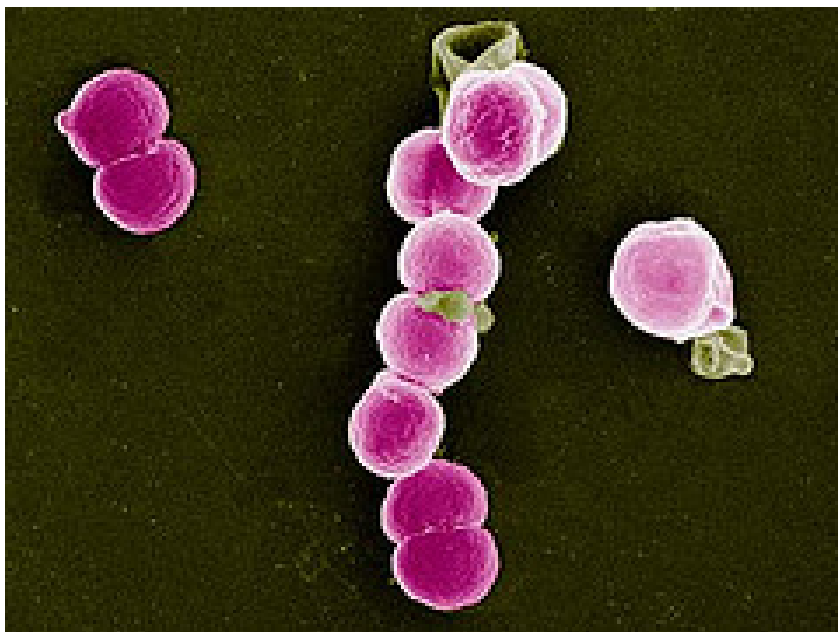




# GRASP

The Gonococcal Resistance  
to Antimicrobials  
Surveillance Programme

Annual Report 2007



# GRASP

## **The Gonococcal Resistance to Antimicrobials Surveillance Programme. Annual Report, Year 2007 Collection.**

GRASP monitors gonococcal antimicrobial resistance at a number of sentinel sites in England & Wales. The programme is coordinated by the Health Protection Agency Centre for Infections.

GRASP is funded by the Department of Health (London)

### **Suggested Citation:**

GRASP Steering Group.  
The Gonococcal Resistance to Antimicrobials Surveillance Programme (GRASP) Year 2007 report.  
London: Health Protection Agency 2008.

### **Further Information:**

GRASP Coordinator  
Health Protection Agency  
Centre for Infections  
61 Colindale Avenue  
London NW9 5EQ

Tel: +44 (0) 208 327 7555  
Fax: +44 (0) 208 200 7868  
Email: [stbrl@hpa.org.uk](mailto:stbrl@hpa.org.uk)

## GRASP Steering Group

**Prof Catherine Ison<sup>1</sup>, Dr Gwenda Hughes<sup>1</sup> Ms Leah de Souza-Thomas<sup>1</sup>, Ms Helen Munro Wild<sup>1</sup>, Dr Stephanie Chisholm,<sup>1</sup> John Anderson<sup>1</sup>, Elisabeth Maclure<sup>1</sup>, Dr Alan Johnson<sup>1</sup>, Prof George Kinghorn<sup>2</sup>, Dr David Livermore<sup>1</sup>, Dr Rohinton Mulla<sup>3</sup>, Mr Tom Nichols<sup>1</sup>, Dr Angela Robinson<sup>4</sup>, Prof Jonathan Ross<sup>5</sup>, Dr Jim Wade<sup>6</sup>, Dr Hugh Young<sup>7</sup>.**

1. Health Protection Agency, Centre for Infections, 61 Colindale Avenue, London NW9 5EQ.
2. Department of Genitourinary Medicine, Royal Hallamshire Hospital, Glossop Road, Sheffield S10 2JF.
3. Luton Microbiology Laboratory, Lewsey Road, Luton LU4 0EP.
4. The Mortimer Market Centre, Camden and Islington NHS Trust, Off Capper Street, London WC1E 6AU.
5. The Whittall Street Clinic, Department of GU Medicine, Whittall Street, Birmingham B4 6DH.
6. Health Protection Agency South London, King's College Hospital, Denmark Hill, London SE5 9RS.
7. Scottish Bacterial Sexually Transmitted Infections Reference Laboratory, Edinburgh Royal Infirmary, Little France, Edinburgh EH16 4SA.

# Contents

1. KEY POINTS.....	4
1.1 STUDY POPULATION.....	4
1.2 ANTIMICROBIAL RESISTANT N. GONORRHOEAE.....	4
2. BACKGROUND.....	5
2.1 EPIDEMIOLOGY OF N. GONORRHOEAE IN ENGLAND AND WALES.....	5
2.2 GLOBAL GONOCOCCAL ANTIMICROBIAL RESISTANCE.....	5
2.3 THE GONOCOCCAL RESISTANCE TO ANTIMICROBIALS SURVEILLANCE PROGRAMME.....	6
2.4 ANTIMICROBIAL RESISTANCE GLOSSARY.....	6
3. SAMPLE DESCRIPTION.....	7
3.1 RETRIEVAL IN 2007.....	7
3.2 WEIGHTING OF DATA.....	7
3.3 SAMPLE DISTRIBUTION IN 2007.....	8
4. PATIENT CHARACTERISTICS.....	9
4.1 DEMOGRAPHIC CHARACTERISTICS.....	9
4.2 CLINICAL CHARACTERISTICS.....	9
4.3 BEHAVIOURAL CHARACTERISTICS.....	9
5. ANTIMICROBIAL SUSCEPTIBILITY.....	12
6. CIPROFLOXACIN.....	13
7. PENICILLIN.....	14
7.1 CHROMOSOMALLY-MEDIATED RESISTANCE (CMRNG).....	14
7.2 PLASMID-MEDIATED RESISTANCE (PPNG OR PP/TRNG).....	14
8. AZITHROMYCIN.....	15
9. OTHER ANTIMICROBIALS.....	16
9.1 TETRACYCLINE.....	16
9.2 CEFIXIME.....	16
9.3 CEFTRIAXONE.....	16
9.4 SPECTINOMYCIN.....	16
10. ANTIMICROBIAL RESISTANCE TRENDS.....	17
11. PRESCRIBING PRACTICE.....	18
12. DISCUSSION.....	19
13. GRASP METHODOLOGY.....	20
13.1 ACKNOWLEDGEMENTS.....	21
14. COLLABORATORS.....	22
15. REFERENCES.....	23

# 1. Key Points

## 1.1 Study Population

A total of 1,514 isolates were collected by the 23<sup>1</sup> GRASP collaborating laboratories during the three month data collection period in 2007, and sent to the Sexually Transmitted Bacteria Reference Laboratory (STBRL) for antimicrobial susceptibility testing. After the exclusion of duplicates 1,400 isolates remained, of which 1,113 (80%) were recovered successfully and confirmed as *Neisseria gonorrhoeae*. Compared with earlier GRASP years there are now relatively more men in the sample; while the number of heterosexual cases has approximately halved, the number of cases in men who have sex with men (MSM) remained relatively constant.

## 1.2 Antimicrobial Resistant *N. gonorrhoeae*

- For the first time two isolates (0.2%) were categorised as exhibiting decreased susceptibility to cefixime (Minimum Inhibitory Concentration (MIC)  $\geq 0.25$ mg/l) a third generation cephalosporin. Confirmation using Etests demonstrated a marginally lower MIC of 0.19mg/l than the 0.25 mg/l determined by the GRASP methodologies. Both isolates were susceptible to ceftriaxone (MIC 0.015mg/l)
- The prevalence of ciprofloxacin (MIC  $\geq 1$ mg/l) resistance increased slightly from 27% to 28% between 2006 and 2007 ( $p=0.61$ ). The prevalence of resistance is highest in MSM and increased to 47% compared with 44% in 2006. Fifty-three percent of resistant isolates were from individuals in the 35-44 year age group.
- Penicillin resistant (MIC  $\geq 1$ mg/l or  $\beta$ -lactamase positive) GRASP isolates increased from 9.5% in 2006 to 24% in 2007 ( $p<0.001$ ). In 2007, 7.9% of isolates demonstrated plasmid-mediated penicillin resistance (PPNG or PP/TRNG), an increase from the 3.4% in 2006 ( $p=0.002$ ), and 15% of isolates demonstrated chromosomally-mediated penicillin resistance (CMRNG), a significant increase from the 3.9% observed in 2006 ( $p<0.001$ ).
- Azithromycin resistance (MIC  $\geq 1$ mg/l) more than doubled between 2006 and 2007 from 1.8% to 4.1%, respectively ( $p=0.09$ ). High-level resistance to azithromycin ( $>256$ mg/l) was detected for the first time.
- Overall, 60% of isolates demonstrated tetracycline resistance (MIC  $\geq 2$ mg/l) in 2007, a significant increase compared to the 37% observed in 2006 ( $p<0.001$ ). Plasmid-mediated tetracycline resistance (TRNG or PP/TRNG) was observed in 11% of isolates and chromosomally –mediated TetR resistance in 32% of isolates in 2007.
- In 2007, no isolates demonstrated resistance to spectinomycin (MIC  $\geq 128$ mg/l), or decreased susceptibility to ceftriaxone (MIC  $\geq 0.125$ mg/l).
- Non-genitourinary medicine (non-GUM) isolates continued to demonstrate lower prevalences of ciprofloxacin resistance (14%), penicillin resistance (12%), tetracycline resistance (37%) and azithromycin resistance (0%), compared with GUM isolates in 2007.

