Sexually Transmitted Disease Surveillance 2006 Supplement

Gonococcal Isolate Surveillance Project (GISP) Annual Report 2006

Division of STD Prevention
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The report is also available by Internet via the CDC home page at: **http://www.cdc.gov/std/GISP2006/**. To view the Clinic Profiles, please use the drop down boxes on **http://www.cdc.gov/std/GISP2006/**.

Any comments and suggestions that would improve the usefulness of future publications are appreciated and should be sent to GISP Coordinator, Epidemiology and Surveillance Branch, Division of STD Prevention, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, Centers for Disease Control and Prevention, 1600 Clifton Road, Mailstop E-02, Atlanta, GA 30333.

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Gonococcal Isolate Surveillance Project (GISP) Annual Report – 2006

Introduction

With 358,366 gonorrhea cases reported in 2006, gonorrhea is the second most frequently reported communicable disease in the United States. Gonorrhea rates in the United States declined 74.3% from 1975 through 1997 following the implementation of national gonorrhea control programs in the mid-1970s.[1,2] After 1997 gonorrhea rates appeared to plateau. However, these rates have increased for the second consecutive year to 120.9 cases per 100,000 persons in 2006 which is a 5.5% increase since 2005. Additionally, gonorrhea rates among women and men have been relatively similar for the past ten years (**Figure 1**).[3,4] Overall, in 2006 the rate of gonorrhea has increased in all regions of the country except the Northeast, among all race/ethnic groups except Asian/Pacific Islanders, and among adolescents and young adults (**Figures 2, 3** and **4**).[3,4] The health impact of gonorrhea is largely related to its role as a major cause of pelvic inflammatory disease, which frequently leads to infertility or ectopic pregnancy.[5] In addition, data suggest that gonorrhea facilitates HIV transmission.[6,7]

The treatment and control of gonorrhea has been complicated by the ability of *Neisseria gonorrhoeae* (or *N. gonorrhoeae*) to develop resistance to antimicrobial agents. The appearance of penicillinase-producing *N. gonorrhoeae* (PPNG) and chromosomally mediated penicillin and tetracycline-resistant *N. gonorrhoeae* (CMRNG) in the 1970s eventually led to the abandonment of these drugs as therapies for gonorrhea.

Since the 1990s, fluoroquinolone-resistant *N. gonorrhoeae* (QRNG) has been reported and has been increasing in many parts of the world, including the United States.[8-14] As a result of increases in QRNG prevalence in defined locations and groups, CDC indicated that quinolones were no longer recommended in certain situations in 2000, 2002, and 2004. In April 2007, CDC reported that quinolones were not recommended to treat gonococcal infections in the U.S., after observing widespread increases in QRNG prevalence to all regions of the country and continued increases among heterosexual males. Currently, the CDC recommended treatment for gonococcal infections is limited to a single class of drug, the cephalosporins.[15]

GISP Overview

GISP was established in 1986 to monitor trends in antimicrobial susceptibilities of strains of *N. gonorrhoeae* in the United States to establish a rational basis for the selection of gonococcal therapies.[16] GISP is a collaborative project among selected sexually transmitted diseases (STD) clinics in different sites, five regional laboratories, and the Centers for Disease Control and Prevention (CDC).

In GISP during 2006, *N. gonorrhoeae* isolates were collected from the first 25 men with urethral gonorrhea attending STD clinics each month in 28 sites in the United States. Clinical and demographic data were abstracted from medical records of GISP

participants. Using agar dilution, regional laboratories determined the susceptibilities of these isolates to penicillin, tetracycline, spectinomycin, cefixime, ceftriaxone, ciprofloxacin, and azithromycin. Minimum inhibitory concentrations (MICs) were measured, and values interpreted according to criteria recommended by the Clinical and Laboratory Standards Institute (CLSI, formerly NCCLS).[17-20]

Important GISP findings have included:

- the continued high prevalence of resistance to both penicillin and tetracycline which has remained above 22%;
- the emergence of multi-drug resistant isolates (resistant to penicillin, tetracycline, and fluoroquinolone) with decreased susceptibility to cefixime;[21]
- the emergence and increasing prevalence of resistance to the fluoroquinolones;[8-15] and
- the appearance, and increasing prevalence of decreased susceptibility to the macrolides.[22]

GISP findings have directly contributed to CDC's STD Treatment Guidelines in 1993, 1998, 2002, and 2006 and updates to the guidelines in 2004 and 2007.[15, 23-26]

2006 GISP Sites and Regional Labs

Twenty-eight sites contributed 6,089 gonococcal isolates to GISP in 2006 (**Figure 5**). Fifteen out of 28 sites (54%) have participated continuously since 1987: Albuquerque, Atlanta, Baltimore, Birmingham, Cincinnati, Denver, Honolulu, Long Beach, New Orleans, Philadelphia, Phoenix, Portland, San Diego, San Francisco, and Seattle. The other thirteen GISP sites joined in the following years: Chicago (1996), Cleveland (1991), Dallas (2000), Detroit (2003), Greensboro (2002), Los Angeles (2003), Las Vegas (2002), Miami (1998), Minneapolis (1992), New York City (2006), Oklahoma City (2003), Orange County (1991), and Tripler (2001). The five GISP regional laboratories are located in Atlanta at Emory University, Birmingham at the University of Alabama, Cleveland at the Cleveland Clinic Foundation, Denver at the University of Colorado Health Sciences Center, and Seattle at the University of Washington.

Description of GISP Data

Aggregate data from all GISP sites are described and illustrated in the first part of this report. Site-specific figures are provided in the second part of this report, to illustrate geographic variations in patient characteristics and antimicrobial susceptibility.

Demographic and Clinical Characteristics

Age: The age distribution of GISP participants compared with nationally reported male gonorrhea patients in 2006 is shown in **Figure 6**. In 2006, GISP had proportionally fewer 20-24 year olds and persons less than 20 years old than were reported nationally and more persons in the older age groups. GISP participants ranged in age from 13 to 85 years, with a median age of 27 years.

Race/Ethnicity: The race/ethnicity distribution of GISP participants as compared with nationally reported male

gonorrhea patients in 2006 is shown in **Figure 7**. White, Hispanic, and Asian males were slightly over represented in GISP while African-American and Native American males were slightly under represented compared with the race/ethnicity distribution of nationally reported male gonorrhea patients in 2006.

Sexual Orientation: The proportion of GISP participants who were MSM increased every year from 1993 to 2002, then in 2003, there was a slight decrease. From 2004 to 2005, this proportion again increased and in 2006 was 21.5%. (**Figure 8**). The majority of GISP participants who were MSM were on the West Coast (**Figure 9**).

Reason for Clinic Attendance: Most (95.2%) GISP participants in 2006 presented to the clinic on their own initiative (volunteers); others were referred as contacts of sexual partners diagnosed with gonorrhea or presented for tests-of-cure (**Figure 10**). There has been little change in this distribution over time from 1999 to 2006.

Report of Symptoms: In 2006, 97.8% of GISP participants reported dysuria and/or urethral discharge; 2.2% had no symptoms. These proportions have been relatively stable over time.

History of Gonorrhea: The percentage of GISP participants reporting ever having had a previous episode of gonorrhea was 51.4% in 2006. The percentage of GISP participants with a documented previous episode of gonorrhea in the last 12 months peaked at 23.6% in 2000 then decreased to 16.1% in 2004, and now has increased from 18.3% in 2005 to 23% in 2006.

Supplemental Patient Data: The proportion of GISP participants who were HIV-positive during 2006 was 7.8% (312/4,014). Of 988 MSM reporting HIV testing information, 276 (27.9%) were HIV positive; 1.1% (34/3,010) of heterosexuals were HIV positive. During the 60 days prior to diagnosis of gonorrhea, GISP patients reported the following behaviors:

- 4.9% (222/4,511) took antibiotics;
- 9% (315/3,521) traveled outside the state where the sentinel site is located;
- 1.8% (68/3,783) used injection recreational drugs;
- 26.3% (888/3,373) used non-injection recreational drugs; and
- 2.1% (71/3,441) exchanged money or drugs for sex or vice versa.

Antimicrobial Treatments Given for Gonorrhea: The antimicrobial agents given to GISP participants for gonorrhea therapy are shown in **Figure 11**. The proportion of GISP patients treated with cephalosporins decreased from a peak of 84.7% in 1990 to 67.7% in 2006. However, 67.7% represented an increase from the proportion treated with cephalosporins in 2005, which was 63.7%. In 2002, the manufacture and distribution of cefixime was halted.[27] With the discontinuation of cefixime, the use of "other cephalosporins" such as cefpodoxime, increased from 4.6% in 2003 to 19.5% in 2006. The proportion of GISP participants treated with fluoroquinolones (ciprofloxacin, ofloxacin or levofloxacin) increased from none in 1987 to a high of 42% in 2003 before declining to 33.7% in 2005 and 30% in 2006.

Antimicrobial Treatments Given for Chlamydia: The antimicrobial agents given to GISP participants for empiric treatment of *Chlamydia trachomatis* infection are shown in **Figure 12**. The proportion of

GISP patients treated with doxycycline or tetracycline decreased from 50.6% in 2005 to 45.7% in 2006; whereas, the proportion treated with azithromycin 1 gram has increased from 45.8% in 2005 to 49.4% in 2006.

Susceptibility to Antimicrobial Agents

Antimicrobial Resistance Criteria

Antimicrobial resistance in *N. gonorrhoeae* is defined by the criteria recommended by the Clinical and Laboratory Standards Institute (CLSI, formerly NCCLS):[17-20]

Penicillin, MIC ≥ 2.0 µg/ml
Tetracycline, MIC ≥ 2.0 µg/ml
Spectinomycin, MIC ≥ 128.0 µg/ml
Ciprofloxacin, MIC 0.125 - 0.5 µg/ml (intermediate resistance)
Ciprofloxacin, MIC ≥ 1.0 µg/ml (resistance)
Ceftriaxone, MIC ≥ 0.5 µg/ml (decreased susceptibility)
Cefixime, MIC ≥ 0.5 µg/ml (decreased susceptibility)

CLSI criteria for resistance to ceftriaxone, cefixime, and azithromycin and for susceptibility to azithromycin have not been established for *N. gonorrhoeae*.

