Sexually Transmitted Disease Surveillance 2007 Supplement

Gonococcal Isolate Surveillance Project (GISP) Annual Report 2007

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/GISP2007/** To view the Clinic Profiles, please use the drop down boxes on **http://www.cdc.gov/std/GISP2007/**

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 – 2007

Introduction

Gonorrhea is the second most frequently reported communicable disease in the United States.[1]

In 2007, 355,991 gonorrhea cases were reported in the United States.[1] Gonorrhea rates in the United States declined 74.3% from 1975 through 1997 following the implementation of national gonorrhea control programs in the mid-1970's.[2,3] Then for the next 10 years, gonorrhea rates appeared to plateau. However, in the past two years until 2007, rates had slightly increased until this year. In 2007, there were 118.9 cases per 100,000 persons in 2007 which is a decrease of 0.7% from 2006.[4] Among women and men, the gonorrhea rates have been relatively similar for over 10 years, with a slightly higher rate among women in the past 6 years (**Figure 1**).[1] Overall, in 2007 the rate of gonorrhea is still high and persists in some geographic areas, among all race/ethnic groups except Asian/Pacific Islanders, and among adolescents and young adults (**Figures 2, 3** and **4**).[1]

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]

In addition, 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.[11-13] 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.[15] Currently, the CDC recommended treatment for gonococcal infections is limited to a single class of drugs, the cephalosporins.

Additional information on gonorrhea surveillance may be found in the 2007 CDC *Sexually Transmitted Disease Surveillance Report*.[1]

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 and their state/local public health authorities, GISP regional laboratories, and the Centers for Disease Control and Prevention (CDC).

In GISP during 2007, *N. gonorrhoeae* isolates were collected monthly from the first 25 men with urethral gonorrhea attending STD clinics. 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, 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] Note that cefixime was discontinued in 2007 from the GISP antimicrobial susceptibility panel.

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 2000, 2004, and 2007.[11-13,15,23-26]

2007 GISP Sites and Regional Labs

In 2007, 30 sentinel sites contributed 6,009 gonococcal isolates in GISP (**Figure 5**). Fifteen of 30 sites (50%) have participated continuously since 1987: Albuquerque, Atlanta, Baltimore, Birmingham, Cincinnati, Denver, Honolulu, Long Beach

(discontinued in November 2007), New Orleans, Philadelphia, Phoenix, Portland, San Diego, San Francisco, and Seattle. The other fifteen GISP sites joined in the following years: Chicago (1996), Cleveland (1991), Dallas (2000), Detroit (2003), Greensboro (2002), Kansas City (1991-2001, 2007), Los Angeles (2003), Las Vegas (2002), Miami (1998), Minneapolis (1992), New York City (2006), Oklahoma City (2003), Orange County (1991), Richmond (2007) and Tripler (2001). The five GISP regional laboratories in 2007 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 2007 is shown in **Figure 6**. In 2007, 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 14 to 78 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 2007 is shown in **Figure 7**. Hispanic and Asian males were slightly over represented in GISP while African-American males were slightly under represented compared with the race/ethnicity distribution of nationally reported male gonorrhea patients in 2007.

Sexual Orientation: The proportion of GISP participants who were MSM has steadily increased for most years. In 2007, the proportion increased to 22.4% from 21.5% in 2006 (**Figure 8**). Additionally, the proportion of isolates from MSM has varied geographically with the largest percentage from the West Coast sites (**Figure 9**).

Reason for Clinic Attendance: Most (94.6%) GISP participants in 2007 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 from 1999 to 2007.

Report of Symptoms: In 2007, 97.5% of GISP participants reported dysuria and/or urethral discharge; 2.6% 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 49.7% in 2007. The percentage of GISP participants with a documented previous episode of gonorrhea in the last 12 months was 21.2% in 2007. These percentages have also been relatively stable over time.

Supplemental Patient Data: The proportion of GISP participants who were HIV-positive during 2007 was 7.9% (331/4,208). Of 1,050 MSM reporting HIV testing information, 273 (26%) were HIV positive; 1.8% (56/3,134) of heterosexuals were HIV positive. During the 60 days prior to diagnosis of gonorrhea, GISP patients reported the following behaviors:

- 5.6% (237/4,243) took antibiotics;
- 8.4% (281/3,350) traveled outside the state where the sentinel site is located;
- 1.4% (54/3,757) used injection recreational drugs;
- 26.1% (933/3,569) used non-injection recreational drugs
- 2% (69/3,429) 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 has increased to 81% in 2007 from 67.7% in 2006. Specifically, 61.5% were treated with ceftriaxone in 2007 compared with 48.1% in 2006. Conversely, the proportion of GISP patients being treated with fluoroquinolones (ciprofloxacin, ofloxacin or levofloxacin) has dramatically decreased to 17.1% in 2007 from 30% in 2006. Treatment with azithromycin has slightly increased to 0.8% in 2007 from 0.5% 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/tetracycline decreased from 45.7% in 2006 to 40% in 2007; the proportion treated with azithromycin or erythromycin has increased from 51.1% in 2006 to 58.2% in 2007.

Susceptibility to Antimicrobial Agents

GISP 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)
*Azithromycin, MIC ≥ 2.0 µg/ml (decreased susceptibility)

The criteria listed are used in the GISP protocol.[27]
*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

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 2007. The percentage of isolates that were PPNG declined annually from a peak of 11.0% in 1991 to 0.4% in 2007. The prevalence of TRNG peaked in 1997 at 7.3% and had been decreasing for several years. However since 2005, it has been slightly increasing from 4.5% to 4.6% in 2006, and 5.6% in 2007. The prevalence of PPNG-TRNG has continued to be low for the last several years and in 2007, it was 0.5%.

Figure 14 shows chromosomally mediated resistance to penicillin and tetracycline among GISP isolates from 1988 to 2007. The percentage of PenR isolates increased annually from 0.5% in 1988 to 5.7% in 1999. It subsequently decreased to 1% in 2004 and then increased slightly to 2.2% in 2007. TetR prevalence for 2007 was 5.1%. The prevalence of CMRNG has stayed the same at 9.3% in 2007.

Susceptibility to Spectinomycin

All isolates were susceptible to spectinomycin in 2007. 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 1987. **Figure 15** demonstrates MIC values for three years: the first year of testing, the current year, and a mid-point year (1997). Note that in 2007 the majority of antimicrobial susceptibility tests for ceftriaxone started at a minimum MIC of 0.008 μg/ml. 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 2007.

Susceptibility to Cefixime

Susceptibility testing for cefixime began in 1992 and was discontinued from the GISP antibiotic panel in 2007. In total from 1992 to 2007, 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

Susceptibility testing for ciprofloxacin began in 1990. A total of 16.1% (968/6,009) of isolates exhibited intermediate resistance or resistance to ciprofloxacin in 2007. This is an increase when compared to 2006 in

compared to 2006 in which 15.1% (918/6,089) of isolates showed intermediate resistance or resistance to ciprofloxacin (**Figure 16**). **Figure 17** demonstrates MIC values for ciprofloxacin for 3 years: the first year of testing, the current year, and a mid-point year (1998). Note that in 2007 the majority of antimicrobial susceptibility tests for ciprofloxacin started at a minimum MIC of 0.008 µg/ml.

Intermediate resistance: In 2007, 1.3% (77/6,009) of all GISP isolates exhibited intermediate resistance to ciprofloxacin, which is a slight increase from 1.2% (75/6,089) in 2006.

Resistance: Eight hundred and ninety-one, or 14.8% of GISP isolates were resistant to ciprofloxacin (MICs ≥ 1.0 µg/ml) in 2007. Ciprofloxacin-resistant isolates were identified in all 29 sites that submitted isolates to GISP in 2007. GISP did not receive any isolates from Tripler in 2007.

Resistance by Location/ Regions: The prevalence of ciprofloxacin resistant *N. gonorrhoeae* at each 2007 GISP site from the years 2004 to 2007 is shown in **Figure 18**. Overall in 2007, QRNG increased most markedly in those regions where prevalence had been relatively low.

