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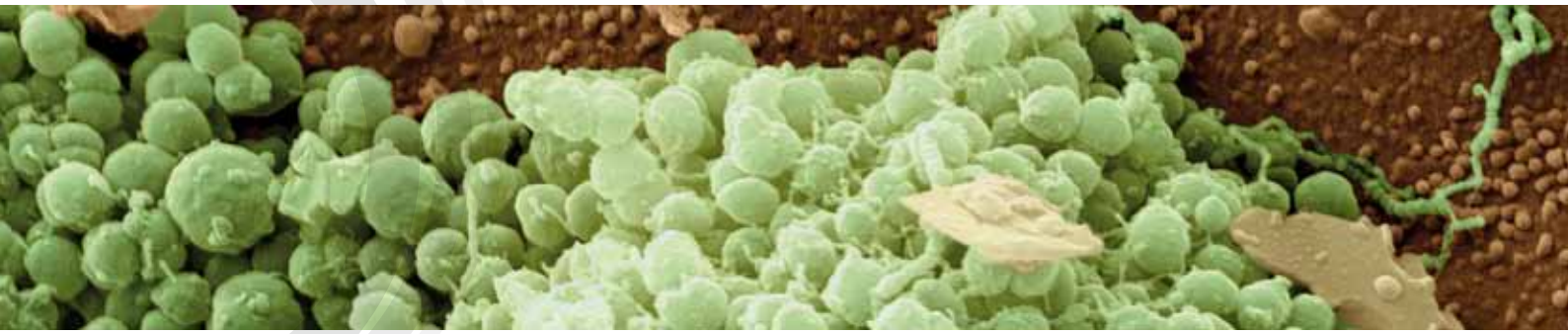

Gonococcal antimicrobial susceptibility surveillance in Europe

2012

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This report of the European Centre for Disease Prevention and Control (ECDC) was coordinated by Gianfranco Spiteri and Andrew J Amato-Gauci, and produced by Public Health England, London, United Kingdom and Örebro University Hospital, Örebro, Sweden.

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Abbreviations

AMR	Antimicrobial resistance
CI	Confidence interval
CT	*Chlamydia trachomatis*
DS	Decreased susceptibility
DV	Dermatovenerology
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
NG	*Neisseria gonorrhoeae*
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 establishment of a European sexually transmitted infection (STI) surveillance network by the European Centre for Disease Prevention and Control (ECDC) greatly strengthened the surveillance of *Neisseria gonorrhoeae* (NG) antimicrobial susceptibility in the EU/EEA. The major elements of ECDC's approach to NG surveillance are: biannual decentralised testing, stronger efforts to increase the number of participating countries, the inclusion of more gonococcal isolates, the collection of epidemiological and behavioural variables, and the continuation of an external quality assurance (EQA) scheme for gonococcal antimicrobial susceptibility.

During 2012, the European Gonococcal Antimicrobial Surveillance Programme (Euro-GASP) followed a biannual decentralised and centralised testing model, which calls for participating laboratories to collect gonococcal isolates between April and May and between October and November. For centralised testing, susceptibility testing was performed on all isolates by Etest or agar dilution for the following antimicrobials: cefixime, ceftriaxone, ciprofloxacin, azithromycin, spectinomycin and gentamicin. Participating laboratories that fulfilled a predefined set of criteria took part in decentralised testing, performed in the participant's own facilities.

In 2012, 20 EU/EEA Member States participated in Euro-GASP, 10 of which did so in decentralised testing. A total of 1 927 isolates were collected and tested. The majority of gonococci (84%) were collected from samples from men. The age range of the patients was less than one year to 78 years, with a median of 28 years; interquartile range was 23 to 37 years, and 33% of patients were younger than 25 years, with men who have sex with men (MSM) and male heterosexuals significantly older than women.

The site of specimen collection was mainly genital (83%), followed by rectal (10%) and pharyngeal (5%). When information on previous diagnosis of gonorrhoea was available, 17% had previously been diagnosed with the disease. Twenty-three per cent of the patients were concurrently diagnosed with chlamydia. When sexual preference was known, 59% stated that they were heterosexual, and 41% said they were MSM. Regarding HIV status, 14% were HIV positive, and 90% of those were MSM.

Applying a breakpoint of >0.125 mg/L, a lower proportion of tested isolates showed decreased susceptibility to cefixime in 2012 (3.9%, compared with 7.6% in 2011). Isolates with this phenotype were detected in 14 countries, three fewer than in 2011. In 2012, patients who acquired a strain displaying decreased susceptibility to cefixime were more likely to be heterosexual and younger than 25 years. Three isolates with decreased susceptibility to ceftriaxone (>0.125 mg/L) were detected compared with 10 in 2011. Rates of ciprofloxacin resistance remained stable (50.1% in 2012, 48.7% in 2011), and azithromycin resistance has continued to decrease (4.5% in 2012, down from 5.3 % in 2011). Three isolates displayed high-level resistance to azithromycin (≥256 mg/L). The minimum inhibitory concentration (MIC) distribution of gentamicin continues to offer hope that gentamicin could be considered for therapy in the future. Overall, the distribution of resistance is similar across patient groups and specimen types, with one exception: ciprofloxacin resistance is associated with heterosexuality, no concurrent chlamydia infection, and age (>25 years).

Nineteen countries participated in the gonococcal antimicrobial resistance EQA scheme. The EQA has continued to document high comparability between participants, which in turn raises confidence in Euro-GASP with respect to the quality and comparability of gonococcal antimicrobial susceptibility testing, particularly for decentralised testing.

The fact that decreased susceptibility levels to cefixime and ceftriaxone remain low is encouraging and may extend the life span of the last remaining treatment options for gonorrhoea across Europe. However, the currently observed lower levels of antimicrobial resistance may be short-lived, and efforts should continue to keep gonorrhoea a treatable infection.

1 Introduction

ECDC has coordinated the enhanced surveillance of STI in the EU/EEA since 2009. STI microbiological work is carried out by an international team coordinated by Public Health England (United Kingdom), with additional support from Örebro University Hospital (Sweden).

The main objectives of the STI microbiology project are:

- to improve the quality of laboratory surveillance of gonorrhoea, syphilis, congenital syphilis and infection with *Chlamydia trachomatis* (including Lymphogranuloma venereum) in EU/EEA Member States; and
- to strengthen the surveillance of NG antimicrobial susceptibility in EU/EEA Member States, by, among other activities, conducting an EQA scheme and offering training courses.

1.1 Background

The emergence and spread of antimicrobial resistance (AMR) in *N. gonorrhoeae* is a serious threat to the treatment and control of gonorrhoea. The therapeutic agents currently recommended in Europe [1] – extended-spectrum cephalosporins, ideally given together with azithromycin – are the last remaining options for effective first-line and alternative antimicrobial monotherapy [2]. The European Gonococcal Antimicrobial Surveillance Programme (Euro-GASP) identified decreasing susceptibility to these agents and documented treatment failures [3], resulting in the establishment of a European response plan to control and manage the threat of multidrug-resistant *N. gonorrhoeae* in Europe [4].

In 2011, Euro-GASP ran a sentinel surveillance programme in 21 EU countries. The major findings were [5]:

- Eight per cent of tested isolates showed decreased susceptibility to cefixime, using a cut-off of >0.125 mg/L. This represents a 3% increase compared with 2009.
- Ten isolates with decreased susceptibility to ceftriaxone, using a cut-off of >0.125 mg/L, were detected for the first time by Euro-GASP.
- Rates of ciprofloxacin and azithromycin resistance decreased but remained high across Europe (49% and 5%, respectively).
- The MIC distribution (*in vitro* susceptibility) of gentamicin suggests that this antimicrobial might be used for therapy in the future.

1.2 Objectives

There is a clear need to monitor *N. gonorrhoeae* AMR in the EU/EEA Member States because 8% of isolates displayed decreased susceptibility to cefixime (tested in Euro-GASP 2011); there are also a number of documented treatment failures.

It is the overall aim of the STI microbiology project to strengthen the surveillance of gonococcal antimicrobial susceptibility in the EU/EEA Member States. The following objectives are focused on achieving this aim:

- Developing and implementing sentinel surveillance of gonococcal antimicrobial susceptibility to a range of therapeutically relevant antimicrobials.
- Improving the timeliness of surveillance to allow more frequent reporting of developments in gonococcal antimicrobial susceptibility across Europe.
- Linking susceptibility data with epidemiological information to better understand the risk factors associated with emerging resistance patterns.
- Implementing an EQA scheme for antimicrobial susceptibility testing across Europe.
- Provision of training in gonococcal culture and antimicrobial susceptibility testing, thereby facilitating better gonococcal antimicrobial susceptibility surveillance, using a standardised methodology across Europe.

This report presents the results of the 2012 gonococcal antimicrobial susceptibility sentinel surveillance and a summary of the results of the second 2012 EQA scheme.

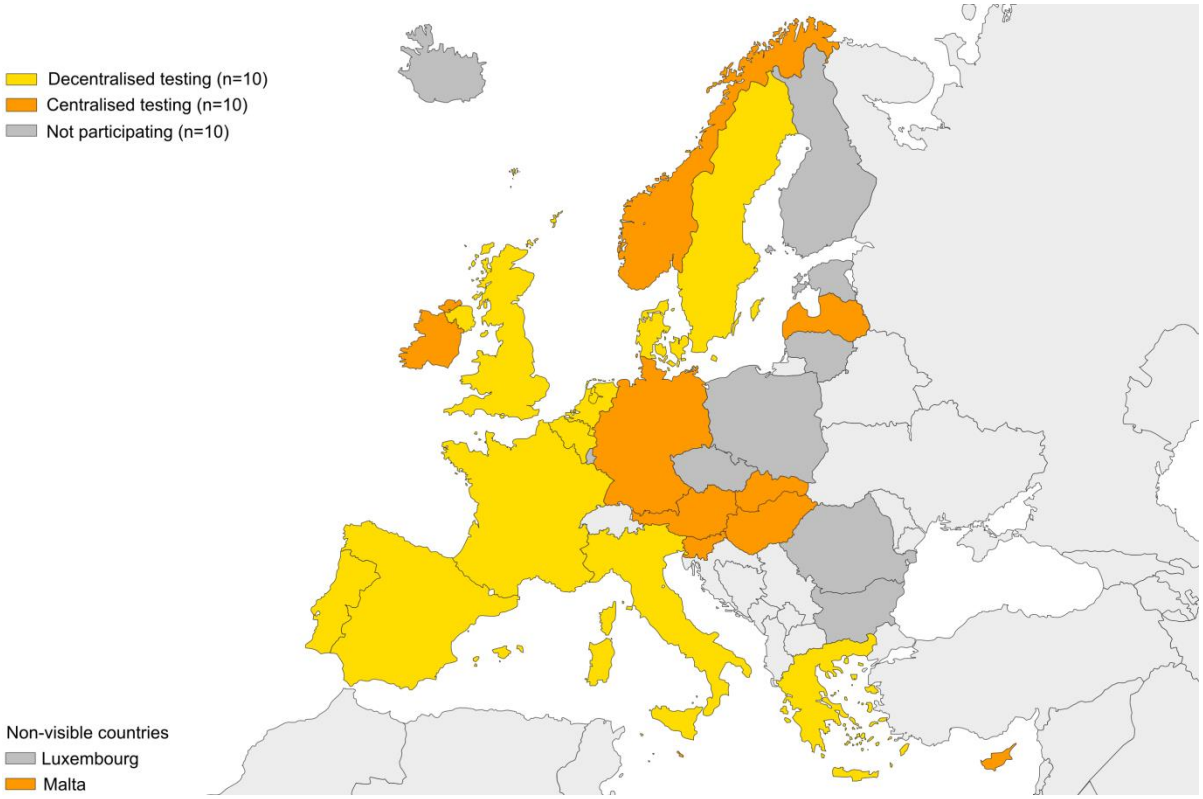
2 Methods

Euro-GASP follows a biannual schedule. Participating laboratories were requested to collect gonococcal isolates during two periods: from April to May and from October to November. The centralised and decentralised testing model continued to be used: in decentralised testing, participating laboratories that fulfilled predefined quality criteria, performed their own susceptibility testing. Laboratories were then requested to upload their results to The European Surveillance System (TESSy) database. Other participating countries followed a centralised testing model, where susceptibility testing was performed at Public Health England (London) and Örebro University Hospital (Örebro, Sweden), using the same methodology (see 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

Nominated contact points for STI surveillance from twenty EU/EEA countries participated in Euro-GASP in 2012 (Map 1), one country fewer (Romania) than in 2011.

Map 1. Countries participating in Euro-GASP, 2012



2.2 National protocol

Each country referring 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 in interpreting data and ensuring accurate linking of laboratory and epidemiological data.

2.3 Isolate collection

Each country was asked to contribute 100 isolates each year (110 from countries which participated in centralised testing, with the aim of retrieving and testing 100 isolates). Countries where 100 isolates represent less than 10% of the total number of cases of gonorrhoea (the Netherlands, Spain and the United Kingdom) were requested to collect up to a maximum of 200 isolates. Half the isolates should be collected between April and May, with the remainder collected in between October and November. In the United Kingdom, the collections took place in July and September to coincide with the collection period of the national Gonococcal Resistance to Antimicrobials Surveillance Programme (GRASP) in England and Wales. Laboratories were requested to collect one isolate from each patient in the following order of preference when multiple sites were infected:

- 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, for susceptibility testing.

2.4 Antimicrobial susceptibility testing

Centralised susceptibility testing

Centralised susceptibility testing was performed using either a breakpoint technique that allows for isolates to be categorised as susceptible or resistant (including intermediate resistance, where applicable), or Etests to determine the MIC to allow monitoring of drift in susceptibility.