Susceptibility to Penicillin and Tetracycline

Overall, 22.3% (1,355/6,089) of isolates collected in 2006 were resistant to penicillin, tetracycline, or both. For GISP analyses in this section, six mutually exclusive categories of resistance are used for describing chromosomally and plasmid-mediated resistance to penicillin and tetracycline:[8]

Categories of Resistance

(1) penicillinase-producing *N. gonorrhoeae* (PPNG): β-lactamase-positive and tetracycline MIC < 16.0 µg/ml;

(2) plasmid-mediated tetracycline resistant *N. gonorrhoeae* (TRNG): β-lactamase-negative and tetracycline MIC ≥ 16.0 µg/ml;

(3) PPNG-TRNG: β-lactamase-positive and tetracycline MIC ≥ 16.0 µg/ml;

(4) chromosomally mediated penicillin-resistant *N. gonorrhoeae* (PenR): non-PPNG and penicillin MIC ≥ 2.0 µg/ml and tetracycline MIC < 2.0 µg/ml;

(5) chromosomally mediated tetracycline-resistant *N. gonorrhoeae* (TetR): non-PPNG and penicillin MIC < 2.0 µg/ml and tetracycline MIC 2.0-8.0 µg/ml; and

(6) chromosomally mediated resistance to both penicillin and tetracycline (CMRNG): non-PPNG and penicillin MIC ≥ 2.0 µg/ml and tetracycline MIC 2.0-8.0 µg/ml.

Figure 13 shows the plasmid-mediated resistance to penicillin and tetracycline among GISP isolates from 1988 to 2006. The percentage of isolates that were PPNG declined annually from a peak of 11.0% in 1991 to 0.4% in 2006. The prevalence of TRNG peaked in 1997 at 7.3% and had been decreasing for several years. Since 2005, it has been slightly increasing from 4.5% to 4.6% in 2006. Additionally, the prevalence of PPNG-TRNG has continued to be low and in 2006, it was 0.5%.

Figure 14 shows chromosomally mediated resistance to penicillin and tetracycline among GISP isolates from 1988 to 2006. The percentage of PenR isolates increased annually from 0.5% in 1988 to 5.7% in 1999, and has subsequently decreased to 1.2% in 2006. TetR prevalence for 2006 was 6.2%. The prevalence of CMRNG increased from 6.1% in 2005 to 9.3% in 2006.

Susceptibility to Spectinomycin

All isolates were susceptible to spectinomycin in 2006. There have been five spectinomycin-resistant isolates in GISP; their locations and years were: St. Louis-1988, Honolulu-1989, San Francisco-1989, Long Beach-1990, and West Palm Beach-1994.

Susceptibility to Ceftriaxone

Susceptibility testing for ceftriaxone began in 1988. There has not been an overall increase in MICs since that time. **Figure 15** demonstrates MIC values for 3 years: the first year of testing, the current year, and a mid-point year (1997). There have been four isolates with decreased susceptibility to ceftriaxone in GISP; all four had MICs of 0.5 μg/ml. Their locations and years were: San Diego-1987, Cincinnati-1992 and 1993, and Philadelphia-1997. No isolates with decreased susceptibility to ceftriaxone were seen in 2006.

Susceptibility to Cefixime

Susceptibility testing for cefixime began in 1992. There has been a decrease in the percentage of isolates with higher MIC values since 1992, as demonstrated in **Figure 16**. In 2004, there were 2 isolates with decreased susceptibility to cefixime reported to GISP; both were from Los Angeles and demonstrated resistance to penicillin, tetracycline and ciprofloxacin. There were no isolates with decreased susceptibility to cefixime in 2002, 2003, and 2005. However, in 2006, there was one isolate from Los Angeles with decreased susceptibility to cefixime that also showed resistance to penicillin, tetracycline, and ciprofloxacin. In total from 1992 to 2006, there have been 48 isolates with decreased susceptibility to cefixime in GISP; their MICs ranged from 0.5-2.0 μg/ml.

Susceptibility to Ciprofloxacin

The correlation of ciprofloxacin MICs of 0.125-0.5 μg/ml with treatment failure is not well established. However, one study of infections with resistant strains treated with ciprofloxacin 500 mg orally showed a treatment failure rate of 45% for strains with MICs of ≥ 4.0 μg/ml.[28] Gonococcal isolates with intermediate resistance (MICs 0.125-0.5 μg/ml) and resistance (≥ 1.0 μg/ml) to ciprofloxacin also demonstrate intermediate resistance and resistance to other fluoroquinolones.

Susceptibility testing for ciprofloxacin began in 1990. A total of 15.1% (918/6,089) of isolates exhibited intermediate resistance or resistance to ciprofloxacin in 2006. This is an increase when compared to 2005 in which 10.5% (648/6,199) of isolates showed intermediate resistance or resistance to ciprofloxacin (**Figure 17**). **Figure 18** demonstrates all MIC values for ciprofloxacin for 3 years: the first year of testing, the current year, and a mid-point year (1997). There was a shift toward higher MIC values from 1997 to 2006.

Intermediate Resistance: In 2006, 1.2% (75/6,089) of all GISP isolates exhibited intermediate resistance to ciprofloxacin, which is a slight increase from 1.1% (67/6,199) in 2005. The seventy-five isolates of *N. gonorrhoeae* exhibiting intermediate resistance to ciprofloxacin in 2006 were found in Baltimore (2), Chicago (11), Cleveland (12), Dallas (2), Honolulu (1), Las Vegas (3), Miami (2), Minneapolis (1), Orange County (1), Phoenix (1), Portland (3), San Diego (4), and Seattle (32).

Resistance: Eight hundred and forty-three, or 13.8% of GISP isolates were resistant to ciprofloxacin (MICs $\geq$ 1.0 μg/ml) in 2006. Ciprofloxacin-resistant isolates were identified in 96% (27/28) of all sites in 2006. Forty percent (337/843) of the 2006 isolates were from California GISP sites and 60% were from non-California GISP sites, compared with 43.9% and 56.1% during 2005, respectively.

Resistance by Location/Regions: The prevalence of ciprofloxacin resistant *N. gonorrhoeae* at each 2006 GISP site from the years 2003 to 2006 is shown in **Figure 19**.

In the West, increases in the proportion of isolates resistant to ciprofloxacin were observed in Honolulu, from 19.3% in 2005 to 35.8% (34 of 95 isolates) in 2006.

In California GISP sites, increases in the number of isolates resistant to ciprofloxacin were identified in all the sites: Los Angeles from 14.5% in 2005 to 22.7% in 2006; Long Beach from 23.5% in 2005 to 28.4% in 2006; Orange County from 27.5% in 2005 to 34.6% in 2006; San Diego from 26.2% in 2005 to 35.1% in 2006; and San Francisco from 31.3% in 2005 to 44.5% in 2006.

Similarly in other West Coast sites, the prevalence of ciprofloxacin-resistant *N. gonorrhoeae* remained high; in Denver the prevalence increased from 10.9% in 2005 to 15.7% in 2006; in Las Vegas from 5.4% in 2005 to 8.7% in 2006; in Phoenix from 7.1% in 2005 to 11.9% in 2006; in Portland from 23.1% in 2005 to 27.2% in 2006; and in Seattle from 11.6% in 2005 to 31.8% in 2006.

Increases also have continued among the Northeastern and Southern GISP sites. In Philadelphia, ciprofloxacin-resistance increased from 14.3% in 2005 to 30.3% in 2006; in Atlanta from 3.8% in 2005 to 5.7% in 2006; in Dallas from 3.2% in 2005 to 6.1% in 2006; in Greensboro from 0.6% in 2005 to 1.7% in 2006; in Miami from 9.1% in 2005 to 19.8% in 2006; in New Orleans from 6.3% in 2005 to 10.2% in 2006; and in Oklahoma City from 2.3% in 2005 to 4.3% in 2006. In Baltimore, there was a slight decrease from 3% in 2005 to 1.4% in 2006 and in Birmingham, the prevalence remained the same at 1.1%.

In the Midwest, Cleveland showed a slight increase in QRNG prevalence from 2.8% in 2005 to 3.1% in 2006; the other Midwestern GISP sites had a decrease in prevalence: Chicago from 4.7% in 2005 to 4.1% in 2006, Cincinnati from 1% in 2005 to 0.7% in 2006, and in Minneapolis from 8% in 2005 to 5.7% in 2006. In Detroit the prevalence remained the same at 0.3%.

Albuquerque identified QRNG isolates for the first time in GISP during 2006 with a QRNG prevalence of 7.3%. New York City, which started participation in GISP in 2006, had a prevalence of 7.6%.

Tripler submitted one isolate during 2006.

Resistance by Sexual Behavior: Resistance to ciprofloxacin among MSM continued to increase from 23.8% of isolates in 2004 to 29% in 2005 and 39% in 2006. Ciprofloxacin resistance also increased among heterosexuals from 2.9% in 2004 to 3.8% in 2005 and 7% in 2006 (**Figure 20**). When excluding data from Hawaii and California GISP sites, ciprofloxacin resistance among MSM continued to increase from 24.3% in 2005 to 34.3% in 2006; and among heterosexuals there was also an increase from 2.7% in 2005 to 5.4% in 2006.

Resistance with other antibiotics: Overall, 25.6% of all 2006 GISP isolates were resistant to penicillin, tetracycline, ciprofloxacin, or some combination of those antibiotics. And 7.5% (457/6,089) of isolates demonstrated resistance to ciprofloxacin, penicillin, and tetracycline (**Figure 21**).

Susceptibility to Azithromycin

Susceptibility testing for azithromycin began in 1992. **Figure 22** demonstrates MIC values for 3 years: the first year of testing, the current year, and a mid-point year (1999). The correlation of azithromycin MICs $\geq$ 0.5 μg/ml with clinical treatment failure when the 2.0 gm azithromycin dose is used to treat a gonococcal infection is not known. However, clinical treatment failures have been reported with the 1.0 gm azithromycin dose for strains with MICs of 0.125-0.5 μg/ml.[29-32]

In previous years, the azithromycin MIC for decreased susceptibility was set at $\geq$ 1.0 μg/ml. However, there was a change in the media used for agar dilution testing among all of the GISP regional laboratories throughout 2005. This media change resulted in an observational shift of the MIC curve, approximately one dilution higher. Caution is needed when interpreting the azithromycin MIC data.

In 2006, 0.2% (14/6,089) of isolates had azithromycin MIC $\geq$ 2.0 μg/ml (range, 2.0-16.0 μg/ml). The following 14 isolates with azithromycin MIC $\geq$ 2.0 μg/ml are listed by location and number of isolates detected in 2006: Dallas (1), Honolulu (1), Las Vegas (2), Minneapolis (1), Orange County (5), Philadelphia (1), Portland (1), San Francisco (1), and Seattle (1).

Susceptibility Reporting Outside of GISP

During 2006-2007, Association of Public Health Laboratories (APHL) were informally surveyed to identify state or city public health laboratories which routinely performed antimicrobial susceptibility testing of *N. gonorrhoeae*. The survey was distributed to 94 APHL labs, of which 24 stated they perform antimicrobial susceptibility testing and the results are presented in **Table 1**.

