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Division of STD Prevention
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Gonococcal Isolate Surveillance Project (GISP) Annual Report - 1999

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This report is available from the Internet via the CDC home page address at
http://www.cdc.gov/nchstp/dstd/Stats_Trends/99GISP.htm
and at
http://www.cdc.gov/ncidod/dastlr/gcdir/Resist/gisp.html.
The 1999 STD Surveillance Report may be found at
http://www.cdc.gov/nchstp/dstd/Stats_Trends/1999SurvRpt.htm.

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GONOCOCCAL ISOLATE SURVEILLANCE PROJECT (GISP)
ANNUAL REPORT - 1999

Introduction

Gonorrhea is the second most frequently reported communicable disease in the United States. Gonorrhea rates in the United States declined 72% during 1975-1997. However, in 1999, the reported rate of gonococcal infections in the United States (133.2 cases per 100,000 persons) increased by 1.2% compared with the 1998 rate (131.6 cases per 100,000 persons) and 9.2% compared with 1997 (122.0 cases per 100,000 persons) (**Figure 1**).[1] Gonorrhea rates remain high in the southeastern states, among minorities, and among adolescents of all racial and ethnic groups (**Figures 2, 3, and 4**).[2, 3] 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.[4] In addition, recent data suggest that gonorrhea facilitates HIV transmission.[5, 6]

Control of gonorrhea has been complicated by the development of resistance to antimicrobial agents. The appearance of penicillinase-producing *Neisseria 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. The currently recommended primary therapies for gonorrhea are two broad-spectrum cephalosporins, ceftriaxone and cefixime, and two fluoroquinolones, ciprofloxacin and ofloxacin.[7] However, fluoroquinolone-resistant *N. gonorrhoeae* have been reported from many parts of the world, including the United States.[8-12]

GISP Overview

The Gonococcal Isolate Surveillance Project (GISP) was established in 1986 to monitor trends in antimicrobial susceptibilities of strains of *N. gonorrhoeae* in the United States in order to establish a rational basis for the selection of gonococcal therapies.[13] GISP is a collaborative project between selected sexually transmitted diseases (STD) clinics, five regional laboratories, and the Centers for Disease Control and Prevention (CDC) (Division of STD Prevention, National Center for HIV, STD, and TB Prevention, and the Division of AIDS, STD, and TB Laboratory Research, National Center for Infectious Diseases).

In GISP, *N. gonorrhoeae* isolates are collected from the first 25 men with urethral gonorrhea attending STD clinics each month in 26 cities in the United States. At regional laboratories, the susceptibilities of these isolates to antimicrobial agents are determined by agar dilution. Minimum inhibitory concentrations (MICs) are measured, and resistance interpreted according to criteria recommended by the National Committee for Clinical Laboratory Standards (NCCLS).[14,15]

Important GISP findings have included:

- the ongoing high prevalence of resistance to penicillin and tetracycline;
- the appearance, with low prevalence, of decreased susceptibility and resistance to the fluoroquinolones;[9-12]
- the absence of resistance to the broad-spectrum cephalosporins;
- the increasing proportion of gonorrhea cases identified in men who have sex with men;[16] and
- the appearance, with low level prevalence, of decreased susceptibility to the macrolides.[12]

GISP findings contributed to the development of CDC's STD treatment recommendations in 1993 and 1998,[7, 17] and stimulated further investigation of the increase in gonorrhea among men who have sex with men.[16]

1999 GISP Sites

A total of 26 STD clinics contributed 5,180 gonococcal isolates to GISP in 1999 (**Figure 5**). Seventeen sites have participated continuously since 1988: Albuquerque, Anchorage, Atlanta, Baltimore, Birmingham, Cincinnati, Denver, Honolulu, Long Beach, New Orleans, Philadelphia, Phoenix, Portland, San Antonio, San Diego, San Francisco, and Seattle. Seven sites joined GISP after 1988: Cleveland, Kansas City, Nassau County, and Orange County in 1991; Minneapolis in 1992; Chicago in 1996; and Miami in 1998. Two sites have had intermittent participation in GISP: Fort Bragg 1987-1990 and 1997-1999, and St. Louis 1987-1993 and 1995-1999. The GISP Regional Laboratories are located in Atlanta, Birmingham, Cleveland, Denver, and Seattle.

DESCRIPTION OF GISP DATA

Aggregate data from all GISP sites are described and illustrated in the first part of this report. The clinic-specific data illustrate substantial geographic variation in patient characteristics and antimicrobial susceptibility of gonococcal strains; clinic-specific figures are provided in the second part of this report.

Demographic and Clinical Characteristics

Age The age distribution of GISP participants compared with nationally reported male gonorrhea patients in 1999 is shown in **Figure 6**; the two groups have similar age distributions. GISP participants in 1999 ranged in age from 12 to 75 years.

Race/Ethnicity The race/ethnicity distribution of GISP participants compared with nationally reported male gonorrhea patients in 1999 is shown in **Figure 7**. The proportion of GISP participants who are Hispanic is higher than among nationally reported male gonorrhea patients; several GISP sites where Hispanic patients account for a high proportion of STD clinic attendees explain this difference.

Sexual Orientation In 1999, 13.1% of GISP participants were men who have sex with men (MSM); compared with 4.0% of GISP participants who were MSM in 1988; the proportion of GISP participants who were MSM has been increasing every year since 1993 (**Figure 8**). Nine

clinics reported the majority (511/613; 83.4%) of MSM in GISP in 1999; in all nine clinics, the proportion of participants who were MSM increased in 1997, 1998, or 1999 or in each of these years. The percentages of isolates that came from MSM in these nine clinics from 1988 through 1999 are shown in **Figure 9**. A study of eight of these cities performed in 1996 showed that in five of the eight (Honolulu, Portland, San Diego, San Francisco, and Seattle) the proportional increases corresponded to absolute increases in numbers of MSM with gonorrhea.[16]

Reason for Clinic Attendance Most GISP participants in 1999 presented to the clinic as volunteers; others were gonorrhea contacts or presented for test-of-cure cultures (**Figure 10**). There has been little change in this distribution over time. Dysuria and/or urethral discharge was present in 92.6% of GISP participants in 1999 and 3.6% had no symptoms; these proportions have been stable over time.

History of Gonorrhea The percentage of GISP participants who reported a history of gonorrhea (ever) increased from 38.3% in 1991, the first year this information was collected, to a peak of 49.9% in 1996, but declined to 45.0% in 1999. The percentage of GISP participants with a documented previous episode of gonorrhea in the last 12 months decreased from 21.5% in 1992, the first year this information was collected, to 17.2% in 1999 (**Figure 11**).