The antimicrobials that were tested included those currently recommended for treatment (cefixime, ceftriaxone and spectinomycin), those considered potential alternatives (azithromycin and gentamicin) and those previously used for treatment (ciprofloxacin and penicillin G, enzyme-mediated high-level resistance only).

The following methods were used for the individual antimicrobial agents:

- azithromycin (breakpoint)
- ciprofloxacin (breakpoint)
- spectinomycin (breakpoint)
- cefixime (Etest)
- ceftriaxone (Etest)
- gentamicin (agar dilution/Etest)
- penicillinase production (nitrocefin).

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

Decentralised susceptibility testing

Countries participating in decentralised testing performed susceptibility testing in their own laboratories (Annex 1); results were interpreted using the Euro-GASP breakpoints (Annex 3). In 2012, the Netherlands did not test for penicillinase production, and France only tested some isolates for penicillinase production. Belgium, Greece, the Netherlands and the United Kingdom did not test gentamicin.

2.5 Background variables

The following data for each isolate were collected via the TESSy gonococcal antimicrobial resistance (GONOAMR) metadata: date specimen obtained, specimen site, sex, age, sexual orientation, previously diagnosed with gonorrhoea, and concurrent STI diagnosed this episode, place of residence, clinical service type, HIV status, and probable country of infection. The full variable list and variable codes are described in Annex 4.

2.6 Data collection and analysis

Data generated by centralised testing were prepared in the appropriate TESSy format and sent to the national contacts, where additional epidemiological data were appended. After the creation of a data source for the GONOAMR data (Annex 5), Member States uploaded and approved data using GONOAMR metadata in TESSy. 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 collected between 2004 and 2009 (note that no data collection was organised in 2005).

Statistical analysis

Statistical analysis was performed in Stata v11.2. The Z-test was used to determine if differences in age distribution and between epidemiological and AMR data collected in 2012 and 2011 were significant. A univariate analysis was performed to investigate associations between patient characteristics and antimicrobial resistance or decreased susceptibility. The odds ratios (OR) and 95% confidence intervals (CI) were calculated, where datasets contained sufficient numbers. 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 sequentially added to the multivariable model. Significance for all tests was assumed when $p<0.05$.

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

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
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

3 Results

3.1 Isolate and patient data

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

Table 2. Characteristics of national protocols for the implementation of Euro-GASP, 2012

Country	Coverage	Specimen Source	Comprehensiveness	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	DV and urology clinic		Selectively
Denmark	National	STI clinics, DV clinics, GPs, hospitals	Comprehensive	Consecutively
France	National	GPs, STI clinics and hospitals	Sentinel	Consecutively
Germany	National	Medical practices, outpatients, 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
Ireland	Regional/capital area	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/inpatients	Other	Consecutively
Malta				
The Netherlands	Regional/Amsterdam	STI clinic	Sentinel	Consecutively
Norway	National	STI clinics, GPs	Unknown	Consecutively
Portugal	National	STI clinics, DV clinics, GPs, hospitals, urology and gynaecology clinics	Sentinel	Consecutively
Slovakia	Regional	DV, urology and gynaecology practices	Comprehensive	Consecutively
Slovenia	Regional	DV and STI clinics	Other	Consecutively
Spain	National	STI clinics and hospitals	Sentinel	Consecutively
Sweden	National	STI clinics	Comprehensive	Consecutively
United Kingdom	National[†]	GUM/STI clinics, GPs and outpatients	Sentinel	Consecutively

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

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

Sentinel: Reporting is based on notifications from a selected group of physicians/hospitals/laboratories or other institutions, and/or cases occurring in 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 a group of physicians (or other institutions) for which no criteria were specified, for example reporting by laboratories which did not specify selection criteria.

[†] *National except for Northern Ireland*

A total of 1 927 isolates were tested over the 2012 collection period, which is an increase of 25 isolates from 2011. During the first collection period, 918 isolates were tested; during the second collection period, 1 009 isolates were tested. The number of isolates tested from each country varied from three (Cyprus) to 262 (United Kingdom) (Table 3). The level of coverage (number of isolates tested compared to the number of reported cases as part of the enhanced epidemiological surveillance of STI in 2012) ranged from 1% (the United Kingdom) to 100% (Slovenia). Hungary, the Netherlands, Spain and the United Kingdom had a coverage of 5% or less; Greece, Hungary, Ireland and Latvia reported on less than the required number of isolates, although there were sufficient cases to reach the 100 required isolates. To monitor the progress of Euro-GASP, the percentage of tested isolates from 2009 to 2011 is also displayed in Table 3. There continues to be a decline in the proportion of isolates tested in Euro-GASP compared to the European epidemiological surveillance data. This is due in part to an increase in the number of gonorrhoea cases from 2011 (37 267) to 2012 (44 632) [5] in Euro-GASP countries.

Table 3. Number of *N. gonorrhoeae* isolates tested in Euro-GASP, number of gonorrhoea cases reported in 2012, percentage of isolates tested; 2009–2012, EU/EEA

Country	Number of isolates tested	Number of cases reported [6]	% isolates tested, 2012	% isolates tested, 2011	% isolates tested, 2010	% isolates tested, 2009
Austria	107	402*	27	23	32	77
Belgium	107	930*	12	13	15	15
Cyprus	3	6*	50	91	52	N/A
Denmark	114	673	17	25	20	20
France	110	933*	12	18	24	32
Germany	106	NR	NR	NR	NR	NR
Greece	68	238	29	26	31	67
Hungary	79	1 487*	5	1	1	NP
Ireland	80	1108	7	8	14	NP
Italy	100	289	35	24	42	48
Latvia	39	601	6	5	6	3
Malta	16	29	55	28	62	92
The Netherlands	146	3 998*	4	6	8	5
Norway	110	443	25	21	11	54
Portugal	110	119	92	91	81	75
Romania	NP	325	NP	5	2	NP
Slovakia	108	283	38	58	70	13
Slovenia	47	45	104	76	64	80
Spain	105	3 042	3	4	5	5
Sweden	110	1 087	10	11	10	18
United Kingdom	262	28 594	1	1	1	1
Total	**1 927**	**44 632**	**4**	**5**	**6**	**6**

** Sentinel data*
NR = not reporting; NP = not participating

As expected – and as documented in previous years – the majority of gonococci (83.7%, n=1 596) were collected from men. Gender was reported as unknown for 21 cases (Table 4). The age range of the patients was <1 year to 78 years, with a median age of 28 years and an interquartile range of 23 to 37 years. A total of 32.9% (617) of patients were younger than 25 years when age was known (Table 5). Infected males (MSM and heterosexual) were significantly older than infected females ($p<0.002$), with the highest and lowest percentage of under 25-year-olds in the female (56%) and MSM patient groups (23%) (Table 5). There was no significant difference between the age distributions in 2012 and 2011.

Site of specimen was mainly genital (83%, n=1537), followed by rectal (10.2%, n=188), pharyngeal (5%, n=92) and other (1.9%, n=35); site of infection was reported as unknown for 75 cases.

Information on previous diagnosis of gonorrhoea was available for 39.3% (757) of cases, of which 17.2% (130) had a previous infection. Information on concurrent STIs was available for 41.5% (800) of cases; 23.4% (187) of patients had concurrent chlamydia, 6.1% (49) were infected with another STI, and 70.6% (564) were not co-infected with other STIs.

Table 4. Overall patient characteristics, 2009–2012

	2009, number (%)	2010, number (%)	2011, number (%)	2012, number (%)
Total number of isolates	1 366	1 766	1 902	1 927
Gender				
Male	1123 (83.7)	1441 (82.4)	1505 (82.4)	1596 (83.7)
Female	219 (16.3)	308 (17.6)	321 (17.6)	310 (16.3)
Unknown	24	17	76	21
Age (years)				
<25	422 (32.0)	599 (34.4)	572 (31.9)	617 (32.9)
≥25	898 (68.0)	1141 (65.6)	1221 (68.10)	1261 (67.1)
Unknown	46	26	109	49
Mode of transmission				
Heterosexual (male and female)	431 (63.2)	605 (60.5)	618 (58.3)	578 (58.6)
Female heterosexual	117 (17.2)	179 (17.9)	195 (18.4)	187 (19)
Male heterosexual	314 (46.1)	426 (42.6)	423 (39.9)	390 (39.6)
Men who have sex with men	251 (36.8)	395 (39.5)	442 (41.7)	408 (41.4)
Other			1 (0.1)	1 (0.1)
Unknown	684	766**	841	940
Site of infection				
Genital	1164 (86.5)	1426 (84.7)	1466 (82.1)	1537 (83)
Pharyngeal	34 (2.5)	62 (3.5)	79 (4.4)	92 (5)
Anorectal	138 (10.3)	191 (11.4)	216 (12.1)	188 (10.2)
Other	9 (0.7)	7 (0.4)	24 (1.3)	35 (1.9)
Unknown	21	80	117	75
Previously diagnosed				
Yes	84 (18.1)	145 (21)	146 (19)	130 (17.2)
No	379 (81.9)	546 (79)	621 (81)	627 (82.8)
Unknown	903	1075	1135	1170
Concurrent STIs				
Concurrent chlamydia	78 (14.3)	172 (22.1)	194 (22.2)	187†† (23.4)
Concurrent other STIs (not HIV)	35 (6.4)	28† (3.6)	43 (4.9)	49ǂ (6.1)
No concurrent STI	433 (79.3)	579 (74.3)	638 (72.9)	564 (70.6)
Unknown	820	987	1027	1127
HIV status*				
Positive	N/D	48 (15.5)	141 (17.6)	104 (13.5)
Negative	N/D	262 (84.5)	661 (82.4)	668 (86.5)
Unknown	N/D	556	1100	1155

N/D: no data
Percentages calculated from known values.
** Data from 866 patients in 2010*
*** Includes one individual with unknown gender but with known mode of transmission; heterosexual*
† Includes two individuals with two concurrent STIs
†† Includes four individuals with two concurrent STIs
ǂ Includes six individuals with chlamydia and an additionally diagnosed STI

Information on probable mode of transmission was available for 51.2% (987) of the cases. In these cases, 58.6% (578) of the *N. gonorrhoeae* infections were reported as heterosexually acquired (19.0% females and 39.6% males) and 41.4% (408) were from MSM. Fifteen additional males with unknown mode of transmission had *N. gonorrhoeae* isolated from the pharynx or anogenital region.

When HIV status was known, 13.5% (104) were HIV positive, of which 90.4% (94) were MSM.

There was little change in the epidemiological data compared with 2011 (Table 4), with one exception: the proportion of samples from patients who are HIV positive decreased significantly from 2011 (p=0.02). Between 2009 and 2012, only a small number of new trends became apparent: a slight decrease in the number of genital infections (86.5% in 2009, 83% in 2012), a slight increase in the number of pharyngeal infections (2.5% in 2009, 5% in 2012), an increase in the number of concurrent chlamydia infections (14.3% in 2009, 23.4% in 2012), and a decrease in the percentage of patients with no concurrent STIs (79.3% in 2009 to 70.6% in 2012).

Table 5. Patient age distribution, 2012

Variable	Number[†]	Age (years)			
		Range	Mode	Median	<25 (%)
All patients	1878	<1–78	20/24	28	617 (32.9)
Gender					
Male	1567	<1–78	24/26	29	443 (28.3)
Female	309	<1–71	20	24	173 (56)
Mode of transmission					
Heterosexual (all)	574	14–68	20	26	237 (41.3)
Male heterosexual	386	14–68	20/26	28	124 (32.1)
Female heterosexual	187	14–53	20	23	112 (59.9)
MSM	404	17–78	26	31	93 (23)

[†] *Where information was available*

As in previous years, the majority of patients (55.8%) attended a dedicated STI or sexual health clinic. Numbers were slightly higher than in 2010 (51.3%) when the clinical service type was known for a case (Table 6).

Table 6. Clinical service type attendance

Grouping	Total 2010 (%), n=866	Total 2011 (%), n=1902	Total 2012 (%), n=1927
STI and sexual health clinics	444 (51.3)	1079 (56.7)	1076 (55.8)
Antenatal	0	0	2 (0.1)
Outpatients clinic	36 (4.2)	128 (6.7)	148 (7.7)
Other	42 (4.9)	60 (3.2)	47 (2.4)
Primary care	88 (10.2)	277 (14.6)	203 (10.5)
Unknown	256 (29.6)	358 (18.8)	451 (23.4)

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

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. Information on country of birth was supplied by 14 countries: Denmark, Germany, Greece, Hungary, Ireland, Italy, Malta, the Netherlands, Slovenia, Slovakia and the United Kingdom all reported foreign-born patients, with the United Kingdom reporting the largest number of nationalities (n=32). Of the 988 cases with country of birth available, 81% (n=797) were diagnosed with gonorrhoea in a reporting country which was also the country of residence of the patient. This number is similar to 2011 (83%) and marks a continued decline from 2010 (87%). Foreign-born patients most frequently came from Brazil (16 patients), Romania (13 patients), Albania (12 patients), Poland (11 patients), Morocco (7 patients), Spain (7 patients), Bulgaria, France and Suriname (6 patients each). Data on the probable country of infection were supplied by 16 countries (two more than 2011); of these 16, namely Belgium, Denmark, France, Germany, Greece, Hungary, Ireland, Italy, Malta, Slovenia, Slovakia, and the United Kingdom, reported patients who were infected with gonorrhoea outside the reporting country. The majority of cases (92%; 790/856) most probably acquired gonorrhoea in the country that also reported the case. The countries that reported the most cases with a probable country of infection outside the reporting country were Thailand (12 male patients; 11 heterosexual, one with unknown sexual orientation; 8/11 isolates were PPNG) and Germany (eight male patients of mixed sexual orientation; one isolate showed decreased susceptibility to cefixime).