Table 1. Non-GISP antimicrobial susceptibility testing of *N. gonorrhoeae* during 2006

STD Project Area	Total # Isolates Tested	FQ S	FQ I	FQ R	Spc S	Spc R	Cfx S	Cfx DS	Cpd S	Cpd DS	Cro S	Cro DS	Azi S	Azi DS [a]
AZ	35 (m)	35	0	0	-	-	-	-	-	-	35	0	-	-
	47 (f)	46	0	1	-	-	-	-	-	-	47	-	-	-
CA (San Diego)[b]	10 (m)	5	0	5	-	-	-	-	-	-	8	0	-	-
	17(f)	14	0	3	-	-	-	-	-	-	17	0	-	-
FL	11 (u)	11	0	0	-	-	-	-	-	-	11	0	-	-
HI	88 (m)	59	6	23	-	-	-	-	88	0	88	0	88	0
	111 (f)	93	2	16	-	-	-	-	111	0	111	0	111	0
IN	1,248 (m)	1,188	5	55	-	-	-	-	-	-	1,248	0	-	-
	628 (f)	626	0	2	-	-	-	-	-	-	628	0	-	-
MA[c]	162 (m)	98	0	64	162	0	162	0	162	0	162	0	132	29
	34 (f)	29	0	5	34	0	34	0	34	0	34	0	30	5
MD	57 (m)	56	0	1	-	-	57	0	-	-	57	0	-	-
	74 (f)	73	1	0	-	-	74	0	-	-	74	0	-	-
	2 (u)	2	0	0	-	-	2	-	-	-	2	0	-	-
MI	349 (m)	327	0	22	349	0	-	-	349	0	349	0	-	-
	209 (f)	206	0	3	209	0	-	-	209	0	209	0	-	-
	7 (u)	5	0	2	7	0	-	-	7	0	7	0	-	-
MN	85 (m)	76	6	3	85	0	85	0	-	-	85	0	85	0
	3 (f)	3	0	0	3	0	3	0	-	-	3	0	3	0
MS	245 (m)	244	0	1	-	-	-	-	-	-	245	0	-	-
	15 (f)	13	0	2	-	-	-	-	-	-	15	0	-	-
	2 (u)	2	0	0	-	-	-	-	-	-	2	-	-	-
MT	7 (m)	3	0	4	7	0	7	0	-	-	7	0	4	3
	5 (f)	4	0	1	5	0	5	0	-	-	5	0	5	0
NH	20 (m)	5	1	14	20	0	14	0	-	-	20	0	10	2
	4 (f)	4	0	0	4	0	3	0	-	-	4	0	3	0
NJ	80 (m)	75	0	5	80	0	80	0	-	-	80	0	-	-
	20 (f)	19	0	1	20	0	20	0	-	-	20	0	-	-
NYC	298 (m)	242	3	53	262	0	259	0	-	-	298	0	293	0
	59 (f)	59	0	0	55	0	53	0	-	-	59	0	59	0
NY (Erie County)	104 (m)	101	0	3	104	0	104	0	-	-	104	0	103	1
	73 (f)	72	0	1	73	0	73	0	-	-	73	0	73	0

STD Project Area	Total # Isolates Tested	FQ S	FQ I	FQ R	Spc S	Spc R	Cfx S	Cfx DS	Cpd S	Cpd DS	Cro S	Cro DS	Azi S	Azi DS [a]
NY State (Wadsworth)	94 (m)	89	0	5	94	0	-	-	-	-	94	0	-	-
	32 (f)	31	0	1	32	0	-	-	-	-	32	0	-	-
OR[d]	91 (m)	52	5	34	-	-	-	-	-	-	-	-	-	-
	56 (f)	50	1	5	-	-	-	-	-	-	-	-	-	-
PA	5 (m)	1	0	4	5	0	5	0	-	-	5	0	5	0
	1 (f)	1	0	0	1	0	1	0	-	-	1	0	1	0
PR	1	1	0	0	1	0	-	-	-	-	-	-	-	-
TX	1	1	0	0	-	-	-	-	-	-	1	0	-	-
UT	101 (m)	92	0	9	-	-	-	-	-	-	101	0	-	-
	34 (f)	34	0	0	-	-	-	-	-	-	34	0	-	-
	1 (u)	-	-	-	-	-	-	-	-	-	1	0	-	-
VA	3 (m)	1	0	2	3	0	3	0	-	-	3	0	1	2
	1 (f)	0	0	1	1	0	1	0	-	-	1	0	0	1
WA[d] (Seattle)	315(m)	175	27	113	-	-	-	-	-	-	-	-	-	-
	134(f)	74	35	25	-	-	-	-	-	-	-	-	-	-
	18 (u)	10	2	6										
WI (Milwaukee)	674 (m)	644	0	30	674	0	-	-	-	-	674	0	668	6
	64 (f)	61	2	1	64	0	-	-	-	-	64	0	63	1
	1 (u)	1	0	0	1	0	-	-	-	-	1	0	1	0
Total[e]	**5,736**	**5,113**	**96**	**526**	**2,355**	**0**	**1,045**	**0**	**960**	**0**	**5,119**	**0**	**1,738**	**50**

Key:

- m = male; f = female; u = unknown gender
- FQ=fluoroquinolone; Spc=spectinomycin; Cfx=cefixime; Cpd=cefpodoxime; Cro=ceftriaxone; Azi=azithromycin
- S=susceptible; DS=decreased susceptibility; I=intermediate resistant; R=resistant.
- Cells containing only "-" indicate that the antibiotic for that column was not tested.

[a] For this table, AziDS is defined as an isolate with azithromycin disk inhibition zone size < 30mm or minimum inhibitory concentration (MIC) ≥ 1.0 µg/ml.

[b] San Diego tested all isolates against ofloxacin, rather than against ciprofloxacin.

[c] Massachusetts used zone size of < 31 mm as marker for decreased susceptibility to azithromycin, < 29 as a marker for resistance to cefpodoxime, and < 35 as a marker for resistance to ceftriaxone.

[d] Oregon and Washington state public health labs do not perform antimicrobial susceptibility testing for GC, this data was received from tests performed at the University of Washington in Seattle, Washington.

[e] Some laboratories did not always test the same number of isolates for each antibiotic. For example, New Hampshire and New York City only performed susceptibility testing on a subset of isolates. Utah had one isolate that was tested for ceftriaxone susceptibility only.

Observation

In 2006-2007, Association of Public Health Laboratories (APHL) and other public health laboratories were informally surveyed to determine the number of state and city public health laboratories that routinely performed antimicrobial susceptibility testing of *N. gonorrhoeae*. These isolates are not representative of the gonorrhea patient population but rather a convenience sample of patients who happen to undergo culture rather than non-culture testing.

Testing methodology used by most of the labs for susceptibility testing was either by disk diffusion or E-test. The survey was distributed to 94 labs, of which 86.2% (81/94) responded and revealed that 29.6% (24/81) labs performed GC susceptibility testing. Data from 5,736 isolates were collected from these 24 labs (**Table 1**). In addition, in contrast to GISP, multiple non-GISP isolates from various anatomic sites may be submitted from a single patient, so the 5,736 non-GISP isolates are likely to represent fewer than 5,736 patients with gonorrhea. Furthermore, the public health laboratories did not always test for resistance with the same antibiotics used in GISP.

The survey revealed that 9.2% (526/5,736) of non-GISP isolates were resistant to ciprofloxacin or ofloxacin. Gender information was available for 5,692 of the 5,736 (99.2%) isolates. Of those, 71.5% (4,071/5,692) were male and 28.5% (1,621/5,692) female. QRNG was found among 11.1% (450/4,071) of all male isolates and 4.2% (68/1,621) of female isolates. In addition, 2.9% (50/1,738) of isolates had decreased susceptibility to azithromycin (as defined by an MIC $\geq$ 1.0 μg/ml in this survey). No resistance was found in the other antibiotics tested.

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We would also like to thank Anthony Tran of the Association of Public Health Laboratories for his assistance with the 2006 survey.

Additional Resources

GISP data was presented at the 17th International Society for STD Research in Seattle, Washington on July 31st, 2007.[33]

Additional information on GISP, as well as useful resources and links, may be found on the: CDC DSTDP Antimicrobial Resistant Gonorrhea website: **http://www.cdc.gov/std/Gonorrhea/arg/default.htm.**

Other United States surveillance data on *N. gonorrhoeae* and other STDs may be found on the CDC DSTDP Surveillance and Statistics website: **http://www.cdc.gov/nchstp/dstd/Stats_Trends/Stats_and_Trends.htm.**