Antimicrobial Treatment The antimicrobial agents given to GISP participants for gonorrhea therapy are shown in **Figure 12**. The proportion of GISP patients treated with cephalosporins decreased from a high of 84.7% in 1990 to 60.4% in 1999, while the proportion treated with fluoroquinolones (ciprofloxacin or ofloxacin) increased from none in 1988 to 34.9% in 1999. The antimicrobial agents given to GISP participants for treatment of *Chlamydia trachomatis* infection are shown in **Figure 13**. The proportion of GISP patients treated with doxycycline or tetracycline decreased from a high of 90.4% in 1990 to 62.5% in 1999, while the proportion treated with azithromycin increased from 0.2% in 1992 (the first year of GISP that azithromycin was identified as being used for *C. trachomatis* therapy) to 28.4% in 1999.

Susceptibility to Antimicrobial Agents

Antimicrobial Resistance Criteria

Antimicrobial resistance in *N. gonorrhoeae* is defined by the criteria recommended by the National Committee on Clinical Laboratory Standards (NCCLS):[15]

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

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

Susceptibility to Penicillin and Tetracycline

Overall, 28.1% (1453/5180) of isolates collected in 1999 were resistant to penicillin, tetracycline, or both (**Figure 14**); this proportion has been relatively constant since 1988. The percentage of penicillinase-producing *N. gonorrhoeae* (PPNG) declined from a peak of 11.0% in 1991 to 2.1% in 1999 (**Figure 15**). In contrast, the percentage of isolates with chromosomally mediated resistance to penicillin (PenR) has increased annually, from 0.5% in 1988 to 5.7% in 1999 (**Figure 16**). The prevalence of plasmid-mediated resistance to tetracycline (TRNG), 5.8% in 1999, has varied little since 1988 (**Figure 15**). Similarly, the prevalence of chromosomally mediated resistance to tetracycline only (TetR), 6.0% in 1999, has been relatively stable since 1989, except for a transient increase in 1995 (**Figure 16**). However, the prevalence of isolates with chromosomally mediated resistance to both penicillin and tetracycline (CMRNG) increased from 3.0% in 1989 to 8.1% in 1999. The prevalence of isolates with plasmid-mediated resistance to both penicillin and tetracycline (PPNG-TRNG), 0.4% in 1999, continues to be very low.

Susceptibility to Spectinomycin

All isolates were susceptible to spectinomycin in 1999. 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

The distributions of MICs to ceftriaxone in 1988 and 1999 are shown in **Figure 17**. Over this time period, there has been a subtle shift towards higher ceftriaxone MICs. In 1999, all isolates were susceptible to ceftriaxone. There have been four isolates with decreased susceptibility to ceftriaxone in GISP; all four had MICs of 0.5 Fg/ml. Their locations and years were: San Diego-1987, Cincinnati-1992 and 1993, and Philadelphia-1997.

Susceptibility to Cefixime

The distributions of MICs to cefixime in 1992 (the first year of cefixime susceptibility testing) and 1999 are shown in **Figure 18**. In 1999, all isolates were susceptible to cefixime. There have been 41 isolates with decreased susceptibility to cefixime in GISP; their MICs have ranged from 0.5-2.0 Fg/ml.

Susceptibility to Ciprofloxacin

The correlation of ciprofloxacin MICs of 0.125-0.5 Fg/ml with treatment failure when a fluoroquinolone is used to treat a gonococcal infection, 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 Fg/ml.[18] Gonococcal isolates with intermediate resistance and resistance to ciprofloxacin also have intermediate resistance and resistance to other fluoroquinolones. Criteria recommended for interpreting ofloxacin MICs are: intermediate resistance, MICs 0.5-1.0 Fg/ml; resistance, MICs $2.0 Fg/ml.[15]

The distributions of MICs to ciprofloxacin in 1990 (the first year of ciprofloxacin susceptibility testing) and 1999 are shown in **Figure 19**. A total of 1.4% (74/5180) of isolates exhibited intermediate resistance or resistance to ciprofloxacin (MICs $0.125 Fg/ml) in 1999 compared with 1.0% (48/4712) of isolates tested in 1998 (**Figure 20**).

Intermediate resistance In 1999, 1.1% (55/5180) of all GISP isolates exhibited intermediate resistance to ciprofloxacin (MICs 0.125-0.5 Fg/ml). Of these isolates, 38.2% (21/55) came from Cincinnati patients, where they accounted for 9.0% (21/233) of isolates and 25.5% (14/55) came from Atlanta patients, where they accounted for 5.3% (14/265) of isolates tested in 1999. In 1999, isolates of *N. gonorrhoeae* exhibiting intermediate resistance to ciprofloxacin were also found in Cleveland (4), Honolulu (1), Miami (1), Minneapolis (1), New Orleans (1), Philadelphia (1), Phoenix (4), Portland (1), San Diego (1), San Francisco (3), Seattle (1), and St. Louis (1).

Resistance Nineteen isolates (0.4%; 19/5180) were resistant to ciprofloxacin (MICs $1.0 Fg/ml) in 1999 compared with 4 (0.1%, 4/4712) GISP isolates in 1998; the locations, numbers, and MICs of the 1999 GISP isolates were: Anchorage (1), 16 Fg/ml; Cincinnati (1), 1.0 Fg/ml; Denver (1), 2.0 Fg/ml; Fort Bragg (2), both 4.0 Fg/ml; Honolulu (7), three 1.0 Fg/ml, three 2.0 Fg/ml, and one 4.0 Fg/ml; New Orleans (1), 1.0 Fg/ml; Orange County (1), 1.0 Fg/ml; San Diego (2), one 4.0 Fg/ml and one 8.0 Fg/ml; Seattle (2), one 4.0 Fg/ml and one 16 Fg/ml; and San Francisco (1), 8.0 Fg/ml. Notably, in Honolulu, 14.3% (7/49) of GISP isolates were resistant to ciprofloxacin in 1999.

Susceptibility to Azithromycin

The correlation of azithromycin MICs $0.5 Fg/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 Fg/ml.[19-22]

The distributions of MICs to azithromycin in 1992 (the first year of azithromycin susceptibility testing) and in 1999 are shown in **Figure 21**. Over this time period, there has been a shift towards higher azithromycin MICs. In 1992, 0.9% (34/3928) of isolates had azithromycin MIC $0.5 Fg/ml compared with 2.9% (151/5180) of such isolates in 1999. In 1992, there were no isolates with azithromycin MIC $1.0 Fg/ml. In 1999, there were 25 isolates with azithromycin MIC $1.0Fg/ml; these isolates by location, number, and MIC are: Cincinnati (1), 1.0 Fg/ml; Denver (1), 1.0 Fg/ml; Honolulu (1), 8.0 Fg/ml; Kansas City (8), five 2.0 Fg/ml and three 4.0 Fg/ml; Long Beach (1), 2.0 Fg/ml; Orange County (1), 1.0 Fg/ml; Philadelphia (1), 1.0 Fg/ml; Phoenix (3), two 1.0 Fg/ml and one 2.0 Fg/ml; and San Diego (3) all three 1.0 Fg/ml.

