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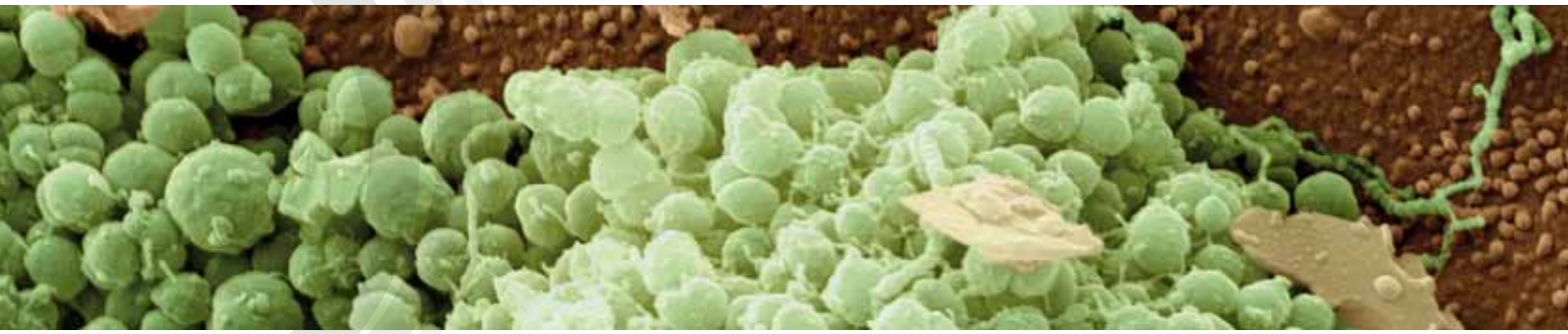

Gonococcal antimicrobial susceptibility surveillance in Europe

2014

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Contents

Figures and maps

Tables

Abbreviations

AMR	Antimicrobial resistance
CI	Confidence interval
CT	*Chlamydia trachomatis*
DV	Dermato-venerology
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
UK-NEQAS	United Kingdom National External Quality Assessment Service
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 revisions of treatment guidelines.

During 2014, 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. Centralised susceptibility testing was performed on all isolates centrally (Etest or agar dilution) for the following antimicrobials: cefixime, ceftriaxone, ciprofloxacin and azithromycin. Testing was decentralised and took place on the premises of participating laboratories fulfilling set quality criteria.

In 2014, 23 EU/EEA Member States participated in Euro-GASP, 17 via decentralised testing. A total of 2 151 isolates were collected and tested. The majority of gonococcal isolates (85.1%) were collected from male patient samples. The age of the patients ranged from under one year to 78 years, with a median age of 30 years. Overall, 28.7% of patients were under 25 years. Males were significantly older than women. The anatomical site of specimen collection was mainly genital (76.3%), followed by rectal (9.5%) and pharyngeal (7.6%). Among cases with information on previous diagnosis of gonorrhoea, 19.7% had previously been diagnosed with the disease. Twenty per cent of the patients were concurrently diagnosed with *Chlamydia trachomatis* infection. Among cases with known sexual preference and gender, 57.4% were heterosexual and 42.5% were men who have sex with men (MSM). Nineteen per cent of all cases were HIV-positive and 88.9% of those were MSM.

In 2014, a significantly lower proportion of tested isolates showed cefixime resistance: 2.0% (42 out of 2 101 isolates), compared with 4.7% (93 out of 1 994 isolates) in 2013. Isolates with this phenotype were detected in 10 countries, three less than in 2013. Five isolates were detected with ceftriaxone resistance (minimum inhibitory concentration (MIC)>0.125 mg/L), compared to seven in 2013. Rates of ciprofloxacin resistance have decreased slightly since 2013 (52.9% in 2013 to 50.7% in 2014). Additionally, the level of azithromycin resistance continued to increase, from 4.5% in 2012 (86 out of 1 927 isolates) to 7.9% in 2014 (169 out of 2 147 isolates); resistance to azithromycin was significantly associated with infection in MSM (9.9%, OR 4.9, $p<0.01$) and male heterosexuals (8.9%, OR 4.4, $p<0.01$) when compared with females (2.2%). One isolate displayed high-level resistance to azithromycin (MIC≥256 mg/L).

The decreasing cefixime and ceftriaxone resistance in Europe is encouraging; however it is predicted that resistance levels will rise again in future years, given the history of *N. gonorrhoeae* and antimicrobial resistance. The increasing resistance to azithromycin, which is used together with ceftriaxone in the currently recommended dual antimicrobial therapy, is also a major concern. 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 slow down the development of resistance to these antimicrobials [1]. Surveillance of the susceptibility to these agents is therefore essential in order to ensure efficient patient management and monitor current and emerging trends in resistance [3].

The European Gonococcal Antimicrobial Surveillance Programme (Euro-GASP) is 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 2013, Euro-GASP ran a sentinel surveillance programme in 21 EU countries. The major findings were [5]:

- Cefixime resistance was observed in 4.7% of tested isolates. This represented a 0.8% increase compared to 2012, prior to which there had been a decreasing trend since 2010.
- Seven isolates resistant to ceftriaxone were detected in Euro-GASP, compared to three in 2012.
- Rates of ciprofloxacin and azithromycin resistance increased slightly compared to 2012. The proportion of isolates resistant to ciprofloxacin remained very high (52.9%); azithromycin resistance remained close to 5% (5.4%).

1.2 Objectives

The overall aim of this project is to strengthen the surveillance of gonococcal antimicrobial susceptibility in the EU/EEA Member States. 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 2014 gonococcal antimicrobial susceptibility sentinel surveillance.

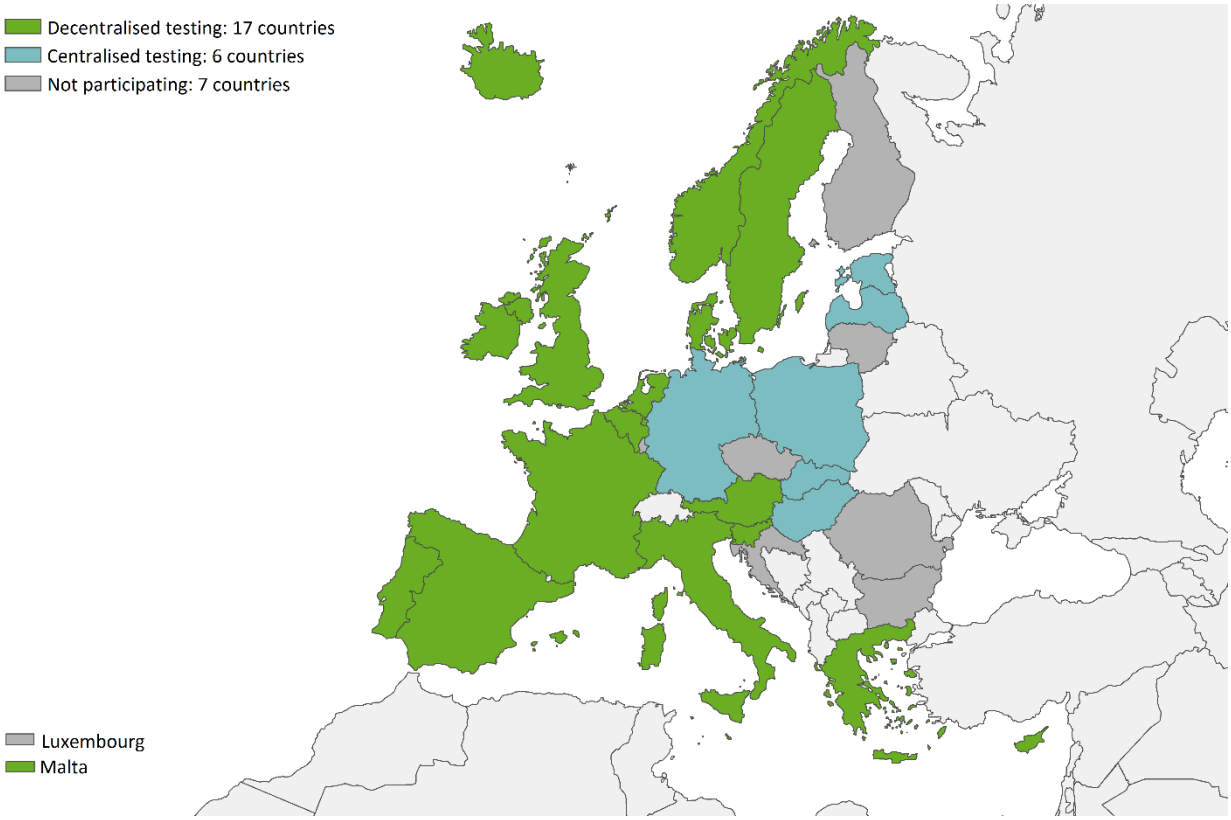
2 Methods

Participating laboratories were requested to collect gonococcal isolates during one period: September–November. This is a change from previous years when the isolates were collected during two periods; April–May and October–November. The centralised and decentralised testing model continued to be used: for decentralised testing, participating laboratories fulfilling set quality criteria performed their own susceptibility testing. Countries were then asked to upload their results to the European Surveillance System (TESSy). 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 Antimicrobial susceptibility testing 2.4). 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 2014, nominated contact points for STI surveillance from 23 EU/EEA countries participated in Euro-GASP (Map 1) which was two countries more (Estonia and Poland) than in 2013.

Map 1. EU/EEA Member States participating in Euro-GASP, 2014



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 centralised-testing model countries with the aim of retrieving and testing 100 isolates). Countries where 100 isolates represent 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 would be able to use isolates from throughout the year. However, in the United Kingdom, the collection was conducted during the period between July and September to coincide with the collection period of the national Gonococcal Resistance to Antimicrobials Surveillance Programme (GRASP) in England and Wales.

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. 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 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 antimicrobial panel in 2014 as these antimicrobials are either not in routine use or are difficult to acquire.

The following methods were used to determine susceptibility:

- Breakpoint (azithromycin and ciprofloxacin)
- Etest (cefixime, ceftriaxone, azithromycin 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) and the results were interpreted using the Euro-GASP standard breakpoints (Annex 3). For 2014, the Netherlands and France did not test for penicillinase production and Greece did not test all isolates for susceptibility to cefixime.

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 and probable country of infection. Diagnostic test and treatment used were new Euro-GASP variables included in 2014. The full variable list and variable codes are described in Annex 4.

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

Data generated by centralised testing were sent to the national contacts; complemented with 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 2004 and 2014 (note that no data collection was organised in 2005).

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

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

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 2014 versus 2013 and whether the differences in age distribution were statistically significant. A univariate analysis was performed to investigate associations between patient characteristics and antimicrobial resistance. Where datasets contained sufficient numbers the odds ratios (OR) and 95% confidence intervals (CI) were calculated and the Pearson's $\chi 2$ test was used to measure if these odds ratios differed significantly from 1. For small cell numbers, Fisher's exact test was performed. Using a forward step-wise approach, the most significant and strongest associations from the univariate analysis were added to a multivariable logistic regression model sequentially. Statistical significance for all tests was assumed when $p<0.05$.

