



GRASP

The Gonococcal Resistance
to Antimicrobials
Surveillance Programme

Annual Report 2006



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The Gonococcal Resistance to Antimicrobials Surveillance Programme. Annual Report, Year 2006 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 2006 report.
London: Health Protection Agency 2007.

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1. Key Points

1.1 Study Population

A total of 1833 isolates were collected by the 24 GRASP collaborating laboratories during the three month data collection period in 2006, and sent to the Sexually Transmitted Bacteria Reference Laboratory (STBRL) for antimicrobial susceptibility testing. After the exclusion of duplicates 1698 isolates remained, of which 1313 (77.3%) were recovered successfully and confirmed as *Neisseria gonorrhoeae*. This represents an increase of 27% in the number of confirmed isolates observed between 2005 and 2006. Whilst retrieval has improved in 2006 the results presented are weighted to allow comparison to previous years.

1.2 Antimicrobial Resistant *N. gonorrhoeae*

- Overall, 26.5% of GRASP isolates were resistant to ciprofloxacin (Minimum Inhibitory Concentration, MIC $\geq 1\text{mg/l}$) in 2006, an increase from the 21.7% observed in 2005 ($p=0.07$). The prevalence of resistance exceeded 10% in all Government Health Regions of England and Wales in 2006. The prevalence of ciprofloxacin resistance increased amongst heterosexual men (18.7%), women (7.5%) and men who have sex with men (MSM) rising to 43.3% in 2006.
- Overall, 9.5% of isolates demonstrated penicillin resistance in 2006 (MIC $\geq 1\text{mg/l}$ or β -lactamase positive), down from 17.9% in 2005 ($p=0.01$). Of this total 3.4% of isolates demonstrated plasmid-mediated penicillin resistance (PPNG or PP/TRNG), a decrease from the 4.3% in 2005 ($p=0.4$), and 3.9% of isolates demonstrated chromosomally-mediated penicillin resistance (CMRNG) in 2006, a significant decrease from the 11.1% seen in 2005 ($p=0.002$).
- Azithromycin resistance (MIC $\geq 1\text{mg/l}$), was identified in 2.0% of isolates in 2006, a small decrease compared with the 2.2% observed in 2005 ($p=0.77$).
- Overall, 36.9% of isolates demonstrated tetracycline resistance (MIC $\geq 2\text{mg/l}$) in 2006, a significant decrease compared to the 48.0% observed in 2005 ($p=0.001$). Plasmid-mediated tetracycline resistance (TRNG or PP/TRNG) was observed in 7.7% of isolates and chromosomally-mediated TetR resistance in 24.5% of isolates in 2006.
- In 2006, no isolates demonstrated resistance to spectinomycin (MIC $\geq 128\text{mg/l}$), or decreased susceptibility to ceftriaxone (MIC $\geq 0.125\text{mg/l}$) or cefixime (MIC $\geq 0.25\text{mg/l}$).
- Non-genitourinary medicine (non-GUM) isolates continued to demonstrate lower prevalences of ciprofloxacin resistance (7.4%), penicillin resistance (2.8%) and tetracycline resistance (17.0%). However, there was a higher prevalence of azithromycin resistance (2.4%), compared with GUM isolates in 2006.

1.3 Patient Characteristics

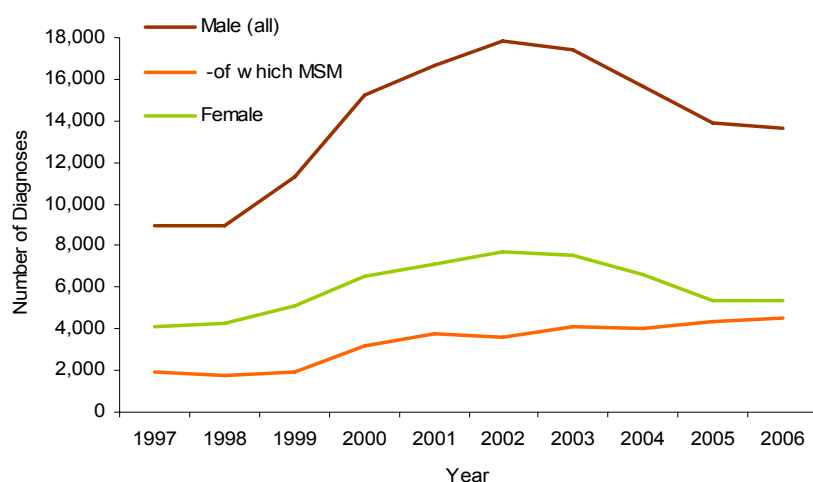
- The clinical and behavioural characteristics of GUM patients represented in the annual GRASP samples have remained relatively constant over time. However, in line with recent trends there are fewer heterosexual men and women represented in 2006, and relatively more MSM (39.3%). The HIV prevalence amongst individuals providing GRASP samples remains stable at 13%.

2. Background

2.1 Epidemiology of *N. gonorrhoeae* in England and Wales

Neisseria gonorrhoeae is the second most common bacterial sexually transmitted infection (STI) in England and Wales, with a total of 19 007 infections diagnosed in GUM clinics in 2006. This represents a 1% decrease compared with the 19 248 diagnoses made in 2005, continuing the decreasing trend in total diagnoses of gonorrhoea seen since 2002¹. However, diagnoses amongst MSM continued to increase by 3% between 2005 and 2006. Young people remain the most commonly infected, with current rates highest in men aged 25-34 years (4587/100 000) and women aged 16-19 years (1969/100 000). Gonococcal infection tends to be concentrated in core risk groups, in the UK these include MSM and black ethnic minority populations².

Figure 1. Diagnoses of uncomplicated gonorrhoea made in GUM clinics (B1B2) by gender and male sexual orientation, UK: 1997 to 2006.



2.2 Global Gonococcal Antimicrobial Resistance

Fluoroquinolone resistance is increasingly prevalent globally, having spread from the Far East³ throughout Asia^{4,5}, Australia⁶, the Middle East⁷ and Western Europe⁸. In the USA, total fluoroquinolone resistance reached 11% in 2005 and the prevalence amongst MSM continued to increase, reaching 29%⁹. Consequently in 2007 CDC treatment guidelines were updated to recommend that fluoroquinolones should no longer be used to treat any patient group¹⁰. The efficacy of fluorquinolones is now compromised in many countries, with resistance prevalences ranging from 8% in Greece⁸ and 31% in Australia⁶ to 99% in China and Hong Kong^{4,5}. Penicillin and tetracycline resistant strains of *N. gonorrhoeae* are well documented throughout the world^{4,5,6,8}. For the first time azithromycin resistance has been documented in Western Europe at a prevalence of 8%⁸. Resistance to azithromycin has also been reported in Cuba¹¹ Brazil¹² and Russia¹³. In addition, there have been reports of reduced susceptibility to azithromycin in a cluster of isolates from infected individuals in the USA¹⁴, and evidence suggests domestic transmission of an azithromycin resistant strain in Sweden¹⁵. While most isolates remain susceptible to cefixime, ceftriaxone and spectinomycin, there have been reports of low-level *in vitro* resistance to ceftriaxone in China⁴, Australia⁶ and Western Europe⁸.

2.3 The Gonococcal Resistance to Antimicrobials Surveillance Programme

The Gonococcal Resistance to Antimicrobials Surveillance Programme (GRASP) was established in June 2000, as a collaboration between the Communicable Disease Surveillance Centre (CDSC), the Genitourinary Infections Reference Laboratory (GUIRL), Bristol and Imperial College, and was funded by the Department of Health¹⁶. 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 23).

