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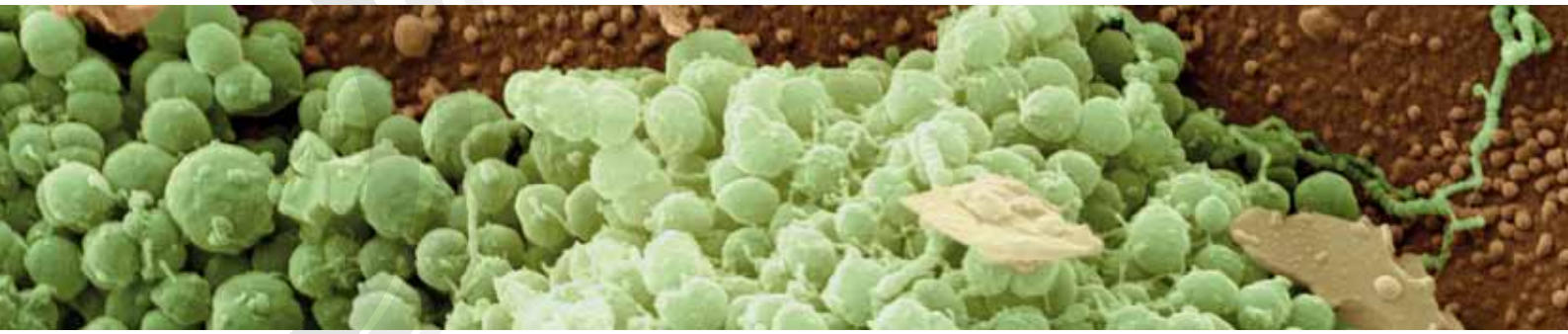

Gonococcal antimicrobial susceptibility surveillance in Europe

2011

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Contents

Abbreviations

AMR	Antimicrobial resistance
CI	Confidence interval
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
PPNG	Penicillinase-producing *Neisseria gonorrhoeae*
STI	Sexually transmitted infection
UK-NEQAS	United Kingdom National External Quality Assessment Service
WHO	World Health Organization

Executive summary

The surveillance of *Neisseria gonorrhoeae* (NG) susceptibility in the European Union/European Economic Area (EU/EEA) has been greatly strengthened since the European Centre for Disease Prevention and Control (ECDC) started running the European sexually transmitted infection (STI) surveillance network. This has been achieved by the advent of biannual decentralised testing, an increase in the number of participating countries and gonococcal isolates, collection of epidemiological and behavioural variables and the continuation of an external quality assurance (EQA) scheme for gonococcal antimicrobial susceptibility.

During 2011, the European Gonococcal Antimicrobial Surveillance Programme (Euro-GASP) followed the biannual decentralised and centralised testing model, where participating laboratories were requested to collect gonococcal isolates during two periods (May/June and November/December). For centralised testing, susceptibility testing was performed on all isolates centrally by Etest or agar dilution for the following antimicrobials: cefixime, ceftriaxone, ciprofloxacin, azithromycin, spectinomycin and gentamicin. Participating laboratories that fulfilled set criteria took part in decentralised testing, where susceptibility testing was performed in the participant's own laboratory.

In 2011, 21 EU/EEA Member States participated in Euro-GASP, ten of which participated in decentralised testing. A total of 1902 isolates were collected and tested. The majority of gonococci (82.4%) were collected from men. The age range of the patients was less than one year to 80 years, with a median of 29 years; 31.9% of patients were younger than 25 years. Men who have sex with men (MSM) and male heterosexuals were significantly older than women. The site of specimen was mainly genital (82%), followed by rectal (12%) and pharyngeal (4%). When information on previous diagnosis of gonorrhoea was available, 19% had previously been diagnosed with the disease. Twenty two per cent of the patients were concurrently diagnosed with chlamydia. When sexual preference was known, 58% stated that they were heterosexual and 40% were men who have sex with men. Regarding HIV status, 18% were HIV-positive and 92% of those were men who have sex with men.

A high proportion of tested isolates showed decreased susceptibility to cefixime in 2011, 7.6%, using a breakpoint of >0.125 mg/L. This is a small (1%) decrease since 2010. Isolates with this phenotype were detected in 17 countries as in 2010, however this included four countries which reported isolates with decreased susceptibility to cefixime for the first time. Compared to the previous year, patients who acquired a strain displaying decreased susceptibility to cefixime were more likely to be female and heterosexual. For the first time in Euro-GASP, ten isolates displayed decreased susceptibility to ceftriaxone (>0.125 mg/L). Rates of ciprofloxacin and azithromycin resistance have both continued to decrease since 2009, but still remain high (48.7% and 5.3%, respectively). For the first time since 2007, two 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 the patient groups and specimen types, other than an association between concurrent chlamydia infection, age and ciprofloxacin susceptibility and also between HIV-positive status and ciprofloxacin susceptibility.

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

The continued high level of decreased susceptibility to cefixime and the ten isolates with decreased susceptibility to ceftriaxone are worrying findings as cefixime and ceftriaxone are recommended therapies for gonorrhoea across Europe. This decreasing susceptibility of gonococcal isolates to these last remaining treatment options, along with the continual detection of treatment failures across Europe, prompted the development of a response plan by ECDC. The response plan aims to control and manage the threat of multi-drug resistant *N. gonorrhoeae* in Europe at a time when action is urgently required to keep gonorrhoea a treatable infection.

1 Introduction

Since 2009, ECDC has co-ordinated the enhanced surveillance STI in the EU/EEA. The STI microbiology project has been contracted with an international team lead by the Health Protection Agency (United Kingdom) and includes the Statens Serum Institut (Denmark) and 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
- to strengthen the surveillance of NG antimicrobial susceptibility in EU/EEA Member States, including an EQA scheme and training.

1.1 Background

The emergence and spread of antimicrobial resistance (AMR) in *N. gonorrhoeae* continues to be a serious threat to the treatment and control of gonorrhoea. The therapeutic agents currently recommended in Europe [1], extended-spectrum cephalosporins, are the last remaining options for effective first-line and alternative antimicrobial therapy [2]. The European Gonococcal Antimicrobial Surveillance Programme (Euro-GASP) has identified decreasing susceptibility to these agents and treatment failures have been documented [3], prompting the creation of a European response plan to control and manage the threat of multi-drug resistant *N. gonorrhoeae* in Europe [4].

In 2010, Euro-GASP ran a sentinel surveillance programme in 21 EU countries. The major findings were [5]:

- Nine per cent of tested isolates had decreased susceptibility to cefixime, using a cut-off of >0.125 mg/L. This was a 4% increase since 2009.
- Ceftriaxone is still a suitable option for therapy; however the upward drift in the MIC for ceftriaxone needs careful and regular monitoring.
- Rates of ciprofloxacin and azithromycin resistance were high across Europe (53% and 7%, respectively).
- The MIC distribution (*in vitro* susceptibility) of gentamicin suggests that this antimicrobial could be used for therapy in the future.

1.2 Objectives

With 9% of isolates (tested in Euro-GASP 2010) displaying decreased susceptibility to cefixime, and the recent documented treatment failures, the need to monitor *N. gonorrhoeae* AMR in the EU/EEA Member States is clear.

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.
- Providing training in gonococcal culture and antimicrobial susceptibility testing, thereby facilitating an enhanced gonococcal antimicrobial susceptibility surveillance, using a standardised methodology across Europe.

This report presents the results from the 2011 gonococcal antimicrobial susceptibility surveillance and a summary of the second distribution from the 2011 EQA scheme.

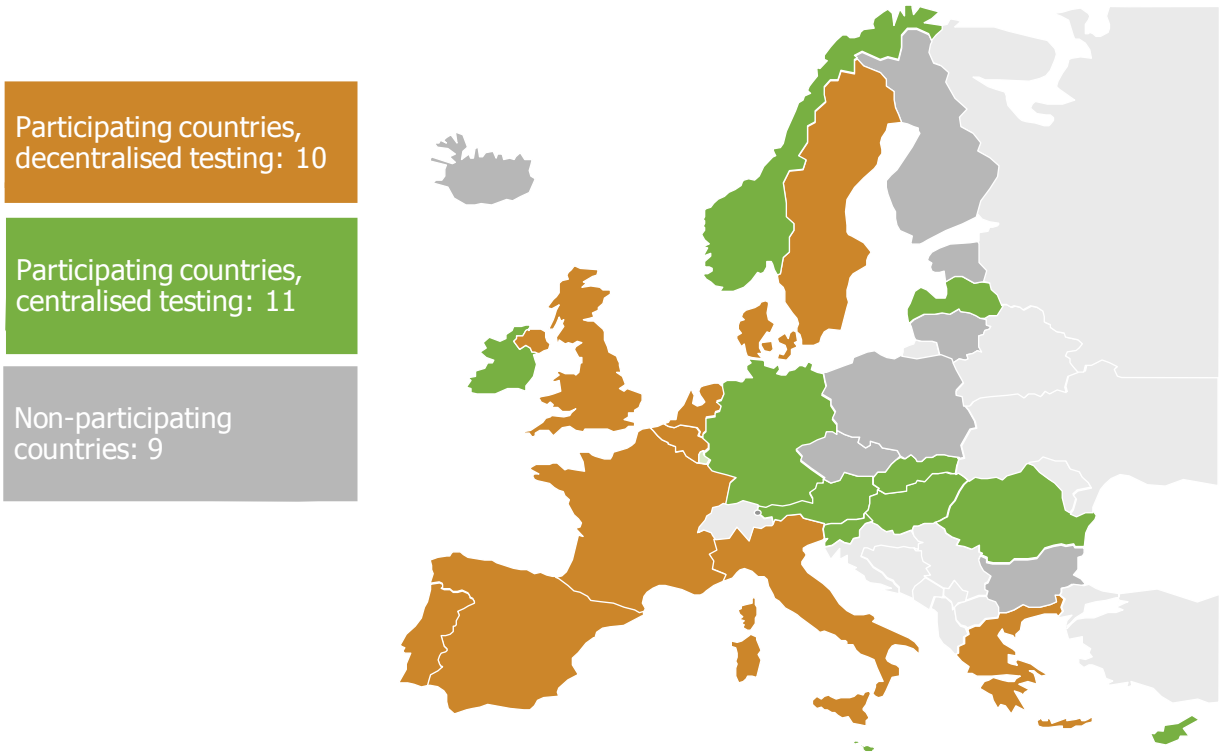
2 Methods

In 2011 Euro-GASP followed a biannual and decentralised testing model. For the biannual testing, participating laboratories were requested to collect gonococcal isolates during two periods; May/June and November/December. For decentralised testing, participating laboratories, who fulfilled set quality criteria, performed susceptibility testing in the participants own laboratory. Subsequently, countries were requested to upload their results to the European Surveillance System. All other participating countries followed the centralised testing model, where susceptibility testing was performed on all isolates at the Health Protection Agency (London), 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

Twenty-one countries participated in Euro-GASP in 2011, as in 2010; all of which were nominated contact points for STI surveillance in EU/EEA countries (Map 1).

Map 1. Countries participating in Euro-GASP, 2011



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 in ensuring accurate linking of laboratory and epidemiological data.

2.3 Isolate collection

Each country was asked to contribute 110 isolates each year, with the aim of retrieving and testing 100 isolates from each country. For countries where 100 isolates represents less than 10% of the total number of cases of gonorrhoea (Spain, The United Kingdom, and the Netherlands), it was requested that up to a maximum of 200 isolates should be collected. The aim was for laboratories to collect half the isolates in May/June and the remainder in November/December. However for the United Kingdom, the first collection was in July and the second in 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 one of the following three laboratories for susceptibility testing: Health Protection Agency, London, United Kingdom; Statens Serum Institut, Copenhagen, Denmark; or Örebro University Hospital, Örebro, Sweden.

