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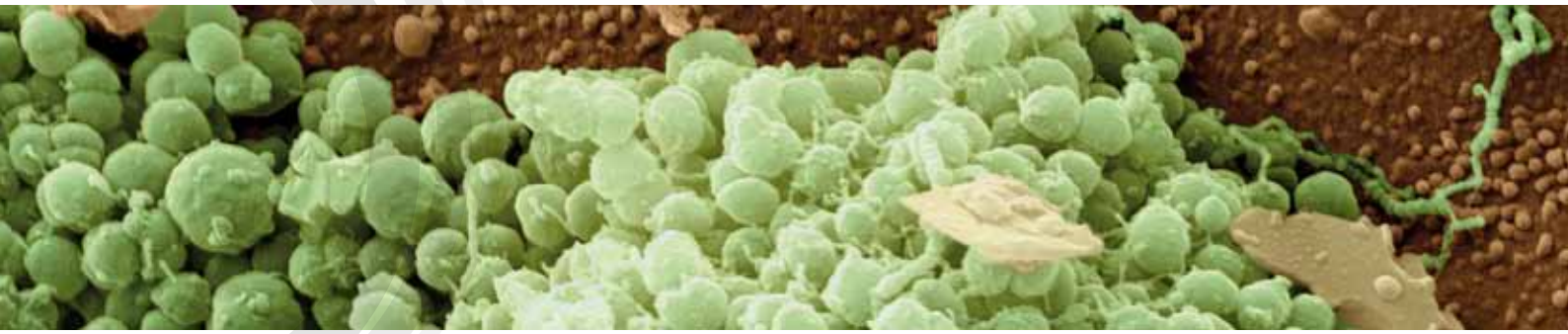

Gonococcal antimicrobial susceptibility surveillance in Europe

2015

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Abbreviations

AMR	Antimicrobial resistance
CI	Confidence interval
CT	*Chlamydia trachomatis*
DV	Dermatology-venereology
ECDC	European Centre for Disease Prevention and Control
EEA	European Economic Area
EQA	External quality assessment
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
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*
STI	Sexually transmitted infection
TESSy	The European Surveillance System
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.

During 2015, 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 and azithromycin. In addition, a β-lactamase test (nitrocefin test) was performed to detect high-level penicillin resistance. Decentralised testing took place on the premises of participating laboratories which met the quality criteria.

In 2015, 24 EU/EEA Member States participated in Euro-GASP, 17 through decentralised testing. A total of 2 134 isolates were collected and tested, covering 3% of the gonorrhoea cases reported by routine surveillance. The majority of gonococcal isolates (81.8%) were samples collected from male patients. The age of the patients ranged from under one year to 79 years, with a median age of 29 years. Overall, 29.5% of the patients were under 25 years, and male patients were significantly older than females. The anatomical site of specimen collection was mainly genital (72.9%), followed by rectal (13.5%) and pharyngeal (8.7%). Among cases with information on previous diagnosis of gonorrhoea, 17.5% had previously been diagnosed with the disease. Nineteen per cent of the patients were concurrently diagnosed with *Chlamydia trachomatis* infection. Among cases with known sexual orientation and gender, 55% were heterosexual men or women, and 45% were men who have sex with men (MSM). Among all cases, 15.3% were HIV-positive, and 96.9% of those were MSM.

The 2015 antimicrobial susceptibility data revealed stable proportions of cefixime, ciprofloxacin and azithromycin resistance compared to 2014; a slightly lower proportion of tested isolates showed cefixime resistance: 1.7% (36 out of 2 132 isolates), compared with 2.0% (42 out of 2 101 isolates) in 2014. Isolates with this phenotype were detected in nine countries, one less than in 2014 and four less than in 2013. Only one isolate with ceftriaxone resistance was detected, compared with five in 2014 and seven in 2013. Ciprofloxacin resistance has decreased since 2013 (52.9% in 2013 to 49.4% in 2015) and the level of azithromycin resistance decreased slightly from 7.9% in 2014 (169 out of 2 147 isolates) to 7.1% in 2015 (152 out of 2 134 isolates). Five isolates displayed high-level resistance to azithromycin (MIC≥256 mg/L), compared with one in 2014.

The decreasing cefixime and ceftriaxone resistance in Europe since 2010 is encouraging and is most probably in part due to the highly-effective dual-therapy regimen (ceftriaxone plus azithromycin) currently recommended. However, the level of resistance to azithromycin is of concern and threatens the effectiveness of this regimen. 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, 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 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].

Since 2009, the European Gonococcal Antimicrobial Surveillance Programme (Euro-GASP) has been coordinated by the European Centre for Disease Prevention and Control (ECDC), supported by an international network led by Public Health England (United Kingdom) and also including Örebro University Hospital (Sweden). Euro-GASP has identified decreasing susceptibility to extended-spectrum cephalosporins, and treatment failures have been documented [3], prompting the creation of a European response plan to control and manage the threat of multidrug-resistant *N. gonorrhoeae* in Europe [4].

In 2014, Euro-GASP ran a sentinel surveillance programme in 23 EU/EEA countries. The major findings were [5]:

- Cefixime resistance was observed in 2.0% of tested isolates. This represented a 2.7% decrease compared to 2013, continuing the decreasing trend observed since 2010, with the exception of a slight increase in 2013.
- Five isolates resistant to ceftriaxone were detected in Euro-GASP, compared with seven in 2013.
- The overall rate of ciprofloxacin resistance in 2014 (50.7%) was similar to the rate in 2013 (52.9%) and remained very high.
- Azithromycin resistance increased significantly from 2.8% in 2013 to 7.9% in 2014.

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 2015 gonococcal antimicrobial susceptibility sentinel surveillance.

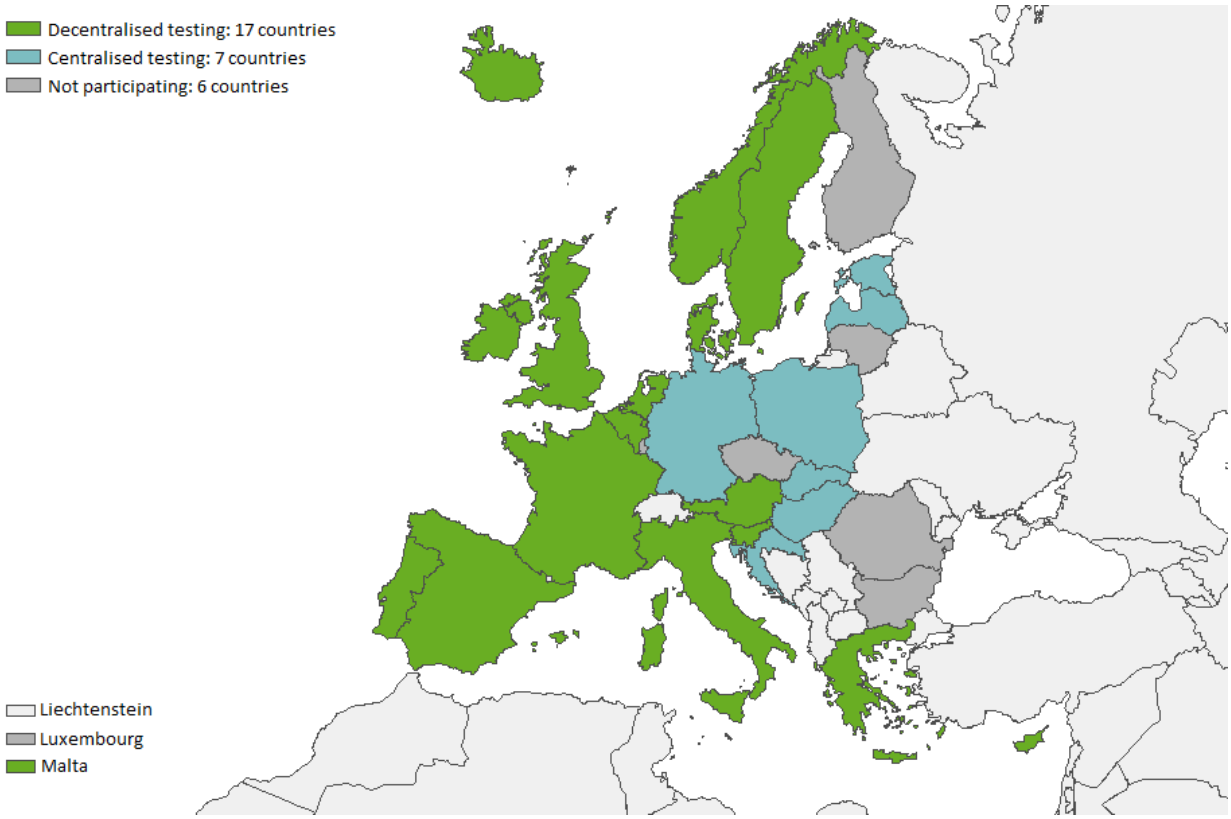
2 Methods

Participating laboratories were requested to collect gonococcal isolates between September and November 2015. 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 2015, nominated contact points for STI surveillance from 24 EU/EEA countries participated in Euro-GASP (Map 1) which was one country more (Croatia) than in 2014.

Map 1. EU/EEA Member States participating in Euro-GASP, 2015



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 for laboratories to collect the isolates between September and November. Countries with low collection numbers were allowed to include isolates collected throughout the year. However, in the United Kingdom, the collection of samples for England and Wales took place between July and September to coincide with the collection period of 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 Etests 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 difficult to acquire. However, gentamicin and spectinomycin will be tested every three years in snapshot studies, starting in 2016.

The following methods were used to determine susceptibility:

- Breakpoint (ciprofloxacin)
- Etest (azithromycin, cefixime, ceftriaxone and ciprofloxacin)
- 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); the results were interpreted using the Euro-GASP (EUCAST) standard breakpoints (Annex 3). In 2015, the Netherlands and France did not test for penicillinase production.

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, previously diagnosed with gonorrhoea and/or concurrent 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 forwarded to the national contacts, complemented with epidemiological data (where available), 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 2006 and 2015 for ceftriaxone, and 2009 to 2015 for all other graphs other than for the azithromycin MIC distribution graph, where data from 2012 to 2015 are displayed due to the high proportion of breakpoint plates (i.e. no MIC data available) prior to 2012. 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 v12.1. The Z-test was used to determine the difference between epidemiological and AMR data collected in 2015 versus 2014 and whether the differences in age distribution were statistically significant. A univariate analysis was performed to investigate associations between patient characteristics and AMR. Where datasets contained sufficient numbers, the odds ratios (OR) and 95% confidence intervals (CI) were calculated and the Pearson's chi-squared test ($\chi 2$) 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 stepwise 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, the reporting completeness was higher in 2015 in the majority of variables (Table 2). Completeness of data remained high for 'gender', 'age' and 'site of infection' (over 97%) and improved for 'mode of transmission', 'previous gonorrhoea', 'clinical service type', 'country of birth' and 'probable country of infection'. The completeness of the new variables introduced in 2014, 'diagnostic test' and 'treatment', also improved. There have been slight decreases in reporting of 'concurrent STI' and 'HIV status'.

Table 2. Completeness of reporting, Euro-GASP, 2015

Variables	2010 (n=1766)		2011 (n=1902)		2012 (n=1927)		2013 (n=1994)		2014 (n=2151)		2015 (n=2134)	
	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
Age	1740	98.5	1793	94.3	1878	97.5	1953	97.9	2106	97.9	2093	98.1
Mode of transmission	1001	56.7	1061	55.8	987	51.2	1044	52.4	1260	58.6	1301	61.0
Site of infection	1683	95.3	1785	93.8	1852	96.1	1938	97.2	2030	94.4	2080	97.5
Diagnostic test	NR	NR	NR	NR	NR	NR	NR	NR	1455	67.6	1644	77.0
Treatment	NR	NR	NR	NR	NR	NR	NR	NR	400	18.6	779	36.5
Previous gonorrhoea	691	39.1	767	40.3	757	39.3	796	39.9	826	38.4	896	42.0
Concurrent STI	779	44.1	875	46.0	800	41.5	841	42.2	851	39.6	806	37.8
Place of residence*	720	83.1	1437	75.6	1541	80.0	1436	72.0	1596	74.2	1579	74.0
Clinical service type*	610	70.4	1544	81.2	1476	76.6	1535	77.0	1619	75.3	1708	80.0
Country of birth*	392	45.3	861	45.3	988	51.3	1029	51.6	879	40.9	1132	53.0
Probable country of infection*	263	30.4	737	38.7	856	44.4	812	40.7	588	27.3	878	41.1
HIV status*	310	35.8	802	42.2	772	40.1	819	41.1	892	41.5	865	40.5

** Inclusion from 2010 second collection period only*
NR – not reported

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, 2015

Country	Coverage	Specimen source	Comprehen-siveness	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
Cyprus	Regional/capital area	DV and urology clinic	Unknown	Unknown
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, outpatients, 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	Local	STI clinic and GPs	Other	Consecutively and some selective isolates where phenotypic resistance detected
Italy	Regional	STI clinics, hospitals, university/hospital microbiology units, DV clinics	Comprehensive	Consecutively
Latvia	National	STI clinics	Other	Consecutively

Country	Coverage	Specimen source	Comprehen-siveness	Sampling method
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 outpatients	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.