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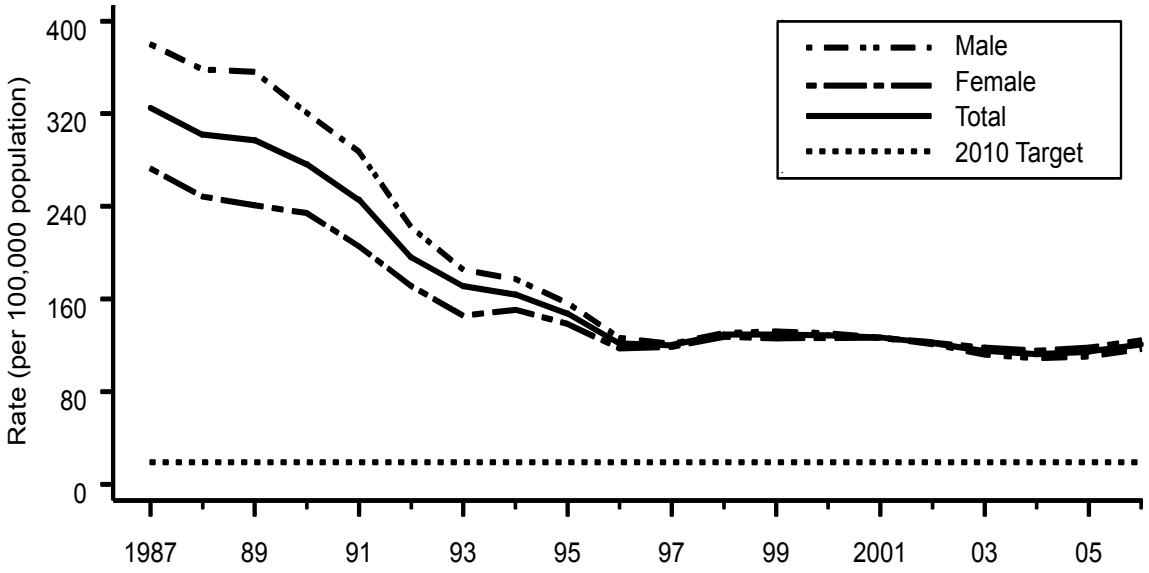
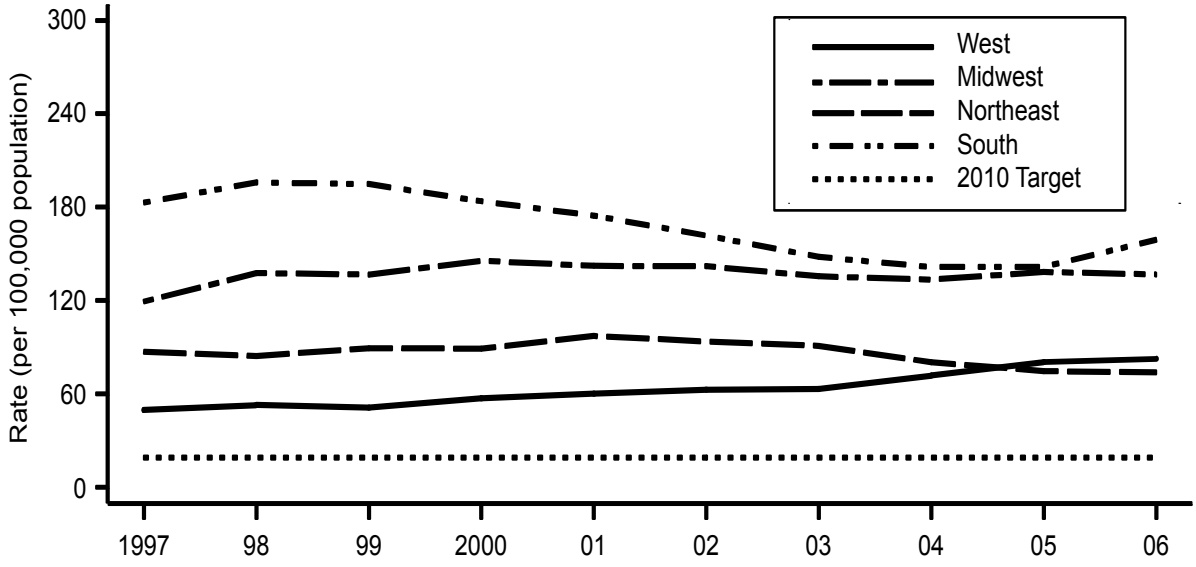
Figure 1. Gonorrhea — Rates: Total and by sex: United States, 1987–2006 and the Healthy People 2010 target



Note: The Healthy People 2010 target for gonorrhea is 19.0 cases per 100,000 population.

Figure 2. Gonorrhea — Rates by region: United States, 1997-2006 and the Healthy People 2010 target



Note: The Healthy People 2010 target for gonorrhea is 19.0 cases per 100,000 population.

Figure 3. Gonorrhea — Rates by race and ethnicity: United States, 1997–2006

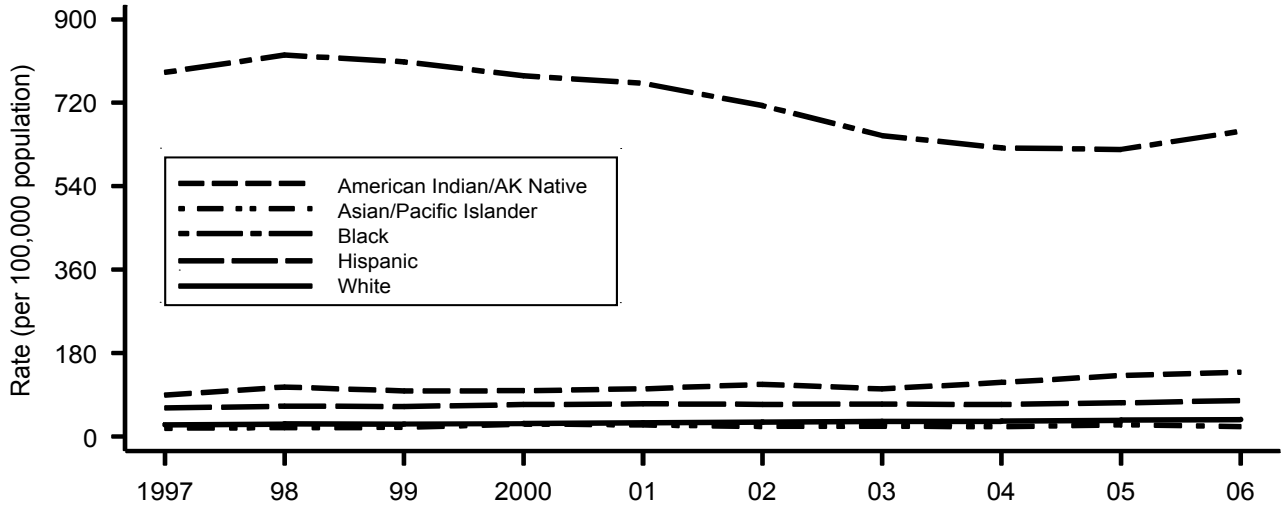


Figure 4. Gonorrhea — Age- and gender-specific rates: United States, 2006

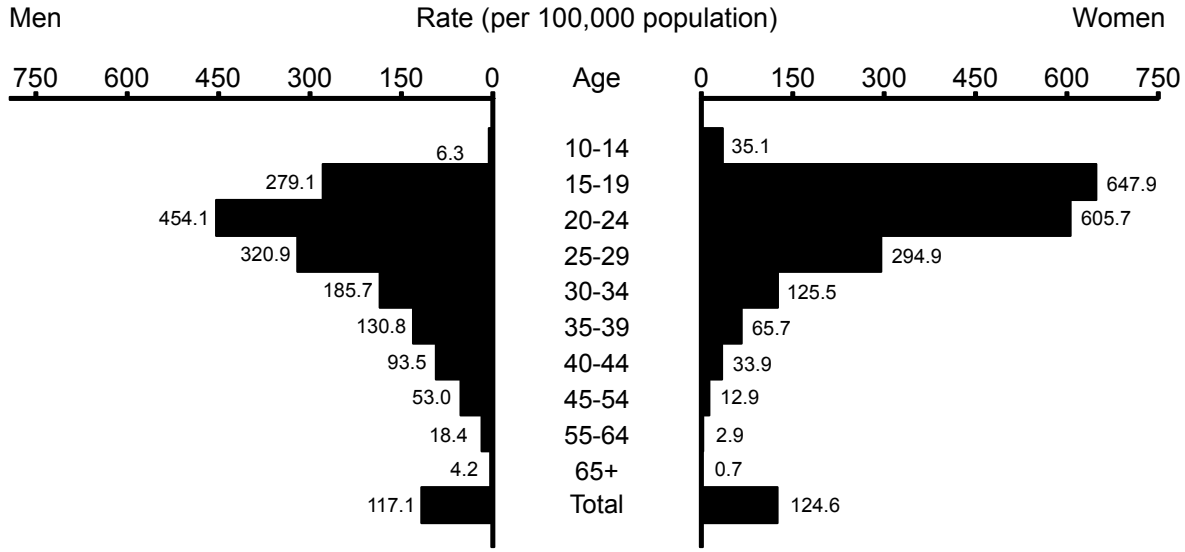
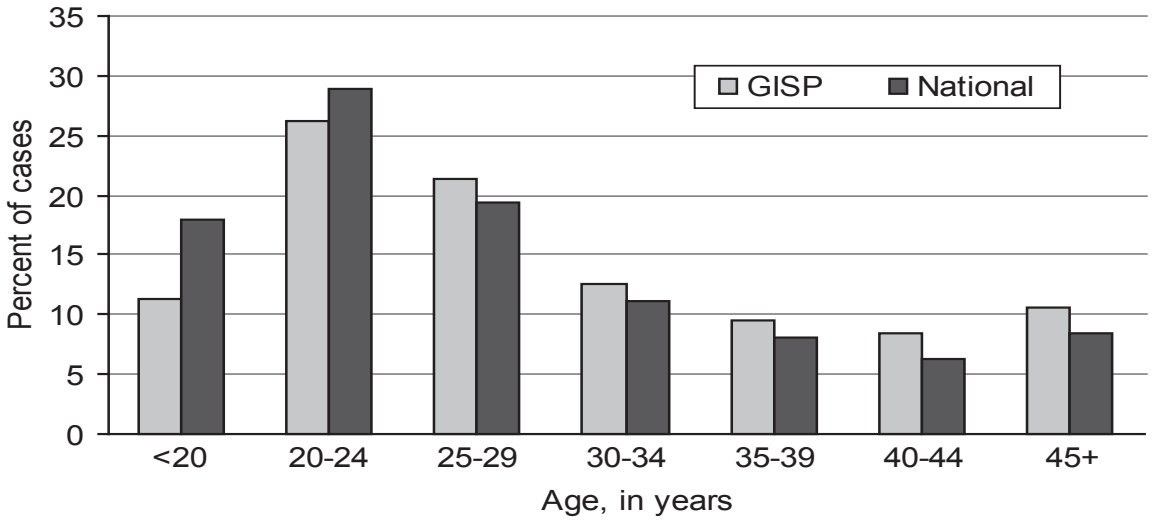


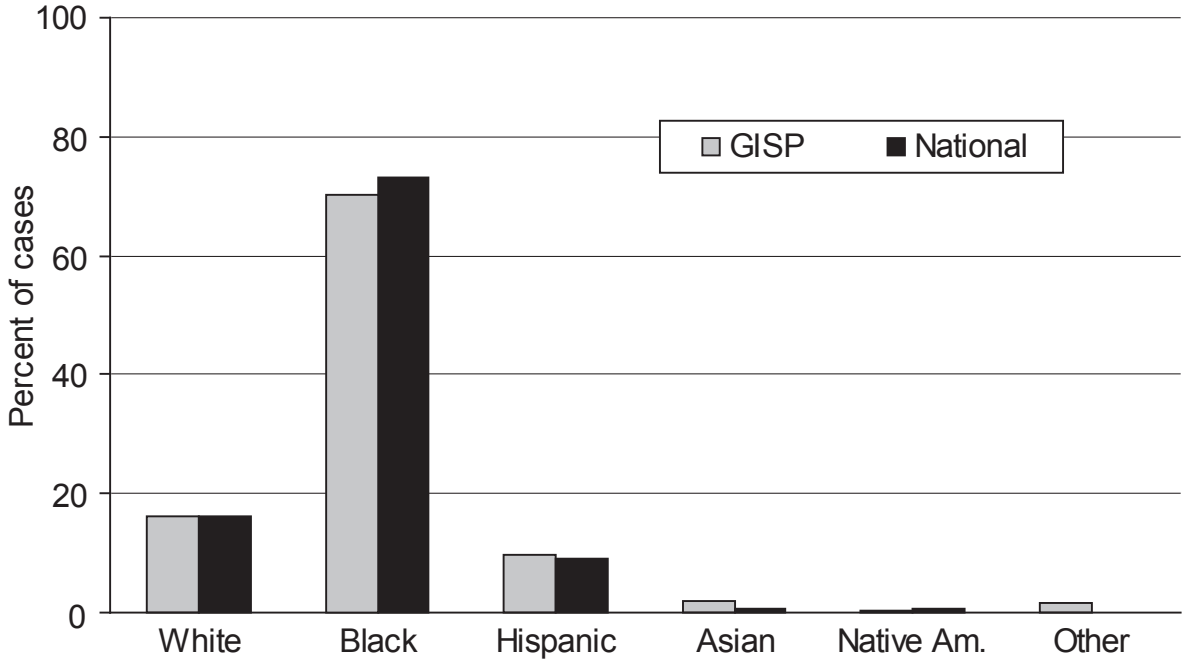
Figure 5. Location of participating GISP clinics and regional laboratories: United States, 2006

Figure 6. Age distribution of GISP participants and nationally reported gonorrhea cases in men, 2006



Note: The age < 20 category includes ages 10-19 for national cases, and ages 13-19 for GISP; 98.7% in GISP are ages 15-19 and for national cases, 97.8% are ages 15-19.