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, enzyme-mediated high-level resistance only).

The following methodologies 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

Laboratories participating in decentralised testing performed susceptibility testing in their own laboratories (Annex 1), and the results were interpreted using the Euro-GASP breakpoints (Annex 2). For 2011, the Netherlands did not test for penicillinase production with all isolates and no spectinomycin with some isolates. Greece and Portugal did not test all isolates with azithromycin and ciprofloxacin respectively. Belgium, Greece and the Netherlands did not test gentamicin. Greece moved from centralised to decentralised testing in 2011.

2.5 Background variables

The following data for each isolate were collected where available via the European Surveillance System (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 where available. After the creation of a data source for the GONOAMR data (Annex 5), the data were uploaded using the GONOAMR metadata in TESSy by each Member State and then approved. Data from centres performing decentralised testing were uploaded to TESSy in the same manner.

Statistical analysis

Statistical analysis was performed in Stata v11.2. The Z-test was used to determine the p-value of the difference between epidemiological and AMR data collected in 2010 versus 2011, and to determine differences in age categories. 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. A Pearson's chi-squared test was used to test if these odds ratios were significantly different from one. For small cell numbers, Fisher's exact test was performed. A multivariable analysis used logistic regression to model the odds of associations between ciprofloxacin susceptibility and concurrent chlamydia infection controlling for other variables. Significance for all tests was when $p<0.05$.

Completeness of data

There is little difference in the completeness of reporting in 2011 compared to 2010, with either slight increases or decreases in the completeness of data. Completeness of data remained high for 'gender' and 'age' (over 94%), along with 'site of infection' (93.8%). Most improvement in completeness of reporting can be seen in clinical service type, probable country of infection and HIV status variables. For the 'place of residence' variable it should be noted that 219 of the 1 437 entries were at the country level only.

Table 1. Completeness of reporting, Euro-GASP 2011

Variables	Number and % of variables, first collection period, 2010 (n=900)		Number and % of variables, second collection period, 2010 (n=866)		Number and % of variables, TOTAL 2010 (n=1766)		Number and % of variables, TOTAL 2011 (n=1902)	
	No	**%**	**No**	**%**	**No**	**%**	**No**	**%**
Gender	892	99.1	857	99.0	1749	99	1826	96
Age	889	98.8	851	98.3	1740	98.5	1793	94.3
Mode of transmission	485	53.9	516	59.6	1001	56.7	1061	55.8
Site of infection	873	97.0	810	93.5	1683	95.3	1785	93.8
Previous gonorrhoea	336	37.3	355	41.0	691	39.1	767	40.3
Concurrent STI	360	40.0	419	48.4	779	44.1	875	46
Place of residence	Not collected		720	83.1	720	83.1	1437	75.6
Clinical service type			610	70.4	610	70.4	1544	81.2
Country of birth			392	45.3	392	45.3	861	45.3
Probable country of infection			263	30.4	263	30.4	737	38.8
HIV status			310	35.8	310	35.8	802	42.2

Clinical service type: To aid clinical service type analysis, the 14 coded variables were merged into six groups (Table 2).

Table 2. 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 'National protocols for the implementation of Euro-GASP, 2011' and/or the data source variable in the European Surveillance System is described in Table 3.

Table 3. Characteristics of national protocols for the implementation of Euro-GASP, 2011

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 STI outreach services	Other	Consecutively
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				
Portugal	National	STI clinics, DV clinics, GPs, hospitals, urology and gynaecology clinics	Sentinel	Consecutively
Romania	Regional/capital area	DV clinics, outpatients	Other	Consecutively
Slovakia	Regional	DV, urology and gynaecology practices.	Comprehensive	Consecutively
Slovenia	Regional	DV and STI clinics	Other	Consecutively
Spain	National	STI clinics and hospitals	Sentinel	Consecutively
Sweden	National	STI clinics	Comprehensive	Consecutively
United Kingdom	National†	GUM/STI clinics, GPs and outpatients	Sentinel	Consecutively

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

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

Sentinel: Reporting is based on a selected group of physicians/hospitals/laboratories/or other institutions' 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.

† National except for Northern Ireland.

A total of 1 902 isolates were tested over the 2011 collection period which is an increase of 136 isolates from 2010; 846 during the first collection period and 1 056 during the second collection period. The number of isolates tested from each country varied from ten (Cyprus) to 251 (UK) (Table 4). 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 2011) ranged from 1% (Hungary and the UK) to 91% (Cyprus and Portugal), and Hungary, Latvia, Romania, Spain and the UK had 5% or less collection coverage. To monitor the progress of Euro-GASP the percentage of isolates tested in 2009 and 2010 Euro-GASP is also displayed in Table 4. Even though an extra 136 isolates were tested in 2011 compared to 2010, there is a 1% decrease in the percentage of isolates tested compared to the European epidemiological surveillance data. This is due to increases in the number of gonorrhoea cases in 2011 (37 267) from 2010 (30 123) [5] from the Euro-GASP participating countries.

Table 4. Number of isolates tested in Euro-GASP 2009–2011 and number of reported gonorrhoea cases, 2011

Country	Number of isolates tested	Number of cases reported[6]	% isolates tested 2011	% isolates tested 2010	% isolates tested 2009
Austria	106	470	23	32	77
Belgium	110	843	13	15	15
Cyprus	10	11	91	52	N/A
Denmark	125	501	25	20	20
France	109	604	18	24	32
Germany	108	--	--	--	--
Greece	100	378	26	31	67
Hungary	13	1369	1	1	N/A
Ireland	64	834	8	14	N/A
Italy	99	407	24	42	48
Latvia	28	544	5	6	3
Malta	13	46	28	62	92
The Netherlands	217	3578	6	8	5
Norway	77	368	21	11	54
Portugal	109	120	91	81	75
Romania	26	521	5	2	N/A
Slovakia	113	194	58	70	13
Slovenia	19	25	76	64	80
Spain	100	2328	4	5	5
Sweden	105	943	11	10	18
United Kingdom	251	23183	1	1	1
Total	**1902**	**37267**	**5**	**6**	**6**

As in the previous years, the majority of gonococci (82.4%, n=1505) were collected from men. Gender was unknown for 76 cases (Table 5). The age range of the patients was <1 year to 80 years, with a mode and median age of 21 and 29 years respectively; a total of 31.9% (572) of patients were younger than 25 years when age was known (Table 6). Males (MSM and heterosexual) were significantly older than females ($p<0.002$), with the highest and lowest number of <25-year-olds in the female (53.9%) and MSM patient groups (21.8%) (Table 6). Compared with the 2010 age data, there was no significant difference between the age categories other than the heterosexuals (male and female) were significantly older in 2011 (36.2% <25 year olds compared to 41.9% in 2010, $p=0.05$).

Site of specimen was mainly genital (82.1%, n=1466), followed by rectal (12.1%, n=216), pharyngeal (4.4%, n=79) and other (1.3%, n=24); site of infection was unknown for 117 cases.

Information on previous diagnosis of gonorrhoea was available for 40.3% (767) of cases, of which 19% (146) had a previous infection. Information on concurrent STI was available for 46% (875) of cases; 22.2% (194) of patients had concurrent chlamydia, 4.9% (43) were infected with another STI, and 72.9% (638) were not co-infected with other STIs.

Table 5. Overall patient characteristics, 2009–2011

	2009, Number (%)	2010, Number (%)	2011, Number (%)
Total number of isolates	1366	1766	1902
Sex			
Male	1123 (83.7)	1441 (82.4)	1505 (82.4)
Female	219 (16.3)	308 (17.6)	321 (17.6)
Unknown	24	17	76
Age (years)			
<25	422 (32.0)	599 (34.4)	572 (31.9)
≥25	898 (68.0)	1141 (65.6)	1221 (68.10)
Unknown	46	26	109
Mode of transmission			
Heterosexual (male and female)	431 (63.2)	605 (60.5)	618 (58.3)
Female heterosexual	117 (17.2)	179 (17.9)	195 (18.4)
Male heterosexual	314 (46.1)	426 (42.6)	423 (39.9)
Men who have sex with men	251 (36.8)	395 (39.5)	442 (41.7)
Other			1 (0.1)
Unknown	684	766**	841
Site of infection			
Genital	1164 (86.5)	1426 (84.7)	1466 (82.1)
Pharyngeal	34 (2.5)	62 (3.5)	79 (4.4)
Anorectal	138 (10.3)	191 (11.4)	216 (12.1)
Other	9 (0.7)	7 (0.4)	24 (1.3)
Unknown	21	80	117
Previously diagnosed			
Yes	84 (18.1)	145 (21)	146 (19)
No	379 (81.9)	546 (79)	621 (81)
Unknown	903	1075	1135
Concurrent STI			
Concurrent chlamydia	78 (14.3)	172 (22.1)	194 (22.2)
Concurrent other STI (not HIV)	35 (6.4)	28† (3.6)	43 (4.9)
No concurrent STI	433 (79.3)	579 (74.3)	638 (72.9)
Unknown	820	987	1027
HIV status*			
Positive	N/D	48 (15.5)	141 (17.6)
Negative	N/D	262 (84.5)	661 (82.4)
Unknown	N/D	556	1100

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

Information on probable mode of transmission was available for 55.8% (1 061) of the cases, of which 58.3% (618) of the *N. gonorrhoeae* infections were reported as heterosexually acquired (18.4% females and 39.9% males) and 41.7% (442) were from MSM. No additional males with unknown mode of transmission had *N. gonorrhoeae* isolated from the pharynx or anogenital region.

When HIV status was known, 17.6% (141) were HIV-positive, of which 92.2% (130) were MSM.

There is little change in the epidemiological data when compared with 2010 (Table 4), other than the number of isolates from the site of infection 'other' increased significantly from 0.4% in 2010 to 1.3% in 2011 (p=0.004).

Table 6. Patient age distribution, 2011

Variable	Number†	Age (years)			
		Range	Mode	Median	<25 (%)
All patients	1793	<1 – 80	21	29	572 (31.9)
Gender					
Male	1475	<1 – 80	25	30	401 (27.2)
Female	317	<1 – 69	19	23	171 (53.9)
Mode of transmission					
Heterosexual (all)	577	15 – 77	21	27	209 (36.2)
Male heterosexual	403	16 – 77	21	29	116 (28.8)
Female heterosexual	174	15 – 59	19	23	93 (53.5)
MSM	385	16 - 80	28	31	84 (21.8)

†where information is available

The majority of patients attended a dedicated STI or sexual health clinic (56.7%), which was slightly more than in 2010 (51.3%) when the clinical service type was known (Table 7).

Table 7. Clinical service type attendance

Grouping	Total 2010 (%) n=866	Total 2011 (%) n=1902
STI and sexual health clinics	444 (51.3)	1079 (56.7)
Antenatal	0	0
Outpatients clinic	36 (4.2)	128 (6.7)
Other	42 (4.9)	60 (3.2)
Primary care	88 (10.2)	277 (14.6)
Unknown	256 (29.6)	358 (18.8)

Note: Grouping of clinical service type as described in Table 2.