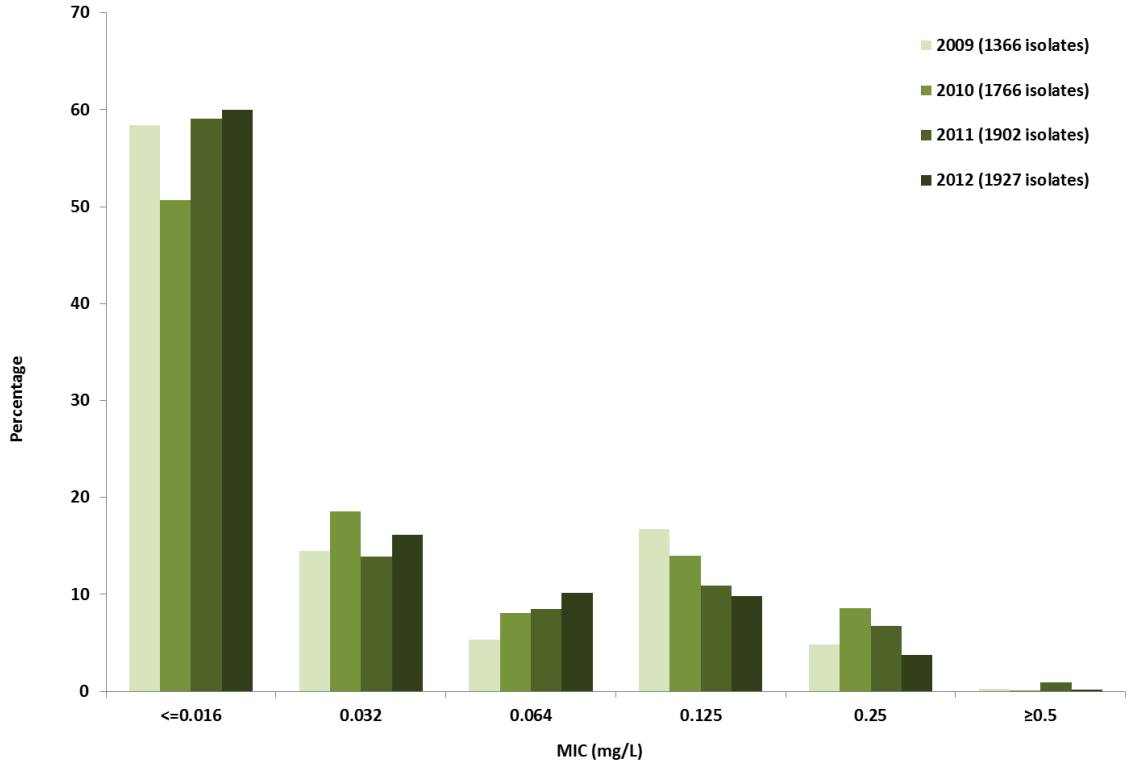
3.2 Antimicrobial susceptibility and resistance

The European guidelines for first-line empirical treatment of gonorrhoea recommend third-generation cephalosporins (either the oral agent cefixime or the parenteral agent ceftriaxone) or spectinomycin, ideally administered with azithromycin [1]. The surveillance of the antimicrobial susceptibility of these agents is therefore essential to ensure efficient patient management and to monitor the currently emerging resistance trends [3].

Ceftriaxone and cefixime

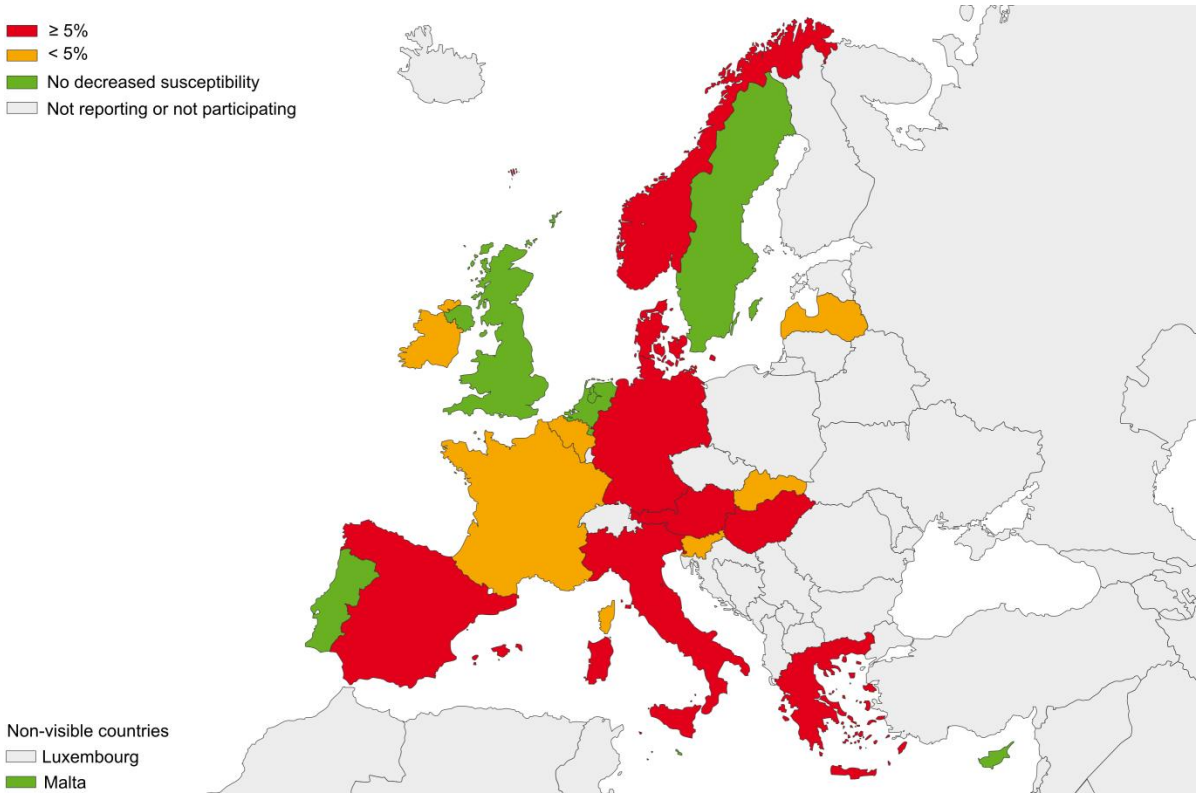
Four percent (3.9%, n=75) of the isolates displayed decreased susceptibility (>0.125 mg/L) to cefixime (Figure 1), a significant decrease compared with 2011 (7.6%, p<0.01). The number of the most susceptible isolates (≤0.016 mg/L) increased slightly between 2011 (59%, n=1 123) and 2012 (60%, n=1 156). This is encouraging, as is the number of isolates displaying an MIC of ≥0.5 mg/L (17 isolates in 2011, 3 isolates in 2012; Figure 1).

Figure 1. MIC to distribution of cefixime, Euro-GASP, 2009–2012



Isolates with decreased susceptibility to cefixime were first isolated in France in 2010; in 2012, they were detected in Latvia for the first time. Decreased susceptibility to cefixime was not detected in the Netherlands and Portugal, and no longer detected in Cyprus, Malta, Sweden and the United Kingdom, lowering the number of countries where decreased susceptibility to cefixime was detected to 14 (Table 7). Eight countries (57%) had more than 5% decreased susceptibility (Table 7) and one country, Spain, reported ≥15% (15.2%) decreased susceptibility, compared with five countries in 2011 (Denmark, Romania, Slovakia, Slovenia and Spain). Map 2 shows the widespread geographical distribution of isolates with decreased susceptibility to cefixime.

Map 2. Proportion of isolates with decreased susceptibility to cefixime in Europe, 2012



As in 2010 and 2011, most of the isolates displaying decreased susceptibility to cefixime were from men (81.3%), which represents a significant increase (up by 14.4% from 2011, p=0.02). Among patients with known sexual orientation, the percentage of heterosexually acquired strains has decreased since 2011 and is now at 37.3%, down from 50.3% (Table 7). Strains with reduced susceptibility to cefixime are still circulating, predominantly in the heterosexual community. It should be noted that the total number of patients with unknown sexual orientation has increased (from 38.6% in 2011 to 52% in 2012), which may account for this statistical decrease. As in Euro-GASP 2009–2011, there were differences across countries with respect to sexual orientation of the cases: depending on the country, isolates were either predominantly from MSM or heterosexuals (Table 7), with the exception of Italy, which showed a 50/50 split. Three individuals infected with isolates that showed decreased susceptibility to cefixime also had concurrent chlamydia infection, and one patient was HIV positive.

The patient characteristics of those with isolates displaying decreased susceptibility to cefixime were quite similar when compared to the overall population, except for mode of transmission. In the univariate analysis, the only association with decreased susceptibility to cefixime was being heterosexual (odds ratio heterosexual vs. MSM=2.54, CI 1.14–5.65, p=0.02; see Annex 7, Table A7.4). The statistical analysis confirms an observation made in 2011 of a move of these isolates into the heterosexual community. It should be noted that the number of unknown variables is large and MSMs may be underreported, so results should be interpreted with caution. Even though the association is not significant, those ≥25 years of age were more likely to be infected with a strain not displaying decreased susceptibility to cefixime (odds ratio <25 years vs. ≥25 years=0.63, CI 0.38–1.03, p=0.06). This is different from 2010 when older people were more likely to be infected with a strain displaying decreased susceptibility to cefixime, and from 2011 when there was no evidence of any association with age (p=0.38). This indicates a concerning move towards a population of younger heterosexuals, which needs to be monitored.

Table 7. Number and percentage of isolates displaying decreased susceptibility to cefixime, by country, age of patient, gender and sexual orientation; 2012

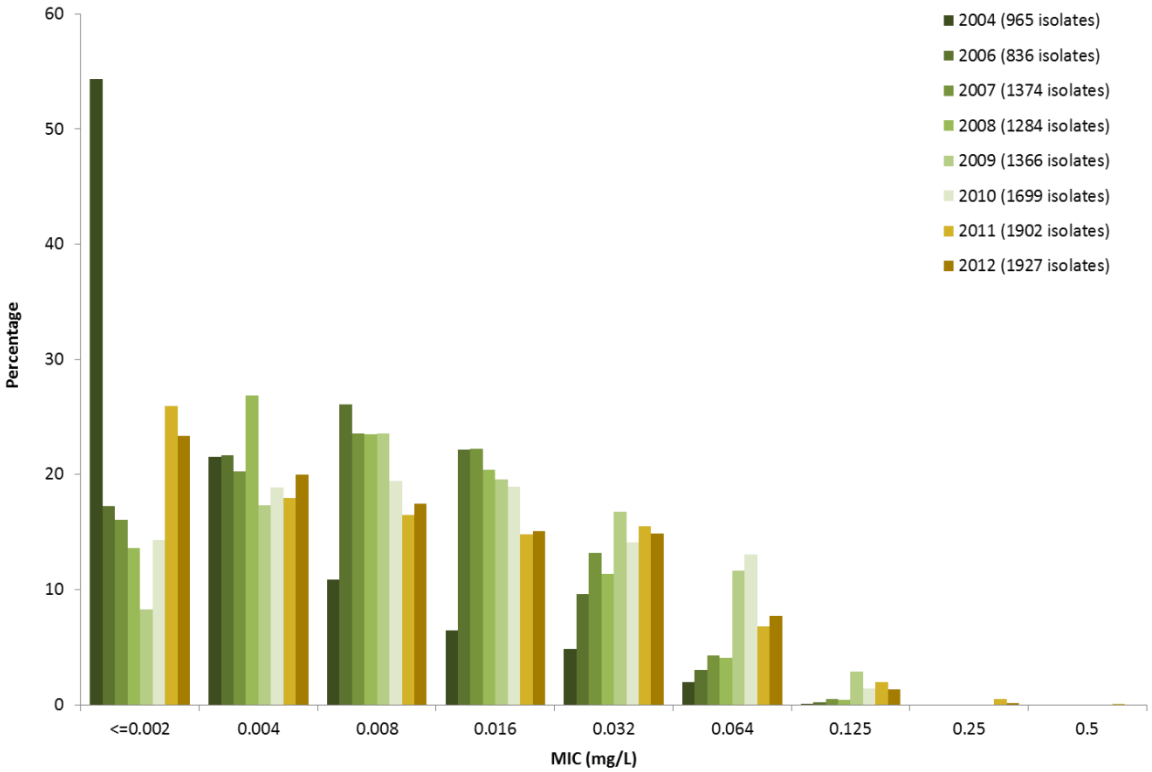
Country	Total number of isolates tested	Isolates with decreased susceptibility to cefixime		Age		Gender						Sexual orientation					
				<25 years		Males		Females		Unknown		MSM		Heterosexual		Unknown	
		No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Austria	107	5	4.7	3	60.0	3	60.0	2	40.0	0	0.0	0	0.0	3	60.0	2	40.0
Belgium	107	1	0.9	0	0.0	1	100.0	0	0.0	0	0.0	0	0.0	0	0.0	1	100.0
Denmark	114	14	12.3	6	42.9	7	50	6	42.9	1	7.1	1	7.1	11	78.6	2	14.3
France	110	2	1.8	1	50.0	2	100.0	0	0.0	0	0.0	0	0.0	0	0.0	2	100.0

Country	Total number of isolates tested	Isolates with decreased susceptibility to cefixime		Age		Gender						Sexual orientation					
				<25 years		Males		Females		Unknown		MSM		Heterosexual		Unknown	
		No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Germany	106	6	5.7	1	16.7	4	66.7	1	16.7	1	16.7	0	0.0	0	0.0	6	100.0
Greece	68	4	5.9	1	25	4	100.0	0	0.0	0	0.0	0	0.0	4	100.0	0	0.0
Hungary	79	5	6.3	2	40.0	5	100.0	0	0.0	0	0.0	2	40.0	1	20.0	2	40.0
Ireland	80	3	3.8	2	66.7	2	66.7	1	33.3	0	0.0	0	0.0	2	66.7	1	33.3
Italy	100	6	6.0	3	50.0	6	100.0	0	0.0	0	0.0	3	50.0	3	50.0	0	0.0
Latvia	39	1	2.6	0	0.0	1	100.0	0	0.0	0	0.0	0	0.0	1	100.0	0	0.0
Norway	110	6	5.5	3	50.0	5	83.3	1	16.7	0	0.0	0	0.0	0	0.0	6	100.0
Slovakia	108	4	3.7	2	50.0	4	100.0	0	0.0	0	0.0	0	0.0	3	75.0	1	25.0
Slovenia	47	2	4.3	1	50.0	2	100.0	0	0.0	0	0.0	2	100.0	0	0.0	0	0.0
Spain	105	16	15.2	4	25.0	15	93.8	1	6.3	0	0.0	0	0.0	0	0.0	16	100.0
Total (with decreased susceptibility to cefixime)	1280	75		29	38.7	61	81.3	12	16	2	2.7	8	10.7	28	37.3	39	52
Total (all isolates)*	1927	75	3.9	617	32.0	1596	82.8	310	16.1	21	1.1	408	21.2	578	30	940	48.8

** Percentages calculated from all values, including 'unknowns'*

Three isolates displayed decreased susceptibility to ceftriaxone (>0.125 mg/L) in 2012 compared with ten in 2011 (Figure 2). These isolates were from Germany (pharyngeal isolate), Ireland (anorectal isolate from an MSM) and Slovenia (pharyngeal isolate from an MSM). Two of the isolates (from Germany and Slovenia) had MICs of cefixime of at least 0.25 mg/L, and all three were also resistant to ciprofloxacin.