3 Results

3.1 Completeness of data

Overall completeness of variables remained quite similar to the 2013 data although there were some minor changes (Table 2). Completeness of data remained high for 'gender', 'age' and 'site of infection' (over 94%). Since 2013, there has been a slight improvement in the completeness of reporting for 'mode of transmission' and 'place of residence', but there have been decreases in 'site of infection', 'previous gonorrhoea', 'concurrent STI' and 'clinical service type' as well as a large downturn in reporting for 'country of birth' and 'probable country of infection'. Compared to 2010, completeness has generally remained stable, except for decreases in 'concurrent STI', 'country of birth' and 'probable country of infection'. Increases were observed for 'clinical service type' and 'HIV status'.

Table 2. Completeness of reporting, Euro-GASP, 2014

Variables	2010 (n=1766)		2011 (n=1902)		2012 (n=1927)		2013 (n=1994)		2014 (n=2151)	
	No	%	No	%	No	%	No	%	No	%
Gender	1749	99.0	1826	96.0	1906	98.9	1978	99.2	2140	99.5
Age	1740	98.5	1793	94.3	1878	97.5	1953	97.9	2106	97.9
Mode of transmission	1001	56.7	1061	55.8	987	51.2	1044	52.4	1260	58.6
Site of infection	1683	95.3	1785	93.8	1852	96.1	1938	97.2	2030	94.4
Diagnostic test	NR	NR	NR	NR	NR	NR	NR	NR	1455	67.6
Treatment	NR	NR	NR	NR	NR	NR	NR	NR	400	18.6
Previous gonorrhoea	691	39.1	767	40.3	757	39.3	796	39.9	826	38.4
Concurrent STI	779	44.1	875	46.0	800	41.5	841	42.2	851	39.6
Place of residence*	720	83.1	1437	75.6	1541	80.0	1436	72.0	1596	74.2
Clinical service type*	610	70.4	1544	81.2	1476	76.6	1535	77.0	1619	75.3
Country of birth*	392	45.3	861	45.3	988	51.3	1029	51.6	879	40.9
Probable country of infection*	263	30.4	737	38.7	856	44.4	812	40.7	588	27.3
HIV status*	310	35.8	802	42.2	772	40.1	819	41.1	892	41.5

* 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, 2014

Country	Coverage	Specimen source	Comprehensive-ness	Sampling method
Austria	Regional/capital area	STI clinics, DV clinics, GPs, hospitals	Sentinel	Consecutively but from a select population
Belgium	National	GPs, hospitals, STI clinics, gynaecologists	Comprehensive	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, out-patients, hospital laboratories, public health departments, STI ambulances and federal armed forces.	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
Italy	Regional	STI clinics, hospitals, university/hospital microbiology units, DV clinics	Comprehensive	Consecutively
Latvia	National	STI clinics	Other	Consecutively
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	Sentinel	Consecutively
Portugal	National	STI clinics, DV clinics, GPs, hospitals, urology and gynaecology clinics	Other	Consecutively
Slovakia	Regional	DV, urology and gynaecology practices	Comprehensive	Consecutively
Slovenia	Regional	DV and STI clinics	Other	Consecutively
Spain	National	STI clinics and hospitals	Sentinel	Consecutively
Sweden	National	STI clinics	Comprehensive	Consecutively
United Kingdom	National†	GUM/STI clinics, GPs and out-patients	Sentinel	Consecutively

DV: Dermatology-venereology, GUM: Genitourinary medicine, GP: General practitioner

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

Sentinel: reporting is based on a selected group of physicians/hospitals/laboratories/or other institutions' notifications and/or cases occurring within a selected population group defined by age, 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 by some laboratories with no selection criteria.

† National except for Northern Ireland.

During 2014, a total of 2 151 isolates were tested. This represents an increase of 157 isolates (7.3%) on 2013. The number of isolates tested from each country varied from two (Cyprus) to 231 (United Kingdom) (Table 4).

The coverage (number of isolates tested compared to the number of reported cases as part of the enhanced epidemiological surveillance of STI in 2014 [5]) ranged from 1% (United Kingdom) to 55% (Portugal). 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. Estonia, Hungary, Italy, Latvia and Poland reported on less than the required 100 isolates although there were sufficient numbers of cases reported to achieve the aim of 100 isolates (except for Italy as data were not available). Reaching this target is, however, not always possible if cases are mainly diagnosed through NAAT. It would not have been possible for Cyprus, Iceland, Malta or Slovenia to achieve 100 isolates as the total number of cases reported through

epidemiological surveillance was less than 100. To monitor the progress of Euro-GASP, the percentage of isolates tested from 2009 to 2014 is also displayed in Table 4. The percentage of isolates tested in Euro-GASP has decreased from 6% in 2009 to 3% in 2014, reflecting the increase in the number of cases reported through epidemiological surveillance during this period.

Table 4. Number of *N. gonorrhoeae* isolates tested in Euro-GASP, gonorrhoea patients reported in 2014, and percentage of isolates tested 2009–2014, EU/EEA

Country	Number of isolates tested 2014	Number of cases reported 2014 [6]	% isolates tested*					
			2014	2013	2012	2011	2010	2009
Austria	101	NR	NR	9	27	23	32	77
Belgium**	140	1119	13	11	12	13	15	15
Cyprus	2	4	50	450	50	91	52	N/A
Denmark	109	1141	10	13	17	25	20	20
Estonia	13	134	10	NP	NP	NP	NP	NP
France**	110	1330	8	8	12	18	24	32
Germany	106	NR	NR	NR	NR	NR	NR	NR
Greece	110	NR	NR	34	29	26	31	67
Hungary**	89	1620	5	6	5	1	1	NP
Iceland	12	38	32	26	NP	NP	NP	NP
Ireland	101	1304	8	8	7	8	14	NP
Italy	50	NR	NR	NR	35	24	42	48
Latvia	21	365	6	7	6	5	6	3
Malta	21	51	41	51	55	28	62	92
Netherlands**	227	10729	2	3	4	6	8	5
Norway	110	682	16	22	25	21	11	54
Poland	46	495	9	NP	NP	NP	NP	NP
Portugal	110	201	55	95	92	91	81	75
Slovakia	109	423	26	29	38	58	70	13
Slovenia	82	61	134	118	104	76	64	80
Spain	151	4562	3	4	3	4	5	5
Sweden	100	1337	7	9	10	11	10	18
United Kingdom	231	38361	1	1	1	1	1	1
Total (number or % isolated tested)	**2151**	**63957**	**3**	**4**	**4**	**5**	**6**	**6**

* Percentages above 100% suggest under-reporting of cases in epidemiological surveillance
** Sentinel data
NR = not reported; NP = not participating.

As in previous years, the majority of gonococci (85%, n=1 821) were collected from men. Gender was reported as unknown for 11 cases (Table 5). The age of the patients ranged from <1 year to 78 years, with a median of 30 years, an interquartile range of 24 to 38 years and 29% (605) of patients being under 25 years (Table 6). Males (median age 30 years) were significantly older than females (median age 26 years) ($p<0.01$), with the highest and lowest percentage of <25-year-olds in the female (45.3%) and MSM patient groups (24.4%), respectively (Table 6).

The anatomical site of specimen collection was mainly genital (76.3%, n=1 549); it was reported as unknown for 121 cases.

Information on previous diagnosis of gonorrhoea was available for 38% (826) of cases, 20% (163) of which had had a previous infection. Information on concurrent STI was available for 40% (851) of cases; 20% (170) of patients had a concurrent chlamydia infection, 4.8% (41) had another STI (hepatitis B n=2, genital herpes n=4, *Lymphogranuloma venereum* (LGV) n=3, *Mycoplasma genitalium* n=2, syphilis n=21 or genital warts n=9) and 75% (640) did not have any other STIs. When HIV status was known (892), 19% (172) were HIV-positive, 89% (153) of whom were MSM (Table 5).

Table 5. Patient characteristics 2009–2014

	2009 N (%)	2010 N (%)	2011 N (%)	2012 N (%)	2013 N (%)	2014 N (%)
Total number of isolates	1366	1766	1902	1927	1994	2151
Gender						
Male	1123 (83.7)	1441 (82.4)	1505 (82.4)	1596 (83.7)	1676 (84.7)	1821 (85.1)
Female	219 (16.3)	308 (17.6)	321 (17.6)	310 (16.3)	302 (15.3)	318 (14.9)
Unknown	24	17	76	21	16	11
Age (years)						
<25	422 (32.0)	599 (34.4)	572 (31.9)	617 (32.9)	554 (28.4)	605 (28.7)
≥25	898 (68.0)	1141 (65.6)	1221 (68.10)	1261 (67.1)	1399 (71.6)	1501 (71.3)
Unknown	46	26	109	49	41	44
Sexual orientation & gender						
Females	219 (27.9)	308 (27.3)	321 (27.1)	310 (28)	302 (25.7)	318 (22.7)
Heterosexual males	314 (40.1)	426 (37.7)	423 (35.6)	390 (35.2)	376 (32)	485 (34.7)
Men who have sex with men	251 (32)	395 (35)	442 (37.3)	408 (36.8)	496 (42.3)	594 (42.5)
Unknown	582	637*	716	819	820	754
Site of infection						
Genital	1164 (86.5)	1426 (84.7)	1466 (82.1)	1537 (83)	1531 (79)	1549 (76.3) ‡‡
Pharyngeal	34 (2.5)	62 (3.5)	79 (4.4)	92 (5)	122 (6.3)	154 (7.6) ‡‡
Anorectal	138 (10.3)	191 (11.4)	216 (12.1)	188 (10.2)	255 (13.2)	192 (9.5)
Other	9 (0.7)	7 (0.4)	24 (1.3)	35 (1.9)	30 (1.5)	135 (6.6) ‡‡
Unknown	21	80	117	75	56	121
Previously diagnosed						
Yes	84 (18.1)	145 (21)	146 (19)	130 (17.2)	142 (17.8)	163 (19.7)
No	379 (81.9)	546 (79)	621 (81)	627 (82.8)	654 (82.2)	663 (80.3)
Unknown	903	1075	1135	1170	1198	1325
Concurrent STI						
Concurrent chlamydia infection	78 (14.3)	172 (22.1)	194 (22.2)	187†† (23.4)	183 (21.8)	170 (20)
Concurrent other STI (not HIV)	35 (6.4)	28† (3.6)	43 (4.9)	49‡ (6.1)	55 (6.5)	41Φ (4.8)
No concurrent STI	433 (79.3)	579 (74.3)	638 (72.9)	564 (70.6)	603 (71.7)	640 (75.2)
Unknown	820	987	1027	1127	1153	1300
HIV status*						
Positive	N/D	48 (15.5)	141 (17.6)	104 (13.5)	144 (17.6)	172 (19.3)
Negative	N/D	262 (84.5)	661 (82.4)	668 (86.5)	675 (82.4)	720 (80.7)
Unknown	N/D	556	1100	1155	1175	1259

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 ($p < 0.05$)

Φ Includes two individuals with chlamydia and an additionally diagnosed STI.

Information on sexual orientation and gender was available for 64.9% (1397) of the cases. In these cases, 57.5% (803) of the *N. gonorrhoeae* infections were reported as heterosexually acquired (39.6% females and 60.4% males) and 42.5% (594) were from MSM. Sixty additional males with unknown mode of transmission had *N. gonorrhoeae* isolated from the pharynx or anogenital region.