Further country-specific data is presented in Annex 6 which includes a breakdown of clinical service type, country of birth, place of residence and probable country of infection.). Information on country of birth was supplied by 14 countries (Belgium, Cyprus, Denmark, Greece, Hungary, Ireland, Italy, Malta, the Netherlands, Portugal, Romania, Slovakia, Slovenia and the UK), of which Cyprus, Denmark, Greece, Ireland, Italy, Malta, the Netherlands and Slovakia reported patients that acquired gonorrhoea in their country but had a different country of birth, with the Netherlands having the largest number of nationalities (n=32). Of the 861 completed variables for country of birth, 83% (n=718) of patients were diagnosed with gonorrhoea in the same reporting country as their country of birth (similar to 2010, 87%). The most common countries reported as different countries of birth to the reporting country were Suriname (15 patients), Brazil (11 patients), Albania (10 patients), Hungary (7 patients) and Bulgaria, Pakistan, Poland and Romania (six patients). Probable country of infection data were supplied by 15 countries for some patients (Belgium, Cyprus, Denmark, France, Greece, Hungary, Italy, Latvia, Malta, Portugal, Romania, Slovenia, Slovakia, Spain and the United Kingdom), of which Belgium, Denmark, France, Greece, Italy, Malta, Slovenia, Slovakia and the United Kingdom reported patients acquiring gonorrhoea outside the reporting country. The majority of cases (95%; 700/737), most probably acquired gonorrhoea in the same country that reported the case. Most common countries reported as probable country of infection, that were different to the reporting country were Thailand (eight patients) and Austria and Germany (four patients).

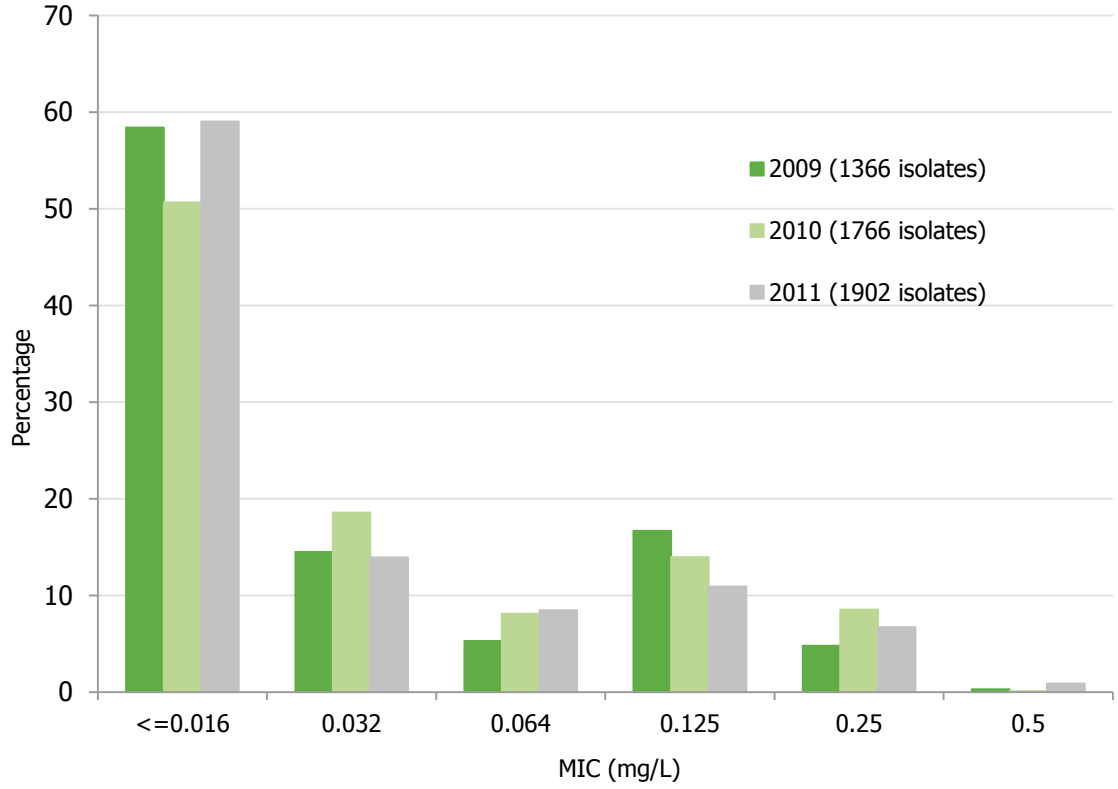
3.2 Antimicrobial susceptibility and resistance

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

Ceftriaxone and cefixime

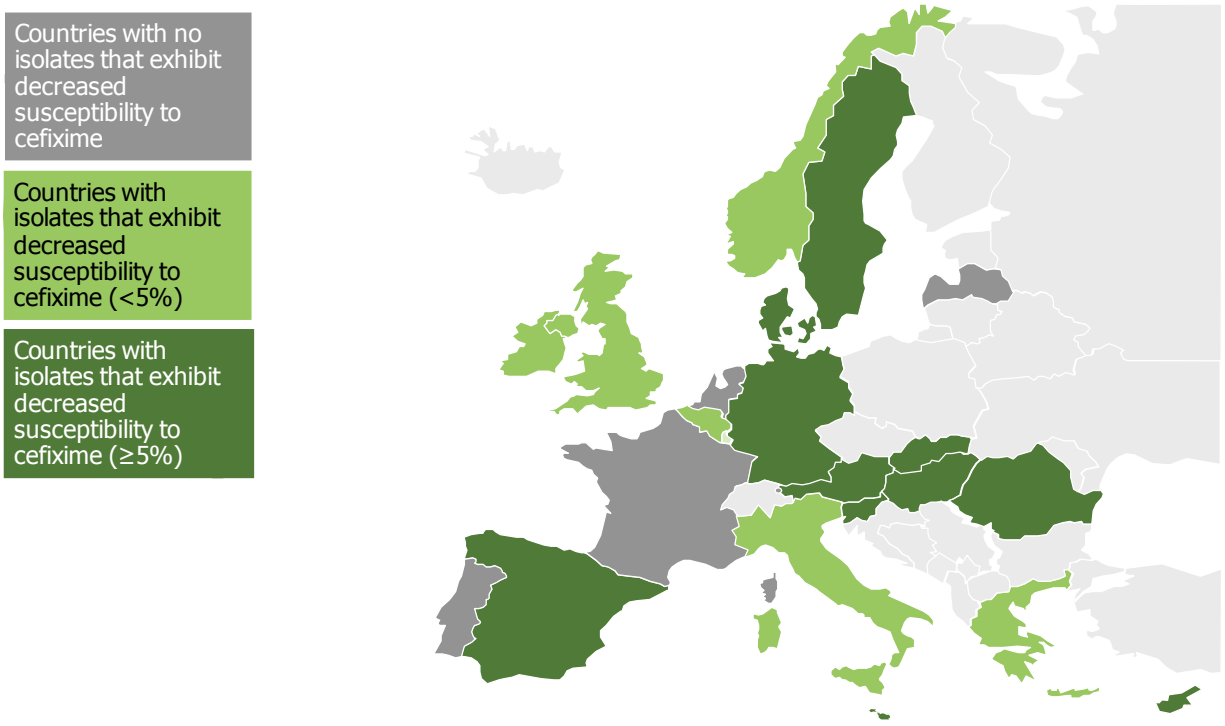
Almost 8% (7.6%, n=145) of the isolates displayed decreased susceptibility (>0.125 mg/L) to cefixime (Figure 1). Even though this is a slight decrease since 2010 (8.7%) the number of isolates with decreased susceptibility to cefixime in 2011 is still significantly higher than in 2009 (5.1% compared to 7.6%, p=0.005). There is an increase in the number of most susceptible isolates (≤0.016 mg/L) from 2010 (50.7%, n=895) to 2011 (59%, n=1 123) (p<0.002), which is close to the 2009 value of 58.4% (n=798). Even though this is encouraging, it is of concern that the proportion of isolates displaying an MIC of 0.5 mg/L has increased to 17 isolates in 2011 from two and four isolates in 2010 and 2009 respectively (Figure 1).

Figure 1. Distribution of MIC with respect to cefixime in Euro-GASP, 2009–2011



There was no change in the number of countries where isolates with decreased susceptibility to cefixime was detected (17 countries, Table 8). There is however a change in which countries provided isolates with decreased susceptibility to cefixime; in 2011 isolates were detected from Hungary, Malta and Romania for the first time. Decreased susceptibility to cefixime was not detected in four countries (France, Latvia, the Netherlands and Portugal). It should be noted that all but Latvia supplied good specimen numbers and had isolates with decreased susceptibility to cefixime in 2010. This data suggests that the problem may be spreading to the eastern part of the EU; however in 2011 more isolates were also tested from the eastern part of the EU, so it was more likely to detect decreased susceptibility to cefixime in these countries. Eleven countries (65%) had more than 5% decreased susceptibility (Table 8) and five countries reported more than 15% decreased susceptibility (Denmark, Romania, Slovakia, Slovenia and Spain). Map 2 displays the widespread geographical distribution of the isolates with decreased susceptibility to cefixime.

Map 2. Geographical distribution of gonococcal isolates with respect to susceptibility to cefixime, 2011



As in 2010, most of the isolates displaying decreased susceptibility to cefixime were from men (66.9%). This was, however, a significant decrease of 17.4% from 2010 ($p<0.0005$). This data, along with an increase in the number of patients who acquired the strains heterosexually when sexual orientation was known (from 28.6% in 2010 to 50.3% in 2011, $p=0.053$) suggest that the strains are now circulating more predominately in the heterosexual community (Table 8). As in Euro-GASP 2009 and 2010, there were differences across countries with respect to sexual orientation of the cases, as the isolates were either predominately from MSM or heterosexuals in each country (Table 8). The exception to this is for Greece where the predominance switched from heterosexual to MSM in 2011, and Slovenia from MSM to heterosexual. Additionally the equality of MSM and heterosexual patients in 2010 changed to become more MSM in 2011 in Italy. It should be noted that the proportion of isolates from MSM patients did decrease in 2011 by 50% in Slovenia, which most probably explains this shift. The mode of transmission proportions in Greece and Italy remained fairly constant however. Nine individuals had concurrent chlamydia infection and one had concurrent syphilis, all of which were from countries with a higher prevalence of cefixime decreased susceptibility (Austria, Slovenia and Slovakia), and one patient was HIV positive. In the previous year, the patient characteristics of those with isolates displaying decreased susceptibility to cefixime were quite similar when compared to the overall population, other than an association with age (more likely to be infected with a decreased susceptible to cefixime strain if older). However in 2011 there was no evidence of an association with age ($p=0.382$). In the univariate analysis, and in contrast to the previous year, there is strong evidence of an association with decreased susceptibility to cefixime and being female, heterosexual and HIV negative ($p=0.003$, $p<0.0001$ and $p=0.012$ respectively. See Annex 7: Table A7.4). However the association between sexual orientation is the only variable that remains significantly associated with cefixime decreased susceptibility in the multivariable model (odds ratio MSM to heterosexual=3.5, CI 1.95-6.44, $p<0.0001$). The statistical analysis confirms the observation of a dominant move of these isolates into the heterosexual community. It should be noted that the number of unknown variables is large and MSMs may be under-reported, so interpretations should be viewed with caution.