From 2006 to 2007, several Western sites demonstrated increases in the number of isolates resistant to ciprofloxacin. In Albuquerque, the prevalence of QRNG more than doubled to 16.7% of isolates collected in 2007 from 7.3% in 2006; in Denver, 17% were resistant to fluoroquinolones in 2007 compared with 15.7% in 2006; in Las Vegas, the prevalence also doubled to 18.7% in 2007 from 8.7% in 2006; in Long Beach, 30.4% were resistant in 2007 compared to 28.4% in 2006; in Orange County, 41% were resistant in 2007 compared with 34.6% in 2006; in Portland, 28.6% were resistant in 2007 compared with 27.2% in 2006; and in San Diego, 36.3% were resistant in 2007 compared with 35.1% in 2006. The prevalence in Los Angeles remained the same at 22.4% in 2007. In other Western sites such as Phoenix, San Francisco, and Seattle, the prevalence of QRNG decreased slightly during the same time period. In Phoenix, 8.7% of isolates were QRNG compared to 11.9% in 2006; in San Francisco, it decreased to 31.3% in 2007 from 44.5% in 2006; and in Seattle to 29.3% in 2007 from 31.8% in 2006.

Twenty (28.6%) of 70 isolates submitted from Honolulu in 2007 demonstrated ciprofloxacin-resistance, a decrease from 34 (35.8%) of 95 isolates in 2006.

In the South from 2006 to 2007, most of the sites continued to observe increases in the prevalence of QRNG. In Baltimore, QRNG resistance increased to 2% in 2007 from 1.4% in 2006; in Birmingham, the prevalence increased about eight fold to 9.4% in 2007 from 1.1% in 2006; in Dallas, the prevalence increased to 7.5% from 6.1%; in Greensboro, it tripled to 5.3% from 1.7%; in New Orleans it increased to 18.1% from 10.2%; and in Oklahoma City, it increased to

6% from 4.3%. However, in Atlanta where isolates were submitted from January to April 2007 only, the prevalence of QRNG decreased to 2.6% in 2007 from 5.7% in 2006. The prevalence of QRNG remained the same in 2007 at 19.6% in Miami.

In the Midwest and Northeast, there were dramatic increases in prevalence of QRNG from 2006 to 2007 in several sites. In Chicago, the prevalence of isolates that were resistant to ciprofloxacin doubled to 8.6% in 2007 from 4.1% in 2006; in Cincinnati, the prevalence almost doubled to 1.2% in 2007 from 0.7% in 2006; in Detroit, it increased five fold to 1.7% in 2007 from 0.3% in 2006; in Minneapolis, it doubled to 10.7% in 2007 from 5.7% in 2006; and in New York City, it also almost doubled to 14.9% in 2007 from 7.6% in 2006. There was a decrease in QRNG prevalence in Cleveland to 0.7% in 2007 from 3.1% in 2006 and in Philadelphia to 29.1% from 30.3%.

New sites in GISP that identified ciprofloxacin-resistant isolates include Kansas City and Richmond. Kansas City rejoined GISP in September 2007 and observed a QRNG prevalence of 16.4% in 2007. Richmond started GISP in November 2007 and QRNG was identified in 17.9% of isolates collected.

Tripler did not submit isolates in 2007.

Resistance by Sexual Behavior: Resistance to ciprofloxacin among MSM decreased slightly to 36.1% in 2007 from 39% in 2006. Ciprofloxacin resistance, however, has continued to increase among heterosexuals to 8.7% in 2007 from 7% in 2006 (**Figure 19**).

Resistance with other antibiotics: Overall, 27% (1,622/6,009) of all 2007 GISP isolates were resistant to penicillin, tetracycline, ciprofloxacin, or some combination of those antibiotics. And 8% (483/6,009) of isolates demonstrated resistance to ciprofloxacin, penicillin, and tetracycline (**Figure 20**).

Susceptibility to Azithromycin

Susceptibility testing for azithromycin began in 1992. **Figure 21** demonstrates MIC values for 3 years: the first year of testing, the current year, and a mid-point year (1999). Note that in 2007 the majority of antimicrobial susceptibility testing for azithromycin started at a minimum MIC of 0.03 µg/ml. The correlation of azithromycin MICs ≥ 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.[28-31]

In previous years, the azithromycin MIC for decreased susceptibility was set at ≥ 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 2007, 0.4% (27/6,009) of isolates had azithromycin MIC ≥ 2.0 µg/ml (range, 2.0-16.0 µg/ml), which is an increase from 2006 of 0.2% of all isolates. The following twenty-seven isolates with azithromycin MIC ≥ 2.0 µg/ml are listed by location and number of isolates detected in 2007: Albuquerque (1), Chicago (3), Denver (6), Las Vegas (8), Long Beach (1), Los Angeles (2), New York (1), Portland (2), San Diego (1), San Francisco (1), and Seattle (1).

Additional Resources

GISP data were presented at the 2008 National STD Conference in Chicago, IL on March 11th, 2008, the 2008 International Conference on Emerging Infectious Disease in Atlanta, GA, on March 19th, 2008, and the 57th Epidemic Intelligence Service Conference in Atlanta, GA on April 15th, 2008.[32-34]

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/std/stats/**

References

[1] CDC. *Sexually Transmitted Disease Surveillance, 2007*. Atlanta, Georgia: U.S. Department of Health and Human Services, 2008.

[2] Fox KK, Whittington WL, Levine WC, Moran JS, Zaidi AA, Nakashima AK. Gonorrhea in the United States, 1981-1996: Demographic and geographic trends. *Sex Transm Dis* 1998;386-93.

[3] CDC. Gonorrhea — United States, 1998 *MMWR* 2000;49:538-542.

[4] CDC. *Sexually Transmitted Disease Surveillance, 2006*. Atlanta, Georgia: U.S. Department of Health and Human Services, 2007.

[5] McCormack WM. Pelvic inflammatory disease. *N Engl J Med* 1994;330:115-119.

[6] Laga M, Manoka A, Kivuvu M, Malele B, Tuliza M, Nzila N, Goeman J, Behets F, Batter V, Alary M. Non-ulcerative sexually transmitted diseases as risk factors for HIV-1 transmission in women: results from a cohort study. *AIDS* 1993;7:95-102.

[7] Cohen MS, Hoffman IF, Royce RA, Kazembe P, Dyer JR, Daly CC, Zimba D, Vernazza PL, Maida M, Fiscus SA, Eron JJ. Reduction of concentration of HIV-1 in semen after treatment of urethritis: implications for prevention of sexual transmission of HIV-1. AIDSCAP Malawi Research Group. *Lancet* 1997;349:1868-73.

[8] Fox KK, Knapp JS, Holmes KK, Hook EW, Judson FN, Thompson SE, Washington JA, Whittington WL. Antimicrobial resistance in *Neisseria gonorrhoeae* in the United States 1988-1994: the emergence of resistance to the fluoroquinolones. *J Infect Dis* 1997;175:1396-1403.

[9] Wang SA, Harvey AB, Conner, SM, Zaidi, AA, Knapp JS, Whittington WLH, del Rio C, Judson FN, and Holmes KK. Antimicrobial resistance for *Neisseria gonorrhoeae* in the United States 1988-2003: the spread of fluoroquinolone resistance. *Ann Internal Med* 2007; 147;2: 81-89.

[10] Iverson CJ, Wang SA, Lee MV, Ohye RG, Trees DL, Knapp JS, Effler PV, O'Connor NP, Levine WC. Fluoroquinolone-resistance among *Neisseria gonorrhoeae* isolates in Hawaii 1990-2000. *Sex Transm Dis* 2004;31:702-8.

[11] CDC. Fluoroquinolone-resistance in *Neisseria gonorrhoeae*, Hawaii 1999, and Decreased Susceptibility to Azithromycin in *Neisseria gonorrhoeae*, Missouri, 1999. *MMWR* 2000;49(37);833-7.

[12] CDC. Increases in fluoroquinolone-resistant *Neisseria gonorrhoeae* – Hawaii and California, 2001. *MMWR* 2002;51:1041-1044.