During 2015, a total of 2 134 isolates were tested. This represents a decrease of 17 isolates (0.8%) compared to 2014. The number of isolates tested from each country varied from three (Cyprus) to 239 (United Kingdom) (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 2015 [5]) ranged from 1% (United Kingdom) to 44% (Croatia and Malta). Cyprus 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, Spain and the United Kingdom had less than 5% coverage, along with Denmark, for the first time, and Latvia, for the first time since 2009. Estonia, Hungary, 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 decreased from 6% in 2009 to 3% in 2014 and remained at 3% in 2015, reflecting the increase in the number of cases reported through epidemiological surveillance and likely also the 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 2015, and percentage of isolates tested compared to reported cases, by country, EU/EEA, 2009–2015

Country	Number of isolates tested 2015	Number of cases reported 2015 [6]	% isolates tested*						
			2015	2014	2013	2012	2011	2010	2009
Austria	61	NR	N/A	N/A	9	27	23	32	77
Belgium**	99	1 368	7	13	11	12	13	15	15
Croatia	8	18	44	NP	NP	NP	NP	NP	NP
Cyprus	3	1	300	50	450	50	91	52	N/A
Denmark	110	2 787	4	10	13	17	25	20	20
Estonia	18	116	16	10	NP	NP	NP	NP	NP
France**	105	1 891	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
Greece	100	237	42	NR	34	29	26	31	67
Hungary**	64	1 246	5	5	6	5	1	1	NP
Iceland	14	45	31	32	26	NP	NP	NP	NP
Ireland	110	1 281	9	8	8	7	8	14	NP
Italy	100	650	15	N/A	N/A	35	24	42	48
Latvia	9	282	3	6	7	6	5	6	3
Malta	29	66	44	41	51	55	28	62	92
Netherlands**	200	5 420	4	2	3	4	6	8	5
Norway	110	851	13	16	22	25	21	11	54
Poland	56	500	11	9	NP	NP	NP	NP	NP

Country	Number of isolates tested 2015	Number of cases reported 2015 [6]	% isolates tested*						
			2015	2014	2013	2012	2011	2010	2009
Portugal	110	427	26	55	95	92	91	81	75
Slovakia	104	341	30	26	29	38	58	70	13
Slovenia	109	73	149	134	118	104	76	64	80
Spain	167	5 006	3	3	4	3	4	5	5
Sweden	100	1 666	6	7	9	10	11	10	18
United Kingdom	239	43 658	1	1	1	1	1	1	1
Total (number or % isolates tested)	**2134**	**67 930**	**3**	**3**	**4**	**4**	**5**	**6**	**6**

** Percentages above 100% suggest underreporting of cases in epidemiological surveillance*

*** Sentinel epidemiological surveillance data*

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

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

As in previous years, the majority of gonococci (81.8%) were collected from men. Gender was reported as unknown for 13 cases (Table 5). The age of the patients ranged from <1 year to 79 years, with a median of 29 years, an interquartile range of 23 to 37 years and 29.5% of patients being under 25 years (Table 6). Males (median age 30 years) were significantly older than females (median age 24.5 years) ($p<0.001$), with the highest and lowest percentage of <25-year-olds in the female (50%) and MSM patient groups (21.6%), respectively (Table 6).

The anatomical site of specimen collection was mainly genital (72.9%); it was reported as unknown for 54 cases (Table 5).

Information on previous diagnosis of gonorrhoea was available for 896 cases (42%), 17.5% of which had had a previous infection. Information on concurrent STI was available for 806 cases (37.8%); 19% had a concurrent chlamydia infection, 6% had another STI, and 75.1% did not have any other STIs. Among 865 cases with known HIV status, 15.3% were HIV positive, 96.9% of whom were MSM (Table 5).

Table 5. Patient characteristics, 2009–2015

	2009 N (%)	2010 N (%)	2011 N (%)	2012 N (%)	2013 N (%)	2014 N (%)	2015 N (%)
Total number of isolates	1366	1766	1902	1927	1994	2151	2134
Gender							
Male	1123 (83.7)	1441 (82.4)	1505 (82.4)	1596 (83.7)	1676 (84.7)	1821 (85.1)	1736 (81.8)‡‡
Female	219 (16.3)	308 (17.6)	321 (17.6)	310 (16.3)	302 (15.3)	318 (14.9)	385 (18.2)‡‡
Unknown	24	17	76	21	16	11	13
Age (years)							
<25	422 (32.0)	599 (34.4)	572 (31.9)	617 (32.9)	554 (28.4)‡‡	605 (28.7)	617 (29.5)
≥25	898 (68.0)	1141 (65.6)	1221 (68.10)	1261 (67.1)	1399 (71.6)	1501 (71.3)	1476 (70.5)
Unknown	46	26	109	49	41	44	41
Sexual orientation and gender							
Females	219 (27.9)	308 (27.3)	321 (27.1)	310 (28)	302 (25.7)	318 (22.7)	385 (26.4)‡‡
Heterosexual males	314 (40.1)	426 (37.7)	423 (35.6)	390 (35.2)	376 (32)	485 (34.7)	419 (28.7)‡‡
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)
Unknown	582	637*	716	819	820	754	673
Site of infection							
Genital	1164 (86.5)	1426 (84.7)	1466 (82.1)	1537 (83)	1531 (79)‡‡	1549 (76.3)‡‡	1517 (72.9)‡‡
Pharyngeal	34 (2.5)	62 (3.5)	79 (4.4)	92 (5)	122 (6.3)	154 (7.6)‡‡	180 (8.7)
Anorectal	138 (10.3)	191 (11.4)	216 (12.1)	188 (10.2)	255 (13.2)‡‡	192 (9.5)	280 (13.5)‡‡
Other	9 (0.7)	7 (0.4)	24 (1.3)	35 (1.9)	30 (1.5)	135 (6.6)‡‡	103 (5.0)‡‡
Unknown	21	80	117	75	56	121	54
Previous gonorrhoea							
Yes	84 (18.1)	145 (21)	146 (19)	130 (17.2)	142 (17.8)	163 (19.7)	157 (17.5)
No	379 (81.9)	546 (79)	621 (81)	627 (82.8)	654 (82.2)	663 (80.3)	739 (82.5)
Unknown	903	1075	1135	1170	1198	1325	1238
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)
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)
No concurrent STI	433 (79.3)	579 (74.3)	638 (72.9)	564 (70.6)	603 (71.7)	640 (75.2)	605 (75.1)
Unknown	820	987	1027	1127	1153	1300	1328

	2009 N (%)	2010 N (%)	2011 N (%)	2012 N (%)	2013 N (%)	2014 N (%)	2015 N (%)
HIV status*							
Positive	N/D	48 (15.5)	141 (17.6)	104 (13.5)	144 (17.6)‡‡	172 (19.3)	132 (15.3)‡‡
Negative	N/D	262 (84.5)	661 (82.4)	668 (86.5)	675 (82.4)‡‡	720 (80.7)	733 (84.7)‡‡
Unknown	N/D	556	1100	1155	1175	1259	1269

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 to previous year (p < 0.05)

Information on sexual orientation and gender was available for 68.5% (1 461) of the cases. In these cases, 55% of the *N. gonorrhoeae* infections were reported as heterosexually acquired (47.9% females and 52.1% males) and 45% were from MSM. Forty-five additional males with unknown or other mode of transmission had *N. gonorrhoeae* isolated from the pharynx (n=20) or anogenital (n=45) region.

Some changes in the epidemiological data have been observed over the last few years (Table 5). The proportion of isolates obtained from men increased each year between 2011 (82.4%) and 2014 (85.1%). However, there was a significant decrease to 81.8% in 2015 (p<0.01). This was mirrored by a concomitant decrease in the proportion of isolates from females (from 17.6% in 2011 to 14.9% in 2014) and a significant increase in 2015 to 18.2% (p<0.01). Between 2009 and 2015, the proportion of isolates from MSM increased from 32% to 45%, whereas those from heterosexual males decreased from 40.1% to 28.7%. Compared to 2014, there was a significant decrease in the proportion of isolates from male heterosexuals in 2015 (28.7%; 2014: 34.7%) (p<0.01). In 2015, there was no significant change in the proportion of patients under 25 years of age compared to the previous year's data. There was a significant decrease in the proportion of HIV-positive patients and an increase in the proportion of HIV-negative patients in 2015 when compared to 2014 (p=0.03). The proportion of genital isolates continued to decrease (from 86.5% in 2009 to 72.9% in 2015), with a significant reduction on the previous year (p=0.013); the proportion of pharyngeal isolates continued to increase (from 2.5% in 2009 to 8.7% in 2015). Since 2014, there has been a significant increase in the proportion of anorectal isolates (p<0.01) and a significant decrease in the proportion of isolates from other sites (p=0.02).

Table 6. Patient age distribution by gender and sexual orientation, 2015

Variable	N†	Age (years)			<25 years N (%)
		Range	Mode	Median	
All patients	2093	0–79	28	29	617 (29.5)
Female	374	0–73	22	24.5	187 (50.0)
Male*	1708	0–79	28	30	426 (24.9)
Male heterosexual	417	13–79	28	30	108 (25.9)
MSM	652	16–71**	28	29	141 (21.6)

† Where information was available
** Including all males, irrespective of sexual orientation*
*** Excludes one patient with age '0' and sexual orientation as MSM; probable coding error*

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 (61.8%). There was a significant increase in the number of patients who attended STI services in 2015 compared to 2014 (p<0.01) (Table 7).

Table 7. Clinical service type attendance, 2010-2015

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 (%)
STI and sexual health clinics	444 (51.3)	1079 (56.7)	1076 (55.8)	1123 (56.3)	1136 (52.8)	1319 (61.8)
Antenatal	0	0	2 (0.1)	0	0	0
Outpatient clinic	36 (4.2)	128 (6.7)	148 (7.7)	122 (6.1)	161 (7.5)	164 (7.7)
Other	42 (4.9)	60 (3.2)	47 (2.4)	75 (3.8)	105 (4.9)	70 (3.3)
Primary care	88 (10.2)	277 (14.6)	203 (10.5)	215 (10.8)	217 (10.1)	155 (7.3)
Unknown	256 (29.6)	358 (18.8)	451 (23.4)	459 (23.0)	532 (24.7)	426 (20.0)

Note: Grouping of clinical service type as described in Table 1

Information on country of birth was supplied by 16 countries. Eleven of these countries (Belgium, Denmark, Greece, Hungary, Ireland, Italy, Malta, the Netherlands, Portugal, Slovenia 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=44). Of the 1 132 cases with known country of birth,

77.5% (n=877) had been diagnosed and reported with gonorrhoea in their country of birth, which is less than in 2014 (82.4%). In cases where country of birth and reporting country differed, the most common countries of birth (with more than five patients) were Brazil (23 patients), Albania (15 patients), Italy and Romania (eleven patients), Spain (ten patients) the United Kingdom (nine patients), Iran and Portugal (eight patients), Egypt and the United States (seven patients), and Poland (six patients). Probable country of infection data were supplied by 18 countries, three more than in 2014, with ten countries reporting patients acquiring gonorrhoea outside the reporting country. The majority of cases (95.3%; 837/878) most probably acquired gonorrhoea in the country reporting the case. Three countries most commonly reported as probable countries of infection (with ≥3 patients) and differing from the reporting country were Spain (four patients), Philippines (three patients) and the United States (three patients).

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

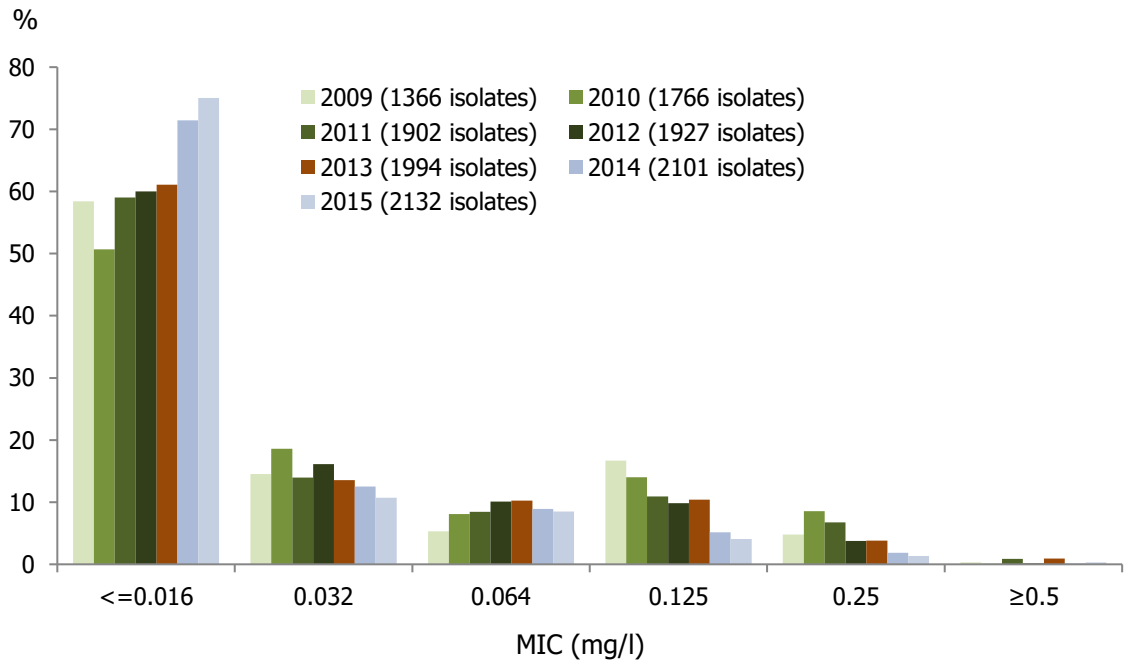
Cefixime and ceftriaxone

Cefixime resistance (MIC>0.125 mg/L) was observed in 1.7% (36/2 132) of isolates (Figure 1), remaining stable compared to 2014 (2.0%, 42 out of 2 101 isolates) (p=0.45, Z-test). A trend of decreasing cefixime resistance has been observed since 2010 (8.7%), except for 2013, when a small increase was observed. The proportion of most susceptible isolates (MIC≤0.016 mg/L) continued to increase (from 61% in 2013 to 71% in 2014 and 75% in 2015). The number of isolates displaying a MIC of ≥0.5 mg/L increased from three isolates in 2014 to seven isolates with a cefixime MIC of 0.5 mg/L in 2015 (19 isolates in 2013, three isolates in 2012 and 17 isolates in 2011).