NON-GISP REPORTING OF RESISTANCE

The American Public Health Laboratories and the 65 STD project areas were informally surveyed in 1999-2000 to identify cities or states that routinely performed antimicrobial susceptibility testing of *N. gonorrhoeae* in 1999. Information was not available on 45 of the 65 project areas. In 1999, no testing outside of GISP occurred in Arkansas, Colorado, Connecticut, Delaware, Indiana, Kansas, Kentucky, Missouri, Nevada, Pennsylvania, Rhode Island, or San Francisco. Information on testing in 1999 was available for 8 sites (**Table 1**).

Table 1 Non-GISP antimicrobial susceptibility testing of *N. gonorrhoeae* in 8 sites in 1999.

City or state	Total # isolates	Cip S	Cip I	Cip R	Spe S	Spe R	Cfx S	Cfx DS	Cro S	Cro DS	Azi S	Azi DS[+]
Hawaii	182	166	1	15	10	0	-	-	10	-	-	-
Massachusetts	319	317	0	2	23	0	-	-	319	0	-	-
Michigan	228	228*	0	0	-	-	228	0	228	0	-	-
Milwaukee	73	69	4	0	-	-	-	-	73	0	-	-
Minnesota	250	250	0	0	250	0	250	0	250	0	-	-
New Hampshire	16	15	1	0	15	0	-	-	16	0	-	-
New York City	1938	1937	1	0	1938	0	-	-	1938	0	-	-
Washington	468	468	1	0	469	0	469	0	469	0	469	0
Total	3475	3450	8	17	2705	0	947	0	3303	0	469	0

The testing methodology for all sites except Washington state was by disk diffusion; Washington used the agar dilution method.

[+]For this table, AziDS is defined as an isolate with azithromycin MIC$1.0 Fg/ml.

*Michigan tested all 228 isolates against ofloxacin, rather than against ciprofloxacin.

Cip=ciprofloxacin; Spe=spectinomycin; Cfx=cefixime; Cro=ceftriaxone; Azi=azithromycin; S=susceptible; DS=decreased susceptibility; I=intermediate resistant; R=resistant.

For their assistance in gathering these data, we acknowledge and thank: Hawaii - Norman O'Connor; Massachusetts - Harvey George; Michigan - Barbara Robinson-Dunn; Milwaukee, WI - Ajaib Singh and M. Stephen Gradus; Minnesota - Timothy Naimi and John Hunt; New Hampshire - Peggy Sweeney; New York City, NY - Aziz Toma, George Williams, and Gladys Schlanger; Washington - Wil Whittington and Judith Hale.

ADDITIONAL RESOURCES

Recent publications using GISP data include MMWR articles in March 1998[11] and September 2000.[12] Presentations of GISP data were made at the International Conference on Emerging Infectious Diseases in July 2000[23, 24] and the Annual Meeting of the Infectious Diseases Society of America in September 2000.[25]

Detailed information on susceptibilities of *N. gonorrhoeae* isolates from each clinic may be obtained through CDC's website (http://www.cdc.gov/ncidod/dastlr/gcdir/Resist/gisp.html). Updates on emerging resistance of *N. gonorrhoeae* strains to the fluoroquinolones may also be obtained through CDC's website (http://www.cdc.gov/ncidod/dastlr/gcdir/gono.html). Additional surveillance data on *N. gonorrhoeae* and other STDs may be found in the 1999 STD Surveillance Report (http://www.cdc.gov/nchstp/dstd/Stats_Trends/1999SurvRpt.htm).

Information on the Draft Public Health Action Plan to Combat Antimicrobial Resistance may be found on the CDC webpage (http://www.cdc.gov/drugresistance/actionplan/).

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Figure 1. Gonorrhea - Reported rates: United States, 1970-1999 and the Healthy People year 2000 objective