Figure 7. Race distribution of GISP participants and nationally reported cases of gonorrhea in men, 2006



Note: Asian includes Native Hawaiians and Pacific Islanders. Other includes participants who selected more than one race category. However, the "Other" category is not used in national gonorrhea reporting.

Figure 8. Gonorrhea — Percentage of GISP cases that occurred among men who have sex with men (MSM), 1988–2006

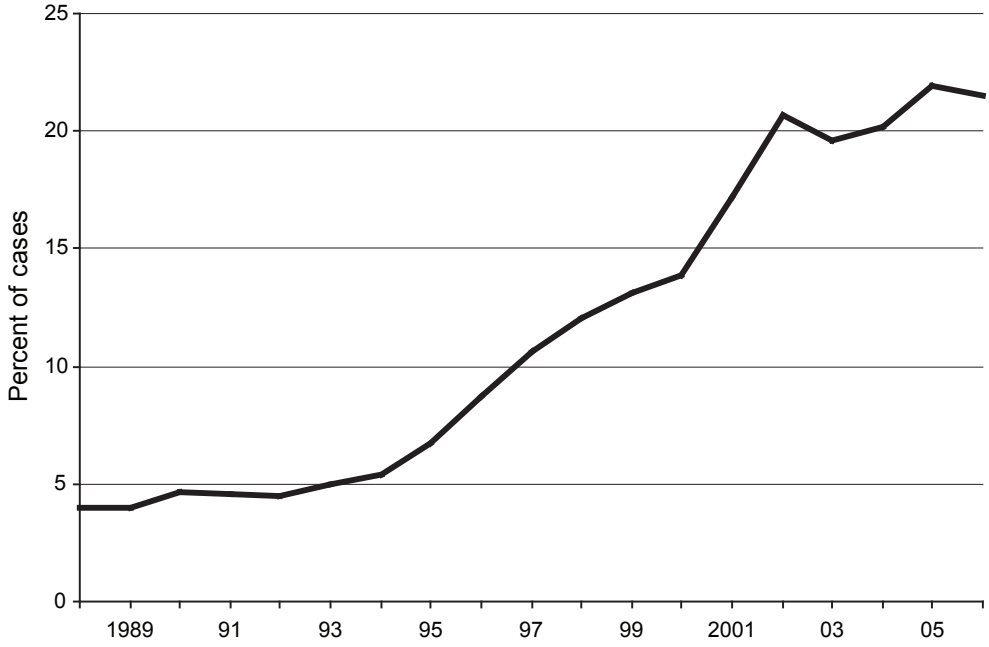
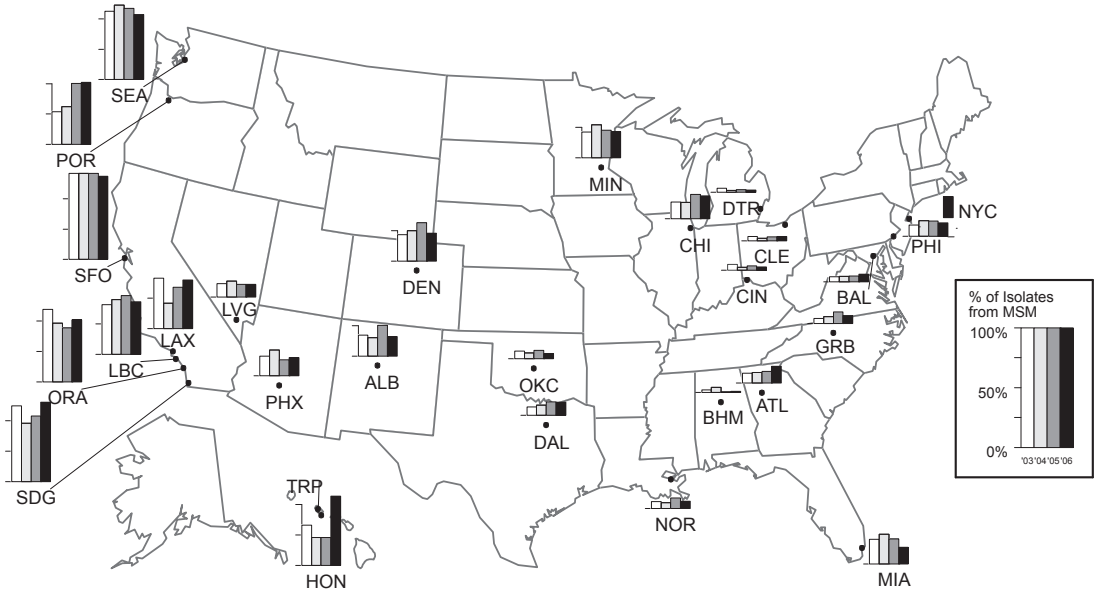
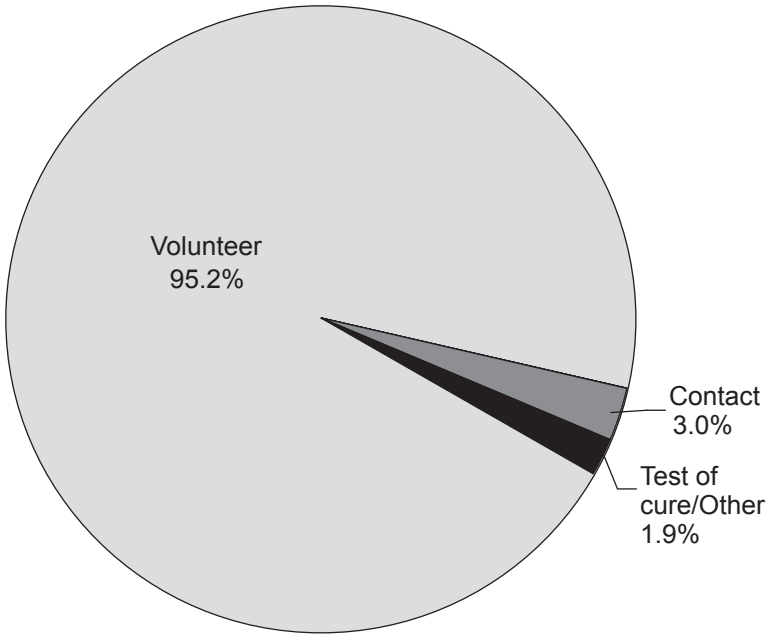


Figure 9. Percent of GISP isolates obtained from MSM attending STD clinics, 2003–2006



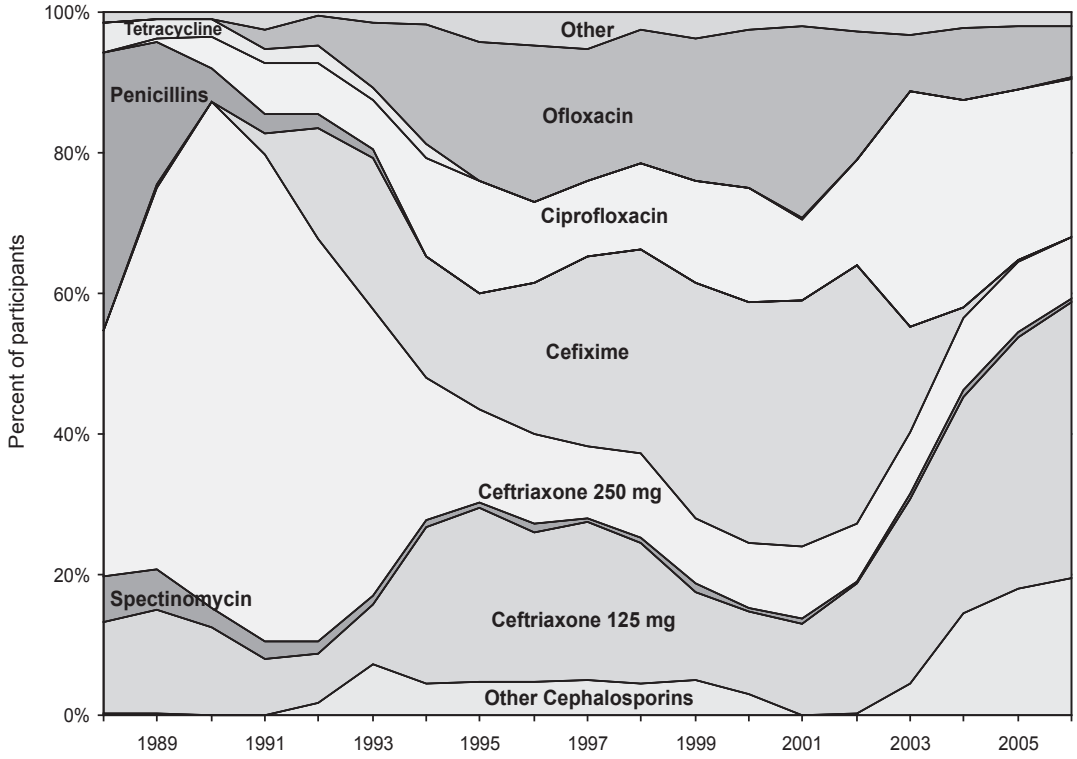
Note: Not all clinics participated in GISP for the last 4 years. Clinics include: ALB=Albuquerque, NM; ATL=Atlanta, GA; BAL=Baltimore, MD; BHM=Birmingham, AL; CHI=Chicago, IL; CIN=Cincinnati, OH; CLE=Cleveland, OH; DAL=Dallas, TX; DEN=Denver, CO; DTR=Detroit, MI; GRB=Greensboro, NC; HON=Honolulu, HI; LAX=Los Angeles, CA; LBC=Long Beach, CA; LVG=Las Vegas, NV; MIA=Miami, FL; MIN=Minneapolis, MN; NOR=New Orleans, LA (restarted in October 2006); NYC=New York City, NY (started in August 2006); OKC=Oklahoma City, OK; ORA=Orange County, CA; PHI=Philadelphia, PA; PHX=Phoenix, AZ; POR=Portland, OR; SDG=San Diego, CA; SEA=Seattle, WA; SFO=San Francisco, CA; and TRP=Tripler Army Medical Center, HI (does not provide sexual risk behavior data).

