	302 (15.3)	318 (14.9)	385 (18.2)‡	395 (14.9) ‡
Unknown	24	17	76	21	16	11	13	9
Age (years)								
<25	422 (32.0)	599 (34.4)	572 (31.9)	617 (32.9)	554 (28.4)‡	605 (28.7)	617 (29.5)	720 (27.5)
≥25	898 (68.0)	1141 (65.6)	1221 (68.10)	1261 (67.1)	1399 (71.6)	1501 (71.3)	1476 (70.5)	1902 (72.5)
Unknown	46	26	109	49	41	44	41	38
Sexual orientation & gender								
Females	219 (27.9)	308 (27.3)	321 (27.1)	310 (28)	302 (25.7)	318 (22.7)	385 (26.4)‡	395 (22.9) ‡
Heterosexual males	314 (40.1)	426 (37.7)	423 (35.6)	390 (35.2)	376 (32)	485 (34.7)	419 (28.7)‡	632 (36.7) ‡
Men who have sex with men	251 (32)	395 (35)	442 (37.3)	408 (36.8)	496 (42.3)‡	594 (42.5)	657 (45.0)	696 (40.4)^ ‡
Unknown	582	637*	716	819	820	754	673	937
Site of infection								
Genital	1164 (86.5)	1426 (84.7)	1466 (82.1)	1537 (83)	1531 (79)‡	1549 (76.3)‡	1517 (72.9)‡	1943 (75.5)
Pharyngeal	34 (2.5)	62 (3.5)	79 (4.4)	92 (5)	122 (6.3)	154 (7.6)‡	180 (8.7)	165 (6.4) ‡
Anorectal	138 (10.3)	191 (11.4)	216 (12.1)	188 (10.2)	255 (13.2)‡	192 (9.5)	280 (13.5)‡	366 (14.2)
Other	9 (0.7)	7 (0.4)	24 (1.3)	35 (1.9)	30 (1.5)	135 (6.6)‡	103 (5.0)‡	100 (3.9)
Unknown	21	80	117	75	56	121	54	86
Previous gonorrhoea								
Yes	84 (18.1)	145 (21)	146 (19)	130 (17.2)	142 (17.8)	163 (19.7)	157 (17.5)	171 (17.2)
No	379 (81.9)	546 (79)	621 (81)	627 (82.8)	654 (82.2)	663 (80.3)	739 (82.5)	824 (82.8)
Unknown	903	1075	1135	1170	1198	1325	1238	1665
Concurrent STI								
Concurrent chlamydia infection	78 (14.3)	172 (22.1)	194 (22.2)	187†† (23.4)	183 (21.8)	170 (20)	153†† (19.0)	203 (23.9)¯ ‡
Concurrent other STI (not HIV)	35 (6.4)	28† (3.6)	43 (4.9)	49‡(6.1)	55 (6.5)	41† (4.8)	48†† (6.0)	53 (6.2) ††
No concurrent STI	433 (79.3)	579 (74.3)	638 (72.9)	564 (70.6)	603 (71.7)	640 (75.2)	605 (75.1)	593 (69.9) ‡
Unknown	820	987	1027	1127	1153	1300	1328	1811
HIV status*								
Positive	N/D	48 (15.5)	141 (17.6)	104 (13.5)	144 (17.6)‡	172 (19.3)	132 (15.3)‡	156 (15.9)
Negative	N/D	262 (84.5)	661 (82.4)	668 (86.5)	675 (82.4)‡	720 (80.7)	733 (84.7)‡	823 (84.1)
Unknown	N/D	556	1100	1155	1175	1259	1269	1681

Percentages calculated from known values.

** Includes one individual of unknown gender, but with mode of transmission reported as heterosexual.*

† Includes two individuals with two concurrent STIs

†† Includes four individuals with two concurrent STIs

‡ Includes six individuals with chlamydia and an additionally diagnosed STI.

‡‡ Significant difference compared with previous year (p < 0.05)

^ Includes one individual of unknown gender, but with mode of transmission reported as MSM.

˜ Includes nine individuals with chlamydia and an additionally diagnosed STI

Table 6. Patient age distribution by gender and sexual orientation, 2016

Variable	N†	Age (years)			<25 years N (%)
		Range	Mode	Median	
All patients	2660	0–93	23	30	720 (27.5)
Female	395	15–93	20	24	203 (51.5)
Male*	2256	0–85	28	30	515 (23.2)
Male heterosexual	632	14–82	28	30	164 (26.1)
MSM	696	17–72	26	30	139 (20.1)

† Where information was available.

** Including all males, irrespective of sexual orientation.*

As in previous years, the majority of patients for whom a clinical service type was known had attended a dedicated STI or sexual health clinic, however there was a significant decrease in patients from this service type between 2015 (61.8%) and 2016 (59.5%) (p=0.01). There was also a significant change in the number of patients who attended 'other' service types in 2016 (3.3%) compared with 2015 (6.6%, p<0.01) (Table 7).

Table 7. Clinical service type attendance, 2010–2016

Grouping	2010 N=866 n (%)	2011 N=1902 n (%)	2012 N=1927 n (%)	2013 N=1994 n (%)	2014 N=2151 n (%)	2015 N=2134 n (%)	2016 N=2660 N (%)
STI and sexual health clinics	444 (51.3)	1079 (56.7)	1076 (55.8)	1123 (56.3)	1136 (52.8)	1319 (61.8)	1583 (59.5)
Antenatal	0	0	2 (0.1)	0	0	0	0
Out-patient clinic	36 (4.2)	128 (6.7)	148 (7.7)	122 (6.1)	161 (7.5)	164 (7.7)	215 (8.1)
Other	42 (4.9)	60 (3.2)	47 (2.4)	75 (3.8)	105 (4.9)	70 (3.3)	176 (6.6)
Primary care	88 (10.2)	277 (14.6)	203 (10.5)	215 (10.8)	217 (10.1)	155 (7.3)	174 (6.5)
Unknown	256 (29.6)	358 (18.8)	451 (23.4)	459 (23.0)	532 (24.7)	426 (20.0)	512 (19.2)

Note: grouping of clinical service type as described in Table 1.

Information on country of birth was supplied by 17 countries. Twelve of these countries (Austria, Belgium, the Czech Republic, Denmark, Greece, Ireland, Italy, Malta, the Netherlands, Portugal, Slovakia and the United Kingdom) reported patients who had acquired gonorrhoea in the reporting country but had a different country of birth, with the Netherlands having the largest number of nationalities (n=38). Of the 1 244 cases with known country of birth, 76.1% (n=946) were diagnosed and reported with gonorrhoea in their country of birth, which was a slight decrease compared with 2015 (77.5%). In cases where country of birth and reporting country differed, the most common continent of birth was Europe (153 patients), with Germany the most common country within Europe (19 patients), followed by Asia (51 patients), South America (44 patients), Africa (27 patients), North America (16 patients), and Australia (seven patients). Data on the probable country of infection were supplied by 13 countries, five less than 2015, with nine countries reporting patients acquiring gonorrhoea outside the reporting country. The majority of cases (92.4%; 668/723) were contracted within the reporting country. The continent most commonly reported as probable country of infection was Europe (38 patients), with Spain the most common country within Europe (eight patients), followed by Asia (10 patients), North and South America (both three patients) and Africa (one patient).

Further country-specific data are presented in Annex 6, which includes a breakdown by clinical service type, country of birth, place of residence and probable country of infection.

3.3 Antimicrobial susceptibility and resistance

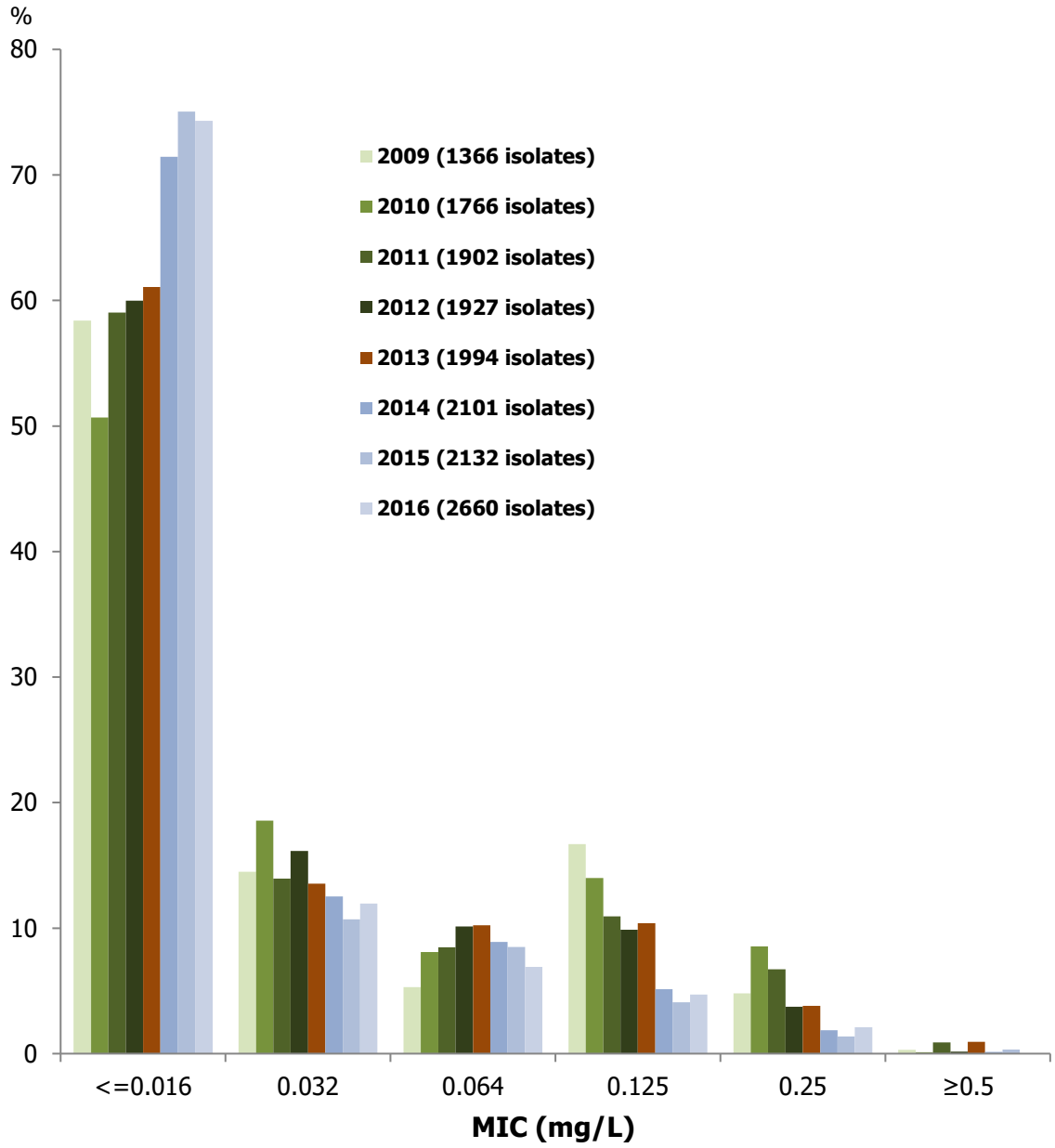
Cefixime and ceftriaxone

Cefixime resistance (MIC>0.125 mg/L) was observed in 2.1% (56/2660) of isolates (Figure 1), remaining stable compared with 2015 (1.7%, 36 out of 2132 isolates) (p=0.26, Z-test). The level of cefixime resistance still remains lower than in 2010–2013 (4.7%–8.7%). The proportion of the most susceptible isolates (MIC≤0.016 mg/L) remained stable at 74.3% in 2016. No isolates with a cefixime MIC of ≥0.5 mg/L were detected in 2016, which is a large decrease from 2015 when seven isolates were detected (three isolates in 2014, 19 isolates in 2013, three isolates in 2012, and 17 isolates in 2011).

In 2016, cefixime resistance was detected in 14 countries (Map 2, Table 8), compared with nine in 2015 and 10 in 2014. In 2016, cefixime resistance in Belgium continued to decrease (12.1% in 2014, 11.1% in 2015, and 8.1% in 2016). Belgium, Germany, Croatia, Hungary, Luxembourg and Poland all reported ≥5% resistance to cefixime in 2016. Slovakia, Spain and the United Kingdom continued to have <5% cefixime resistance. As in previous years, no resistance to Cefixime was detected in Denmark, Estonia, Iceland, Latvia, Malta, the Netherlands, Portugal, Slovenia and Sweden. Austria, Croatia, France, Italy and Poland did not report isolates with cefixime resistance in 2015 but in 2016 resistant isolates were detected. Five countries observed a reduction in cefixime resistance from 2015 to 2016 (Belgium, Greece, Ireland, Slovakia and Spain), with two countries (Greece and Ireland) reporting zero cefixime-resistant isolates in 2016. Greece saw the largest reduction in cefixime resistance: from 11% in 2015 to 0% in 2016.

Cefixime resistance according to sexual orientation and gender was stable (no significant differences) in 2016 compared with 2015; cefixime resistance in MSM continued to decline (0 in 2016, 0.5% in 2015; peak of 7.3% in 2010) (Figure 2). Cefixime resistance has also been declining among females and heterosexual males since 2011. After the increase in 2015 (2.2% in 2016 from 4.1% in 2015). This decline continued among heterosexual males, while in females an increase from 1% in 2015 to 2% in 2016 was observed (Figure 2).