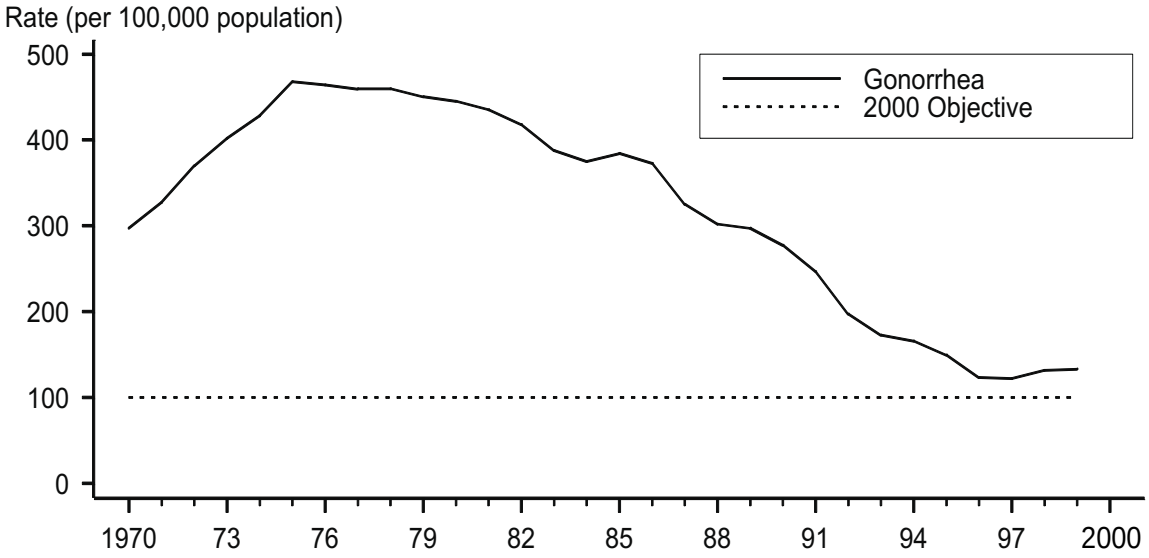
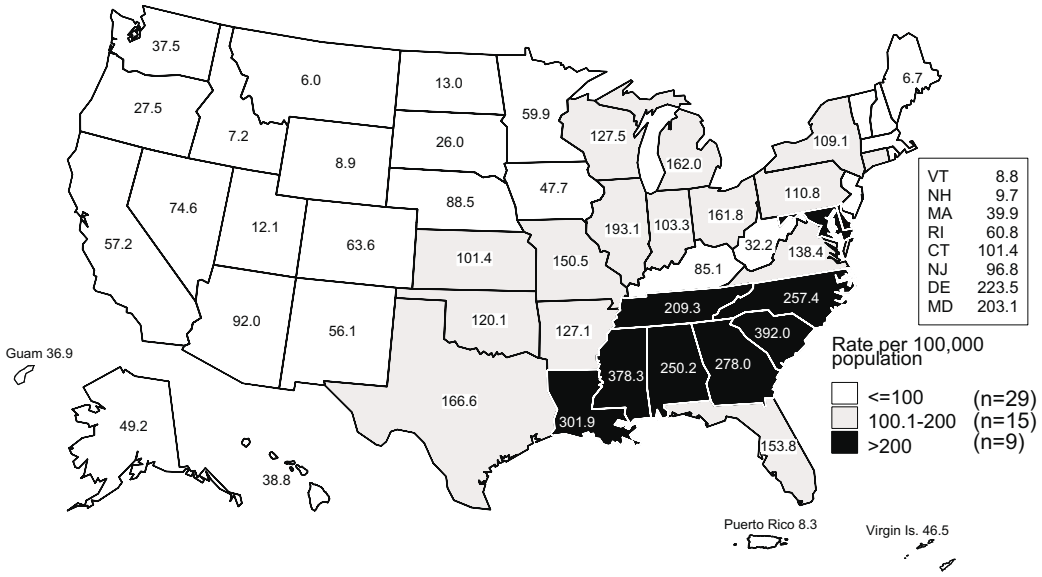
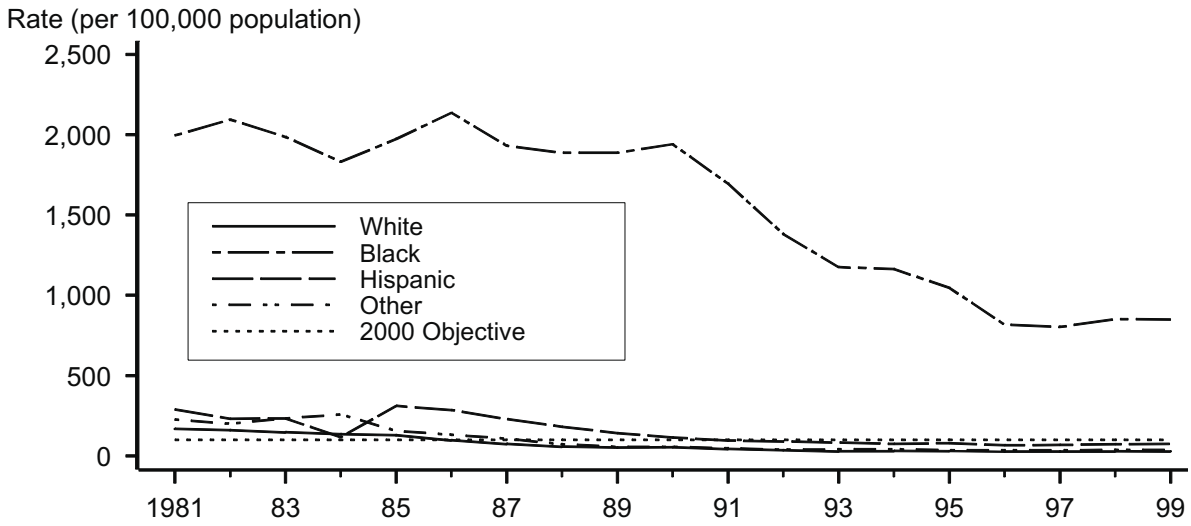


Figure 2. Gonorrhea - Rates by state: United States and outlying areas, 1999



Note: The total rate of gonorrhea for the United States and outlying areas (including Guam, Puerto Rico and Virgin Islands) was 131.4 per 100,000 population. The Healthy People year 2000 objective is 100 per 100,000 population.

Figure 3. Gonorrhea - Rates by race and ethnicity: United States, 1981-1999 and the Healthy People year 2000 objective



Note: "Other" includes Asian/Pacific Islander and American Indian/Alaska Native populations. Black, White, and Other are non-Hispanic.

Figure 4. Gonorrhea - Age- and gender-specific rates: United States, 1999

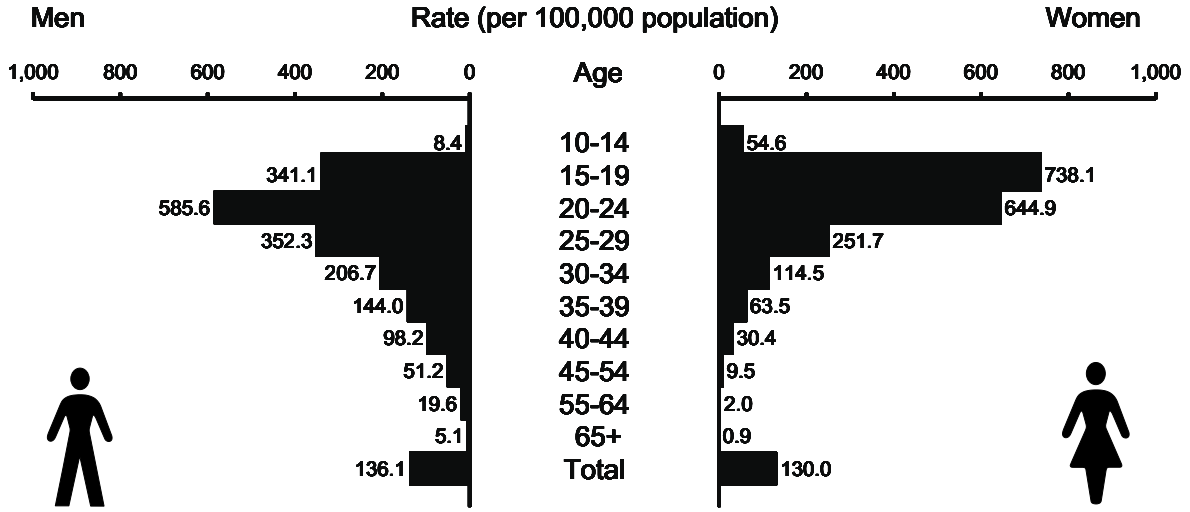


Figure 5. Gonococcal Isolate Surveillance Project (GISP) -- Location of participating clinics and regional laboratories: United States, 1999