Table 8. Countries with isolates displaying decreased susceptibility (DS) to cefixime and epidemiological information, 2011

Country	Total number of isolates tested	Isolates with DS to cefixime		Age*				Gender						Sexual orientation					
				Age		<25 years		Males		Females		Unknown		MSM		Heterosexual		Unknown	
		No.	(%)	Mean	Mode	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Austria	106	14	13.2	23.4	21	10	71.4	6	42.9	8	57.1	0	0.0	0	0.0	9	64.3	5	35.7
Belgium	110	1	0.9	19†	N/A	1	100.0	0	0.0	1	100.0	0	0.0	0	0.0	0	0.0	1	100.0
Cyprus	10	1	10.0	71†	N/A	0	0.0	1	100.0	0	0.0	0	0.0	0	0.0	0	0.0	1	100.0
Denmark	125	25	20.0	31	21	9	36.0	18	72.0	7	28.0	0	0.0	1	4.0	20	80.0	4	16.0
Germany	108	11	10.2	31	N/A	0	0.0	1	9.1	0	0.0	10	90.9	0	0.0	0	0.0	11	100.0
Greece	100	3	3.0	30.7	36	1	33.3	3	100.0	0	0.0	0	0.0	2	66.7	1	33.3	0	0.0
Hungary	13	1	7.7	44†	N/A	0	0.0	1	100.0	0	0.0	0	0.0	0	0.0	1	100.0	0	0.0
Ireland	64	2	3.1	26	N/A	1	50.0	2	100.0	0	0.0	0	0.0	2	100.0	0	0.0	0	0.0
Italy	99	3	3.0	32.7	N/A	0	0.0	3	100.0	0	0.0	0	0.0	2	66.7	1	33.3	0	0.0
Malta	13	1	7.7	29†	N/A	0	0.0	1	100.0	0	0.0	0	0.0	1	100.0	0	0.0	0	0.0
Norway	77	1	1.3	34†	N/A	0	0.0	1	100.0	0	0.0	0	0.0	0	0.0	0	0.0	1	100.0
Romania	26	4	15.4	32.3	31	0	0.0	4	100.0	0	0.0	0	0.0	0	0.0	4	100.0	0	0.0
Slovakia	113	41	36.3	33.2	39	8	19.5	29	70.7	12	29.3	0	0.0	1	2.4	31	75.6	9	22.0
Slovenia	19	7	36.8	34.1	26	1	14.3	5	71.4	2	28.6	0	0.0	2	28.6	5	71.4	0	0.0
Spain	100	15	15.0	34	28	10	13	12	80.0	2	13.3	1	6.7	0	0.0	0	0.0	15	100.0
Sweden	105	8	7.6	27.4	27	3	37.5	5	62.5	3	37.5	0	0.0	0	0.0	0	0.0	8	100.0
United Kingdom	251	7	2.8	33.3	32	2	33.3	5	71.4	1	14.3	1	14.3	5	71.4	1	14.3	1	14.3
Total (with DS-cef)	1439	145		31.5	31	37	25.5	97	66.9	36	24.8	12	8.3	16	11	73	50.3	56	38.6
Total (all isolates)	1902	145	7.6	31	21	572	30.1	1505	79.1	321	16.9	76	4.0	442	23.2	618	32.5	841	44.2

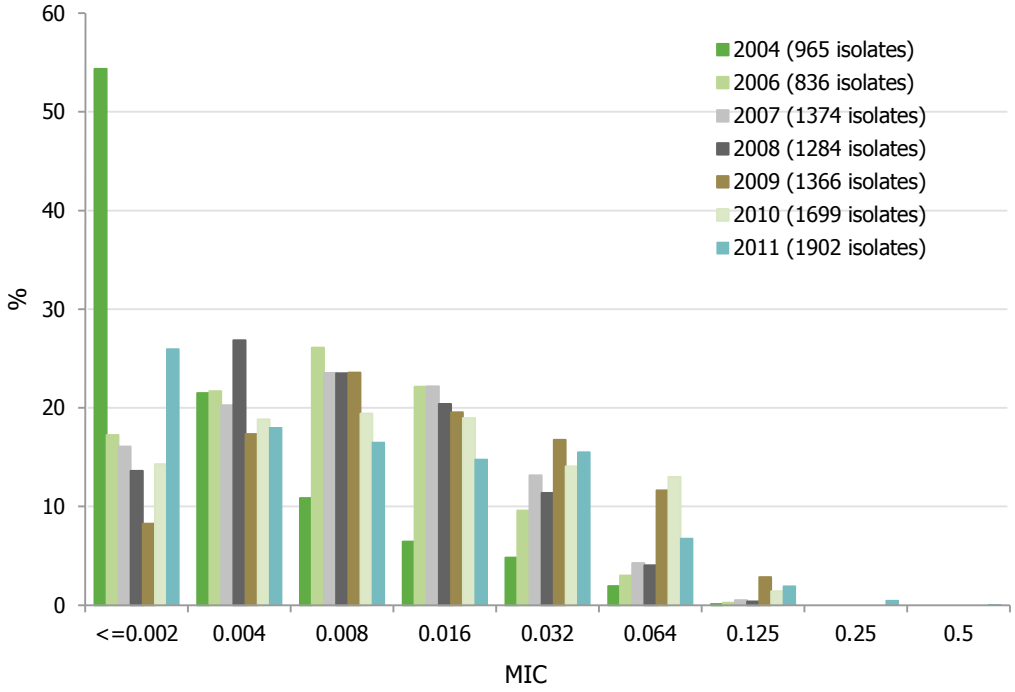
N/A – not enough data to establish a modal age

**Where age is known*

†Actual age of the single individual

For the first time in Euro-GASP, ten isolates displayed decreased susceptibility to ceftriaxone (>0.125 mg/L) in 2011 (Figure 2). Interestingly they are all from the same geographical area (Austria and Germany). Unfortunately there is very little additional epidemiological data with these isolates; when the data is known the cohort is composed of five males, one heterosexual and one concurrently infected with chlamydia. All the isolates have MICs to cefixime of at least 0.125 mg/L and are additionally resistant to ciprofloxacin. Like the cefixime data (Figure 1), the number of isolates in the more susceptible category has increased significantly since 2010 (from 14.3% in 2010 to 26% in 2011, $p<0.0002$).

Figure 2. Distribution of MIC for ceftriaxone, 2004–11



Other antimicrobials

The overall gonococcal resistance for ciprofloxacin, azithromycin and penicillin (high-level resistance only) is presented in Table 9.

Table 9. Resistance to ciprofloxacin, azithromycin and penicillin antimicrobials, 2011

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	72	106	67.9	13	106	12.3	14	106	13.2	Centralised
Belgium	61	110	55.5	4	110	3.6	12	110	10.9	Decentralised – MIC
Cyprus	8	10	80	1	10	10	1	10	10	Centralised
Denmark	73	125	58.4	15	125	12	22	125	17.6	Decentralised – Etest
France	49	109	45	2	109	1.8	11	109	10.1	Decentralised – Etest
Germany	55	108	50.9	1	108	0.9	12	108	11.1	Centralised
Greece	74	100	74	5	63	7.9	9	100	9	Decentralised – Etest
Hungary	8	13	61.5	0	13	0	0	13	0	Centralised
Ireland	9	64	14.1	5	64	7.8	1	64	1.6	Centralised
Italy	60	99	60.6	4	99	4	2	99	2	Decentralised – Etest
Latvia	8	28	28.6	1	28	3.6	0	28	0	Centralised
Malta	9	13	69.2	0	13	0	0	13	0	Centralised
The Netherlands	56	217	25.8	12	217	5.5	N/T			Decentralised – Etest
Norway	25	77	32.5	3	77	3.9	18	77	23.4	Centralised
Portugal	46	99	46.5	8	109	7.3	4	109	3.7	Decentralised – Etest
Romania	21	26	80.8	2	26	7.7	5	26	19.2	Centralised
Slovakia	80	113	70.8	7	113	6.2	5	113	4.4	Centralised
Slovenia	14	19	73.7	1	19	5.3	6	19	31.6	Centralised
Spain	59	100	59	14	100	14	13	100	13	Decentralised – MIC
Sweden	60	105	57.1	1	105	1	31	105	29.5	Decentralised – Etest
United Kingdom	75	251	29.9	0	251	0	10	251	4	Decentralised – MIC
Total	922	1892	48.7	99	1865	5.3	176	1685	10.4	
95% CI	46.5 - 51			4.3 - 6.4			9 - 11.9			
Median	58.4			4.7			10			

CI: confidence interval of the total % mean

NT: not tested

Ciprofloxacin

Resistance (≥1 mg/L) in 2011 ranged from 14.1% (Ireland) to 80.8% (Romania); the mean was 48.7% (Table 9). The ciprofloxacin resistance rates have decreased significantly between 2010 (52.7%) and 2011 (48.7%) (p=0.01, Z-test) continuing the trend seen since 2009 (Figure 3). Nonetheless the resistance levels remain high across Europe.

Azithromycin

Resistance (≥1 mg/L) levels of azithromycin in 2011 ranged from 0% (Hungary, Malta and the United Kingdom) to 14% (Spain), with a mean of 5.3% (Table 9). Two isolates displayed high-level resistance to azithromycin (>256 mg/L); one was isolated from a male heterosexual in Italy and the other from a MSM from Ireland. This is the first time since 2007 that isolates with this high level-resistance have been detected in Euro-GASP; one and four isolates from Scotland were detected in 2006 and 2007 respectively. Since 2004 there is no apparent trend with azithromycin resistance, but resistance levels since 2009 are decreasing. The decrease from 2010 (7.2%) to 2011 (5.3%) is significant (p=0.019, Z-test) (Figure 3). As in previous years, the modal MIC of resistant isolates to azithromycin was 1 mg/L, which is the breakpoint used for categorising resistance. Isolates with an MIC on the breakpoint are just one doubling dilution from giving a susceptible category, which may explain the fluctuating resistance rates observed from 2004 to 2011.

Penicillin

High-level plasmid-mediated resistance to penicillin (penicillinase-producing *N. gonorrhoeae*, (PPNG)) ranged from 0% (Hungary, Latvia and Malta) to 31.6% (Slovenia), with a mean of 10.4% (Table 9). High-level resistance to penicillin (PPNG) continues to remain fairly constant over the years at 8.6–13% (Figure 3).

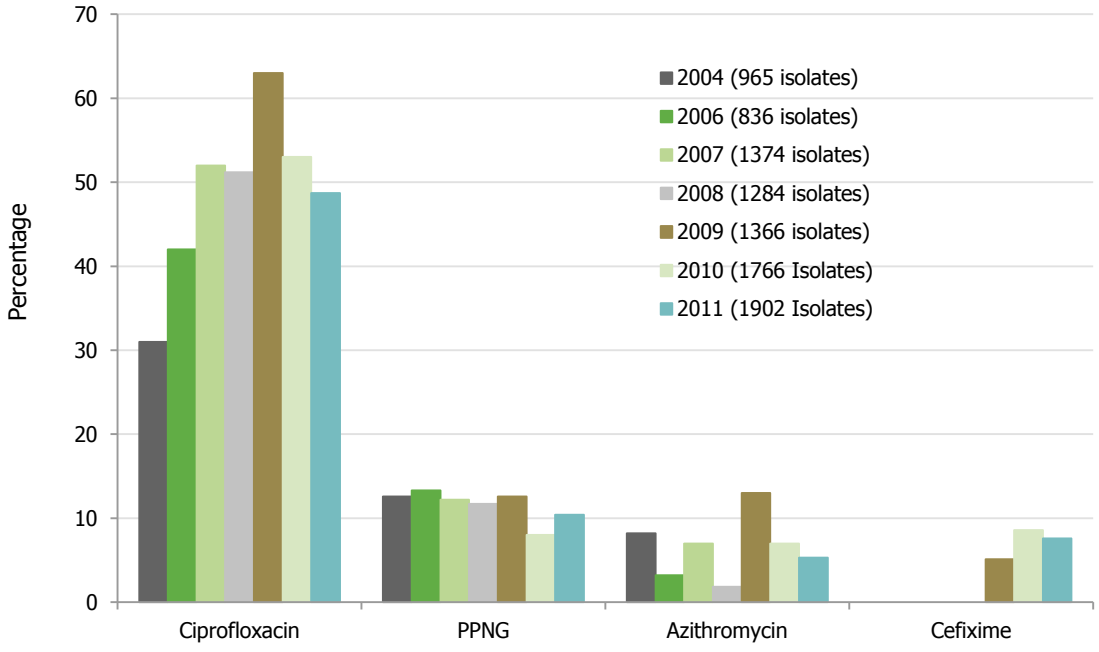
Spectinomycin

No resistance to spectinomycin (>0.64 mg/L) was detected in 2011 (1 879 isolates tested). No resistance to spectinomycin was demonstrated in 2008 to 2011, the years when this agent was tested.