Figure 1. Distribution of MIC for cefixime in Euro-GASP, 2009–2016



Map 2. Proportion of gonococcal isolates with cefixime resistance by country, EU/EEA, 2016

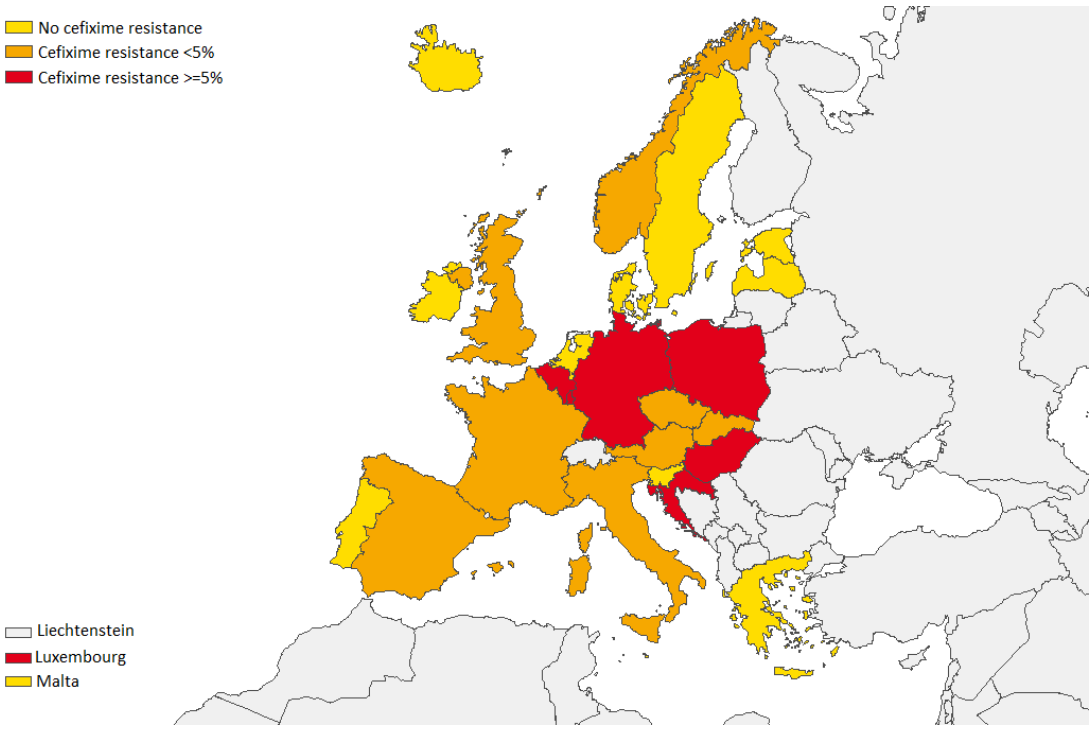
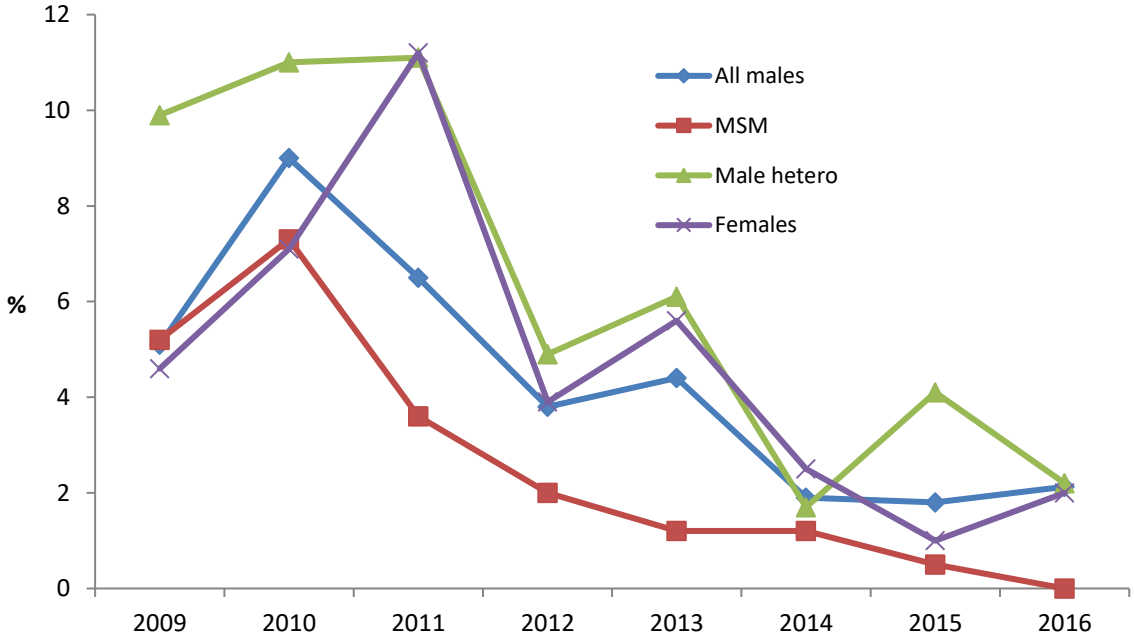


Figure 2. Percentage of isolates with cefixime resistance by gender and male sexual orientation, Euro-GASP, 2009–2016



No isolates displayed ceftriaxone resistance (MIC>0.125 mg/L) in 2016 compared with one in 2015, five in 2014, and seven in 2013 (Figure 3). The MIC distribution for ceftriaxone in 2016, compared with 2015, showed a slightly lower proportion of more susceptible gonococcal isolates (MIC≤0.016 mg/L) along with an increased proportion of isolates with higher MICs (0.032 mg/L to 0.125 mg/L) (Figure 3).

It should be noted that the comparison of resistance between years is limited by the low number of cephalosporin-resistant isolates as well as the small number of isolates submitted to Euro-GASP from some countries.

Figure 3. Distribution of MIC for ceftriaxone in Euro-GASP, 2007–2016

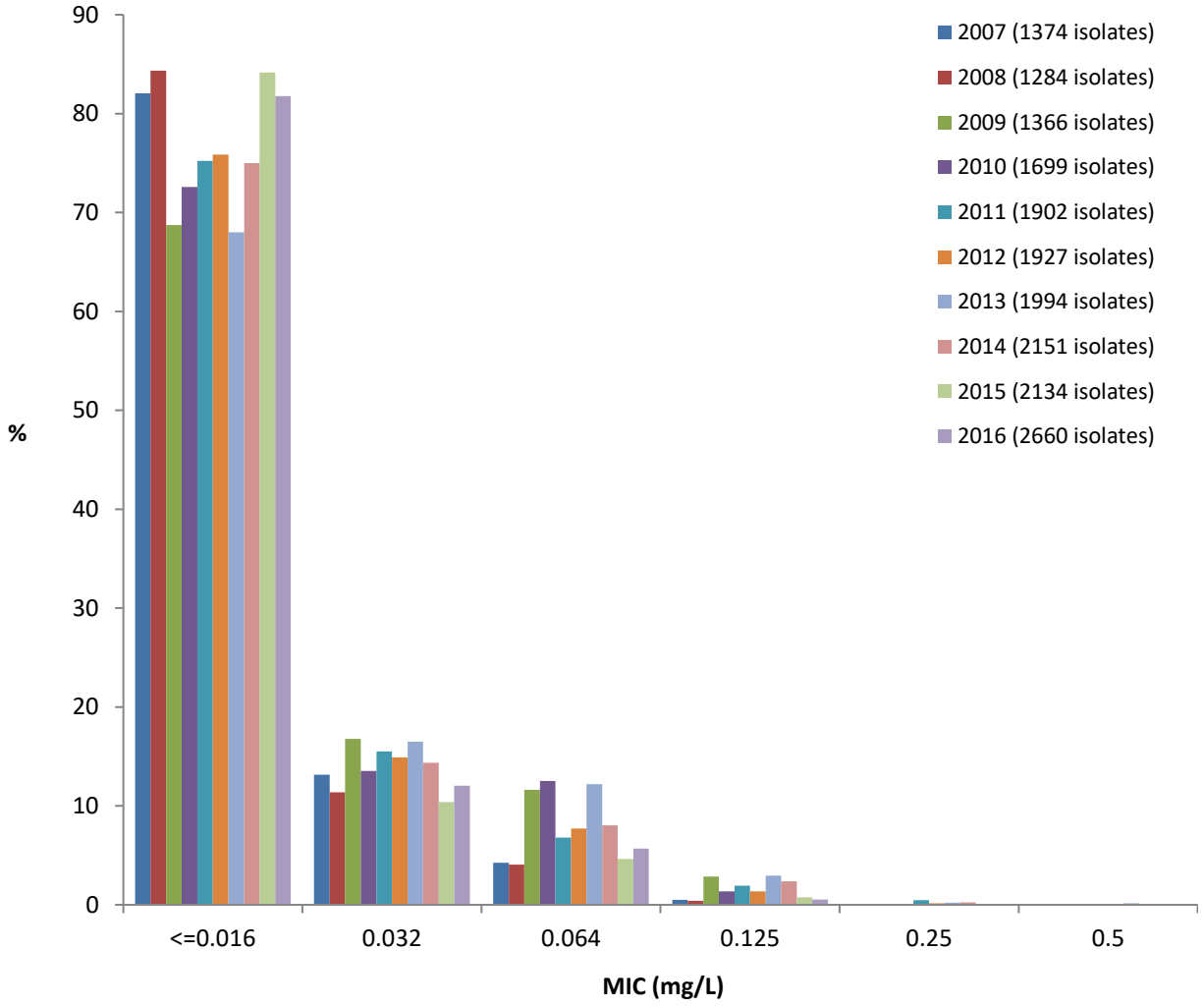


Table 8. Resistance to cefixime, azithromycin, ciprofloxacin and penicillin G (only plasmid-mediated high-level resistance; PPNG) by country, Euro-GASP, 2016

Country	Number of isolates tested	Resistance								Method of testing
		Cefixime		Azithromycin		Ciprofloxacin		PPNG		
		No.	%	No.	%	No.	%	No.	%	
Austria	192	8	4.2	9	4.7	126	65.6	36*	23.1	Decentralised – Etest
Belgium	99	8	8.1	9	9.1	44	44.4	16	16.2	Decentralised – MIC
Croatia	9	1	11.1	0	0	6	66.7	1	11.1	Centralised – BKP/Etest
Czech Republic	90	1	1.1	9	10	47	52.2	19	21.1	Centralised – Etest
Denmark	111	0	0	2	1.8	21	18.9	8	7.2	Decentralised – Etest
Estonia	2	0	0	0^	0	0	0	N/T		Decentralised – Etest
France	99	1	1	7	7.1	37	37.4	N/T		Decentralised – Etest
Germany	109	7	6.4	1	0.9	64	58.7	9	8.3	Centralised – BKP/Etest
Greece	100	0	0	14	14	60	60	20	20	Decentralised – Etest
Hungary	94	8	8.5	15	16	38	40.4	8	8.5	Centralised - Etest
Iceland	35	0	0	5	14.3	27	77.1	0^	0	Decentralised – Etest
Ireland	100	0	0	15	15	42	42	11	11	Decentralised – Etest
Italy	100	2	2	11	11	53	53	8	8	Decentralised – Etest
Latvia	8	0	0	0	0	2	25	1	12.5	Centralised – Etest
Luxembourg	20	2	10	0	0	14	70	2	10	Centralised – Etest
Malta	25	0	0	2	8	11	44	5	20	Decentralised – Etest
Netherlands	255	0	0	5	2	75	29.4	N/T		Decentralised – MIC
Norway	111	2	1.8	18	16.2	51	46	18	16.2	Decentralised – MIC
Poland	77	4	5.2	2	2.6	44	57.1	14	18.2	Centralised – Etest
Portugal	110	0	0	38	34.5	51	46.4	13	11.8	Decentralised – Etest
Slovakia	110	4	3.6	1	0.9	62	56.4	19	17.3	Centralised – BKP/Etest

Country	Number of isolates tested	Resistance								Method of testing
		Cefixime		Azithromycin		Ciprofloxacin		PPNG		
		No.	%	No.	%	No.	%	No.	%	
Slovenia	106	0	0	9	8.5	35	33	15	14.2	Decentralised – Etest
Spain	365	6	1.6	15	4.1	210	57.5	59	16.2	Decentralised – Etest
Sweden	100	0	0	5	5	47	47	24	24	Decentralised – Etest
United Kingdom	233	2	0.9	7	3	69	29.6	27	11.6	Decentralised – MIC/BKP/Etest
Total										
Cefixime	2660	56	2.1							
Ciprofloxacin	2660					1236	46.5			
Azithromycin	2659			199	7.5					
PPNG	2228							333	14.9	
95% CI			1.6-2.7		6.5-8.5		44.6-48.4		13.5-16.4	

** 150 isolates tested*

^ 1 isolate tested

N/T: not tested

BKP: Breakpoint

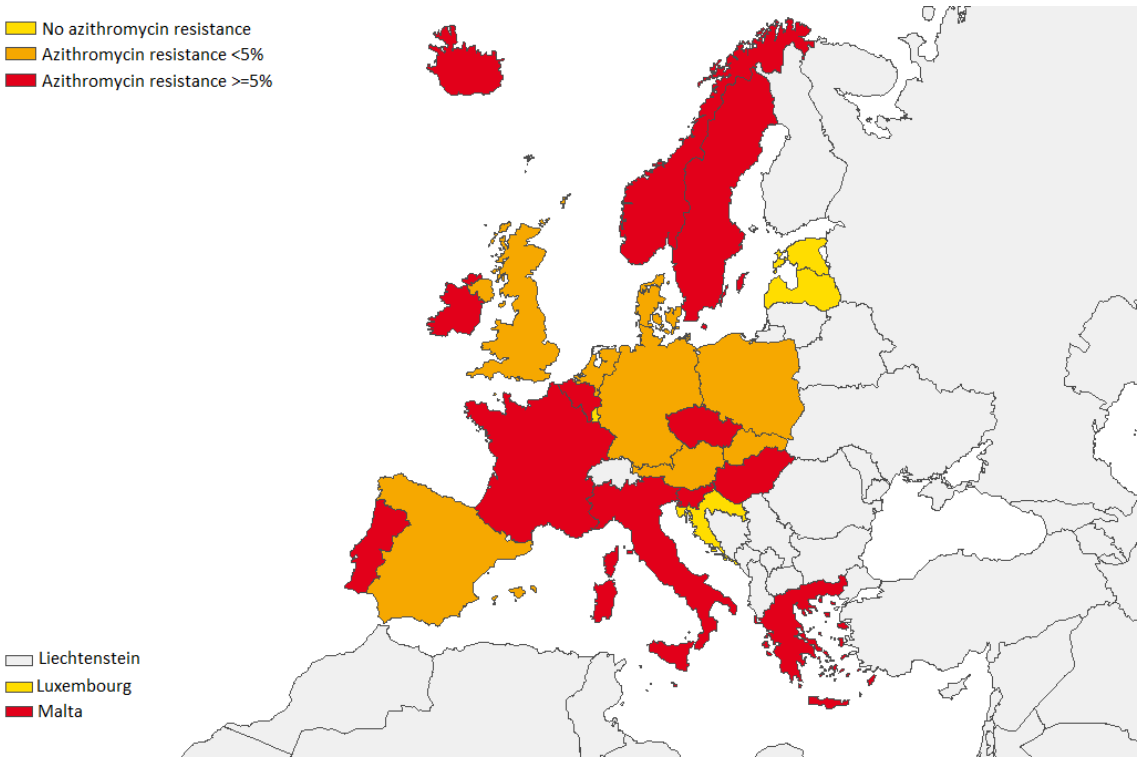
PPNG: Penicillinase-producing Neisseria gonorrhoeae