[13] CDC. Increases in Fluoroquinolone-Resistant *Neisseria gonorrhoeae* Among Men Who Have Sex with Men --- United States, 2003, and Revised Recommendations for Gonorrhea Treatment, 2004. *MMWR* 2004;53:335-338.

[14] WHO Western Pacific Gonococcal Antimicrobial Surveillance Programme. Surveillance of antibiotic resistance in *Neisseria gonorrhoeae* in the WHO Western Pacific Region, 2001. Communicable Disease Intelligence 2002;26:541-545.

[15] CDC. Update to CDC's Sexually Transmitted Diseases Treatment Guidelines, 2006: Fluoroquinolones No Longer Recommended for Treatment of Gonococcal Infections. *MMWR* 2007;56 (14):332-336.

[16]Schwarcz SK, Zenilman JM, Schnell D, Knapp JS, Hook EW, Thompson S, Judson FN, Holmes KK, The Gonococcal Isolate Surveillance Project. National surveillance of antimicrobial resistance in *Neisseria gonorrhoeae*. *JAMA* 1990;264:1413-1417.

[17]National Committee for Clinical Laboratory Standards. 1993. Approved standard M7 - A3. Methods for dilution antimicrobial susceptibility tests for bacteria that grow aerobically. National Committee for Clinical Laboratory Standards, Villanova, PA.

[18]National Committee for Clinical Laboratory Standards. 1998. Approved standard M100-38. Performance standards for antimicrobial susceptibility testing. National Committee for Clinical Laboratory Standards, Wayne, PA.

[19]National Committee for Clinical Laboratory Standards. 2002. Approved standard M100-S12, 22. Performance standards for antimicrobial susceptibility testing. National Committee for Clinical Laboratory Standards, Wayne, PA.

[20]Clinical and Laboratory Standards Institute. January 2007. Approved standard M100-S17, 27 (1). Performance standards for antimicrobial susceptibility testing; Seventeenth Informational Supplement.

[21]Wang SA, Lee MVC, O'Connor N, Iverson CJ, Ohye RG, Whiticar PM, Hale JA, Knapp JS, Effler PV, Weinstock HS. Multi-drug resistant *Neisseria gonorrhoeae* with decreased susceptibility to cefixime – Hawaii, 2001. *Clin Infect Dis* 2003;37:849-852.

[22]McLean CA, Wang SA, Hoff GL, Dennis LY, Trees DL, Knapp JS, Markowitz LE, Levine WC. The emergence of *Neisseria gonorrhoeae*, with decreased susceptibility to azithromycin in Kansas City, Missouri, 1999-2000. *Sexually Transmitted Diseases* 2004;31:73-78.

[23]CDC. 1993 Sexually transmitted diseases treatment guidelines. *MMWR* 1993;42(No. RR-14).

[24]CDC. 1998 Guidelines for treatment of sexually transmitted diseases. *MMWR* 1998;47(No. RR-1).

[25]CDC. Sexually transmitted diseases treatment guidelines 2002. *MMWR* 2002;51(No. RR-6).

[26]CDC. Sexually transmitted diseases treatment guidelines 2006. *MMWR* 2006;55(No. RR-11).

[27] Gonococcal Isolate Surveillance Project (GISP) Protocol. Available at: http://www.cdc.gov/std/gisp/protocol2006_web_version_rev12_2007.pdfAccessed December 10, 2008.

[28]Steingrimsson O, Olafsson JH, Thorarinsson H, Ryan RW, Johnson RB, Tilton RC. Azithromycin in the treatment of sexually transmitted disease. J Antimicrob Chemother 1990;25(Suppl A):109-114.

[29]Waugh MA. Open study of the safety and efficacy of a single dose of azithromycin for the treatment of uncomplicated gonorrhea in men and women. J Antimicrob Chemother 1993;31(Suppl E):193-198.

[30]Young H, Moyes A, McMillan A. Azithromycin and erythromycin resistant *Neisseria gonorrhoeae* following treatment with azithromycin. *Int J STD AIDS* 1997;8:299-302.

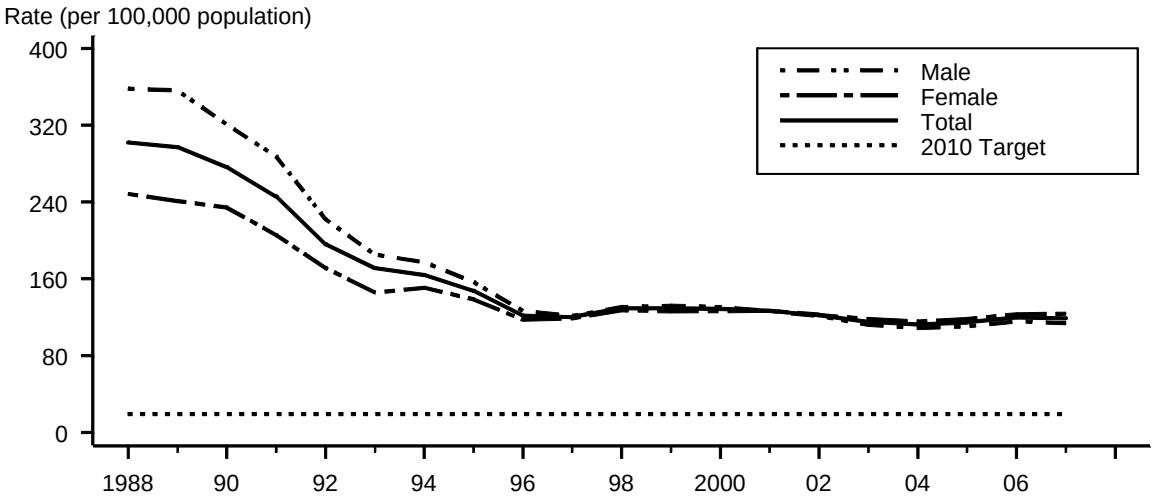
[31]Tapsall JW, Shultz TR, Limnios EA, Donovan B, Lum G, Mulhall BP. Failure of azithromycin therapy in gonorrhea and discorrelation with laboratory test parameters. *Sex Transm Dis* 1998;25:505-508.

[32]Yee EL. Monitoring Emerging Resistance in *N. Gonorrhoeae* in the U.S. [Abstract 6: Symposium-the Changing Epidemiology of STDs in the United States] 2008 National STD Conference in Chicago, IL, March 11th, 2008.

[33]Yee EL. Multidrug-Resistant Gonorrhea-The GC Isolate Surveillance Program [Concurrent Panel Session J3: Sexually Transmitted Diseases] 2008 International Conference on Emerging Infectious Disease, Atlanta, GA, March 19th, 2008.

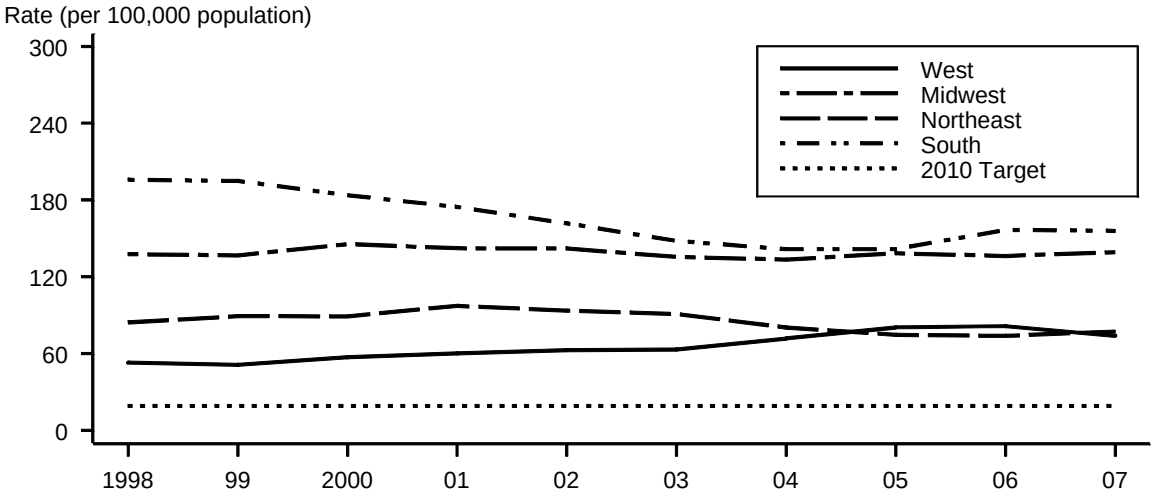
[34]Dowell, DR, Peterman T, Newman L, Yee E, and Weinstock H. Evaluation of the Impact of Revised Treatment Recommendations on the Use of Fluoroquinolones for Gonorrhea Treatment-United States, 2007. [Session H2: She Blinded Me with Science] 57th Epidemic Intelligence Service Conference, Atlanta, GA, April 15th, 2008.