---

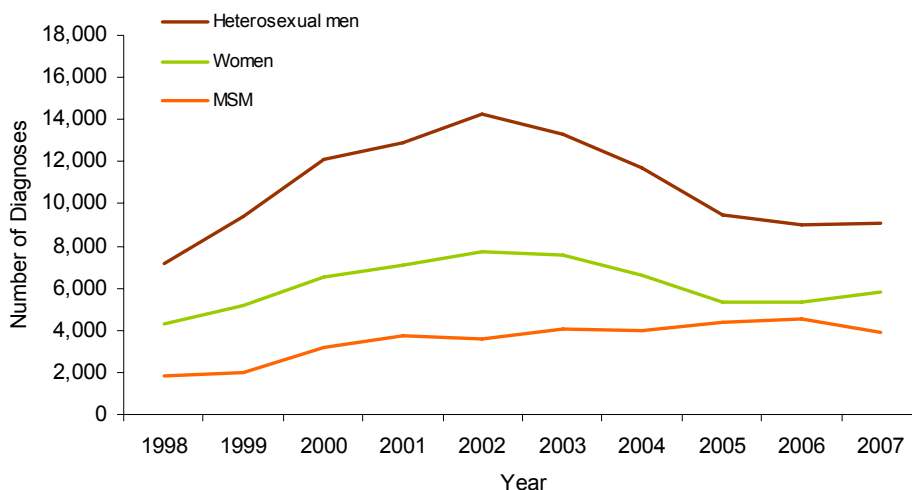
<sup>1</sup> Ordinarily there are 24 microbiological laboratories that participate in GRASP. However, in 2007 one laboratory was unable to participate.

## 2. Background

### 2.1 Epidemiology of *N. gonorrhoeae* in the United Kingdom

*Neisseria gonorrhoeae* is the second most common bacterial sexually transmitted infection (STI) in the United Kingdom, with a total of 18 710 uncomplicated infections diagnosed in GUM clinics in 2007. This represents a 1% decrease compared with the 18 898 diagnoses made in 2006, continuing the decreasing trend in total diagnoses of gonorrhoea seen since 2002<sup>1</sup>. Gonococcal diagnoses tend to be concentrated in core risk groups in the UK. These include black ethnic populations and men who have sex with men (MSM). For the first time since 1998 diagnoses amongst MSM started to decline in 2007. However, of the 12,933 new episodes of gonorrhoea in men, 30% were among MSM<sup>2</sup>. Young people remain the most likely to be infected, with current rates highest in men aged 20-24 years (174.2/100 000) and women aged 16-19 years (136.9/100 000).

Figure 1. Diagnoses of uncomplicated gonorrhoea made in GUM clinics by gender and male sexual orientation, UK: 1998 to 2007.



### 2.2 Global Gonococcal Antimicrobial Resistance

Antimicrobial resistance in *N. gonorrhoeae* remains a problem worldwide and providing effective therapy will be a challenge in future years. The current status is:

- There is growing evidence of decreased susceptibility to the third generation cephalosporins<sup>3,4</sup> but as yet there are no reported therapeutic failures to ceftriaxone or cefixime.
- Fluoroquinolone resistance continues to be prevalent worldwide, including reports of resistance of 99% in the Nanjing city of China<sup>5</sup>, 48% in Russia<sup>6</sup>, 70% in Japan<sup>7</sup> and Sweden<sup>8</sup> and 21% in New Zealand<sup>9</sup>.
- Ciprofloxacin is no longer recommended first line therapy in most countries including the USA<sup>10</sup> and UK<sup>11</sup>.
- Azithromycin is not recommended as first line therapy for gonorrhoea but is often used to treat co-infection with *C. trachomatis* and there are reports from a number of countries of increasing resistance. The percentage of isolates resistant to azithromycin was reported to be 80% in a recent study in Japan<sup>7</sup>, and the emergence of strains with high-level azithromycin resistance (>256 mg/L) identified in Scotland in 2004, has been reported recently<sup>12</sup>. The increasing prevalence of resistance to this antimicrobial in England and Wales has also been highlighted in this report, as has the emergence of high-level resistant strains. The United States<sup>10</sup> has reported the appearance and increasing prevalence of isolates with decreased susceptibility.

## 2.3 The Gonococcal Resistance to Antimicrobials Surveillance Programme

The Gonococcal Resistance to Antimicrobials Surveillance Programme (GRASP) was established in June 2000, as collaboration between the Communicable Disease Surveillance Centre (CDSC), the Genitourinary Infections Reference Laboratory (GUURL), Bristol and Imperial College, and was funded by the Department of Health<sup>13</sup>. In 2000 the pilot collection was carried out across 30 participating GUM clinics and laboratories. From 2001 the annual GRASP collection has consisted of 26 collaborating GUM clinics covered by 24 laboratories (see page 22)<sup>2</sup>.

In 2007, the GRASP annual collection was undertaken by the Health Protection Agency, Centre for Infections. GRASP has proven a successful collaboration with participating laboratories and GUM clinics collecting data on about 17 000 isolates since the first collection.

This report presents the findings of the eighth year of isolate collection for this programme, highlighting the changes observed in antimicrobial susceptibility and gonococcal epidemiology between 2006 and 2007.

## 2.4 Antimicrobial Resistance Glossary

Table 1. Glossary of antimicrobial resistance and classification types.

Classification	Definition
Penicillin Resistant	Penicillin: MIC $\geq$ 1mg/l or $\beta$ -lactamase +ve
Tetracycline Resistant	Tetracycline: MIC $\geq$ 2mg/l
PPNG	Penicillin: $\beta$ -lactamase +ve AND tetracycline: MIC < 16mg/l
TRNG	Penicillin $\beta$ -lactamase -ve AND tetracycline: MIC $\geq$ 16mg/l
PP/TRNG	Penicillin: $\beta$ -lactamase +ve AND tetracycline: MIC $\geq$ 16mg/l
CMRNG	Penicillin: $\beta$ -lactamase -ve AND MIC $\geq$ 1mg/l AND tetracycline: MIC between 2-8mg/l
PenR	Penicillin: MIC $\geq$ 1mg/l but $\beta$ -lactamase -ve AND tetracycline: MIC < 2mg/l
TetR	Penicillin: $\beta$ -lactamase -ve AND MIC < 1mg/l AND tetracycline: MIC between 2-8mg/l
Ciprofloxacin Resistant	MIC $\geq$ 1mg/l
Ciprofloxacin Decreased Susceptibility	MIC $\geq$ 0.125mg/l to 0.5mg/l
Ciprofloxacin Decreased Susceptible or Resistant	MIC $\geq$ 0.125mg/l
Spectinomycin	MIC $\geq$ 128mg/l
Azithromycin	MIC $\geq$ 1mg/l
Ceftriaxone (Decreased susceptibility)	MIC $\geq$ 0.125mg/l
Cefixime (Decreased susceptibility)	MIC $\geq$ 0.25mg/l

<sup>2</sup> In 2007 one laboratory was unable to participate.

## 3. Sample Description

### 3.1 Retrieval in 2007

A total of 1514 isolates were collected by the 23 GRASP collaborating laboratories during the three month data collection period in 2007, and sent to STBRL for antimicrobial susceptibility testing. After the exclusion of duplicates 1400 isolates were retained, of which 1113 (80%) were retrieved successfully and the identity confirmed as *N. gonorrhoeae*.

The retrieval rates for 2007 by region are shown in detail in table 2. The overall retrieval rate in London was 86% compared with 74% of isolates outside of London, where retrieval ranged from 47% in the South West to 92% in the East Midlands.

The demographic, clinical and behavioural data presented in this report includes information on all patients for whom a gonococcal isolate was referred, whilst the antimicrobial resistance data uses information only on patients for whom an isolate was retrieved.

Table 2. The proportion of GRASP isolates confirmed as *N.gonorrhoeae* by region in the 2007 collection.

Region	Submitted Isolates N (%)		Total
	Retrieved	Not retrieved	
East Midlands	88 (92)	8 (8)	96
East of England	17 (63)	10 (37)	27
London	537 (86)	88 (14)	625
North East	30 (86)	5 (14)	35
North West	105 (72)	40 (28)	145
South East	79 (81)	19 (19)	98
South West	24 (47)	27 (53)	51
Wales	50 (86)	8 (14)	58
West Midlands	97 (87)	15 (13)	112
Yorkshire & Humberside	86 (56)	67 (44)	153
<b>Total</b>	<b>1113 (80)</b>	<b>287 (21)</b>	<b>1400</b>

### 3.2 Weighting of Data

Since 2005, the percentage of isolates that are resistant to a particular antibiotic has been estimated using a weighted analysis. This is because a simple percentage would under weight isolates from sites that have a lower retrieval rate. Estimates for 2000-2004 have been recalculated in this way and so values presented in this report may differ to the unweighted estimates that have appeared in previous GRASP reports. The weight for a particular clinic in a particular year is inversely proportional to its retrieval rate and each estimate of the percentage resistant to a particular antibiotic in a particular year is a weighted average of the percentages from the participating sites in that year.

### 3.3 Sample Distribution in 2007

Of the total 1113 retrieved isolates in 2007, 1059 isolates were from patients who had attended a GUM clinic, whilst 54 attended a primary care setting such as general practice, or hospital in- or out-patient departments (table 3). Where more than one isolate per individual was received during the data collection period, results for the second isolate were only included in the analyses if the date of isolation of the second isolate was  $\geq 28$  days after the first isolate. In 2007, as in previous years, such patients accounted for 1% of all isolates.