In 2006, 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 over 15 000 isolates since the first collection in 2000. GRASP has enabled us to calculate reliable prevalence estimates of gonococcal antimicrobial resistance in England and Wales^{17,18}. It has also allowed epidemiological investigations of gonococcal antimicrobial resistance. Most importantly the prevalence estimates produced by GRASP have informed national antimicrobial prescribing policy^{17,19}.

This report presents the findings of the 7th year of isolate collection in this programme, highlighting the changes observed in antimicrobial susceptibility and gonococcal epidemiology from 2005 to 2006.

2.4 Antimicrobial Resistance Glossary

Table 1. Glossary of antimicrobial resistance and classification types.

Classification	Definition
Penicillin Resistant	Penicillin: MIC \geq 1mg/l or β -lactamase +ve
Tetracycline Resistant	Tetracycline: MIC \geq 2mg/l
PPNG	Penicillin: β -lactamase +ve AND tetracycline: MIC <16mg/l
TRNG	Tetracycline: MIC \geq 16mg/l AND penicillin β -lactamase -ve
PP/TRNG	Penicillin: β -lactamase +ve AND tetracycline: MIC \geq 16mg/l
CMRNG	Penicillin: MIC \geq 1mg/l but β -lactamase -ve AND tetracycline: MIC between 2-8mg/l
PenR	Penicillin: MIC \geq 1mg/l but β -lactamase -ve AND tetracycline: MIC <2mg/l
TetR	Tetracycline: MIC between 2-8mg/l AND penicillin: MIC <1mg/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

3. Sample Description

3.1 Retrieval in 2006

The retrieval problems identified in 2005 have been addressed and retrieval rates in 2006 were much improved. A total of 1833 isolates were collected by the 24 GRASP collaborating laboratories during the three month data collection period in 2006, and sent to STBRL for antimicrobial susceptibility testing. After the exclusion of duplicates 1698 isolates were retained, of these isolates 1313 (77.3%) were recovered successfully and confirmed as *N. gonorrhoeae*, compared to a retrieval rate of 56.5% in 2005. This represents a 27% increase in the number of confirmed isolates observed in 2006 compared to 2005.

The retrieval rates by region are shown in detail in table 2. The overall retrieval rate in London was 75.5 % compared with 78.9% of isolates outside of London, where retrieval ranged from 62.3% in Yorkshire & Humberside to 93.1% in the South East.

Table 2. The proportion of GRASP isolates confirmed as *N.gonorrhoeae* by region in the 2006 collection.

Region	Submitted Isolates N (%)		Total
	Confirmed	Unconfirmed	
East Midlands	99 (79.2)	26 (20.8)	125
East of England	24 (72.7)	9 (27.3)	33
London	591 (75.5)	192 (24.5)	783
North East	28 (63.6)	16 (33.4)	44
North West	182 (88.8)	23 (11.2)	205
South East	95 (93.1)	7 (6.9)	102
South West	41 (69.5)	18 (30.5)	59
Wales	67 (85.9)	11 (14.1)	78
West Midlands	95 (77.2)	28 (22.8)	123
Yorkshire & Humberside	91 (62.3)	55 (37.7)	146
Total	1313 (77.3)	385 (22.7)	1698

3.2 Weighting of Data

Since 2005, it is has been decided to estimate the percentage of isolates that are resistant to a particular antibiotic using a weighted analysis. This is to avoid estimates being under representative of sites that have a lower retrieval rate and over representative of sites that have a higher retrieval rate. Estimates for 2000-2004 have been recalculated in this new way and so values presented in this report may be slightly different to the unweighted estimates that have appeared in previous GRASP reports. 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.

3.3 Sample Distribution in 2006

Of the total 1313 confirmed isolates in 2006, 1242 isolates were from patients who had attended a GUM clinic, whilst 71 attended another primary care setting such as general practice, 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 ≥ 28 days after the first isolate. In 2006, as in previous years, such patients accounted for 1% of all isolates.

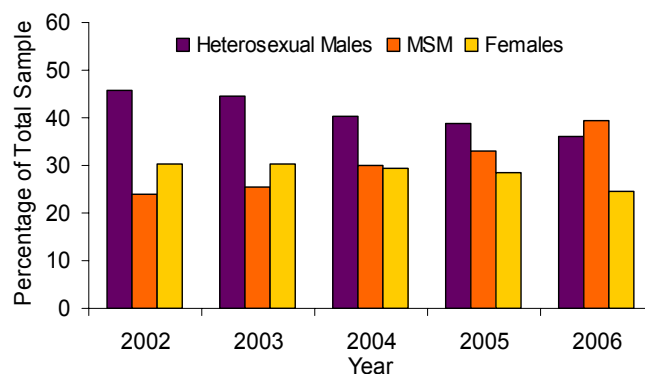
Table 3. Numbers of gonococcal isolates obtained in the GRASP collection: June-August 2006.

Region	Total number of confirmed isolates (%)	Non-GUM isolates N (%)	GUM Clinic data	
			Number of Isolates (%)	Number of Patients (%)
East Midlands	99 (7.5)	7 (10.0)	92 (7.4)	90 (7.3)
East of England	24 (18.2)	2 (2.8)	22 (1.8)	22 (1.8)
London	591 (45.0)	18 (25.3)	573 (46.1)	565 (46.1)
North East	28 (2.1)	0 (0.0)	28 (2.3)	27 (2.2)
North West	182 (13.9)	5 (7.0)	177 (14.3)	175 (14.3)
South East	95 (7.2)	4 (5.6)	91 (7.3)	90 (7.3)
South West	41 (3.1)	11 (15.4)	30 (2.4)	30 (2.4)
Wales	67 (5.1)	10 (14.0)	57 (4.6)	56 (4.6)
West Midlands	95 (7.2)	9 (12.6)	86 (6.9)	85 (6.9)
Yorkshire & Humberside	91 (6.9)	5 (7.0)	86 (6.9)	85 (6.9)
Total	1313	71	1242	1225

In 2006, 46.1% of the confirmed isolates were from London and 53.9% were from outside of London compared to the 52.3% and 49.2% observed respectively in 2005. The proportion of GUM isolates contributed to the total by each region is shown in table 3. Within each region the burden of gonococcal infection remains concentrated within the urban area served by each GUM clinic.

The trend observed over recent years of an increasing proportion of isolates from MSM continued in 2006, with 39.3% of isolates coming from MSM compared with 34.1% in 2005, whilst the proportion of isolates from heterosexual men and women decreased to 36.2% (38.7% in 2005), and 24.4% (28.4 in 2005) respectively, which is in-line with the latest KC60 trends¹ (figure 2).

Figure 2. The proportion of confirmed gonococcal isolates by gender and sexual orientation GRASP 2002 to 2006.



4. Antimicrobial Susceptibility

In the 2006 GRASP collection, ciprofloxacin resistance was observed in 26.5% of isolates, with a further 1.7% showing decreased susceptibility. Penicillin resistance was observed in 9.5% of isolates, with plasmid-mediated resistance (PPNG or PP/TRNG) due to β -lactamase in 3.4% of isolates and chromosomally-mediated (CMRNG or PenR) resistance in 4.4% of isolates. Tetracycline resistance was observed in 36.9% of isolates, with high-level plasmid-mediated tetracycline resistance (TRNG or PP/TRNG) found in 7.7% of isolates and chromosomally-mediated tetracycline resistance (TetR) found in 24.5% of isolates. Azithromycin resistance was identified in 2.0% of isolates, whilst no isolates were resistant to spectinomycin in 2006. As observed in previous years, no isolates in 2006 showed decreased susceptibility to ceftriaxone or cefixime.

A significant difference was observed between the prevalence of azithromycin resistance in London (1.1%) and non-London (2.7%) clinics ($p=0.05$) in 2006. No significant differences were observed between the London and non-London prevalence's, for ciprofloxacin, PPNG or PP/TRNG, TRNG or PP/TRNG, or CMRNG resistance in 2006.