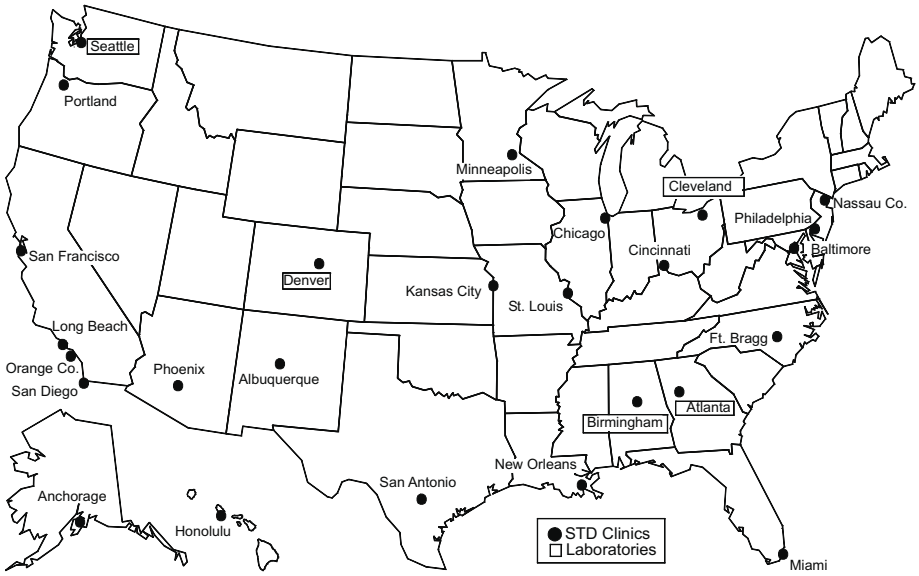
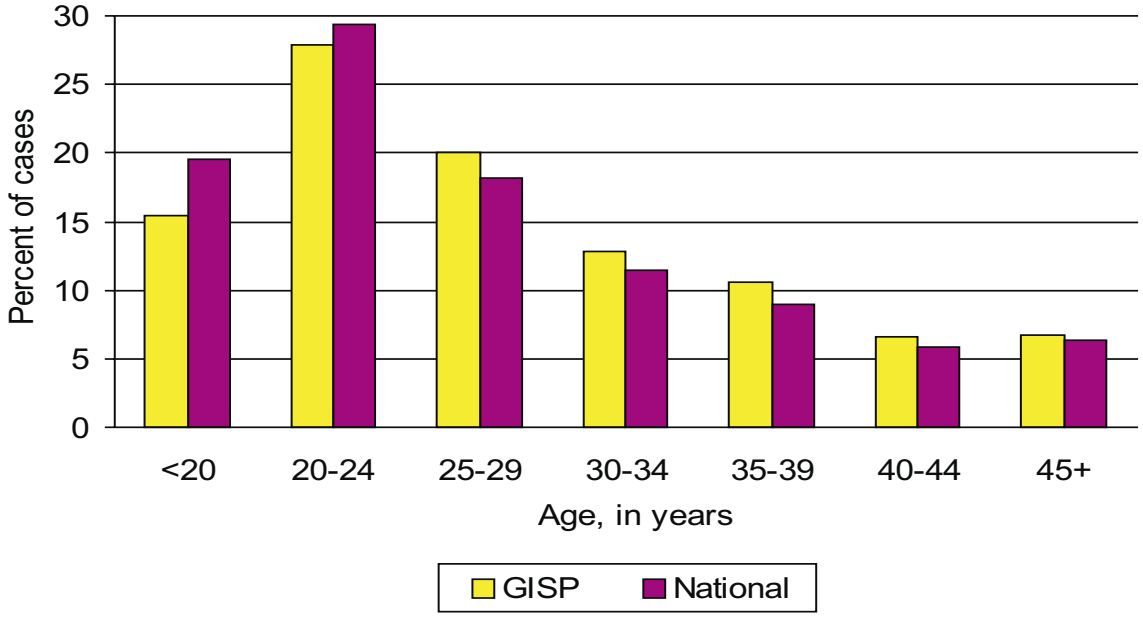
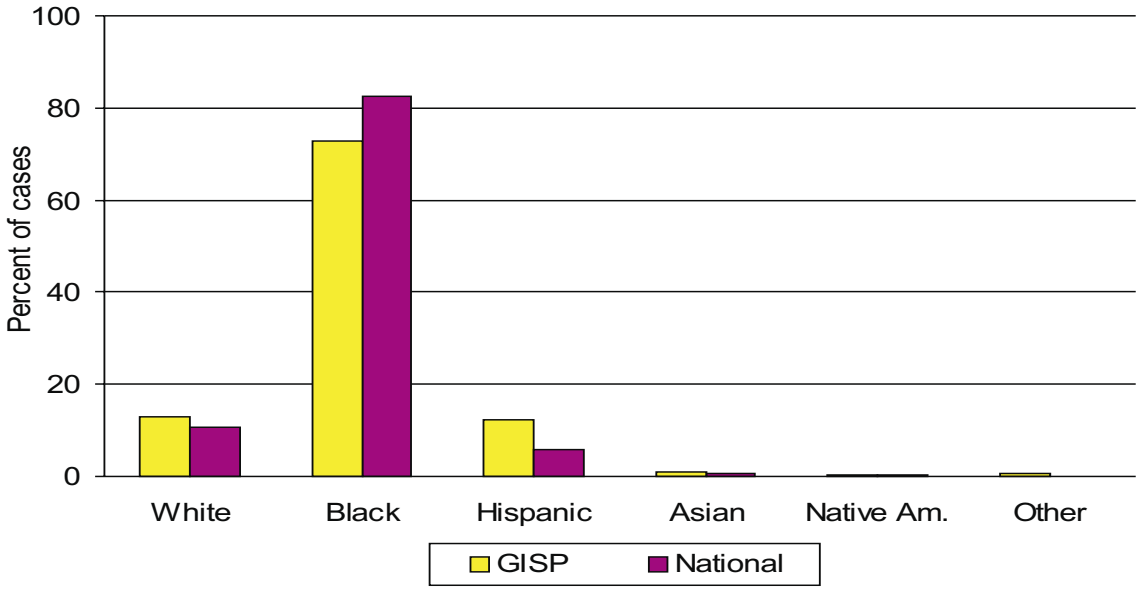


Figure 6. Age distribution of GISP participants and nationally reported gonorrhea cases in men, 1999



Note: The age <20 category includes ages 10-19 for national cases, and ages 13-19 for GISP; over 99% of the GISP cases in the <20 category are ages 15-19. National cases with unknown ages were excluded.

Figure 7. Race distribution of GISP participants and nationally reported cases of gonorrhea in men, 1999



Note: The "Other" category is not used in national gonorrhea reporting. National cases with unknown race were excluded.