Gentamicin

As yet, there are no breakpoints for gentamicin, but the overall MIC distribution continues to be low in all European countries (MIC50 4 mg/L and MIC90 8 mg/L). The MIC50 is one dilution lower than the previous years of 8 mg/L, however the MIC range was the same as the previous year (0.5–16 mg/L, 1473 isolates tested).

Figure 3. Overall percentage of resistant Neisseria gonorrhoeae, 2004–2011



Resistance by patient characteristics was calculated (Table 10), and statistical analysis was performed to explore associations between resistance and patient characteristics (Annex 7). Overall the distribution of resistance is similar across patient groups and specimen types, other than for the following.

By univariate analysis there continues to be strong evidence of an association between ciprofloxacin resistance and no concurrent chlamydia infection, and heterosexuals (p=<0.0001, Table A7.1, Annex 7). Ciprofloxacin resistance is additionally associated with age (>25 years, p=0.027). This association remains strong following multivariable analysis for concurrent chlamydia infection and sexual orientation (odds ratio concurrent chlamydia to no concurrent chlamydia=2, CI 1.39–2.9, p=<0.0001, and odds ratio MSM to heterosexual=1.7, CI 1.24-2.26, p=0.001). The association with age becomes borderline in the multivariable analysis (odds ratio <25 years to ≥25 years=1.4, CI 1–1.89, p=0.053). Strong evidence of an association between HIV-negative status and ciprofloxacin resistance was observed (p=0.0014), but this association was not included in the multivariable analysis (likelihood ratio p=0.38).

Interestingly, the level of antibiotic resistance seems to be reducing in MSM as there are strong associations between heterosexuals and ciprofloxacin, penicillinase and cefixime resistance (p=<0.0001, Tables A7.1-A7.4, Annex 7). It should be noted that reporting on sexuality is low (56%), so MSM patients may be under-reported; however susceptibility profiles of MSM are also mirrored in specimens from the ano-rectal region.

The association between patient characteristics and decreased susceptibility to cefixime has been described previously (section 3.2).

Table 10. Resistance to ciprofloxacin, azithromycin, cefixime and penicillin by patient characteristics, 2011

Country	Ciprofloxacin			Azithromycin			Cefixime			PPNG		
	Total tested	No. resistant	%	Total tested	No. resistant	%	Total tested	No. decreased susceptible	%	Total tested	No. resistant	%
Gender												
Male	1496	732	48.9	1469	78	5.3	1505	97	6.5	1333	128	9.6
Female	320	145	45.3	321	18	5.6	321	36	11.2	276	42	15.2
Age												
<25 years	568	251	44.2	566	24	4.2	572	37	6.5	504	49	9.7
≥25 years	1215	605	49.8	1190	65	5.5	1221	93	7.6	1072	116	10.8
Transmission												
MSM	440	165	37.5	437	21	4.8	442	16	3.6	302	7	2.3
Heterosexual	617	336	54.5	587	38	6.5	618	73	11.8	541	62	11.5
Site of infection												
Genital	1456	743	51	1429	76	5.3	1466	119	8.1	1355	151	11.1
Pharyngeal	79	31	39.2	79	6	7.6	79	8	10.1	68	8	11.8
Anorectal	216	78	36.1	216	15	6.9	216	7	3.2	122	3	2.5
Other	24	9	37.5	24	0	0	24	0	0	23	2	8.7
Previous gonorrhoea infection												
Yes	146	69	47.3	140	5	3.6	146	12	8.2	146	11	7.5
No	618	338	54.7	592	39	6.6	621	84	13.5	621	49	7.9
Concurrent chlamydia												
Yes	192	57	29.7	194	5	2.6	194	9	4.6	130	6	4.6
No	679	315	46.4	669	36	5.4	681	58	8.5	528	34	6.4
HIV status												
Positive	141	46	32.6	141	5	3.6	141	5	3.6	68	2	2.9
Negative	658	312	47.4	651	30	4.6	661	68	10.3	522	42	8.1
Overall resistance	1892	922	48.7	1845	99	5.4	1902	145	7.6	1685	176	10.4

4 External quality assessment

4.1 Background

Comparability and concordance of antimicrobial susceptibility data across the testing centres is a priority of any surveillance programme especially where decentralised testing is a desired component. Implementation of an EQA scheme facilitates this monitoring.

An EQA scheme for *N. gonorrhoeae* has been available for laboratories participating in Euro-GASP since 2009. The United Kingdom National External Quality Assessment Service (UK-NEQAS) provides a genital pathogens scheme for pathogen identification and antimicrobial susceptibility testing. Two pathogens are distributed three times a year with an additional panel of isolates from the European STI network to allow more extensive antimicrobial susceptibility testing analysis. Successful performance in the EQA scheme is essential for participation in decentralised susceptibility testing across Europe (Annex 1).

A summary of the second 2011 EQA distribution dataset is described and a full report is available upon request from ECDC. The first 2011 EQA distribution data has been summarised in the Euro-GASP 2010 report [5].

4.2 Antimicrobial susceptibility testing external quality assessment scheme

In October 2011 participating laboratories received the UK-NEQAS genital pathogens EQA scheme for identification and susceptibility testing and an additional five gonococcal isolates from the European GC AMR EQA programme for susceptibility testing only. In order to monitor intra-laboratory reproducibility, one isolate was provided in duplicate (QA11-07/QA11-10). The gonococcal isolates were selected to provide a range of different susceptibility profiles and were chosen from a well-characterised global panel of strains and recently isolated clinical strains.

The October 2011 panel (QA11_2) was received by 21 participating laboratories within 18 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 where possible:

- Azithromycin
- Cefixime
- Ceftriaxone
- Ciprofoxacin
- Gentamicin
- Spectinomycin
- Beta-lactamase testing

4.3 Results

Results for the UK-NEQAS panel were reported back directly to UK-NEQAS (data not shown) whilst results for the European GC AMR panel were submitted centrally onto 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 resistance (resistant, intermediate or susceptible) for each antimicrobial tested. The majority of laboratories used the Clinical Laboratory Standards Institute [7] guidelines, however other guidelines/susceptibility criteria used included those from GRASP, the European Committee on Antimicrobial Susceptibility Testing [8] and the World Health Organization (WHO).

Results for each isolate were reported as the category of resistance and the MIC for the Etest and agar dilution methods or the zone of inhibition for the disc diffusion method. After results were received they were decoded and referred back to the laboratories to allow observation of intra-laboratory reproducibility and for any issues identified to be immediately addressed.

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

Table 11. Overall consensus results from October 2011 EQA

Consensus category

Modal (range) MIC for Etest and agar dilution method (mg/L)

Mean (Range) diameter for disc diffusion method (mm)

Strain	Azithromycin Consensus	Cefixime Consensus	Ceftriaxone Consensus	Ciprofloxacin Consensus	Gentamicin Consensus	Spectinomycin Consensus	Beta-lactamase Consensus
	S	**S**	**S**	**R**	**S**	**S**	
QA11-06	0.5 (0.25 – 1)	0.125 (0.032 – 1)	0.064 (0.008 – 0.25)	>32 (>1 - >32)	4 (4 – 16)	16 (8 -32)	NEG
(G10-1494)	28 (26 – 30)	31 (28 – 34)	36 (34 – 39)	6 (0 – 12)	15 (No range)	25 (23 -27)	100%
	47	81	100	100	100	100	
	S	S	S	S	S	R	
QA11-07	0.25 (0.125 – 1)	0.016 (0.016 – 0.25)	0.016 (<0.016 – 0.064)	0.008 (0.004 – 0.064)	4 (2 – 8)	>1024 (>64 - >1024)	POS
QA11-10	32 (30 – 35)	36 (36 – 37)	40 (36 – 41)	41 (8 – 46)	15 (13 – 16)	3 (0 – 7)	94%
(WHO O)	88	94	100	97	100	100	
	S	S	S	R	S	S	
QA11-08	0.064 (0.016 – 0.125)	0.016 (0.008 – 0.25)	0.008 (<0.016 – 0.125)	4 (>1 – 8)	4 (2 – 8)	8 (4 -16)	POS
(G10-1892)	34 (30 – 36)	36 (No range)	43 (40 – 44)	15 (12 – 19)	16 (15 -16)	27 (24 – 30)	100%
	100	94	100	100	100	100	
	S	S	S	S	S	S	
QA11-09	0.125 (0.032 – 0.125)	<0.016 (<0.016 – 0.016)	<0.002 (<0.002 – 0.016)	0.004 (<0.002 – 0.032)	4 (2 – 8)	16 (8 – 32)	NEG
(WHO F)	33 (31 – 34)	46 (44 – 47)	46 (41 – 50)	43 (38 – 46)	17 (16 – 17)	24 (21 – 26)	100%
	100	100	100	95	100	100	

% concordance of resistance category

No range: two countries with the same disc diffusion value.

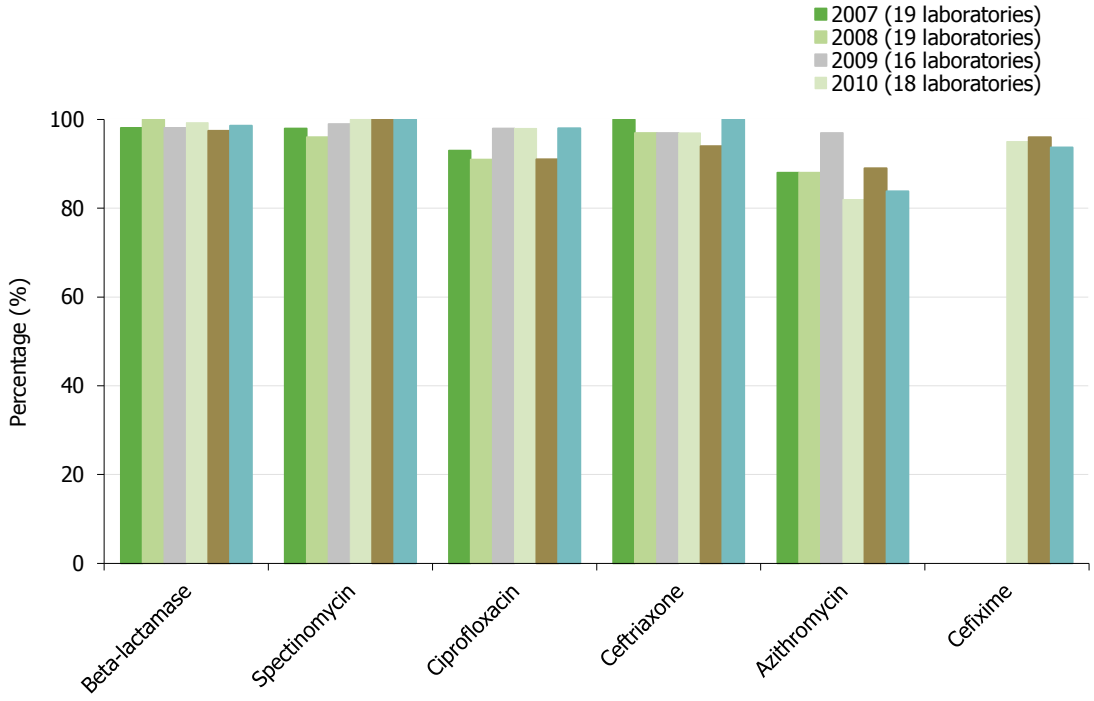
Number of centres used to calculate disc diffusion mean diameter: azithromycin = 4; cefixime= 2; ceftriaxone = 4; ciprofloxacin = 5; gentamicin = 2; spectinomycin = 4

4.3.1. Resistance category concordance

The highest resistance category concordance was seen for ceftriaxone, gentamicin and spectinomycin (100%), whilst the lowest was seen for azithromycin (84%). The agar dilution method gave the highest concordance between laboratories (100%) although it should be noted that just two laboratories used the agar dilution method.