Some of the epidemiological data have changed over time (Table 5). Between 2011 and 2014, isolates from men increased each year (from 82.4% to 85.1%), with a concomitant decrease in the proportion of isolates from females (from 17.6% to 14.9%) during the same period. Between 2009 and 2014, the proportion of isolates from MSM increased from 32% to 42.5%. In 2014, there was a significant increase in the proportion of MSM patients under 25 years compared to the previous year's data ($p=0.012$) (Table 6). The proportion of genital isolates continued to decrease (from 87% in 2009 to 76.3% in 2014), with a significant reduction on the previous year ($p=0.04$); the proportion of pharyngeal isolates continued to increase (from 2.5% in 2009 to 7.6% in 2014). Since 2013, there has been a significant decrease in the proportion of anorectal isolates ($p<0.01$) and a significant increase in the proportion of isolates from other sites ($p<0.01$).

Table 6. Patient age distribution by gender and sexual orientation, 2014

Variable	N†	Age (years)			Proportion <25 years (%)
		Range	Mode	Median	
All patients	2106	0–78	23	30	605 (28.7)
Female	311	0–76	19/21	26	141 (45.3)
Male*	1787	13–78	23	30	461 (25.8)
Male heterosexual	482	14–71	24	31	130 (27.0)
MSM	594	13–73	23	30	145 (24.4)

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

As in previous years, the majority of patients for whom a clinical service type was known had attended a dedicated STI or sexual health clinic (53%). There was a slight but significant decrease in the number of patients who attended STI services in 2014 compared to 2013 (p=0.02) (Table 7).

Table 7. Clinical service type attendance

Grouping	2010 N=866 n (%)	2011 N=1902 n (%)	2012 N=1927 n (%)	2013 N=1994 n (%)	2014 N=2151 n (%)
STI and sexual health clinics	444 (51.3)	1079 (56.7)	1076 (55.8)	1123 (56.3)	1136 (52.8)
Antenatal	0	0	2 (0.1)	0	0
Out-patient clinic	36 (4.2)	128 (6.7)	148 (7.7)	122 (6.1)	161 (7.5)
Other	42 (4.9)	60 (3.2)	47 (2.4)	75 (3.8)	105 (4.9)
Primary care	88 (10.2)	277 (14.6)	203 (10.5)	215 (10.8)	217 (10.1)
Unknown	256 (29.6)	358 (18.8)	451 (23.4)	459 (23.0)	532 (24.7)

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

Information on country of birth was supplied by 14 countries. Ten of these countries (Belgium, Denmark, Greece, Ireland, Italy, Malta, the Netherlands, Slovakia, 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=37). Of the 879 cases with known country of birth, 82.4% (n=724) had been diagnosed and reported with gonorrhoea in their country of birth, which is similar to the percentage for 2013 (83%). In cases where country of birth and reporting country differed, the most common countries of birth (with >5 patients) were Brazil (16 patients), the United Kingdom (13 patients), Albania (nine patients), Suriname (eight patients) and Venezuela (seven patients). Probable country of infection data were supplied by 15 countries, two less than 2013, with nine countries reporting patients acquiring gonorrhoea outside the reporting country. The majority of cases (94%; 553/588) most probably acquired gonorrhoea in the country reporting the case. The two countries most commonly reported as probable countries of infection (with ≥4 patients) and differing from the reporting country were Poland, with five patients (all male, four with known sexual orientation: two MSM and two heterosexual) and Thailand with four patients (three males, two of which were heterosexual, and one female).

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

Ceftriaxone and cefixime

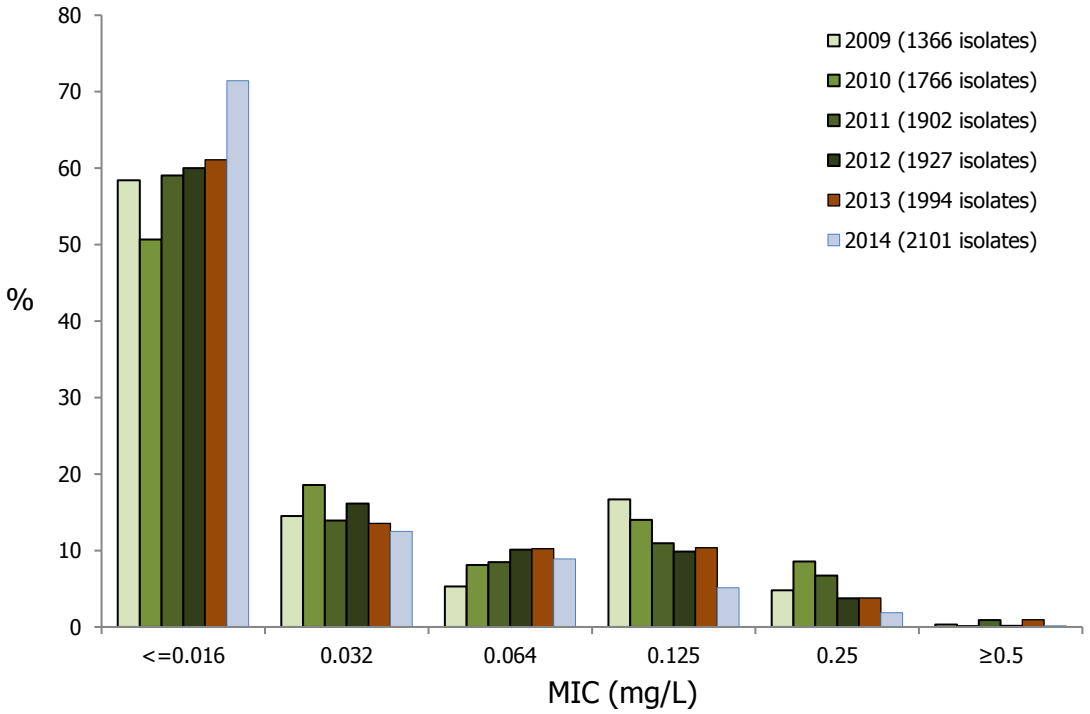
Cefixime resistance (MIC>0.125 mg/L) was observed in 2.0% (42/2 101) of isolates (Figure 1). This is a significant decrease (p<0.01) on 2013 (4.7%, 93 out of 1994 isolates). A trend of decreasing cefixime resistance has been documented since 2010 (8.7%), except for 2013, when a small increase was seen. The proportion of most susceptible isolates (MIC≤0.016 mg/L) increased (from 61% in 2013 to 71% in 2014). The number of isolates displaying a MIC of ≥0.5 mg/L also decreased from 19 isolates in 2013 to three isolates in 2014 (three isolates in 2012 and 17 isolates in 2011).

In 2014, cefixime resistance was detected in 10 countries (Map 2, Table 8), compared to 13 in 2013. Since 2013 there has been a decrease in cefixime resistance in all countries other than Belgium, which has continued to see a rise in resistance (0.9% in 2012, 6.4% in 2013, and 12.1% in 2014), Italy, the Netherlands and Norway. Cefixime resistance was no longer detected in Austria, Latvia, Spain and the United Kingdom. Spain saw a large reduction in cefixime resistance from 15.1% in 2013 to 0% in 2014. It should be noted that the switch to Etests from agar dilution in 2014 by the referring laboratory in Spain may have contributed to this adjustment. Compared to 2013,

three countries (Belgium, Denmark and Greece) continued to have ≥5% resistance in 2014; in addition, resistance in Norway reached 5.5% in 2014. France, Slovakia and Slovenia continued to have <5% cefixime resistance, with resistance in Hungary decreasing to <5% in 2014. Italy and the Netherlands did not report isolates with cefixime resistance in 2013 but detected resistant isolates in 2014.

In 2014, cefixime resistance among MSM remained at the same level as 2013, (1.2%) which represents a decline since 2010 (7.3%). Cefixime resistance has been declining among females and heterosexual males since 2011 to 2.5% and 1.7%, respectively (Figure 2).

Figure 1. Distribution of MIC for cefixime in Euro-GASP, 2009–2014



Map 2. Proportion of isolates with cefixime resistance in Europe, 2014

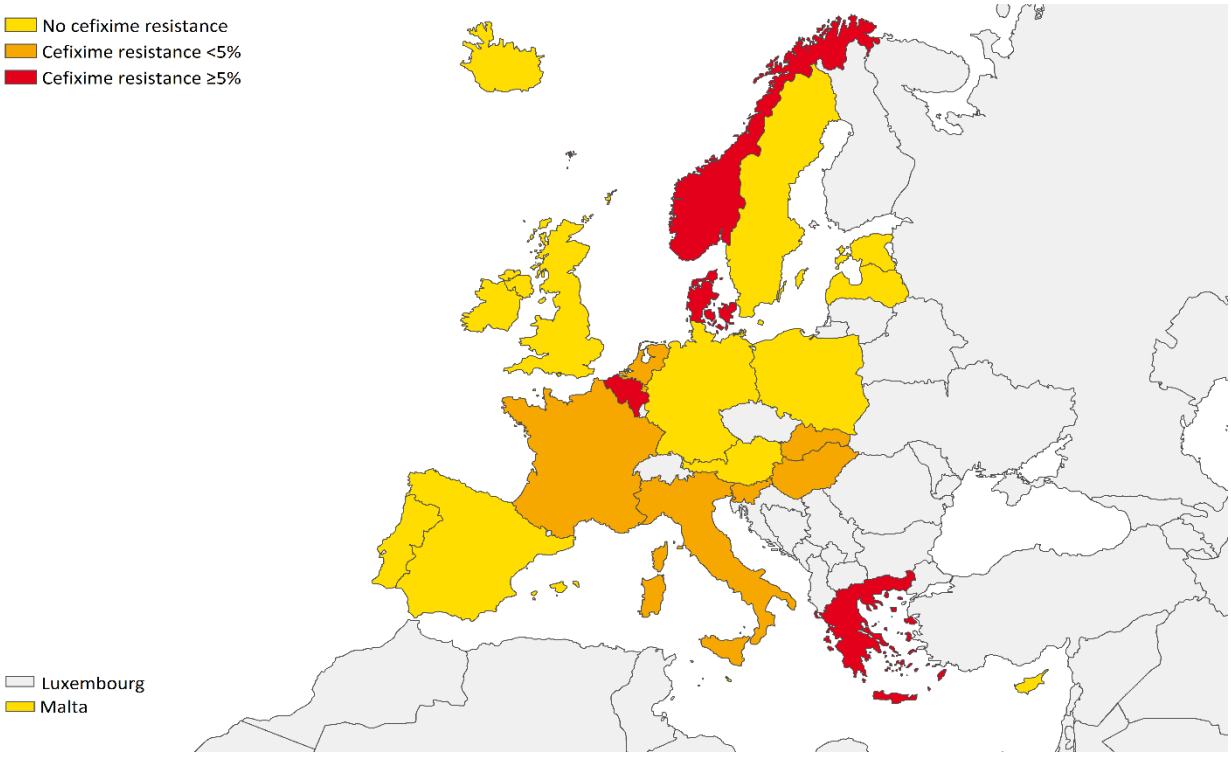
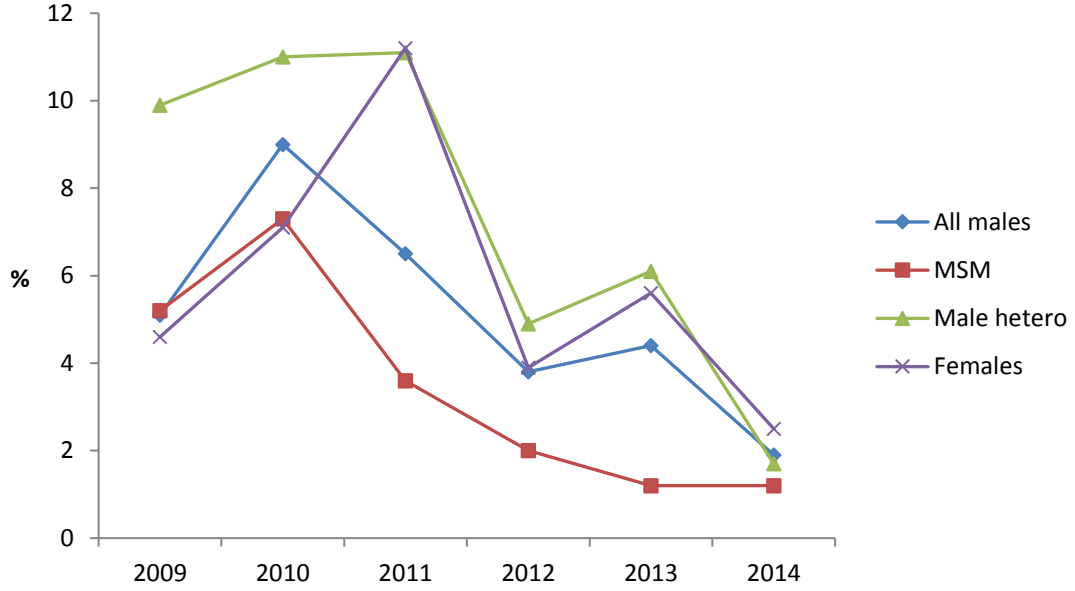