In 2015, cefixime resistance was detected in nine countries (Map 2, Table 8), compared to 10 in 2014 and 13 in 2013. In 2014, the increase of cefixime resistance in Belgium seems to have stalled (0.9% in 2012, 12.1% in 2014 and 11.1% in 2015). An increase in cefixime resistance was observed in Greece from 5% in 2014 to 11% in 2015; a decrease in resistance was observed in Norway (5.5% in 2014 to 0.9% in 2015). Belgium and Greece were the only two countries reporting ≥5% resistance to cefixime in 2015. Hungary and Slovakia continued to have <5% cefixime resistance. Cefixime resistance was no longer detected in Denmark, France, Italy, the Netherlands and Slovenia. Germany, Ireland, Spain and the United Kingdom did not report isolates with cefixime resistance in 2014 but detected resistant isolates in 2015. Denmark saw the largest reduction in cefixime resistance: from 5.5% in 2014 to 0% in 2015.

Cefixime resistance among MSM continued to decline to 0.5% in 2015 (7.3% in 2010). Cefixime resistance has also been declining among females and heterosexual males since 2011, and this decline continues in females (1% in 2015), while in heterosexual males an increase from 1.7% in 2014 to 4.1% in 2015 was observed (Figure 2). This is mainly due to isolates with cefixime resistance from male heterosexuals reported from Belgium and Greece.

Figure 1. Distribution of MIC for cefixime in Euro-GASP, 2009–2015



Map 2. Proportion of gonococcal isolates with cefixime resistance in Europe, 2015

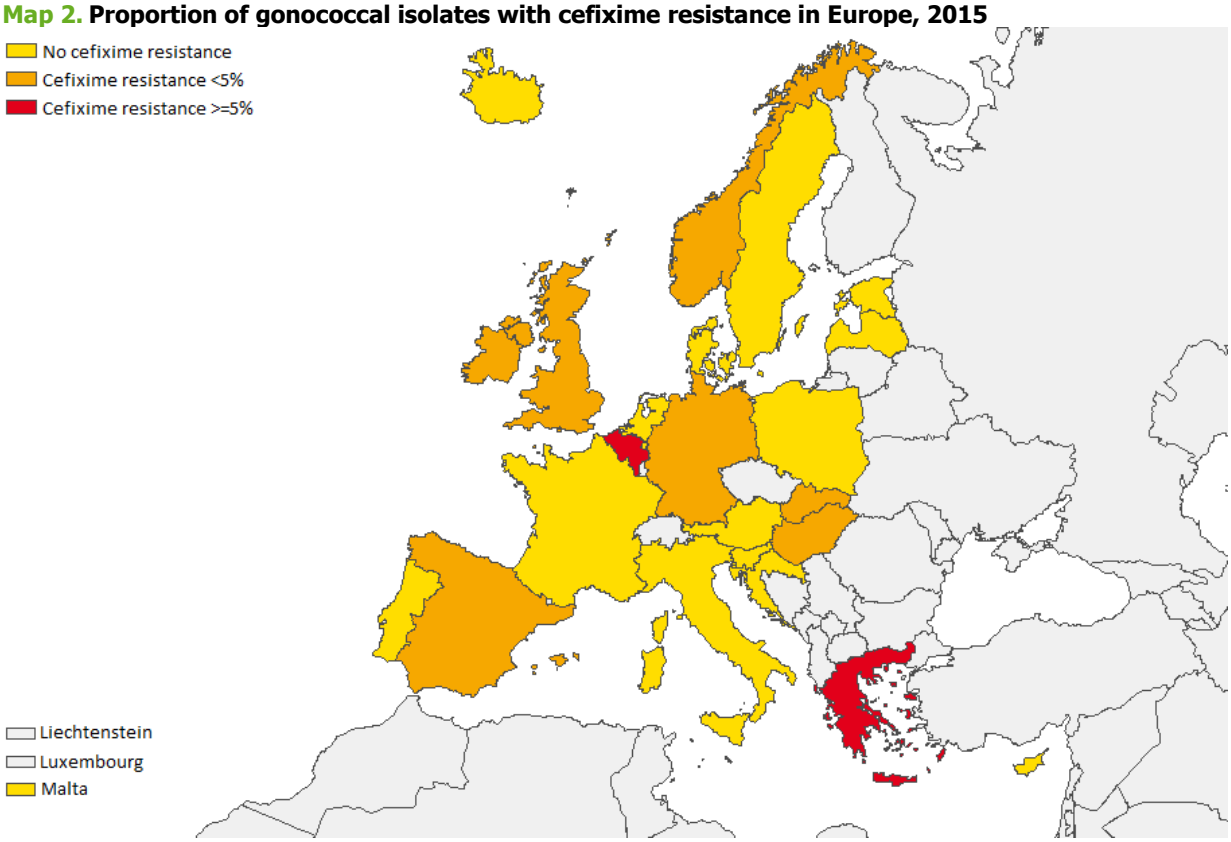
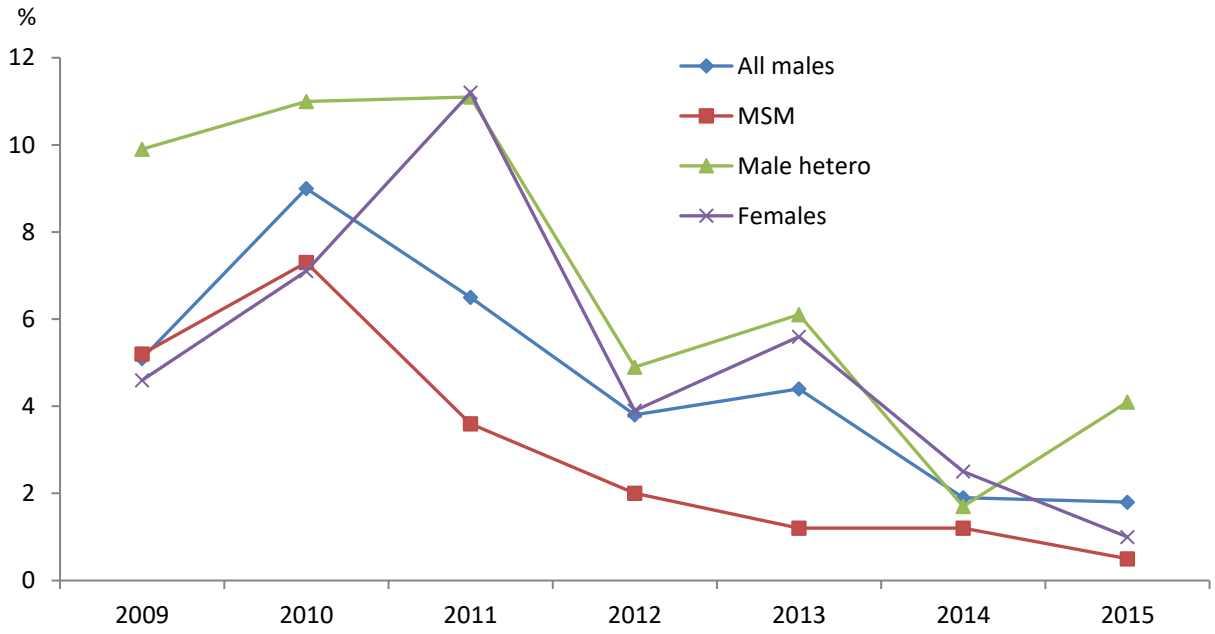


Figure 2. Percentage of isolates with cefixime resistance by gender and male sexual orientation, Euro-GASP, 2009–2015



One isolate displayed ceftriaxone resistance (MIC>0.125 mg/L) in 2015 compared with five in 2014, seven in 2013 and three in 2012 (Figure 3). The single isolate in 2015 (MIC=0.25 mg/L) was from Greece, a genital isolate from a heterosexual male, which also displayed the classical NG-MAST sequence type 1407 profile of cefixime and ciprofloxacin resistance. The MIC distribution for ceftriaxone in 2015, compared to the recent years, showed a higher proportion of more susceptible gonococcal isolates (MIC≤0.016 mg/L), along with a decreased 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, 2006–2015

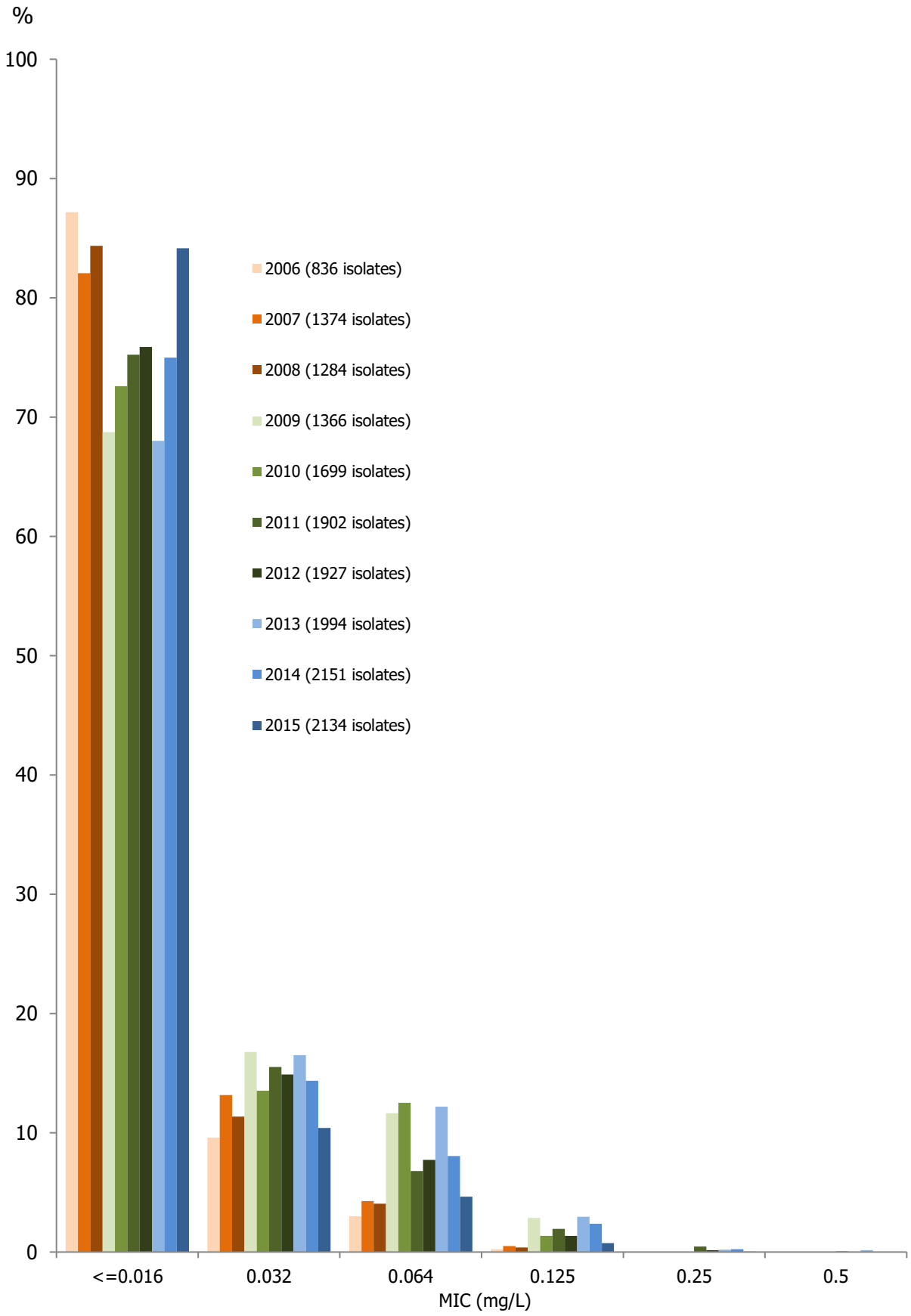


Table 8. Resistance to cefixime, azithromycin, ciprofloxacin and penicillin G (only plasmid-mediated high-level resistance; PPNG) by country, Euro-GASP, 2015

Country	Number of isolates tested	Resistance								Method of testing
		Cefixime		Azithromycin		Ciprofloxacin		PPNG		
		No.	%	No.	%	No.	%	No.	%	
Austria	61	0	0.0%	2	3.3%	40	65.6%	16	32.0% *	Decentralised – Etest
Belgium	99	11	11.1%	3	3.0%	49	49.5%	14	14.1%	Decentralised – MIC
Croatia	8	0	0.0%	0	0.0%	3	37.5%	1	12.5%	Centralised – Etest
Cyprus	3	0	0.0%	0	0.0%	2	66.7%	0	0.0%	Decentralised – Etest
Denmark	110	0	0.0%	3	2.7%	34	30.9%	10	9.1%	Decentralised – Etest
Estonia	18	0	0.0%	0	0.0%	5	27.8%	0	0.0%	Centralised – Etest
France	105	0	0.0%	6	5.7%	44	41.9%	N/T	N/T	Decentralised – Etest
Germany	109	2	1.8%	2	1.8%	67	61.5%	17	15.6%	Centralised – BKP/Etest
Greece	100	11	11.0%	22	22.0%	77	77.0%	11	11.0%	Decentralised – Etest
Hungary	64	1	1.6%	3	4.7%	34	53.1%	9	14.1%	Centralised - BKP/Etest
Iceland	14	0	0.0%	0	0.0%	4	28.6%	0	0.0%	Decentralised – Etest
Ireland	110	1	0.9%	20	18.2%	50	45.5%	12	10.9%	Decentralised – Etest
Italy	100	0	0.0%	2	2.0%	71	71.0%	7	7.0%	Decentralised – Etest
Latvia	9	0	0.0%	0	0.0%	1	11.1%	0	0.0%	Centralised - Etest
Malta	29	0	0.0%	4	13.8%	19	65.5%	7	24.1%	Decentralised – Etest
Netherlands	200	0	0.0%	8	4.0%	74	37.0%	N/T	N/T	Decentralised – Etest
Norway	110	1	0.9%	4	3.6%	64	58.7%**	27	24.5%	Decentralised – MIC
Poland	56	0	0.0%	3	5.4%	32	57.1%	3	5.4%	Centralised – Etest
Portugal	110	0	0.0%	19	17.3%	41	37.3%	9	8.2%	Decentralised – Etest
Slovakia	104	4	3.8%	2	1.9%	56	53.8%	27	26.0%	Centralised – Etest
Slovenia	109	0	0.0%	0	0.0%	38	34.9%	5	4.6%	Decentralised – Etest
Spain	167	4	2.4%	5	3.0%	109	65.3%	33	19.8%	Decentralised – Etest
Sweden	100	0	0.0%	14	14.0%	45	45.0%	13	13.0%	Decentralised – Etest
United Kingdom	239	1	0.4%	30	12.6%	95	39.7%	46	19.2%	Decentralised – MIC/Etest
Total										
Cefixime	2132	36	1.7%							
Ciprofloxacin	2133					1054	49.4%			
Azithromycin	2134			152	7.1%					
PPNG	1806							267	14.8%	
95% CI			1.2–2.3		6.1-8.3		47.3-51.5		13.2-16.5	