Figure 2. MIC distribution for ceftriaxone, 2004–12



Other antimicrobials

The gonococcal resistance to ciprofloxacin, azithromycin and penicillin G (high-level resistance only) is presented in Table 8.

Table 8. Resistance to ciprofloxacin, azithromycin and penicillin G, 2012

Country	Antimicrobial									Method of testing
	Ciprofloxacin			Azithromycin			Penicillinase-producing *Neisseria gonorrhoeae* (PPNG)			
	No. resistant	No. tested	%	No. resistant	No. tested	%	No. resistant	No. tested	%	
Austria	79	107	73.8	3	107	2.8	34	107	31.8	Centralised
Belgium	60	107	56.1	2	107	1.9	11	107	10.3	Decentralised – MIC
Cyprus	3	3	100.0	0	3	0.0	1	3	33.3	Centralised
Germany	78	106	73.6	2	106	1.9	20	106	18.9	Centralised
Denmark	67	114	58.8	15	114	14.0	20	114	17.5	Decentralised – Etest
Spain	61	105	58.1	10	105	9.5	16	105	15.2	Decentralised – MIC
France	43	110	39.1	0	110	0.0	4	55	7.3	Decentralised – Etest
Greece	47	68	69.1	4	68	5.9	8	68	11.8	Decentralised – Etest
Hungary	52	79	65.8	0	79	0.0	1	79	1.3	Centralised
Ireland	18	80	22.5	7	80	8.8	2	80	2.5	Centralised
Italy	65	100	65.0	2	100	2.0	9	100	9.0	Decentralised – Etest
Latvia	15	39	38.5	2	39	5.1	0	39	0.0	Centralised
Malta	9	16	56.3	0	16	0.0	3	16	18.8	Centralised
Netherlands	50	146	34.2	1	146	0.7			Not tested	Decentralised – Etest
Norway	61	110	55.5	14	110	12.7	30	110	27.3	Centralised
Portugal	45	110	40.9	2	110	1.8	9	110	8.2	Decentralised – Etest
Sweden	63	110	57.3	7	110	6.4	34	110	30.9	Decentralised – Etest
Slovenia	19	47	40.4	7	47	14.9	4	47	8.5	Centralised
Slovakia	58	108	53.7	3	108	2.8	6	108	5.6	Centralised
United Kingdom	73	262	27.9	5	262	1.9	12	262	4.6	Decentralised – MIC
Total	966	1 927	50.1	86	1 927	4.5	224	1 726	13	
95% CI			47.9 – 52.4			3.6 – 5.5			11.4 – 14.6	
Median			56.2			2.4			10.3	

CI: confidence interval of the mean %

Ciprofloxacin

Resistance (≥1 mg/L) in 2012 ranged from 22.5% (Ireland) to 100% (Cyprus); the mean was 50.1% (Table 8). Overall resistance levels were similar to 2011 (48.7%), but the slight increase also means that the downward trend observed since 2009 (Figure 3) has come to an end.

Azithromycin

Resistance (≥1 mg/L) levels of azithromycin in 2012 ranged from 0% (Cyprus, France, Hungary, and Malta) to 14.9% (Slovenia), with a mean of 4.5% (a decrease from 5.3% in 2011) (Table 8). Three isolates displayed high-level resistance to azithromycin (≥256 mg/L); one each were isolated from a male of unknown sexual orientation and a female from Sweden. The remaining isolate was from a male heterosexual from Ireland. Isolates displaying high-level resistance to azithromycin were previously detected in 2006 (n=1), 2007 (n=4) and 2011 (n=2).

Resistance levels have been on the decline since 2009 (Figure 3). As in previous years, the modal MIC of isolates resistant to azithromycin was 1 mg/L, which is the breakpoint used for categorising resistance. Isolates with an MIC at the breakpoint are within one doubling dilution from the susceptible breakpoint, which may explain the fluctuating resistance rates prior to 2009.

Penicillin G

High-level plasmid-mediated resistance to penicillin G (penicillinase-producing *N. gonorrhoeae* (PPNG)) ranged from 0% (Latvia) to 31.8% and 33.3% (Austria and Cyprus, respectively), with a mean of 13% (Table 8). High-level resistance to penicillin G continues to remain fairly constant over the years at 8.6–13% (Figure 3).

Spectinomycin

No resistance to spectinomycin (>0.64 mg/L) was detected in 2012 (1927 isolates tested). No resistance to spectinomycin has been detected since 2008, when this agent was tested first.

Gentamicin

As yet, there are no breakpoints for gentamicin, but overall, the MICs of gentamicin continue to be low in all European countries (MIC50 and MIC90 8 mg/L). This is the same as in previous years, with the exception of 2011 when the MIC50 was 4 mg/L. The MIC range in 2012 (0.75–16 mg/L) was similar to 2011 (0.5–16 mg/L, 1340 tested isolates).

Figure 3. Overall percentage of resistant *Neisseria gonorrhoeae*, 2004–2012

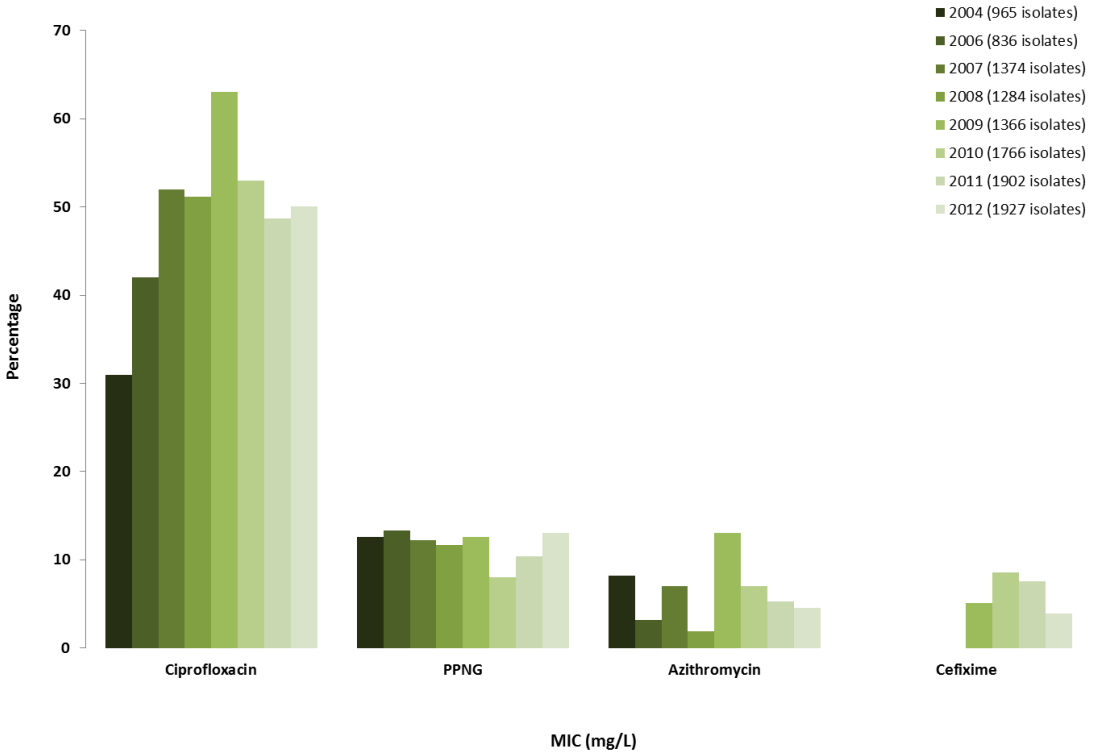


Table 9 shows resistance by patient characteristics; further statistical analysis of associations is available in Annex 7. Overall, the distribution of resistance is similar across patient groups and specimen types – with the following exceptions:

- By univariate analysis, a continuing association was observed between ciprofloxacin resistance and age (≥25 years, p<0.01), heterosexual transmission (p<0.01), and no concurrent chlamydia infection (p=0.03) (Table A7.1, Annex 7). These associations remained following multivariable analysis (odds ratio ≥25 years compared with <25 years: 1.89, CI 1.34–2.66, p<0.01; odds ratio for heterosexual transmission compared with transmission by MSM: 1.46, CI 1.05–2.01, p=0.02, and odds ratio for no concurrent chlamydia compared with concurrent chlamydia: 1.77, CI 1.2–2.6, p<0.01).
- Univariate analysis revealed associations between PPNG and heterosexual transmission (p<0.001) and age (≥25 years, p=0.07) (Table A7.3, Annex 7). However, these associations did not remain in the multivariable model. The association between patient characteristics and decreased susceptibility to cefixime has been described previously (Section 3.2). In 2012, heterosexual transmission continued to be associated with resistance to ciprofloxacin (by multivariable analysis), PPNG, and cefixime decreased susceptibility (by univariate analysis). However, as in the previous year, reporting on sexual orientation was low (51.2%), so MSM patients may be underreported.

Table 9. Resistance to ciprofloxacin, azithromycin, cefixime, and penicillin G, by patient characteristics, 2012

Country	Ciprofloxacin			Azithromycin			Cefixime			PPNG		
	Total tested	No. resistant	%	Total tested	No. resistant	%	Total tested	No. de-creased susceptible	%	Total tested	No. resistant	%
Gender												
Male	1596	806	50.5	1596	73	4.6	1596	61	3.8	1434	184	12.8
Female	310	150	48.4	310	11	3.6	310	12	3.9	271	39	14.4
Age												
<25 years	617	276	44.7	617	31	5	617	29	4.7	542	60	11.1
≥25 years	1261	664	52.7	1261	51	4	1261	38	0.1	1135	162	14.3
Transmission												
MSM	408	165	40.4	408	14	3.4	408	8	2	316	12	3.8
Heterosexual	578	288	49.8	578	27	4.7	578	28	4.8	524	76	14.5
Site of infection												
Genital	1537	793	51.6	1537	67	4.3	1537	65	4.2	1410	199	14.1
Pharyngeal	92	32	34.8	92	7	7.6	92	4	4.4	85	7	8.2
Anorectal	188	73	38.8	188	8	4.3	188	3	1.6	121	6	5
Other	35	19	54.3	35	0	0	35	1	2.9	35	3	8.6
Previous gonorrhoea infection												
Yes	130	62	47.7	130	6	4.6	130	5	3.9	130	8	6.2
No	627	294	46.9	627	30	4.8	627	28	4.5	627	67	10.7
Concurrent chlamydia												
Yes	187	69	36.9	187	5	2.7	187	3	1.6	140	10	7.1
No	613	281	45.8	613	15	2.5	613	16	2.6	485	58	12
HIV status												
Positive	104	44	42.3	104	3	2.9	104	1	1	60	4	6.7
Negative	668	301	45.1	668	25	3.7	668	24	3.6	565	57	10.1
Overall resistance	1927	966	50.1	1927	86	4.5	1927	75	3.9	1726	224	13

3.3 Completeness of data

Overall completeness of variables remained similar to 2011 (Table 10). Completeness of data remained high for 'gender' and 'age' (over 94%), along with 'site of infection' (96.1%). Most improvement in completeness of reporting can be seen in the 'probable country of infection' variable and the 'place of residence' variable since 2011, although the completeness of this variable is still lower than in 2010. The continuing decrease in the completeness of reporting since 2010 for 'mode of transmission' is disappointing.