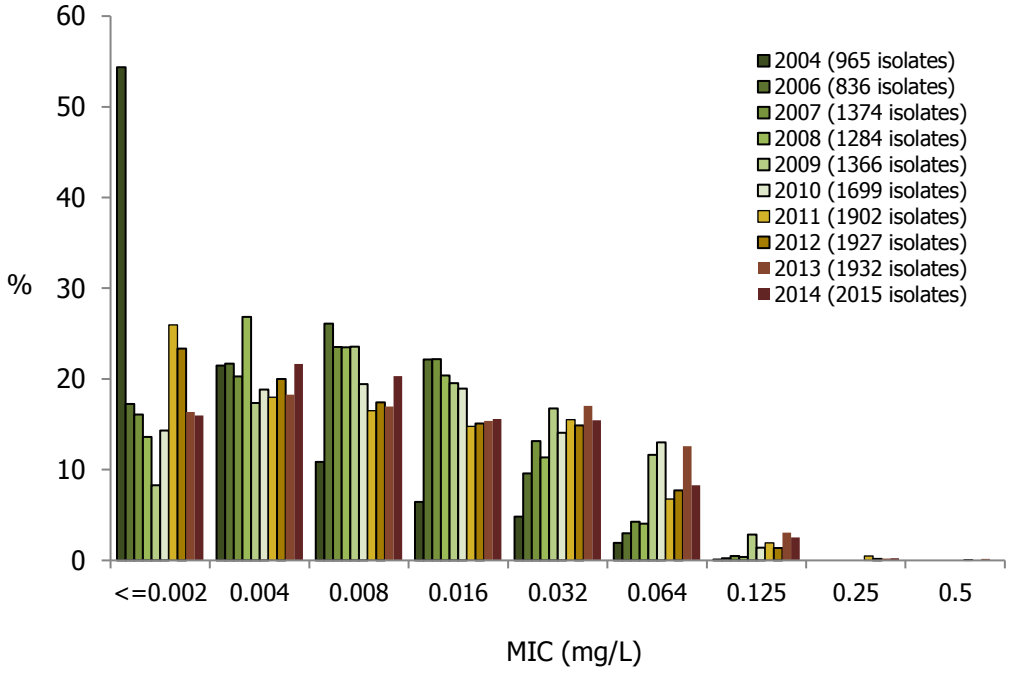
Figure 2. Percentage of isolates with cefixime resistance by gender and male sexual orientation, Euro-GASP, 2009–2014



Five isolates displayed ceftriaxone resistance (MIC>0.125 mg/L) in 2014 compared to seven in 2013 and three in 2012 (Figure 3). Three isolates were from Greece and one each from Germany and Norway. All were from men and were genital isolates. All displayed the classical *Neisseria gonorrhoeae* Multi Antigen Sequence Typing (NG-MAST) sequence type 1407 profile of cefixime and ciprofloxacin resistance. The MIC distribution for ceftriaxone in 2014 showed a similar proportion of highly susceptible gonococcal isolates (MIC≤0.002 mg/L) as in 2013, along with an increased proportion of isolates with lower MICs (0.004 mg/L and 0.008 mg/L) and a decreased proportion of isolates with higher MICs (0.064 mg/L and 0.125 mg/L) (Figure 3).

It should be noted that the comparison of resistance between years is limited by the small number of 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, 2004–2014



Note: 2014 MIC distribution data do not include four isolates from Portugal, 17 from Malta, 41 from Ireland or 74 from Spain as Etests with the lowest concentration of 0.016 mg/L were used. In 2013, there were 33 isolates from Ireland and 29 from Malta which were also not included. Susceptibility testing was not performed on isolates from 2005.

Table 8. Resistance to cefixime, azithromycin, ciprofloxacin and penicillin G (only plasmid-mediated high-level resistance; PPNG) by country, Euro-GASP, 2014

Country	Number of isolates tested	Resistance								Method of testing
		Cefixime		Azithromycin		Ciprofloxacin		PPNG		
		No.	%	No.	%	No.	%	No.	%	
Austria	101	0	0.0%	2	2.0%	53	52.5%	24	23.8%	Decentralised – Etest
Belgium	140	17	12.1%	5	3.6%	81	57.9%	27	19.3%	Decentralised – MIC
Cyprus	2	0	0.0%	0	0.0%	2	100.0%	0	0.0%	Decentralised – Etest
Denmark	109	6	5.5%	4	3.7%	36	33.0%	10	9.2%	Decentralised – Etest
Estonia	13	0	0.0%	0	0.0%	2	15.4%	0	0.0%	Centralised- BKP/Etest
France	110	1	0.9%	12	10.9%	56	50.9%	N/T		Decentralised – Etest
Germany	106	0	0.0%	3	2.8%	67	63.2%	14	13.2%	Centralised - Etest
Greece	110	3	5.0%[ł]	42	39.6%*	77	70.0%	6	5.5%	Decentralised – Etest
Hungary	89	1	1.1%	1	1.1%	49	55.1%	12	13.5%	Centralised- Etest
Iceland	12	0	0.0%	0	0.0%	7	58.3%	2	22.2%**	Decentralised – Etest
Ireland	101	0	0.0%	38	37.6%	35	34.7%	2	2.0%	Decentralised – Etest
Italy	50	1	2.0%	3	6.0%	39	78.0%	4	8.0%	Decentralised – Etest
Latvia	21	0	0.0%	3	14.3%	4	19.0%	0	0.0%	Centralised-Etest
Malta	21	0	0.0%	1	4.8%	12	57.1%	2	9.5%	Decentralised – Etest
Netherlands	227	5	2.2%	4	1.8%	73	32.2%	N/T		Decentralised – Etest
Norway	110	6	5.5%	6	5.5%	81	73.6%	32	29.1%	Decentralised – Etest
Poland	46	0	0.0%	4	8.7%	30	65.2%	0	0.0%	Centralised- BKP/Etest
Portugal	110	0	0.0%	19	17.3%	40	36.4%	8	7.3%	Decentralised – Etest
Slovakia	109	1	0.9%	4	3.7%	74	67.9%	27	24.8%	Centralised- BKP/Etest
Slovenia	82	1	1.2%	2	2.4%	37	45.1%	18	22.0%	Decentralised – Etest
Spain	151	0	0.0%	10	6.6%	102	67.5%	28	18.5%	Decentralised – Etest
Sweden	100	0	0.0%	4	4.0%	57	57.0%	19	19.0%	Decentralised – Etest
UK	231	0	0.0%	2	0.9%	77	33.3%	21	9.1%	Decentralised – MIC
Total:										
Cefixime	2101	42	2.0%							
Ciprofloxacin	2151					1091	50.7%			
Azithromycin	2147			169	7.9%					
PPNG	1811							256	14.1%	
95% CI			1.5–2.7		6.8-9.1		48.6-52.8		12.6-15.8	

[ł]Calculated from 60 isolates with cefixime results

*Calculated from 106 isolates with azithromycin results

**Calculated from nine isolates with PPNG results

N/T not tested

BKP: Break-point

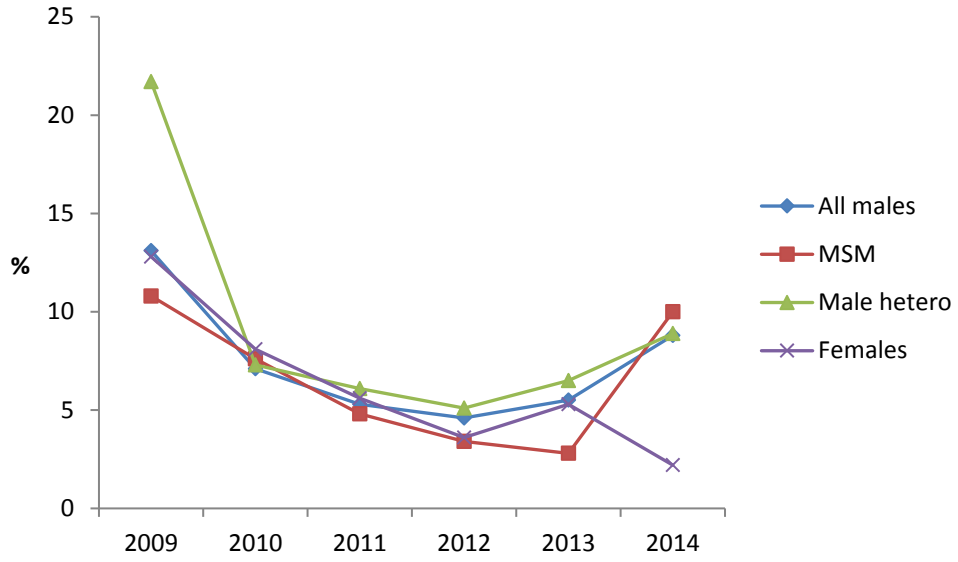
PPNG: Penicillinase-producing *Neisseria gonorrhoeae*

Azithromycin

In 2014, the mean resistance to azithromycin (MIC>0.5 mg/L) was 7.9% (169 out of 2 147 isolates) and ranged from 0% (Cyprus, Estonia and Iceland) to 40% in Greece (Table 8). Resistance levels have continued to increase since 2012 (4.5%, 86 of 1 927 isolates). In 2014, only one isolate displayed high-level resistance to azithromycin (MIC≥256 mg/L) and this was from a male in Italy. Isolates displaying this type of high-level resistance to azithromycin were detected in 2006 (n=1), 2007 (n=4), 2011 (n=2), 2012 (n=3) and 2013 (n=1).

In 2014, the highest resistance (10.0%) was observed in MSM, the lowest resistance (2.2%) in females (Figure 4). The trend in azithromycin resistance varied between the genders: among males, and particularly among MSM, resistance has been increasing again since 2012/2013, in contrast to females where the decreasing trend has continued (Figure 4).