Table 4 presents the percentage of isolates resistant to specific antimicrobials in London and non-London GRASP clinics in 2006, compared with 2005, and table 5 shows the percentage resistant to different types of penicillin and tetracycline resistance in London and non-London GRASP clinics in 2006 compared with 2005.

Table 4. Percentage of isolates resistant to specific antimicrobials 2005 to 2006 in London and Non-London.

Antimicrobial*	London % (95% CI)		Non-London % (95% CI)		Total % (95% CI)	
	2005	2006	2005	2006	2005	2006
Penicillin ($\geq 1\text{mg/l}$ or β -lactamase +)	25.4 [16.4,37.1]	10.9 [5.7,19.9]	11.2 [7.5,16.5]	8.4 [5.4,12.8]	17.9 [12.8,24.5]	9.5 [6.7,13.4]
Tetracycline ($\geq 2\text{mg/l}$)	56.4 [38.6,72.8]	43.0 [28.5,58.8]	40.3 [32.1,49.2]	31.6 [23.3,41.3]	48.0 [38.8,57.2]	36.9 [29.0,45.6]
Ciprofloxacin ($\geq 1\text{mg/l}$)	24.7 [13.0,41.9]	31.4 [21.7,42.9]	19.0 [12.9,27.2]	22.2 [16.4,29.3]	21.7 [15.5,29.5]	26.5 [20.8,33.0]
Ciprofloxacin ($\geq 0.125\text{mg/l}$)	25.9 [13.4,44.3]	32.4 [22.7,44.0]	20.4 [14.1,28.6]	24.5 [18.5,31.8]	23.0 [16.5,31.3]	28.2 [22.6,34.7]
Azithromycin ($\geq 1\text{mg/l}$)	2.2 [0.8,6.1]	1.1 [0.6,2.1]	2.2 [1.1,4.5]	2.7 [1.2,5.7]	2.2 [1.3,3.8]	2.0 [1.1,2.6]
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 [-,-]	0.0 [-,-]	0.0 [-,-]	0.0 [-,-]	0.0 [-,-]	0.0 [-,-]

Table 5. Percentage of isolates resistant to penicillin and tetracycline 2005 to 2006, in London and Non-London.

Resistance Classification*	London % (95% CI)		Non-London % (95% CI)		Total % (95% CI)	
	2005	2006	2005	2006	2005	2006
PPNG	5.1 [2.7,9.3]	1.0 [0.5,2.2]	1.5 [0.6,3.7]	1.5 [0.7,3.2]	3.2 [1.8,5.6]	1.3 [0.8,2.2]
TRNG	8.2 [5.2,12.8]	7.1 [4.6,10.9]	4.0 [2.2,7.3]	4.3 [2.7,6.6]	6.0 [4.2,8.5]	5.6 [3.9,7.9]
PP/TRNG	0.7 [0.2,2.6]	2.0 [1.0,4.2]	1.5 [0.5,4.6]	2.1 [1.2,3.5]	1.1 [0.5,2.6]	2.1 [1.3,3.2]
CMRNG	16.0 [7.2,32.0]	5.5 [2.0,14.7]	6.7 [4.8,9.4]	2.4 [1.0,5.4]	11.1 [6.8,17.7]	3.9 [2.1,7.2]
PenR	1.5 [0.6,4.1]	1.4 [0.5,4.0]	0.5 [0.1,4.5]	1.5 [0.4,4.9]	1.0 [0.4,2.4]	1.5 [0.6,3.2]
TetR	26.6 [17.5,38.2]	27.8 [20.0,27.2]	26.8 [20.9,33.7]	21.6 [14.3,31.3]	26.7 [21.7,32.4]	24.5 [18.6,31.5]
PPNG or PP/TRNG	5.8 [2.9,11.2]	3.0 [1.4,6.3]	3.0 [1.3,6.8]	3.7 [2.4,5.6]	4.3 [2.6,7.2]	3.4 [2.3,4.8]
TRNG or PP/TRNG	8.9 [6.2,12.7]	9.1 [6.4,12.8]	5.5 [2.9,10.1]	6.4 [4.5,9.0]	7.1 [5.1,9.8]	7.7 [6.0,9.8]

*Resistance category definitions are listed on page 6.

5. Ciprofloxacin

In 2006, 26.5% of isolates were resistant to ciprofloxacin, an increase from the 21.7% observed in 2005. A further 1.7% of isolates demonstrated a decreased susceptibility to ciprofloxacin (cf. 1.3% in 2005)

The prevalence of ciprofloxacin resistance varied significantly by region ($p < 0.005$) in 2006, ranging from 10.5% in the East Midlands to 48.0% in the North East. In all regions the prevalence remained greater than 10% in 2006 (figure 3).

The prevalence of resistance increased in women rising to 7.5% (cf. 6.3% in 2005) and heterosexual men 18.7% (cf. 11.8% in 2005), although these increases were not significant. The prevalence amongst MSM continued to rise reaching 43.3% in 2006 (cf. 42.4% in 2005), this increase however was not significant (figure 4).

The prevalence of ciprofloxacin resistance by ethnic group is shown in figure 5. In 2006, 52.0% of isolates from Asian and 28.7% of isolates from white individuals were ciprofloxacin resistant. The high prevalence of resistance amongst isolates from Asian individuals continues to be driven by heterosexual men having sexual contact abroad²⁰. Whilst the high prevalence of resistance amongst isolates from white individuals is due to the high proportion of white MSM with high prevalences of resistance in both endemic (41.3%) and imported strains (51.7%).

Despite the disproportionate burden of gonorrhoea in black ethnic groups, the prevalence of ciprofloxacin resistance has previously remained much lower in these groups compared to other ethnic groups; however in 2006 the prevalence of ciprofloxacin resistance rose to 12.0% in black Caribbean and 27.2% in black African populations, indicating increased transmission of ciprofloxacin resistant strains is occurring in these populations.

Figure 3. The prevalence of ciprofloxacin resistance by region 2002 to 2006.

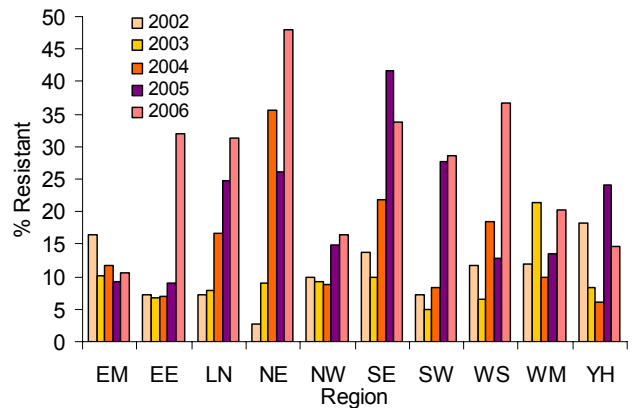


Figure 4. The prevalence of ciprofloxacin resistance by gender and male sexual orientation, 2002 to 2006.