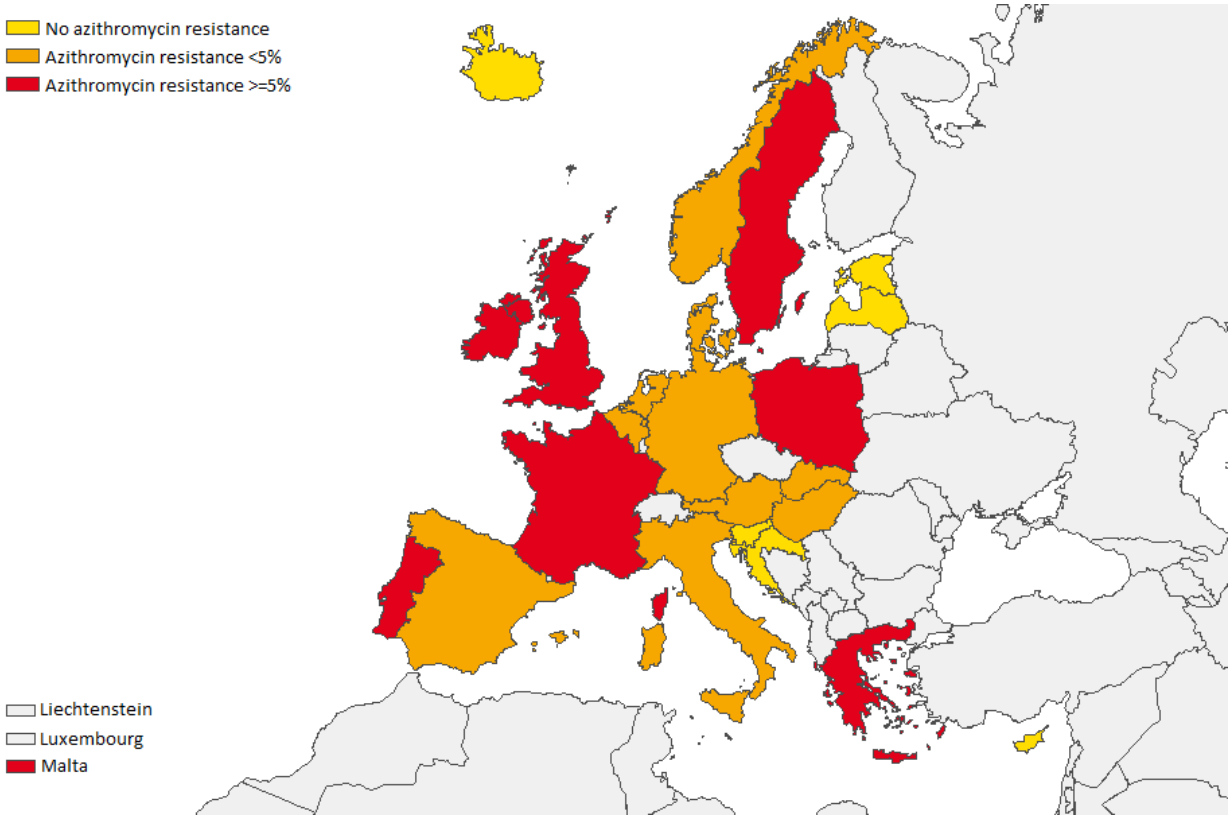
* Calculated from 50 isolates with PPNG results
** Calculated from 109 isolates with ciprofloxacin results
N/T: Not tested
BKP: Breakpoint
PPNG: Penicillinase-producing *Neisseria gonorrhoeae*

Azithromycin

In 2015, the mean resistance to azithromycin (MIC>0.5 mg/L) was 7.1% (152 out of 2 134 isolates) and ranged from 0% (Croatia, Cyprus, Estonia, Iceland, Latvia and Slovenia) to 22% in Greece (Table 8). Although overall proportion of azithromycin resistance was similar in 2015 compared to 2014 (7.9% p=0.35), five isolates displayed high-level resistance to azithromycin (MIC≥256 mg/L), which is the highest number since the beginning of Euro-GASP surveillance. These five isolates comprised three isolates from Ireland, one from Norway and one from the United Kingdom and were susceptible to the other antimicrobials tested, except for the Norwegian 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) and 2014 (n=1).

In 2015, >10% azithromycin resistance was detected in six countries: Greece, Ireland, Malta, Portugal, Sweden and the United Kingdom. More than 10% azithromycin resistance was also detected in Greece, Ireland and Portugal in 2014, with an increase in resistance to >10% observed in Malta, Sweden and the United Kingdom, where resistance was 4.8%, 4.0% and 0.9% in 2014, respectively. The highest resistance levels were detected in Greece (22.0%) and Ireland (18.2%), which is similar to 2014 when Greece and Ireland documented 39.6% and 37.6% resistance, respectively, and most isolates were submitted from men. If data from Greece and Ireland are excluded, the overall azithromycin resistance in 2015 would decrease to 4.8% (4.5% in 2014). Azithromycin resistance in France and Latvia decreased from 10.9% and 14.3% in 2015 to 5.7% and 0.0% in 2014, respectively.

Map 3. Proportion of isolates with azithromycin resistance in Europe, 2015



In 2015, azithromycin resistance remained highest in MSM and heterosexual males (both 8.1%) and lowest in females (4.9%) (Figure 4). The trend in azithromycin resistance varied by gender, although changes compared to 2014 were not significant. The MIC distribution for azithromycin in 2015 was similar to previous years; the majority of resistant isolates had an MIC of 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, 2009–2015

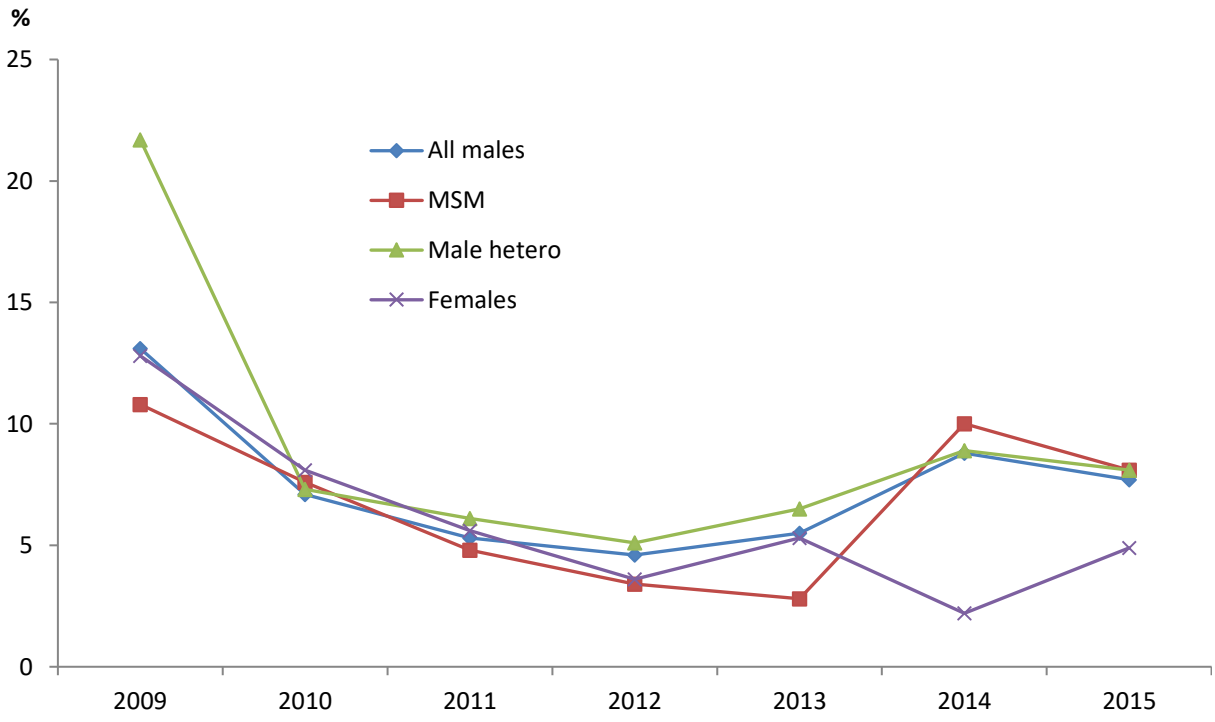
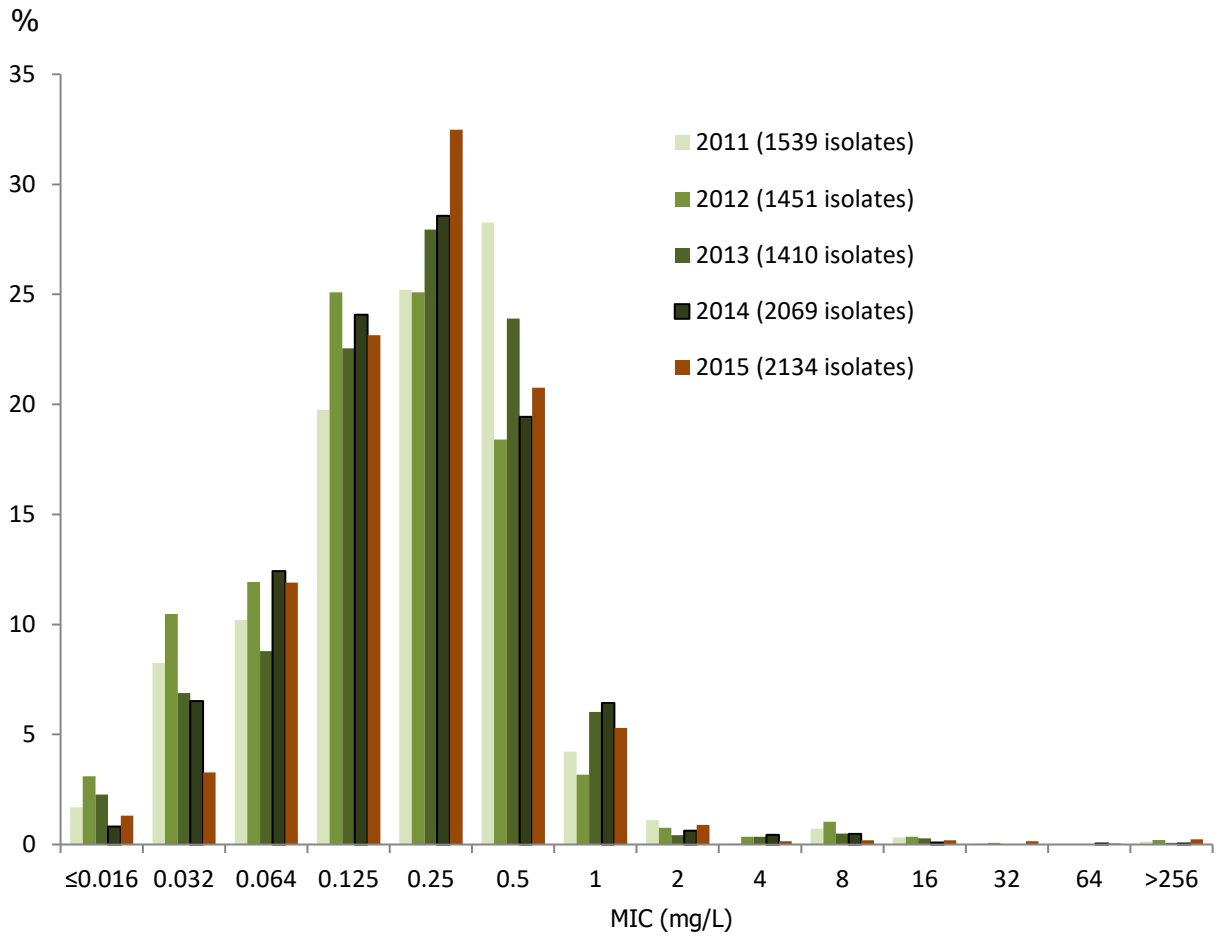