Table 3. Numbers of gonococcal isolates obtained in the GRASP collection: June-August 2007.

Region	Total number of isolates referred	Non-GUM clinic data		GUM clinic data		
		Number of isolates referred (%)	Number of isolates retrieved	Number of isolates referred (%)	Number of isolates retrieved	Number of patients
East Midlands	96	12 (13)	10	84 (88)	78	83
East of England	27	0 (0)	0	27 (100)	17	27
London	625	8 (1)	6	617 (99)	531	614
North East	35	1 (3)	0	34 (97)	30	34
North West	145	3 (2)	3	142 (98)	102	141
South East	98	6 (6)	4	92 (94)	75	91
South West	51	10 (20)	8	41 (80)	16	41
Wales	58	10 (17)	9	48 (83)	41	48
West Midlands	112	5 (4)	5	107 (96)	92	106
Yorkshire & Humberside	153	13 (8)	9	140 (92)	77	139
<b>Total</b>	<b>1400</b>	<b>68 (5)</b>	<b>54</b>	<b>*1332 (95)</b>	<b>1059</b>	<b>1324</b>

\* includes eight patients each represented twice due to more than one episode of infection

In 2007, 46% of the isolates referred were from patients attending GUM clinics in London and 54% were from outside of London. The percentage of GUM clinic isolates contributing to the total by each region is shown in table 3.

The trend observed over recent years of an increasing proportion of isolates from MSM has not continued in 2007, with 35% of isolates coming from MSM compared with 39% in 2006. The proportion of isolates from heterosexual men and women have increased slightly since 2006, to 39% (36% in 2006), and 26% (24% in 2006) respectively, which is in-line with the latest KC60 trends<sup>1</sup> (figures 1 and 2).

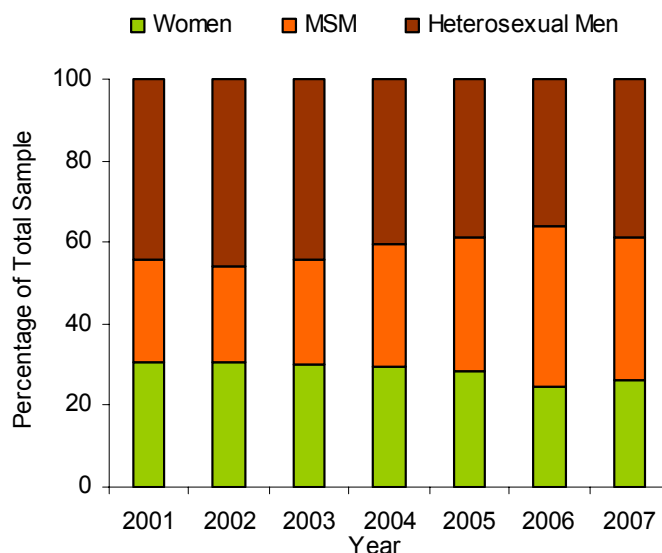


Figure 2. The proportion of gonococcal isolates from GUM patients by gender and male sexual orientation. GRASP 2001 to 2007.

# 4. Patient Characteristics

## 4.1 Demographic Characteristics

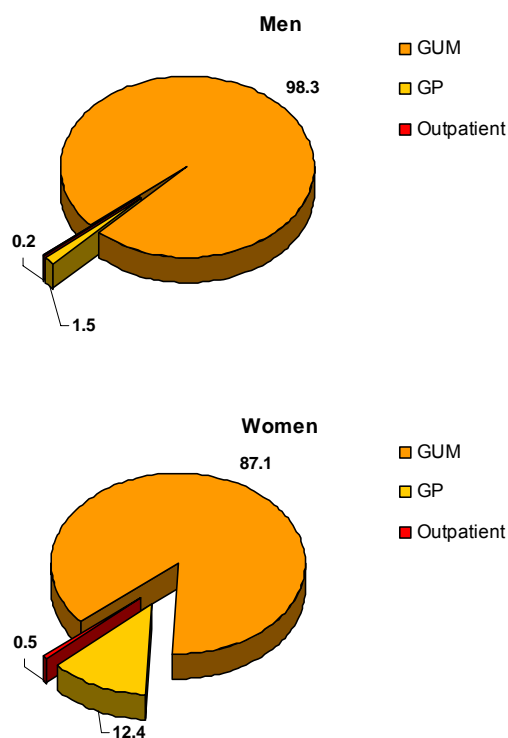
Tables 4 and 5 present characteristics of all the GUM and non-GUM clinic patients referred to GRASP (including patients from whom we could not retrieve their isolates for testing).

In 2007, most of the patients were diagnosed in GUM clinics. Although 12.4% of women had been diagnosed at their GP compared with 1.5% of men (figure 3), outpatient diagnoses were much fewer in both men and women.

Of the 68 non-GUM clinic patients, 88% of diagnoses were made outside of London, principally in Yorkshire & Humberside, East Midlands, the South West and Wales. In contrast, only 54% of all GUM clinic diagnoses were made outside of London, with the highest number in the North West (11%).

The majority of non-GUM clinic gonorrhoea diagnoses were made in patients under the age of 25 whereas GUM clinic diagnoses were more common in a wider age range of patients; those aged 20-34 years.

Figure 3. Proportion of patients (%) by diagnoses service and gender 2007.



## 4.2 Clinical characteristics

The presence of symptoms (discharge or dysuria) was most prevalent in heterosexual men and MSM, but almost half (47%) of women had no symptoms associated with their infection. Ninety-eight percent of women and heterosexual men and 61% of MSM presented with a genital infection, followed by throat isolates in 5.7% of women and 3.0% of heterosexual men (Table 4). Forty percent of MSM presented with rectal isolates. Previous gonorrhoea diagnoses were reported for 29% of all patients and 43% of MSM in 2007. As in previous years chlamydia was the most prevalent concurrent STI, reported in 34% of women, 31% of heterosexual men and 17% of MSM. HIV prevalence among all GRASP patients with known status was 13% as in 2006. This prevalence varied by gender and male sexual orientation, and was highest among MSM (32%).

## 4.3 Behavioural Characteristics

In 2007, 51% of all individuals reported having between two and five partners (either in the UK or abroad) in the past three months. Ten percent reported sexual contact abroad in the past three months compared with 11% in 2006.

Table 4. Demographic, clinical and behavioural characteristics of GUM clinic patients with gonorrhoea from participating GUM clinics by gender and sexual orientation\*: GRASP 2007.

Characteristics	Women%	Heterosexual men %	MSM %	Total§ %
<b>GUM Clinic Locality</b>				
London	39	41	57	46
Outside London	61	59	43	54
Total (Baseline†)	343	506	459	1332
<b>Ethnicity</b>				
White	57	41	85	61
Asian or Asian British	3.7	6.3	4.1	4.9
Black Caribbean	21	30	1.6	18
Black African	4.0	7.4	1.6	4.4
Other Black	8.7	9.7	1.6	6.5
Other	5.3	5.7	5.9	5.7
Total (Baseline†)	321	475	437	1243
<b>Age Group</b>				
≤15	4.4	0.6	0.0	1.4
16-19	39	15	5.2	18
20-24	33	35	22	30
25-34	19	31	40	31
35-44	2.3	11	23	13
45+	2.0	7.7	11	7.3
Total (Baseline†)	343	506	459	1331
<b>Symptoms</b>				
Discharge and or dysuria	54	90	65	72
No discharge or dysuria	47	9.7	36	28
Total Baseline†)	325	496	439	1267
<b>Previously diagnosed with gonorrhoea</b>				
Yes	18	23	43	29
No	82	77	57	71
Total (Baseline†)	325	487	433	1251
<b>Concurrent STI‡</b>				
Syphilis	0.9	0.6	2.4	1.3
Chlamydia	34	31	17	27
Herpes	0.9	1.0	0.4	0.8
Warts	1.2	0.8	1.8	1.2
Other	13	4.0	6.0	7.0
Total (Baseline) †	330	498	452	1286
<b>Site of Infection‡</b>				
Genital	96	99	61	85
Rectal	4.2	0.4	40	15
Throat	5.7	3.0	14	7.6
Other	1.2	0.6	0.4	0.7
Total (Baseline) †	331	499	457	1294
<b>HIV Status</b>				
Negative	100	99	68	87
Positive	0.0	0.8	32	13
Total (Baseline) †	256	369	411	1043
<b>UK Partners (past 3 months)</b>				
0-1	67	45	27	45
2-5	31	50	56	47
6-10	0.3	4.0	10	5.2
11+	1.5	0.4	7.1	3.0
Total (Baseline) †	329	494	422	1251
<b>Sex Abroad (past 3 months)</b>				
Yes	4.3	14	11	10
Total (Baseline) †	329	497	426	1258

\* Sexual orientation was reported for 98% (965/988) of males at participating GRASP clinics.

§ Total includes women, heterosexual men, MSM, individuals of unknown gender (1) and men of unknown sexual orientation (23) and includes eight patients for which there was more than one episode of infection.

† Baseline figure is the number of patients for whom that variable is known.

‡ A patient may present with more than 1 site of infection and/or concurrent STI.

Table 5. Demographic characteristics among non-GUM clinic patients with gonorrhoea from participating GRASP centres, 2003 to 2007.