Figure 1. Gonorrhea — Reported rates: United States, 1988–2007 and the Healthy People 2010 target



Note: The Healthy People 2010 (HP2010) objective for gonorrhea is 19.0 cases per 100,000 population.

Figure 2. Gonorrhea — Rates by region: United States, 1998–2007 and the Healthy People 2010 target



Note: The Healthy People 2010 (HP2010) objective for gonorrhea is 19.0 cases per 100,000 population.

Figure 3. Gonorrhea — Rates by race/ethnicity: United States, 1998–2007

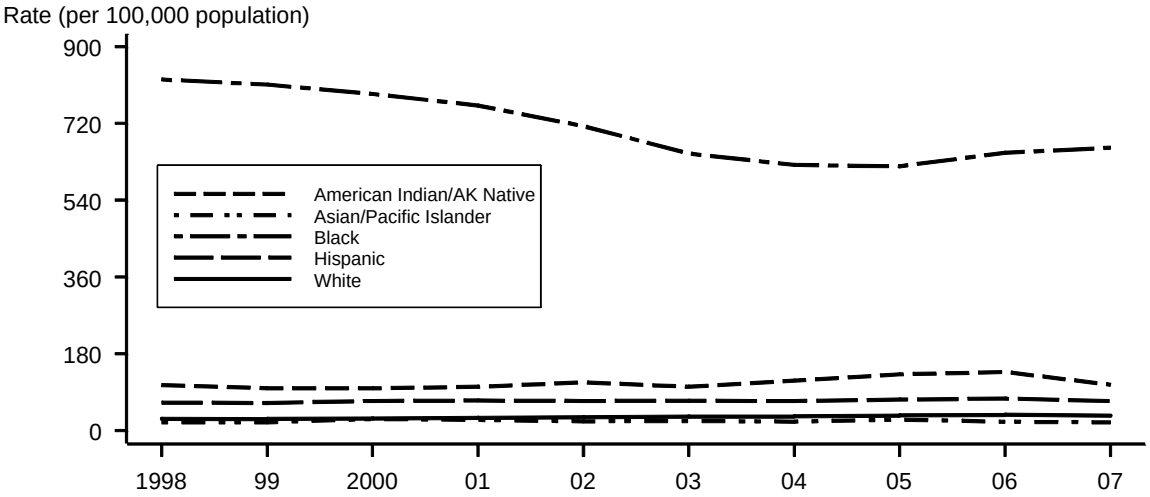


Figure 4. Gonorrhea — Age- and gender-specific rates: United States, 2007

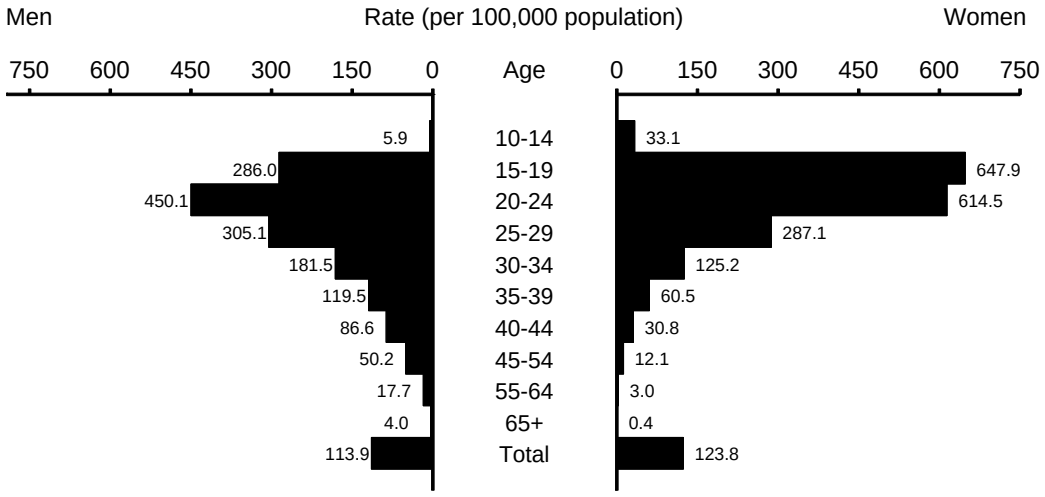
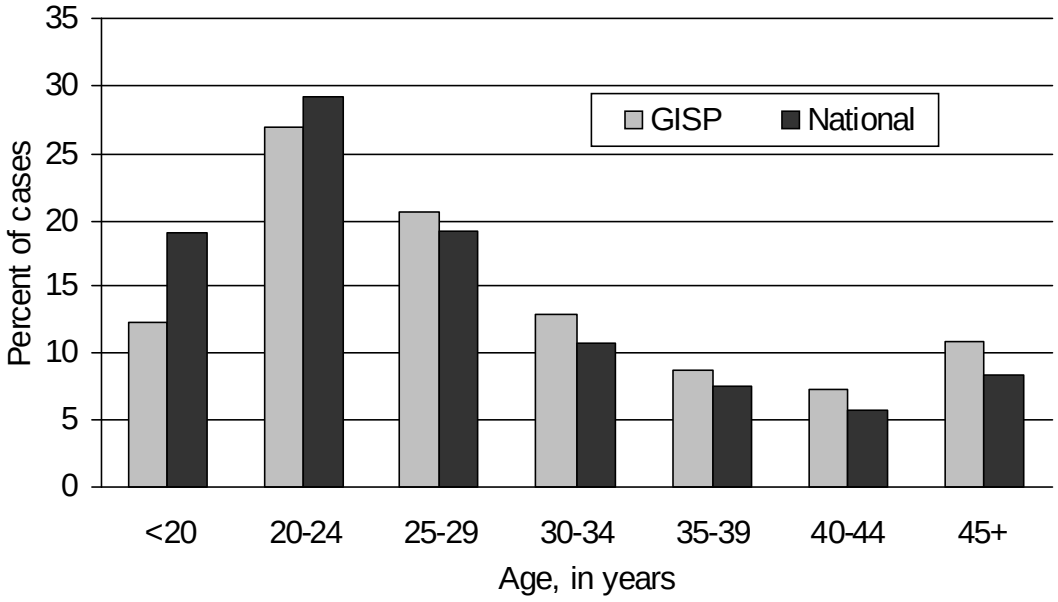