Table 10. Completeness of reporting, Euro-GASP 2012

Variables	Number and % of variables, total 2010 (n=1766)		Number and % of variables, total 2011 (n=1902)		Number and % of variables, total 2012 (n=1927)	
	Number	%	Number	%	Number	%
Gender	1749	99	1826	96	1906	98.9
Age	1740	98.5	1793	94.3	1878	97.5
Mode of transmission	1001	56.7	1061	55.8	987	51.2
Site of infection	1683	95.3	1785	93.8	1852	96.1
Previous gonorrhoea	691	39.1	767	40.3	757	39.3
Concurrent STI	779	44.1	875	46	800	41.5
Place of residence*	720	83.1	1437	75.6	1541	80
Clinical service type*	610	70.4	1544	81.2	1476	76.6
Country of birth*	392	45.3	861	45.3	988	51.3
Probable country of infection*	263	30.4	737	38.8	856	44.4
HIV status*	310	35.8	802	42.2	772	40

** Variable data collection from 2010 second collection period only*

4 External quality assessment

4.1 Background

The concordance and comparability of generated data, for example antimicrobial susceptibility data, should be a priority of any surveillance programme featuring decentralised testing. The utilisation of an EQA scheme facilitates the monitoring of this kind of data across, and within, different testing centres.

An EQA scheme for *N. gonorrhoeae* has been available for laboratories participating in the European Sexually Transmitted Infections (STI) surveillance network since 2009. In addition, the United Kingdom National External Quality Assessment Service (UK-NEQAS) runs a genital pathogens scheme of two pathogens distributed three times a year (February, June and October) for pathogen identification and antimicrobial susceptibility testing, which is also available to the European STI surveillance network. In 2012, an extended panel of *N. gonorrhoeae* from the European Gonococcal Antimicrobial Resistance Quality Assessment Programme (GC AMR EQA) was incorporated into the second (June) distribution of this scheme to provide more in-depth antimicrobial susceptibility assessment. Successful performance in the EQA scheme was essential for participation in decentralised susceptibility testing across Europe (Annex 1).

This chapter summarises the results of the second EQA distribution dataset; a full report is available upon request from ECDC [7].

4.2 Antimicrobial susceptibility testing external quality assessment scheme

In June 2012, participating laboratories received the UK-NEQAS genital pathogens EQA panel for identification and susceptibility testing, with an additional ten gonococcal isolates (QA12) from the European GC AMR EQA programme for susceptibility testing only. In order to monitor intra-laboratory reproducibility, one isolate was supplied in triplicate (QA12-01, QA12-04, QA12-09), two were supplied in duplicate (QA12-02,QA12-07 and QA12-03, QA12-10). The remaining three isolates were supplied only once, resulting in six different isolate strains. The isolates in the panel were selected to demonstrate a range of different susceptibility profiles to therapeutic antimicrobials and were chosen from a well-characterised global panel of strains and recently isolated clinical strains.

Panel QA12 was received by 22 participating laboratories in 20 countries. Nineteen of these laboratories returned results for analysis.

Susceptibility testing methods

Participating laboratories used their local routine testing methodologies to test the isolates. Laboratories were requested to test the isolates against the following antimicrobial agents:

- Azithromycin
- Cefixime
- Ceftriaxone
- Ciprofloxacin
- Gentamicin
- Spectinomycin
- Beta-lactamase

4.3 Results

Results for the UK-NEQAS panel were reported back directly to the UK-NEQAS (data not shown) while results for the European GC AMR panel were submitted centrally to the European *N. gonorrhoeae* Antimicrobial Resistance EQA Programme website[1] for analysis.

Laboratories reported details of testing methodology and the breakpoints used for determining categories of susceptibility (resistant, intermediate susceptible, or susceptible) for each antimicrobial tested. The majority of laboratories used the Clinical and Laboratory Standards Institute [8] guidelines and their breakpoints for interpretation. Other laboratories reported use of the guidelines from the European Committee on Antimicrobial

[1] http://www.hpa-bioinformatics.org.uk/amr_eqa/home.php

Susceptibility Testing (EUCAST) [9] and the World Health Organization (WHO), while a number of laboratories used a combination of breakpoints from these three different organisations.

Results for each isolate were reported as the category of susceptibility and the MIC for the Etest and agar dilution methods, or zone of inhibition for the disc diffusion method (Table 11). Received results were decoded and referred back to the laboratories to allow observation of intralaboratory reproducibility and the identification of any potential problems.

Table 11. Overall consensus results from the June 2012 EQA

Consensus category							
Modal (range) MIC for Etest and agar dilution (mg/L)							
Mean (range) diameter for disc diffusion (mm)							
% concordance of resistance category							
Strain	**Azithromycin consensus**	**Cefixime consesus**	**Ceftriaxone consensus**	**Ciprofloxacin consensus**	**Gentamicin consensus**	**Spectinomycin consensus**	**Beta-lactamase consensus**
QA12-01/QA12-04/QA12-09 (WHO O) (PPNG, SpecR)	S	S	S	S	N/A	R	
	0.25 (0.032-0.5)	0.016 (<0.016-0.5)	0.016 (0.008-0.064)	0.008 (0.004-0.064)	4 (1-16)	>1024 (16->1024)	POS
	31 (28->35)	35 (>31-39)	42 (>35-49)	45 (>35-52)	15 (14-15)	9 (6-14)	98%
	94.1	94.1	100	94.7	N/A	94.4	
QA12-02/QA12-07 (H120240088) (CipR)	S	S	S	R	N/A	S	
	0.25 (0.032-0.5)	0.016 (<0.016-0.5)	0.016 (0.008-0.064)	>32 (16->32)	4 (1-16)	16 (4-32)	NEG
	34 (32-36)	33 (>31-35)	40 (>35-45)	12 (6-19)	15 (no range)	26 (22-28)	100%
	100	94.1	100	100	N/A	100	
QA12-03/QA12-10 (H105060806) (AzmR, CipR)	R	S	S	R	N/A	S	
	1 (0.064-2)	0.125 (0.032-1)	0.064 (0.016-0.25)	>32 (16->32)	8 (1-16)	16 (1-32)	NEG
	33 (25-40)	32 (>31-34)	40 (>35-47)	16 (6-<27)	12 (no range)	27 (23-31)	97%
	61.8	70.6	94.7	100	N/A	100	
QA12-05 (WHO F) (Fully susceptible)	S	S	S	S	N/A	S	
	0.064 (0.032-0.25)	<0.016 (<0.02-0.064)	<0.002 (<=0.001-<=0.016)	0.004 (<0.002-0.032)	4 (1-4)	16 (4-32)	NEG
	34 (31-36)	44 (>31-56)	51 (>35-60)	44 (33-53)	18 (no range)	24 (20-26)	100%
	100	100	100	100	N/A	100	
QA12-06 (H105060805) (CipR)	S	S	S	R	N/A	S	
	0.25 (0.032-0.5)	0.25 (0.064-1)	0.064 (0.008-0.25)	>32 (16->32)	4 (1-16)	16 (2-32)	NEG
	37 (31-47)	32 (>31-33)	41 (35-46)	13 (6-19)	13 (no range)	28 (23-24)	94%
	94.1	70.6	94.7	100	N/A	100	
QA12-08 (F89) (CefR, CeftR, CipR)	S	R	R	R	N/A	S	
	0.25 (0.032-0.5)	2 (>0.125-8)	1 (0.25-4)	>32 (8->32)	4 (2-8)	8 (2-32)	NEG
	32 (30-33)	18 (13-23)	36 (34-40)	13 (6-20)	13 (no range)	26 (24-29)	100%
	94.1	100	84.2	100	N/A	100	

N/A: No consensus category of resistance was assigned to gentamicin, as there are currently no published breakpoints for this antimicrobial. No range was assigned where disc diffusion zones were the same.

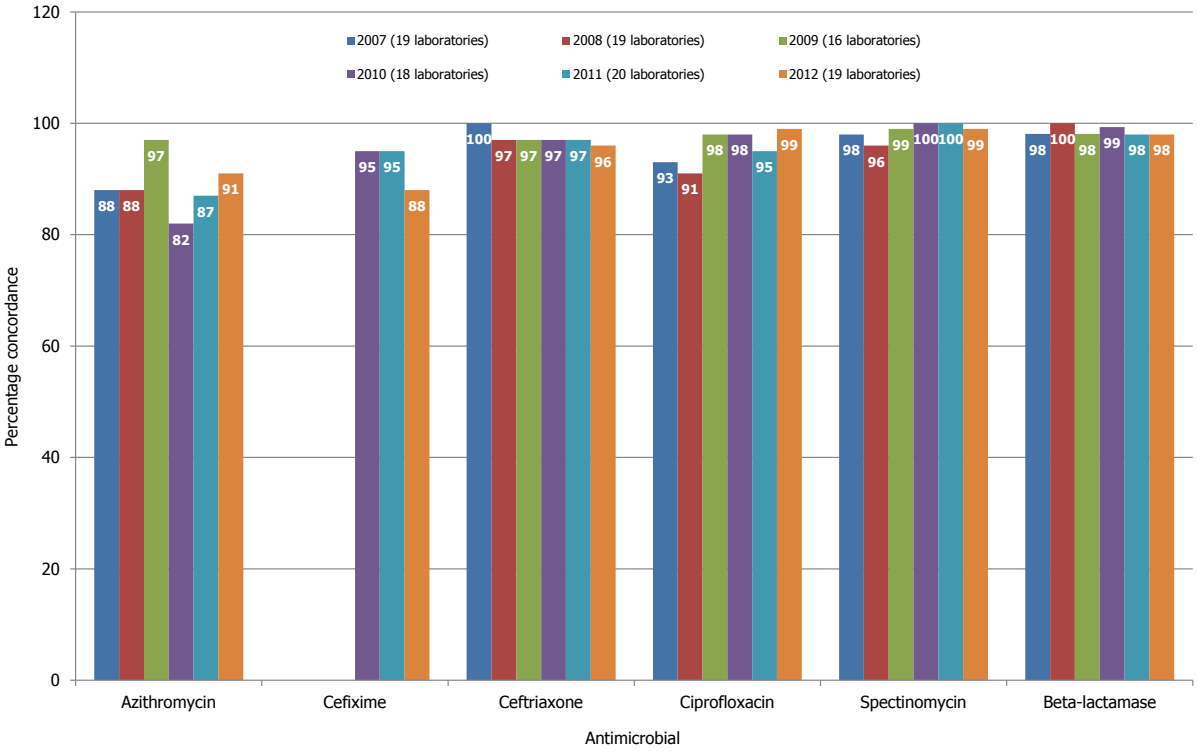
Antibiotic susceptibility concordance

An incomplete set of results was returned from one laboratory due to a problem with the retrieval of strain QA12-05.

The highest levels of susceptibility category concordance were seen for ciprofloxacin and spectinomycin (99.1%) while the lowest level was seen for cefixime (88.2%). None of the antimicrobials tested by Etest gave 100% concordance, although in three of the five antimicrobials tested, concordance was above 95%. Agar dilution and disc diffusion methods both showed higher levels of concordance than Etest, however the number of laboratories performing antimicrobial susceptibility testing using these techniques were in the minority.

Overall susceptibility concordance in QA12 was compared with results from the European Surveillance of Sexually Transmitted Infections project (ESSTI) (QA panel distributions QA2007, QA2008 and QA2009) and previous ECDC Euro-GASP EQA panels (QA2010 and QA2011). Levels appeared relatively stable for most antimicrobials tested, with the exception of cefixime, which showed a 7% decrease in concordance while azithromycin concordance increased by 4% in this distribution (Figure 4).

Figure 4. EQA interlaboratory antimicrobial susceptibility category concordance, 2007–2012



Note: Cefixime was added to the EQA scheme in 2010. ESSTI EQA distributions comprised 30 isolates (10 strains in triplicate).

Beta-lactamase concordance

Seventeen of the nineteen centres returned results for beta-lactamase testing. Of those seventeen, two centres incorrectly identified duplicate strains while one laboratory incorrectly identified a single strain (QA12-06). Overall concordance of beta-lactamase detection has remained stable since the previous distribution at 98%.

Minimum inhibitory concentration concordance

Overall, 89.7% of the submitted MIC results were within one doubling dilution of the modal MIC recorded for all tested antimicrobials, 7.2% were within two doubling dilutions, and the remaining 3.1% differed from the modal MIC by more than two doubling dilutions. Highest MIC concordances were seen for ciprofloxacin (92.0%) and spectinomycin (91.8%) while the lowest were seen in cefixime (87.2%) and ceftriaxone (88.6%). Despite the minor decrease in overall MIC concordance from previous EQA panels (90% in QA2010 and 94% in QA2011), concordance remained high, demonstrating comparability of different testing methods and robust laboratory performance.

5 Conclusions

5.1 Gonococcal antimicrobial susceptibility and resistance

Isolates exhibiting decreased susceptibility to cefixime continue to decline in the EU/EEA (3.9% in 2012, compared with 8.7% in 2010). This may be due to a number of factors, including clinics using ceftriaxone and thus reducing cefixime selection pressure and/or increased use of molecular tests which offer better detection and treatment of infections. The decrease may also be linked to a reduction of isolates belonging to ST1407, which was linked to decreased susceptibility to cefixime in 2010 [10]. However, isolates with higher cefixime MICs (0.75 and 2 mg/L), the continued detection of isolates exhibiting decreased susceptibility to ceftriaxone, and the continued detection of isolates with very high MICs of azithromycin (≥256 mg/L) are of major concern as the risk of treatment failures remains high. The European response plan to control the threat of multidrug-resistant *N. gonorrhoeae* in Europe [4] should continue to be implemented in order to assist in the identification and reporting of treatment failures; at the same time, AMR surveillance should be stepped up to keep gonorrhoea a treatable infection.

Rates of ciprofloxacin resistance increased slightly since 2011 (50.1%), and azithromycin resistance has continued to decrease since 2009 (4.5%). However, none of those antimicrobials are recommended treatment options, unless the isolates are first shown to be susceptible. To date there is no known resistance to spectinomycin, but it is feared that resistance might rapidly emerge if spectinomycin is more frequently used; currently, this antimicrobial can be difficult to obtain.