Figure 8. Percentage of GISP cases that occurred among men who have sex with men (MSM), 1988-1999

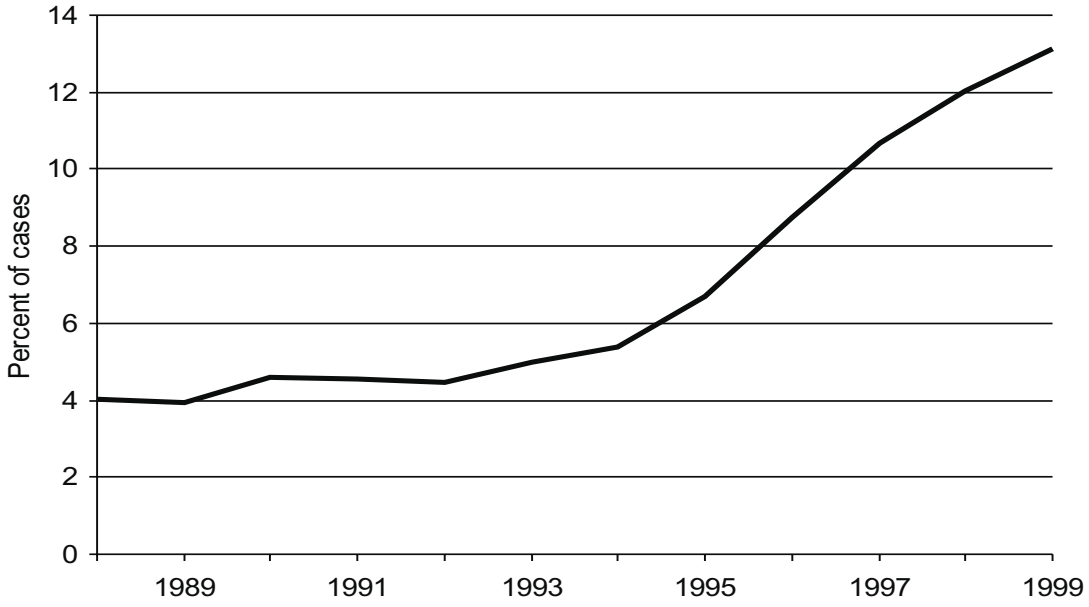
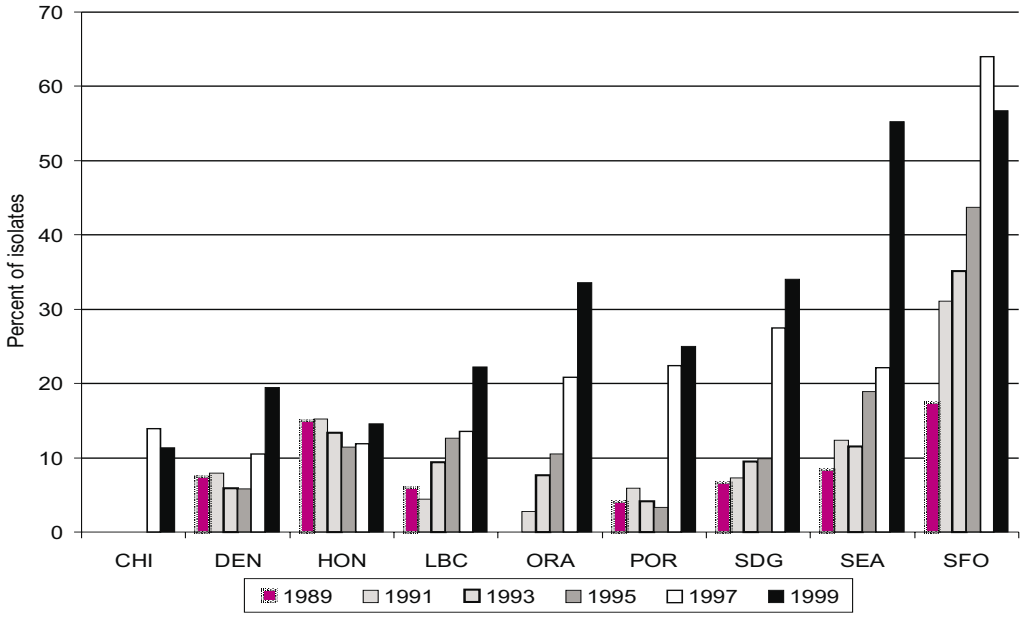
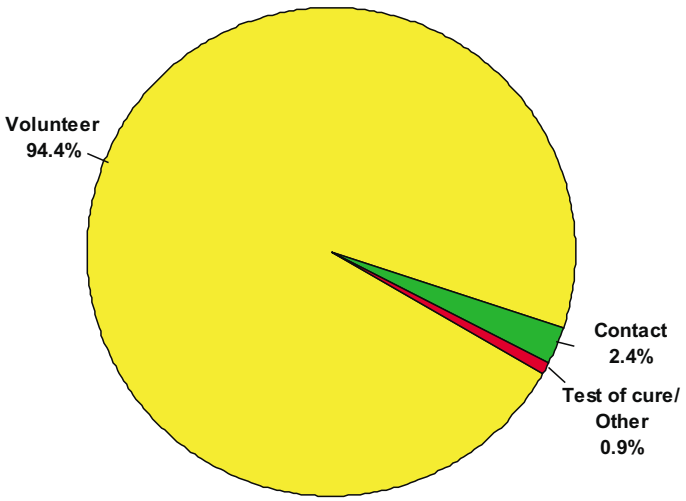


Figure 9. Percentage of GISP isolates from men who have sex with men in nine clinics, 1989-1999



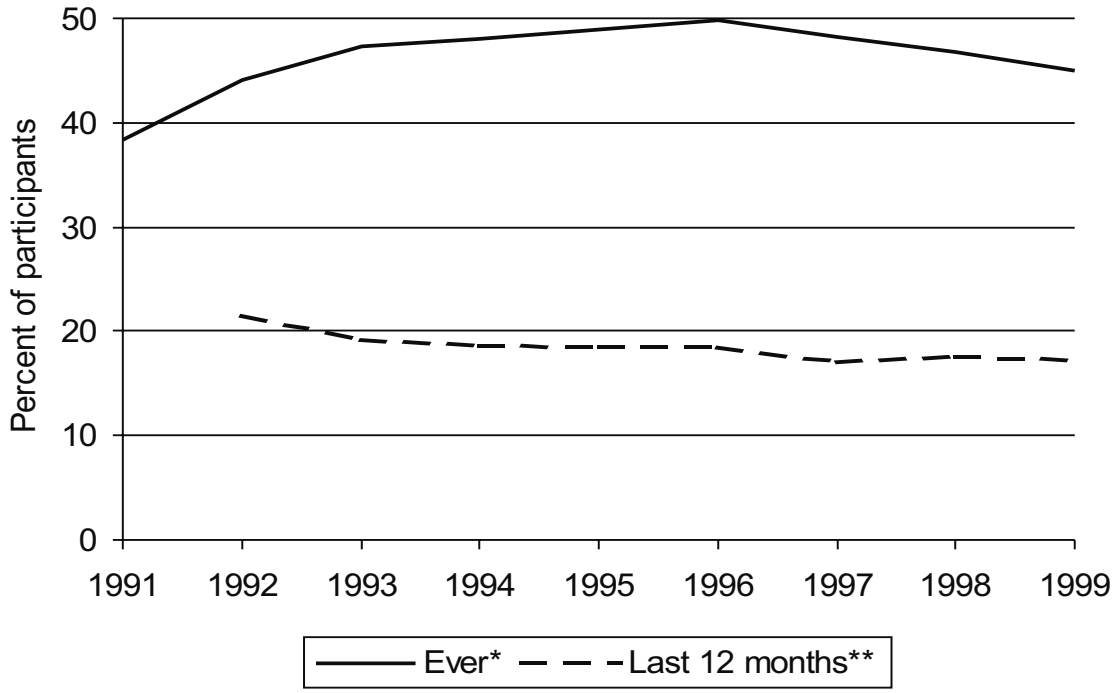
Clinics include: CHI=Chicago, IL (first year 1996 for this site); DEN=Denver, CO; HON=Honolulu, HI; LBC=Long Beach, CA; ORA=Orange County, CA (first year 1991 for this site); POR=Portland, OR; SDG=San Diego, CA; SEA=Seatlle, WA; SFO=San Francisco, CA.