Comparison of the overall concordance from previous 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) shows that concordance of resistance categories was very good across the different distributions (Figure. 4).

Figure 4. Inter-laboratory concordance



**Testing of cefixime became part of the EQA scheme from 2010. During the ESSTI AMR project cefixime was not part of the antimicrobial panel but is now included in the ECDC Euro-GASP AMR project.*

It should be noted that the ESSTI panels contained 30 isolates (10 in triplicate) and the European gonococcal antimicrobial resistance EQA panels contained 10 isolates per year.

4.3.2. Beta-lactamase concordance

Eighteen of the nineteen centres returned results tested for beta-lactamase production. Seventeen of the eighteen centres achieved full concordance, the remaining centre incorrectly identified isolates QA11-07 and QA11-10 as beta-lactamase negative. Overall concordance has increased from 97.4% in the previous EQA distribution to 98.6%.

4.3.3. Minimum inhibitory concentration concordance

A high proportion of the MIC results for the panel, using the agar dilution and Etest methods, were within one doubling dilution of the modal MIC (93%) and just 4% within two doubling dilutions. On ten occasions (2%), isolate MICs differed from the modal MICs by more than two dilutions; five of which were cefixime, three ciprofloxacin and two ceftriaxone. Spectinomycin (100%) followed by gentamicin (98%) gave the highest MIC concordance within one doubling dilution and cefixime (87%) and ceftriaxone (89%) gave the lowest. Overall, the MIC concordance demonstrates the high level of comparability between the Etest and agar dilution methods in the participating laboratories.

5 Conclusions

5.1 Gonococcal antimicrobial susceptibility and resistance

The percentage of isolates displaying decreased susceptibility to cefixime is still highly worrying, even with the observed slight decrease since 2010, from 8.7% to 7.6% in 2011. The decrease could be due to a number of factors and may include clinics using ceftriaxone and as such reducing cefixime selection pressure and/or increased use of molecular tests which offer better detection and subsequent treatment of infections.

The ten isolates with decreased susceptibility to ceftriaxone (>0.125 mg/L) add to the concern that gonorrhoea may become an untreatable infection, at least using antimicrobial monotherapy, due to the emergence of resistance to the last remaining treatment option ceftriaxone.

Rates of ciprofloxacin and azithromycin resistance have both continued to decrease since 2009, but still remain high (48.7% and 5.3%, respectively) and therefore are not recommended treatment options unless the isolates are first shown to be susceptible. For the first time since 2007, two isolates displayed high-level resistance to azithromycin (>256 mg/L) and the potential spread of these isolates will be monitored closely.

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. There continues to be no resistance to spectinomycin, but this antimicrobial can be difficult to acquire.

5.2 Quality assessment

Antimicrobial susceptibility testing methods across Europe continue to have common features which allow comparison using EQA schemes. Overall concordance remains high (>90%) for all antimicrobials other than azithromycin (84%) which reflects the results seen in previous distributions. Azithromycin concordance was lower due to strains being close to breakpoints and/or different interpretative criteria used by laboratories. The variation in breakpoint classification for azithromycin appears to have reduced suggesting breakpoint harmonisation.

The continued high level of concordance between laboratories in the STI surveillance network recommends confidence in and lends support to decentralised testing for Euro-GASP. Further participation with the UK-NEQAS genital pathogens scheme and the European GC AMR EQA scheme should be encouraged to help build confidence, competence and capability in the isolation and identification of *N. gonorrhoeae*.

5.3 Further developments of Euro-GASP

This decreasing susceptibility of gonococcal isolates to the last remaining treatment options of cefixime and ceftriaxone, along with the continual detection of treatment failures across Europe, prompted ECDC to develop a response plan [4]. The response plan aims to control and manage the threat of multi-drug resistant *N. gonorrhoeae* in Europe at a time when action is required to keep gonorrhoea a treatable infection. Euro-GASP has a major role to play in fulfilling the objectives of the response plan which include:

- Strengthening the surveillance of gonococcal antimicrobial susceptibility by increasing the number of participating countries and isolates, improving representativeness of the programme and collecting more epidemiological variables. Country visits to Latvia and Romania, and a prospective visit to Bulgaria may assist in the inclusion of additional centres and isolate numbers. Isolate numbers from Hungary should increase in the future as some storage problems have been resolved. More isolates are required from Spain and the number of cases from the UK is too large to achieve 5% coverage in Euro-GASP. Improved completeness of reporting is required if robust statistical analysis is to be performed on the linked susceptibility and patient data.
- Providing 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 in training where required and eventually move towards decentralised testing.
- Ensuring that all Euro-GASP laboratories participate in the EQA programme. Even though the concordance with the EQA is high, full participation by all Euro-GASP countries needs to be achieved.

The results from Euro-GASP 2011 re-enforces the requirements for improved antimicrobial susceptibility surveillance, as the situation with the extended-spectrum cephalosporins needs to be monitored very closely. The loss of these last treatment options would have serious public health implications.

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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 UK, 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 2.4 susceptibility testing). All other laboratories will continue with centralised testing. In those laboratories performing decentralised testing, data is 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 (E-test)
- ceftriaxone (E-test)
- ciprofloxacin (breakpoint)
- gentamicin (agar dilution/E-test)
- 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 the 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 E-tests, 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 in 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 vs sexual orientation and gender (bar graph/line graph)
- Cefixime DS vs age group and gender
- Similar analysis as for number 9 and 10 for Ceftriaxone (if examples of DS observed)

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

Each country referring gonococcal isolates or 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 (E-test/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 gonococcal antimicrobial susceptibility testing

- Isolates are shipped frozen to one of the three testing centres:
  - Health Protection Agency , London, UK
  - Statens Serum Institut, Copenhagen, Denmark
  - 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 (Launch 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		
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 [10] are used, with the exception of ciprofloxacin and azithromycin intermediate resistance. The ciprofloxacin resistance breakpoint in this study is more clinically relevant to treatment failure. 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 dept, 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/homo or bisexual male, Mother-to-child transmission, Other, Unknown	**Test method:** E-test, 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. Patient characteristics

Table A6.1. Patient characteristics; all countries and by country, 2011

	All countries		Austria		Belgium		Cyprus		Denmark		France		Germany		Greece		Hungary	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
	1902		106		110		10		125		109		108		100		13	
Sex																		
Male	1505	79.1	62	58.5	98	89.1	10	100.0	95	76.0	90	82.6	30	27.8	100	100.0	13	100.0
Female	321	16.9	44	41.5	12	10.9	0	0.0	30	24.0	19	17.4	11	10.2	0	0.0	0	0.0
Unknown	76	4.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	67	62.0	0	0.0	0	0.0
Age (years)																		
<25	572	30.1	45	42.5	30	27.3	2	20.0	34	27.2	45	41.3	15	13.9	14	14.0	4	30.8
≥25	1221	64.2	61	57.6	76	69.1	8	80.0	91	72.8	62	56.9	26	24.1	84	84.0	9	69.2
Unknown	109	5.7	0	0.0	4	3.6	0	0.0	0	0.0	2	1.8	67	62.0	2	2.0	0	0.0
Mode of transmission																		
Heterosexual (male and female)	618	32.5	77	72.6	5	4.6	0	0.0	77	61.6	0	0.0	0	0.0	78	78.0	11	84.6
Male heterosexual	423	22.2	34	32.1	5	4.5	0	0.0	51	40.8	0	0.0	0	0.0	78	78.0	11	84.6
MSM	442	23.2	6	5.7	1	0.9	0	0.0	33	26.4	0	0.0	0	0.0	20	20.0	0	0.0
Other	1	0.05	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Unknown	841	44.2	23	21.7	104	94.5	10	100.0	15	12.0	109	100.0	108	100.0	2	2.0	2	15.4
Site of infection																		
Genital	1466	77.1	95	89.6	94	85.5	10	100.0	113	90.4	96	88.1	37	34.3	98	98.0	13	100.0
Pharyngeal	79	4.2	2	1.9	0	0.0	0	0.0	5	4.0	1	0.9	0	0.0	0	0.0	0	0.0
Anorectal	216	11.4	9	8.5	5	4.5	0	0.0	7	5.6	4	3.7	3	2.8	0	0.0	0	0.0
Other	24	1.3	0	0.0	10	9.1	0	0.0	0	0.0	7	6.4	1	0.9	0	0.0	0	0.0
Unknown	117	6.2	0	0.0	1	0.9	0	0.0	0	0.0	1	0.9	67	62.0	2	2.0	0	0.0
Previously diagnosed																		
Yes	146	7.7	20	18.9	2	1.8	0	0.0	18	14.4	0	0.0	0	0.0	12	12.0	0	0.0
No	621	32.7	12	11.3	12	10.9	0	0.0	107	85.6	0	0.0	0	0.0	82	82.0	0	0.0
Unknown	1135	59.7	74	69.8	96	87.3	10	100.0	0	0.0	109	100.0	108	100.0	6	6.0	13	100.0
Concurrent STI																		
Concurrent CT	194	10.2	21	19.8	1	0.9	0	0.0	0	0.0	10	9.2	1	0.9	0	0.0	0	0.0
Concurrent other	47	2.5	0	0.0	1	0.9	0	0.0	0	0.0	2	1.8	0	0.0	1	1.0	0	0.0
No concurrent STI	638	33.5	71	67.0	0	0.0	0	0.0	0	0.0	27	24.8	2	1.9	32	32.0	0	0.0
Unknown	1027	54	14	13.2	108	98.2	10	100.0	125	100.0	70	64.2	105	97.2	67	67.0	13	100.0
HIV status																		
Positive	141	7.4	2	1.9	2	1.8	0	0.0	6	4.8	2	1.8	0	0.0	0	0.0	0	0.0
Negative	661	34.8	28	26.4	2	1.8	0	0.0	86	68.8	0	0.0	1	0.9	31	31.0	0	0.0
Unknown	1100	57.8	76	71.7	106	96.4	10	100.0	33	26.4	107	98.2	107	99.1	69	69.0	13	100.0

Table A6.1. Patient characteristics; all countries and by country, 2011 (continued)