Azithromycin

In 2016, the mean proportion of resistance to azithromycin (MIC>0.5 mg/L) was 7.5% (199 out of 2659 isolates) and ranged from 0% (Croatia, Estonia, Latvia and Luxembourg) to 34.5% in Portugal (Table 8). Although overall azithromycin resistance was stable in 2016 compared with 2015 (7.1% p=0.74), seven isolates displayed high-level resistance to azithromycin (MIC≥256 mg/L), two more than in 2015. This is the highest number since the beginning of the Euro-GASP surveillance. These seven isolates came from Iceland (2), Italy (2), the Czech Republic, Ireland and the United Kingdom (one each); all were susceptible to the other antimicrobials tested, except for the Czech isolate which displayed ciprofloxacin resistance. Isolates displaying high-level resistance to azithromycin were also detected in 2006 (n=1), 2007 (n=4), 2011 (n=2), 2012 (n=3), 2013 (n=1), 2014 (n=1), and 2015 (n=5).

In 2016, azithromycin resistance above 10% was detected in seven countries: Greece, Hungary, Iceland, Ireland, Italy, Norway and Portugal. In 2015, resistance in Hungary (4.7%), Iceland (2.0%), Italy (0.0%), and Norway (3.6%) was still well below 10%. Resistance to azithromycin was also above 10% in 2014 and 2015 in Greece, Ireland and Portugal. The highest resistance levels were detected in Portugal (34.5%) and Norway (16.2%). In 2015, the highest resistance levels were reported by Greece (22.0%) and Ireland (18.2%). If Portugal and Norway are excluded, the overall azithromycin resistance in 2016 would decrease to 5.9%. Azithromycin resistance decreased in 2016 in Germany, Denmark, Greece, Malta, the Netherlands, Poland, Slovakia and the United Kingdom.

Map 3. Proportion of isolates with azithromycin resistance in Europe, 2016



In 2016, azithromycin resistance remained highest among heterosexual males (7.6%), followed by MSM (5.6%). It was lowest in females (5.3%) (Figure 4). The MIC distribution for azithromycin in 2016 was similar to previous years; the majority of resistant isolates had an MIC just above the breakpoint (0.5 mg/L), and the modal MIC continues to be 0.25 mg/L (Figure 5).

Figure 4. Percentage of isolates with azithromycin resistance by gender and male sexual orientation, Euro-GASP, 2009–2016

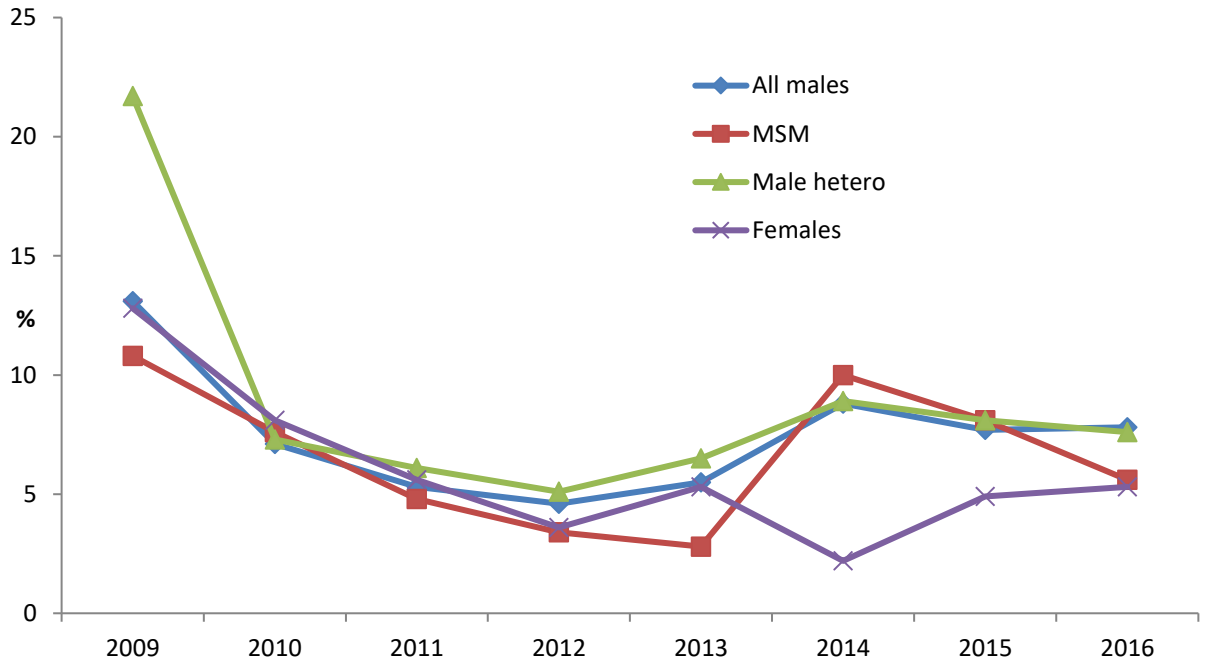
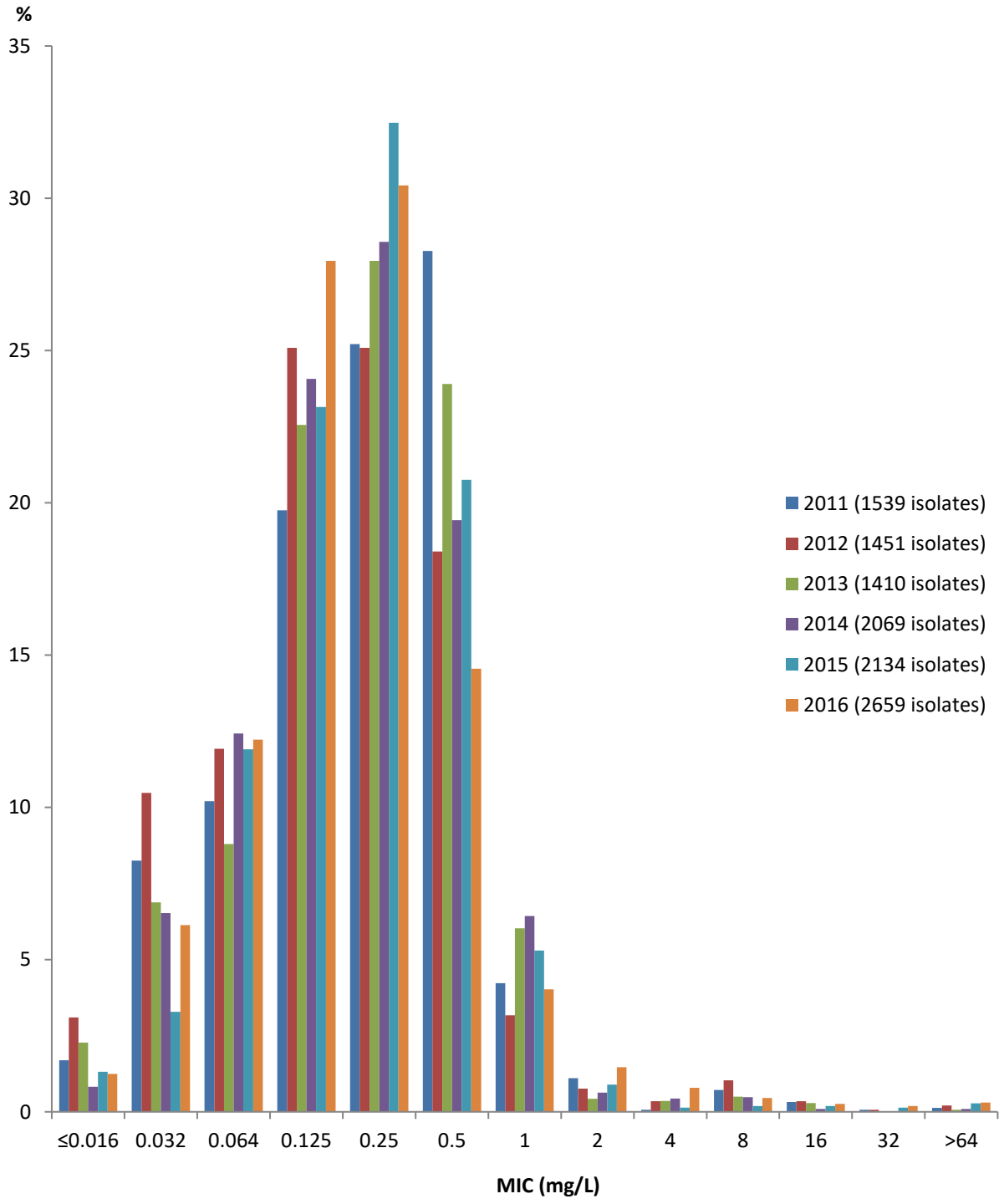


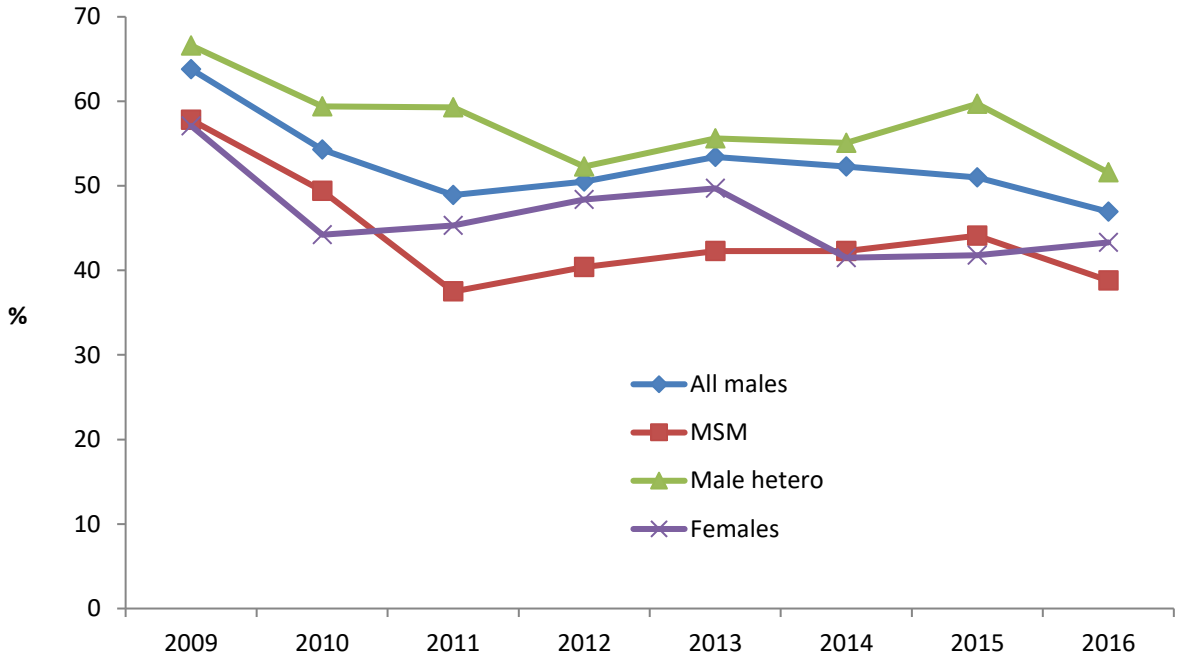
Figure 5. Distribution of MIC for azithromycin in Euro-GASP, 2011–2016



Ciprofloxacin

In 2016, resistance to ciprofloxacin (MIC>0.06 mg/L) ranged from 0% in Estonia to 77.1% in Iceland (Table 8). Overall resistance levels in 2016 (46.5%, 1 236 out of 2 660) were lower than in 2015 (49.4%) although the difference was not statistically significant (p=0.06). Resistance was highest among heterosexual males (51.6%) and lowest in MSM (38.8%), with a significant decrease in resistant isolates from heterosexual males (p=0.01) and MSM (p=0.05) between 2015 and 2016.(Figure 6).

Figure 6. Percentage of isolates with ciprofloxacin resistance by gender and male sexual orientation, Euro-GASP, 2009–2016



Penicillin G

High-level plasmid-mediated resistance to penicillin G (penicillinase-producing *N. gonorrhoeae* (PPNG)) ranged from 0% in Iceland to 24.0% in Sweden, with an overall resistance level of 14.9% (Table 8). In 2016, PPNG prevalence was at the highest level ever recorded by Euro-GASP. A steadily increasing trend in PPNG prevalence has been observed since 2010 (Figure 7).