Characteristics	Year %					Total
	2003	2004	2005	2006	2007	
<b>Location</b>						
London	11	25	22	34	12	21
Outside London	90	75	78	66	88	79
Total (Baseline) ‡	152	159	143	99	68	621
<b>Region</b>						
East Midlands	1.3	4.4	4.9	9.1	18	6.0
East of England	7.2	3.8	2.1	3.0	0.0	3.7
London	11	25	22	34	12	21
North East	1.3	0.6	2.8	2.0	1.5	1.6
North West	11	3.1	1.4	6.1	4.4	5.2
South East	7.2	3.1	3.5	4.0	8.8	5.0
South West	39	28	22	14	15	26
Wales	14	12	22	11	15	15
West Midlands	5.9	6.3	15	11	7.4	9.2
Yorkshire & Humberside	3.3	13	3.5	5.1	19	7.9
Total (Baseline) ‡	152	159	143	99	68	621
<b>Gender</b>						
Male	32	33	38	22	25	31
Female	68	67	62	78	75	69
Total (Baseline) ‡	148	158	143	98	68	615
<b>Age Group</b>						
≤15	6.1	1.3	2.2	0.0	1.5	2.5
16-19	32	33	27	33	30	31
20-24	25	26	33	27	33	28
25-34	25	28	20	24	27	25
35-44	10	9.8	13	7.1	4.5	9.6
45+	2.0	2.6	5.0	10	4.5	4.5
Total (Baseline) ‡	147	153	139	98	67	604

‡ Baseline figure is the number of patients for whom that variable is known.

Table 6. Percentage of isolates resistant to specific antimicrobials among GUM and non-GUM patients, 2006 to 2007.

Antimicrobial*	2006 % (95% CI)		2007 % (95% CI)	
	GUM	Non-GUM	GUM	Non-GUM
Penicillin (≥ 1mg/l or β-lactamase +)	9.5 [6.7,13.4]	2.8 [0.6,12.3]	24 [18.3,30.1]	12 [4.9,25.1]
Tetracycline (≥ 2mg/l)	37 [29.0,45.6]	17 [11.1,25.2]	60 [51.3,67.5]	37 [23.1,54.2]
Ciprofloxacin (≥ 1mg/l)	27 [20.8,33.0]	7.4 [3.0,17.4]	28 [20.9,35.6]	14 [6.4,26.9]
Azithromycin (≥ 1mg/l)	1.8 [0.9,3.4]	1.0 [0.1,8.3]	4.1 [2.2,7.2]	0.0 [-,-]
Spectinomycin (≥128mg/l)	0.0 [-,-]	0.0 [-,-]	0.0 [-,-]	0.0 [-,-]
Ceftriaxone (≥ 0.125mg/l)	0.0 [-,-]	0.0 [-,-]	0.0 [-,-]	0.0 [-,-]
Cefixime (≥ 0.25mg/l)	0.0 [-,-]	0.0 [-,-]	0.2 [0.0,0.6]	0.0 [-,-]

\*Resistance category definitions are listed on page 6

## 5. Antimicrobial Susceptibility

Variation was observed in the 2007 collection in the proportion of isolates resistant to specific antimicrobials (Table 6).

- Penicillin resistance in GUM clinic isolates increased from 9.5 % in 2006 to 24% in 2007 ( $p < 0.001$ ) and also increased in non-GUM clinic isolates from 2.8% in 2006 to 12% in 2007 ( $p = 0.05$ ).
- Tetracycline resistance increased significantly in non-GUM and GUM clinic isolates to 37% and 60% in 2007 ( $p < 0.001$ ), respectively.
- Ciprofloxacin resistant GUM clinic isolates increased only slightly to 28% in 2007, compared with non-GUM clinic isolates which increased from 7.4% in 2006 to 14% in 2007 ( $p = 0.17$ ).
- Azithromycin resistance increased from 1.8% in 2006 to 4.1% in 2007 in GUM clinic isolates but was not detected in non-GUM clinic isolates in 2007.
- Decreased susceptibility to cefixime remains unusual but was detected in two isolates (0.2%) from GUM clinic patients in 2007, but was not present in non-GUM clinic isolates.
- No isolates demonstrated resistance to spectinomycin or showed decreased susceptibility to ceftriaxone.

In 2007 the prevalence of resistance in GUM clinic isolates did not vary significantly between London and non-London clinics for any of the antimicrobials tested (Tables 7 and 8).

Table 7. Percentage of isolates resistant to specific antimicrobials 2006 to 2007 in London and Non-London.

Antimicrobial*	London % (95% CI)		Non-London % (95% CI)		Total % (95% CI)	
	2006	2007	2006	2007	2006	2007
Penicillin ( $\geq 1\text{mg/l}$ or $\beta$ -lactamase +)	11 [5.7,19.9]	27 [17.6,37.9]	8.4 [5.4,12.8]	21 [16.0,27.6]	9.5 [6.7,13.4]	24 [18.3,30.1]
Tetracycline ( $\geq 2\text{mg/l}$ )	43 [28.5,58.8]	63 [49.7,74.3]	32 [23.3,41.3]	57 [46.7,66.4]	37 [29.0,45.6]	60 [51.2,67.5]
Ciprofloxacin ( $\geq 1\text{mg/l}$ )	31 [21.7,42.9]	29 [18.0,43.7]	22 [16.4,29.3]	26 [19.6,34.2]	27 [20.8,33.0]	28 [20.9,35.6]
Azithromycin ( $\geq 1\text{mg/l}$ )	1.1 [0.6,2.1]	3.2 [1.5,6.4]	2.3 [1.0,5.6]	4.8 [2.1,10.8]	1.8 [0.9,3.4]	4.1 [2.2,7.3]
Spectinomycin ( $\geq 128\text{mg/l}$ )	0.0 [-,-]	0.0 [-,-]	0.0 [-,-]	0.0 [-,-]	0.0 [-,-]	0.0 [-,-]
Ceftriaxone ( $\geq 0.125\text{mg/l}$ )	0.0 [-,-]	0.0 [-,-]	0.0 [-,-]	0.0 [-,-]	0.0 [-,-]	0.0 [-,-]
Cefixime ( $\geq 0.25\text{mg/l}$ )	0.0 [-,-]	0.3 [0.1,1.1]	0.0 [-,-]	0.0 [-,-]	0.0 [-,-]	0.2 [0.0,0.6]

Table 8. Percentage of isolates resistant to penicillin and tetracycline 2006 to 2007, in London and Non-London.

Resistance Classification*	London % (95% CI)		Non-London % (95% CI)		Total % (95% CI)	
	2006	2007	2006	2007	2006	2007
PPNG	1.0 [0.5,2.2]	1.2 [0.6,2.3]	1.5 [0.7,3.2]	1.0 [0.4,2.8]	1.3 [0.8,2.2]	1.1 [0.6,2.0]
TRNG	7.1 [4.6,10.9]	4.7 [3.1,6.9]	4.3 [2.7,6.6]	4.0 [1.9,8.3]	5.6 [3.9,7.9]	4.3 [2.8,6.6]
PP/TRNG	2.0 [1.0,4.2]	6.4 [4.2,9.7]	2.1 [1.2,3.5]	7.1 [4.2,11.6]	2.1 [1.3,3.2]	6.8 [4.8,9.4]
CMRNG	5.5 [2.0,14.7]	19 [12.0,27.7]	2.4 [1.0,5.4]	12 [9.4,16.1]	3.9 [2.1,7.2]	15 [11.4,20.2]
PenR	1.4 [0.5,4.0]	0.0 [-,-]	1.5 [0.4,4.9]	0.6 [0.2,1.7]	1.5 [0.6,3.2]	0.3 [0.1,1.0]
TetR	28 [20.0,27.2]	32 [27.8,37.1]	22 [14.3,31.3]	32 [25.6,39.7]	25 [18.6,31.5]	32 [28.1,36.8]
PPNG or PP/TRNG	3.0 [1.4,6.3]	7.6 [4.9,11.6]	3.7 [2.4,5.6]	8.1 [4.8,13.4]	3.4 [2.3,4.8]	7.9 [5.6,11.0]
TRNG or PP/TRNG	9.1 [6.4,12.8]	11 [8.1,15.0]	6.4 [4.5,9.0]	11 [7.5,16.2]	7.7 [6.0,9.8]	11 [8.6,14.2]

\*Resistance category definitions are listed on page 6

## 6. Ciprofloxacin

Overall, the prevalence of ciprofloxacin resistance increased slightly from 27% in 2006 to 28% in 2007 ( $p=0.61$ ).

There was significant regional variation ( $P<0.001$ ), ranging from 9.3% in the East of England to 46% in the South East (figure 4).

Resistance was more common in older age groups and varied from 7.7% in the under 20's to 53% in those aged 35-44 years.

Figure 4. The prevalence of ciprofloxacin resistance by region, 2003 to 2007.

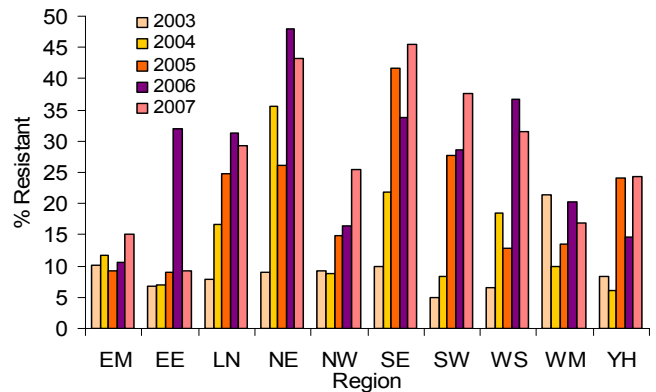


Figure 5. The prevalence of ciprofloxacin resistance by gender and male sexual orientation, 2003 to 2007.