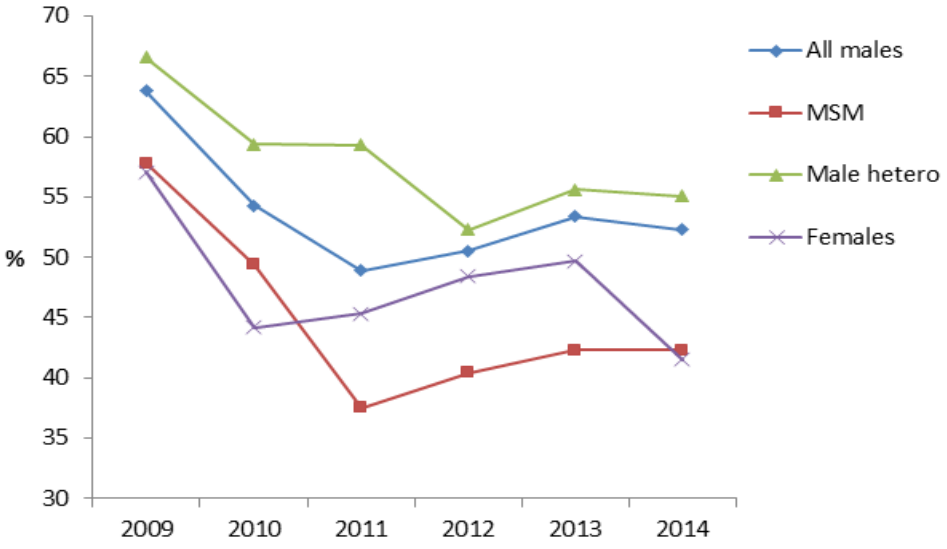
Figure 4. Percentage of isolates with azithromycin resistance by gender and male sexual orientation, Euro-GASP, 2009–2014



Ciprofloxacin

In 2014, resistance to ciprofloxacin (MIC>0.06 mg/L) ranged from 15% in Estonia to 78% in Italy and 100% in Cyprus, although it should be noted that only two isolates were available from Cyprus (Table 8). Overall resistance levels in 2014 (50.7%) were similar to those in 2013 (53%). Resistance was highest in heterosexual males (55%) and lowest in females (42%) (Figure 5).

Figure 5. Percentage of isolates with ciprofloxacin resistance by gender and male sexual orientation, Euro-GASP, 2009–2014

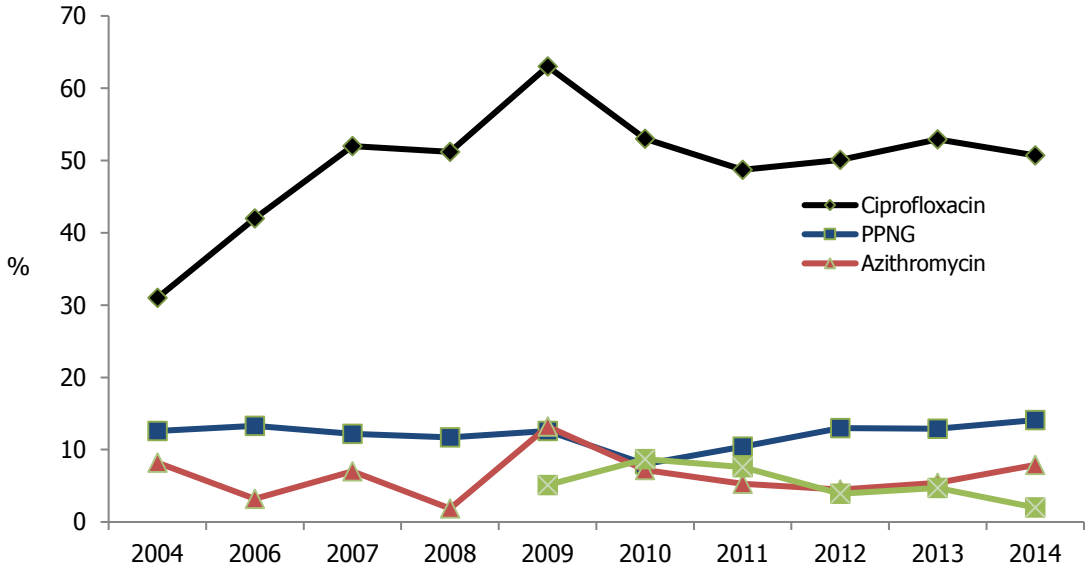


Penicillin G

High-level plasmid-mediated resistance to penicillin G (penicillinase-producing *N. gonorrhoeae* (PPNG)) ranged from 0% (Cyprus, Estonia, Latvia and Poland) to 29% (Norway), with an overall resistance level of 14.1% (Table 8). High-level resistance to penicillin G continues to remain fairly constant at 8.0–14.1% (Figure 6).

The percentages of *N. gonorrhoeae* isolates resistant to ciprofloxacin, azithromycin, cefixime and producing β-lactamase from 2004 to 2014 are summarised in Figure 6.

Figure 6. Percentage of resistant *Neisseria gonorrhoeae* by antimicrobial and year, Euro-GASP, 2004–2014



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 resistance is similar across patient groups and specimen types, other than for the following:

- Cefixime: no patient characteristics or infection site were significantly associated with cefixime resistance in 2014. This is a change from last year when both heterosexual males and females had a significant association with cefixime resistance.
- Azithromycin: MSM (9.9%) and male heterosexuals (8.9%) had a much higher level of azithromycin resistance in 2014 than in 2013, with higher levels of resistance compared to females (2.2%). Univariate analysis confirmed an association between azithromycin resistance and being MSM or male heterosexual compared to females (MSM: OR 4.9, CI 2.19-10.95, p<0.01. Male heterosexuals: OR 4.4, CI 1.92-9.88, p<0.01). This association was not observed in 2013. 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. There was no significant association between the site of infection and azithromycin resistance, unlike the 2013 data which demonstrated a significant association (p<0.01) in genital and pharyngeal sites harbouring isolates with more resistance than anorectal sites (Table A7.2, Annex 7).
- Ciprofloxacin: univariate analysis revealed that most of the associations were the same as in 2012 and 2013, and these related to ciprofloxacin resistance and age (≥25 years, OR 1.55, CI 1.28-1.87, p<0.01), being a heterosexual male compared to MSM (OR 1.67, CI 1.3-2.12, p<0.01), and the absence of a concurrent chlamydial infection (OR 1.58, 1.11-2.24, p=0.01) (Table A7.3, Annex 7). Being female compared to MSM was not associated with ciprofloxacin resistance in 2014 as it was in 2013 and 2012. Following multivariable analysis, ciprofloxacin resistance remained associated with age (odds ratio for age ≥25 years compared to <25 years: 1.49, CI 1.07–2.08, p=0.02) and the absence of a concurrent chlamydial infection (odds ratio for no concurrent chlamydia infection: 1.54, CI 1.05-2.26, p=0.03). As in 2013 and 2012, isolates from the anorectal and pharyngeal sites were less likely to harbour ciprofloxacin resistance than isolates from genital sites (anorectal OR 0.66, CI 0.49-0.9, p<0.01; pharyngeal OR 0.65, CI 0.47-0.91, p=0.01) (Table A7.1, Annex 7).

- PPNG: compared to MSM, univariate analysis revealed an association between PPNG and being female (OR 1.9, CI 1.15-3.15, p=0.01) and being a heterosexual male (OR 2.7, CI 1.74-4.19, p<0.01) (Table A7.4, Annex 7). The association with females was also observed in 2012 and 2013, and the association between PPNG and being a heterosexual male was last observed in 2012. Isolates from the anorectal site were less likely to be PPNG than isolates from genital sites (anorectal OR 0.35, CI 0.15-0.81, p=0.01) (Table A7.4, Annex 7) which was previously observed in 2012.

Table 9. Resistance to cefixime, azithromycin, ciprofloxacin and penicillin G (only plasmid-mediated high-level resistance) by patient characteristic, Euro-GASP, 2014

	Cefixime			Azithromycin			Ciprofloxacin			PPNG		
	Tested	Resistant	%	Tested	Resistant	%	Tested	Resistant	%	Tested	Resistant	%
Sexual orientation and gender												
Female	318	8	2.5	318	7	2.2	318	132	41.5	275	37	13.5
Male	1771	34	1.9	1817	161	8.9	1821	952	52.3	1524	217	14.2
Heterosexual male	449	8	1.8	482	43	8.9	485	267	55.1	454	82	18.1
MSM	583	7	1.2	594	59	9.9	593	252	42.4	424	32	7.6
Age (years)												
<25 years	597	7	1.2	604	41	6.8	605	260	43.0	500	70	14.0
≥25 years	1459	33	2.3	1498	124	8.3	1501	808	53.8	1273	182	14.3
Site of infection												
Genital	1499	34	2.3	1545	120	7.8	1549	828	53.5	1426	222	15.6
Anorectal	192	2	1.0	192	20	10.4	192	83	43.2	99	6	6.1
Pharyngeal	154	0	0.0	154	13	8.4	154	66	42.9	119	11	9.2
Other	135	4	3.0	135	11	8.2	135	67	49.6	46	8	17.4
Previously diagnosed												
Yes	150	3	2.0	163	27	16.6	163	87	53.4	163	14	8.6
No	629	13	2.1	659	69	10.5	663	309	46.6	663	80	12.1
Concurrent chlamydia												
Yes	170	2	1.2	170	9	5.3	170	58	34.1	102	9	8.8
No	673	8	1.2	681	53	7.8	681	306	44.9	481	66	13.7
HIV status												
Positive	172	1	0.6	172	11	6.4	172	63	36.6	107	12	11.2
Negative	713	13	1.8	720	53	7.4	720	306	42.5	556	65	11.7
Overall resistance	2101	42	2.0	2147	169	7.9	2151	1091	50.7	1811	256	14.1

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 67.6% (1 455/2 151) of cases. The majority (88.7%, n=1 291) were diagnosed using culture-based methods, and of these, 153 patients also had microscopy performed, 80 patients had microscopy and a nucleic acid amplification test (NAAT) performed, seven patients were diagnosed by culture and NAAT, eight patients by culture, NAAT and another unspecified test, and one patient had culture, microscopy and another test (unspecified) 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 112 patients, 30 patients were diagnosed by microscopy, and of these 13/30 patients also had another test performed (unspecified), 4/30 patients also had a NAAT performed, and 4/30 patients had a NAAT and an additional diagnostic test performed. An unspecified test was used in 22 patients and, upon investigation, these were deemed to be culture methods.

Data on which antimicrobial was used to treat the patient infected with *N. gonorrhoeae* were only available for 18.6% of patients (400/2 151). Of these, 68.5% (274/400) received the recommended treatment of ceftriaxone and azithromycin, although the dosages were not available. More MSM received the recommended treatment (78.3%, n=126) than heterosexual men (66.3%, n=112) and females (66.7%, n=32).

Among the 126 patients who did not receive the recommended treatment for their gonococcal infection [1], 37 (29.4%) were given cefixime only, 30 (23.8%) ceftriaxone only, 26 (20.6%) ciprofloxacin, while four patients were administered azithromycin only, three were administered spectinomycin and azithromycin, two patients were prescribed cefixime and azithromycin and one patient was given only spectinomycin. Twenty-three patients (18.3%) were given an unspecified treatment, and upon investigation, the other treatments administered included doxycycline, penicillins and other cephalosporins. One patient given azithromycin harboured a resistant strain (MIC=0.75 mg/L) and 18 of 26 patients given ciprofloxacin harboured ciprofloxacin-resistant strains (all with MIC>0.5 mg/L). It is not known whether any treatments were administered based on prior susceptibility testing results.