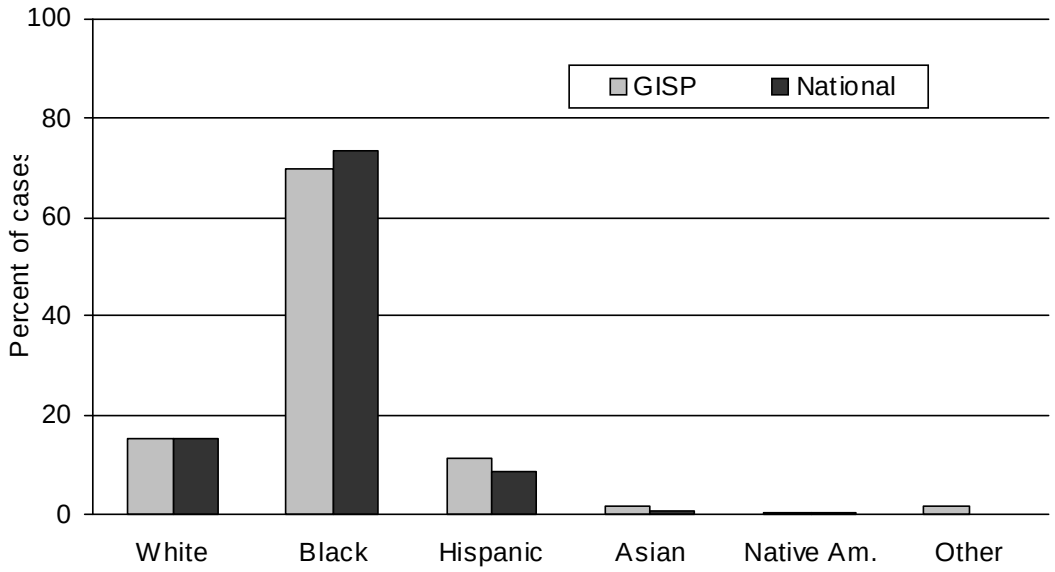
Figure 5. Location of participating GISP clinics and regional laboratories: United States, 2007

Figure 6. Age distribution of GISP participants and nationally reported gonorrhea cases in men, 2007



Note: The age < 20 category includes ages 10-19 for national cases, and ages 14-19 for GISP; 99% in GISP are ages 15-19 and for national cases, 98% are ages 15-19.

Figure 7. Race distribution of GISP participants and nationally reported cases of gonorrhea in men, 2005



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), 1988–2007

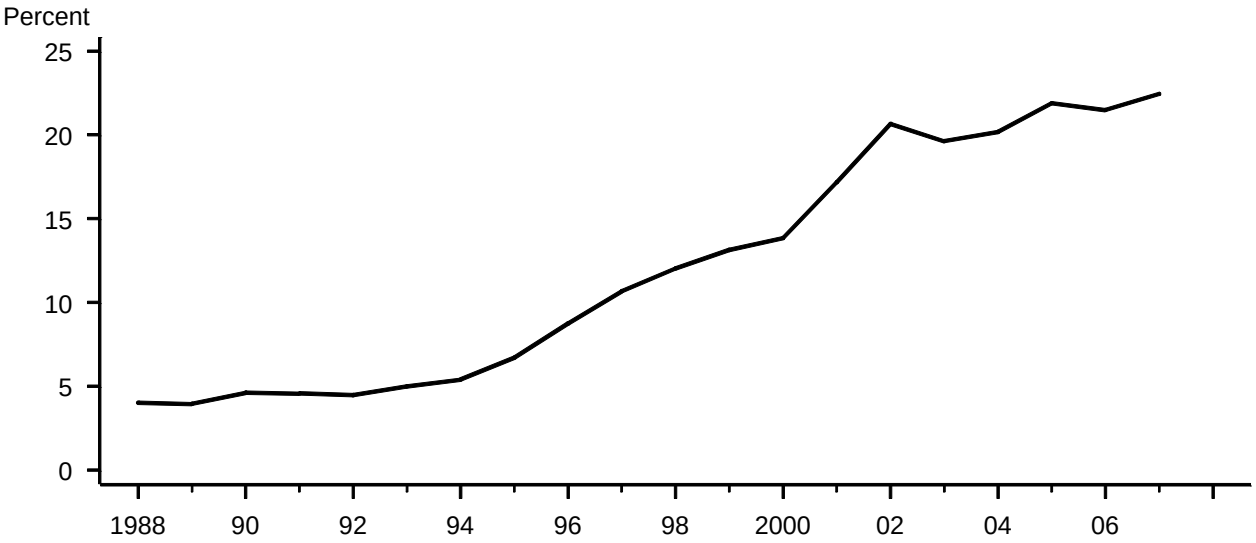
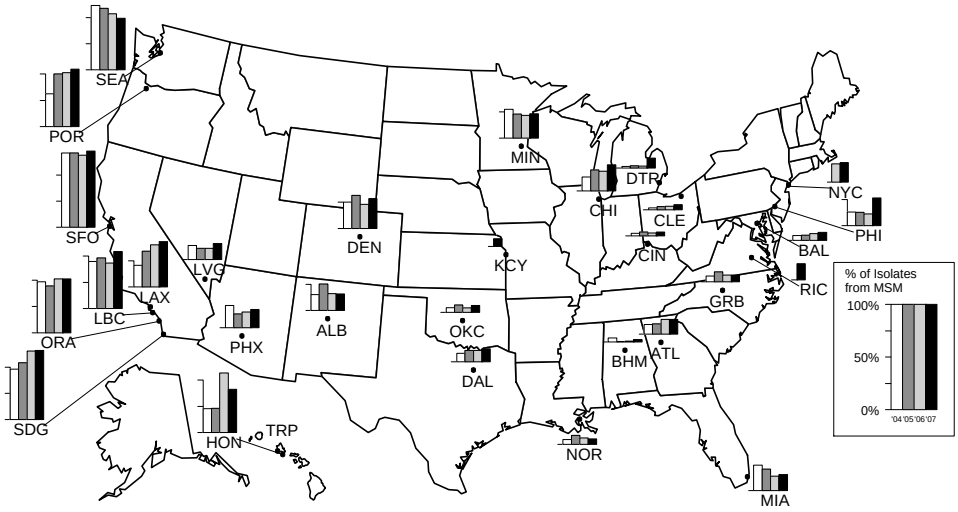
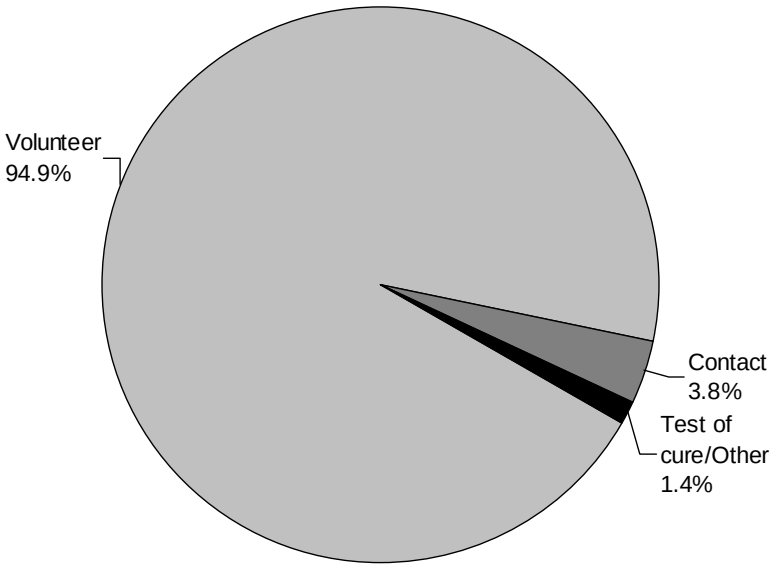


Figure 9. Percent of GISP *Neisseria gonorrhoeae* isolates obtained from MSM attending STD clinics, 2004–2007