Figure 7 shows the percentages of *N. gonorrhoeae* isolates resistant to ciprofloxacin, azithromycin and cefixime, as well as the percentage of penicillinase-producing isolates from 2007 to 2016

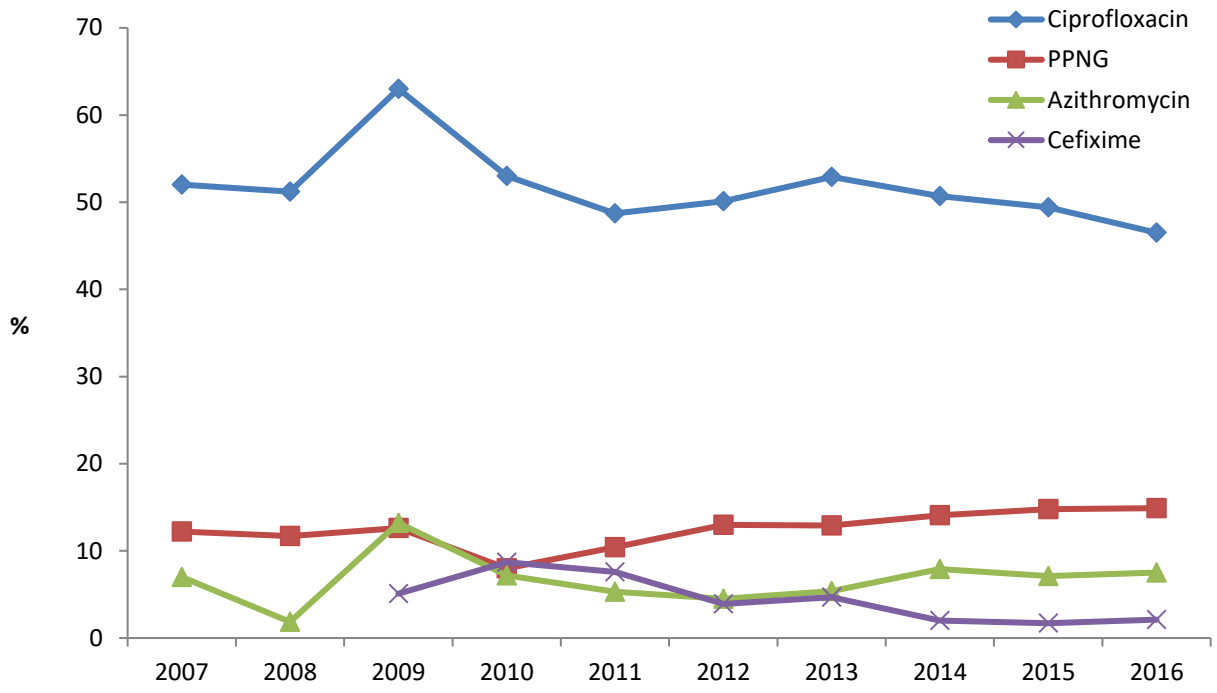
Spectinomycin

No resistance to spectinomycin (MIC>64 mg/L) was detected in 2016 (2 018 isolates tested). Resistance to spectinomycin has not been detected since 2008, when Euro-GASP first started testing for it.

Gentamicin

Gentamicin data were available for 1 507 isolates. No data were reported from Austria, Estonia, France, Greece, Iceland, Ireland, Malta, the Netherlands, Norway, Sweden and the United Kingdom. As of yet, there are no breakpoints for gentamicin, but MICs of gentamicin continue to be low in all European countries (MIC_{50} and MIC_{90} 4 mg/L and 8 mg/L, respectively), with lower MIC_{50} and MIC_{90} observed than in 2013 (MIC_{50} and MIC_{90} 8 mg/L and 12 mg/L, respectively). This is likely due to a change in methodology that increased the use of Etests in 2016 (83.4% tested by Etest in 2016, 43.6% in 2013) that frequently read one dilution lower than agar dilution for gentamicin. The MIC range in 2016 was similar to the results of the previous test in 2013; 0.5–16 mg/L in 2016, 1–16 mg/L in 2013.

Figure 7. Percentage of resistant *Neisseria gonorrhoeae* by antimicrobial and year, Euro-GASP, 2007–2016



PPNG: penicillinase-producing *N. gonorrhoeae*

3.4 Diagnostic tests and treatment

Data on the type of diagnostic test are summarised in Table 9. Culture was the most common diagnostic test, used in 92.7% of cases overall, which is comparable to 2015 (90.2%), while the total amount of microscopy and NAAT testing decreased in 2015 (17.6% and 21.1%, respectively). Data on treatment are summarised in Figure 8. Three patients who received only azithromycin harboured an intermediate strain (MIC=0.5 mg/L), and one patient treated with cefixime and ciprofloxacin harboured a cefixime- and ciprofloxacin-resistant strain (MIC>0.125 mg/L and >0.06 mg/L, respectively). Four patients treated with ciprofloxacin alone harboured ciprofloxacin-resistant strains (MIC>0.06 mg/L). It is not known whether any treatments were administered based on prior susceptibility testing results. As in 2015, ceftriaxone with azithromycin was the most commonly administered treatment in all groups (433/779, or 55.6%, in 2015; 520/991, or 52.5%, in 2016); this treatment continues to be more frequently used in heterosexual males than MSM or females where ceftriaxone usage alone accounted for a larger percentage of treatments in these groups (Figure 8).

Table 9. Summary of 2016 diagnostic tests

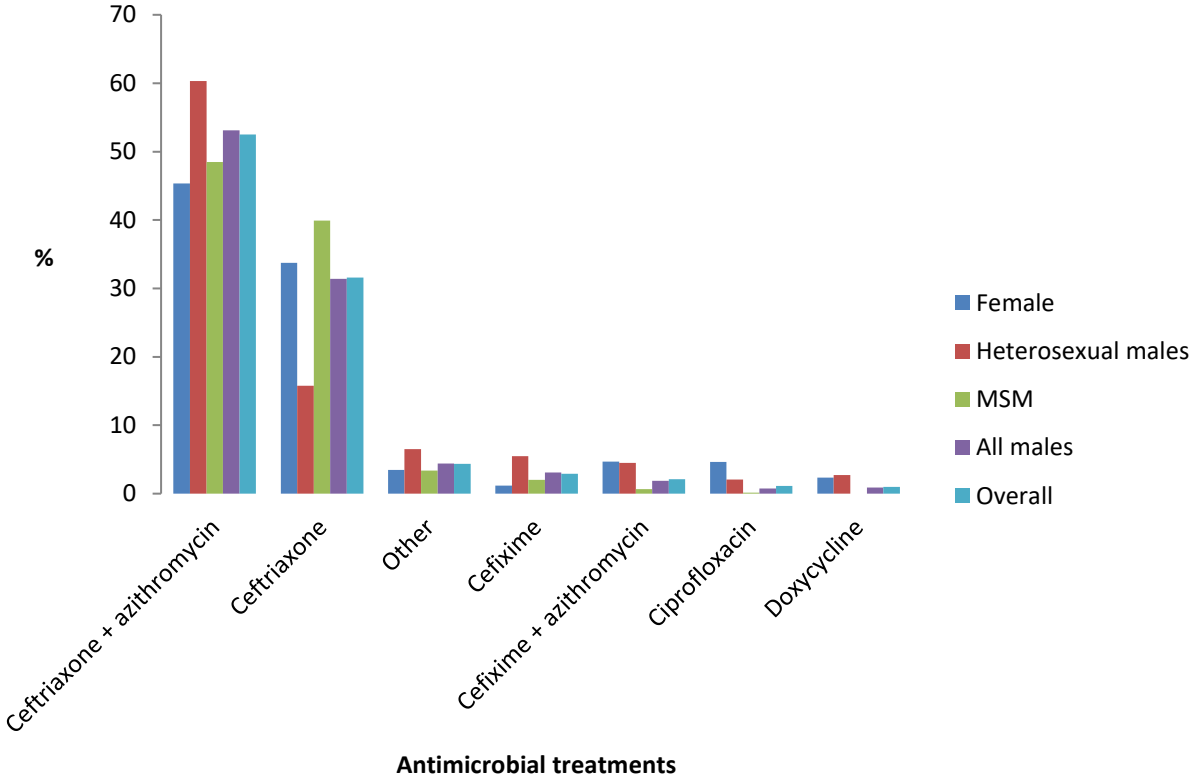
	Culture		NAAT		Microscopy	
	No.	%	No.	%	No.	%
Primary diagnostic test only	1805	84.9	154	7.2	0	0
Primary test plus other diagnostic tests	164*	7.7	140†	6.6	111‡	5.2
Total	**1969**	**92.7**	**294**	**13.8**	**111**	**5.2**

** Includes 26 tests with microscopy, 55 with NAAT, and 83 with both microscopy and NAAT*

† Includes 55 tests with culture, 2 with microscopy, and 83 with culture and microscopy

‡ Includes 26 tests with culture, 2 with NAAT, and 83 with culture and NAAT

Figure 8. Percentage of known treatments used by gender and transmission type for the most frequently used therapies, 2016



Note: Twenty-two different combinations of antimicrobials were recorded in 2016; only treatments with ≥2% in any gender/ transmission group are shown.

4 Conclusions

Cefixime resistance overall remained stable across the EU/EAA between 2014 and 2016; compared with 2013 (4.7%), cefixime resistance dropped (2.1% in 2016). Resistant isolates were detected in fourteen (56%) of the 25 countries covered in 2016, an increase of nine countries over 2015. Cefixime resistance rates increased slightly compared with 2015 (1.7%). It should, however, be noted that the proportion of highly resistant isolates (≥0.5 mg/L) decreased to zero in 2016, the lowest value recorded since 2009. Cefixime resistance continues to be lowest among MSM (0%) and highest in male and female heterosexuals (2.2% and 2.0%, respectively). No isolates displayed ceftriaxone resistance in 2016, compared with one isolate in 2015, five in 2014, and seven in 2013.

The ceftriaxone MIC distribution shifted slightly in 2016, with a decreased proportion of more susceptible isolates (MIC≤0.016 mg/L) and an increased proportion of isolates with higher MICs (0.032 mg/L to 0.125 mg/L). The continuing low resistance to third generation cephalosporins is particularly good news considering that these are the last remaining options for empiric first-line treatment. Among patients for whom treatment regimen was reported, 86.2% were administered ceftriaxone, with or without azithromycin, so the use of the recommended dual antimicrobial therapy (ceftriaxone plus azithromycin) and/or ceftriaxone monotherapy has likely contributed to increased cephalosporin susceptibility.

The overall rate of ciprofloxacin resistance decreased to 46.5%, down from a rate of around 50% between 2010 and 2015. Azithromycin resistance was stable at 7.5% in 2016 (7.1% in 2015 and 7.9% in 2014). Neither azithromycin nor ciprofloxacin are recommended for monotherapy, unless the isolates are shown to be susceptible first. The higher azithromycin resistance in heterosexual men (7.8% vs 5.3% in females) may be driven by the frequent use of azithromycin to treat male non-gonococcal urethritis, although azithromycin is often used to treat chlamydia in both genders. In MSM, azithromycin resistance decreased to 5.6%. In Portugal and Norway, a bias towards submitting isolates from males may skew the overall azithromycin resistance data. Accordingly, when isolates from Portugal and Norway are removed from the overall prevalence calculation, azithromycin resistance decreases to 5.9%. It should be noted that the majority of resistant isolates are just above the resistance breakpoint (53.8% of resistant isolates had MICs≤1 mg/L and 73.4% MICs≤2 mg/L), and fluctuations in azithromycin resistance are most probably due to the proximity of isolates to this breakpoint. In addition, azithromycin susceptibility testing is sensitive to minor differences in agar media composition, pH and CO_2 levels.

In previous years, MSM had a tendency towards a lower risk of harbouring resistant isolates [7], which was supported by a lower resistance rate among anorectal isolates. However, in 2014, there was a significant rise in azithromycin resistance in MSM (from 2.8% in 2013 to 10% in 2014), followed by a decline in 2015 (8.1%) and 2016 (5.6%). Among MSM, cefixime resistance has remained fairly steady since 2013. A decrease in ciprofloxacin resistance was reported between 2015 (44.1%) and 2016 (38.8%). In females, slight increases in azithromycin, cefixime and ciprofloxacin resistance were recorded between 2015 and 2016, the first time since 2013, with the exception of an increase in azithromycin resistance in 2015.

Although overall resistance levels remained stable for cefixime, ceftriaxone and azithromycin in 2016, the European response plan to control the threat of multidrug-resistant *N. gonorrhoeae* in Europe [4] should be observed to help identify and report treatment failures and ensure that gonorrhoea remains a treatable infection. Euro-GASP has a major role in fulfilling the objectives of the response plan, which include:

- Strengthening the surveillance of gonococcal antimicrobial susceptibility by increasing the number of participating countries and isolates and improving representativeness of the programme. The Czech Republic and Luxembourg joined Euro-GASP in 2016, further strengthening the surveillance programme. Cyprus collected and tested isolates for 2016 but the results had to be excluded due to media problems. Overall completeness of variables in 2016 remained quite similar to 2015, with decreases in reporting of a few variables such as probable country of infection (41.1% to 27.2%), country of birth (53.0% to 46.7%) and concurrent STI (37.8% to 31.9%). Reporting has to improve for many variables in order to achieve a robust statistical analysis that links susceptibility and patient data.
- More country visits to support the inclusion of additional countries and centres, improve isolate numbers/representativeness, and reporting of epidemiological data.
- Strengthening capacity for the surveillance of gonococcal antimicrobial susceptibility by developing capacity for culture and susceptibility testing across countries. Training in STI diagnostics and susceptibility testing is provided, and experts (or related staff) are encouraged to participate in these activities; the goal is to introduce decentralised testing where possible.
- Advocating the use of recommended dual therapy (ceftriaxone and azithromycin) to treat gonorrhoea [1]. Even though data completeness for 'treatment used' has improved since 2014, the overall level (37.3%) is still disappointing. It has been shown that the majority of the patients (54.1%) received appropriate dual therapy, which is a decrease from 2015 (57.6%) and 2014 (68.5%). Encouragingly, 86.2% received 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, in particular those who harboured

strains resistant to the administered therapy. The high azithromycin resistance detected in Euro-GASP is a threat to the effectiveness of dual therapy and needs to be monitored closely.