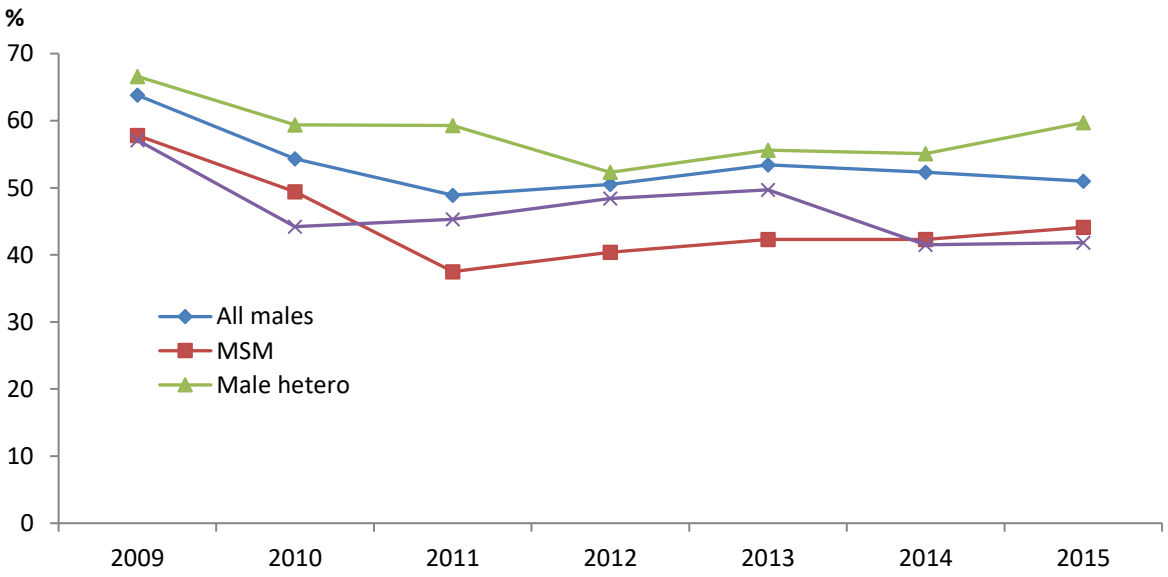
Figure 5. Distribution of MIC for azithromycin in Euro-GASP, 2011–2015



Ciprofloxacin

In 2015, resistance to ciprofloxacin (MIC>0.06 mg/L) ranged from 11.1% in Latvia to 77.0% in Greece (Table 8). Overall resistance levels in 2015 (49.4%, 1 054 out of 2 133) were similar to those in 2014 (50.7%) (p=0.4). Resistance was highest in heterosexual males (59.7%) and lowest in females (41.8%) (Figure 6).

Figure 6. Percentage of isolates with ciprofloxacin resistance by gender and male sexual orientation, Euro-GASP, 2009–2015

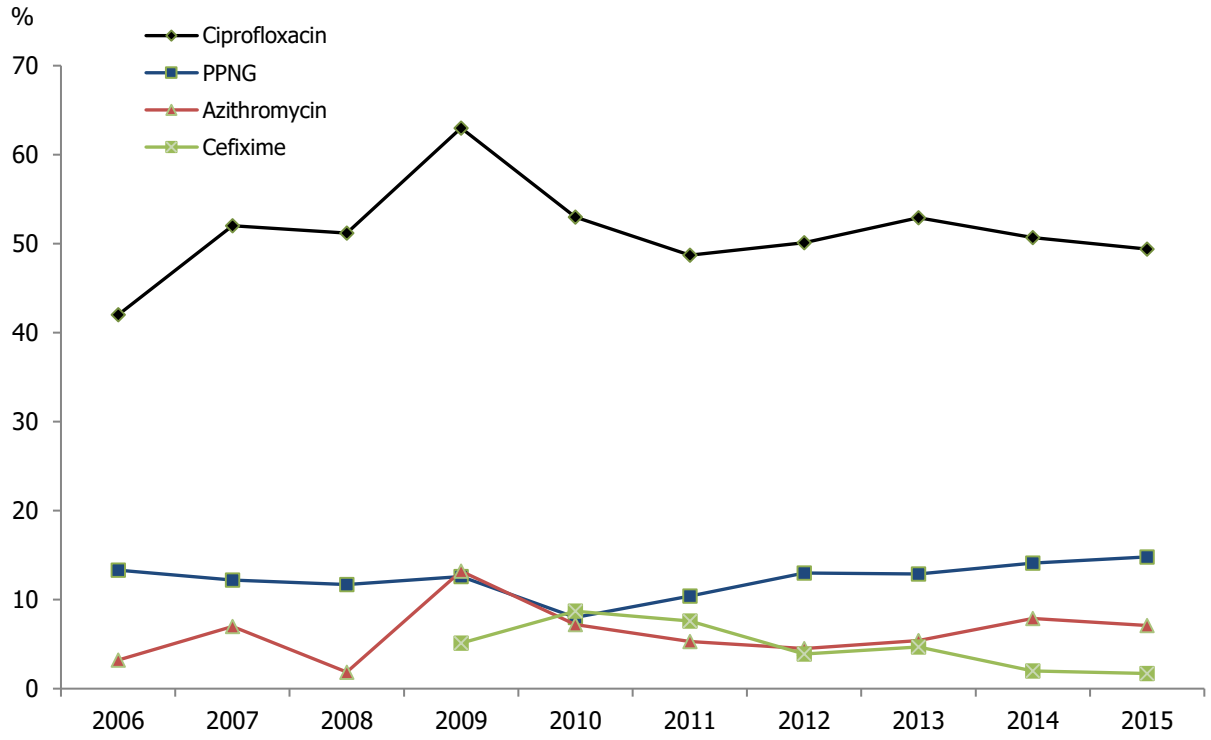


Penicillin G

High-level plasmid-mediated resistance to penicillin G (penicillinase-producing *N. gonorrhoeae* (PPNG)) ranged from 0% (Cyprus, Estonia, Iceland and Latvia) to 32% (Austria), with an overall resistance level of 14.8% (Table 8). PPNG prevalence is at the highest ever seen in Euro-GASP, and there has been a steadily increasing trend since 2010 (Figure 7).

The percentages of *N. gonorrhoeae* isolates resistant to ciprofloxacin, azithromycin, cefixime and producing β-lactamase from 2006 to 2015 are summarised in Figure 7.

Figure 7. Percentage of resistant *Neisseria gonorrhoeae* by antimicrobial and year, Euro-GASP, 2006–2015



PPNG: Penicillinase-producing N. gonorrhoeae

Associations between patient characteristics and resistance

Table 9 shows resistance by patient characteristic. Further statistical analysis of the associations is available in Annex 7. Overall, the distribution of AMR is similar across patient groups and specimen types, other than for the following exceptions:

- Cefixime: In 2015, cefixime resistance was significantly associated with male heterosexuals (4.1%, p<0.01, Fisher's exact test) when compared with females (1%) and MSM (0.5%); in comparison, no patient characteristics or infection sites were significantly associated with cefixime resistance in 2014. Additionally in 2015 genital specimens were more likely to harbour resistant strains (2.2%, p<0.01, Fisher's exact test) than anorectal (0%) and pharyngeal specimens (0%).
- Azithromycin: As in 2014, in 2015 MSM (8.1%) and male heterosexuals (8.1%) had higher levels of resistance compared to females (4.9%), but this difference was no longer significant in 2015. For the first time, an association between previous gonorrhoea and azithromycin resistance was observed in 2014 (OR 1.7, CI 1.05-2.76, p=0.03) although this did not remain significant in the multivariable analysis. In 2015, the association between previous gonorrhoea and azithromycin resistance was stronger (OR 2.07, CI 1.21-3.51, p<0.01). Unlike 2014, there was a significant association of anorectal (OR 1.65, CI 1.07-2.56, p=0.02) and pharyngeal (OR 1.79, CI 1.08-2.98, p=0.02) sites harbouring isolates with azithromycin resistance (Table A7.2, Annex 7) compared to genital sites.
- Ciprofloxacin: The only association with ciprofloxacin resistance in 2015 was being a heterosexual male compared to MSM (OR 1.87, CI 1.46-2.41, p<0.01); by contrast, between 2012 and 2014, ciprofloxacin resistance was also associated with age (≥25 years) and the absence of a concurrent chlamydial infection. As in 2012–2014, isolates from the anorectal and pharyngeal sites were less likely to harbour ciprofloxacin

resistance than isolates from genital sites (anorectal OR 0.73, CI 0.56-0.94, p=0.02; pharyngeal OR 0.48, CI 0.35-0.67, p<0.01) (Table A7.3, Annex 7).

- PPNG: Univariate analysis revealed for the first time an association between PPNG and no previous gonorrhoea infection (OR 2.45, CI 1.28-4.67, p<0.01) (Table A7.4, Annex 7). The association of PPNG and females observed in 2011–2014 and the association between PPNG and being a heterosexual male observed in 2012 and 2014 were not observed in 2015. In 2014, 2012 and 2011, isolates from the anorectal site were less likely to be PPNG than isolates from genital sites, however in 2015 isolates from the pharynx were less likely to be PPNG than isolates from genital sites (OR 0.38, CI 0.19-0.77, p<0.01) (Table A7.4, Annex 7).

Table 9. Resistance to cefixime, azithromycin, ciprofloxacin and penicillin G (only plasmid-mediated high-level resistance; PPNG) by patient characteristic, Euro-GASP, 2015

	Cefixime			Azithromycin			Ciprofloxacin			Penicillin G		
	Tested	Resistant	%	Tested	Resistant	%	Tested	Resistant	%	Tested	Resistant	%
Sexual orientation and gender												
Female	384	4	1.0	385	19	4.9	385	161	41.8	331	42	12.7
Male	1735	32	1.8	1736	133	7.7	1735	885	51.0	1462	224	15.3
Heterosexual male	419	17	4.1	419	34	8.1	419	250	59.7	398	60	15.1
MSM	657	3	0.5	657	53	8.1	657	290	44.1	495	79	16.0
Age (years)												
<25 years	617	5	0.8	617	50	8.1	617	286	46.4	519	65	12.5
≥25 years	1474	28	1.9	1476	99	6.7	1475	745	50.5	1248	198	15.9
Site of infection												
Genital	1517	34	2.2	1517	99	6.5	1516	792	52.2	1401	223	15.9
Anorectal	280	0	0.0	280	29	10.4	280	124	44.3	200	23	11.5
Pharyngeal	180	0	0.0	180	20	11.1	180	62	34.4	133	9	6.8
Other	103	2	1.9	103	3	2.9	103	52	50.5	28	4	14.3
Previous gonorrhoea												
Yes	157	3	1.9	157	22	14.0	157	71	45.2	157	11	7.0
No	739	15	2.0	739	54	7.3	739	364	49.3	739	115	15.6
Concurrent chlamydia												
Yes	153	0	0.0	153	7	4.6	153	61	39.9	101	12	11.9
No	653	7	1.1	653	44	6.7	653	306	46.9	475	75	15.8
HIV status												
Positive	132	0	0.0	132	7	5.3	132	49	37.1	89	14	15.7
Negative	731	9	1.2	733	51	7.0	733	320	43.7	569	79	13.9
Overall resistance	**2132**	**36**	**1.7**	**2134**	**152**	**7.1**	**2133**	**1054**	**49.4**	**1806**	**267**	**14.8**

3.4 Diagnostic test and treatment used

Data on which diagnostic test was used to initially identify the *N. gonorrhoeae* infection in the patients were available for 1 644 (77.0%) of 2 134 cases. The majority (90.2%, n=1 483) were diagnosed using culture-based methods, and of these, 146 patients also had microscopy performed; 119 patients had microscopy and a NAAT performed; 57 patients were diagnosed by culture and NAAT; 14 patients by culture, NAAT and another unspecified test; and six patients had culture, microscopy and another unspecified test to diagnose their infection. Of those patients that did not have culture specified as their diagnostic test, a NAAT was used to diagnose gonorrhoea in 139 patients, and 19 patients were diagnosed by microscopy (18 of these also had a NAAT). An unspecified test was used in three patients.

Data on which antimicrobials were used to treat the gonorrhoea were available for 36.5% of patients (779/2 134). Of these, 57.6% received the recommended treatment of ceftriaxone and azithromycin, although the dosages were not available. More heterosexual males received the recommended treatment (67.4%) than females (57.4%) and MSM (51.7%). Sixteen patients who received ceftriaxone and azithromycin also received an additional unspecified antimicrobial.

Among the 330 patients who did not receive the recommended treatment for their gonococcal infection [1], 228 (69.1%) were given ceftriaxone only, 46 (13.9%) cefixime only, 12 (3.6%) ciprofloxacin, 7 (2.1%) azithromycin only, four patients were given spectinomycin and azithromycin, one patient was given azithromycin and an unspecified treatment, and one patient was administered spectinomycin, azithromycin and an unspecified treatment. Thirty-one patients (9.4%) were given an unspecified treatment. Two patients given azithromycin harboured either a resistant strain (MIC=1 mg/L) or an intermediate strain (MIC=0.5 mg/L), and 7 of 12 patients given ciprofloxacin harboured ciprofloxacin-resistant strains (all with MIC>2 mg/L). It is not known whether any treatments were administered based on prior susceptibility testing results.

4 Conclusions

A decrease in cefixime resistance has been observed across the EU/EEA (from 4.7% in 2013 to 1.7% in 2015), with resistant isolates detected in just nine of the 24 countries in 2015. It should be noted that some countries submitted a low number of isolates. The increase in the proportion of highly cefixime-susceptible isolates in 2015 further showed that the gonococcal population across Europe is becoming more susceptible to cefixime. However, there was a slight increase in the number of isolates displaying a MIC of 0.5 mg/L: seven in 2015 compared with three in 2014. Cefixime resistance continues to be lowest among MSM, decreasing in females and highest in heterosexual males. Only one isolate displayed ceftriaxone resistance in 2015, compared with five in 2014 and seven in 2013. Overall, the ceftriaxone MIC distribution of the isolates in 2015 has shifted slightly to higher susceptibility than in 2014. The continuing increase in cephalosporin susceptibility is good news considering that these are among the last remaining options for treatment. Among patients for whom treatment was reported, 86.9% were administered ceftriaxone with or without azithromycin, so the use of the recommended and more appropriate ceftriaxone may have contributed to this increase in cephalosporin susceptibility.