Figure 10. Reason for clinic attendance among GISP participants, 2006



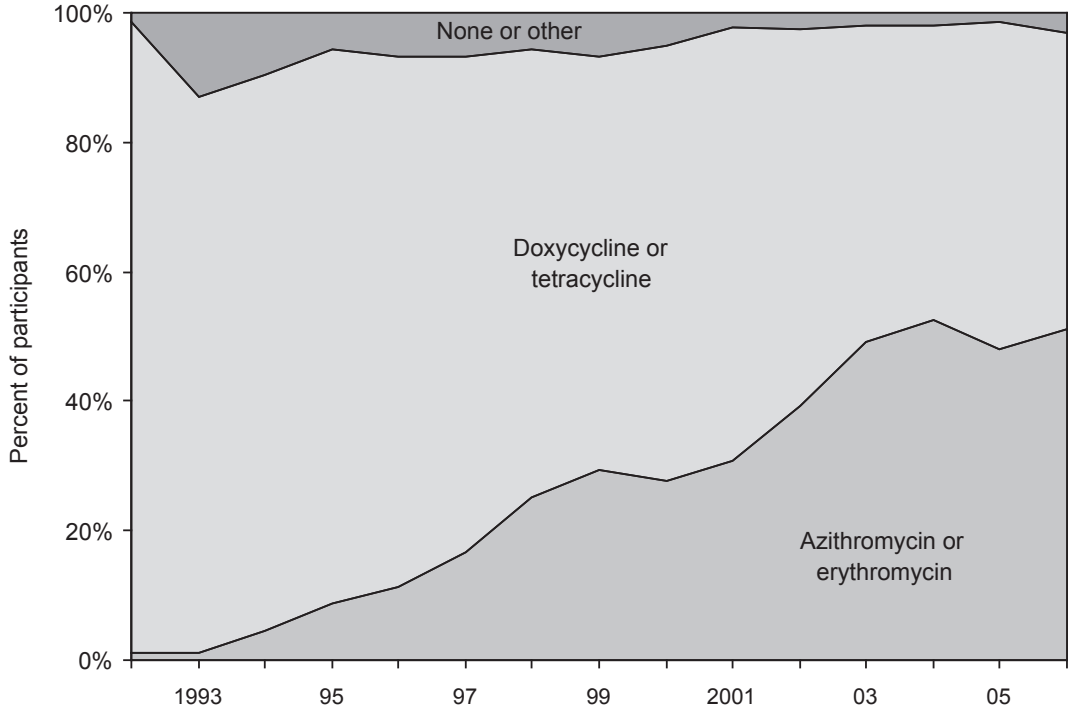
Note: Contact=has sexual partner with gonorrhea.

Figure 11. Drugs used to treat gonorrhea in GISP participants, 1988–2006



Note: For 2006, "Other" includes no therapy (1.3%), azithromycin 2 g (0.5%), levofloxacin (0.1%), and other less frequently used drugs.

Figure 12. Drugs used to treat *Chlamydia trachomatis* infection in GISP participants, 1992–2006



Note: For each year, "Other" accounted for only 0 - 0.9% of C. trachomatis treatment and erythromycin accounted for only 0.1 – 2.1% of C. trachomatis treatment.

Figure 13. Plasmid-mediated resistance to penicillin and tetracycline among GISP isolates, 1988–2006

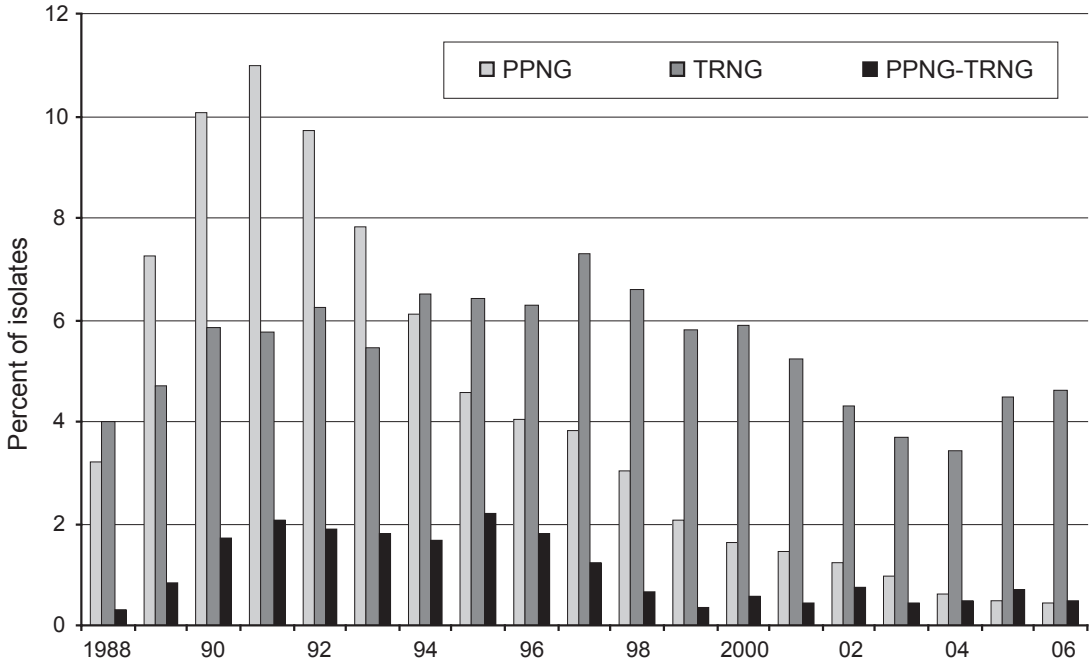


Figure 14. Chromosomally mediated resistance to penicillin and tetracycline among GISP isolates, 1988–2006

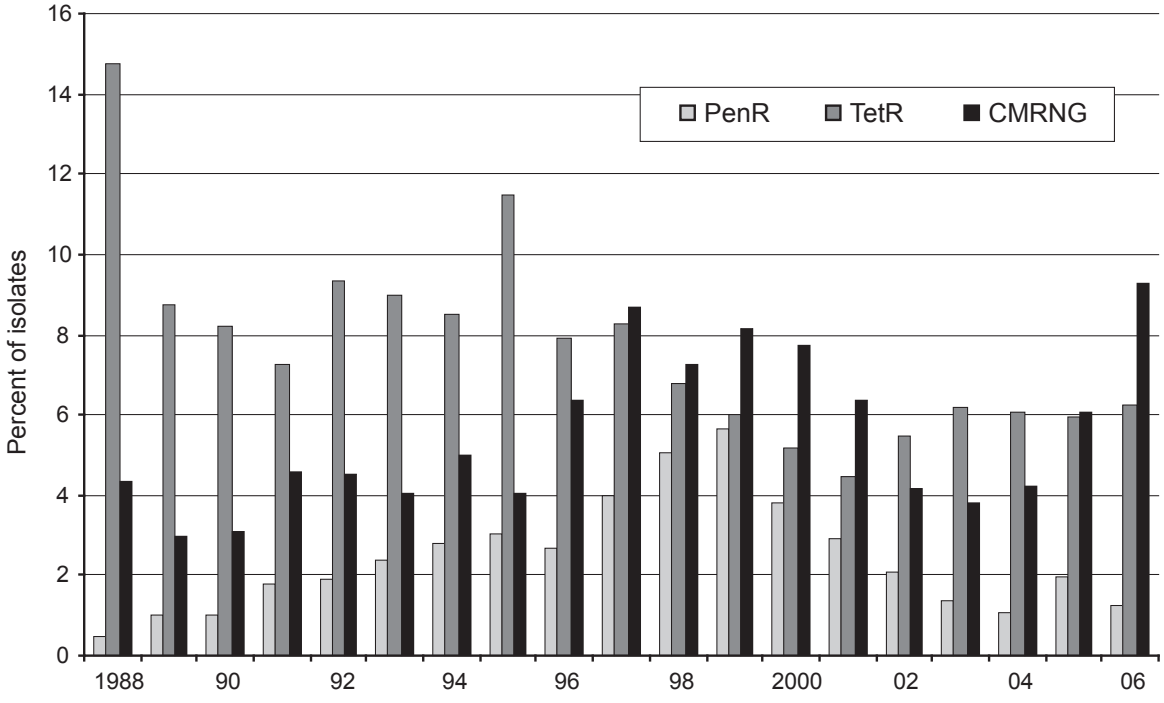
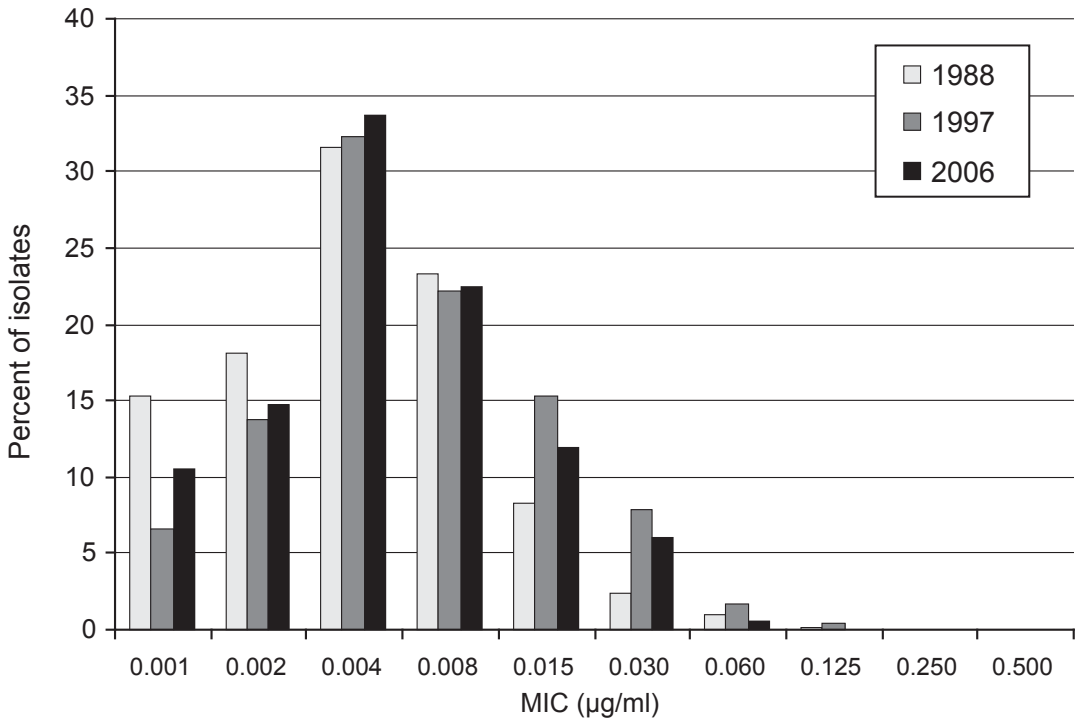
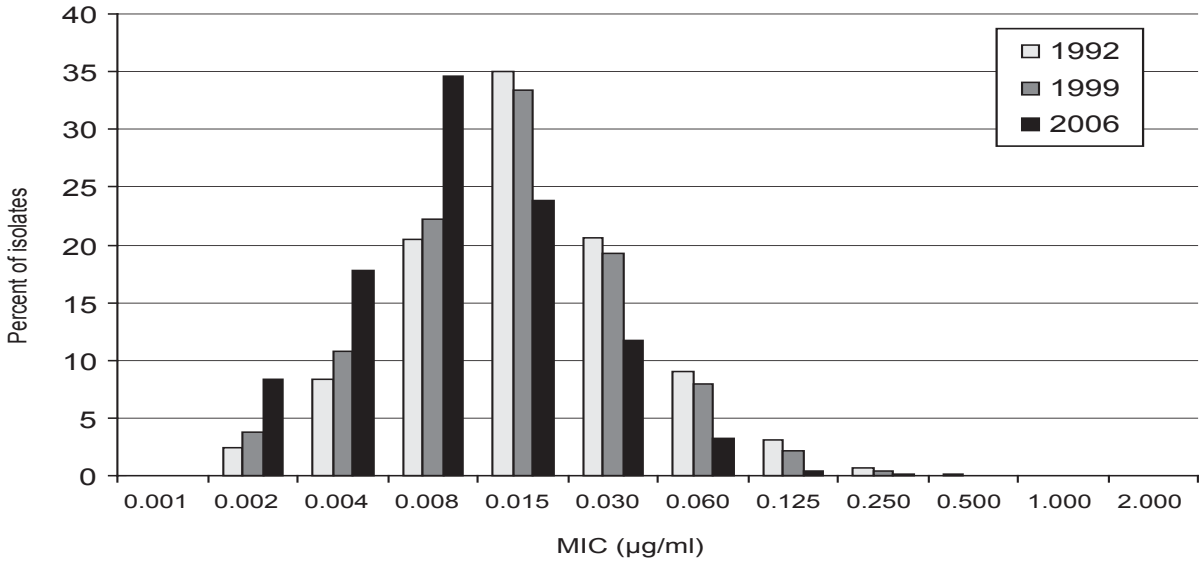