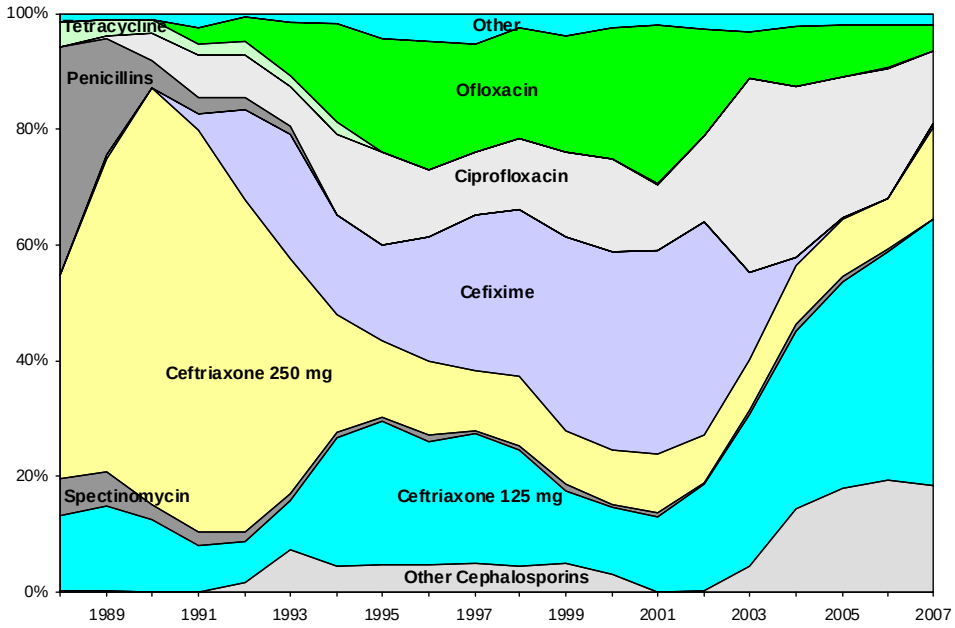
Note: Not all clinics participated in GISP for the last 4 years. Clinics include: ALB=Albuquerque, NM; ATL=Atlanta, GA; BAL=Baltimore, MD; BHM=Birmingham, AL; CHI=Chicago, IL; CIN=Cincinnati, OH; CLE=Cleveland, OH; DAL=Dallas, TX; DEN=Denver, CO; DTR=Detroit, MI; GRB=Greensboro, NC; HON=Honolulu, HI; KCY=Kansas City, MO (started in September 2007); LAX=Los Angeles, CA; LBC=Long Beach, CA; LVG=Las Vegas, NV; MIA=Miami, FL; MIN=Minneapolis, MN; NOR=New Orleans, LA; NYC=New York City, NY; OKC=Oklahoma City, OK; ORA=Orange County, CA; PHI=Philadelphia, PA; PHX=Phoenix, AZ; POR=Portland, OR; RIC=Richmond, VA (started in November 2007); 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, 2007



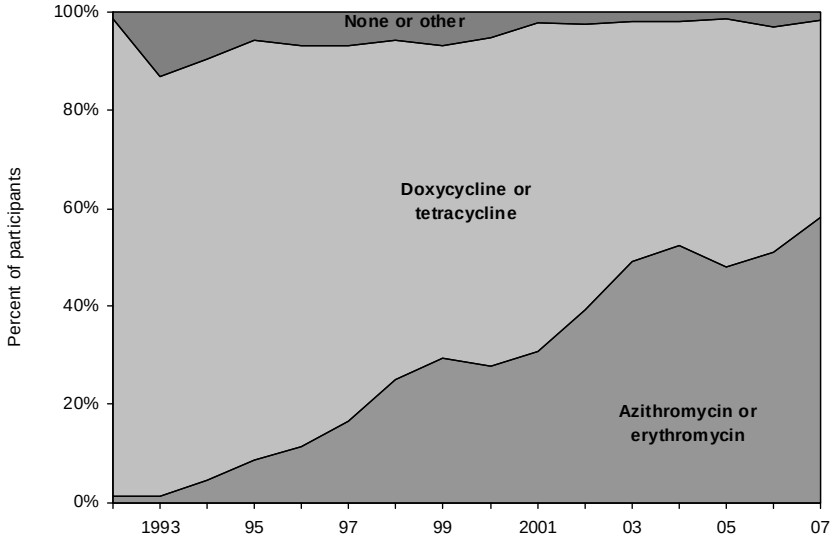
Note: Contact=has sexual partner with gonorrhea.

Figure 11. Drugs used to treat gonorrhea in GISP participants, 1988–2007



Note: For 2007, "Other" includes no therapy (0.8%), azithromycin 2 g (0.8%), levofloxacin (0.2%), and other less frequently used drugs.

Figure 12. Drugs used to treat *Chlamydia trachomatis* infection in GISP participants, 1992–2007



Note: For each year, "Other" accounted for only 0 - 0.9% of *C. trachomatis* treatment and erythromycin accounted for only 0.1 – .1% of *C. trachomatis* treatment.

Figure 13. Plasmid-mediated resistance to penicillin and tetracycline among GISP isolates, 1988–2007

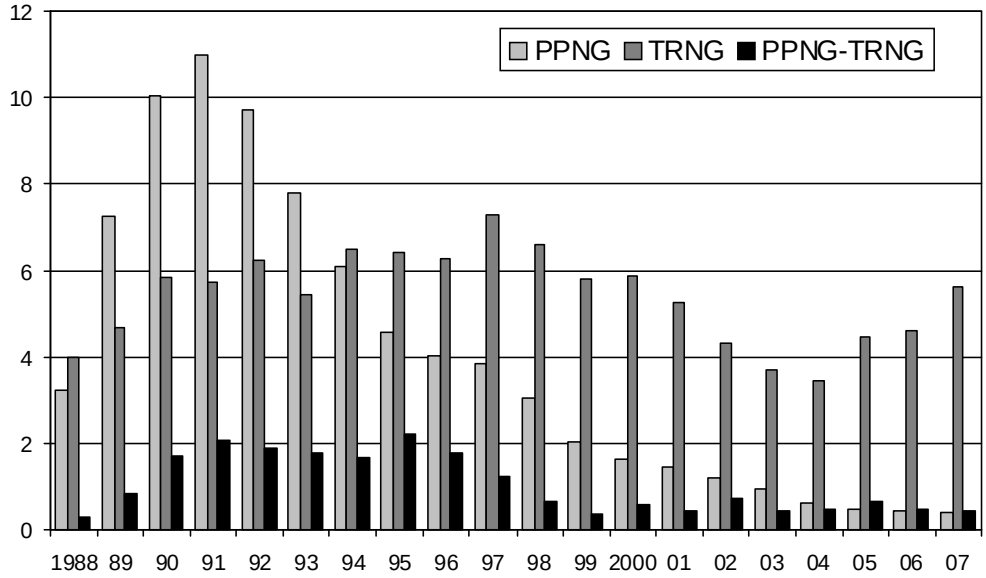


Figure 14. Chromosomally mediated resistance to penicillin and tetracycline among GISP isolates, 1988–2007