- Ensuring that all Euro-GASP laboratories continue to participate in the EQA programme.

The number of isolates tested (2 660) was higher in 2016 compared with previous years (2015: 2 134, 2014: 2 151), and although the percentage of tested isolates compared to the number of reported gonorrhoea cases decreased from 6% in 2009 to 4% in 2016, the proportion increased slightly when compared to more recent years (3% in both 2014 and 2015). These low proportions are a result of the increase in the overall number of gonorrhoea cases diagnosed in the EU/EEA while the required isolate numbers in Euro-GASP remained static. A review of the number of isolates submitted to Euro-GASP is required in order to ensure that Euro-GASP data remain representative of the European *N. gonorrhoeae* population.

Even though Euro-GASP detected stable cefixime, ceftriaxone and azithromycin resistance in 2016, the continued high azithromycin resistance and the detection of seven isolates with a very high MIC of azithromycin (≥256 mg/L) is of major concern. Treatment failures are still possible, as documented by Fifer et al. [8] who described the first treatment failure with the recommended dual-therapy regimen. Therefore, continuous implementation and a review of the response plan that takes into account developments in recent years is essential, along with the development of novel antimicrobials and/or new dual antimicrobial therapy regimens.

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Annex 1. Framework for the European Gonococcal Antimicrobial Surveillance Programme: isolates collected in 2016 and 2017

Isolate collection

Submitted isolates

Each country should aim to collect a minimum of 110 gonococcal isolates each year, with the overall aim to retrieve and test a minimum of 100 isolates. For countries where 110 isolates represent less than 10% of the total number of cases of gonorrhoea (Spain, the United Kingdom and the Netherlands), additional isolates should be collected in order to provide a more representative sample, e.g. at least 200.

Selection criteria

Isolates should be selected from consecutive patients and from patients representing different patient groups and geographical regions within the country to reflect the distribution of gonorrhoea cases in that country, if known. Consecutive isolate selection may not be possible if particular patient groups/regions are selected or if isolates with corresponding epidemiological data are selected in place of isolates with no data. Care should be taken to avoid selection bias.

Multiple isolates from a single patient should be considered as a single episode of infection if the isolates were recovered within a period of ≤4 weeks, and only one isolate should be submitted, according to the hierarchy below. Where more than one isolate is collected from a patient, then a hierarchy of desired isolates for collection would be:

Males: 1. Pharyngeal 2. Rectal 3. Urethral 4. Other

Females: 1. Pharyngeal 2. Cervical 3. Other anogenital (high vaginal swab/rectal/urethral) 4. Other

Given the current view that cephalosporin resistance emerged through interaction between commensal *Neisseria* species and *N. gonorrhoeae* in the pharynx and the fact that cephalosporins and most other antimicrobials have a lower efficacy in the pharynx, pharyngeal samples (where available) should be selected first as cephalosporin resistance is most likely to develop at this site.

Submission of isolates for centralised testing

Each participating laboratory will be provided with cryopreservative beads to store gonococcal isolates (see Annex 1) until collection by courier once annually.

Schedule of isolate collection 2016

As agreed at the Euro-GASP coordination meeting in December 2013, only one isolate collection will be collected each year, until further notice, in order to simplify processes and aim for a more efficient collection, analysis and reporting of data. The collection dates are between September and November. Countries with low collection numbers would be able to use isolates from throughout the year. In addition, isolates outside of the September–November collection period may be submitted if this enables a more representative isolate set from patients to be submitted (i.e. isolates representing different patient groups and geographical regions within the country to reflect the distribution of gonorrhoea cases in that country).

Data collection

It is the aim of the Euro-GASP surveillance system to link *N. gonorrhoeae* susceptibility data with basic epidemiological data to get an overview of risk groups and to target prevention measures. All data from the AMR susceptibility testing should be submitted to TESSy. The set of variables and validation rules are described in the GONOAMR metadata set.

Epidemiological information

Epidemiological data are collected as part of enhanced STI surveillance and submitted by the national STI surveillance contact points. The GONOAMR surveillance database should use consistently formatted epidemiological information based on an identical set of variables (see Annex 4) in order to make it possible to link epidemiological information with microbiological information in case-based formats.

The method of obtaining epidemiological data could be implemented as follows:

- The STI microbiology contact points who submit or test isolates for AMR surveillance can liaise with national contact points for STI surveillance and request the epidemiological data for cases included in AMR surveillance. This will require a patient identifier – at national level – to link the information. However, the patient identifier should not be sent to TESSy and only be used for internal purposes.
- If data submitted by the national contact points for STI surveillance cannot be linked to gonococcal isolates and associated antimicrobial susceptibility data (e.g. if the data for STI surveillance are aggregate, or there is no shared patient identifier between the epidemiological and microbiological data), the national contact points for STI microbiology submit the available epidemiological data (either data submitted with the isolate or data requested from the location where the sample was collected).

In both instances, the epidemiological and microbiology data are submitted to TESSy by the national STI contact point (microbiologists, epidemiologists or data managers).

Please note that the submission of AMR results should not be delayed if some epidemiological data are still missing; AMR results should be uploaded as soon as they become available. Datasets can be completed at a later stage.

Centralised testing

For countries participating in Euro-GASP through centralised testing, the Euro-GASP hub sends results back to laboratories in the Member States. Epidemiological and AMR data should then be entered in TESSy by the Member States. This could be done by the microbiology or epidemiological focal point, as explained above. The hub will be able to check with the TESSy helpdesk on whether all cases tested were reported through TESSy.

Susceptibility testing

Centralised testing

Isolates sent directly to the hub will be tested for susceptibility to the following panel of therapeutically relevant antimicrobials. An extended panel including gentamicin and spectinomycin will be tested every three years (introduced in 2016). Further details on the testing methodology can be found in Annex 3.

- Ciprofloxacin (breakpoint or Etest on all isolates)
- Azithromycin (breakpoint, resistance confirmed by Etest; alternatively all isolates tested by Etest)
- Cefixime (Etest)
- Ceftriaxone (Etest)
- β-lactamase test (nitrocefin test) for detection of high-level penicillin resistance
- Gentamicin (full agar dilution or Etest on all isolates) for 2016 isolates only
- Spectinomycin (breakpoint or Etest on all isolates) for 2016 isolates only

Samples will no longer be tested for gentamicin and spectinomycin susceptibility as neither spectinomycin nor gentamicin is routinely used for the treatment of gonorrhoea; spectinomycin is also difficult to acquire. However, a snapshot of the current antibiotic susceptibility situation should be performed every third year (2016, 2019) using an extended panel of antibiotics, including spectinomycin and gentamicin. Testing for specinomycin and gentamicin is not mandatory.

Laboratories participating in centralised testing are encouraged to shift to decentralised testing through training, country visits and twinning activities.

Decentralised testing

Laboratories from individual countries that meet the below criteria described will perform their own susceptibility testing and enter their results directly into TESSy. Even though susceptibility testing methods may vary, it is important that breakpoints are harmonised and meet Euro-GASP criteria (Annex 3).

Selection criteria for decentralised testing

To ensure data quality, laboratories can use their own testing methods to test the agreed core antimicrobial panel if they meet the following criteria:

- Laboratories that perform consistently well in the EQA (no more than 5% of MIC results differ by more than two doubling dilutions of the modal MICs).
- Laboratories with good comparability (at least 90% concordance between resistance category and no more than 5% of MIC results differ by more than two doubling dilutions) between the laboratories' own national or regional susceptibility testing data and susceptibility data generated by centralised susceptibility testing.

If participating laboratories wish to include data from gonococcal isolates that were tested for antimicrobial susceptibility by third-party laboratories, the laboratory needs to ensure that these laboratories also meet the above criteria. Details for these additional laboratories should be provided to the hub.

If laboratories significantly change their susceptibility testing methods, e.g. by changing from agar dilution to Etest, the Euro-GASP hub should be informed. Local validation data can be submitted to Euro-GASP for review, but this is not mandatory; laboratories that take part in decentralised testing are expected to use appropriate control strains to identify potential issues and ensure consistency in the longitudinal data.

Procedure for decentralised testing

Laboratories identified as suitable candidates for decentralised testing are required to:

- submit MIC data and corresponding resistance category, generated by Etest, the agar dilution method or the agar breakpoint method;
- use appropriate control strains supplied by ECDC; IQC data should be submitted annually to the Euro-GASP hub for quality assurance purposes. MICs of the control strains should be within the modal MIC ranges. The Euro-GASP hub can troubleshoot if deviations from these MIC ranges are noted;
- test a core group of antimicrobials, ideally as close as possible to the core panel tested by the laboratories that use the centralised approach. As an absolute minimum, this should include ceftriaxone, cefixime and azithromycin. Additional antimicrobials which may be tested include:
  - Ciprofloxacin
  - β-lactamase/penicillinase activity
  - Gentamicin (2016 isolates)
  - Spectinomycin (2016 isolates)
- use the lowest available Etest MIC range (currently <0.002–32 mg/L) for ceftriaxone; and
- submit susceptibility data to TESSy in a timely fashion.

For the short term it is anticipated that data will be submitted by one laboratory per country. If multiple testing sites exist within a country, data should be collected and submitted by the (main) national STI laboratory contact.

Confirmation of resistant isolates

The susceptibility testing and *N. gonorrhoeae* species identification should be repeated for all isolates that are resistant to ceftriaxone (MICs>0.125 mg/L), on isolates that show elevated resistance to cefixime (MICs>0.25 mg/L), and all isolates showing high-level resistance to azithromycin (MICs>256 mg/L). Those isolates are also recommended to be sent to the Reference Laboratory Hub (London/Örebro) for further verification and molecular typing including determination of genetic resistance determinants. If necessary, a material transfer agreement can be signed by the ECDC/Reference Laboratory Hub and the owner of the isolates.

National protocol

Each country that reports susceptibility data should provide additional information on *N. gonorrhoeae* surveillance at the national level. This information is critical for the interpretation of data and ensures accurate linking of laboratory and epidemiological data. The national protocol template is available in Annex 2. The following information should be included:

- Sampling strategy: information on the geographical coverage of submitted isolates (complete, national, regional, local).
- Information on regions of the country covered (or place of residence)
- Data source and sampling frame: where were the isolates collected (STI clinics, DV clinics, GPs, hospitals etc.); how were they sampled (consecutive patients; sampling)
- Linking between AMR data and epidemiological data (e.g. isolate sent to the laboratory came with documentation containing epidemiological data; epidemiological data were requested from the source of the isolate, e.g. STI clinic, GP surgery; epidemiological data were requested by the epidemiologist)
- MIC range of testing method for each antimicrobial
- Control strains tested for each batch of media/reagent or for each antimicrobial tested
- Institute/laboratory/person submitting the AMR and epidemiological AMR data recorded in TESSy

Gonococcal susceptibility data analysis

Collated data for each report are analysed for emerging trends in AMR. The following types of analyses are currently used and a selection is included in the surveillance report. Additional analyses can be included in the report, based on emerging trends:

- Summary of isolates received and tested for each country (table)
- Overall incidence of resistance for each included antimicrobial for each testing year (line graph)
- MIC distribution by year for ceftriaxone (bar graph)
- % ceftriaxone resistant isolates by country per year (bar graph, table or, if low numbers, additional text)
- MIC distribution by year for cefixime (bar graph)
- % cefixime resistance by country per year (bar graph or map and table)
- MIC distribution by year for azithromycin (bar graph)
- % azithromycin resistance by country per year (bar graph or map and table)
- Ciprofloxacin resistance by country by year (table)
- Summary of epidemiological data received by each country (table)
- Cefixime resistance vs sexual orientation and gender (bar graph/line graph)
- Cefixime resistance vs age group and gender
- Similar analysis as for #11 and #12 for ceftriaxone and azithromycin (if examples of resistance observed).

Annex 2. Protocol for Euro-GASP implementation at the national level

Each country referring gonococcal isolates or susceptibility data should provide the following additional information to implement Euro-GASP at national level. This information is critical in interpreting data and in ensuring accurate linking of laboratory and epidemiological data.

Table A2.10. Euro-GASP information form

1. Identifying information Name: Laboratory/name of institute: Date form completed:			
2. Sampling strategy. Please provide information on the geographical coverage of isolates submitted (complete, national, regional, local)			
3. Please provide information on covered regions of the country. Alternatively, provide patient's place of residence.			
4. Please describe the source of the isolates (STI clinics, DV clinics, GPs, hospitals etc.)			
5. How are the isolates sampled (consecutively, selectively)?			
6. How were the epidemiological data obtained (e.g. isolate sent to the laboratory came with documentation containing epidemiological data; epidemiological data were requested from the source of the isolate, e.g. STI clinic, GP surgery; epidemiological data were requested by the epidemiologist)?			
7. How are the AMR data and epidemiological data linked?			
8. Institute/laboratory/person submitting the GC AMR data to TESSy.			
9. Institute/laboratory/person submitting the epidemiological data to TESSy.			
10. For laboratories performing decentralised testing, please provide the following antimicrobial information:			
	Methodology (Etest/agar dilution/breakpoint)	Agar base (GC, chocolate, DST, etc.)	MIC range (min – max)
Ceftriaxone	_____	_____	_____
Cefixime	_____	_____	_____
Azithromycin	_____	_____	_____
Ciprofloxacin	_____	_____	_____
Spectinomycin	_____	_____	_____
Gentamicin	_____	_____	_____
β-lactamase	_____	_____	_____
11. Please list the control strains tested for each media/reagent batch or for each antimicrobial tested.			