4 Conclusions

A decrease in cefixime resistance was observed in 2014 across the EU/EEA (from 4.7% in 2013 to 2.0% in 2014), with resistant isolates detected in just 10 of the 23 countries, although it should be noted that some countries submitted a low number of isolates. The increase in the proportion of highly susceptible isolates in 2014, as well as the decreased number of isolates displaying a MIC of ≥0.5 mg/L, shows that the gonococcal population across Europe is becoming more susceptible to cefixime. Cefixime resistance continues to be lowest among MSM and highest in heterosexual males and females. Five isolates displayed ceftriaxone resistance in 2014, compared to seven in 2013 and three in 2012. Overall, the ceftriaxone MIC distribution of the isolates in 2014 shows more susceptibility than in 2013. These increases in cephalosporin susceptibility are very encouraging. Among patients for whom treatment was reported, 9.8% were administered cefixime, so the use of the recommended and more appropriate ceftriaxone, particularly in combination with azithromycin, may have contributed to this increase in cephalosporin susceptibility.

Rates of ciprofloxacin resistance were similar to 2013 at just over 50%. Worryingly, azithromycin resistance has continued to increase significantly, from 5.4% in 2013 to 7.9% in 2014. However, none of those antimicrobials are recommended for monotherapy, unless the isolates are first shown to be susceptible.

In previous years, there was a tendency for MSM to have a lower risk of harbouring resistant isolates [7], which was supported by a lower risk of resistance among anorectal isolates. However in 2014, there was a dramatic rise in azithromycin resistance in MSM (2.8% in 2013 to 10% in 2014), and the cefixime and ciprofloxacin resistance levels have remained the same since 2013, while large decreases in azithromycin, cefixime and ciprofloxacin resistance have been demonstrated in females.

Even though the overall resistance levels have fallen for cefixime and ceftriaxone in 2014, 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; improving representativeness of the programme and collecting more epidemiological variables, such as diagnostic tests and treatment used in 2014. Estonia and Poland joined Euro-GASP in 2014, thereby further strengthening the surveillance programme. Even though the overall completeness of variables remained quite similar to 2013, the fact that information on site of infection, previous gonorrhoea, concurrent STI and country of birth decreased slightly, along with a large decrease in reporting of probable country of infection, is disappointing. Reporting needs to improve if statistical analysis of the linked susceptibility and patient data is to be robust.
- Continuing country-support visits to promote the inclusion of additional centres and increase isolate numbers.
- 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 recommended dual therapy (ceftriaxone and azithromycin) to treat gonorrhoea [1]. The low data completeness for 'treatment used' is disappointing, however it was the first year that this variable was included. It has shown that the majority of the patients (68.5%) received appropriate therapy. However, it is of major concern that some patients still did not receive appropriate therapy which included ciprofloxacin, in particular those who harboured strains that were resistant to the administered therapy. The increasing azithromycin resistance detected in Euro-GASP is a threat to the effectiveness of dual therapy and needs to be monitored closely.
- Ensuring that all Euro-GASP laboratories participate in the EQA programme. Even though participation in the EQA is high, all Euro-GASP countries need to ensure full implementation.

Even though the number of isolates tested in Euro-GASP is increasing year on year, the percentage of isolates tested in Euro-GASP has decreased from 6% in 2009 to 3% in 2014. 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. A review of the number of isolates submitted to Euro-GASP is required.

Even though Euro-GASP detected decreases in cefixime and ceftriaxone resistance in 2014, the increase in azithromycin resistance and the detection of one isolate with a very high MIC of azithromycin (≥256 mg/L) is of major concern. Treatment failures are still possible, therefore continuous implementation 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 2014

Isolate collection

Submitted isolates

Each country should aim to collect a minimum of 110 gonococcal isolates each year, with the overall aim to retrieve and test a minimum of 100 isolates. For countries where 110 isolates represent less than 10% of the total number of gonorrhoea cases (Spain, 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 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 2014

As agreed at the Euro-GASP co-ordination meeting in December 2013, isolates were only collected once in 2014 in order to simplify processes and aim for a more efficient collection, analysis and reporting of data. The collection dates in 2014 were 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 for obtaining epidemiological data could be 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, to request it. This will require a patient identifier – at national level - to link to 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 the laboratory could retrieve (either data submitted with the isolate or data 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 due to 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 (2016 reporting protocol to be updated appropriately). Further details on the testing methodology can be found in Annex 2.

- Ciprofloxacin (breakpoint or all isolates tested by Etest)
- 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 tested annually since neither spectinomycin nor gentamicin is 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 penicillin, tetracycline, spectinomycin and gentamicin, beginning in 2016. This will not be mandatory and will not be quality assured using external quality assessments (EQAs) so a basic separate analysis should be undertaken.

Laboratories participating through centralised testing will be supported to move to decentralised testing through training, 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 4).

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 then 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.

Procedure for decentralised testing

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

- Submit MIC data and the 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 – 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 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 data collection should be organised locally and data 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). It is also recommended that the isolates 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 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.) and how are they sampled (consecutive patients; sampling);
- How is the AMR data linked to the epidemiological data (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);
- 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 is linked.

Gonococcal susceptibility data analysis

Collated data for each report will be analysed for emerging trends in antimicrobial resistance. As this continues to evolve it may be necessary to adapt the approach to analysis, but it is provisionally proposed that the following would be examined and presented in each report, if the data for that period indicate that it would be informative:

1. Summary of isolates received and tested for each country (table).
2. Overall incidence of resistance for each antimicrobial included for each testing year (bar graph).
3. MIC distribution by year for Ceftriaxone (bar graph).
4. % Ceftriaxone resistant isolates by country per year (bar graph).
5. MIC distribution by year for Cefixime (bar graph).
6. % Ceftriaxone resistance by country per year (bar graph).
7. Ciprofloxacin resistance by country by year.
8. Summary of epidemiological data received by each country (table).
9. Cefixime resistance versus sexual orientation and gender (bar graph/line graph).
10. Cefixime resistance versus age group and gender.
11. Similar analysis to for numbers 9 and 10 for Ceftriaxone (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

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

Centralised testing protocol

1. Isolates are shipped frozen to Public Health England, London, UK or Örebro University Hospital, Örebro, Sweden.
2. The isolates are stored at −70°C or in liquid nitrogen.
3. 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 5% CO_2.
4. 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 sub-culture is grown.
5. If there is a high level of contamination, cultures are repeatedly transferred to selective agar.
6. Susceptibility testing is performed using the agar dilution breakpoint technique or Etest for ciprofloxacin and azithromycin. Suspensions of cultures aged 18 to 24 hours are prepared equivalent to McFarland standard 0.5 (approximately 10^4 cfu/µl) in 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	Intermediate	Resistant
Ciprofloxacin	0.06*	0.5**
Azithromycin	0.25	0.5

*For low-level resistance
**For high-level resistance

7. The ceftriaxone and cefixime MICs are determined using Etests according to the manufacturer's instructions.
8. All isolates are tested for penicillinase production using the chromogenic reagent Nitrocefin.
9. Etests are performed on isolates that are resistant to azithromycin using the agar dilution breakpoint technique.
10. 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)
11. 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	0.5*	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)
**Reported as low-level resistance (I)

12. 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.

Note: Changes from previous versions are highlighted.

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 5**. If you use different RecordType versions the data will be rejected.	5	
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 as invalidated). If set to NEW/UPDATE or left empty, the record is added to the database as a new entry.	Status of reporting NEW/UPDATE or DELETE (inactivate).	
Subject	Subject corresponding to the RecordType	GONOAMR	Mandatory
ReportingCountry	The country reporting the record.	ISO coded value list	Mandatory
DataSource	The data source for AMR NG (laboratory) that the record originates from.	Coded value list; codes maintained by each Member State in the data source editing interface in TESSy	Mandatory
DateUsedForStatistics	Date the specimen was taken from the patient, alternatively use date received in laboratory	Preferred format: yyyy-mm-dd	Mandatory
Gender	Gender of the infected person	F = Female M = Male O = Other UNK = Unknown	Mandatory
Age	Age in years of patient as reported in the national system	0-120, UNK	Mandatory
PlaceOfResidence	Place of residence of patient, NUTS level 0-3 (region)	NUTS code 0-3	
ClinicalServiceType	Type of clinical service where patient was first seen	ANC - ANC COMB - Combined service DV - Dermatology-venereology clinic ED - Hospital Emergency Dept FPC - Family Planning Clinic GP - General Practitioner GYN - Gynaecology clinic ID - Infectious disease clinic OPC - Other primary care STI - Dedicated STI clinic URO - Urology YTH - Youth clinics O - Other UNK - Unknown	

Variable	Variable description	Coding	Validation rules
CountryOfBirth	Country of birth of patient	ISO coded value list, UNK	
ProbableCountryOfInfection	Probable country(ies) of infection, country(ies) visited during the incubation period of the reported disease. Repeatable field.	ISO coded value list, UNK	
Transmission	Mode of transmission	HETERO = Heterosexual contact MSM = MSM/homo or bisexual male MTCT = Mother-to-child transmission O = Other UNK = Unknown	Error if Transmission = MSM and Gender = F
SiteOfInfection	Site of infection	AR = Ano-Rectal GEN = Genital PH = Pharyngeal O = Other NA = Not applicable UNK = Unknown	
PrevGono	Existing evidence about previous gonorrhoea	Y = Yes N = No UNK =Unknown	
HIVStatus	HIV status of patient at time of diagnosis	POS = Positive POSKNOWN = Known HIV positive POSNEW = New HIV diagnosis NEG = Negative UNK = Unknown	
ConcurrentSTI	Concurrent STI	CHLAM = Chlamydia HEPB = Hepatitis B HEPC = Hepatitis C HERP = Genital herpes LGV = *Lymphogranuloma venereum* SYPH = Syphilis WARTS = Genital warts MYCO = *Mycoplasma genitalium* NO = No concurrent STI UNK = Unknown	
ResultPor	Por allele number generated from a 490 nucleotide por 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 Por 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	CULT = culture MICRO = microscopy NA = Not applicable NUCLACID = detection of nucleic acid O = Other Unk = Unknown	

Variable	Variable description	Coding	Validation rules
TreatmentUsed	Treatment used	CFM = Cefixime CRO = Ceftriaxone SPT = Spectinomycin CIP = Ciprofloxacin GEN = Gentamicin AZM = Azithromycin CROAZM = Ceftriaxone and Azithromycin UNK = Unknown O = Other	
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, 2014