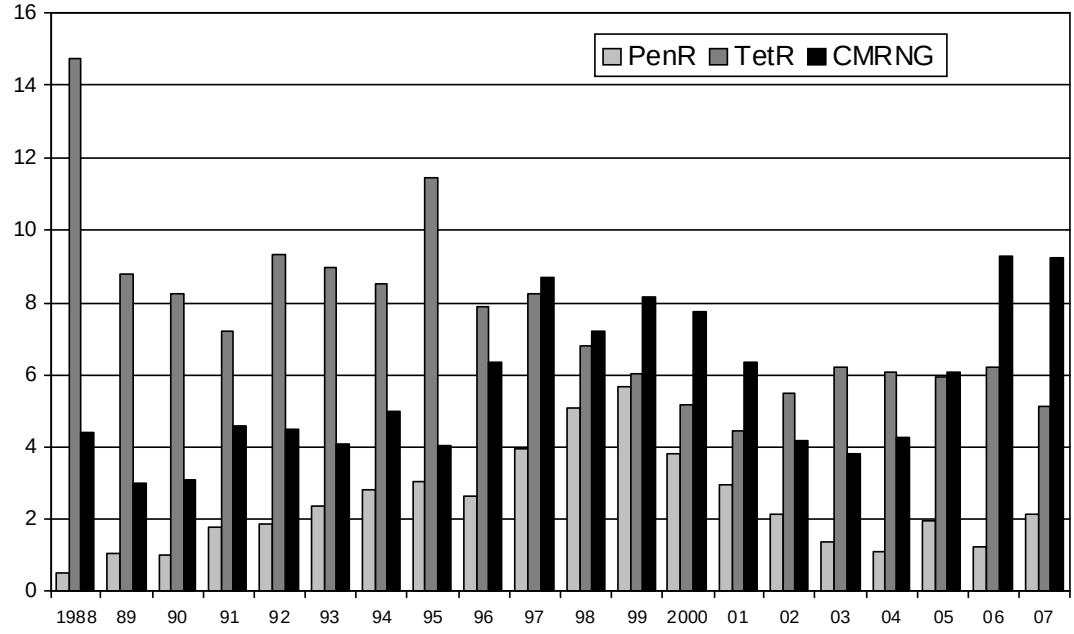
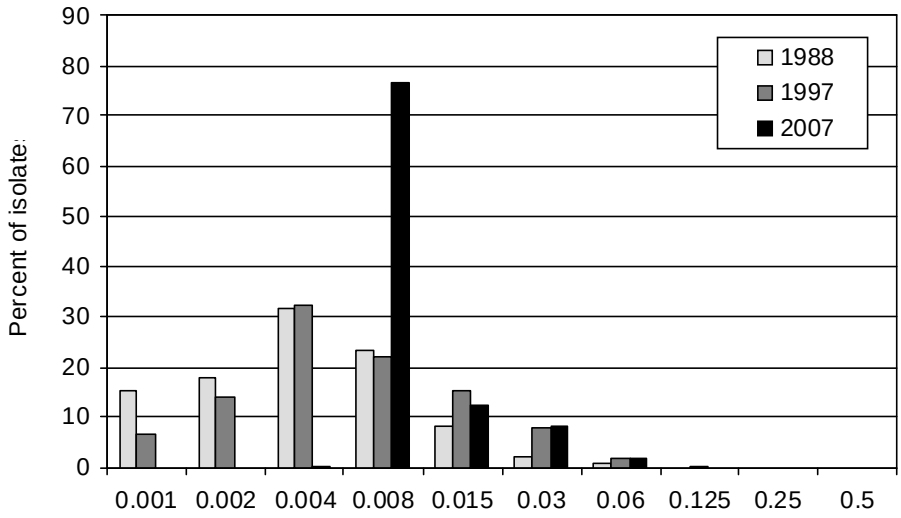
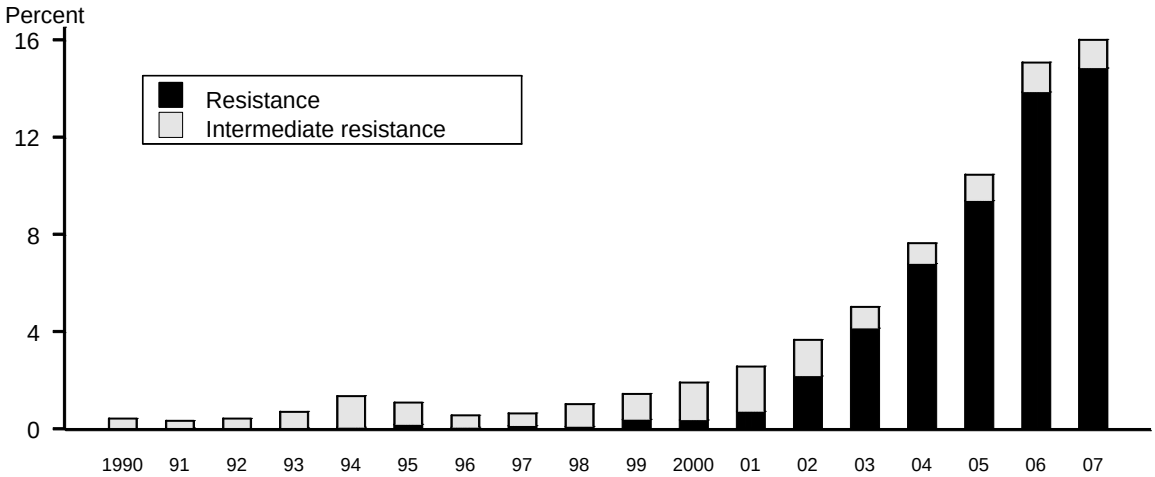


Figure 15. Distribution of MICs to ceftriaxone among GISP isolates, 1988, 1997, and 2007



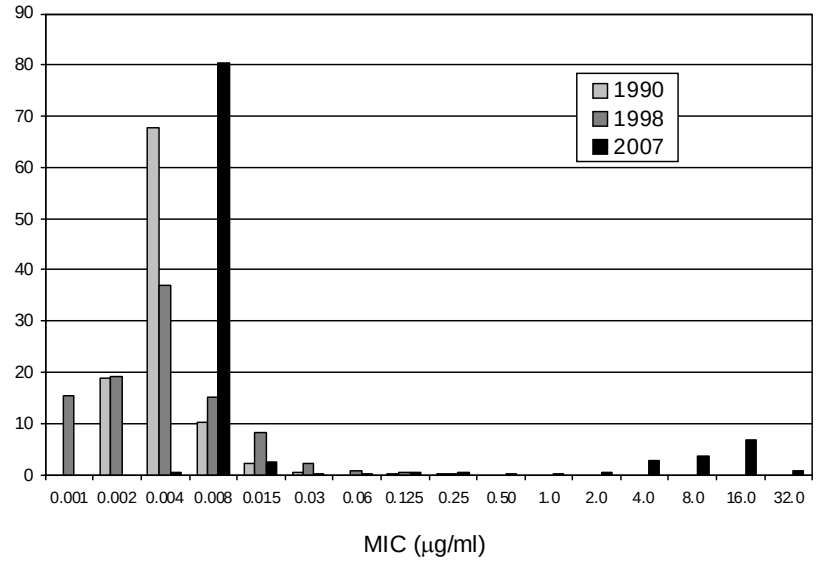
Note: In 1997, there was one isolate with MIC 0.5 µg/ml. In 2007, the majority of susceptibility tests for ceftriaxone started at a minimum MIC of 0.008 µg/ml.

Figure 16. Percentage of GISP isolates with intermediate resistance or resistance to ciprofloxacin, 1990-2007



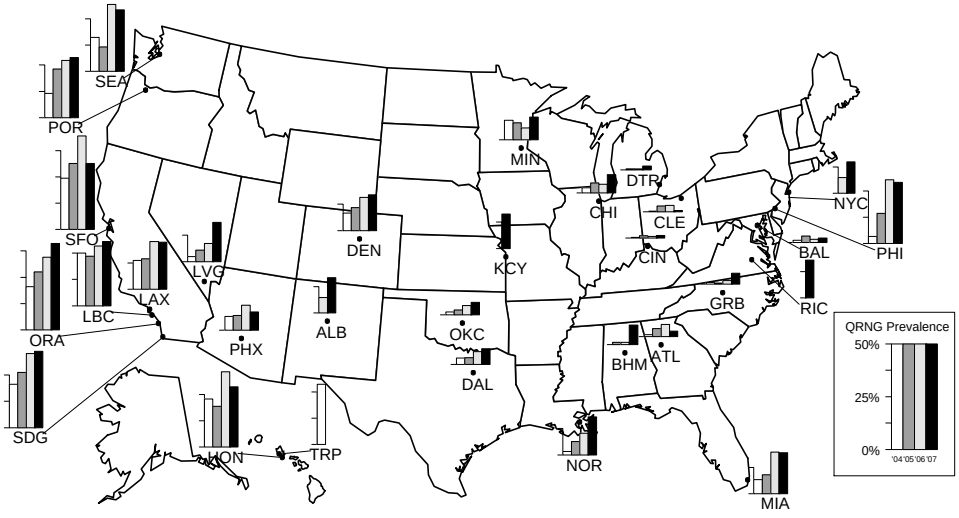
Note: Resistant isolates have ciprofloxacin MICs ≥ 1 µg/ml. Isolates with intermediate resistance have ciprofloxacin MICS of 0.125 – 0.5 µg/ml. Susceptibility to ciprofloxacin was first measured in GISP in 1990.

Figure 17. Distribution of MICs to ciprofloxacin among GISP isolates, 1990, 1998, and 2007



Note: In 1998, there were 2 isolates with MIC 1.0 µg/ml, 1 isolate with MIC 2.0 µg/ml, and 1 isolate with MIC 8.0 µg/ml. In 2007, there were 9 isolates with MIC 1.0 µg/ml, 40 isolates with MIC 2.0 µg/ml, 170 isolates with MIC 4.0 µg/ml, 220 with MIC 8.0 µg/ml, 402 isolates with MIC 16.0 µg/ml, and 50 isolates with MIC 32.0 µg/ml. The majority of susceptibility tests for ciprofloxacin in 2007 started at a minimum MIC of 0.008 µg/ml.