The MIC distribution of gentamicin has not changed over the years, and gentamicin may therefore be a potential future therapeutic option. However, this is based on in vitro data only, and appropriately designed and quality-assured clinical trials are needed.

5.2 Quality assessment

Antimicrobial susceptibility testing methods across Europe continue to have common features which allow comparisons between EQA schemes. Overall concordance remains high (>90%) for all antimicrobials other than cefixime (88%). Cefixime concordance was lower due to strains being close to breakpoints and/or different interpretative criteria used by laboratories.

The continued high level of concordance between laboratories in the STI surveillance network justifies confidence in, and lends support to, decentralised testing for Euro-GASP. Further participation in the European GC AMR EQA scheme should be encouraged to help build confidence, competence and capability in isolation techniques, and thus improve the identification and antimicrobial susceptibility testing of *N. gonorrhoeae*.

5.3 Euro-GASP: further developments

The response plan [4] which aims to control and manage the threat of multidrug-resistant *N. gonorrhoeae* in Europe should continue to be implemented to keep gonorrhoea a treatable infection. Euro-GASP has a major role in fulfilling the objectives of the response plan:

- Euro-GASP strengthens the surveillance of gonococcal antimicrobial susceptibility by increasing the number of participating countries and the number of tested isolates; this improves the representativeness of the programme and provides more epidemiological variables. Additional country visits should assist in the inclusion of additional centres and increase the number of collected isolates. Numbers of collected isolates from countries that previously supplied low numbers are increasing (Hungary, Ireland, Latvia, Norway and Slovenia). However, isolate numbers from Greece and the Netherlands have dropped (note: the Netherlands did not submit any data from the second collection period). More isolates are required from Spain, and the number of gonorrhoea diagnoses from the United Kingdom (28 594) was too large to achieve the 5% coverage for isolates required by Euro-GASP. Improved completeness of reporting of patient variables is required if robust statistical analysis is to be performed on the linked susceptibility and patient data.
- Euro-GASP provides training to strengthen the surveillance of gonococcal antimicrobial susceptibility and develop 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 so that countries can eventually move towards decentralised testing.
- The Euro-GASP programme needs to ensure that all Euro-GASP laboratories participate in the EQA programme. Although concordance with the EQA is already high, full participation by all Euro-GASP countries needs to be achieved.

The results from Euro-GASP 2012 are encouraging, yet we cannot be complacent. Improved antimicrobial susceptibility surveillance is essential to avoid the loss of the last few treatment options.

References

1) Bignell C, Unemo M. 2012 European guideline on the diagnosis and treatment of gonorrhoea in adults. Int J STD AIDS. 2013;24:85-92. Available from: http://www.iusti.org/regions/Europe/pdf/2012/Gonorrhoea_2012.pdf

2) Lewis DA. The Gonococcus fights back: is this time a knock out? Sex Transm Infect. 2010;86:415–421.

3) Van de Laar M, Spiteri G. Increasing trends of gonorrhoea and syphilis and the threat of drug-resistant gonorrhoea in Europe. Euro Surveill. 2012;17:pii=20225.

4) European Centre for Disease Prevention and Control. Response plan to control and manage the threat of multidrug- resistant gonorrhoea in Europe. Stockholm: ECDC; 2012. Available from: http://www.ecdc.europa.eu/en/publications/Publications/1206-ECDC-MDR-gonorrhoea-response-plan.pdf

5) European Centre for Disease Prevention and Control. Gonococcal antimicrobial susceptibility surveillance in Europe 2011. Stockholm: ECDC; 2012. Available from: http://www.ecdc.europa.eu/en/publications/publications/gonococcal-antimicrobial-susceptibility-surveillance-27-mar-2013.pdf

6) European Centre for Disease Prevention and Control. Sexually transmitted infections in Europe 1990–2012. Stockholm: ECDC; 2014.

7) European Centre for Disease Prevention and Control. External quality assessment (EQA) scheme, 2012 for Neisseria gonorrhoeae as part of the European Sexually Transmitted Infections (STI) surveillance network. Stockholm: ECDC; 2013. [Available upon request]

Annex 1. Framework for the European Gonococcal Antimicrobial Surveillance Programme, 2010–2012: reporting protocol and analysis plan

A gonococcal antimicrobial surveillance programme will be implemented from 2010, which allows for more frequent reporting of developments in antimicrobial resistance in Europe.

A1.1 Isolate collection

Numbers

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 represents less than 10% of the total number of cases of gonorrhoea (Spain, the United Kingdom and the Netherlands), up to a maximum of 200 isolates should be collected.

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: pharyngeal; rectal; urethral; other
- Females: pharyngeal; cervical; other anogenital (high vaginal swab/rectal/urethral); 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) will be selected first as resistance is most likely to develop at this site.

Frequency

The timeliness of testing needs to be improved to allow for more frequent reporting of AMR. It is proposed that this is implemented in phases so laboratories can work to the model of 'best practice', ideally to ultimately achieve biannual decentralised testing.

Submission of isolates for centralised testing

Each participating laboratory will be provided with cryopreservative beads to store gonococcal isolates until collection by courier at intervals (twice yearly minimum for countries collecting the full 110 strains).

Improving timeliness in 2010–2012

The following testing scheme for 2010 to 2012 is proposed and summarised in Table A1.

AMR surveillance, year 2010

This period will introduce biannual centralised testing for all laboratories and also pilot decentralised testing in a subset of laboratories. It is proposed that laboratories collect up to 55 isolates (or 110 for Spain, the United Kingdom, and the Netherlands) twice per year in a six-week period starting in Q2 and Q4:

- Q2 – May/June (week 20–25): National samples of isolates will be sent to and tested by the three sentinel laboratories. Centralised testing in the short term will continue to collect longitudinal data on the new antimicrobial panel.
- Q4 – November/December (week 45–50): A pilot project on decentralised testing will be carried out by laboratories fulfilling the EQA criteria (see Section 2.4: susceptibility testing). All other laboratories will continue with centralised testing. In laboratories that perform decentralised testing, data are required from 50 or 100 isolates.

For laboratories with low collection rates, the collection period can be extended to include the time period preceding the collection start dates (Q1 and Q3) until up to 55 isolates are collected.

AMR surveillance, years 2011–2012 (Table A1)

- It is proposed that decentralised testing will be extended, but for laboratories unable to do this, biannual centralised testing will continue.
- The biannual collection period will remain in Q2 (May/June, week 20–25) and Q4 (November/December, week 45–50) in 2011 and 2012.

Table A1. Summary of proposed collection schedules to achieve biannual centralised and decentralised testing and piloting of quarterly testing

Year	Quarter	Isolate collection (centralised testing)	AMR data collection (biannual decentralised testing*)
2010	**Q1** (Jan–Mar)		
	Q2 (Apr–Jun)	55 isolates	Not applicable
	Q3 (Jul–Sep)		
	Q4 (Oct–Dec)	55 isolates	50 isolates
2011	**Q1** (Jan–Mar)		
	Q2 (Apr–Jun)	55 isolates	50 isolates
	Q3 (Jul–Sep)		
	Q4 (Oct–Dec)	55 isolates	50 isolates
2012	**Q1** (Jan–Mar)		
	Q2 (Apr–Jun)	55 isolates	50 isolates

**Only for countries fulfilling the selection criteria described in Section 2.4*

A1.2 Data collection

This surveillance system aims to link NG susceptibility data to basic epidemiological data in order to get an overview of risk groups and target prevention measures. All data from the AMR susceptibility testing should be submitted to TESSy. The set of variables are described in Annex 4.

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. To avoid duplication in data collection, it is suggested that the same source of epidemiological information is used for the AMR NG surveillance database if the epidemiological information can be linked to the microbiological information, which is presented in a case-based format.

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

- The microbiology national contact points who submit or test isolates for AMR surveillance will contact the national contact points for STI surveillance and request the collected epidemiological data. This will require a patient identifier – at national level – to link the information. However, the patient identifier should not be sent to TESSy; it should be used for internal purposes only.

- If the information submitted by the national contact points for STI surveillance cannot be linked to gonococcal isolates and associated antimicrobial susceptibility data (e.g. if the data for STI surveillance is aggregate, or there is no shared patient identifier between the epidemiological and microbiological data), the national contact points for STI microbiology will enter whatever epidemiological data the laboratory could retrieve, e.g. data submitted with the isolate, or data that was requested from the place of isolate submission.

In both instances the epidemiological and microbiology data will be submitted to TESSy by the national STI contact point (microbiologist, epidemiologist, or data manager).

Please note that the submission of AMR results should not be delayed by incomplete epidemiological data; AMR results should be uploaded as soon as they become available. Incomplete datasets can be replaced by complete data at a later stage. The set of variables for gonococcal AMR surveillance is listed in Annex 4.

Centralised testing

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

A1.3 Antimicrobial susceptibility testing

While a centralised testing strategy offers the advantage of ensuring stricter comparability of testing methodology and data, this approach is a barrier to the timeliness of reporting surveillance data. As described above, decentralised testing will be trialled in a limited number of pilot laboratories in the 2010 (November) NG strain collection period.

Centralised testing

Testing will initially be centralised and performed at one of the three centres. All isolates will be tested for susceptibility to the following panel of therapeutically relevant antimicrobials:

- azithromycin (breakpoint)
- cefixime (Etest)
- ceftriaxone (Etest)
- ciprofloxacin (breakpoint)
- gentamicin (agar dilution/Etest)
- spectinomycin (breakpoint)

Penicillin and tetracycline will not be tested as they are no longer used to treat gonorrhoea. Further details on the testing methodology can be found in Annex 3.

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 3). The remaining laboratories will collect and refer isolates for centralised testing as described above. Within this group, some laboratories may be identified that could submit their own data in the future after further training, support, harmonisation, and quality assurance of methods, etc.

Selection criteria for decentralised testing

To ensure data quality is maintained for decentralised testing, the following criteria will be applied when selecting individual laboratories which use their own methods to test the agreed core antimicrobial panel:

- Laboratories have to 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 need to demonstrate 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 the susceptibility data generated by centralised susceptibility testing.

Procedure for decentralised testing

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

- submit MIC data and the corresponding resistance category, generated by Etests, agar dilution method or agar breakpoint method;
- use appropriate control strains (supplied by ECDC) and submit internal quality control data for quality assurance purposes;
- test a core group of antimicrobials, ideally identical to the core panel tested by the centralised approach (absolute minimum requirement for testing: ceftriaxone and cefixime):
  - ceftriaxone
  - cefixime
  - azithromycin
  - gentamicin
  - ciprofloxacin
  - spectinomycin
  - any other antimicrobial that is used in their country/region for first line therapy for uncomplicated urogenital gonorrhoea.
- submit susceptibility data to TESSy in a timely manner to ensure timely reporting.

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

A1.4 Data analysis

Collated data for each report will be analysed for emerging trends in antimicrobial resistance. It may be necessary to adapt the analysis mechanism to accommodate potential changes, but it is proposed that the following items should be examined and graphically represented in each report:

- Summary of isolates received and tested for each country (table)
- Overall incidence of resistance and decreased susceptibility (DS) for each of the following AMR for each testing year (bar graph):
  - cefixime
  - ceftriaxone
  - ciprofloxacin
  - spectinomycin
  - azithromycin
  - gentamicin
  - penicillinase-producing *Neisseria gonorrhoeae*
- MIC distribution by year for ceftriaxone (bar graph)
- Percentage ceftriaxone DS isolates by country per year (bar graph)
- MIC distribution by year for cefixime (bar graph)
- Percentage ceftriaxone DS isolates by country per year (bar graph)
- Ciprofloxacin resistance by country by year
- Summary of epidemiological data received by each country (table)
- Cefixime DS versus sexual orientation and gender (bar graph/line graph)
- Cefixime DS versus age group and gender
- Ceftriaxone DS versus sexual orientation and gender (bar graph/line graph) (if examples of DS observed)
- Ceftriaxone DS versus age group and gender (if examples of DS observed)

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

All countries analysing gonococcal isolates or collecting susceptibility data should provide the following information to implement Euro-GASP at the 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 (consecutive, selective)?			
6. How were the epidemiological data obtained (available with isolate submitted to the laboratory; data were requested from the isolate source, such as the STI clinic/GP surgery; data were 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

- Isolates are shipped frozen to one of the two testing centres:
  - Public Health England, London, United Kingdom
  - Örebro University Hospital, Örebro, Sweden
- The isolates are stored at −70 °C or in liquid nitrogen.
- Isolates are transferred to non-selective agar (such as GCVIT with 1% Vitox (Oxoid)) and incubated for 18 to 24 hours at 36 °C in 5% CO_2.
- The purity and the identity of the isolates are confirmed by Gram stain, oxidase and the *N. gonorrhoeae* MicroTrak (Trinity Biotech) test or the Phadebact (MKL Diagnostics) test. A further sub-culture is grown.
- If there is a high level of contamination, cultures are repeatedly transferred to selective agar.
- Susceptibility testing is performed using the agar dilution breakpoint technique for ciprofloxacin, spectinomycin and azithromycin, and the full agar dilution technique or Etest for gentamicin. 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 and the full agar dilution technique

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

- The ceftriaxone and cefixime MICs are determined using Etests according to the manufacturer's instructions.
- All isolates are tested for penicillinase production, using the chromogenic reagent nitrocefin.
- Etests are performed on isolates that are resistant to azithromycin, using the agar dilution breakpoint technique.
- Etests are performed on all isolates with MIC>8 mg/L of gentamicin, using the agar dilution technique.
- The following control strains are tested on the poured agar dilution plates and each batch of Etests:
  - WHO G (QA07–10)
  - WHO K (QA09–03)
  - WHO M (QA09–09)
  - WHO O (QA09–10)
  - WHO P (QA09–05)
- Bacterial growth is recorded for the agar dilution plates. MIC is recorded from the Etest plates. 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	1	-	0.5
Cefixime*	0.25		0.125
Ceftriaxone*	0.25		0.125
Ciprofloxacin	1	0.12–0.5	0.06
Gentamicin	To be determined		
Spectinomycin	128		64

**Decreased susceptibility, reported as I in The European Surveillance System.*

European Committee on Antimicrobial Susceptibility Testing breakpoints [9] are used, with the exception of the breakpoints for ciprofloxacin and azithromycin intermediate susceptibility. The ciprofloxacin resistance breakpoint used in Euro-GASP is more clinically relevant. Azithromycin intermediate resistance has not been recorded as the clinical significance of this is currently unknown.