The overall level of ciprofloxacin resistance was similar to 2014 at around 50% – a steady trend since 2010. The recent increase in azithromycin resistance stabilised at 7.1% in 2015. Neither azithromycin nor ciprofloxacin are recommended for monotherapy, unless the isolates are first shown to be susceptible. The higher azithromycin resistance in men may be driven by the use of azithromycin to treat non-gonococcal urethritis, although azithromycin is often used to treat chlamydia in both genders. The bias in Greece and Ireland towards submitting isolates from males, along with the submission of non-consecutive isolates from the Irish laboratory may skew the overall azithromycin resistance data. Accordingly, when isolates from Greece and Ireland are removed from the overall prevalence calculation, azithromycin resistance is only 4.8%. It should be noted that the majority of resistant isolates are just above the resistance breakpoint, and fluctuations in azithromycin resistance are most probably due to the proximity of isolates around this breakpoint. Azithromycin susceptibility testing is also sensitive to minor differences in agar media composition, pH and CO_2 levels. The increase of azithromycin resistance in the United Kingdom is in part due to a recent change in the media used in susceptibility testing [7].

In previous years, there was a tendency for MSM to have a lower risk of harbouring resistant isolates [8], which was supported by a lower risk of resistance 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), with a slight non-significant decrease in 2015 (8.1%, p=0.25). The cefixime and ciprofloxacin resistance levels in this group have remained fairly steady since 2013. By contrast, large decreases in azithromycin, cefixime and ciprofloxacin resistance have been demonstrated in females since 2013, although an increase in azithromycin resistance in females in 2015 has now been observed.

Even though the overall resistance levels have fallen further for cefixime and ceftriaxone in 2015, the European response plan to control the threat of multidrug-resistant *N. gonorrhoeae* in Europe [4] should continue to 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. Croatia and Northern Ireland (as part of the submission from the United Kingdom) joined Euro-GASP in 2015, thereby further strengthening the surveillance programme. Overall completeness of variables either increased or remained quite similar to 2014, in particular improvements in reporting of treatment (18.6% to 36.5%) and probable country of infection (27.3% to 41.1%) are encouraging. However, reporting needs to improve for many variables if statistical analysis of the linked susceptibility and patient data is to be robust. The increase in the proportion of isolates from females is a positive development.
- Continuing country visits to support the inclusion of additional countries and centres and 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 annually and experts (or related staff) are encouraged to participate, where required, and eventually move towards decentralised testing.
- Advocating the use of the recommended dual therapy (ceftriaxone and azithromycin) to treat gonorrhoea [1]. Even though the data completeness for 'treatment used' has improved since 2014, the level (36.5%) is still disappointing. It has shown that the majority of the patients (57.6%) received appropriate dual therapy, which is a decrease from 2014 (68.5%). Encouragingly, 86.9% 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 also needs to be monitored closely.

- Ensuring that all Euro-GASP laboratories participate in the EQA programme. Even though participation in the EQA is high, all Euro-GASP countries need to ensure full implementation to continue to produce high quality and comparable results.

The number of isolates tested in 2015 (2 134) was slightly less than in 2014 (2 151), and the percentage of isolates tested in Euro-GASP compared to the number of gonorrhoea cases reported has decreased from 6% in 2009 to 3% in both 2014 and 2015. This is mainly due to the increase in the overall number of cases diagnosed in the EU/EEA while the required isolate numbers in Euro-GASP have remained static. The number of isolates submitted to Euro-GASP might need to be increased in order to ensure that Euro-GASP data remain representative of the European *N. gonorrhoeae* population.

Even though Euro-GASP detected stabilising cefixime and ceftriaxone resistance in 2015, the high azithromycin resistance and the detection of five isolates with a very high MIC of azithromycin (≥256 mg/L), the highest number since the beginning of the Euro-GASP surveillance, is of major concern. Treatment failures are still possible, as documented by Fifer et al. [9] who described the first treatment failure with the recommended dual-therapy regimen. Therefore, continuous implementation and update of the response plan 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 2015

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 100 isolates represent less than 10% of the total number of cases of gonorrhoea (Spain, the United Kingdom and the Netherlands), additional isolated 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 (HVS)/rectal/urethral) 4. Other

Given the current view that cephalosporin resistance emerged through interaction between commensal *Neisseria* species and *N. gonorrhoeae* in the pharynx[4] 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 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 2015

As agreed at the Euro-GASP co-ordination 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.

Data collection

It is the aim of this 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 section *GONOAMR metadata set*. This section also includes the variables which are part of the 'Datasource'. Instructions on data reporting can be found in the section *Reporting to TESSy.*

Epidemiological information

A set of variables is collected as part of the enhanced STI surveillance and submitted by the national STI surveillance contact points in each country. It is suggested that the same source of epidemiological information is used for the GONOAMR surveillance database where it is possible to link the epidemiological information with the microbiological information in case-based formats.

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

1. The STI microbiology contact points who are submitting or testing isolates for AMR surveillance, will contact the national contact points for STI surveillance, who will already have collated this information, and request the information. This will require a patient identifier – at national level - to link the information. However the patient identifier should not be sent to TESSy, it should be used for internal purposes only.
2. If the information submitted by the national contact points for STI surveillance cannot be linked with gonococcal isolates and associated antimicrobial susceptibility data (e.g. if the data for STI surveillance is aggregate, or there is no shared patient identifier between the epidemiological and microbiological data), the national contact points for STI microbiology would enter the available epidemiological data that was possible for the laboratory to retrieve (either data submitted with the isolate or data is requested from place of isolate submission).

In both instances the epidemiological and microbiology data will be submitted by the national STI contact point (either microbiologist or epidemiologist or data managers) in TESSy.

Please note that the submission of AMR results should not be delayed by missing epidemiological data; AMR results should be uploaded as soon as they become available and the data can be replaced by complete data at a later stage.

Centralised testing

Where centralised testing is being carried out, the hub will send results back to member states' laboratories. Epidemiological and AMR data should then be entered in TESSy by member states. This could be done by the microbiology or epidemiological focal point as discussed above. As a quality control process, the hub will be able to check with the TESSy helpdesk on whether all cases tested have been reported through TESSy so further follow-up can be organised with individual laboratory/epidemiological contacts.

Susceptibility testing

Centralised testing

For countries participating through centralised testing, all isolates sent 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 (from 2016). Further details on the testing methodology can be found in Annex 2.

- 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 and spectinomycin will no longer be routinely tested annually as spectinomycin and gentamicin are not routinely used for treatment of gonorrhoea. Spectinomycin is also difficult to acquire. However, a snapshot of the current antibiotic susceptibility situation should be performed every third year using an extended panel of antibiotics, including spectinomycin (breakpoint or Etest on all isolates) and gentamicin (full agar dilution or Etest on all isolates), beginning in 2016. This will not be mandatory. Discussions on the value of performing snapshot testing of penicillin and tetracycline are underway. Any future testing of these antimicrobials will again not be mandatory and will not be quality assured using EQAs so a basic separate analysis will be undertaken.

Laboratories participating through centralised testing will be supported to move to decentralised testing through training and including country visits and twinning activities where necessary.

Decentralised testing

Laboratories from individual countries meeting the criteria described below will perform their own susceptibility testing and enter their results directly into TESSy. Even though susceptibility testing methods may vary, it is important that the breakpoints are harmonised and breakpoints used in Euro-GASP are adhered to (Annex 2).

Selection criteria for decentralised testing

To ensure the data quality is maintained for decentralised testing, the criteria for selecting individual laboratories to use their own methods to test the agreed core antimicrobial panel would include:

- Laboratories that perform consistently well in the EQA (no more than 5% of MIC results should 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 should 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 laboratories participating in decentralised testing wish to include data from gonococcal isolates that have undergone antimicrobial susceptibility testing in other laboratories, the decentralised laboratory needs to ensure that all submitting laboratories additionally pass the decentralised criteria stated above. Details of these additional laboratories should be provided to the hub.

If laboratories significantly change their susceptibility testing methods i.e. changing from agar dilution to Etests, then local validation data should be submitted to Euro-GASP to ensure consistency in the longitudinal data.

Procedure for decentralised testing

- Laboratories identified as suitable candidates for participating in decentralised testing are required to:
- Submit MIC data and corresponding resistance category assigned, that has been generated using Etests, the agar dilution method or the agar breakpoint method.
- Use appropriate control strains supplied by ECDC and IQC data should be submitted for quality assurance purposes.
- Test a core group of antimicrobials, ideally as close as possible to the core panel tested by the centralised approach, but as an absolute minimum to include ceftriaxone, cefixime and azithromycin:
  - Ceftriaxone
  - Cefixime
  - Azithromycin
  - Ciprofloxacin
  - ß-lactamase/penicillinase activity
- The lowest available Etest MIC range (currently <0.002-32 mg/L) should be used for ceftriaxone and cefixime
- Submit susceptibility data to TESSy in a timely fashion.

In the short-term it is anticipated that data should be submitted from one laboratory per country. If multiple testing sites exist within a country then there should be local organisation of data collection and data should be 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 cefixime and ceftriaxone (MICs>0.125 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 (MTA) can be signed by the ECDC/Reference Laboratory Hub and the owner of the isolates.

National protocol

Each country reporting susceptibility data should provide the following additional information on how surveillance for *N. gonorrhoeae* is implemented at national level. This information is critical in interpreting data and in ensuring accurate linking of laboratory and epidemiological data. The National Protocol template is available in Annex 2 and data to be provided includes:

- Sampling strategy – providing information on the geographical coverage of isolates submitted (complete, national, regional, local)
- Information on regions of the country covered (or place of residence)
- Describe the Data source and sampling frame: where the isolates come from (STI clinics, DV clinics, GPs, hospitals etc.); how they are sampled (consecutive patients; sampling)
- How is the AMR data linked to the epidemiological data (available with isolate submitted to the laboratory, data is requested from the isolate source, such as the STI clinic/GP surgery, data is requested from the epidemiologist)
- MIC range of testing method for each antimicrobial;
- Control strains tested for each media/reagent batch or for each antimicrobial tested
- Institute/Laboratory/Person submitting the AMR and epidemiological AMR data in TESSy
- Information on how the AMR data and epidemiological data are linked.

Gonococcal susceptibility data analysis

Collated data for each report will be analysed for emerging trends in AMR. The following analyses are currently performed and a selection included in the surveillance report. Additional analyses might be included in the report based on emerging trends:

1. Summary of isolates received and tested for each country (Table).
2. Overall incidence of resistance for each included antimicrobial for each testing year (line graph).
3. MIC distribution by year for ceftriaxone (bar graph).
4. % ceftriaxone resistant isolates by country per year (bar graph, table or if low numbers then description in the text).
5. MIC distribution by year for cefixime (bar graph).
6. % cefixime resistance by country per year (bar graph or map and table).
7. Ciprofloxacin resistance by country by year (Table).
8. Summary of epidemiological data received by each country (Table).
9. Cefixime resistance vs sexual orientation and gender (bar graph/line graph).
10. Cefixime resistance vs age group and gender.
11. Similar analysis as for #9 and #10 for ceftriaxone, ciprofloxacin and azithromycin (if examples of resistance observed).

Annex 2. Protocol for implementing Euro-GASP at national level

Each country referring gonococcal isolates or susceptibility data should provide the following information to implement Euro-GASP at national level. This information is crucial for the interpretation of data, and ensures that laboratory and epidemiological data are linked accurately.

1. Identifying information Name: Laboratory/institute name: 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 regions of the country covered (or 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 (available with isolate submitted to the laboratory; data requested from the isolate source, such as the STI clinic/GP surgery; data requested from the epidemiologist)?			
7. How are the AMR data and epidemiological data linked?			
8. Institute/laboratory/person submitting the GC AMR data to TESSy. Please indicate if you would like the hub to submit the data.			
9. Institute/laboratory/person submitting the epidemiological data to TESSy. Please indicate if you would like the hub to submit the data.			
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 Beta-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 5 times to mix up the organism with the fluid.
- Using a fine-tip pastette remove as much liquid as possible, and close the cryovial tightly.
- Place in the freezer (preferable −70 °C, range −50 °C to −80 °C) in a designated box.
- Record the data for that strain and study number.