Figure 15. Distribution of MICs to ceftriaxone among GISP isolates, 1988, 1997, and 2006



Note: In 1988, there was one isolate with MIC 0.25 µg/ml. In 1997, there were three isolates with MIC 0.25 µg/ml and one isolate with MIC 0.5 µg/ml. In 2006, there were no isolates with MIC > 0.125 µg/ml.

Figure 16. Distribution of MICs to cefixime among GISP isolates, 1992, 1999, and 2006



Note: In 1992, there were six isolates with MIC 0.5 µg/ml, three isolates with MIC 1.0 µg/ml, and two isolates with MIC 2.0 µg/ml. In 1999, there were no isolates with MIC > 0.25 µg/ml. In 2006, there was one isolate with MIC 0.5 µg/ml.

Figure 17. Percentage of GISP isolates with intermediate resistance or resistance to ciprofloxacin, 1990–2006

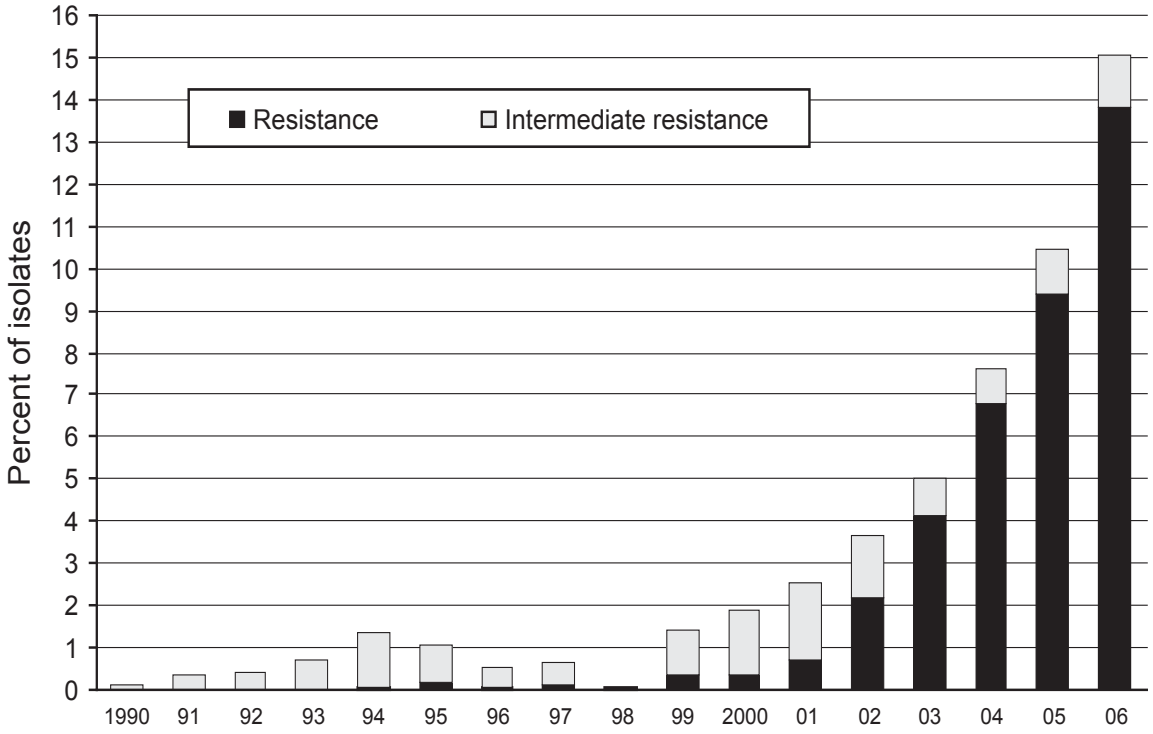
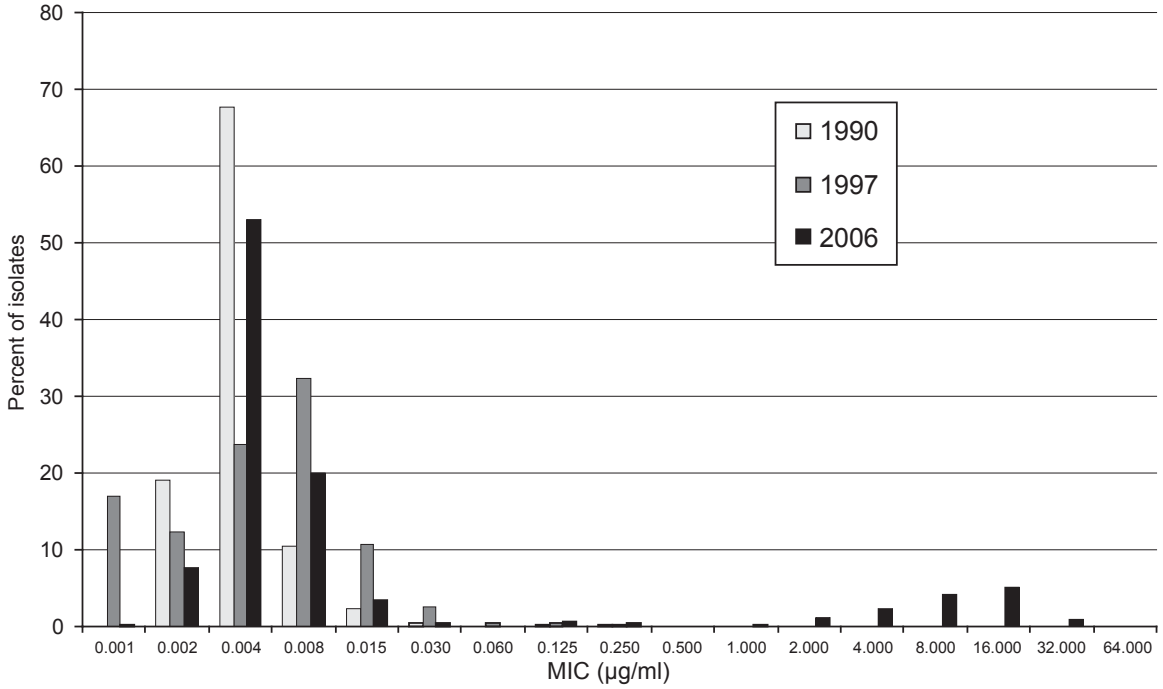
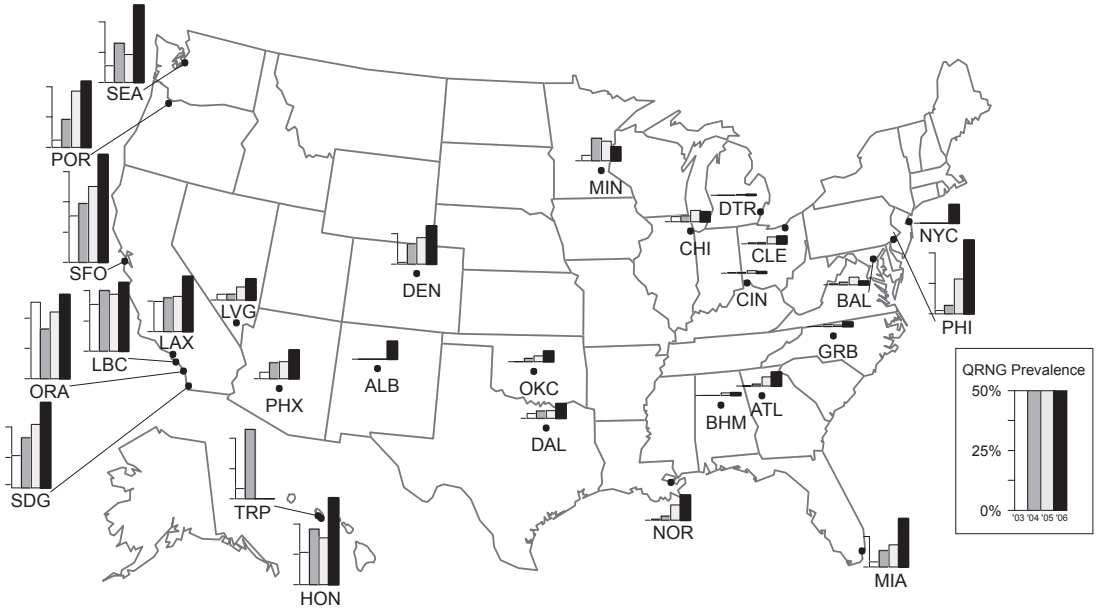