Isolates that are contaminated in the original vial or are slow to grow are resaved with a pure culture.

Annex 4. Set of variables for gonococcal antimicrobial susceptibility testing

The following table contains the set of basic variables for all diseases as well as the disease-specific and AMR data variables for Euro-GASP.

Variables		
Common set	**Disease specific**	**AMR**
Record Id	**Place of residence:** NUTS code 0–3	**Record Id**
Record type	**Clinical service type:** ANC, combined service, dermatology-venereology clinic, hospital emergency department, family planning clinic, general practitioner gynaecology clinic, infectious disease clinic other primary care, dedicated STI clinic, urology, youth clinics, other, unknown	**Record type**
Record type version	**Country of birth:** ISO-coded value list, UNK	**Parent Id**
Status	**Probable country of infection:** ISO coded value list, UNK	**Antibiotic:** Ceftriaxone, cefixime, azithromycin, ciprofloxacin, spectinomycin, gentamicin, penicillinase
Subject	**Transmission:** Heterosexual contact, MSM/homosexual or bisexual male, mother-to-child transmission, other, unknown	**Test method:** Etest, MIC, breakpoint, penicillinase
Reporting country: ISO coded value list	**Site of infection:** Anorectal Genital Pharyngeal Other Not applicable Unknown	**Result sign:** < Less than <= Less than or equal = Equal > Greater than ≥ Greater than or equal
Data source	**Prev Gono:** Yes No Unknown	**Result value**
Date used for statistics: yyyy-mm-dd	**HIV status:** Positive Known HIV positive New HIV diagnosis Negative Unknown	**SIR:** Sensitive Intermediate/decreased susceptibility Resistant Unknown
Gender: Female, male, unknown	**Concurrent STI:** Chlamydia Hepatitis B Hepatitis C Genital herpes LGV Syphilis Genital warts Mycoplasma Ureaplasma No concurrent STI Unknown	
Age: Years or unknown	**Result por:** NG-MAST *por* allele number	
	Result TbpB: NG-MAST *tbpb* allele number	
	Result Seq Type: NG-MAST sequence type number	

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	
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	
Star tSurv Sys	Start year for data collection in the surveillance system	YYYY	
Internal quality control	WHO-recommended strains used for quality control procedures	G = WHO G K = WHO K M = WHO M O = WHO O P = WHO P OTH = Other control strains used NT = Not tested	

Annex 6. Summary of patient characteristics

Table A6.1. Patient characteristics for cases reported to Euro-GASP; overall and by country, 2012

	All countries		Austria		Belgium		Cyprus		Denmark		France		Germany		Greece		Hungary	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
	1927		107		107		3		114		110		106		68		79	
Gender																		
Male	1596	82.8	67	62.6	91	85	3	100	80	70.2	92	83.6	88	83	68	100	67	84.8
Female	310	16.1	40	37.4	15	14	0	0	28	24.6	18	16.4	15	14.2	0	0	8	10.1
Unknown	21	1.1	0	0	1	0.9	0	0	6	5.3	0	0	3	2.8	0	0	4	5.1
Age (years)																		
<25	617	32.0	35	32.7	22	20.6	2	66.7	44	38.6	43	39.1	30	28.3	13	19.1	20	25.3
≥25	1261	65.4	72	67.3	83	77.6	1	33.3	64	56.1	67	60.9	74	69.8	52	76.5	54	68.4
Unknown	49	2.5	0	0	2	1.9	0	0	6	5.3	0	0	2	1.9	3	4.4	5	6.3
Mode of transmission																		
Heterosexual (male and female)	578	30.0	71	66.4	9	8.4	0	0	76	66.7	0	0	1	0.9	35	51.5	32	40.5
Male heterosexual	390	20.2	34	31.8	8	7.5	0	0	48	42.1	0	0	0	0	35	51.5	29	36.7
MSM	408	21.2	3	2.8	4	3.7	1	33.3	23	20.2	0	0	1	0.9	24	35.3	6	7.6
Other	1	0.1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Unknown	940	48.8	33	30.8	94	87.9	2	67.7	15	13.2	110	100	104	98.1	9	13.2	41	51.9
Site of infection																		
Genital	1537	79.8	100	93.5	86	80.4	3	100	95	83.3	103	93.6	105	99.1	64	94.1	38	48.1
Pharyngeal	92	4.8	2	1.9	0	0	0	0	6	5.3	0	0	1	0.9	0	0	0	0
Anorectal	188	9.8	4	3.7	3	2.8	0	0	6	5.3	5	4.5	0	0	1	1.5	0	0
Other	35	1.8	1	0.9	17	15.9	0	0	1	0.9	2	1.8	0	0	0	0	0	0
Unknown	75	3.9	0	0	1	0.9	0	0	6	5.3	0	0	0	0	3	4.4	41	51.9
Previously diagnosed																		
Yes	130	6.7	16	15	4	3.7	0	0	15	13.2	0	0	3	2.8	11	16.2	0	0
No	627	32.5	11	10.3	28	26.2	0	0	99	86.8	0	0	0	0	41	60.3	0	0
Unknown	1170	60.7	80	74.8	75	70.1	3	100	0	0	110	100	103	97.2	16	23.5	79	100
Concurrent STI																		
Concurrent CT	187	9.7	9	8.4	6	5.6	0	0	0	0	11	10	13	12.3	1	1.5	0	0
Concurrent other	49	2.5	1	0.9	0	0	0	0	0	0	7	6.4	3	2.8	2	2.9	0	0
No concurrent STI	564	29.3	68	63.6	4	3.7	0	0	0	0	36	32.7	3	2.8	25	36.8	0	0
Unknown	1127	58.5	29	27.1	97	90.7	3	100	114	100	56	50.9	87	82.1	40	58.8	79	100
HIV status																		
Positive	104	5.4	0	0	2	1.9	0	0	3	2.6	1	0.9	4	3.8	0	0	1	1.3
Negative	668	34.7	35	32.7	14	13.1	0	0	69	60.5	0	0	7	6.6	27	39.7	9	11.4
Unknown	1155	60.0	72	67.3	91	85	3	100	42	36.8	109	99.1	95	89.6	41	60.3	69	87.3

Table A6.1. Patient characteristics for cases reported to Euro-GASP; overall and by country, 2012 (continued)

	Ireland		Italy		Latvia		Malta		Netherlands		Norway		Portugal		Slovakia	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
	80		100		39		16		146		110		110		108	
Gender																
Male	70	87.5	89	89	35	89.7	15	93.8	118	80.8	100	90.9	97	88.2	85	78.7
Female	10	12.5	5	5	4	10.3	1	6.3	28	19.2	10	9.1	13	11.8	23	21.3
Unknown	0	0	6	6	0	0	0	0	0	0	0	0	0	0	0	0
Age (years)																
<25	40	50	24	24	12	30.8	3	18.8	52	35.6	32	29.1	41	37.3	29	26.9
≥25	40	50	68	68	27	69.2	12	75	94	64.4	78	70.9	69	62.7	79	73.1
Unknown	0	0	8	8	0	0	1	6.3	0	0	0	0	0	0	0	0
Mode of transmission																
Heterosexual (male and female)	24	30	42	42	35	89.7	8	50	54	37	0	0	12	10.9	71	65.7
Male heterosexual	14	17.5	37	37	31	79.5	7	43.8	26	17.8	0	0	8	7.3	56	51.9
MSM	47	58.8	47	47	2	5.1	7	43.8	92	63	0	0	12	10.9	3	2.8
Other	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0.9
Unknown	9	11.3	11	11	2	5.1	1	6.3	0	0	110	100	86	78.2	33	30.6
Site of infection																
Genital	51	63.8	77	77	39	100	13	81.3	75	51.4	91	82.7	107	97.3	106	98.1
Pharyngeal	13	16.3	1	1	0	0	1	6.3	7	4.8	3	2.7	3	2.7	0	0
Anorectal	16	20	20	20	0	0	2	12.5	64	43.8	9	8.2	0	0	0	0
Other	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	1.9
Unknown	0	0	2	2	0	0	0	0	0	0	7	6.4	0	0	0	0
Previously diagnosed																
Yes	5	6.3	15	15	3	7.7	0	0	0	0	0	0	8	7.3	14	13
No	72	90	76	76	0	0	15	93.8	0	0	0	0	16	14.5	94	87
Unknown	3	3.8	9	9	36	92.3	1	6.3	146	100	110	100	86	78.2	0	0
Concurrent STI																
Concurrent CT	9	11.3	15	15	18	46.2	4	25	41	28.1	0	0	4	3.6	7	6.5
Concurrent other	0	0	0	0	3	7.7	2	12.5	15	10.3	0	0	1	0.9	12	11.1
No concurrent STI	68	85	73	73	0	0	10	62.5	90	61.6	0	0	19	17.3	74	68.5
Unknown	3	3.8	12	12	18	46.2	0	0	0	0	110	100	86	78.2	15	13.9
HIV status																
Positive	7	8.8	11	11	1	2.6	1	6.3	43	29.5	0	0	0	0	0	0
Negative	68	85	81	81	0	0	15	93.8	103	70.5	0	0	24	21.8	92	85.2
Unknown	5	6.3	8	8	38	97.4	0	0	0	0	110	100	86	78.2	16	14.8

Table A6.1. Patient characteristics for cases reported to Euro-GASP; overall and by country, 2012 (end)

	Slovenia		Spain		Sweden		United Kingdom	
	No.	%	No.	%	No.	%	No.	%
	47		105		110		262	
Gender								
Male	45	95.7	101	96.2	80	72.7	205	78.2
Female	2	4.3	4	3.8	30	27.3	56	21.4
Unknown	0	0	0	0	0	0	1	0.4
Age (years)								
<25	9	19.1	28	26.7	51	46.4	87	33.2
≥25	35	74.5	58	55.2	59	53.6	175	66.8
Unknown	3	6.4	19	18.1	0	0	0	0
Mode of transmission								
Heterosexual (male and female)	14	29.8	0	0	0	0	94	35.9
Male heterosexual	12	25.5	0	0	0	0	45	17.2
MSM	24	51.1	0	0	0	0	112	42.7
Other	0	0	0	0	0	0	0	0
Unknown	9	19.1	105	100	110	100	56	21.4
Site of infection								
Genital	28	59.6	102	97.1	76	69.1	178	67.9
Pharyngeal	10	21.3	0	0	19	17.3	26	9.9
Anorectal	8	17	2	1.9	0	0	48	18.3
Other	1	2.2	1	1	0	0	10	3.8
Unknown	0	0	0	0	15	13.6	0	0
Previously diagnosed								
Yes	2	4.3	0	0	0	0	34	13
No	24	51.1	0	0	0	0	151	57.6
Unknown	21	44.7	105	100	110	100	77	29.4
Concurrent STI								
Concurrent CT	0	0	0	0	0	0	49	18.7
Concurrent other	0	0	0	0	0	0	3	1.1
No concurrent STI	0	0	0	0	0	0	94	35.9
Unknown	47	100	105	100	110	100	116	44.3
HIV status								
Positive	5	10.6	0	0	0	0	25	9.5
Negative	19	40.4	0	0	0	0	105	40.1
Unknown	23	48.9	105	100	110	100	132	50.4

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, 2012

	Austria (n=107)	Belgium (n=107)	Cyprus (n=3)	Denmark (n=114)	France (n=110)	Germany (n=106)	Greece (n=68)	Hungary (n=79)
Clinical service types								
ANC – antenatal clinic	0	0	0	0	0	0	0	0
COMB – combined service	0	0	0	0	0	11	13	0
DV – dermatology-venereology clinic	29	0	1	0	1	11	0	41
ED – Hospital emergency dept	0	0	0	0	9	3	0	0
FPC – family planning clinic	0	0	0	0	2	0	0	0
GP – general practitioner	33	0	0	63	64	11	0	0
GYN – gynaecology clinic	0	0	0	0	6	10	0	0
ID – infectious disease clinic	0	0	0	0	0	0	0	0
OPC – other primary care	0	0	0	0	0	5	0	0
STI – dedicated STI clinic	41	7	0	42	18	0	55	0
URO – urology	0	0	1	0	2	52	0	0
YTH – youth clinics	0	0	0	0	0	1	0	0
O – other	4	0	1	3	8	0	0	0
UNK – unknown	0	100	0	6	0	2	0	38
Place of residence								
NUTS level 0–3 (region)	2=AT12	20=BE1	3=CY000	59=DK0	110=FR	40=DE	1=DE	4=HU101
	81=AT13	66=BE2		19=DK011		1=DE125	6=GR	2=HU211
	3=AT21	17=BE3		2=DK012		5=DE3	1=GR122	4=HU221
	15=AT22	4=UNK		4=DK013		12=DE6	2=GR14	1=HU312
	1=AT32			3=DK021		3=DE922	1=GR142	68=UNK
	5=AT33			2=DK022		3=DEA2	1=GR242	
				1=DK031		9=DEA24	4=GR30	
				5=DK032		2=DEA4	49=GR300	
				3=DK041		15=DEA41	3=UNK	
				11=DK042		2=DEA42		
				5=DK05		1=DEA43		
						7=DED2		
						4=DED22		
						2=UNK		
Country of birth								
ISO coded value list. UNK	107=UNK	16=BE	2=CY	1=CM. ES. GH. IQ. JP. KE. LK. MA. NP. PL. RO. SY	110=UNK	1=BG	1=BG. CY. DE. IR. PK. PL. RO	1=CN. RO
		91=UNK	1=UNK	83=DK		17=DE	8=AL	56=HU
				4=GL		88=UNK	47=GR	2=NG
				2=PH. TR			2=IQ	19=UNK
				11=UNK			4=UNK	
Probable country of infection								
ISO coded value list. UNK	107=UNK	12=BE	3=CY	1=DE. IN. PL. RO	27=FR	1=UZ	56=GR	1=DE
		1=TH		77=DK	1=MA. MG. TH	105=UNK	2=PH	51=HU
		94=UNK		3=GL. PH	80=UNK		10=UNK	2=IT
				7=TH				25=UNK
				20=UNK				