Centralised testing protocol

- Isolates are shipped frozen to Public Health England, London, United Kingdom, 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 (Launch Diagnostics) test. A further subculture 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. 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 A3.1. Concentrations (mg/L) of antimicrobials used for the agar dilution breakpoint technique

Antimicrobial	Resistant (low-level)	Resistant (high-level)
Ciprofloxacin	0.06	0.5
	Intermediate	Resistant
Azithromycin	0.25	0.5

- The ceftriaxone and cefixime MICs are determined using Etests according to 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:
  - WHO G (QA07-10)
  - WHO K (QA09-03)
  - WHO M (QA09-09)
  - WHO P (QA09-05)
- 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 A3.2. 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 (0.5*;0.12 – 0.5**)		0.06

Note: European Committee on Antimicrobial Susceptibility Testing breakpoints are used (www.eucast.org/clinical_breakpoints).
** Reported as high-level resistance (R) in TESSy*
*** Reported as low-level resistance (I) in TESSy*

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

Annex 4. GONOAMR metadata

Table A4.1. 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 – MS selected and generated	Text	Mandatory
RecordType	RecordType corresponding to the Subject	GONOAMR	Mandatory
RecordTypeVersion	Version of the RecordType used. This should be reported as 6. If you use different RecordType versions the data will be rejected.	6	
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 MS 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 – antenatal clinic COMB – combined service DV – dermatology–venereology clinic ED – hospital emergency department 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	

Variable	Variable description	Coding	Validation rules
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
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
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 UNK = unknown	
PenicillinaseActivityGONO	Penicillinase activity	POS = positive NEG = negative UNK = unknown	
AZMResultSign	Sign	< Less than <= Less than or equal = Equal > Greater than >= Greater than or equal	
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		

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 A6.1. Patient characteristics for cases reported to Euro-GASP; overall and by country, 2015

	All countries		Austria		Belgium		Croatia		Cyprus		Denmark		Estonia		France		Germany	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
	2134		61		99		8		3		110		18		105		109	
Sexual orientation and gender																		
Female	385	18.0	47	77.0	19	19.2	1	12.5	0	0.0	47	42.7	7	38.9	25	23.8	15	13.8
Male heterosexual	419	19.6	13	21.3	12	12.1	0	0.0	0	0.0	41	37.3	1	5.6	0	0.0	1	0.9
MSM	657	30.8	0	0.0	17	17.2	0	0.0	0	0.0	7	6.4	2	11.1	0	0.0	2	1.8
Unknown	673	31.5	0	0.0	51	51.5	7	87.5	3	100.0	15	13.6	8	44.4	80	76.2	91	83.5
Gender																		
All males	1736	81.3	13	21.3	78	78.8	7	87.5	3	100.0	63	57.3	11	61.1	80	76.2	94	86.2
Female	385	18.0	47	77.0	19	19.2	1	12.5	0	0.0	47	42.7	7	38.9	25	23.8	15	13.8
Unknown	13	0.6	1	1.6	2	2.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Age (years)																		
<25	617	28.9	28	45.9	23	23.2	3	37.5	1	33.3	55	50.0	8	44.4	35	33.3	25	22.9
≥25	1476	69.2	33	54.1	72	72.7	5	62.5	0	0.0	55	50.0	10	55.6	70	66.7	84	77.1
Unknown	41	1.9	0	0.0	4	4.0	0	0.0	2	66.7	0	0.0	0	0.0	0	0.0	0	0.0
Site of infection																		
Genital	1517	71.1	55	90.2	78	78.8	NR	NR	3	100.0	103	93.6	16	88.9	23	21.9	104	95.4
Anorectal	280	13.1	5	8.2	8	8.1	NR	NR	0	0.0	3	2.7	1	5.6	5	4.8	2	1.8
Pharyngeal	180	8.4	1	1.6	0	0.0	NR	NR	0	0.0	2	1.8	1	5.6	2	1.9	1	0.9
Other	103	4.8	0	0.0	12	12.1	NR	NR	0	0.0	1	0.9	0	0.0	75	71.4	2	1.8
Unknown	54	2.5	0	0.0	1	1.0	NR	NR	0	0.0	1	0.9	0	0.0	0	0.0	0	0.0
Previously diagnosed																		
No	739	34.6	0	0.0	33	33.3	NR	NR	0	0.0	103	93.6	0	0.0	0	0.0	3	2.8
Yes	157	7.4	0	0.0	6	6.1	NR	NR	0	0.0	7	6.4	1	5.6	0	0.0	0	0.0
Unknown	1074	58.0	61	100.0	60	60.6	NR	NR	3	100.0	0	0.0	17	94.4	105	100.0	106	97.2
Concurrent STI																		
Concurrent CT	153	7.2	0	0.0	11	11.1	2	25.0	0	0.0	0	0.0	5	27.8	11	10.5	1	0.9
Concurrent other	48	2.2	0	0.0	5	5.1	1	12.5	0	0.0	0	0.0	0	0.0	1	1.0	0	0.0
No concurrent STI	605	28.4	0	0.0	10	10.1	0	0.0	0	0.0	0	0.0	0	0.0	18	17.1	5	4.6
Unknown	1328	62.2	61	100.0	73	73.7	5	62.5	3	100.0	110	100.0	13	72.2	75	71.4	103	94.5
HIV status																		
Positive	132	6.2	0	0.0	8	8.1	0	0.0	0	0.0	1	0.9	0	0.0	0	0.0	1	0.9
Negative	733	34.3	0	0.0	19	19.2	0	0.0	0	0.0	66	60.0	0	0.0	0	0.0	2	1.8
Unknown	1269	59.5	61	100.0	72	72.7	8	100.0	3	100.0	43	39.1	18	100.0	105	100.0	106	97.2

NR = Not reported any data in this category

Table A6.1. Patient characteristics for cases reported to Euro-GASP; overall and by country, 2015 (continued)

	Greece		Hungary		Iceland		Ireland		Italy		Latvia		Malta		Netherlands		Norway	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
	100		64		14		110		100		9		29		200		110	
Sexual orientation and gender																		
Female	0	0.0	8	12.5	1	7.1	8	7.3	2	2.0	3	33.3	4	13.8	19	9.5	20	18.2
Male heterosexual	66	66.0	0	0.0	0	0.0	9	8.2	36	36.0	6	66.7	6	20.7	19	9.5	0	0.0
MSM	20	20.0	1	1.6	0	0.0	92	83.6	57	57.0	0	0.0	18	62.1	162	81.0	0	0.0
Unknown	14	14.0	55	85.9	13	92.9	1	0.9	5	5.0	0	0.0	1	3.4	0	0.0	90	81.8
Gender																		
Male	100	100.0	55	85.9	13	92.9	102	92.7	97	97.0	6	66.7	25	86.2	181	90.5	83	75.5
Female	0	0.0	8	12.5	1	7.1	8	7.3	2	2.0	3	33.3	4	13.8	19	9.5	20	18.2
Unknown	0	0	1	1.6	0	0.0	0	0.0	1	1.0	0	0.0	0	0.0	0	0.0	7	6.4
Age (years)																		
<25	21	21.0	14	21.9	3	21.4	31	28.2	18	18.0	4	44.4	9	31.0	54	27.0	28	25.5
≥25	68	68.0	40	62.5	11	78.6	79	71.8	79	79.0	5	55.6	17	58.6	146	73.0	82	74.5
Unknown	11	11.0	10	15.6	0	0.0	0	0.0	3	3.0	0	0.0	3	10.3	0	0.0	0	0.0
Site of infection																		
Genital	99	99.0	51	79.7	0	0.0	30	27.3	84	84.0	9	100.0	19	65.5	81	40.5	88	80.0
Anorectal	0	0.0	0	0.0	0	0.0	36	32.7	13	13.0	0	0.0	7	24.1	74	37.0	9	8.2
Pharyngeal	0	0.0	0	0.0	0	0.0	44	40.0	1	1.0	0	0.0	3	10.3	45	22.5	5	4.5
Other	0	0.0	1	1.6	0	0.0	0	0.0	2	2.0	0	0.0	0	0.0	0	0.0	0	0.0
Unknown	1	1.0	12	18.8	14	100.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	8	7.3
Previously diagnosed																		
No	57	57.0	0	0.0	0	0.0	91	82.7	82	82.0	9	100.0	26	89.7	0	0.0	0	0.0
Yes	23	23.0	0	0.0	0	0.0	17	15.5	11	11.0	0	0.0	3	10.3	0	0.0	0	0.0
Unknown	20	20.0	64	100.0	14	100.0	2	1.8	7	7.0	0	0.0	0	0.0	200	100.0	110	100.0
Concurrent STI																		
Concurrent CT	0	0	0	0.0	0	0.0	12	10.9	8	8.0	5	55.6	3	10.3	41	20.5	0	0.0
Concurrent other	0	0	0	0.0	0	0.0	3	2.7	1	1.0	0	0.0	13	44.8	15	7.5	0	0.0
No concurrent STI	5	5.0	0	0.0	0	0.0	93	84.5	78	78.0	4	44.4	13	44.8	144	72.0	0	0.0
Unknown	95	95.0	100	100.0	14	100.0	2	1.8	13	13.0	0	0.0	0	0.0	0	0.0	110	100.0
HIV status																		
Positive	1	1.0	0	0.0	0	0.0	21	19.1	14	14.0	0	0.0	5	17.2	43	21.5	0	0.0
Negative	5	5.0	1	1.6	14	100.0	87	79.1	73	73.0	9	100.0	22	75.9	154	77.0	0	0.0
Unknown	94	94.0	63	98.4	0	0.0	2	1.8	13	13.0	0	0.0	2	6.9	3	1.5	110	100.0

** Includes one patient with 'other'*

Table A6.1. Patient characteristics for cases reported to Euro-GASP; overall and by country, 2015 (end)

	Poland		Portugal		Slovakia		Slovenia		Spain		Sweden		United Kingdom	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
	56		110		104		109		167		100		239	
Sexual orientation and gender														
Female	NR	NR	28	25.5	20	19.2	4	3.7	32	19.2	NR	NR	30	12.6
Male heterosexual	NR	NR	0	0.0	43	41.3	32	29.4	99	59.3	NR	NR	35	14.6
MSM	NR	NR	7	6.4	13	12.5	64	58.7	34	20.4	NR	NR	161	67.4
Unknown	NR	NR	75	68.2	28	26.9	9	8.3	1	1.2	NR	NR	12	5.0
Gender														
Male	55	98.2	82	74.5	84	80.8	105	96.3	134	80.2	56	56.0	209	87.4
Female	1	1.8	28	25.5	20	19.2	4	3.7	32	19.2	44	44.0	30	12.6
Unknown	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6	0	0.0	0	0.0
Age (years)														
<25	10	17.9	51	46.4	19	18.3	24	22.0	42	25.1	45	45.0	66	27.6
≥25	46	82.1	59	53.6	84	80.8	84	77.1	125	74.9	55	55.0	167	69.9
Unknown	0	0.0	0	0.0	1	1.0	1	0.9	0	0.0	0	0.0	6	2.5
Site of infection														
Genital	54	96.4	107	97.3	100	96.2	55	50.5	149	89.2	62	62.0	147	61.5
Anorectal	0	0.0	0	0.0	2	1.9	26	23.9	12	7.2	11	11.0	66	27.6
Pharyngeal	2	3.6	2	1.8	0	0.0	28	25.7	4	2.4	20	20.0	19	7.9
Other	0	0.0	1	0.9	2	1.9	0	0.0	2	1.2	1	1.0	4	1.7
Unknown	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	6	6.0	3	1.3
Previously diagnosed														
No	NR	NR	7	6.4	94	90.4	80	73.4	0	0.0	NR	NR	154	64.4
Yes	NR	NR	0	0.0	10	9.6	16	14.7	0	0.0	NR	NR	63	26.4
Unknown	NR	NR	103	93.6	0	0.0	13	11.9	167	100.0	NR	NR	22	9.2
Concurrent STI														
Concurrent CT	NR	NR	0	0.0	6	5.8	7	6.4	0	0.0	NR	NR	41	17.2
Concurrent other	NR	NR	0	0.0	2	1.9	5	4.6	0	0.0	NR	NR	2	0.8
No concurrent STI	NR	NR	7	6.4	80	76.9	89	81.7	0	0.0	NR	NR	59	24.7
Unknown	NR	NR	103	93.6	16	15.4	8	7.3	167	100.0	NR	NR	137	57.3
HIV status														
Positive	NR	NR	1	0.9	1	1.0	6	5.5	0	0.0	NR	NR	30	12.6
Negative	NR	NR	6	5.5	87	83.7	90	82.6	0	0.0	NR	NR	98	41.0
Unknown	NR	NR	103	93.6	16	15.4	13	11.9	167	100.0	NR	NR	111	46.4

NR = Did not report data in this category

Table A6.2. Clinical service type, place of residence, country of birth and probable country of infection for cases reported to Euro-GASP, by country, 2015

	Austria (n=61)	Belgium (n=99)	Croatia (n=8)	Cyprus (n=3)	Denmark (n=110)	Estonia (n=18)	France (n=105)	Germany (n=109)
Clinical service types								
ANC – antenatal clinic	0	0	0	0	0	0	0	0
COMB – combined service	0	0	0	0	0	1	0	0
DV – dermatology-venereology clinic	0	0	0	0	0	4	0	7
ED – Hospital emergency department	0	0	0	0	0	0	7	0
FPC – family planning clinic	0	0	0	0	0	0	0	0
GP – general practitioner	0	0	5	0	53	3	70	8
GYN – gynaecology clinic	0	0	0	0	1	6	6	13
ID – infectious disease clinic	0	0	0	0	0	0	1	1
OPC – other primary care	0	0	3	0	0	0	0	0
STI – dedicated STI clinic	61	10	0	0	55	0	16	0
URO – urology	0	0	0	1	0	2	0	66
YTH – youth clinics	0	0	0	0	0	0	0	0
O – other	0	0	0	0	1	0	5	8
UNK – unknown	0	89	0	2	0	2	0	6
Place of residence								
NUTS level 0-3 (region)[1]	UNK=61	UNK=99	HR=8	CY000=1	DK011=37	EE001=9	FR=105	DE=7
				UNK=2	DK012=11	EE004=7		DE3=16
					DK013=7	EE008=2		DE6=20
					DK021=5			DE11=1
					DK022=3			DE212=4
					DK031=8			DE271=6
					DK032=11			DE929=9
					DK041=4			DEA=1
					DK042=16			DEA13=5
					DK050=6			DEB1=10
					UNK=2			DED2=7
								DED2D=1
								DED45=2
								DED51=9
								DED52=4
								DEF0=7
Country of birth								
ISO coded value list[2]	UNK=61	AL=1	HR=8	CY=1	BA=1, BR=1	EE=18	UNK=105	DE=9
		BD=1		UNK=2	DE=1			UNK=100
		BE=34			DK=94			
		IN=1			GL=2, IN=1			
		MA=1			IQ=2, IR=1			
		NL=1			PH=1, RU=1			
		UNK=60			SE=1, SO=1			
					SY=1, TR=1			
					UNK=1			
Probable country of infection								
ISO coded value list[2]	UNK=61	BE=20	HR=8	CY=1	BR=1	AU=1	UNK=105	DE=3
		CN=1		UNK=2	DK=88	UNK=17		UNK=106
		IN=1			ID=1, JM=1			
		UNK=77			LK=1, PH=1			
					TR=1, US=1			
					UNK=15			