	Ireland		Italy		Latvia		Malta		Netherlands		Norway		Portugal		Romania		Slovakia	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
	64		99		28		13		217		77		109		26		113	
Sex																		
Male	58	90.6	91	91.9	17	60.7	12	92.3	172	79.3	71	92.2	101	92.7	26	100.0	87	77.0
Female	6	9.4	3	3.0	11	39.3	1	7.7	45	20.7	6	7.8	8	7.3	0	0.0	26	23.0
Unknown	0	0.0	5	5.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Age (years)																		
<25	25	39.1	22	22.2	11	39.3	4	30.8	68	31.3	9	11.7	38	34.9	8	30.8	30	26.6
≥25	39	60.9	68	68.7	17	60.7	9	69.2	149	68.7	68	88.3	71	65.1	18	69.2	83	73.5
Unknown	0	0.0	9	9.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Mode of transmission																		
Heterosexual (male and female)	12	18.8	34	34.3	26	92.9	9	69.2	77	35.5	0	0.0	5	4.6	26	100.0	73	64.6
Male heterosexual	8	12.5	32	32.3	15	53.6	8	61.5	32	14.7	0	0.0	3	2.8	26	100.0	55	48.7
MSM	42	65.6	58	58.6	1	3.6	3	23.1	140	64.5	0	0.0	7	6.4	0	0.0	8	7.1
Other	1	1.6	1	1.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Unknown	10	15.6	6	6.1	1	3.6	1	7.7	0	0.0	77	100.0	97	89.0	0	0.0	32	28.3
Site of infection																		
Genital	33	51.6	80	80.8	28	100.0	10	76.9	111	51.2	67	87.0	105	96.3	26	100.0	112	99.1
Pharyngeal	11	17.2	0	0.0	0	0.0	1	7.7	11	5.1	1	1.3	1	0.9	0	0.0	0	0.0
Anorectal	20	31.3	10	10.1	0	0.0	2	15.4	94	43.3	6	7.8	1	0.9	0	0.0	0	0.0
Other	0	0.0	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	2	1.8	0	0.0	1	0.9
Unknown	0	0.0	9	9.1	0	0.0	0	0.0	0	0.0	3	3.9	0	0.0	0	0.0	0	0.0
Previously diagnosed																		
Yes	5	7.8	10	10.1	3	10.7	0	0.0	0	0.0	0	0.0	2	1.8	0	0.0	8	7.1
No	58	90.6	62	62.6	0	0.0	13	100.0	0	0.0	0	0.0	10	9.2	26	100.0	104	92.0
Unknown	1	1.6	27	27.3	25	89.3	0	0.0	217	100.0	77	100.0	97	89.0	0	0.0	1	0.9
Concurrent STI																		
Concurrent CT	5	7.8	8	8.1	10	35.7	1	7.7	64	29.5	0	0.0	7	6.4	0	0.0	5	4.4
Concurrent other	6	9.4	2	2	3	10.7	0	0.0	14	6.5	0	0.0	3	2.8	0	0.0	8	7.1
No concurrent STI	31	48.4	63	63.6	15	53.6	12	92.3	139	64.1	0	0.0	6	5.5	0	0.0	88	77.9
Unknown	22	34.4	27	27.3	0	0.0	0	0.0	0	0.0	77	100.0	93	85.3	26	100.0	12	10.6
HIV status																		
Positive	5	7.8	15	15.2	1	3.6	0	0.0	73	33.6	0	0.0	1	0.9	0	0.0	0	0.0
Negative	18	28.1	77	77.8	0	0.0	12	92.3	139	64.1	0	0.0	11	10.1	0	0.0	90	79.6
Unknown	41	64.1	7	7.1	27	96.4	1	7.7	5	2.3	77	100.0	97	89.0	26	100.0	23	20.4

** Data only collected during the second collection period*

Table A6.1. Patient characteristics; all countries and by country, 2011 (end)

	Slovenia		Spain		Sweden		UK	
	No.	%	No.	%	No.	%	No.	%
	19		100		105		251	
Sex								
Male	17	89.5	90	90.0	65	61.9	200	79.7
Female	2	10.5	8	8.0	40	38.1	49	19.5
Unknown	0	0.0	2	2.0	0	0.0	2	0.8
Age (years)								
<25	5	26.3	10	10.0	50	47.6	103	41.0
≥25	14	73.7	67	67.0	55	52.4	146	58.2
Unknown	0	0.0	23	23.0	0	0.0	2	0.8
Mode of transmission								
Heterosexual (male and female)	12	63.2	0	0.0	0	0.0	96	38.3
Male heterosexual	10	52.6	0	0.0	0	0.0	55	21.9
MSM	6	31.6	0	0.0	0	0.0	117	46.6
Other	0	0.0	0	0.0	0	0.0	0	0.0
Unknown	1	5.3	100	100.0	105	100.0	38	15.2
Site of infection								
Genital	14	73.7	96	96.0	71	67.6	157	62.6
Pharyngeal	3	15.8	1	1.0	18	17.1	24	9.6
Anorectal	2	10.5	2	2.0	0	0.0	51	20.3
Other	0	0.0	1	1.0	0	0.0	1	0.4
Unknown	0	0.0	0	0.0	16	15.2	18	7.2
Previously diagnosed								
Yes	1	5.3	0	0.0	0	0.0	65	25.9
No	17	89.5	0	0.0	0	0.0	118	47.0
Unknown	1	5.3	100	100.0	105	100.0	68	27.1
Concurrent STI								
Concurrent CT	4	21.1	0	0.0	0	0.0	57	22.7
Concurrent other	0	0.0	0	0.0	0	0.0	5	2.0
No concurrent STI	15	78.9	0	0.0	0	0.0	137	54.6
Unknown	0	0.0	100	100.0	105	100.0	53	21.1
HIV status								
Positive	2	10.5	0	0.0	0	0.0	32	12.8
Negative	16	84.2	0	0.0	0	0.0	150	59.8
Unknown	1	5.3	100	100.0	105	100.0	69	27.5

Table A6.2. Clinical service type, place of residence, country of birth and probable country of infection

	Austria (n=106)	Belgium (n=110)	Cyprus (n=10)	Denmark (n=125)	France (n=109)	Germany (n=108)	Greece (n=100)	Hungary (n=13)
Clinical service types								
ANC – antenatal clinic	0	0	0	0	0	0		0
COMB – combined service	0	0	0	0	0	0	9	3
DV – dermatology-venereology clinic	17	0	8	0	5	1	0	9
ED – Hospital emergency dept	0	0	0	0	12	0	0	0
FPC – family planning clinic	0	0	0	0	0	0	0	0
GP – general practitioner	41	0	0	66	67	0	0	0
GYN – gynaecology clinic	0	0	0	1	5	1	0	0
ID – infectious disease clinic	0	0	0	0	2	0	0	0
OPC – other primary care	0	0	0	0	0	0	0	0
STI – dedicated STI clinic	48	11	0	52	7	0	91	0
URO – urology	0	0	1	0	1	2	0	0
YTH – youth clinics	0	0	0	0	0	0	0	0
O – other	0	0	1	3	6	36	0	0
UNK – unknown	0	99	0	3	4	68	0	1
Place of residence								
NUTS level 0-3 (region)	104=AT13	24=BE1	10=CY000	125=UNK	109=FR	14=DE	2=GR	13=UNK
	1=AT32	60=BE2				1=FR	7=GR122	
	1=AT33	17=BE3				1=SE	87=GR300	
		1=FR				92=UNK	1=GR242, GR253, GR241	
		8=UNK					1=UNK	
Country of birth								
ISO coded value list, UNK	106=UNK	1=BE	7=CY	100=DK	109=UNK	108=UNK	81=GR	12=HU
		109=UNK	1=GR	1=DE, ES			1=DZ	1=UNK
			2=UNK	2=GL			8=AL	
				1=IT			2=BD	
				2=LB			1=SD	
				1=PH, PK, RO, SL,TH, UK, US, VN			2=BG	
				10=UNK			5=PK	
Probable country of infection								
ISO coded value list, UNK	106=UNK	3=BE	10=CY	2=DE	1=CN	108=UNK	94=GR	12=HU
		1=TH		100=DK	35=FR		1=MX	1=UNK
		1=ZA		1=GM, IR, IT, LB, LK, PK, RO	1=TH		1 =TH	
		105=UNK		3=TH	72=UNK		4=UNK	
				1=TR, US				
				11=UNK				

Table A6.2. Clinical service type, place of residence, country of birth and probable country of infection (continued)

	Ireland (n=64)	Italy (n=99)	Latvia (n=28)	Malta (n=13)	Netherlands (n=217)	Norway (n=77)	Portugal (n=109)	Romania (n=26)
Clinical service types								
See first table for codes	10=GP	38=DV	28=ID	12=STI	217=STI	77=UNK	80=OPC	21=DV
	54=STI	5=ID		1=O			29=STI	5=OPC
		52=STI						
		4=O						
Place of residence								
NUTS level 0-3 (region)	26=IE	1=FR	1=LV003	11= MT001	1=NL122	77=UNK	1=PT11	26=RO321
	38=IE0	22=ITC11	1=LV005	2=UNK	2=NL225		1=PT112	
		1=ITC14, ITC17, ITC34, ITC4, ITC41, ITC43	19=LV006		3=NL230		2=PT113	
		40=ITC45	5=LV007		4=NL310		16=PT114	
		1=ITC46	1=LV008, LV009		1=NL321, NL322, NL324		2=PT115	
		5=ITC47			3=NL325		3=PT150	
		4=ITD55			178=NL326		26=PT17	
		1=ITE22, ITE41			5=NL327		51=PT171	
		8=ITE43			1=NL331, NL332, NL334		7=PT172	
		1=ITE44, ITF41			2=NL336			
		8=UNK			13=UNK			
Country of birth								
ISO-coded value list, UNK	1=BR, ES, MX, MY, RU	1=EC, FR, GR, IN, IR, PL, SV, TR	28=UNK	10=MT	1=ANHH, BE, BG, CA, CD, CM, CN, CV, ES, HN, JO, MY, RU, PH, PL, SY, TN, US, UK, VN	77=UNK	109 = PT	26=RO
	26=IE	2=AL, BG, PE, RO		1=BG, SO, NG	6=BR			
	2=LT	4=BR			2=DE, EG, ID, IT, MA, SE			
	4=PL	68=IT			4=FR			
	27=UNK	3=MA			7=HU			
		8=UNK			149=NL			
					3=RO			
					15=SR			
Probable country of infection								
ISO coded value list, UNK	64=UNK	1=CU, ES, US	27=LV	10=MT	217=UNK	77=UNK	109 = PT	26=RO
		86=IT	1=UNK	1=SO				
		10=UNK		2=UNK				

UNK: unknown

Table A6.2. Clinical service type, place of residence, country of birth and probable country of infection (end)

	Slovakia (n=113)	Slovenia (n=19)	Spain (n=100)	Sweden (n=105)	UK (n=251)
Clinical Service types					
See first table for codes	41=DV	17=DV	86=COMB	105=UNK	242=STI
	19=GYN	2=STI	6=STI		6=GP
	1=OPC		8=O		1=OPC
	51=URO				1=O
	1=YTH				1=UNK
Place of residence					
NUTS level 0-3 (region)	1=CZ	19=SI	43=ES	105=UNK	1=UKC
	67=SK01		2=ES114		3=UKC2
	21=SK021		22=ES120		1=UKC22
	6=SK022		14=ES300		1=UKD2
	13=SK023		3=ES419		9=UKD3
	1=SK032		2=ES422		2=UKD43
	2=SK041		3=ES511		4=UKD52
	1=SK042		3=ES523		5=UKE32
	1=UA		1=ES611		1=UKE41
			7=UNK		11=UKE42
					6=UKF14
					2=UKF23
					1=UKG3
					2=UKG12
					1=UKG13
					12=UKG31
					1=UKG32
					7=UKG35
					2=UKH12
					3=UKH21
					2=UKH23
					46=UKI
					23=UKI1
					14=UKI11
					7=UKI12
					2=UKI2
					1=UKI22, UKJ13
					5=UKJ21
					1=UKJ22
					3=UKJ23
					1=UKJ42
					2=UKK1
					3=UKK11
					1=UKK13
					2=UKL21
					9=UKL22
					6=UKM2
					3=UKM22
					19=UKM25
					8=UKM3
					1=UKM5
					2=UKM6
					14=UNK
Country of birth					
ISO-coded value list, UNK	108=SK	19=SI	100=UNK	105=UNK	2=UK
	1= GR, RS, CM, UA				249=UNK