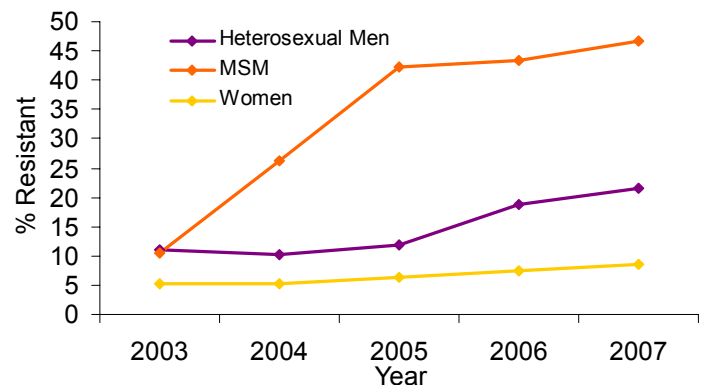
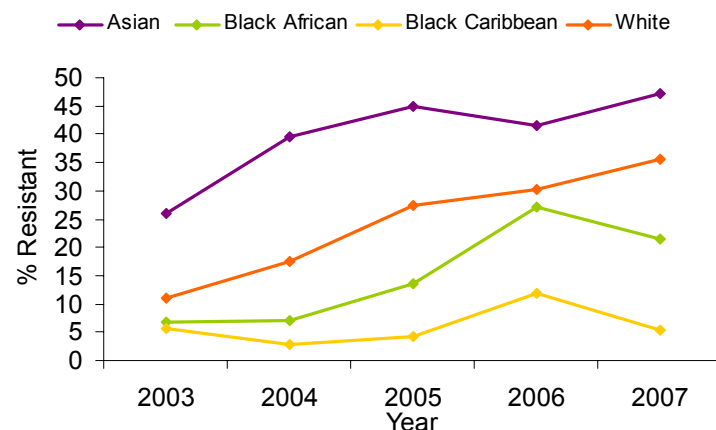


Figure 6. The prevalence of ciprofloxacin resistance by ethnic group, 2003 to 2007.



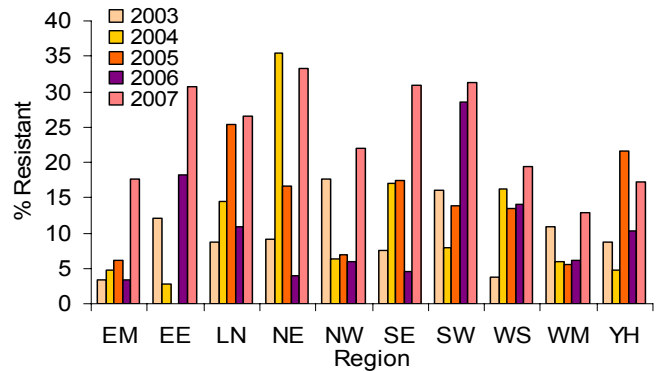
Between 2006 and 2007, ciprofloxacin resistance decreased among black ethnic groups but increased among whites and Asians (figure 6). The prevalence of resistance remains highest amongst Asians with 47% of isolates resistant in 2007 compared to 36% in whites. Following a gradual increase up to 2006, levels of ciprofloxacin resistance among black Africans and black Caribbeans have declined in 2007 to 22% and 5.3% respectively.

# 7. Penicillin

Penicillin resistance increased significantly from 9.5% to 24% between 2006 and 2007 ( $p < 0.001$ ). The prevalence of resistance ranged from 13% in the West Midlands to 33% in the North East although differences were not statistically significant ( $p = 0.2$ ) (figure 7).

Significant differences were observed by ethnic group, with the lowest prevalence observed in the black Caribbean (3.8%) and black other (6.1%) ethnic groups. In contrast, 49% of Asian, 30% of white and 23% of black African individuals had isolates that demonstrated penicillin resistance.

Figure 7. The prevalence of penicillin resistance by region, 2003 to 2007.

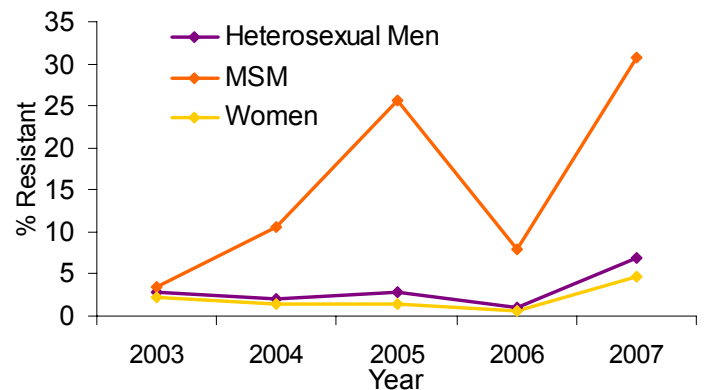


## 7.1 Chromosomally-mediated resistance (CMRNG)

Fifteen percent of isolates in the 2007 collection showed chromosomally-mediated penicillin resistance (CMRNG), compared with 3.9% in 2006 ( $p < 0.001$ ).

The hydrophobic nature of the cell wall of CMRNG increases the likelihood that it will be isolated from rectal isolates and consequently it is more likely to be associated with MSM. In 2007, 31% (cf. 8.0% in 2006) of MSM were infected with CMRNG isolates compared with 6.9% of heterosexual men and 4.6% of women (figure 8).

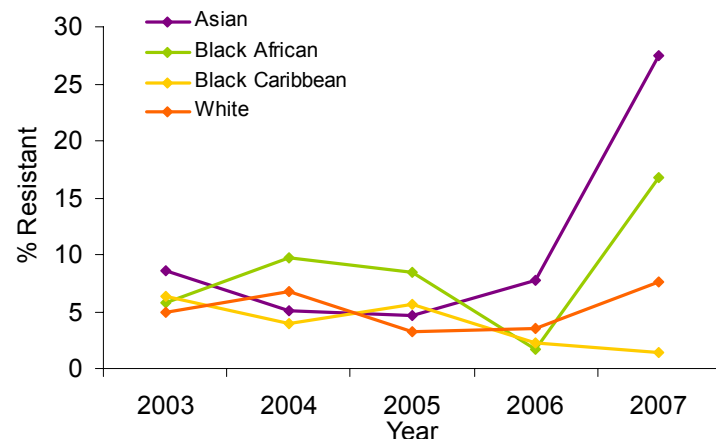
Figure 8. The prevalence of CMRNG by gender and male sexual orientation, 2003 to 2007.



## 7.2 Plasmid-mediated resistance (PPNG or PP/TRNG)

In 2007, 7.9% of isolates demonstrated plasmid-mediated penicillin resistance (PPNG or PP/TRNG), compared with 3.4% in 2006 ( $p = 0.002$ ). Resistance was higher among individuals reporting sexual contact abroad and has increased since 2006, (19% cf 13%,  $p = 0.31$ ). Resistance increased markedly in black Africans (17% of isolates in 2007 cf. 1.7% in 2006) and Asians (28% in 2007 compared with 7.8% in 2006).

Figure 9. The prevalence of PPNG or PP/TRNG by ethnicity, 2003 to 2007.



# 8. Azithromycin

Overall, 4.1% of isolates demonstrated azithromycin resistance in 2007 (figure 10), an increase from the 1.8% in 2006 (p=0.09). The prevalence of azithromycin resistance varied significantly by age, with the highest prevalence observed in those over the age of 45 (10%).

In 2007, 4.6% of heterosexual men and 4.7% of MSM had isolates that were resistant to azithromycin (figure 11). Increases in the prevalence have been observed in women since 2005 and heterosexual men since 2006. In 2007, high-level resistance (MIC >256mg/L) was observed for the first time in six isolates, with an even split between heterosexual men and women.

Significant regional variation in the prevalence of resistance was observed in 2007 (p<0.001). The prevalence ranged from 0% in the East of England, East Midlands and Yorkshire and Humberside to 25% in the South West (figure 12).

The prevalence of resistance was 7.1% in those who had had reported recent sexual contact abroad (cf. 3.8% in those with no recent sexual contact abroad). Nineteen percent of individuals reporting recent sexual contact in the Indian subcontinent were found to have azithromycin resistant isolates (cf. 4% in those with no recent sexual contact in the Indian subcontinent p=0.02).

In 2007, 15 (1.1%) of patients with gonorrhoea were treated with azithromycin alone. These isolates were from patients attending clinics in the West Midlands, North West, East Midlands and London.

Figure 10. The prevalence of azithromycin resistance, 2003 to 2007.

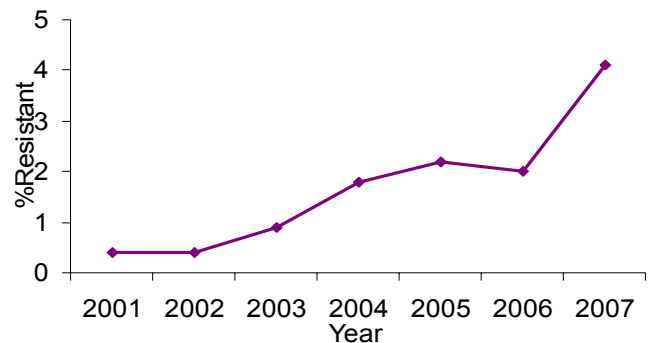


Figure 11. The prevalence of azithromycin resistance by gender and male sexual orientation, 2003 to 2007.