Figure 18. Prevalence of ciprofloxacin resistant *Neisseria gonorrhoeae* by GISP site, 2004–2007



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; KCY=Kansas City, MO (started in September 2007); LAX=Los Angeles, CA; LBC=Long Beach, CA; LVG=Las Vegas, NV; MIA=Miami, FL; MIN=Minneapolis, MN; NOR=New Orleans, LA; NYC=New York City, NY; OKC=Oklahoma City, OK; ORA=Orange County, CA; PHI=Philadelphia, PA; PHX=Phoenix, AZ; POR=Portland, OR; RIC=Richmond, VA (started in November 2007); SDG=San Diego, CA; SEA=Seattle, WA; SFO=San Francisco, CA; and TRP=Tripler Army Medical Center, HI.

Figure 19. Prevalence of GISP isolates with resistance to ciprofloxacin by sexual behavior, 2001–2007

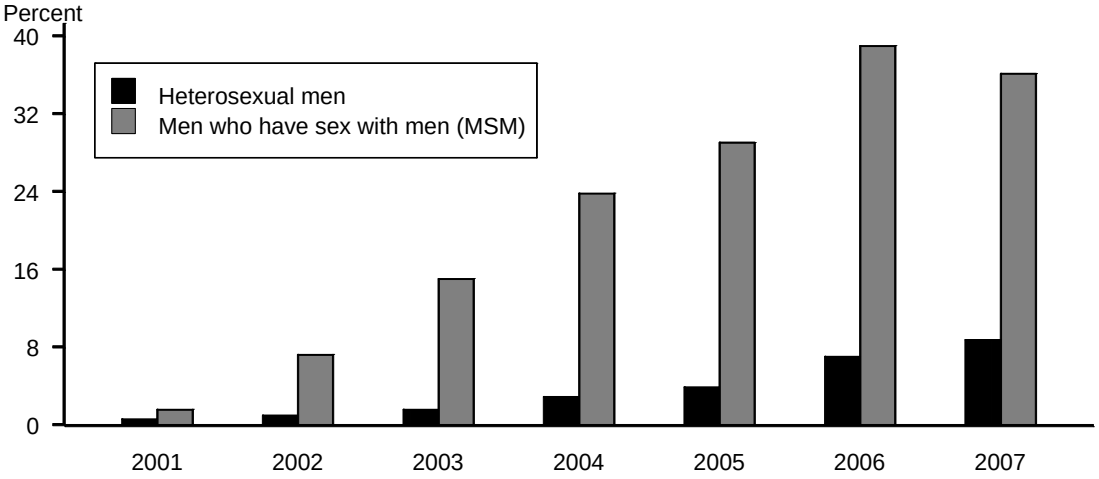


Figure 20. Penicillin, tetracycline, and ciprofloxacin resistance among GISP isolates, 2007

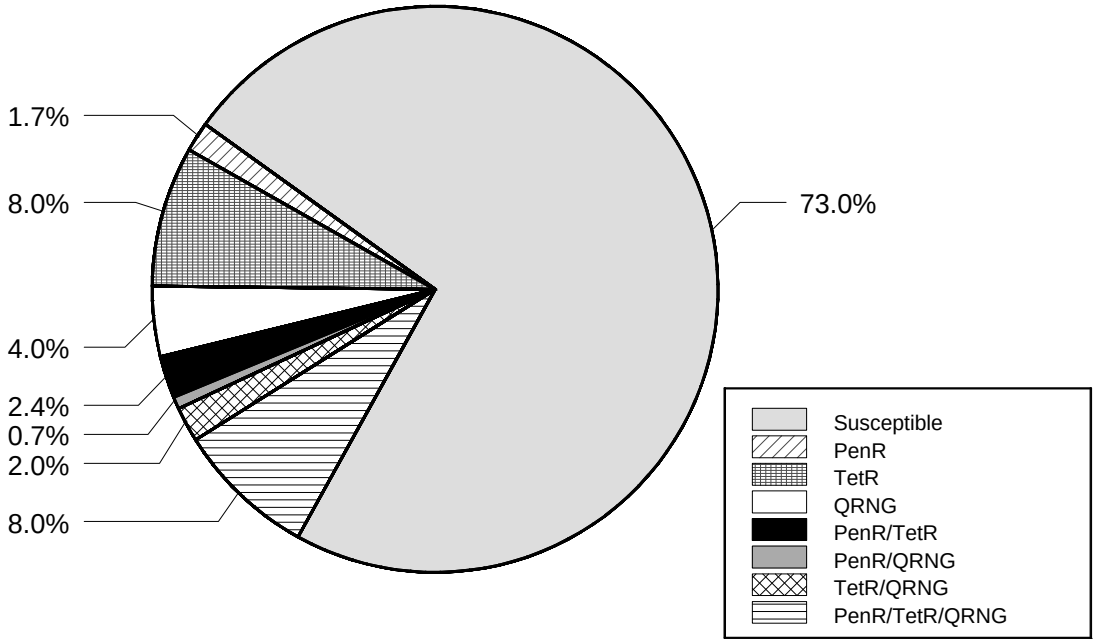
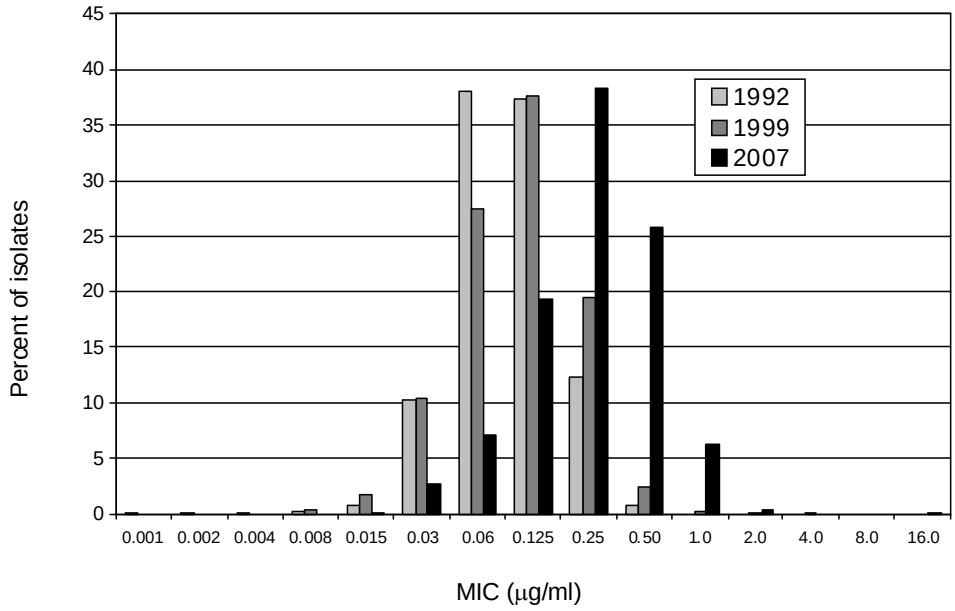


Figure 21. Distribution of MICs to azithromycin among GISP isolates, 1992, 1999 and 2007



Note: In 1999, there were 11 isolates with MIC 1.0 µg /ml, 8 isolates with MIC 2.0 µg /ml, 5 isolates with MIC 4.0 µg/ml, and 1 isolate with MIC 8.0 µg /ml. In 2005, there was a change in the media used for agar dilution testing among all of the GISP regional laboratories which resulted in an observational shift of the MIC curve, approximately one dilution higher. In 2007, there were 18 isolates with MIC 2.0 µg /ml, 3 isolates with MIC 8.0 µg /ml, and 6 isolates with MIC 16.0 µg /ml. The majority of susceptibility tests for azithromycin in 2007 started at a minimum MIC of 0.03 µg /ml.