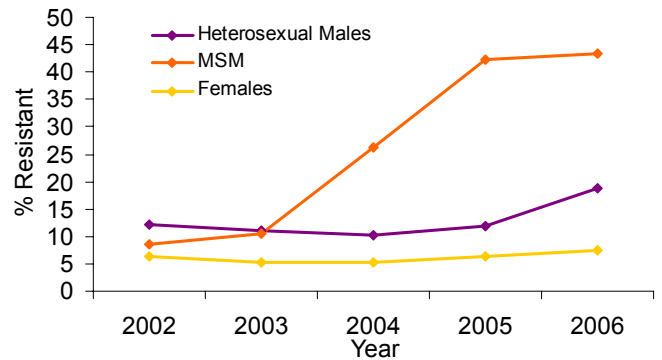
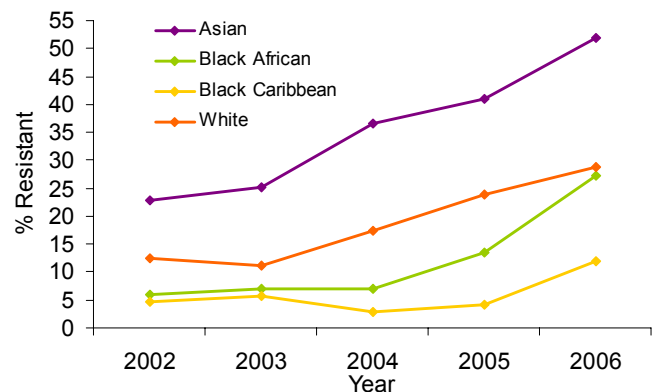


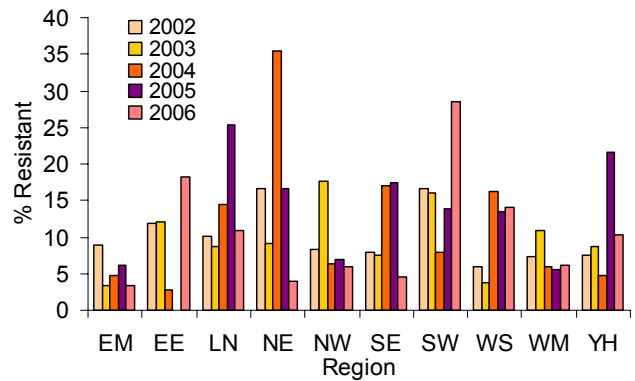
Figure 5. The prevalence of ciprofloxacin resistance by ethnic group: 2002 to 2006.



6. Penicillin

Overall, 9.5% of isolates demonstrated penicillin resistance in 2006, a significant decrease from the 17.9% seen in 2005 ($p=0.01$). The prevalence of penicillin resistance varied significantly by region in 2006 ($p<0.005$), ranging from 3.4% in the East Midlands to 28.5% in the South West in 2006, figure 6.

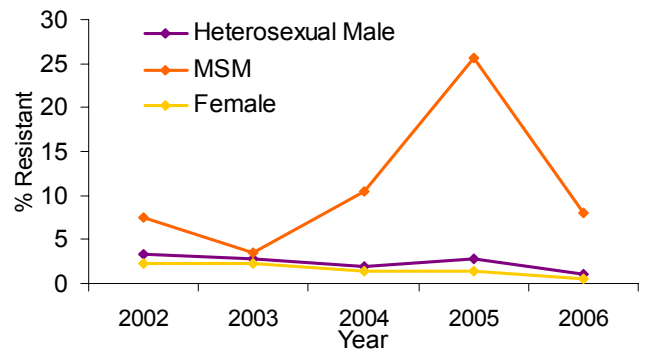
Figure 6. The prevalence of penicillin resistance by region over time: 2002 to 2006.



6.1 Chromosomally-mediated resistance (CMRNG)

In 2006, 3.9% of isolates demonstrated chromosomally-mediated penicillin resistance (CMRNG), compared with 11.1% in 2005 ($p<0.005$). No significant differences were observed in the prevalence of CMRNG amongst heterosexual men (1.1% cf. 2.8%) and women (1.4% cf. 0.6%) in 2006 compared with 2005. However, a significant decrease in the prevalence of CMRNG amongst MSM was observed, declining from 25.6% in 2005 to 8.0% in 2006 ($p<0.0005$), figure 7.

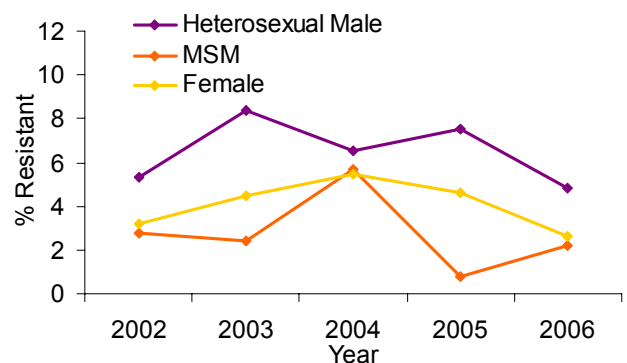
Figure 7. The prevalence of CMRNG by gender and male sexual orientation: 2002 to 2006



6.2 Plasmid-mediated resistance (PPNG or PP/TRNG)

In 2006, 3.4% of isolates demonstrated plasmid-mediated penicillin resistance (PPNG or PP/TRNG), compared with 4.3% in 2005 ($p=0.5$). A decrease was observed in both the prevalence of PPNG or PP/TRNG in heterosexual males from 7.5% in 2005 to 4.8% in 2006 ($p=0.2$), and amongst women from 4.6% in 2005 to 2.6% in 2006 ($p=0.2$). Whilst an increase in the prevalence amongst MSM was observed, rising from 0.8% in 2005 to 2.2% in 2006, this increase was not significant ($p=0.09$), figure 8.

Figure 8. The prevalence of PPNG or PP/TRNG by gender & male sexual orientation: 2002 to 2006.



7. Other Antimicrobials

7.1 Tetracycline

In 2006, 36.9% of isolates demonstrated tetracycline resistance, compared with 48.0% in 2005 ($p=0.001$). Chromosomally-mediated tetracycline resistance (TetR) was observed in 24.5% of isolates in 2006 a decrease from the 26.7% seen in 2005 ($p=0.4$). Plasmid-mediated tetracycline resistance (TRNG or PP/TRNG) was observed in 7.7% of isolates in 2006 compared to 7.1% in 2005 ($p=0.5$).

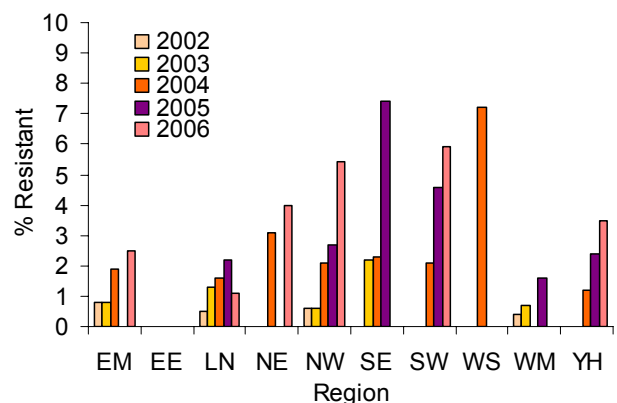
There were increases in the prevalence of TRNG or PP/TRNG amongst both heterosexual men 9.1% in 2006 (6.5% in 2005) and women 6.1% in 2006 (5.4% in 2005). Whilst the prevalence decreased in MSM from 8.8% in 2005 to 7.0% in 2006, although none of these changes were significant. The prevalence of TetR decreased amongst heterosexual males from 18.3% in 2005 to 14.5% in 2006 and in MSM from 45.0% in 2005 to 42.9% in 2006, but these changes were not significant. However, the prevalence of TetR amongst women decreased significantly from 14.6% in 2005 to 7.5% in 2006 ($p=0.05$).

7.2 Azithromycin

In 2006, 2.0% of isolates demonstrated resistance to azithromycin, compared to the 2.2% observed in 2005 although this decrease was not significant ($p=0.8$). The prevalence of resistance in 2006 ranged from 0% in the East of England, South East, West Midlands and Wales to over 5% in the South West (5.9%) and North West (5.4%) see figure 9.

In 2006 the prevalence of azithromycin resistance decreased in heterosexual men to 0.5% (1.9% in 2005), whilst increasing amongst females to 1.0% (0.5% in 2005) and MSM to 4.0% (3.7% in 2005) although these changes were not significant.