Annex 3. Protocol for centralised gonococcal antimicrobial susceptibility testing

Procedure for saving gonococcal isolates

- Label a cryovial with a study number using a permanent marker, or the labels provided.
- Using a loop, gather as much growth as possible from a pure fresh culture and re-suspend in the microbank fluid.
- Close the cryovial tightly and invert five times to mix up the organism with the fluid.
- Using a fine-tip pastette (transfer pipette), remove as much liquid as possible and close the cryovial tightly.
- Place in the freezer (preferable -70 °C, range -50 °C to -80 °C) into designated box.
- Record data for strain and study number.

Centralised testing protocol

- Isolates are shipped frozen to Public Health England, London, UK, or Örebro University Hospital, Örebro, Sweden
- The isolates are stored at -70°C or in liquid nitrogen.
- Isolates are transferred to non-selective agar (such as GCVIT with 1% Vitox (Oxoid)) and incubated for 18 to 24 hours at 36 °C in humid 5% CO_2-enriched atmosphere.
- The purity and the identity of the isolates are confirmed by Gram stain, oxidase and Maldi-TOF or the Phadebact Monoclonal GC test (Launch Diagnostics) or the API NH test (BioMérieux). A further subculture from a single colony (to avoid mixed infections) is grown.
- If there is a high level of contamination, cultures are repeatedly transferred to selective agar.
- Susceptibility testing is performed using the agar dilution breakpoint technique or Etest for ciprofloxacin, azithromycin, spectinomycin and gentamicin (spectinomycin and gentamicin tested in snapshot years only; 2016 and 2019). Suspensions of cultures aged 18 to 24 hours are prepared equivalent to McFarland standard 0.5 (approximately 10^4 colony forming units (cfu)/µL) in sterile saline. Using a multipoint inoculator, suspensions are inoculated onto GC agar plates with 1% Vitox, containing a panel of antimicrobials at the following breakpoint concentrations:

Table A3.11. Concentrations (mg/L) of antimicrobials used for the agar dilution breakpoint technique

Antimicrobial	Intermediate	Resistant
Ciprofloxacin	0.03	0.06
Azithromycin	0.25	0.5
Spectinomycin♯		64
Gentamicin♯ (no breakpoint determined yet)	1, 2, 4, 8, 16	

♯ Testing in snapshot years; 2016 and 2019

- The ceftriaxone and cefixime MICs are determined using Etests in accordance with the manufacturer's instructions.
- All isolates are tested for penicillinase production using the chromogenic reagent Nitrocefin.
- Etests are performed on isolates that are resistant to azithromycin using the agar dilution breakpoint technique.
- The following control strains are tested on the poured agar dilution plates and each batch of Etests (Table A3.12):
  - WHO G
  - WHO K
  - WHO M
  - WHO P
- WHO O (for use when testing spectinomycin resistance)

Table A3.12. WHO control strains for use in Euro-GASP – MICs and susceptibility categories obtained from Euro-GASP data

		Azithromycin		Cefixime		Ceftriaxone		Ciprofloxacin		Gentamicin		Spectinomycin	
Strain	β-lactamase	SC	MIC	SC	MIC	SC	MIC	SC	MIC	SC	MIC	SC	MIC
WHO G	NEG	S	0.25	S	≤0.016	S	0.008	R	0.125	UK	4	S	16
WHO K	NEG	S	0.25	R	0.25	S	0.064	R	>32	UK	4	S	16
WHO M	POS	I	0.5	S	≤0.016	S	0.008	R	2	UK	4	S	16

		Azithromycin		Cefixime		Ceftriaxone		Ciprofloxacin		Gentamicin		Spectinomycin	
Strain	β-lactamase	SC	MIC	SC	MIC	SC	MIC	SC	MIC	SC	MIC	SC	MIC
WHO O	POS	S	0.25	S	0.016	S	0.016	S	0.008	UK	4	R	>1024
WHO P	NEG	R	4	S	≤0.016	S	0.004	S	0.004	UK	4	S	16

SC = susceptibility category

Notes: MIC data collated from the centralised/decentralised testing centres and the Euro-GASP EQAs to establish modal MICs and SCs. Laboratories that carry out decentralised testing should also establish their own local modal MIC data. Control strain MICs should be no more than one doubling dilution different to the MICs in the Table A3.12. The modal MICs in Table A3.12 may be updated once further data are collected. Laboratories that carry out decentralised testing are ultimately responsible for their own QC data; however, QC data should always be sent to ECDC to ensure the data are within the expected range.

Bacterial growth is recorded for the agar dilution plates, and the MIC is recorded from the Etests plated. The category of resistance is determined using the following breakpoints:

Table A3.13. MIC breakpoints for specific antimicrobials

Antimicrobial	MIC breakpoint (mg/L)		
	R >	I	S ≤
Azithromycin	0.5	0.5	0.25
Cefixime	0.12		0.12
Ceftriaxone	0.12		0.12
Ciprofloxacin	0.06*	0.06**	0.03
Spectinomycin	64		64
Gentamicin	No breakpoint determined yet		

Note: European Committee on Antimicrobial Susceptibility Testing breakpoints are used (www.eucast.org/clinical_breakpoints).

**Previously 0.5 and reported as high-level resistance (R)*

*** Previously 0.12–0.5 and reported as low-level resistance (I)*

Isolates that are contaminated in the original vial or are slow to grow are re-saved.

Annex 4. GONOAMR metadata

Table A4.14. Description of the variables collected for the European Gonococcal Antimicrobial Surveillance Programme

Variable	Variable description	Coding	Validation rules
RecordId	Unique identifier for each record within and across the national surveillance system – Member State selected and generated. A unique identifier must be used for all years; repeat use of a specific identifier will replace the contents of the original entry. We suggest to include the isolate year in the RecordId to avoid overwriting data.	Text	Mandatory
RecordType	RecordType corresponding to the Subject	GONOAMR	Mandatory
RecordTypeVersion	Version of the RecordType used. **This should be reported as 7.** If you use different RecordType versions the data will be rejected.	7	
Status	Default if left out: NEW/UPDATE. If set to DELETE, the record with the given RecordId will be deleted from the TESSy database (or better stated, invalidated). If set to NEW/UPDATE or left empty, the record is newly entered into the database.	Status of reporting NEW/UPDATE or DELETE (inactivate).	
Subject	Subject corresponding to the RecordType	GONOAMR	Mandatory
ReportingCountry	The country reporting the record.	ISO coded value list	Mandatory
DataSource	The data source for AMR NG (laboratory) that the record originates from.	Coded value list; codes maintained by each Member State in the Data Source editing interface in TESSy	Mandatory
DateUsedForStatistics	Date the specimen was taken from the patient, alternatively use date received in laboratory	Preferred format: yyyy-mm-dd	Mandatory
Gender	Gender of the infected person	F = Female M = Male O = Other UNK = UNK	Mandatory
Age	Age in years of patient as reported in the national system	0-120, UNK	Mandatory
PlaceOfResidence	Place of residence of patient, NUTS level 0-3 (region)	NUTS code 0-3	
ClinicalServiceType	Type of clinical service where patient was first seen	ANC - ANC COMB - Combined service DV - Dermatology-venereology clinic ED - Hospital Emergency Dept FPC - Family Planning Clinic GP - General Practitioner GYN - Gynaecology clinic ID - Infectious disease clinic OPC - Other primary care STI - Dedicated STI clinic URO - Urology YTH - Youth clinics O - Other UNK - Unknown	
CountryOfBirth	Country of birth of patient	ISO coded value list, UNK	
ProbableCountryOfInfection	Probable country(ies) of infection, country(ies) visited during the incubation period of the reported disease. Repeatable field.	ISO coded value list, UNK	
Transmission	Mode of transmission	HETERO = Heterosexual contact MSM = MSM/homo or bisexual male MTCT = Mother-to-child transmission O = Other UNK = Unknown	Error if Transmission = MSM and Gender = F
SiteOfInfection	Site of Infection	AR = Ano-Rectal GEN = Genital PH = Pharyngeal O = Other NA = Not applicable UNK = Unknown	
PrevGono	Existing evidence about previous gonorrhoea	Y = Yes N = No UNK =Unknown	
HIVStatus	HIV Status of patient at time of diagnosis	POS = Positive POSKNOWN = Known HIV positive POSNEW = New HIV diagnosis NEG = Negative UNK = Unknown	
ConcurrentSTI	Concurrent STI	CHLAM = Chlamydia HEPB = Hepatitis B HEPC = Hepatitis C HERP = Genital herpes LGV = LGV SYPH = Syphilis WARTS = Genital warts MYCO = Mycoplasma genitalium NO = No concurrent STI UNK = Unknown	
ResultPor	*porB* allele number generated from a 490 nucleotide *porB* sequence submitted to the NG-MAST website (http://www.ng-mast.net)	Number	number should be >=1 and an integer
ResultTbpB	*tbpB* allele number generated from a 390 nucleotide *tbpB* sequence submitted to the NG-MAST website (http://www.ng-mast.net)	Number	number should be >=1 and an integer

Variable	Variable description	Coding	Validation rules
ResultSeqType	NG-MAST sequence type. A combination of the *porB* and *tbpB* allele numbers, obtained by submission to the NG-MAST website (http://www.ng-mast.net)	Number	number should be >=1 and an integer
Genogroup	NG-MAST genogroup as established via molecular typing surveys	'G' and number e.g. G1407	
DiagnosticTest	Diagnostic test used Note: this is a repeatable field and multiple columns with this variable name can be included.	CULT = culture (including methods used to identify *N. gonorrhoeae* from culture, such as MALDI-TOF, API and Phadebact) MICRO = microscopy NA = Not applicable NUCLACID = detection of nucleic acid O = Other UNK = Unknown	
TreatmentUsed	Treatment used Note: this is a repeatable field and multiple columns with this variable name can be included.	AZM = Azithromycin CFM = Cefixime CIP = Ciprofloxacin CRO = Ceftriaxone CROAZM = Ceftriaxone and Azithromycin GEN = Gentamicin O = Other SPT = Spectinomycin **CFMAZM = Cefixime and azithromycin** **DOX = Doxycycline** **PEN = Penicillin** UNK = Unknown	
PenicillinaseActivityGONO	Penicillinase activity	POS = Positive NEG = Negative UNK = Unknown	
AZMResultSign	Sign	< Less than <= Less than or equal = Equal > Greater than	
CFMResultSign	Sign		
CIPResultSign	Sign		
CROResultSign	Sign		
GENResultSign	Sign		
SPTResultSign	Sign		
AZMResultValue	Value	Number	
CFMResultValue	Value		
CIPResultValue	Value		
CROResultValue	Value		
GENResultValue	Value		
SPTResultValue	Value		
AZMSIR	Final interpretation result	S = Sensitive I = Intermediate/decreased susceptibility R = Resistant UNK = Unknown	
CFMSIR	Final interpretation result		
CIPSIR	Final interpretation result		
CROSIR	Final interpretation result		
GENSIR	Final interpretation result		
SPTSIR	Final interpretation result		
AZMTestMethod	Test method	ETEST = Etest MIC = MIC BKP = Breakpoint	
CFMTestMethod	Test method		
CIPTestMethod	Test method		
CROTestMethod	Test method		
GENTestMethod	Test method		
SPTTestMethod	Test method		

Note: Changes from previous versions are highlighted.

Annex 5. Description of variables: data source for Euro-GASP

Annex 5 contains the definitions of variables to be used as part of the data source description; includes information on laboratory methods and other aspects related to the surveillance programme.

Variable	Variable description	Coding	Validation rule
Subject mnemonic	Mnemonic of country data source	Coded value list	
Subject name	Name of country data source	Coded value list	
Comment	Short description of the surveillance system for the disease. Important details for the analysis.	Text	
Coverage	Coverage of the surveillance system	NAT = National REG = Regional LOC = Local UNK = Unknown	Mandatory
Comprehensive	Comprehensive: Reporting is based on cases occurring within the whole population of the geographical area where the surveillance system is set up (national, regional, etc.). Sentinel: Reporting is based on a selected group of physicians/hospitals/laboratories/or other institutions' notifications and/or cases occurring within a selected group of population defined by age group, gender, exposure or other selection criteria. Other: Reporting is based on a part of the population or group of physicians (or other institutions) which is not specified, for example reporting of some laboratories with no selection criteria.	Comp = Comprehensive O = Other Sent = Sentinel Unk = Unknown	Mandatory
StartSurvSys	Start year for data collection in the surveillance system.	YYYY	
InternalQualityControl	WHO-recommended strains used for quality control procedures.	WHOCS = WHO control strains OTH = Other control strains used NT = Not tested UNK = Unknown	

Annex 6. Summary of patient characteristics

Table A6.15. Patient characteristics for cases reported to Euro-GASP; overall and by country, 2016