Figure 10. Reason for clinic attendance among GISP participants, 1999



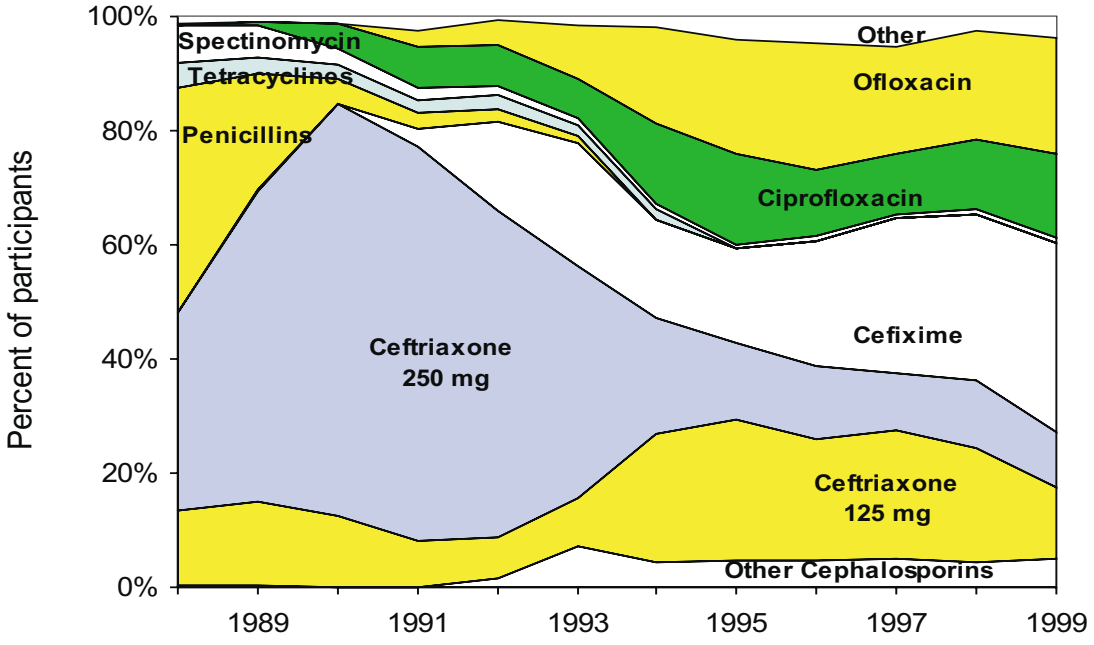
Contact=has sexual partner with gonorrhea

Figure 11. History of gonorrhea in GISP participants, 1991-1999



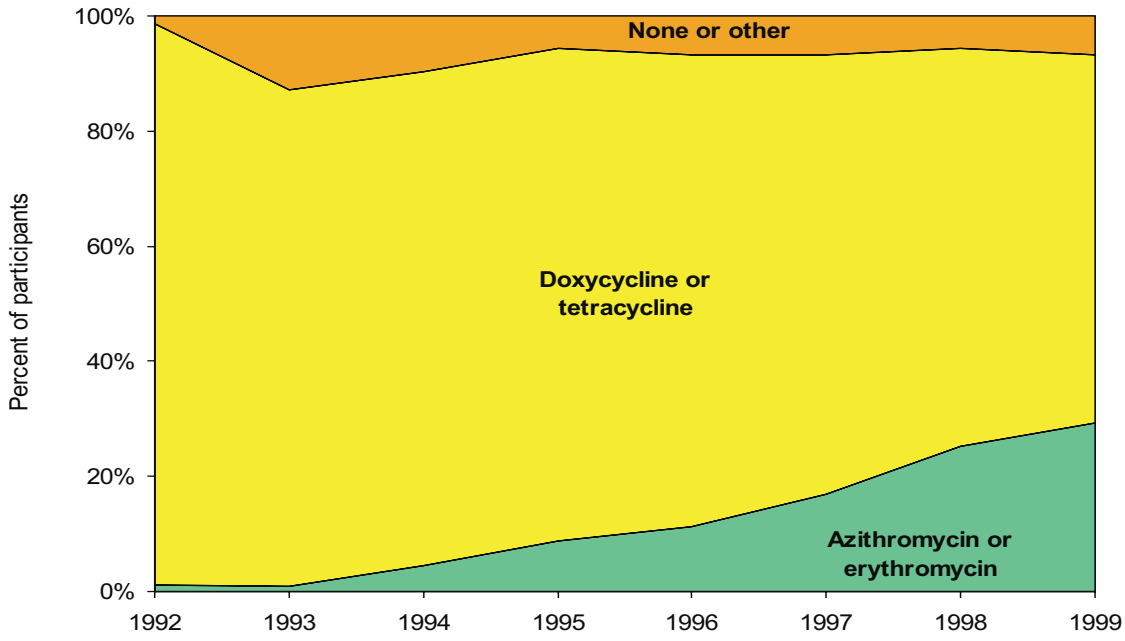
*Data first collected in 1991.
**Data first collected in 1992.