Figure 9. The prevalence of azithromycin resistance by region:2002 to 2006.



7.3 Ceftriaxone and Cefixime

As observed in previous years, no isolates demonstrated decreased susceptibility to ceftriaxone or cefixime in 2006.

7.4 Spectinomycin

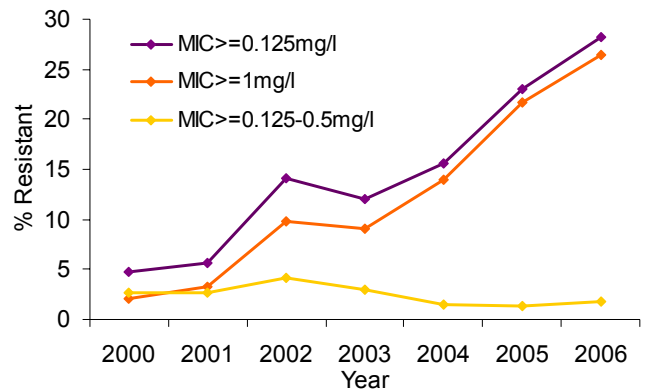
As seen in 2005 no isolates in 2006 were resistant to spectinomycin.

8. Antimicrobial Resistance Trends

The trends in antimicrobial resistance observed between 2000 and 2006 are highlighted in the figures below.

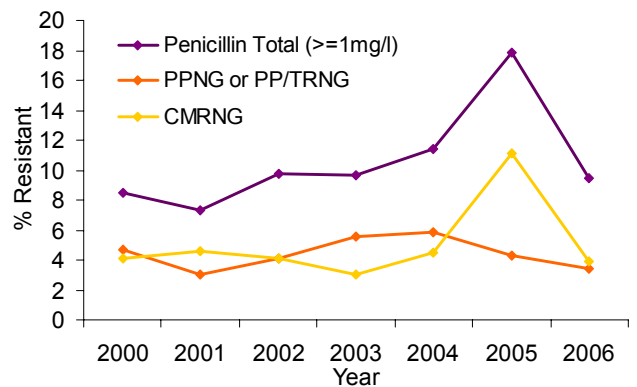
Between 2000 and 2006 there was a significant increase in the prevalence of both ciprofloxacin resistance ($\geq 1\text{mg/l}$), $p < 0.0005$, and those isolates that had decreased susceptibility ($\geq 0.125\text{mg/l}$), $p < 0.0005$. However the increase in ciprofloxacin resistance seen between 2005 and 2006, 21.7% to 26.5% was not significant ($p = 0.07$). Intermediate resistance ($\geq 0.125\text{--}0.5\text{mg/l}$), has remained at a stable low level between 2000 and 2006, (figure 10).

Figure 10. Trends in ciprofloxacin resistance GRASP 2000 to 2006.



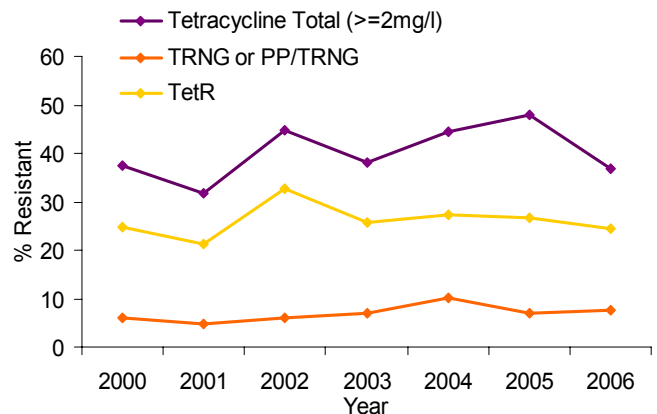
There was no significant difference in the prevalence of penicillin resistance ($\geq 1\text{mg/l}$ or β -lactamase +ve) between 2000 and 2006 (8.5% cf. 9.5%, $p = 0.5$), however there was a significant decrease between 2005 and 2006 (17.9% to 9.5%, $p = 0.01$). PPNG or PP/TRNG resistance shows no significant difference in prevalence over time between 2000 and 2006 or between 2005 and 2006. Whilst there is no significant difference in the prevalence of CMRNG resistance between 2000 and 2006, there was a significant decrease between 2005 and 2006 (11.1% to 3.9%, $p = 0.002$), (figure 11).

Figure 11. Trends in penicillin resistance GRASP 2000 to 2006.



There was no significant difference in the prevalence of tetracycline resistance ($\geq 2\text{mg/l}$) between 2000 and 2006 (37.4% cf. 36.9%, $p = 0.9$), however there was a significant decrease between 2005 and 2006 (48.0% to 36.9%, $p = 0.001$). This decrease reflects the decrease observed in CMRNG. Neither, plasmid mediated-TRNG or PP/TRNG nor, chromosomally – mediated TetR resistance have shown any significant difference in prevalence over time between 2000 and 2006 or between 2005 and 2006, (figure 12).

Figure 12. Trends in tetracycline resistance GRASP 2000 to 2006.



9. Prescribing Practice

Current treatment guidelines recommend cephalosporins as first-line treatment for gonococcal infection¹⁹. The prescribing pattern observed across the regions in the 2006 collection compared to 2005 is shown in Table 6. Overall 81.3% of patients were prescribed a cephalosporin to treat gonococcal infection in 2006, an increase from the 71.2% observed in 2005. Prescribing differences were observed across the regions, with the proportion of individuals prescribed a cephalosporin ranging from 73.1% in the North West region to 93.0% in the West Midlands ($p < 0.0005$). Prescribing also differed significantly by gender and male sexual orientation; with 79.4% of heterosexual men, 91.5% of MSM and 67.3% of women prescribed cephalosporins in 2006 ($p < 0.0005$). Of those prescribed, the most commonly administered were cefixime (70% of patients) and ceftriaxone (30% of patients).

In 2006, 14.0% of GRASP patients were prescribed fluoroquinolones, compared with the 18.6% observed in 2005. Fluoroquinolone prescribing ranged from 4.0% in the West Midlands region to 23.9% in the North West. Prescribing also varied significantly by gender and male sexual orientation, with 23.6% of women, 15.9% of heterosexual men and 6.6% of MSM receiving fluoroquinolones in 2006 ($p = 0.007$).

Penicillin (ampicillin) was prescribed to 2.9% of individuals in 2006 compared with 5.7% in 2005. Only clinics in London (5.9%) and the North West (1.0%) prescribed penicillin to GRASP patients in 2006, and this was only to a small proportion of individuals. Prescribing varied significantly by gender and male sexual orientation, with 5.0% of women, 3.8% of heterosexual men and 1% of MSM being prescribed penicillin in 2006 ($p = 0.02$).

Azithromycin is used to treat patients with concurrent chlamydial infection and in 2006 was prescribed to 40.1% of individuals compared to 28.2% in 2005. The proportion of individuals prescribed azithromycin in 2006 was highest in the West Midlands (69.0%), South East (59.8%), London (52.5%), and South West (40.0%) regions. Azithromycin was prescribed to 40.2% of MSM, 40.8% of females and 39.8% of heterosexual males in 2006 ($p = 0.9$).

Although not shown in table 6, tetracycline (doxycycline) is also used to treat patients with concurrent chlamydial infection. In 2006, it was prescribed to 30.4% of individuals compared to 43.0% in 2005. The proportion of individuals prescribed tetracycline in 2006 ranged from 4.6% in the North West to 69.0% in the Eastern Region. Tetracycline was prescribed 29.6% of MSM, 19.0% of females and 38.3% of heterosexual males in 2006 ($p = 0.1$).