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, 2012 (continued)

	Ireland (n=80)	Italy (n=100)	Latvia (n=39)	Malta (n=16)	Netherlands (n=146)	Norway (n=110)	Portugal (n=110)
Clinical service types							
See first table for codes	9=GP	10=DV	38=COMB	16=STI	146=STI	110=UNK	3=ED
	71=STI	1=GYN	1=ID				1=GP
		3=ID					26=STI
		15=O					79=UNK
		71=STI					1=YTH
Place of residence							
NUTS level 0-3 (region)	80=IE	32=ITC11	3=LV003	11=MT001	1=NL111	110=UNK	1=PT112
		2=ITC16	1=LV005	5=UNK	1=NL212		1=PT113
		1=ITC17	22=LV006		2=NL230		11=PT114
		1=ITC31	9=LV007		11=NL310		1=PT116
		1=ITC42	3=LV008		1=NL321		5=PT150
		25=ITC45	1=LV009		2=NL322		1=PT163
		2=ITC47			4=NL323		1=PT165
		1=ITD37			1=NL325		65=PT171
		5=ITD44			101=NL326		20=PT172
		1=ITD53			2=NL327		1=PT183
		7=ITD55			1=NL331		3=PT185
		1=ITD58			1=NL335		
		4=ITE21			18=UNK		
		6=ITE43					
		1=ITF41					
		1=ITF61					
		9=UNK					
Country of birth							
ISO-coded value list. UNK	5=BR	4=AL	39=UNK	2=LY	2=BG. CM. CW	110=UNK	110=PT
	1=CL. ES. FR. GE. NG. PK. PL. RU. TR. UK	1=BG. CO. DO. DZ. EG. FR. TN		10=MT	4=BR. PL		
	29=IE	68=IT		4=UNK	1=CD. CN. CO. ES. FR. GM. IN. LK. NG. RO. RU		
	36=UNK	2=MA. PE			3=DE. ID. MA		
		7=RO			104=NL		
		10=UNK			6=SR		
					2=UNK		
Probable country of infection							
ISO coded value list. UNK	22=IE	43=IT	38=LV	1=AE. DE	146=UNK	110=UNK	110=PT
	58=UNK	1=TH	1=UNK	10=MT			
		56=UNK		2=TH			
				2=UNK			

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, 2012 (end)

	Slovakia (n=108)	Slovenia (n=47)	Spain (n=105)	Sweden (n=110)	United Kingdom (n=262)
Clinical service types					
See first table for codes	2=ANC	27=DV	103=COMB	110=UNK	9=GP
	46=DV	1=ED	2=O		2=O
	1=ED	12=O			245=STI
	14=GYN	4=OPC			6=UNK
	4=OPC	3=STI			
	41=URO				
Place of residence					
NUTS level 0–3 (region)	46=SK01	1=BA	1=ES112	110=UNK	2=UKC
	28=SKO21	1=CN	3=ES113		1=UKC2
	4=SK022	40=SI	5=ES114		1=UKC21
	19=SK023	5=UNK	30=ES120		11=UKD3
	5=SK041		26=ES30		2=UKD4
	4=SK042		3=ES411		1=UKD52
	2=UNK		3=ES418		1=UKD53
			3=ES419		1=UKD54
			1=ES422		5=UKE32
			7=ES511		6=UKE42
			6=ES523		1=UKE43
			16=ES611		1=UKF1
			1=ES614		5=UKF14
					4=UKF23
					1=UKG13
					14=UKG31
					1=UKG34
					4=UKG35
					4=UKH21
					1=UKH23
					92=UKI
					5=UKJ21
					2=UKJ23
					1=UKJ24
					3=UKK11
					2=UKK13
					10=UKM2
					4=UKM21
					1=UKM22
					2=UKM27
					18=UKM3
					4=UKM50
					1=UKM6
					50=UNK
Country of birth					
ISO-coded value list. UNK	1=CZ. TR	2=BA	105=UNK	110=UNK	1=AO. AU. BG. CD. CZ. GH. IE. IN. IT. LV. MA. MX. NG. PK. SE. SO. TH. UA. ZW
	105=SK	1=CN. NZ			7=BR
	1=UNK	35=SI			2=CO. DE. JM. PT. RO. US
		8=UNK			4=ES. PL. ZA
					3=FR. ZM
					123=UK
					83=UNK

	Slovakia (n=108)	Slovenia (n=47)	Spain (n=105)	Sweden (n=110)	United Kingdom (n=262)
Probable country of infection					
ISO-coded value list. UNK	1=AT. HR. HU. RU	2=AT	105=ES	110=UNK	1=AU. BB. GR. MA. RO. US
	68=SK	1=BA. ES. IT. PT. RS. UK			2=BR. DE. FR. JM. PT
	36=UNK	3=DE			3=ES
		19=SI			149=UK
		17=UNK			94=UNK

UNK = unknown

Annex 7. Statistical tables

Table A7.1. Association of ciprofloxacin resistance/susceptibility and patient characteristics, Euro-GASP, 2012

	Ciprofloxacin resistant (%, 95% CI)	Odds ratio	95% CI	P value
Site of infection, n=1852				
Genital (1537)	793 (51.6, 49.1 – 54.1)	1		
Anorectal (188)	73 (38.8, 32.2 – 46.0)	0.6	0.44 – 0.81	0.001
Pharyngeal (92)	32 (34.8, 25.8 – 44.9)	0.5	0.32 – 0.78	0.0017
Other (35)	19 (54.3, 38.2 – 69.5)	1.11	0.57 – 2.18	0.7528
Gender, n=1906				
Male (1596)	806 (50.5, 48.1 – 53.0)	1		
Female (310)	150 (48.4, 42.9 – 53.9)	0.92	0.72 – 1.17	0.496
Previous GC, n=757				
Yes (130)	62 (47.7, 39.3 – 56.2)	1.03	0.71 – 1.51	0.8676
No (627)	294 (46.9, 43.0 – 50.8)	1		
Mode of transmission, n=986				
MSM (408)	165 (40.4, 35.8 – 45.3)	1		
Heterosexual (578)	288 (49.8, 45.8 – 53.9)	1.46	1.13 – 1.89	0.0036
Concurrent chlamydia, n=800				
Yes (187)	69 (36.9, 30.3 – 44.0)	1		
No (613)	281 (45.8, 41.9 – 49.8)	1.45	1.03 – 2.03	0.0311
HIV status, n=772				
Positive (104)	44 (42.3, 33.3 – 51.9)	1		
Negative (668)	301 (45.1, 41.3 – 48.9)	1.12	0.74 – 1.7	0.5997
Age, n=1878				
<25 years (617)	276 (44.7, 40.9 – 48.7)	1		
≥25 years (1261)	664 (52.7, 49.9 – 55.4)	1.37	1.13 – 1.67	0.0013

Note: P value obtained from Pearson's chi-squared tests

Table A7.2. Association of azithromycin resistance/susceptibility and patient characteristics, Euro-GASP, 2012

	Azithromycin resistant (%, 95% CI)	Odds ratio	95% CI	P value
Site of infection, n=1852				
Genital (1537)	67 (4.4, 3.5 – 5.5)	1		
Anorectal (188)	8 (4.3, 2.2 – 8.2)	0.98	0.46 – 2.06	0.9475
Pharyngeal (92)	7 (7.6, 3.7 – 14.9)	1.81	0.8 – 4.06	0.1461
Other (35)	0 (0)	N/A		
Gender, n=1906				
Male (1596)	73 (4.6, 3.7 – 5.7)	1		
Female (310)	11 (3.6, 2.0 – 6.2)	0.77	0.4 – 1.46	0.4209
Previous GC, n=757				
Yes (130)	6 (4.6, 2.1 – 9.7)	0.96	0.39 – 2.36	0.9343
No (627)	30 (4.8, 3.4 – 6.7)	1		
Mode of transmission, n=986				
MSM (408)	14 (3.4, 2.1 – 5.7)	1		
Heterosexual (578)	27 (4.7, 3.2 – 6.7)	1.38	0.71 – 2.67	0.337
Concurrent chlamydia, n=800				
Yes (187)	5 (2.7, 1.2 – 6.1)	1		
No (613)	15 (2.5, 1.5 – 4.0)	0.91	0.33 – 2.55	0.862
HIV status, n=772				
Positive (104)	3 (2.9, 1.0 – 8.1)	1		
Negative (668)	25 (3.7, 2.6 – 5.5)	1.31	0.39 – 4.42	0.6636
Age, n=1878				
<25 years (617)	31 (5, 3.6 – 7.0)	1		
≥25 years (1261)	51 (4, 3.1 – 5.3)	0.8	0.5 – 1.26	0.3292

Note: P value obtained from Pearson's chi-squared tests
N/A = Expected cells less than five – analysis not performed

Table A7.3. Association of penicillinase activity and patient characteristics, Euro-GASP, 2012

	PPNG resistant (%, 95% CI)	Odds ratio	95% CI	P value
Site of infection, n=1651				
Genital (1410)	199 (14.1, 12.4 – 16.0)	1		
Anorectal (121)	6 (5, 2.3 – 10.4)	0.32	0.14 – 0.73	0.0046
Pharyngeal (85)	7 (8.2, 4.1 – 16.0)	0.55	0.25 – 1.2	0.1269
Other (35)	3 (8.6, 3.0 – 22.4)	N/A		
Gender, n=1705				
Male (1434)	184 (12.8, 11.2 – 14.7)	1		
Female (271)	39 (14.4, 10.7 – 19.1)	1.14	0.79 – 1.66	0.485
Previous GC, n=757				
Yes (130)	8 (6.2, 3.2 – 11.7)	0.55	0.26 – 1.17	0.1157
No (627)	67 (10.7, 8.5 – 13.4)	1		
Mode of transmission, n=840				
MSM (316)	12 (3.8, 2.2 – 6.5)	1		
Heterosexual (524)	76 (14.5, 11.8 – 17.8)	4.3	2.3 – 8.1	<0.0001
Concurrent chlamydia, n=625				
Yes (140)	10 (7.1, 3.9 – 12.7)	1		
No (485)	58 (12, 9.4 – 15.2)	1.77	0.88 - 3.56	0.1072
HIV status, n=625				
Positive (60)	4 (6.7, 2.6 – 15.9)			
Negative (565)	57 (10.1, 7.9 – 12.9)			0.498*
Age n=1677				
<25 years (542)	60 (11.1, 8.7 – 14.0)	1		
≥25 years (1135)	162 (14.3, 12.4 – 16.4)	1.34	0.98 – 1.84	0.0704

Note: P value obtained from Pearson's chi-squared tests
**Expected value for one cell < 5, so Fisher's exact test performed*
N/A = Expected cells less than five – analysis not performed.

Table A7.4. Association of decreased susceptibility to cefixime and patient characteristics, Euro-GASP, 2012

	Cefixime decreased susceptibility (%, 95% CI)	Odds ratio	95% CI	P value
Site of infection, n=1852				
Genital (1537)	65 (4.2, 3.4 – 5.4)			
Anorectal (188)	3 (1.6, 0.6 – 4.6)			0.309*
Pharyngeal (92)	4 (4.4, 1.7 – 10.7)			
Other (35)	1 (2.9, 0.5 – 14.5)			
Gender, n=1906				
Male (1596)	61 (3.8, 3 – 4.9)	1		
Female (310)	12 (3.9, 2.2 – 6.6)	1.01	0.54 – 1.9	0.967
Previous GC, n=757				
Yes (130)	5 (3.9, 1.7 – 8.7)	1		
No (627)	28 (4.5, 3.1 – 6.4)	0.86	0.32 – 2.26	0.753
Mode of transmission, n=986				
MSM (408)	8 (2, 1.0 – 3.8)	1		
Heterosexual (578)	28 (4.8, 3.4 - 7)	2.54	1.14 – 5.65	0.0175
Concurrent chlamydia, n=800				
Yes (187)	3 (1.6, 0.5 – 4.6)			
No (613)	16 (2.6, 1.6 – 4.2)			0.587*
HIV status, n=772				
Positive (104)	1 (1, 0.2 – 5.2)			
Negative (668)	24 (3.6, 2.4 – 5.3)			0.234*
Age, n=1878				
<25 years (617)	29 (4.7, 3.3 – 6.7)	1		
≥25 years (1261)	38 (3.01, 2.2 – 4.1)	0.63	0.38 – 1.03	0.064

Note: P value obtained from Pearson's chi-squared tests
** Expected value for one cell <5, so Fisher's Exact test performed*