	Slovakia (n=113)	Slovenia (n=19)	Spain (n=100)	Sweden (n=105)	UK (n=251)
	1=UNK				
Probable country of infection					
ISO-coded value list, UNK	4=AT	2=DE	100=ES	105=UNK	2=UK
	1=AU	1=GR			249=UNK
	3=CZ	13=SI			
	73=SK	2=TH			
	32=UNK	1=UNK			

UNK = unknown

Annex 7. Statistical tables

Table A7.1. Patient characteristics vs. ciprofloxacin resistance/susceptibility

	Ciprofloxacin resistant (%, 95% CI)	Ciprofloxacin susceptible (%, 95% CI)	Odds ratio	95% CI	P value
Site of infection n=1775					
Genital (1456)	743 (51, 48.5 – 53.6)	713 (49, 46.4 – 51.5)	1		
Anorectal (216)	78 (36.1, 30 – 42.7)	138 (63.9, 57.3 - 70)	0.54	0.4 – 0.73	<0.0001
Pharyngeal (79)	31 (39.2, 29.2 – 50.3)	48 (60.8, 49.7 – 70.8)	0.62	0.39 – 0.99	0.041
Other (24)	9 (37.5, 21.2 – 57.3)	15 (62.5, 42.7 – 78.4)	0.58	0.25 – 1.33	0.189
Gender n=1816					
Male (1496)	732 (48.9, 46.4 – 51.5)	764 (51.1, 48.5 – 53.6)	1		
Female (320)	145 (45.3, 39.9 – 50.8)	175 (54.7, 49.2 – 60.1)	0.86	0.68 – 1.1	0.24
Previous GC n=764					
Yes (146)	69 (47.3, 39.3 – 55.3)	77 (52.7, 44.7 – 60.7)	0.74	0.52 – 1.07	0.106
No (618)	338 (54.7, 50.8 – 58.6)	280 (45.3, 41.4 – 49.3)	1		
Mode of transmission n=1057					
MSM (440)	165 (37.5, 33.1 – 42.1)	275 (62.5, 57.9 – 66.9)	1		
Heterosexual (617)	336 (54.5, 50.5 – 58.4)	281 (45.5, 41.7 – 49.5)	2	1.55 – 2.57	<0.0001
Concurrent chlamydia n=871					
Yes (192)	57 (29.7, 23.7 – 36.5)	135 (70.3, 63.5 – 76.3)	1		
No (679)	315 (46.4, 42.7 – 50.2)	364 (53.6, 49.9 – 57.3)	2.05	1.45 – 2.9	<0.0001
HIV status n=799					
Positive (141)	46 (32.6, 25.4 – 40.7)	95 (67.4, 59.3 – 74.6)	1		
Negative (658)	312 (47.4, 43.6 – 51.2	346 (52.6, 48.5 – 56.4)	1.86	1.27 – 2.74	0.0014
Age n=1783					
< 25 years (568)	251 (44.2, 40.2 – 48.3)	317 (55.8, 51.7 – 59.8)	1		
≥25 years (1215)	605 (49.8, 47 – 52.6)	610 (50.2, 47.4 - 53)	1.25	1.03 – 1.53	0.027

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

Baseline variables: Site of infection – genital; gender – male; previous GC – no; mode of transmission – MSM; concurrent chlamydia – yes; HIV status – positive; age – <25 years

Table A7.2. Patient characteristics vs. azithromycin resistance/susceptibility

	Azithromycin resistant (%, 95% CI)	Azithromycin susceptible (%, 95% CI)	Odds ratio	95% CI	P value
Site of infection n=1748					
Genital (1429)	76 (5.3, 4.3 – 6.6)	1353 (94.7, 93.4 – 95.7)	1		
Anorectal (216)	15 (6.9, 4.6 – 11.1)	201 (93.1, 88.9 – 95.8)	1.33	0.75 – 2.36	0.33
Pharyngeal (79)	6 (7.6, 3.5 – 15.6)	73 (92.4, 84.4 – 96.5)	1.46	0.62 – 3.47	0.385
Other (24)	0 (0, 0 – 13.8)	24 (100, 86.2 – 100)	N/A		
Gender n=1789					
Male (1469)	78 (5.3, 4.3 – 6.6)	1390 (94.7, 93.4 – 95.7)	1		
Female (321)	18 (5.6, 3.6 – 8.7)	303 (94.4, 91.3 – 96.4)	1.06	0.63 – 1.79	0.832
Previous GC n= 732					
Yes (140)	5 (3.6, 1.5 – 8.1)	135 (96.4, 91.9 – 98.5)	0.52	0.2 – 1.36	0.177
No (592)	39 (6.6, 4.9 – 8.9)	553 (93.4, 91.1 – 95.1)	1		
Mode of transmission n=1024					
MSM (437)	21 (4.8, 3.2 – 7.2)	416 (95.2, 92.8 – 96.8)	1		
Heterosexual (587)	38 (6.5, 4.8 – 8.8)	549 (93.5, 91.2 – 95.3)	1.37	0.79 – 2.37	0.257
Concurrent chlamydia n=863					
Yes (194)	5 (2.6, 1.1 – 5.9)	189 (97.4, 94.1 – 98.9)	1		
No (669)	36 (5.4, 3.9 – 7.4)	633 (94.6, 92.6 – 96.1)	2.15	0.83 – 5.57	0.106
HIV status n=792					
Positive (141)	5 (3.6, 1.5 - 8)	136 (96.5, 92 – 98.5)	1		
Negative (651)	30 (4.9, 3.4 – 6.9)	621 (95.4, 93.5 – 96.8)	1.31	0.5 – 3.45	0.578
Age n=1756					
< 25 years (566)	24 (4.2, 2.9 – 6.2)	542 (95.8, 93.8 – 97.1)	1		
≥25 years (1190)	65 (5.5, 4.3 – 6.9)	1125 (94.5, 93.1 – 95.7)	1.31	0.81 – 2.11	0.275

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

Baseline variables: Site of infection – genital; gender – male; previous GC – no; mode of transmission – MSM; concurrent chlamydia – yes; HIV status – positive; age – <25 years

N/A = Expected cells less than five – analysis not performed

Table A7.3. Patient characteristics vs. penicillinase activity

	PPNG resistant (%, 95% CI)	PPNG susceptible (%, 95% CI)	Odds ratio	95% CI	P value
Site of infection n=1568					
Genital (1355)	151 (11.1, 9.6 – 12.9)	1204 (88.9, 87.1 – 90.4)	1		
Anorectal (122)	3 (2.5, 0.8 - 7)	119 (97.5, 93 – 99.2)	0.2	0.06 – 0.64	0.0027
Pharyngeal (68)	8 (11.8, 6.1 – 21.5)	60 (88.2, 78.5 – 93.9)	1.06	0.5 – 2.27	0.874
Other (23)	2 (8.7, 2.4 – 26.8)	21 (91.3, 73.2 – 97.6)	N/A		
Gender n=1609					
Male (1333)	128 (9.6, 8.1 – 11.3)	1205 (90.4, 88.7 – 91.9)	1		
Female (276)	42 (15.2, 11.5 – 19.9)	234 (84.8, 80.1 – 88.5)	1.69	1.16 – 2.46	0.006
Previous GC n=767					
Yes (146)	11 (7.5, 4.3 - 13)	135 (92.5, 87 – 95.7)	0.95	0.48 – 1.88	0.885
No (621)	49 (7.9, 6 – 10.3)	572 (92.1, 89.7 - 94)	1		
Mode of transmission n=843					
MSM (302)	7 (2.3, 1.1 – 4.7)	295 (97.7, 95.3 – 98.9)	1		
Heterosexual (541)	62 (11.5, 9 – 14.4)	479 (88.5, 85.6 - 91)	5.46	2.44 – 12.21	<0.0001
Concurrent chlamydia n=658					
Yes (130)	6 (4.6, 2.1 – 9.7)	124 (95.4, 90.3 – 97.9)	1		
No (528)	34 (6.4, 4.6 – 8.9)	494 (93.6, 91.1 – 95.4)	1.42	0.58 – 3.47	0.436
HIV status n=590					
Positive (68)	2 (2.9, 0.8 – 10.1)	66 (97.1, 89.9 – 99.2)			0.215*
Negative (522)	42 (8.1, 6 – 10.7)	480 (91.9, 98.3 - 94)			
Age n=1576					
< 25 years (504)	49 (9.7, 7.4 – 12.6)	455 (90.3, 87.4 – 92.6)	1		
≥25 years (1072)	116 (10.8, 9.1 – 12.8)	956 (89.2, 87.2 - 91)	1.13	0.79 – 1.6	0.51

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

**Expected value for one cell = 5 so Fisher's Exact test performed*

Baseline variables: Site of infection – genital; gender – male; previous GC – no; mode of transmission – MSM; concurrent chlamydia – yes; HIV status – positive; age – <25 years

N/A = Expected cells less than five – analysis not performed.

Table A7.4. Patient characteristics vs. cefixime decreased susceptibility/susceptibility

	Cefixime decreased susceptibility (%, 95% CI)	Cefixime susceptible (%, 95% CI)	Odds ratio	95% CI	P value
Site of infection n=1785					
Genital (1466)	119 (8.1, 6.8 – 9.6)	1347 (91.9, 90.4 – 93.2)	1		
Anorectal (216)	7 (3.2, 1.6 – 6.5)	209 (96.8, 93.5 – 98.4)	0.38	0.17 – 0.83	0.011
Pharyngeal (79)	8 (10.1, 5.2 – 18.7)	71 (89.9, 81.3 – 94.8)	1.28	0.6 – 2.71	0.527
Other (24)	0 (0, 0 – 13.8)	24 (100, 86.2 – 100)	N/A		
Gender n=1826					
Male (1505)	97 (6.5, 5.3 – 7.8)	1408 (93.6, 92.2 – 94.7)	1		
Female (321)	36 (11.2, 8.2 – 15.1)	285 (88.8, 84.9 – 91.8)	1.83	1.22 – 2.75	0.003
Previous GC n=767					
Yes (146)	12 (8.2, 4.8 – 13.8)	134 (91.8, 86.2 – 95.2)	0.57	0.3 – 1.08	0.081
No (621)	84 (13.5, 11.1 – 16.5)	537 (86.5, 83.6 – 88.9)	1		
Mode of transmission n=1060					
MSM (442)	16 (3.6, 2.2 – 5.8)	426 (96.4, 94.2 – 97.8)	1		
Heterosexual (618)	73 (11.8, 9.5 – 14.6)	545 (88.2, 85.4 – 90.5)	3.57	2.03 – 6.26	<0.0001
Concurrent chlamydia n=875					
Yes (194)	9 (4.6, 2.5 – 8.6)	185 (95.4, 91.4 – 97.5)	1		
No (681)	58 (8.5, 6.7 – 10.9)	623 (91.5, 89.1 – 93.4)	1.91	0.93 – 3.94	0.07
HIV status n=802					
Positive (141)	5 (3.6, 1.5 - 8)	136 (96.4, 92 – 98.5)	1		
Negative (661)	68 (10.3, 8.2 – 12.8)	593 (89.7, 87.2 – 91.8)	3.12	1.23 – 7.92	0.012
Age n=1793					
< 25 years (572)	37 (6.5, 4.7 – 8.8)	535 (93.5, 91.2 – 95.3)	1		
≥25 years (1221)	93 (7.6, 6.3 – 9.3)	1128 (92.4, 90.8 – 93.8)	1.19	0.8 – 1.77	0.382

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

Baseline variables: Site of infection – genital; gender – male; previous GC – no; mode of transmission – MSM; concurrent chlamydia – yes; HIV status – positive; age – <25 years

N/A: Expected cells less than five – analysis not performed