Table 6. The proportion of patients (%) receiving selected antimicrobials to treat gonorrhoea and/or chlamydial infection in 2006 compared with 2005.

Region	Fluoroquinolones		Cephalosporins		Azithromycin		Penicillin	
	2005	2006	2005	2006	2005	2006	2005	2006
East Midlands	18.4	9.9	76.9	86.5	38.5	28.8	0.0	0.0
East of England	47.6	20.6	52.4	82.8	7.9	6.9	0.0	0.0
London	18.2	14.8	66.5	77.2	38.0	52.5	10.5	5.9
North East	2.4	9.8	95.1	87.8	0.0	0.0	0.0	0.0
North West	44.1	23.9	49.4	73.1	1.6	1.0	0.0	1.0
South East	11.3	14.1	88.7	88.0	54.9	59.8	0.0	0.0
South West	12.1	7.5	87.9	90.0	35.4	40.0	0.0	0.0
Wales	8.7	14.9	65.9	83.0	7.9	14.9	20.4	0.0
West Midlands	3.1	4.0	84.6	93.0	15.6	69.0	0.0	0.0
Yorkshire & Humberside	12.7	8.0	89.9	91.3	27.3	37.0	0.0	0.0
Overall Percentage	18.6	14.0	71.2	81.3	28.2	40.1	5.7	2.9

10. Patient Characteristics

10.1 Demographic characteristics

As in previous years, the 2006 data highlights the burden of gonococcal infection in core groups including MSM, young people and ethnic minorities (table 7)²¹. A continued increase in the proportion of infection diagnosed in MSM was observed rising from 32.9% to 39.3% in 2006. This is mainly due to a decrease in diagnoses amongst heterosexual men and women. The majority of gonococcal infections in young women were diagnosed in those aged 16-19yrs (36.3%), and in heterosexual men (20.7%) and MSM (44.4%) aged 25-34yrs. Ethnic minorities accounted for a decreasing proportion of the total diagnoses in 2006, 36.0% compared to 40.2% in 2005.

10.2 Clinical Characteristics

In 2006 an increasing proportion of individuals reported having a previous diagnosis of gonorrhoea, 30.6% (rising to 45.1% in MSM), compared to 29.4% in 2005. A concurrent STI was reported by 33.0% of individuals (rising to 45.7% in females) in 2006 compared to 35.9% in 2005. Chlamydia was the most commonly reported concurrent STI, found in 37.3% of women, 30.4% of heterosexual men, and 15.4% of MSM. The majority of women (97.9%) and heterosexual men (97.7%) presented with genital infection, whilst 55.4% of MSM presented with rectal and/or pharyngeal gonorrhoea. The prevalence of HIV amongst patients diagnosed with gonorrhoea with a known HIV status remained stable in 2006 at 13.2% compared to 14.0% in 2005. This varied by gender and sexual orientation with 28.3% of MSM, 1.0% of heterosexual men and 0.4% of women diagnosed as HIV positive.

10.3 Behavioural Characteristics

In 2006, 66.9% of women reported 0-1 partners in the past three months, compared with 37.5% of heterosexual men and 30.9% of MSM. Overall, 58.3% of individuals reported 2 or more sexual partners in the last 3 months, significantly higher than is estimated for the general population²². In 2006 the prevalence of individuals reporting a sexual partner abroad in the past 3 months remained stable at 11%. Sexual contact abroad varied by gender and male sexual orientation and was reported in 9.9% of heterosexual men, 15.1% of MSM and 6.7% of women in 2006. Of the individuals reporting sexual partners abroad in 2006 for whom region of sexual contact was known, 33% reported a sexual contact in Western Europe, 15% in the Far East, 10% in America and 10% in Africa or the Caribbean (figure 13).

Figure 13. Geographic location of sexual contact abroad in the past 3 months for individuals diagnosed with gonorrhoea, GRASP 2006 (n=165).

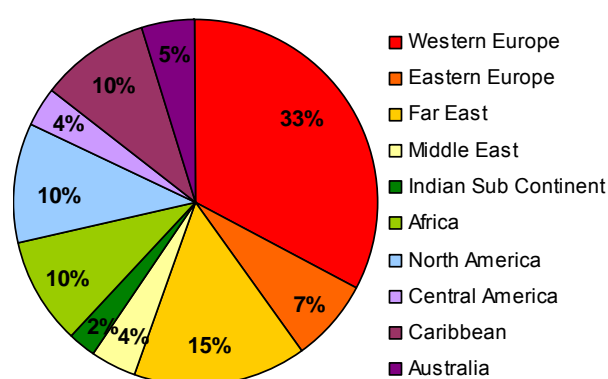


Table 7. Demographic, clinical and behavioural characteristics among all GUM patients with gonorrhoea from participating GUM clinics by gender and sexual orientation*: GRASP 2006.

Characteristics	Females %	Heterosexual males %	MSM %	Total %
GUM Clinic Locality				
London	43.2	36.2	59.5	46.8
Outside London	56.8	63.8	40.5	53.2
Total (Baseline) ‡	375	556	603	1599
Ethnicity				
White	57.5	44.6	86.0	64.3
Asian or Asian British	1.8	5.8	1.9	3.3
Black Caribbean	22.5	28.7	2.9	17.1
Black African	2.7	7.5	2.2	4.3
Other Black	8.4	7.5	1.6	5.3
Other	7.2	6.0	5.3	6.0
Total (Baseline) ‡	334	534	580	1458
Age Group				
≤15	2.2	0.5	0.3	0.8
16-19	36.3	20.3	2.8	17.0
20-24	31.2	27.5	17.3	24.3
25-34	20.7	32.0	44.4	34.2
35-44	7.3	13.9	27.5	17.9
45+	2.4	5.8	7.7	5.8
Total (Baseline) ‡	372	553	601	1591
Symptoms				
Discharge and or dysuria	55.5	89.3	72.1	74.9
No discharge or dysuria	44.5	10.7	27.9	25.1
Total Baseline ‡	337	551	577	1472
Previously diagnosed with gonorrhoea				
Yes	15.2	24.7	45.1	30.8
No	84.8	75.3	54.9	69.2
Total (Baseline) ‡	343	539	581	1469
Concurrent STI †				
Syphilis	0.3	0.9	4.0	2.0
Chlamydia	37.3	30.4	15.4	26.1
Herpes	1.7	0.9	0.3	0.9
Warts	1.7	1.8	0.9	1.4
Other	8.7	2.0	4.2	4.4
Total (Baseline) ‡	346	546	578	1478
Site of Infection †				
Genital	97.9	97.7	61.0	83.0
Rectal	5.3	1.6	40.0	17.6
Throat	2.4	2.0	15.4	7.4
Other	0.5	0.0	0.0	0.1
Total (Baseline) ‡	375	556	603	1598
HIV Status				
Negative	99.6	99.0	71.7	86.8
Positive	0.4	1.0	28.3	13.2
Total (Baseline) ‡	257	391	523	1180
UK Partners (past 3 months)				
0-1	66.9	37.5	31.0	41.5
2-5	32.2	58.6	51.9	50.0
6-10	0.6	3.3	9.2	5.0
11+	0.3	0.6	8.0	3.4
Total (Baseline) ‡	338	544	578	1467
Sex Abroad (past 3 months)				
Yes	6.7	9.9	15.1	11.2
Total (Baseline) ‡	341	545	582	1476

*Sexual orientation was reported for 94.7% (1159/1224) of males at participating GRASP clinics.

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

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

11. Data from non-GUM settings

The GRASP collection receives both GUM and non-GUM isolates each year. In 2006 non-GUM isolates accounted for 5.8% of the total sample compared to 7.8% in 2005. These isolates come from a range of settings such as General Practice, and in-patient or out-patient hospital services such as family planning. The GRASP analyses presented in each annual report consists of GUM data only, as limited clinical information is available on non-GUM patients. However in table 8 and 9 we present the available data on the non-GUM sample collected annually as part of GRASP.