	All countries		Austria		Belgium		Cyprus		Denmark		Estonia		France		Germany		Greece	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
	2151		101		140		2		109		13		110		106		110	
Sexual orientation & gender																		
Female	318	22.7	21	27.6	26	39.4	0	0.0	43	46.2	4	100	16	100	7	58.3	2	1.9
Male heterosexual	485	34.7	46	60.5	22	33.3	0	0.0	29	31.2	0	0.0	0	0.0	2	16.7	71	68.9
MSM	594	42.5	9	11.8	18	27.3	0	0.0	21	22.6	0	0.0	0	0.0	3	25.0	30	29.1
Unknown	754		25		74		2		16		9		94		94		7	
Gender																		
All males	1821	85.1	80	79.2	109	80.7	2	100	66	60.6	9	69.2	94	85.5	99	93.4	108	98.2
Female	318	14.9	21	20.8	26	19.3	0	0.0	43	39.4	4	30.8	16	14.5	7	6.6	2	1.8
Unknown	11		0		5*		0		0		0		0		0		0	
Age (years)																		
<25	605	28.7	36	35.6	31	79.2	1	50.0	54	49.5	4	33.3	35	34.0	18	17.1	23	21.5
≥25	1501	71.3	65	64.4	106	20.8	1	50.0	55	50.5	8	66.7	68	66.0	87	82.9	84	78.5
Unknown	44		0		3		0		0		1		7		1		3	
Site of infection																		
Genital	1549	76.3	96	95.0	106	79.7	2	100	103	94.5	12	92.3	15	13.6	92	88.5	106	100.0
Anorectal	192	9.5	2	2.0	8	6.0	0	0.0	4	3.7	0	0.0	6	5.5	4	3.8	0	0.0
Pharyngeal	154	7.6	3	3.0	0	0.0	0	0.0	2	1.8	0	0.0	0	0.0	1	1.0	0	0.0
Other	135	6.6	0	0.0	19	14.3	0	0.0	0	0.0	1	7.7	89	80.9	7	6.7	0	0.0
Unknown	121		0		7		0		0		0		0		2		4	
Previously diagnosed																		
No	663	80.3	2	25.0	40	85.1	0	0.0	100	91.7	1	100	0	0.0	6	66.7	66	65.3
Yes	163	19.7	6	75.0	7	14.9	0	0.0	9	8.3	0	0.0	0	0.0	3	33.3	35	34.7
Unknown	1325		93		93		2		0		12		110		97		9	
Concurrent STI																		
Concurrent CT	170	20.0	9	11.5	4	13.3	0	0.0	0	0.0	1	50.0	11	26.8	3	37.5	0	0.0
Concurrent other	41	4.8	0	0.0	3	10.0	0	0.0	0	0.0	0	0.0	1	2.4	0	0.0	3	17.6
No concurrent STI	640	75.2	69	88.5	23	76.7	0	0.0	0	0.0	1	50.0	29	70.7	5	62.5	14	82.4
Unknown	1300		23		110		2		109		11		69		98		93	
HIV status																		
Positive	172	19.3	2	12.5	15	31.3	0	0.0	3	4.7	0	0.0	5	100	5	100.0	3	20.0
Negative	720	80.7	14	87.5	33	68.8	0	0.0	61	95.3	1	100	0	0.0	0	0.0	12	80.0
Unknown	1259		85		92		2		45		12		105		101		95	

*Include one patient with 'other'

Table A6.1 Patient characteristics for cases reported to Euro-GASP; overall and by country, 2014 (continued)

	Hungary		Iceland		Ireland		Italy		Latvia		Malta		Netherlands		Norway		Poland	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
	89		12		101		50		21		21		227		110		46	
Sexual orientation & gender																		
Female	13	72.2	1	100	4	4.3	1	2.2	6	31.6	2	9.5	26	11.5	24	100	1	100
Male heterosexual	4	22.2	0	0.0	19	20.2	14	30.4	13	68.4	3	14.3	31	13.7	0	0.0	0	0.0
MSM	1	5.6	0	0.0	71	75.5	31	67.4	0	0.0	16	76.2	170	74.9	0	0.0	0	0.0
Unknown	71		11		7		4		2*		0		0		86		45	
Gender																		
Male	74	85.1	11	91.7	97	96.0	48	98.0	15	71.4	19	90.5	201	88.5	84	77.8	45	97.8
Female	13	14.9	1	8.3	4	4.0	1	2.0	6	28.6	2	9.5	26	11.5	24	22.2	1	2.2
Unknown	2		0		0		1		0		0		0		2		0	
Age (years)																		
<25	16	25.8	1	8.3	28	27.7	9	18.4	7	33.3	6	28.6	69	30.4	42	38.2	8	17.4
≥25	46	74.2	11	91.7	73	72.3	40	81.6	14	66.7	15	71.4	158	69.6	68	61.8	38	82.6
Unknown	27		0		0		1		0		0		0		0		0	
Site of infection																		
Genital	77	96.3	10	90.9	50	49.5	40	80.0	20	100	14	66.7	106	46.7	91	87.5	40	87.0
Anorectal	0	0.0	1	9.1	26	25.7	9	18.0	0	0.0	6	28.6	86	37.9	10	9.6	5	10.9
Pharyngeal	3	3.8	0	0.0	25	24.8	0	0.0	0	0.0	1	4.8	35	15.4	3	2.9	1	2.2
Other	0	0.0	0	0.0	0	0.0	1	2.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Unknown	9		1		0		0		1		0		0		6		0	
Previously diagnosed																		
No	0	0.0	0	0.0	73	76.8	40	85.1	18	85.7	20	95.2	0	0.0	0	0.0	0	0.0
Yes	0	0.0	0	0.0	22	23.2	7	14.9	3	14.3	1	4.8	0	0.0	0	0.0	0	0.0
Unknown	89		12		6		3		0		0		227		110		46	
Concurrent STI																		
Concurrent CT	0	0.0	0	0.0	19	20.0	3	6.3	5	23.8	5	23.8	57	25.1	0	0.0	0	0.0
Concurrent other	0	0.0	0	0.0	3	3.2	0	0.0	0	0.0	7	33.3	10	4.4	0	0.0	0	0.0
No concurrent STI	0	0.0	0	0.0	73	76.8	45	93.8	16	76.2	9	42.9	160	70.5	0	0.0	0	0.0
Unknown	89		12		6		2		0		0		0		110		46	
HIV status																		
Positive	1	100	0	0.0	11	11.8	5	10.6	0	0.0	4	19.0	60	26.8	0	0.0	0	0.0
Negative	0	0.0	0	0.0	82	88.2	42	89.4	21	100	17	81.0	164	73.2	0	0.0	0	0.0
Unknown	88		12		8		3		0		0		0		0		46	

*Include one patient with 'other'

Table A6.1 Patient characteristics for cases reported to Euro-GASP; overall and by country, 2014 (end)

	Portugal		Slovakia		Slovenia		Spain		Sweden		UK	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
	110		109		82		151		100		231	
Sexual orientation & gender												
Female	13	39.4	18	26.5	8	11.6	15	9.9	31	100	36	16.1
Male heterosexual	5	15.2	42	61.8	28	40.6	119	78.8	0	0.0	37	16.5
MSM	15	45.5	8	11.8	33	47.8	17	11.3	0	0.0	151	67.4
Unknown	77		41		13		0		69		7	
Gender												
Male	97	88.2	91	83.5	74	90.2	136	90.1	69	69.0	193	84.3
Female	13	11.8	18	16.5	8	9.8	15	9.9	31	31.0	36	15.7
Unknown	0		0		0		0		0		2	
Age (years)												
<25	30	27.3	13	11.9	21	25.9	42	28.0	41	41.0	70	30.3
≥25	80	72.7	96	88.1	60	74.1	108	72.0	59	59.0	161	69.7
Unknown	0		0		1		1		0		0	
Site of infection												
Genital	105	95.5	108	99.1	60	73.2	145	96.0	63	72.4	88	58.7
Anorectal	0	0.0	0	0.0	3	3.7	1	0.7	5	2.3	16	10.7
Pharyngeal	3	2.7	1	0.9	19	23.2	1	0.7	22	25.3	34	22.7
Other	2	1.8	0	0.0	0	0.0	4	2.6	0	0.0	12	8.0
Unknown	0		0		0		0		10		81	
Previously diagnosed												
No	14	63.6	104	95.4	64	92.8	0	0.0	0	0.0	115	68.9
Yes	8	36.4	5	4.6	5	7.2	0	0.0	0	0.0	52	31.1
Unknown	88		0		13		151		100		64	
Concurrent STI												
Concurrent CT	1	4.5	8	8.9	8	12.3	0	0.0	0	0.0	36	41.9
Concurrent other	2	9.1	1	1.1	4	6.2	0	0.0	0	0.0	7	8.1
No concurrent STI	19	86.4	81	90.0	53	81.5	0	0.0	0	0.0	43	50.0
Unknown	88		19		17		151		100		145	
HIV status												
Positive	5	22.7	3	3.4	5	8.3	0	0.0	0	0.0	45	28.0
Negative	17	77.3	85	96.6	55	91.7	0	0.0	0	0.0	116	72.0
Unknown	88		21		22		151		100		70	

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, 2014

	Austria (n=101)	Belgium (n=140)	Cyprus (n=2)	Denmark (n=109)	Estonia (n=13)	France (n=110)	Germany (n=106)	Greece (n=110)
Clinical service types								
ANC – antenatal clinic	0	0	0	0	0	0	0	0
COMB – combined service	0	0	0	0	0	0	0	10
DV – dermatology-venereology clinic	19	0	2	0	4	0	9	0
ED – Hospital emergency department	0	0	0	0	0	8	0	0
FPC – family planning clinic	0	0	0	0	0	0	0	0
GP – general practitioner	61	0	0	58	0	76	6	0
GYN – gynaecology clinic	0	0	0	2	1	3	5	0
ID – infectious disease clinic	0	0	0	1	0	0	0	0
OPC – other primary care	0	0	0	0	0	0	0	0
STI – dedicated STI clinic	12	11	0	46	0	15	0	100
URO – urology	0	0	0	1	1	4	64	0
YTH – youth clinics	0	0	0	0	0	0	0	0
O – other	0	0	0	1	2	4	20	0
UNK – unknown	9	129	0	0	5	0	2	0
Place of residence								
NUTS level 0-3 (region)[1]	AT12=2	UNK=140	CY000=2	DK011=24	EE001=2	FR=110	DE113=1	CY0=1
	AT13=84			DK012=6	EE004=7		DE126=1	DE=1
	AT21=2			DK013=4	EE006=1		DE21H=3	EL=57
	AT22=4			DK021=1	EE008=2		DE3=26	EL122=1
	AT31=7			DK022=5	UNK=1		DE6=27	EL253=1
	AT32=2			DK031=14			DEA13=3	EL30=2
				DK032=16			DEA15=9	EL300=47
				DK041=4			DEA24=1	
				DK042=7			DEA43=3	
				DK050=8			DEB17=4	
				UNK=20			DED2=9	
							DED2D=4	
							DED45=1	
							DED52=14	
Country of birth								
ISO coded value list[2]	UNK=101	AL=1	CY=2	AF=2	EE=13	UNK=110	DE=24	AF=2
		BE=39		CG=1			UNK=82	AL=7
		CL=1		DK=77				BG=3
		NL=1		IQ=1				EG=2
		UK=1		LB=1				EL=83
		UNK=97		UNK=27				MA=1
								MD=1
								PK=3
								RO=2
								SO=1
								SY=1
								UNK=4
Probable country of infection								
ISO coded value list[2]	UNK=101	BE=13	CY=2	AU=1	UNK=13	UNK=110	PL=2	DE=1
		RU=1		DK=80			UNK=104	UNK=109
		TG=1		IQ=1, PH=1				
		TH=1		TH=1, US=1				
		UNK=124		UNK=24				

UNK: unknown

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

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, 2013 (continued)