	All countries		Austria		Belgium		Croatia		Czech Republic		Denmark		Estonia		France		Germany		Greece	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
	2660		192		99		9		90		111		2		99		109		100	
Sexual orientation & gender																				
Female	395	14.8	53	27.6	22	22.2	0	0.0	5	5.6	56	50.5	2	100	25	25.3	12	11.0	0	0.0
Male heterosexual	632	23.8	20	10.4	14	14.1	0	0.0	46	51.1	23	20.7	0	0	0	0.0	1	0.9	55	55.0
MSM	696	26.2	6	3.1	18	18.2	0	0.0	39	43.3	8	7.2	0	0	0	0.0	0	0.0	21	21.0
Unknown	937	35.2	113	58.9	45	45.5	9	100.0	0	0.0	24	21.6	0	0	74	74.7	96	88.1	24	24.0
Gender																				
All males	2256	84.8	136	70.8	76	76.8	6	66.7	85	94.4	54	48.6	0	0	74	74.7	97	89.0	100	100.0
Female	35	14.9	53	27.6	22	22.2	0	0.0	5	5.6	56	50.5	2	100	25	25.3	12	11.0	0	0.0
Unknown	9	0.3	3	1.6	1	1.0	3	33.3	0	0.0	1	0.9	0	0	0	0.0	0	0.0	0	0.0
Age																				
<25	720	27.1	36	18.8	20	20.2	2	22.2	20	22.2	56	50.5	1	50	35	35.4	28	25.7	11	11.0
≥25	1902	71.5	156	81.3	76	76.8	4	44.4	70	77.8	55	49.5	1	50	64	64.6	81	74.3	73	73.0
Unknown	38	1.4	0	0.0	3	3.0	3	33.3	0	0.0	0	0.0	0	0	0	0.0	0	0.0	16	16.0
Site of infection																				
Genital	1943	73.0	167	87.0	74	74.7	9	100.0	80	88.9	103	92.8	2	100	23	23.2	98	89.9	99	99.0
Anorectal	366	13.8	9	4.7	6	6.1	0	0.0	5	5.6	2	1.8	0	0	9	9.1	4	3.7	0	0.0
Pharyngeal	165	6.2	6	3.1		0.0	0	0.0	5	5.6	5	4.5	0	0	1	1.0	3	2.8	0	0.0
Other	100	3.8	9	4.7	16	16.2	0	0.0	0	0.0	0	0.0	0	0	61	61.6	4	3.7	0	0.0
Unknown	86	3.2	1	0.5	3	3.0	0	0.0	0	0.0	1	0.9	0	0	5	5.1	0	0.0	1	1.0
Previously diagnosed																				
No	824	31.0	38	19.8	37	37.4	0	0.0	58	64.4	106	95.5	2	100	0	0.0	2	1.8	56	56.0
Yes	171	6.4	14	7.3	6	6.1	0	0.0	32	35.6	5	4.5	0	0	0	0.0	0	0.0	21	21.0
Unknown	1665	62.6	140	72.9	56	56.6	9	100.0	0	0.0	0	0.0	0	0	99	100.0	107	98.2	23	23.0
Concurrent STI																				
Concurrent CT	203	7.6	14	7.3	0	0.0	1	11.1	14	15.6	0	0.0	1	50	10	10.1	0	0.0	0	0.0
Concurrent other	53	2.0	1	0.5	0	0.0	0	0.0	4	4.4	0	0.0	0	0	1	1.0	0	0.0	0	0.0
No concurrent STI	593	22.3	0	0.0	0	0.0	4	44.4	72	80.0	0	0.0	0	0	19	19.2	4	3.7	6	6.0
Unknown	1811	68.1	177	92.2	99	100.0	4	44.4	0	0.0	111	100.0	1	50	69	69.7	105	96.3	94	94.0
HIV status																				
Positive	156	5.9	2	1.0	5	5.1	0	0.0	11	12.2	3	2.7	0	0	1	1.0	0	0.0	4	4.0
Negative	823	30.9	17	8.9	26	26.3	0	0.0	78	86.7	55	49.5	0	0	0	0.0	0	0.0	2	2.0
Unknown	1681	63.2	173	90.1	68	68.7	9	100.0	1	1.1	53	47.7	2	100	98	99.0	109	100.0	94	94.0

Table A6.15 Patient characteristics for cases reported to Euro-GASP; overall and by country, 2016 (continued)

	Hungary		Iceland		Ireland		Italy		Latvia		Luxembourg		Malta		Netherlands		Norway		Poland	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
	94		35		100		100		8		20		25		255		111		77	
Sexual orientation & gender																				
Female	7	7.4	8	22.9	14	14.0	1	1.0	0	0.0	4	20.0	3	12.0	25	9.8	21	18.9	2	2.6
Male heterosexual	0	0.0	0	0.0	13	13.0	42	42.0	7	87.5	0	0.0	6	24.0	19	7.5	0	0.0	0	0.0
MSM	0	0.0	0	0.0	73	73.0	49	49.0	1	12.5	0	0.0	16	64.0	210	82.4	0	0.0	0	0.0
Unknown	87	92.6	27	77.1	0	0.0	8	8.0	0	0.0	16	80.0	0	0.0	1	0.4	90	81.1	75	97.4
Gender																				
All males	87	92.6	27	77.1	86	86.0	99	99.0	8	100.0	15	75.0	22	88.0	230	90.2	90	81.1	75	97.4
Female	7	7.4	8	22.9	14	14.0	1	1.0	0	0.0	4	20.0	3	12.0	25	9.8	21	18.9	2	2.6
Unknown	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	5.0	0	0.0	0	0.0	0	0.0	0	0.0
Age																				
<25	15	16.0	9	25.7	41	41.0	23	23.0	0	0.0	5	25.0	5	20.0	67	26.3	37	33.3	21	27.3
≥25	69	73.4	26	74.3	59	59.0	76	76.0	8	100.0	14	70.0	20	80.0	188	73.7	74	66.7	56	72.7
Unknown	10	10.6	0	0.0	0	0.0	1	1.0	0	0.0	1	5.0	0	0.0	0	0.0	0	0.0	0	0.0
Site of infection																				
Genital	76	80.9	0	0.0	43	43.0	91	91.0	8	100.0	4	20.0	14	56.0	96	37.6	76	68.5	65	84.4
Anorectal	0	0.0	0	0.0	42	42.0	8	8.0	0	0.0	0	0.0	10	40.0	119	46.7	28	25.2	6	7.8
Pharyngeal	2	2.1	0	0.0	15	15.0	1	1.0	0	0.0	0	0.0	1	4.0	40	15.7	2	1.8	6	7.8
Other	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Unknown	16	17.0	35	100.0	0	0.0	0	0.0	0	0.0	16	80.0	0	0.0	0	0.0	5	4.5	0	0.0
Previously diagnosed																				
No	0	0.0	0	0.0	82	82.0	79	79.0	7	87.5	0	0.0	23	92.0	0	0.0	0	0.0	0	0.0
Yes	0	0.0	0	0.0	15	15.0	11	11.0	1	12.5	0	0.0	2	8.0	0	0.0	0	0.0	0	0.0
Unknown	94	100.0	35	100.0	3	3.0	10	10.0	0	0.0	20	100.0	0	0.0	255	100.0	111	100.0	77	100.0
Concurrent STI																				
Concurrent CT	0	0.0	0	0.0	14	14.0	8	8.0	2	25.0	2	10.0	9	36.0	62	24.3	0	0.0	0	0.0
Concurrent other	0	0.0	0	0.0	6	6.0	1	1.0	4	50.0	0	0.0	3	12.0	9	3.5	0	0.0	0	0.0
No concurrent STI	0	0.0	0	0.0	78	78.0	75	75.0	2	25.0	0	0.0	12	48.0	184	72.2	0	0.0	0	0.0
Unknown	94	100.0	35	100.0	2	2.0	16	16.0	0	0.0	18	90.0	1	4.0	0	0.0	111	100.0	77	100.0
HIV status																				
Positive	0	0.0	0	0.0	10	10.0	11	11.0	1	12.5	0	0.0	2	8.0	56	22.0	0	0.0	0	0.0
Negative	0	0.0	0	0.0	86	86.0	71	71.0	0	0.0	0	0.0	22	88.0	187	73.3	0	0.0	0	0.0
Unknown	94	100.0	35	100.0	4	4.0	18	18.0	7	87.5	20	100.0	1	4.0	12	4.7	111	100.0	77	100.0

Table A6.15. Patient characteristics for cases reported to Euro-GASP; overall and by country, 2016 (end)

	Portugal		Slovakia		Slovenia		Spain		Sweden		UK	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
	110		110		106		365		100		233	
Sexual orientation & gender												
Female	9	8.2	21	19.1	8	7.5	47	12.9	21	21.0	29	12.4
Male heterosexual	0	0.0	40	36.4	33	31.1	264	72.3	0	0.0	49	21.0
MSM	3	2.7	14	12.7	57	53.8	53	14.5	0	0.0	128	54.9
Unknown	98	89.1	35	31.8	8	7.5	1	0.3	79	79.0	27	11.6
Gender												
All males	101	91.8	89	80.9	98	92.5	318	87.1	79	79.0	204	87.6
Female	9	8.2	21	19.1	8	7.5	47	12.9	21	21.0	29	12.4
Unknown	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Age												
<25	33	30.0	23	20.9	26	24.5	104	28.5	40	40.0	62	26.6
≥25	77	70.0	87	79.1	79	74.5	258	70.7	60	60.0	171	73.4
Unknown	0	0.0	0	0.0	1	0.9	3	0.8	0	0.0	0	0.0
Site of infection												
Genital	102	92.7	107	97.3	58	54.7	342	93.7	68	68.0	138	59.2
Anorectal	6	5.5	0	0.0	22	20.8	8	2.2	12	12.0	70	30.0
Pharyngeal	0	0.0	1	0.9	26	24.5	10	2.7	18	18.0	23	9.9
Other	2	1.8	2	1.8	0	0.0	4	1.1	1	1.0	1	0.4
Unknown	0	0.0	0	0.0	0	0.0	1	0.3	1	1.0	1	0.4
Previously diagnosed												
No	1	0.9	104	94.5	75	70.8	0	0.0	0	0.0	154	66.1
Yes	2	1.8	6	5.5	20	18.9	0	0.0	0	0.0	36	15.5
Unknown	107	97.3	0	0.0	11	10.4	365	100.0	100	100.0	43	18.5
Concurrent STI												
Concurrent CT	1	0.9	10	9.1	7	6.6	0	0.0	0	0.0	48	20.6
Concurrent other	0	0.0	5	4.5	13	12.3	0	0.0	0	0.0	6	2.6
No concurrent STI	2	1.8	75	68.2	47	44.3	0	0.0	0	0.0	13	5.6
Unknown	107	97.3	20	18.2	39	36.8	365	100.0	100	100.0	166	71.2
HIV status												
Positive	2	1.8	5	4.5	16	15.1	1	0.3	0	0.0	26	11.2
Negative	2	1.8	80	72.7	75	70.8	0	0.0	0	0.0	122	52.4
Unknown	106	96.4	25	22.7	15	14.2	364	99.7	100	100.0	85	36.5

Table A6.16. Clinical service type, place of residence, country of birth and probable country of infection for cases reported to Euro-GASP, by country, 2016

	Austria (n=192)	Belgium (n=99)	Croatia (n=9)	Czech Republic (n=90)	Denmark (n=111)	Estonia (n=2)	France (n=99)
Clinical service type							
ANC – antenatal clinic							
COMB – combined service							1
DV – dermatology-venereology clinic	40			90	2	1	
ED – Hospital emergency department	3						3
FPC – family planning clinic							
GP – general practitioner	10				45		63
GYN – gynaecology clinic	7					1	6
ID – infectious disease clinic	1						
OPC – other primary care	3						
STI – dedicated STI clinic	39	7			64		23
URO – urology	61						
YTH – youth clinics							
O – other	17						3
UNK – unknown	11	92	9				
Place of residence							
NUTS level 0-3 (region)[1]	UNK=192	UNK=99	HR=9	CZ=90	DK011=25	EE001=1	FR=99
					DK012=10	EE007=1	
					DK013=6		
					DK022=5		
					DK031=8		
					DK032=5		
					DK041=1		
					DK042=8		
					DK050=4		
					UNK=39		
Country of birth							
ISO coded value list[2]	AT=53	BE=55	HR=9	CU=1	BA=1	EE=2	UNK=99
	BF=1	FR=1		CZ=68	BO=1		
	BG=1	IQ=1		DE=1	CO=1		
	CN=3	NL=1		ES=2	DK=64		
	CZ=1	SY=1		HU=1	GH=1		
	DE=4	UNK=40		KR=1	GL=1		
	GH=1			PL=2	KE=1		
	HU=14			RO=1	LB=1		
	IN=2			RS=1	LT=1		
	RO=5			SK=7	UNK=39		
	TH=2			UA=3			
	UA=1			US=1			
	UK=1			VN=1			
	UNK=103						
Probable country of infection							
ISO coded value list[2]	UNK=192	BE=26	HR=9	CZ=81	DK=66	UNK=2	UNK=99
		UNK=73		ES=2	ES=1		
				FR=1	TR=1		
				LB=1	UNK=43		
				SK=1			
				TH=2			
				US=1			
				VN=1			

Table A6.16. Clinical service type, place of residence, country of birth and probable country of infection for cases reported to Euro-GASP, by country, 2015 (continued)

	Germany (n=109)	Greece (n=100)	Hungary (n=94)	Iceland (n=35)	Ireland (n=100)	Italy (n=100)	Latvia (n=8)
Clinical service type							
ANC – antenatal clinic							
COMB – combined service		12				3	8
DV – dermatology-venereology clinic	7		4	29		12	
ED – hospital emergency department	10			1			
FPC – family planning clinic							
GP – general practitioner	20			3	4		
GYN – gynaecology clinic	6					2	
ID – infectious disease clinic						1	
OPC – other primary care	9						
STI – dedicated STI clinic		88			96	56	
URO – urology	51						
YTH – youth clinics							
O – other	2		89	2		26	
UNK – unknown	4		1				
Place of residence							
NUTS level 0-3 (region)[1]	DE=8	EL=40	UNK=94	UNK=35	IE012=2	ITC11=28	LV003=1
	DE212=7	EL3=47			IE013=12	ITC15=1	LV006=6
	DE271=7	TR1=1			IE021=71	ITC47=1	LV007=1
	DE3=19	UNK=12			IE022=5	ITC4C=25	
	DE6=22				IE023=9	ITF33=1	
	DE929=18				IE025=1	ITF44=1	
	DEA1=1					ITF46=1	
	DEA13=3					ITG12=1	
	DEB1=8					ITG25=1	
	DED2=5					ITH42=1	
	DED45=5					ITH44=1	
	DED5=1					ITH55=14	
	DEF0=5					ITH58=1	
						ITI21=4	
						ITI43=11	
						ITI44=1	
						UNK=7	
Country of birth							
ISO coded value list[2]	DE=3	AF=1	HU=13	UNK=35	AR=1	AL=2	UNK=8
	UNK=106	AL=7	UNK=81		BR=11	AU=1	
		BD=1			DE=2	CO=2	
		BE=1			ES=2	CU=1	
		BG=1			HU=1	DE=1	
		EG=1			IE=47	EG=2	
		EL=79			IT=1	ES=1	
		IR=2			LB=1	FI=1	
		PK=1			LT=1	GH=1	
		PS=1			PL=2	GN=1	
		TN=1			UK=4	IT=77	
		TR=1			UNK=25	MA=2	
		UNK=3			VE=2	NG=1	
						RO=4	
						SN=1	
						UNK=2	
Probable country of infection							
ISO coded value list[2]	UNK=109	EL=74	HR=13	UNK=35	IE=63	AL;IT=1	LV=8