UNK: unknown

Table A6.2. Clinical service type, place of residence, country of birth and probable country of infection for cases reported to Euro-GASP, by country, 2015 (continued)

	Greece (n=100)	Hungary (n=64)	Iceland (n=14)	Ireland (n=110)	Italy (n=100)	Latvia (n=9)	Malta (n=29)	Netherlands (n=200)
Clinical service types								
See first table for codes	COMB=14	DV=7	GP=2	GP=3	COMB=2	COMB=7	GP=2	STI=200
	STI=86	OPC=2	STI=10	STI=107	DV=21	DV=1	STI=27	
		O=3	O=2		GYN=1	OPC=1		
		UNK=52			ID=2			
					STI=64			
					O=10			
Place of residence								
NUTS level 0–3 (region)[1]	EL=31	HU=26	IS=13	IE02=4	ITC11=41	LV003=3	MT001=27	NL121=1
	EL112=1	UNK=38	UNK=1	IE011=1	ITC16=2	LV006=6	BG=1	NL123=1
	EL300=55			IE012=3	ITC18=1		UNK=1	NL226=1
	RO126=1			IE021=91	ITC47=2			NL230=2
	UNK=12			IE022=6	ITC4A=1			NL310=4
				IE023=1	ITC4C=25			NL322=2
				IE024=1	ITF46=1			NL324=1
				UNK=3	ITF65=2			NL325=2
					ITG17=1			NL326=172
					ITH36=1			NL327=9
					ITH55=4			NL333=1
					ITI14=1			NL337=2
					ITI19=1			NL342=1
					ITI43=13			NL411=1
					UNK=4			
Country of birth								
ISO-coded value list[2]	AL=14	HU=15	UNK=14	BR=17	EG=2	UNK=9	BG=1	AF=1, AM=1
	BG=1	TR=1		CA=1,	FR=1		CZ=1	ANHH=1
	EG=2	UNK=48		CN=1	IT=88		ES=1	AT=1, AU=2
	EL=68			CO=1	KE=1		MT=20	AW=2, BE=2
	IR=2			CZ=1	RO=5		RU=1	BG=1, BR=2
	LY=1			ES=4	UA=1		SE=1	CA=1, CO=2
	RO=3			GE=1	UNK=2		SY=1	CV=1, CW=1
	UNK=9			IE=55			TN=1	CY=1, CZ=1
				IR=1			UK=2	DO=1, EG=2
				IT=4				ES=1, FR=1
				LT=1				GH=1, HR=1
				LV=1				HU=1, ID=1
				MY=1				IL=2, IQ=1
				NG=2				IR=1, IT=4
				NZ=1				LT=1, MA=1
				PL=2				MT=1, MX=1
				PT=2				MY=1, NL=137
				PY=1				NZ=1, PL=1
				RO=1				RO=2, RS=1
				TW=1				RU=1, SO=1
				UK=5				SR=4; TR=1
				US=1				UA=1, UK=2
				VE=3				US=4, VE=1
				UNK=2				UNK=1
Probable country of infection								
ISO coded value list[2]	EL=82	HU=13	DE=1	ES=1	EG=1, FR=2	LV=9	MT=26	UNK=200
	UNK=18	UNK=51	IS=3	IE=97	IT=82		PH=1, TH=1	
			US=2	NZ=1	UK=1		TR=1	
			UNK=8	UNK=11	UNK=14			

Table A6.2. Clinical service type, place of residence, country of birth and probable country of infection for cases reported to Euro-GASP, by country, 2015 (end)

	Norway (n=110)	Poland (n=56)	Portugal (n=110)	Slovakia (n=104)	Slovenia (n=109)	Spain (n=167)	Sweden (n=100)	United Kingdom (n=239)
Clinical service types								
See first table for codes	UNK=110	DV=56	COMB=38	DV=44	DV=60	COMB=167	UNK=100	STI=239
			STI=7	GP=3	GYN=2			
			UNK=65	GYN=15	STI=8			
				URO=40	O=39			
				O=2				
Place of residence								
NUTS level 0–3 (region)[1]	UNK=110	UNK=56	PT11A=28	SK01=47	SL=101	ES7=3, ES111=1	UNK=100	UK=14, UKC2=2
			PT11C=2	SK021=21	UNK=8	ES113=3, ES114=8		UKC21=1, UKD3=2
			PT16B=7	SK022=2		ES120=38, ES220=23		UKD7=6, UKE32=3
			PT16D=2	SK023=25		ES243=1, ES300=33		UKE42=11, UKF14=3
			PT16F=4	SK041=8		ES411=1, ES413=3		UKG12=1, UKG31=8
			PT16G=2	SK042=1		ES417=1		UKG32=2, UKH3=1
			PT16I=1			ES422=4		UKH21=2
			PT112=6			ES511=15		UKI=108
			PT119=5			ES513=1		UKJ4=1
			PT150=6			ES521=6		UKJ14=1
			PT170=35			ES523=3		UKJ21=6
			PT181=2			ES611=15		UKJ23=1
			PT185=7			ES613=2		UKK11=4
			PT186=1			ES614=4		UKK13=3
			PT187=2			ES616=1		UKM=1
						ES617=1		UNK=58
Country of birth								
ISO-coded value list[2]	UNK=110	UNK=56	GW=1	SK=103	KG=1	UNK=167	UNK=100	AR=1, AU=3
			PT=6	UNK=1	RS=1			BE=1, BG=1
			UNK=103		SI=99			BR=3, CA=1
					UNK=8			CN=2, CO=1
								DE=3, EG=1
								EL=1, ES=4
								FR=2, GE=1
								GH=1, HK=1
								HU=1, IE=5
								IN=1, IR=3
								IT=3, JM=3
								JP=1, LK=1
								LT=1, MX=2
								NG=1, NL=1
								NO=1, NZ=2
								PL=3, PT=6
								SE=1, SG=1
								SK=2, SL=1
								SO=1, TT=1
								UK=122
								US=2, ZA=3
								UNK=43
Probable country of infection								
ISO-coded value list[2]	UNK=110	UNK=56	PT=7	CZ=2, DE=1	AT=1, ES=2	ES=167	UNK=100	BR=1, CN=1
			UNK=103	HU=2, PH=1	HR=2, SE=1			EE=1, EG=1
				SK=69	SI=58			ES=1, MW=1
				UNK=29	UNK=45			PL=1, UK=104
								UNK=128

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

Annex 7. Statistical tables

Table A7.1. Univariate association of cefixime resistance/susceptibility and patient characteristics, Euro-GASP, 2015

	Cefixime resistance N (%, 95% CI)	Odds ratio	95% CI	P value
Site of infection (n=2080)				
Genital (1517)	34 (2.2, 1.6 – 3.1)	1.0		
Anorectal (280)	0 (0.0, 0.0 – 1.4)			
Pharyngeal (180)	0 (0.0, 0.0 – 2.1)			
Other (103)	2 (1.9, 0.5 – 6.8)	0.86	0.21 – 3.65	**<0.01***
Sexual orientation and gender (n=1460)				
MSM (657)	3 (0.5, 0.2 – 1.3)	1.0		
Male heterosexual (419)	17 (4.1, 2.6 – 6.4)	9.22	2.66 – 32.01	
Female (384)	4 (1.0, 0.4 – 2.7)	2.30	0.51 – 10.32	**<0.001***
Previous GC (n=896)				
Yes (157)	3 (1.9, 0.7 – 5.5)	0.94	0.27 – 3.29	1.0*
No (739)	15 (2.0, 1.2 – 3.3)	1.0		
Concurrent chlamydia (n=806)				
Yes (153)	0 (0.0, 0.0 – 2.5)			0.36*
No (653)	7 (1.1, 0.5 – 2.2)			
HIV status (n=863)				
Positive (132)	0 (0.0, 0.0 – 2.8)			0.37*
Negative (731)	9 (1.2, 0.7 – 2.3)			
Age (n=2091)				
<25 years (617)	5 (0.8, 0.3 – 1.9)	1.0		
≥25 years (1474)	28 (1.9, 1.3 – 2.7)	2.37	0.91 - 6.17	0.07

** Expected value for one cell < 5, so Fisher's exact test performed*

Table A7.2. Univariate association of azithromycin resistance/susceptibility and patient characteristics, Euro-GASP, 2015

	Azithromycin resistance N (%, 95% CI)	Odds ratio	95% CI	P value
Site of infection (n=2080)				
Genital (1517)	99 (6.5, 5.4 – 7.9)	1.0		
Anorectal (280)	29 (10.4, 7.3 – 14.5)	1.65	1.07 – 2.56	0.02
Pharyngeal (180)	20 (11.1, 7.3 – 16.5)	1.79	1.08 – 2.98	0.02
Other (103)**	3 (2.9, 1.0 – 8.2)	0.43	0.133 – 1.38	
Sexual orientation and gender (n=1461)				
MSM (657)	53 (8.1, 6.2 – 10.4)	1.0		
Male heterosexual (419)	34 (8.1, 5.9 – 11.1)	1.0	0.64 – 1.58	0.98
Female (385)	19 (4.9, 3.2 – 7.6)	0.59	0.34 – 1.02	0.06
Previous GC (n=896)				
Yes (157)	22 (14.0, 9.4 – 20.3)	2.07	1.22 – 3.52	**<0.01**
No (739)	54 (7.3, 5.6 – 9.4)	1.0		
Concurrent chlamydia (n=806)				
Yes (153)	7 (4.6, 2.2 – 9.1)	0.66	0.29 – 1.51	0.32
No (653)	44 (6.7, 5.1 – 8.9)	1.0		
HIV status (n=865)				
Positive (132)	7 (5.3, 2.6 – 10.5)	0.75	0.33 – 1.69	0.48
Negative (733)	51 (7.0, 5.3 – 9.0)	1.0		
Age (n=2093)				
<25 years (617)	50 (8.1, 6.2 – 10.5)	1.0		
≥25 years (1476)	99 (6.7, 5.5 – 8.1)	0.82	0.57 – 1.16	0.25

** Expected value for one cell < 5, so Fisher's exact test performed. ** Not included in univariate analysis due to low cell numbers*

Table A7.3. Univariate association of ciprofloxacin resistance/susceptibility and patient characteristics, Euro-GASP, 2015

	Ciprofloxacin resistance N (%, 95% CI)	Odds ratio	95% CI	P value
Site of infection (n=2079)				
Genital (1516)	792 (52.2, 49.7 – 54.8)	1.0		
Anorectal (280)	124 (44.3, 38.6 – 50.1)	0.73	0.56 – 0.94	0.01
Pharyngeal (180)	62 (34.4, 27.9 – 41.7)	0.48	0.35 – 0.67	**<0.001**
Other (103)	52 (50.5, 41.0 – 60.0)	0.93	0.63 – 1.39	0.73
Sexual orientation and gender (n=1461)				
MSM (657)	290 (44.1, 40.4 – 48.0)	1.0		
Male heterosexual (419)	250 (59.7, 54.9 – 64.3)	1.87	1.46 – 2.41	**<0.001**
Female (385)	161 (41.8, 37.0 – 46.8)	0.91	0.71 – 1.17	0.47
Previous GC (n=896)				
Yes (157)	71 (45.2, 37.7 – 53.0)	0.85	0.60 – 1.20	0.36
No (739)	364 (49.3, 45.7 – 52.9)	1.0		
Concurrent chlamydia (n=806)				
Yes (153)	61 (39.9, 32.5 – 47.8)	0.75	0.53 – 1.08	0.12
No (653)	306 (46.9, 43.1 – 50.7)	1.0		
HIV status (n=865)				
Positive (132)	49 (37.1, 29.4 – 45.6)	0.76	0.52 – 1.12	0.16
Negative (733)	320 (43.7, 40.1 – 47.3)	1.0		
Age (n=2092)				
<25 years (617)	286 (46.4, 42.5 – 50.3)	1.0		
≥25 years (1475)	745 (50.5, 48.0 – 53.1)	1.18	0.98 – 1.43	0.08

Table A7.4. Univariate association of penicillinase activity and patient characteristics, Euro-GASP, 2015

	Penicillinase activity N (%, 95% CI)	Odds ratio	95% CI	P value
Site of infection (n=1762)				
Genital (1401)	223 (15.9, 14.1 – 17.9)	1		
Anorectal (200)	23 (11.5, 7.8 – 16.7)	0.69	0.43 – 1.09	0.11
Pharyngeal (133)	9 (6.8, 3.6 – 12.4)	0.38	0.19 – 0.77	<0.01
Other (28)**	4 (14.3, 5.7 – 31.5)			
Sexual orientation and gender (n=1224)				
MSM (495)	79 (16, 13 – 19.4)	1.0		
Male heterosexual (398)	60 (15.1, 11.9 – 18.9)	0.94	0.65 – 1.35	0.72
Female (331)	42 (12.7, 9.5 – 16.7)	0.77	0.51 – 1.15	0.19
Concurrent chlamydia (n=576)				
Yes (101)	12 (11.9, 6.9 – 19.6)	0.72	0.38 – 1.38	0.32
No (475)	75 (15.8, 12.8 – 19.3)	1.0		
Previous GC (n=896)				
Yes (157)	11 (7.01, 4.0 – 12.1)	0.41	0.21 – 0.78	**<0.01**
No (739)	115 (15.6, 13.1 – 18.4)	1.0		
HIV status (n=658)				
Positive (89)	14 (15.7, 9.6 – 24.7)	1.16	0.62 – 2.15	0.64
Negative (569)	79 (13.9, 11.3 – 17)	1.0		
Age (n=1767)				
<25 years (519)	65 (12.5, 10.0 – 15.7)	1.0		
≥25 years (1248)	198 (15.9, 13.9 – 18.0)	1.32	0.97 – 1.78	0.07

** Expected value for one cell < 5, so Fisher's exact test performed. ** Not included in univariate analysis due to low cell numbers*

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