11.1 Demographic characteristics

Table 8 presents the demographic data available for the non-GUM isolates collected as part of GRASP from 2002 to 2006. In 2006, 34.3% of non-GUM isolates were from London representing a rise in the proportion of non-GUM isolates from London. This is in contrast to the pattern seen in the 2006 GUM sample where the London and outside London sample is more evenly split (46.8% cf. 53.2%). In 2006, the regions outside of London with the largest number of non-GUM isolates were the South West (14.1%), Wales (11.1%) and the West Midlands (11.1%). In contrast the North East (2.0%) and East of England region (3.0%) had relatively few non-GUM isolates in 2006.

The majority of non-GUM isolates are from female patients, 77.6% in 2006 compared with 58.6% in 2005. This is the opposite of the gender breakdown of the GUM sample which are predominantly from male patients in 2006 (76.5%). Consequently the non-GUM sample also consists of younger patients, with the median age of non-GUM patients in 2006 being 22 whilst the median age of GUM patients in 2006 is 26.

11.2 Antimicrobial Susceptibility

The percentages of non-GUM isolates resistant to specific antimicrobials during the 2002 to 2006 GRASP collections are shown in table 9. In 2006 ciprofloxacin resistance was observed in 7.4% of non-GUM isolates, a decrease from the 14.2% observed in 2005 ($p=0.22$). Penicillin resistance was observed in 2.8% of isolates in 2006 a large decrease from the 11.5% prevalence observed in 2005 ($p=0.07$). The prevalence of tetracycline resistance also decreased from 42.0% in 2005 to 17.0% of isolates in 2006 ($p=0.002$). However, the prevalence of azithromycin resistance increased to 2.4% compared to 1.7% in 2005 ($p=0.79$). No non-GUM isolates demonstrated resistance to spectinomycin or decreased susceptibility to ceftriaxone or cefixime between 2002 and 2006.

In each year's GRASP collection the GUM isolates demonstrated higher prevalences of resistance to each antimicrobial than the corresponding year's non-GUM isolates. In 2006, 26.5% of GUM isolates demonstrated ciprofloxacin resistance compared with 7.4% of non-GUM isolates. Likewise, 9.5% of GUM isolates were penicillin resistant compared with 2.8% of non-GUM isolates, 36.9% compared with 17.0% were tetracycline resistant. Azithromycin resistance is an exception to this, with a prevalence of 2.0% in GUM isolates compared with 2.4% in non-GUM isolates. This is most likely due to the large proportion of non-GUM isolates from the South West region which has the highest prevalence of azithromycin resistance in 2006 (5.9%).

Table 8. Demographic characteristics among non-GUM patients with confirmed gonorrhoea from participating GRASP centres over time 2002 to 2005.

Characteristics	Year %					Total
	2002	2003	2004	2005	2006	
Location						
London	22.5	10.5	25.2	23.1	34.3	23.1
Outside London	77.5	89.5	74.8	76.9	65.7	76.9
Total (Baseline) ‡	120	152	159	143	99	673
Region						
East Midlands	2.5	1.3	4.4	4.9	9.1	4.4
East of England	7.5	7.2	3.8	2.1	3.0	4.7
London	22.5	10.5	25.2	21.7	34.3	22.8
North East	4.2	1.3	0.6	2.8	2.0	2.2
North West	5.8	10.5	3.1	1.4	6.1	5.4
South East	1.7	7.2	3.1	3.5	4.0	3.9
South West	28.3	38.8	28.3	22.4	14.1	25.8
Wales	13.3	13.8	11.9	22.4	11.1	14.5
West Midlands	5.0	5.9	6.3	15.4	11.1	8.7
Yorkshire & Humberside	9.2	3.3	13.2	3.5	5.1	6.9
Total (Baseline) ‡	120	152	159	143	99	673
Gender						
Male	29.1	33.7	35.1	41.4	22.4	32.3
Female	70.9	66.3	64.9	58.6	77.6	67.7
Total (Baseline) ‡	118	148	158	143	98	665
Age Group						
≤15	9.3	5.3	0.8	3.7	0.0	3.8
16-19	28.6	32.3	29.9	16.8	33.7	28.3
20-24	20.7	25.0	25.5	30.1	25.5	25.4
25-34	23.5	24.8	29.4	26.0	23.5	25.4
35-44	12.3	10.2	10.9	14.6	7.1	11.0
45+	5.6	2.4	3.5	8.7	10.2	6.1
Total (Baseline) ‡	114	147	153	139	98	651

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

Table 9. Percentage and number of isolates resistant to specific antimicrobials among non-GUM patients with confirmed gonorrhoea from participating GRASP centres over time 2002 to 2006.

Antimicrobial	Year % (95% CI)				
	2002	2003	2004	2005	2006
Penicillin (≥ 1mg/l or β lactamase +ve)	10.6 [5.7, 18.7]	8.5 [4.7, 14.9]	8.4 [4.6, 14.8]	11.5 [5.0, 24.3]	2.8 [0.6, 11.9]
Tetracycline (≥ 2mg/l)	33.8 [20.6, 50.0]	22.9 [16.7, 30.4]	33.4 [25.2, 42.7]	42.0 [30.4, 54.6]	17.0 [11.2, 25.0]
Ciprofloxacin (≥ 1mg/l)	7.1 [3.7, 13.0]	4.7 [1.7, 12.1]	8.4 [3.4, 19.3]	14.2 [7.6, 25.1]	7.4 [3.0, 17.2]
Ciprofloxacin (≥ 0.125mg/l)	8.8 [5.2, 14.7]	5.6 [2.2, 13.6]	9.0 [4.1, 18.7]	14.2 [7.6, 25.1]	9.8 [4.7, 19.2]
Azithromycin (≥ 1mg/l)	0.0 [-,-]	0.7 [0.1, 5.8]	0.0 [-,-]	1.7 [0.3, 9.2]	2.4 [0.6, 9.3]
Spectinomycin (≥ 128mg/l)	0.0 [-,-]	0.0 [-,-]	0.0 [-,-]	0.0 [-,-]	0.0 [-,-]
Ceftriaxone (≥ 0.125mg/l)	0.0 [-,-]	0.0 [-,-]	0.0 [-,-]	0.0 [-,-]	0.0 [-,-]
Cefixime (≥ 0.25mg/l)	N/A	N/A	0.0 [-,-]	0.0 [-,-]	0.0 [-,-]

12. Discussion

GRASP has proven to be a successful collaboration, with *N. gonorrhoeae* isolates obtained from 24 laboratories and 26 GUM clinics collecting data on over 15 000 isolates over seven years. The data have allowed us to determine annual antimicrobial susceptibility patterns of *N. gonorrhoeae* in England and Wales over time¹⁶⁻¹⁸. In addition, they have enabled us to characterise the demographic and behavioural characteristics of patients with infections caused by antibiotic resistant gonococci and have informed the national treatment guidelines¹⁹.

The prevalence of ciprofloxacin resistance continued to rise in 2006 reaching 26.5% in England and Wales, which is comparable to the 34.8% found in Scotland²³. The prevalence of ciprofloxacin resistance remained highest in MSM (43.3%), more than double the prevalence seen in heterosexual men (18.7%), and five times higher than the prevalence amongst women (7.5%). The prevalence remained high amongst white ethnic groups where it is largely driven by MSM and amongst Asian individuals, where it remains largely driven by sexual contact abroad. Despite seeing previously low prevalences of ciprofloxacin resistance in black ethnic groups, the prevalence began to rise in 2006, doubling to 27.2% in black Africans, and quadrupling to 12.0% in black Caribbeans, suggesting endemic resistant strains are now being transmitted amongst these heterosexual sexual networks.