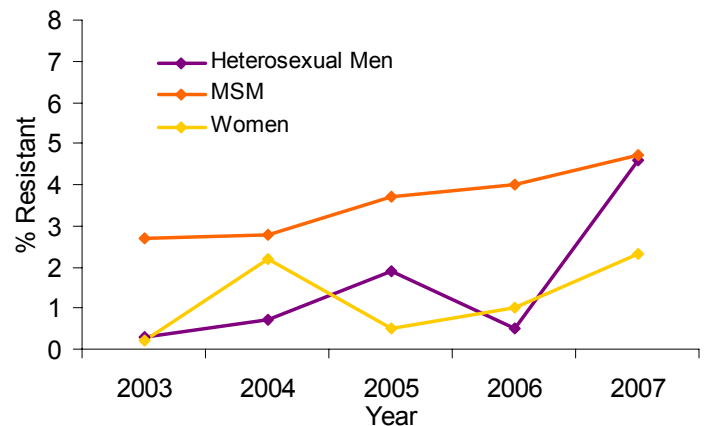
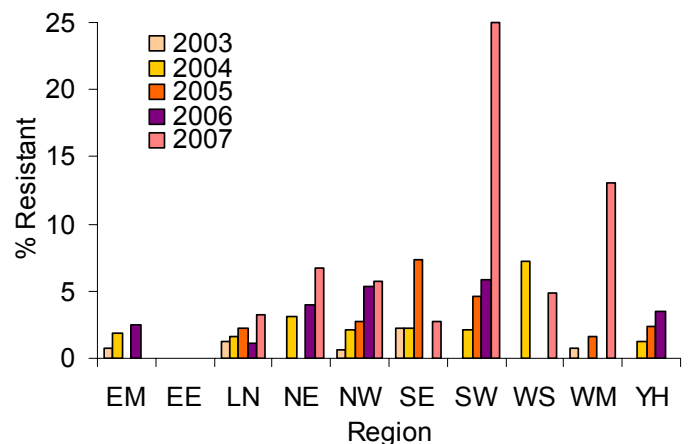


Figure 12. The prevalence of azithromycin resistance by region, 2003 to 2007.



# 9. Other Antimicrobials

## 9.1 Tetracycline

Overall, 60% of isolates demonstrated resistance to tetracycline, compared to the 37% observed in 2006 ( $p < 0.001$ ). Tetracycline resistant isolates varied significantly by age, ranging from 38% in the under 20s to 84% in the 35-44 year age group ( $p < 0.001$ ).

In 2007, the prevalence of tetracycline resistance increased in MSM, heterosexual men and women (figure 13). The prevalence among females was 35%, whilst among heterosexual men and MSM it was 49% and 88% respectively.

Tetracycline resistance was highest among white (68%) and Asian (78%) patients.

## 9.2 Cefixime

- For the first time since sensitivity testing for cefixime began in 2004, GRASP detected two isolates with decreased susceptibility to cefixime in the 2007 collection. Confirmatory testing by E-test demonstrated a marginally lower MIC of 0.19 mg/L than the 0.25 mg/L determined by GRASP methodologies. Nevertheless these are the highest MICs recorded in GRASP to date. Accordingly, the prevalence increased from 0% in 2006 to 0.2% in 2007, although this was not a significant increase ( $p = 0.12$ ). Both isolates were susceptible to ceftriaxone (MIC 0.015mg/l), which reflects the general finding that gonococci are less sensitive to cefixime than to ceftriaxone. These isolates were observed in MSM from London who did not report sexual contact abroad. Therapies for these patients were ceftriaxone and cefixime.

## 9.3 Ceftriaxone

As in previous years, no isolates demonstrated decreased susceptibility to ceftriaxone in 2007. Figure 14 shows the MIC drift in this antimicrobial. The graph clearly shows a shift towards higher MIC values as the years have progressed.

## 9.4 Spectinomycin

Since 2005 no isolates have been observed to be resistant to spectinomycin.

Figure 13. The prevalence of tetracycline resistance by gender & male sexual orientation, 2003 to 2007.

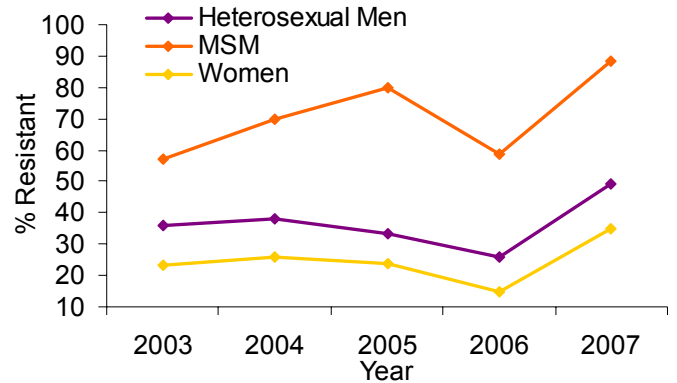
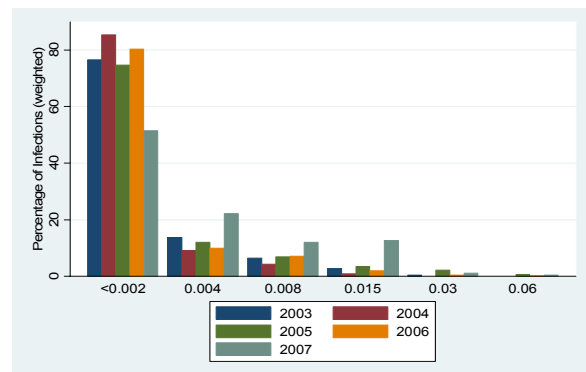


Figure 14. The MIC drift in ceftriaxone: 2003 to 2007.



# 10. Antimicrobial Resistance Trends

The trends in antimicrobial resistance observed between 2000 and 2007 are highlighted in the figures below.

There was a significant increase in the prevalence of ciprofloxacin resistance ( $\geq 1\text{mg/l}$ ), between 2000 and 2007 (2.1% cf. 28%  $p < 0.0001$ ). Figure 15 shows that the prevalence of resistance has continued to rise since the change in treatment guidelines in 2002/03, although the increase in recent years has appeared to have slowed. The increase between 2006 and 2007 was not statistically significant (27% cf. 28%  $p = 0.61$ ).

Figure 15. Trends in ciprofloxacin resistance, GRASP, 2000 to 2007.

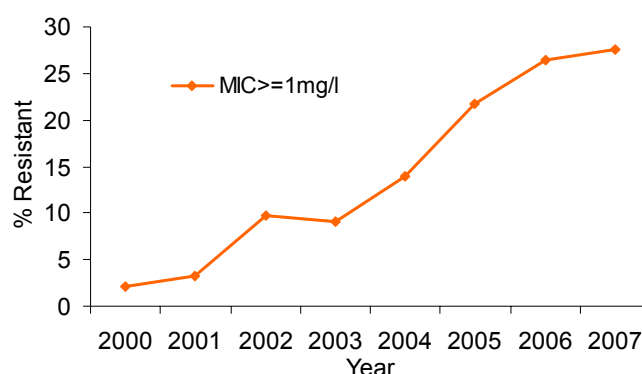
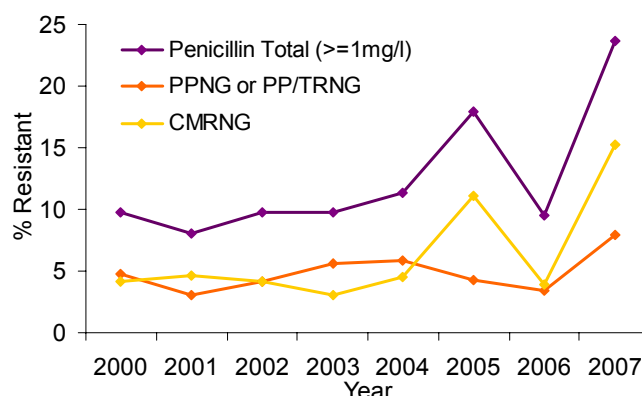


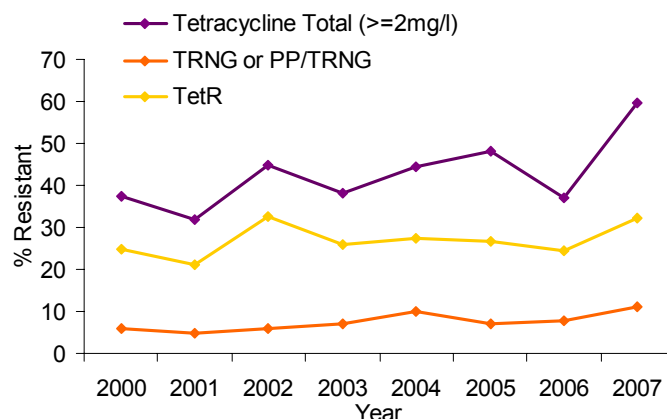
Figure 16 shows a significant increase in the prevalence of penicillin resistance between 2000 and 2007 ( $p < 0.001$ ) and between 2006 and 2007 (9.5% cf. 24%  $p < 0.001$ ). Increases were observed in the prevalence of PPNG or PP/TRNG between 2000 and 2007 (4.7% cf. 7.9%  $p = 0.05$ ), and between 2006 and 2007 (3.4% cf. 7.9%  $p = 0.002$ ). The prevalence of CMRNG resistance increased between 2000 and 2007 (4.1% cf. 15%  $p < 0.0001$ ) and 2006 and 2007 (3.9% cf. 15%  $p < 0.001$ ).

Figure 16. Trends in penicillin resistance, GRASP, 2000 to 2007.