Figure 18. Distribution of MICs to ciprofloxacin among GISP isolates, 1990, 1997, and 2006



Note: In 1990, there were no isolates with MIC > 0.25 µg/ml. In 1997, there was one isolate with MIC 0.5 µg/ml, one isolate with MIC 1.0 µg/ml, two isolates with MIC 2.0 µg/ml, and two isolates with MIC 16.0 µg/ml. In 2006, there were four isolates with MIC 0.5 µg/ml, eight isolates with MIC 1.0 µg/ml, 66 isolates with MIC 2.0 µg/ml, 141 isolates with MIC 4.0 µg/ml, 260 isolates with MIC 8.0 µg/ml, 315 isolates with MIC 16.0 µg/ml, 52 isolates with MIC 32.0 µg/ml, and one isolate with MIC 64.0 µg/ml.

Figure 19. Prevalence of ciprofloxacin resistant *Neisseria gonorrhoeae* by GISP site, 2003–2006



Note: Not all clinics participated in GISP for the last 4 years. Clinics include: ALB=Albuquerque, NM; ATL=Atlanta, GA; BAL=Baltimore, MD; BHM=Birmingham, AL; CHI=Chicago, IL; CIN=Cincinnati, OH; CLE=Cleveland, OH; DAL=Dallas, TX; DEN=Denver, CO; DTR=Detroit, MI; GRB=Greensboro, NC; HON=Honolulu, HI; LAX=Los Angeles, CA; LBC=Long Beach, CA; LVG=Las Vegas, NV; MIA=Miami, FL; MIN=Minneapolis, MN; NOR=New Orleans, LA (restarted in October 2006); NYC=New York City, NY (started in August 2006); OKC=Oklahoma City, OK; ORA=Orange County, CA; PHI=Philadelphia, PA; PHX=Phoenix, AZ; POR=Portland, OR; SDG=San Diego, CA; SEA=Seattle, WA; SFO=San Francisco, CA; and TRP=Tripler Army Medical Center, HI.

Figure 20. Percentage of GISP isolates with resistance to ciprofloxacin by sexual behavior, 2001–2006

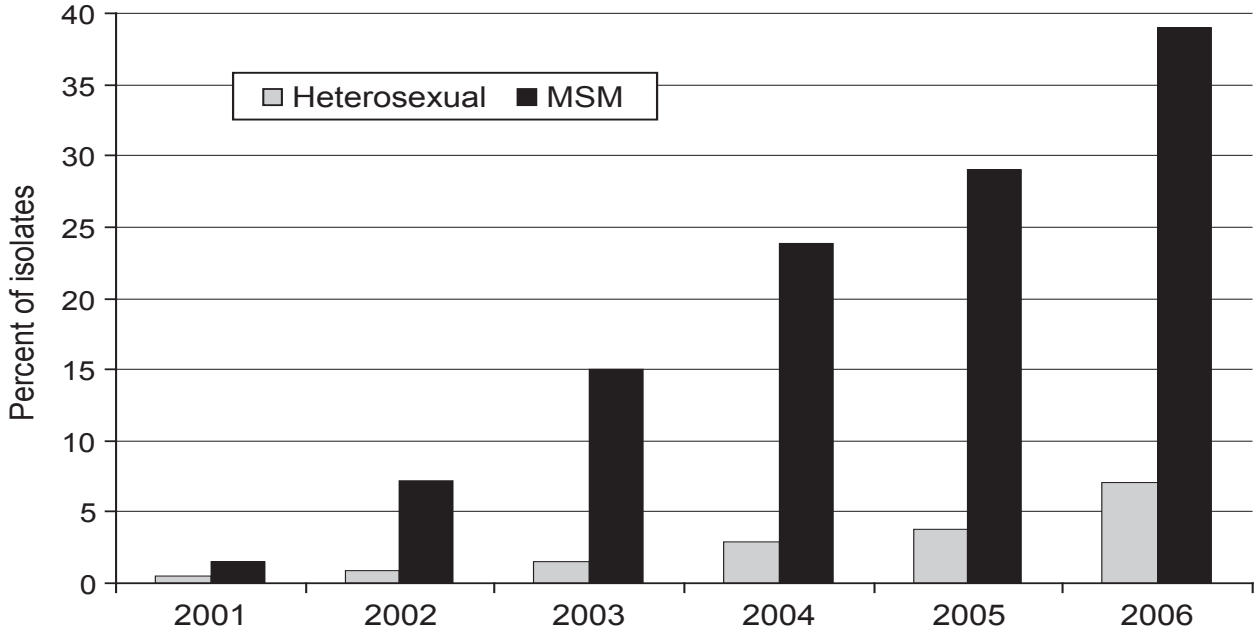
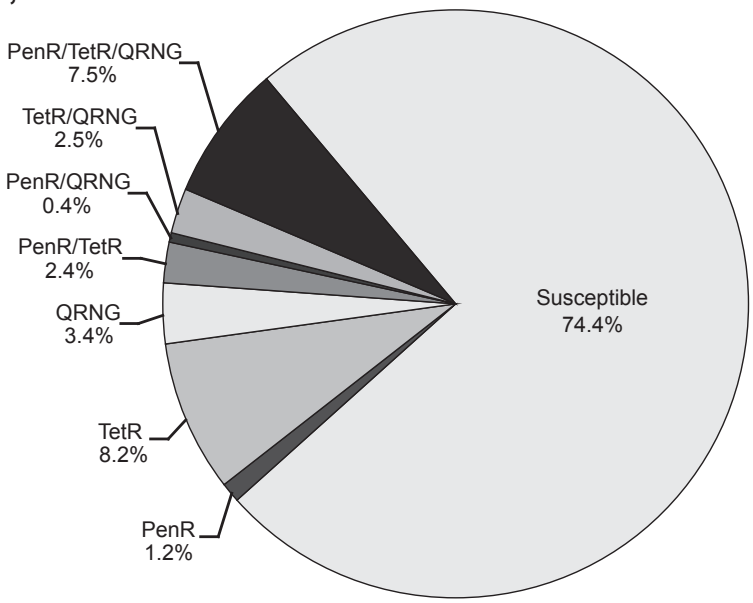
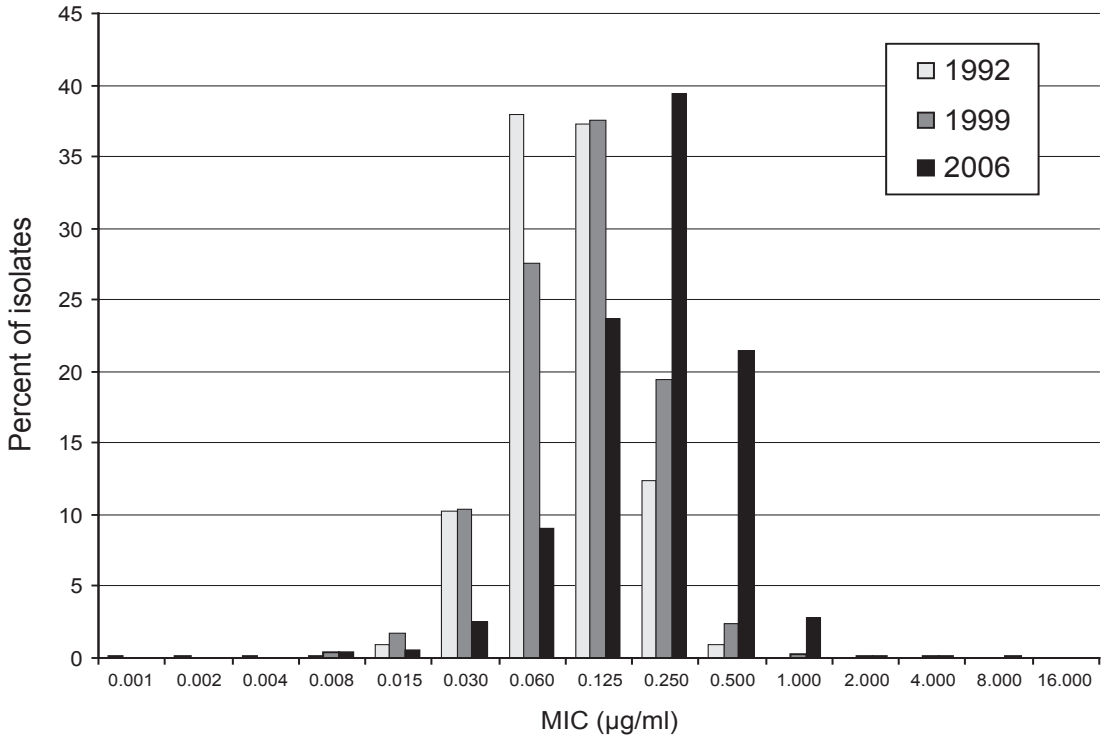


Figure 21. Penicillin, tetracycline, and ciprofloxacin resistance among GISP isolates, 2006



PenR = penicillinase-producing *N. gonorrhoeae* and chromosomally mediated penicillin-resistant *N. gonorrhoeae*
TetR = chromosomally and plasmid mediated tetracycline-resistant *N. gonorrhoeae*
QRNG = ciprofloxacin resistant *N. gonorrhoeae*

Figure 22. Distribution of MICs to azithromycin among GISP isolates, 1992, 1999, and 2006



Note: In 1992, there were no isolates with MIC > 0.5 µg/ml. In 1999, there were 11 isolates with MIC 1.0 µg/ml, eight isolates with MIC 2.0 µg/ml, five isolates with MIC 4.0 µg/ml, and one isolate with MIC 8.0 µg/ml. In 2006, there were four isolates with MIC 2.0 µg/ml, four isolates with MIC 4.0 µg/ml, five isolates with MIC 8.0 µg/ml, and one isolate with MIC 16.0 µg/ml.