	Germany (n=109)	Greece (n=100)	Hungary (n=94)	Iceland (n=35)	Ireland (n=100)	Italy (n=100)	Latvia (n=8)
		TR=1	UNK=81		UK=1	AT=1	
		UNK=25			UNK=36	CO=1	
						ES=1	
						ES;IT=2	
						IT=79	
						UNK=15	

Table A6.16 Clinical service type, place of residence, country of birth and probable country of infection for cases reported to Euro-GASP, by country, 2015 (continued)

	Luxembourg (n=20)	Malta (n=25)	Netherlands (n=255)		Norway (n=111)	Poland (n=77)	Portugal (n=110)
Clinical service type							
ANC – antenatal clinic							
COMB – combined service							
DV – dermatology-venereology clinic							
ED – Hospital emergency department	1						
FPC – family planning clinic	4						
GP – general practitioner	14	1					
GYN – gynaecology clinic							
ID – infectious disease clinic							
OPC – other primary care							
STI – dedicated STI clinic		24	255				3
URO – urology	1						
YTH – youth clinics							
O – other							
UNK – unknown					111	77	107
Place of residence							
NUTS level 0-3 (region)[1]	LU=20	MT001=25	NL326=242		UNK=111	UNK=77	PT112=9
			NL327=8				PT119=3
			NL337=2				PT11A=26
			NL338=1				PT11C=1
			NL339=1				PT11D=1
			UNK=1				PT150=5
							PT16B=5
							PT16D=3
							PT16E=1
							PT16F=2
							PT16G=3
							PT16H=1
							PT170=42
							PT18=1
							PT185=5
							PT186=1
							PT300=1
Country of birth							
ISO coded value list[2]	UNK=20	BR=1	ANHH=2	KZ=1	UNK=111	UNK=77	CH=1
		CG=1	AT=2	LB=2			PT=2
		CO=1	AU=1	LV=1			UNK=107
		DE=1	BE=1	MA=1			
		IT=2	BG=1	MD=1			
		MK=1	BR=5	MX=2			
		MT=14	CO=2	NL=174			
		RS=1	CV=1	NZ=1			
		RU=1	CW=3	PH=1			
		UK=1	DDDE=5	PL=4			

	Luxembourg (n=20)	Malta (n=25)	Netherlands (n=255)		Norway (n=111)	Poland (n=77)	Portugal (n=110)
		ZA=1	DE=1	SK=1			
			DO=2	SR=7			
			EL=1	SUHH=1			
			ES=1	SY=1			
			FR=4	TH=2			
			HK=1	TR=2			
			ID=4	UK=5			
			IN=1	VE=1			
			IR=3	VN=2			
			IT=4				
Probable country of infection							
ISO coded value list[2]	UNK=20	CO=1	UNK=255		UNK=111	UNK=77	PT=3
		FR=1					UNK=107
		MT=20					
		NO=1					
		TH=1					
		UK=1					

Table A6.16. Clinical service type, place of residence, country of birth and probable country of infection for cases reported to Euro-GASP, by country, 2015 (end)

	Slovakia (n=110)	Slovenia (n=106)	Spain (n=365)	Sweden (n=100)	UK (n=233)
Clinical service type					
ANC – antenatal clinic					
COMB – combined service			358		
DV – dermatology-venereology clinic	48	64	3		
ED – Hospital emergency department			2		
FPC – family planning clinic					
GP – general practitioner	1		1		
GYN – gynaecology clinic	17	1			
ID – infectious disease clinic	2				
OPC – other primary care					
STI – dedicated STI clinic		9			233
URO – urology	38				
YTH – youth clinics					
O – other	4	32	1		
UNK – unknown				100	
Place of residence					
NUTS level 0-3 (region)[1]	SK01=69	BA=2	ES111=4	UNK=100	UKC21=1
	SK021=9	CA=1	ES113=2		UKC22=2
	SK022=3	CH=1	ES114=22		UKD33=6
	SK023=19	IT=1	ES120=45		UKD34=3
	SK032=1	SI=92	ES220=44		UKD37=1
	SK041=4	UNK=9	ES300=136		UKD71=1
	SK042=4		ES411=2		UKD72=3
	UNK=1		ES413=1		UKE32=1
			ES417=3		UKE42=11
			ES419=3		UKF14=2
			ES422=7		UKG31=13
			ES432=3		UKG32=2
			ES511=26		UKG37=3
			ES521=9		UKH21=1
			ES523=13		UKI31=4
			ES611=29		UKI32=11
			ES613=9		UKI33=11
			ES614=4		UKI34=5
			ES616=2		UKI41=14
			ES618=1		UKI42=8
					UKI43=11
					UKI44=17

	Slovakia (n=110)	Slovenia (n=106)	Spain (n=365)	Sweden (n=100)	UK (n=233)
					UKI45=18
					UKI51=3
					UKI53=1
					UKI54=1
					UKI61=2
					UKI62=1
					UKI63=4
					UKI71=4
					UKI72=4
					UKI73=4
					UKI74=2
					UKJ21=6
					UKK11=3
					UKK12=1
					UNK=48
Country of birth					
ISO coded value list[2]	SK=108	SI=65	UNK=365	UNK=100	AO=2
	VN=1	UNK=41			AU=6
	UNK=1				BD=1
					BG=1
					BR=5
					CD=1
					CH=1
					CN=1
					CO=3
					CU=1
					CY=1
					DE=4
					ES=3
					FR=2
					GW=1
					HU=1
					IE=2
					IN=1
					IR=1
					IT=8
					JM=1
					LB=2
					MY=1
					NG=1
					PK=1
					PL=3
					PT=2
					RO=1
					SK=1
					SO=1
					ST=1
					TH=1
					UK=113
					UNK=53
					US=1
					VE=1
					YE=1
					ZA=2
Probable country of infection					
ISO coded value list[2]	AT=1	AT=2	UNK=365	UNK=100	EL=1
	CZ=2	BR=1			ES=2
	HR=1	CH=1			IT=1
	HU=2	CZ=1			MA=1
	SK=60	DE=2			PH=1
	UNK=44	EL=1			PT=1
		HR=2			TH=1
		HU=1			UK=131

	Slovakia (n=110)	Slovenia (n=106)	Spain (n=365)	Sweden (n=100)	UK (n=233)
		ID=1			UNK=94
		RS=1			
		SI=44			
		TH=2			
		UNK=45			
		US=2			

UNK: unknown. [1] http://ec.europa.eu/eurostat/web/nuts/overview. [2] http://www.iso.org/iso/country_codes.

Annex 7. Statistical tables

Table A7.17 Univariate association of cefixime resistance/susceptibility and patient characteristics, Euro-GASP, 2016

	Cefixime resistance N (%, 95% CI)	Odds ratio	95% CI	P value
Site of infection (n=2574)				
Genital (1943)	47 (2.4, 1.8-3.2)	1.00		
Anorectal (366)	0 (0.0, 0.0-1.0)	0.00		
Pharyngeal (165)	1 (0.6, 0.1-3.4)	0.25	0.03-1.80	
Other (100)	5 (5.0, 2.2-11.2)	2.12	0.82-5.47	**<0.01***
Sexual orientation & gender (n=1723)				
MSM (696)	0 (0.0, 0.0-0.5)	0.00		
Male heterosexual (632)	14 (2.2, 1.3-3.7)	1.00		
Female (395)	8 (2.0, 1.0-4.0)	0.91	0.38-2.20	**<0.01***
Previous GC (n=995)				
Yes (171)	1 (0.6, 0.1-3.2)	0.48	0.06-3.77	0.70*
No (824)	10 (1.2, 0.7-2.2)	1.00		
Concurrent chlamydia (n=849)				
Yes (203)	1 (0.5, 0.1-2.7)	0.4	0.05-3.2	0.70*
No (646)	8 (1.2, 0.6-2.4)	1.00		
HIV status (n=979)				
Positive (156)	0 (0.0, 0.0-2.4)			
Negative (823)	8 (0.97, 0.5-1.9)			0.37*
Age (n=2622)				
<25 years (720)	13 (1.8, 1.1-3.1)	1.00		
≥25 years (1902)	43 (2.3, 1.7-3.0)	1.26	0.67-2.35	0.47

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

Table A7.18 Univariate association of azithromycin resistance/susceptibility and patient characteristics, Euro-GASP, 2016

	Azithromycin resistance N (%, 95% CI)	Odds ratio	95% CI	P value
Site of infection (n=2573)				
Genital (1942)	149 (7.7, 6.6-8.9)	1.00		
Anorectal (366)	17 (4.6, 2.9-7.3)	0.59	0.35-0.98	**0.04**
Pharyngeal (165)	13 (7.9, 4.7-13.0)	1.03	0.57-1.86	0.92
Other (100)	10 (10.0, 5.5-17.4)	1.34	0.68-2.63	0.40
Sexual orientation & gender (n=1722)				
MSM (696)	39 (5.6, 4.1-7.6)	1.00		
Male heterosexual (632)	48 (7.6, 5.8-10.0)	1.38	0.89-2.14	0.14
Female (394)	21 (5.3, 3.5-8.0)	0.95	0.55-1.64	0.84
Previous GC (n=994)				
Yes (171)	11 (6.4, 3.6-11.2)	0.86	0.44-1.67	0.65
No (823)	61 (7.4, 5.8-9.4)	1.00		
Concurrent chlamydia (n=848)				
Yes (202)	8 (4.0, 2.0-7.6)	0.51	0.24-1.11	0.08
No (646)	48 (7.4, 5.6-9.7)	1.00		
HIV status (n=979)				
Positive (156)	9 (5.8, 3.1-10.6)	0.91	0.44-1.88	0.79
Negative (823)	52 (6.32, 4.9-8.2)	1.00		
Age (n=2621)				
<25 years (719)	57 (7.9, 6.2-10.1)	1.00		
≥25 years (1902)	139 (7.3, 6.2-8.6)	0.92	0.66-1.26	0.59

Table A.7.19. Univariate association of ciprofloxacin resistance/susceptibility and patient characteristics, Euro-GASP, 2016

	Ciprofloxacin resistance N (%, 95% CI)	Odds ratio	95% CI	P value
Site of infection (n=2574)				
Genital (1943)	940 (48.4, 46.2-50.6)	1.00		
Anorectal (366)	132 (36.1, 31.3-41.1)	0.60	0.48-0.76	**<0.01**
Pharyngeal (165)	64 (38.8, 31.7-46.4)	0.68	0.49-0.94	**0.02**
Other (100)	44 (44.0, 34.7-53.8)	0.84	0.56-1.26	0.39
Sexual orientation & gender (n=1723)				
MSM (696)	270 (38.8, 35.2-42.5)	1.00		
Male heterosexual (632)	326 (51.6, 47.7-55.5)	1.68	1.35-2.09	**<0.01**
Female (395)	171 (43.3, 38.5-48.2)	1.20	0.94-1.55	0.15
Previous GC (n=995)				
Yes (171)	86 (50.3, 42.9-57.7)	1.46	1.05-2.04	**0.02**
No (824)	337 (40.9, 37.6-44.3)	1.00		
Concurrent chlamydia (n=849)				
Yes (203)	73 (36.0, 29.7-42.8)	0.76	0.55-1.05	0.10
No (646)	275 (42.6, 38.8-46.4)	1.00		
HIV status (n=979)				
Positive (156)	59 (37.8, 30.6-45.6)	0.93	0.66-1.33	0.70
Negative (823)	325 (39.5, 36.2-42.9)	1.00		
Age (n=2622)				
<25 years (720)	276 (38.3, 34.9-41.9)	1.00		
≥25 years (1902)	936 (49.2, 47.0-51.5)	1.56	1.31-1.86	<0.01

Table A7.20. Univariate association of penicillinase activity and patient characteristics, Euro-GASP, 2016

	Penicillinase activity N (%, 95% CI)	Odds ratio	95% CI	P value
Site of infection (n=2181)				
Genital (1789)	281 (15.7, 14.1-17.5)	1.00		
Anorectal (235)	31 (13.2, 9.5-18.1)	0.82	0.55-1.22	0.32
Pharyngeal (119)	11 (9.2, 5.2-15.8)	0.55	0.29-1.03	0.06
Other (38)**	4 (10.5, 4.2-24.1)			
Sexual orientation & gender (n=1396)				
MSM (486)	61 (12.6, 9.9-15.8)	1.00		
Male heterosexual (613)	103 (16.8, 14.1-20.0)	1.41	1.00-1.98	**0.05**
Female (297)	39 (13.1, 9.8-17.5)	1.05	0.69-1.62	0.81
Previous GC (n=958)				
Yes (161)	27 (16.8, 11.8-23.3)	1.39	0.87-2.21	0.16
No (797)	101 (12.7, 10.5-15.2)	1.00		
Concurrent chlamydia (n=556)				
Yes (123)	17 (13.8, 8.81-21.0)	0.94	0.53-1.68	0.84
No (433)	63 (14.6, 11.5-18.2)	1.00		
HIV status (n=732)				
Positive (99)	14 (14.1, 8.6-22.4)	1.06	0.58-1.96	0.85
Negative (633)	85 (13.4, 11.0-16.3)	1.00		
Age (n=2190)				
<25 years (593)	76 (12.8, 10.4-15.8)	1.00		
≥25 years (1597)	250 (15.7, 14.0-17.5)	1.26	0.96-1.66	0.10

*Note: ** Not included in univariate analysis due to low cell numbers*

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