The prevalences of resistance to other antimicrobials remained relatively stable in 2006. In 2005 the prevalence of CMRNG among isolates from MSM was 26% but in 2006 this fell back to 8% similar to levels previously observed. In MSM in 2005, CMRNG was significantly higher if reporting sex abroad, whereas in 2006 it was only slightly higher. This suggests that the large prevalence seen previously was due to imported CMRNG resistant strains no longer circulating in 2006. Azithromycin resistance remained at low levels in 2006; however, in two regions of England and Wales it has now exceeded 5%. Importantly no GRASP isolates have yet been found to have decreased susceptibility to ceftriaxone or cefixime.

The recommended first-line treatments for gonorrhoea in the UK are ceftriaxone (intramuscular) or cefixime (oral)¹⁹. The majority of patients are now prescribed cephalosporins (81%). Importantly, of the cephalosporins prescribed 99% were given cefixime or ceftriaxone as recommended²⁴. Only 14% of individuals were prescribed a fluoroquinolone in 2006, however this varied by gender and sexual orientation, rising from 7% of MSM to 24% of women and 16% of heterosexual men. This is of particular concern considering the increase in ciprofloxacin resistance seen amongst certain black ethnic groups in 2006.

The demographic, clinical and behavioural characteristics remained relatively similar to previous years although the proportion of MSM in the GRASP sample is increasing (39%) in 2006. This is mainly due to a decreasing number of diagnoses from heterosexual men and women, as the number of diagnoses from MSM has not changed a great deal since 2000. Notably, the prevalence of HIV amongst patients diagnosed with gonorrhoea with a known HIV status remained stable in 2006 at 13%. Whilst the prevalence of individuals reporting a sexual partner abroad remained stable at 11% in 2006, important in terms of the potential for importation of new resistant strains into the UK. As in previous years, the non-GUM sample in 2006 was predominantly composed of women, whilst the GUM sample was predominantly composed of men. Antimicrobial susceptibilities among the non-GUM sample were lower for all antibiotics except azithromycin, which was seen at a similar prevalence to that found in GUM patients.

The findings discussed in this report continue to highlight the changes in prevalence of antimicrobial resistance observed in England and Wales, alongside the changing epidemiology of gonococcal infection in 2006. Moreover, the continued heterogeneity of antimicrobial resistance prevalence seen across the regions highlights the sustained need for local and national monitoring of antimicrobial resistance, so treatment strategies can remain responsive to the changing epidemiology of antimicrobial resistant gonorrhoea.

13. Future Challenges for GRASP

13.1 GRASP collaborator's meeting

The second GRASP collaborator's meeting was held on 6 June 2007 at the HPA Head Office at Holborn Gate. In the morning session there were four presentations; Can better prescribing turn the tide of resistance? (David Livermore); Global overview of gonococcal resistance to antimicrobials (Cathy Ison); Demographic and behavioural characteristics of the GRASP sample 2000 to 2005 (Laura James) and Analysis of antimicrobial resistance data from GRASP 2006 (Beth Maclure). In the afternoon there was an interactive session to discuss the future challenges of GRASP and many helpful comments were made, many of which are described below. The meeting was well attended and we would encourage as many collaborators as possible to attend future meetings as GRASP faces its future challenges

13.2 Timely production of results

It has always been the aim to produce timely clinical and annual reports for GRASP to enable the results to be used to inform therapeutic choice. The problems of retrieval of isolates in 2005 have largely been overcome but the pressure on the laboratory staff to provide information on retrieval in real-time subsequently led to technical problems during testing which have again delayed the 2006 report. It was, therefore decided at the collaborator's meeting to change the reporting of retrieval rates for 2007 such that STBRL would no longer retrieve isolates immediately on arrival in the laboratory but would give timely feedback to collaborating laboratories only if specifically requested or to laboratories with previous low retrieval rates. Preliminary indications are that this has been a very successful approach.

13.3 Effect of molecular testing on GRASP sample

The potential for increased usage of nucleic acid amplification tests (NAAT) for the detection of gonorrhoea to effect how representative the sample remains was discussed in the 2005 report^{25,26}. At the collaborator's meeting the discussion produced the following two scenarios:

Scenario 1: In some centres patients who are considered likely to have gonorrhoea infection, have a culture as well as a NAAT performed. Clarification on the selection criteria will need to be ascertained but this should not present any major concerns for obtaining cultures from these centres for GRASP

Scenario 2: Some centres will go over to NAATs entirely and do very little culture. These centres could however take a second specimen from patients for culture over the three month sampling period of GRASP. Concerns were raised about whether the skills in GC culture would be adequately maintained to ensure that the sensitivity would be as good as at present.

In the coming months the GRASP team will be contacting centres to gain information on their individual approach with a view to further discussion at the next collaborator's meeting.

13.4 Representative nature of GRASP

The centres selected as sentinel sites for GRASP were chosen to give regional representation. Preliminary analysis has shown that the proportion of gonorrhoea tested through GRASP in different regions varies. Work is currently underway to weight the analysis for KC60 data to determine whether this influences the resistance trends. This will inform any changes which we feel may be necessary to the composition of the sentinel sites.

13.5 Community acquired gonorrhoea

As highlighted in the 2005 report community acquired gonorrhoea only accounts for a small percentage of isolates (6% in 2006, 8% in 2005) and is not used for the full analysis because of the lack of clinical data. There is increasing evidence of gonorrhoea in the community and this is probably an under-representation. It is clear that for the future of GRASP we need to undertake pilot studies to improve the data collection of non-GUM patients for GRASP.

13.6 Web-based data collection

Data (both clinical and demographic) for GRASP has been collected using paper system followed by manual data entry at the HPA. We feel this is inefficient in time and has led to complications with data management which often delay the production of the final analysis. It is planned that in future years all data collection will be web-based and it is hoped to achieve this for the 2008 collection, with all the data being held on a single database. This should reduce the time taken to collect the data and minimise the corrections needed and hence improve the production of a timely report.

14. 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 protocol²⁷.

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 were sent to STBRL for susceptibility testing. At each local laboratory, primary isolates of *N. gonorrhoeae* were sub-cultured to obtain a pure growth and frozen in glycerol broth for transportation or sent on chocolate agar slopes. At the reference laboratory, MICs were determined for the following antimicrobial agents (the range of concentrations tested is shown in parentheses): penicillin (0.03-4.0mg/l), ciprofloxacin (0.002-32mg/l) spectinomycin (2-64mg/l), tetracycline (1-32mg/l), ceftriaxone (0.002 to 0.125mg/l), azithromycin (0.03-2mg/l) and cefixime (0.002-0.25mg/l).

As a quality control, a two-way panel of isolates was exchanged twice between the GRASP reference laboratory and the Scottish *Neisseria gonorrhoeae* Reference Laboratory (SNGRL) during the isolate collection period. Isolates were 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 were compared and an error was recorded if a laboratory result was more than one or two doubling dilutions from the other. These results 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 in the 2006 collection.

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

All results (except those in section 11) are based on GUM patients only. A weighted analysis for antimicrobial resistance is hoped to produce estimates that reflect all GUM patients. 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. An analysis of antibiotic prescribing practice and the characteristics of patients diagnosed with gonorrhoea at GUM clinics has not been weighted.

14.1 Acknowledgements

This report was only made possible due to the continued enthusiastic cooperation of the collaborating centres listed on page 23. We would like 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 Iona Martin, Stephanie Chisholm, Elisabeth Maclure and John Anderson for their hard work in testing such large numbers of isolates at our reference laboratory and Elizabeth Rudd for her invaluable help with preparation of the data for analysis and the clinical and annual reports.

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