Between 2000 and 2007, there was a significant increase in the prevalence of tetracycline resistance from 37% to 60% (figure 17) and between 2006 and 2007 (37% cf. 60%  $p < 0.001$ ). The prevalence of TRNG or PP/TRNG significantly increased between 2000 and 2007 (6.1% cf. 11%  $p = 0.005$ ), and also between 2006 (7.7% cf. 11%) and 2007 ( $p = 0.01$ ). There was no significant difference in the prevalence of TetR between 2000 and 2007 ( $p = 0.09$ ). However, there was an increase in the prevalence between 2006 and 2007 (25% cf. 32%  $p = 0.004$ ).

Figure 17. Trends in tetracycline resistance, GRASP, 2000 to 2007.



# 11. Prescribing Practice

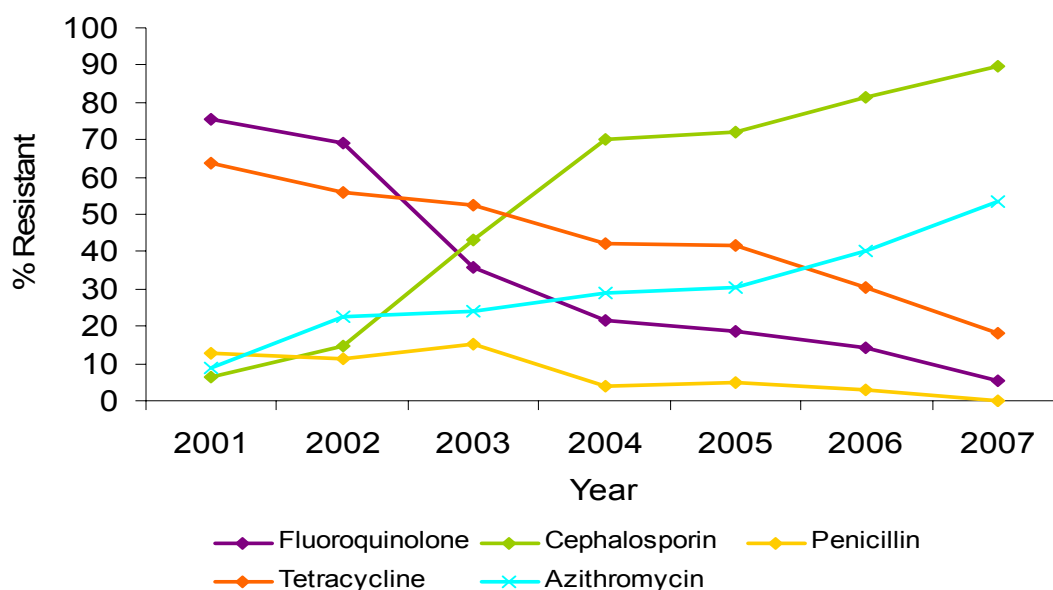
The third generation cephalosporins; ceftriaxone, cefixime and spectinomycin are recommended as first line treatment for gonorrhoea<sup>11</sup>. Overall, in 2007 90% of patients were treated with the recommended antimicrobials, cefixime or ceftriaxone. There was little variation in prescribing practice by region, ranging from 83% of patients in the North West to 97% of patients in the North East being prescribed a cephalosporin ( $p=0.22$ ). Eighty-four percent of women were prescribed a cephalosporin, compared with 92% of heterosexual men and 91% of MSM ( $p<0.0001$ ).

Fluoroquinolones are no longer recommended as first-line therapy for gonococcal infections. However, national guidelines highlight the need for region specific prescribing strategies. In 2007, 5.4% of GRASP patients were prescribed either ciprofloxacin or ofloxacin, compared with 14% in 2006 ( $p<0.01$ ). Prescribing of a fluoroquinolone varied significantly by region, ranging from 0% in the East of England and Wales to 14% in the South East ( $p=<0.001$ ). Fluoroquinolone prescribing also varied by gender and male sexual orientation with higher proportions of women being treated (8.6%) than heterosexual men (4.0%) and MSM (4.6%); differences were significant ( $p=0.005$ ).

There was a decrease in the use of penicillin (ampicillin) between 2006 and 2007 (2.9% cf. 0.2%). Only female patients in London received this antimicrobial.

Patients with gonorrhoea are often co-infected with *C. trachomatis* and so azithromycin or doxycycline are used to treat patients known to be co-infected or when a patient is unlikely to return. In 2007, 54% of patients in GRASP were treated with azithromycin compared with 40% in 2006 and 8.6% in 2001 in addition to specific gonorrhoea therapy. There was significant regional variation, ranging from 6.1% in the North East to 71% in London clinics ( $p<0.0001$ ). There was no significant difference in therapy between women (45%), heterosexual men (60%) and MSM (53%) ( $p=0.13$ ). In a similar manner tetracycline (doxycycline) was used for 18% of patients treated in 2007, with significant regional variation in prescribing. This variation ranged from 6.6% in Yorkshire & Humberside to 67% in the East of England ( $p<0.0001$ ).

Figure 18. Trends in the proportion of patients (%) receiving selected antimicrobials to treat gonorrhoea and/or chlamydial infection 2001 to 2007.



## 12. Discussion

GRASP aims to provide timely data on antimicrobial resistance profiles<sup>13,14</sup> to inform national guidelines<sup>11</sup>, and provide enhanced demographic and behavioural data to identify high risk groups<sup>15</sup>. This report, of the eighth year of GRASP, confirms that the first line therapies recommended in national guidelines of ceftriaxone, cefixime and spectinomycin remain effective. It is, however, a concern that two isolates have been detected with decreased susceptibility to cefixime. This is consistent with findings in other countries<sup>3,4</sup>, where there is growing evidence of a drift towards resistance and highlights that continued surveillance is essential to identify drift or emergence of resistance to these highly effective agents. It is very encouraging that 90% of the patients treated at the sentinel clinics within GRASP in 2007 have been treated with a third generation cephalosporin, and that there are few patients treated with ciprofloxacin or ampicillin, ensuring rapid and effective therapy.

The burden of antimicrobial resistance detected by GRASP is among MSM, with high levels of ciprofloxacin resistant and CMRNG. Asian individuals who have acquired infection by sexual contact in their country of origin<sup>16</sup> are a smaller group (11 individuals) than MSM but have a high prevalence of ciprofloxacin resistant gonorrhoea (63%), as reported in previous GRASP reports. The increase in ciprofloxacin resistant gonorrhoea among black Africans and Caribbeans identified in the GRASP 2006 report has not been maintained in 2007. However, despite the decline in gonorrhoea among black heterosexuals<sup>15</sup>, the trend in this group is important and needs monitoring as this group continues to be disproportionately affected and the spread of resistant strains threaten to impede efforts to control transmission.

The ability of *N. gonorrhoeae* to continue to evade antimicrobial therapy is evident in this year's results with the emergence of high-level resistance to azithromycin. The mechanism of this resistance and identification of possible selective pressures that may have contributed to this are yet to be elucidated. However, it is a constant reminder that this organism is versatile and has been adept at becoming resistant to all the previous antimicrobial agents that have been used.

# 13. GRASP Methodology

The GRASP collection combines laboratory and clinical data from sentinel laboratories. GRASP covers two distinct geographical regions: London, which includes seven laboratories and nine GUM clinics and outside of London where 17 GUM clinics and laboratories were purposely selected to provide good geographic coverage (with representation of all NHS regions) and to maximise the number of isolates collected. Further details on the policies and procedures of GRASP can be found in the GRASP protocol<sup>17</sup>.

All gonococcal isolates from consecutive patients (one from each patient episode, according to a hierarchy of preferred swab sites) identified in participating laboratories during the months of June, July and August are sent to the GRASP reference laboratory within STBRL for susceptibility testing. At each local laboratory, primary isolates of *N. gonorrhoeae* are sub-cultured to obtain a pure growth and frozen in glycerol broth for transportation via courier or sent on chocolate agar slopes or on Amies charcoal swabs. Following retrieval and confirmation of identity of *N. gonorrhoeae* at STBRL, the MICs are determined for the following antimicrobial agents (the range of concentrations tested is shown in parentheses): penicillin (0.03-4.0mg/l), ciprofloxacin (0.002-64mg/l) spectinomycin (2-64mg/l), tetracycline (1-32mg/l), ceftriaxone (0.002 to 0.125mg/l), azithromycin (0.03–256mg/l) and cefixime (0.002-0.25mg/l).

As part of the quality control, a two-way panel of isolates is exchanged biannually between the GRASP reference laboratory and the Scottish Bacterial Sexually Transmitted Infections Reference Laboratory. Isolates are tested, blinded to the originator's results, using the agar dilution method for susceptibility to azithromycin, ceftriaxone, ciprofloxacin, penicillin, spectinomycin and tetracycline. The results for each isolate/antimicrobial combination are compared and an error recorded if a laboratory result is more than one or two doubling dilutions from the other. The results in 2007 showed that the MICs obtained by the two laboratories were within one dilution of each other in 78% of cases and within two dilutions of each other in 89% of cases.

GUM clinics provide demographic, behavioural and clinical data for each GUM patient included in the GRASP collection. Routinely collected clinical data are utilised. These included: gender, age, ethnic background, sexual orientation, postal area, previous gonococcal infection, symptom presence, concurrent STIs, HIV status, number of partners in the UK and abroad, test of cure and therapy received. This data from patients (from GUM clinics) and susceptibility data (from the reference laboratory) of their isolates are then linked.