	Hungary (n=89)	Iceland (n=12)	Ireland (n-101)	Italy n=50)	Latvia (n=21)	Malta (n=21)	Netherlands (n=227)	Norway (n=110)
Clinical service types								
See first table for codes	UNK=89	DV=11	GP=6	COMB=2	COMB=18	STI=21	STI=227	UNK=110
		GP=1	STI=95	DV=6	OPC=3			
				ID=1				
				STI=29				
				O=12				
Place of residence								
NUTS level 0-3 (region) [1]	UNK=89	UNK=12	IE=101	ITC11=13	LV003=2	MT001=21	NL213=1	UNK=110
				ITC47=1	LV006=14		NL221=1	
				ITC4A=1	LV007=3		NL230=6	
				ITC4C=17	LV008=1		NL310=7	
				ITH55=6	LV009=1		NL322=4	
				ITI21=2			NL323=3	
				ITI22=1			NL324=4	
				ITI43=6			NL325=1	
				UNK=3			NL326=184	
							NL327=4	
							NL332=2	
							NL337=3	
							NL339=1	
							NL413=1	
							UNK=5	
Country of birth								
ISO-coded value list[2]	HU=29	UNK=12	AU=1	BR=1	UNK=21	DE=1	AF=1, AL=1	UNK=110
	UNK=60		BE=1	DO=1		ES=4	ANHH=1	
			BR=11	EG=2		HR=1	AT=1, AU=2	
			CA=1	ES=1		IT=1	AW=1, BE=2	
			CN=1	GH=1		MT=14	BG=1, BQ=1	
			CZ=1	IT=40			BR=4, CN=1	
			FR=1	SN=1			CO=3, CV=1	
			HR=1	UNK=3			CW=5, DE=2	
			HU=1				EE=1, FR=1	
			IE=56				GH=1, HN=1	
			MD=1				IE=1, IT=1	
			MX=1				MA=2, MY=1	
			PL=3				NG=1	
			PT=1				NL=160	
			SK=1				PK=1, PL=1	
			UK=5				PT=1, RU=1	
			UNK=8				SE=1, SG=1	
			VE=5				SR=8, SY=1	
			ZA=1				TR=3, UK=7	
							US=3, VE=2	
Probable country of infection								
ISO coded value list[2]	HU=7	UNK=12	IE=85	IT=45	LV=20	MT=21	UNK=227	UNK=110
	UNK=82		PL=1	UNK=5	UNK=1			
			TH=1, UK=2					
			UNK=12					

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, 2013 (end)

	Poland (n=46)	Portugal (n=110)	Slovakia (n=109)	Slovenia (n=82)	Spain (n=151)	Sweden (n=100)	UK (n=231)
Clinical service types							
See first table for codes	UNK=46	O=46	DV=39	DV=52	COMB=151	UNK=100	GP=2
		STI=22	GP=1	ED=1			STI=229
		UNK=42	GYN=15	O=19			
			ID=2	OPC=3			
			O=1	STI=6			
			URO=51	URO=1			
Place of residence							
NUTS level 0-3 (region)[1]	UNK=46	PT111=2	SK01=43	SI=75	ES111=2	UNK=100	UKD3=8
		PT113=6	SK021=25	UNK=7	ES113=2		UKD72=2
		PT114=21	SK022=10		ES114=22		UKE2=1
		PT115=6	SK023=28		ES120=24		UKE31=1
		PT150=3	SK041=2		ES220=11		UKE32=5
		PT163=1	SK042=1		ES300=48		UKE42=5
		PT16B=5			ES411=1		UKE45=1
		PT171=56			ES413=3		UKF14=5
		PT172=9			ES419=2		UKF24=2
		PT184=1			ES422=4		UKG31=11
					ES432=1		UKG32=1
					ES511=6		UKG37=1
					ES521=6		UKG38=2
					ES523=10		UKH24=1
					ES611=9		UKH25=2
							UKI=128
							UKJ11=4
							UKJ12=1
							UKJ21=8
							UKJ23=2
							UKJ24=1
							UKK11=5
							UKK13=1
							UKM2=2
							UKM27=1
							UKM3=6
							UKM50=1
							UKM6=1
							UNK=22
Country of birth							
ISO-coded value list[2]	UNK=46	UNK=110	CZ=1	BA=1	UNK=151	UNK=100	DE=1
			SK=106	RS=1			IE=1
			UNK=2	SI=71			UK=10
				UNK=9			UNK=219
Probable country of infection							
ISO-coded value list[2]	UNK=46	PL=1	AT=1	CH=1	ES=151	UNK=100	AU=2, BR=1
		UNK=109	CZ=1	DE=1			CN=1, ES=1
			SK=63	ES=2			FR=1, GH=1
			UNK=44	GQ=1			IL=1, PK=1
				SI=66			PL=1, SO=1
				UNK=11			TH=1, UNK=219

UNK: unknown

Annex 7. Statistical tables

Table A7.1 Univariate association of cefixime resistance/susceptibility and patient characteristics, Euro-GASP, 2014

	Cefixime resistance (%, 95% CI)	Odds ratio	95% CI	P value
Site of infection (n=1980)				
Genital (1499)	34 (2.3, 1.6 – 3.2)			
Anorectal (192)	2 (1.0, 0.3 – 3.7)			
Pharyngeal (154)	0 (0, 0 – 2.4)			
Other (135)	4 (3, 1.2 – 7.4)			0.128*
Sexual orientation & gender (n=1350)				
MSM (583)	7 (1.2, 0.6 – 2.5)	4.9	2.19 – 10.95	<0.0001
Male heterosexual (449)	8 (1.8, 0.9 – 3.5)	4.4	1.92 – 9.88	0.0001
Female (318)	8 (2.5, 1.3 – 4.9)			
Previous GC (n=779)				
Yes (150)	3 (2, 0.7 – 5.7)			
No (629)	13 (2.1, 1.2 – 3.5)			1.0*
Concurrent chlamydia (n=843)				
Yes (170)	2 (1.2, 0.3 – 4.2)			
No (673)	8 (1.2, 0.6 – 2.3)			1.0*
HIV status (n=885)				
Positive (172)	1 (0.6, 0.1 – 3.2)			
Negative (713)	13 (1.8, 1.1 – 3.1)			0.326*
Age (n=2056)				
<25 years (597)	7 (1.2, 0.6 – 2.4)			
≥25 years (1459)	33 (2.3, 1.6 – 3.2)	1.95	0.86 – 4.44	0.1046

Note: *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, 2014

	Azithromycin resistance (%, 95% CI)	Odds ratio	95% CI	P value
Site of infection (n=2026)				
Genital (1545)	120 (7.8, 6.5 – 9.2)			
Anorectal (192)	20 (10.4, 6.8 – 15.5)	1.38	0.84 – 2.28	0.2035
Pharyngeal (154)	13 (8.4, 5 – 13.9)	1.1	0.6 – 1.99	0.7664
Other (135)	11 (8.2, 4.6 – 14)	1.05	0.55 – 2.01	0.8742
Sexual orientation & gender (n=1394)				
MSM (594)	59 (9.9, 7.8 – 12.6)			
Male heterosexual (482)	43 (8.9, 6.7 – 11.8)	0.89	0.59 – 1.34	0.5734
Female (318)	7 (2.2, 1.1 – 4.5)	0.2	0.09 – 0.46	<0.001
Previous GC (n=822)				
Yes (163)	27 (16.6, 11.6 – 23)	1.7	1.05 – 2.76	0.0302
No (659)	69 (10.5, 8.4 – 13)			
Concurrent chlamydia (n=851)				
Yes (170)	9 (5.3, 2.8 – 9.8)			
No (681)	53 (7.8, 6 – 10)	1.51	0.73 – 3.13	0.2644
HIV status (n=892)				
Positive (172)	11 (6.4, 3.6 – 11.1)			
Negative (720)	53 (7.4, 5.7 – 9.5)	1.16	0.59 – 2.28	0.6594
Age (n=2102)				
<25 years (604)	41 (6.8, 5 – 9.1)			
≥25 years (1498)	124 (8.3, 7 – 9.8)	1.24	0.86 – 1.79	0.2506

Table A7.3 Univariate association of ciprofloxacin resistance/susceptibility and patient characteristics, Euro-GASP, 2014

	Ciprofloxacin resistance (%, 95% CI)	Odds ratio	95% CI	P value
Site of infection n= (2030)				
Genital (1549)	828 (53.5, 51 – 55.9)			
Anorectal (192)	83 (43.2, 36.4 – 50.3)	0.66	0.49 – 0.9	0.0075
Pharyngeal (154)	66 (42.9, 35.3 – 50.8)	0.65	0.47 – 0.91	0.012
Other (135)	67 (49.6, 41.3 – 58)	0.86	0.6 – 1.22	0.3932
Sexual orientation & gender (n=1397)				
MSM (594)	252 (42.4, 38.5 – 46.4)			
Male heterosexual (485)	267 (55.1, 50.6 – 59.4)	1.67	1.3 – 2.12	<0.001
Female (318)	132 (41.5, 36.2 – 47)	0.96	0.73 – 1.27	0.7898
Previous GC (n=826)				
Yes (163)	87 (53.4, 45.7 – 60.9)	1.31	0.93 – 1.85	0.1215
No (663)	309 (46.6, 42.8 – 50.4)			
Concurrent chlamydia (n=851)				
Yes (170)	58 (34.1, 27.4 – 41.5)			
No (681)	306 (44.9, 41.2 – 48.7)	1.58	1.11 – 2.24	0.0108
HIV status (n=892)				
Positive (172)	63 (36.6, 29.8 – 44.1)			
Negative (720)	306 (42.5, 38.9 – 46.1)	1.28	0.91 – 1.8	0.1603
Age (n=2106)				
<25 years (605)	260 (43, 39.1 – 47)			
≥25 years (1501)	808 (53.8, 51.3 – 56.3)	1.55	1.28 – 1.87	<0.001

Table A7.4 Univariate association of penicillinase activity and patient characteristics, Euro-GASP, 2014

	Penicillinase activity (%, 95% CI)	Odds ratio	95% CI	P value
Site of infection (n=1690)				
Genital (1426)	222 (15.6, 13.8 – 17.5)			
Anorectal (99)	6 (6.1, 2.8 – 12.6)	0.35	0.15 – 0.81	0.01
Pharyngeal (119)	11 (9.2, 5.2 – 15.8)	0.55	0.29 – 1.05	0.0641
Other (49)	8 (17.4, 9.1 – 30.7)	1.14	0.53 – 2.48	0.7375
Sexual orientation & gender (n=1153)				
MSM (424)	32 (7.6, 5.4 – 10.5)			
Male heterosexual (454)	82 (18.1, 14.8 – 21.9)	2.7	1.74 – 4.19	<0.001
Female (275)	37 (13.5, 9.9 – 18)	1.9	1.15 – 3.15	0.0106
Previous GC n=826				
Yes (163)	14 (8.6, 5.2 – 13.9)	0.69	0.38 – 1.24	0.2107
No (663)	80 (12.1, 9.8 – 14.8)			
Concurrent chlamydia (n=583)				
Yes (102)	9 (8.8, 4.7 – 15.9)			
No (481)	66 (13.7, 10.9 – 17.1)	1.64	0.79 – 3.42	0.18
HIV status (n=663)				
Positive (107)	12 (11.2, 6.5 – 18.6)			
Negative (556)	65 (11.7, 9.3 – 14.6)	1.05	0.55 – 2.02	0.8882
Age (n=1773)				
<25 years (500)	70 (14, 11.2 – 17.3)			
≥25 years (1273)	182 (14.3, 12.5 – 16.3)	1.03	0.76 – 1.38	0.872

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