All results (unless otherwise specified) are based on GUM patients only. A weighted analysis for antimicrobial resistance is hoped to produce estimates that reflect all GUM patients that have been sampled (i.e. including those that could not be successfully retrieved). Each estimate of the percentage resistant to a particular antibiotic is a weighted average of the percentages from the participating sites. The weight for a particular clinic in a particular year is inversely proportional to the retrieval rate. Analysis of antibiotic prescribing practice and the characteristics of patients diagnosed with gonorrhoea at GUM clinics is not dependent on the successful retrieval of isolates and has not been weighted.

## **13.1 Acknowledgements**

This report was only made possible due to the continued enthusiastic cooperation of the collaborating centers listed on page 22. We would like to thank everyone from the participating laboratories for sending isolates to the reference laboratory, and all GUM staff involved in the collection of clinical data. We would also like to thank Stephanie Chisholm, Elisabeth Maclure and John Anderson for their hard work in testing such large numbers of isolates at our reference laboratory, Leah de Souza-Thomas for data preparation and the production of the annual report, Tom Nichols for the statistical analysis and generation of figures, Geraldine Leong for preparation and analysis of clinic-specific data, and Rachel Denholm, Stephen Duffell, Wilhelmine Meeraus, Kay Nolan and Mandy Yung for collecting some of the clinical data.

# 14. Collaborators

**EAST MIDLANDS: Northampton:** Dr Minassian, Department of Microbiology, Dr Riddell Department of GU Medicine, Northampton General Hospital. **Nottingham:** Dr Boswell, Nottingham Microbiology Laboratory, University Hospital Queens Medical Centre; Dr Bignell, Department of GU Medicine, Nottingham City Hospital.

**EAST of ENGLAND: Cambridge:** Dr Farrington, HPA East of England Cambridge Laboratory & Dr Carne, Department of GU Medicine, Addenbrooke's NHS Trust. **Luton:** Dr Mulla, Luton Microbiology Laboratory, Dr Balachandran, Department of GU Medicine, Luton & Dunstable Hospital.

**LONDON: Charing Cross:** Dr Azadian, Department of Microbiology, Chelsea and Westminster Hospital; Dr McLean, The West London Centre for Sexual Health, Charing Cross Hospital; Dr McOwan, The Victoria Clinic; Dr Boag, John Hunter Clinic, St Stephen's Centre, Chelsea and Westminster Hospital. **Homerton:** Dr Claxton, Department of Medical Microbiology, & Dr Nathan, Department of GU Medicine, Homerton Hospital. **Kings:** Ms M Graver, HPA South London, & Dr Tenant-Flowers, The Caldecot Centre, King's Healthcare NHS Trust. **St George's:** Dr Holliman, Department of Medical Microbiology, & Dr Hay, Department of GU Medicine, St George's Hospital. **St Mary's:** Dr Jepson, Department of Bacteriology, & Dr Smith, Jefferiss Wing Centre for Sexual Health, St Mary's Hospital. **UCH:** Dr Morris Jones, Microbiology Laboratory & Dr Robinson, The Mortimer Market Centre. University College London Hospitals. **Woolwich:** Dr Bragman, Department of Microbiology, & Dr Russell, Trafalgar Clinic for Sexual Health, Queen Elizabeth Hospital.

**NORTH EAST: Newcastle:** Dr Magee, HPA North East Newcastle Laboratory, & Dr Sankar, Department of GU Medicine, Newcastle General Hospital.

**NORTH WEST: Liverpool:** Dr Neal, Medical Microbiology Department, & Dr Carey, Department of GU Medicine, Royal Liverpool Hospital. **Manchester:** Dr Qamruddin, Department of Microbiology, & Dr Sukthankar, Manchester Centre for Sexual Health, Manchester Royal Infirmary.

**SOUTH EAST: Brighton:** Dr Paul, Brighton Microbiology Department & Dr Dean & Dr Warwick, Department of GU Medicine, The Royal Sussex County Hospital. **Reading:** Dr Stacey, Microbiology Department, & Dr Wildman 'Florey Unit' Department of GU Medicine, Royal Berkshire Hospital.

**SOUTH WEST: Bristol:** Dr Spencer, HPA South West, & Dr Horner, Milne Sexual Health Centre, Bristol Royal Infirmary. **Gloucester:** Dr Logan, Gloucester Microbiology Laboratory, & Dr Sulaiman, Department of GU Medicine, Gloucestershire Royal Hospital.

**WALES: Cardiff:** Dr Hosein, NPHS Microbiology Cardiff, & Dr Birley, Department of GU Medicine, Cardiff Royal Infirmary. **Newport:** Dr Kubriak, Department of Clinical Microbiology & Infection Control, & Dr Das, Department of GU Medicine, Royal Gwent Hospital.

## **WEST MIDLANDS**

**Birmingham:** Dr Gill, Department of Clinical Microbiology, Queen Elizabeth Hospital & Dr Ross, Whittall Street Clinic, Department of GU Medicine. **Wolverhampton:** Dr Jones, Department of Microbiology, & Dr Tariq, The Fowler Centre for GU Medicine, New Cross Hospital.

**YORKSHIRE & HUMBERSIDE: Leeds:** Dr Gascoyne-Binzi, Department of Microbiology, & Dr Clarke, Centre for Sexual Health, Leeds General Infirmary. **Sheffield:** Dr Zadik, Sheffield Microbiology Laboratory, Northern General Hospital; Dr Kinghorn, Department of GU Medicine, Royal Hallamshire Hospital

# 15. References

1. Health Protection Agency. All new STI episodes at genitourinary medicine (GUM) clinics in the United Kingdom: 1998-2007. Available at: [http://www.hpa.org.uk/web/HPAwebFile/HPAweb\\_C/1215589014474](http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1215589014474).
2. The UK collaborative Group for HIV and STI surveillance. Testing Times. HIV and other Sexually Transmitted Infections in the United Kingdom: 2007. London: Health Protection Agency, Centre for Infections. November 2007.
3. Yokoi S, Deguchi T, Ozawa T *et al*. Threat to cefixime treatment for gonorrhoea [letter]. *Emerg Infect Dis*. [serial on the Internet]. Aug 2007. Available at: [www.cdc.gov/EID/content/13/8/1275.htm](http://www.cdc.gov/EID/content/13/8/1275.htm)
4. Wang SA, Veneranda LC, O'Connor N *et al*. Multidrug-Resistant *Neisseria gonorrhoeae* with decreased susceptibility to cefixime – Hawaii, 2001. *Clin Infect Dis* 2003;**37**: 849-52.
5. Xiaohong Su, Faxing Jiang, Qimuge *et al*. Surveillance of Antimicrobial Susceptibilities in *Neisseria gonorrhoeae* in Nanjing, China, 1999-2006. *Sex Transm Dis* 2007;**34**: 995-99
6. Kubanova A, Frigo N, Kubanov A, *et al*. National surveillance of antimicrobial susceptibility in *Neisseria gonorrhoeae* in 2005-2006 and recommendations of first-line antimicrobials for gonorrhoea treatment in Russia. *Sex Transm Inf*. 2008; 84:258-9
7. Matsumoto T. Trends of sexually transmitted diseases and antimicrobial resistance in *Neisseria gonorrhoeae*. *Int J Antimicrob Agents* 2008; 31:S35-S39.
8. European Centre for Disease Prevention and Control. Antibiotic use in Sweden – the Swedres report 2007 has been published. *Eurosurveillance* **13**, Issue 25, 19 June 2008
9. Institute of Environmental Science & Research. Antimicrobial resistance among *Neisseria gonorrhoeae* October to December 2007. Available at:[http://www.surv.esr.cri.nz/antimicrobial/neisseria\\_gonorrhoeae.php](http://www.surv.esr.cri.nz/antimicrobial/neisseria_gonorrhoeae.php).
10. CDC. Sexually Transmitted Disease Surveillance 2006 Supplement, Gonococcal Isolate Surveillance Project (GISP) Annual Report 2006. Atlanta, Georgia: U.S. Department of Health and Human Services, CDC. April 2008 [www.cdc.gov/std/gisp2006/default.htm](http://www.cdc.gov/std/gisp2006/default.htm)
11. National Guidelines on the Management of gonorrhoea in adults. Clinical Effectiveness Group (BASHH, British Association of Sexual Health & HIV). [http:// www.bashh.org/cegguidelines.html](http://www.bashh.org/cegguidelines.html).
12. Palmer HM, Young H, Winter A, Dave J. Emergence and spread of azithromycin-resistant *Neisseria gonorrhoeae* in Scotland. *J Antimicrob Chemother*. Advance Access published online on June 13, 2008
13. Paine TC, Fenton KA, Herring A, *et al*. GRASP: a new national sentinel surveillance initiative for monitoring gonococcal antimicrobial resistance in England and Wales. *Sex Trans Inf* 2001; **77**: 398-401.
14. Fenton KA, Ison C, Johnson AP, *et al*. Ciprofloxacin resistance in *Neisseria gonorrhoeae* in England and Wales in 2002. *Lancet* 2003; **361**: 1867-69.
15. de Souza L, Hughes G and Ison C. Changing trends in the characteristics of patients diagnosed with gonorrhoea in England and Wales. BASHH-ASTDA 2008. Brooklyn, New York. 7-10 May 2008. Poster Presentation (B-11)
16. de Souza-Thomas L, Chen M, Martin I, *et al*. The role of sex abroad, gender/male sexual orientation and ethnicity in the importation of resistant gonococcal strains into England and Wales: An analysis of data from GRASP. Health Protection 2006. University of Warwick, England. 11-13 September 2006. Poster presentation.
17. The Gonococcal Resistance to Antimicrobials Surveillance Programme (GRASP). Protocol of operational aspects and data management of GRASP. HIV & STI Division PHLS Communicable Disease Surveillance Centre. 2000.