Figure 12. Drugs used to treat gonorrhea in GISP participants, 1988-1999



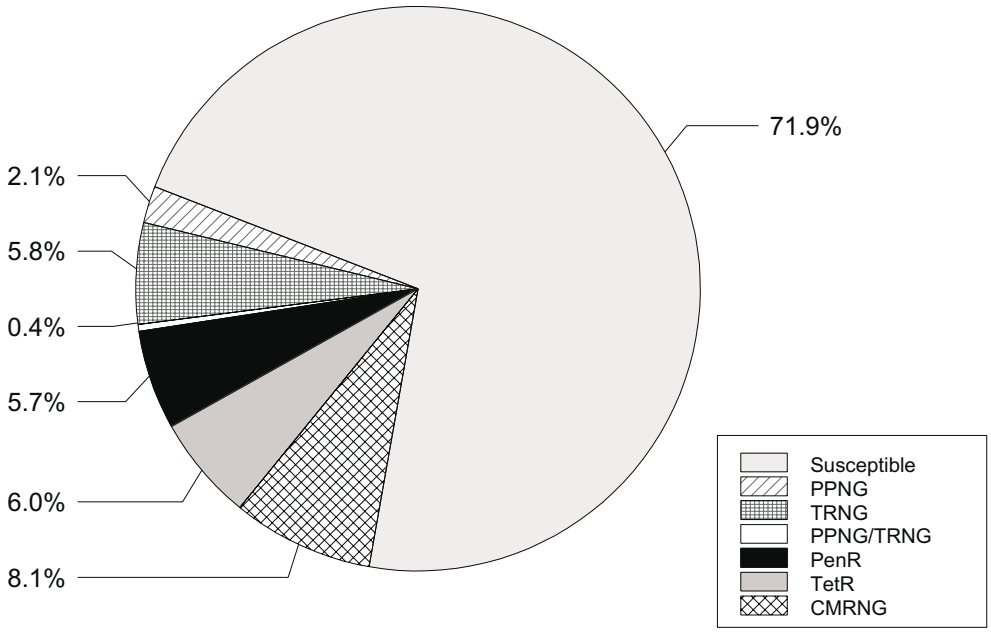
Note: “Other” includes macrolide or no drug therapy.

Figure 13. Drugs used to treat *Chlamydia trachomatis* infection in GISP participants, 1992-1999



For each year, "Other" accounted for only 0.1 - 1.0% of *C. trachomatis* treatment and erythromycin accounted for only 0.3 - 1.0% of *C. trachomatis* treatment.

Figure 14. Penicillin and tetracycline resistance among GISP isolates, 1999



Note: PPNG=penicillinase-producing *N. gonorrhoeae;* TRNG=plasmid-mediated tetracycline resistant *N. gonorrhoeae;* PPNG-TRNG=plasmid-mediated penicillin and tetracycline resistant *N. gonorrhoeae;* PenR=chromosomally mediated penicillin resistant *N. gonorrhoeae;* TetR=chromosomally mediated tetracycline resistant *N. gonorrhoeae;* CMRNG=chromosomally mediated penicillin and tetracycline resistant *N. gonorrhoeae*

Figure 15. Plasmid-mediated resistance to penicillin and tetracycline among GISP isolates, 1988-1999

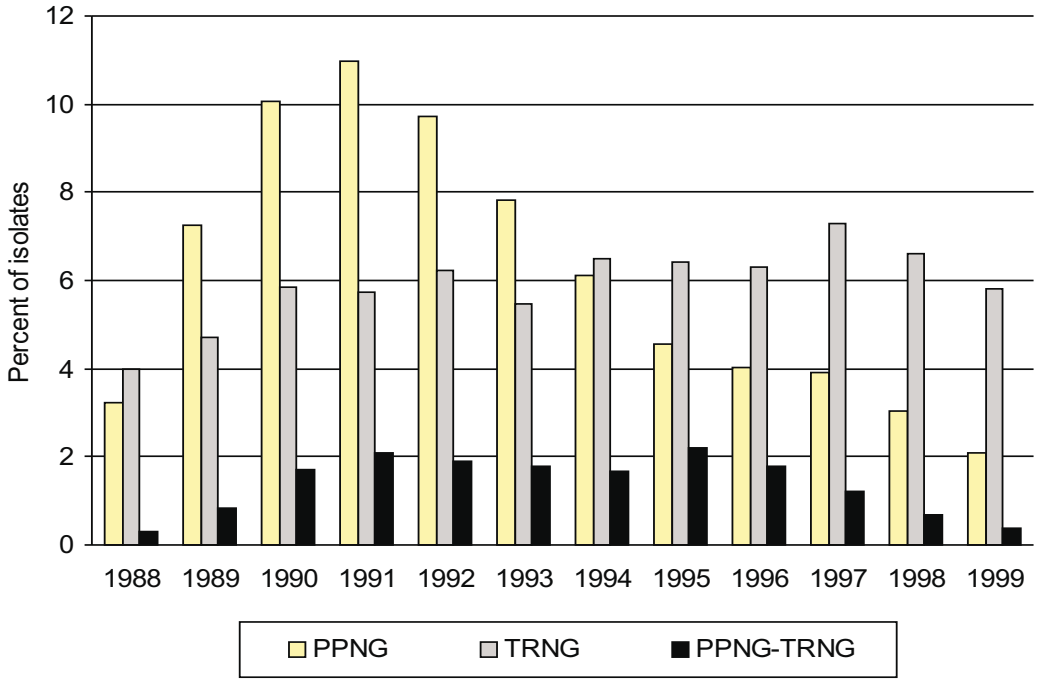


Figure 16. Chromosomally mediated resistance to penicillin and tetracycline among GISP isolates, 1988-1999

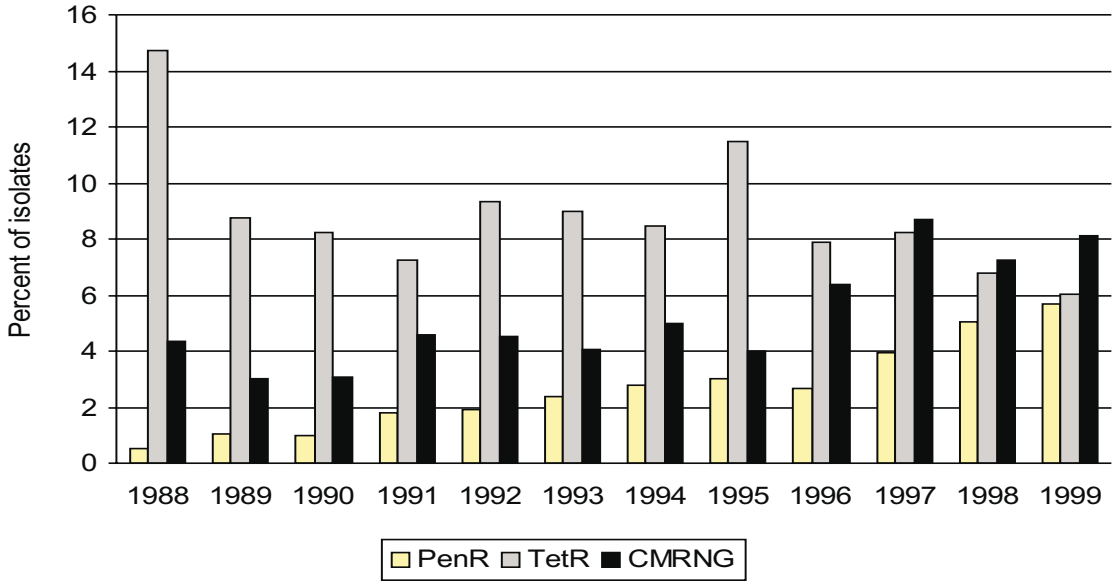


Figure 17. Distribution of MICs to ceftriaxone among GISP isolates, 1988 and 1999

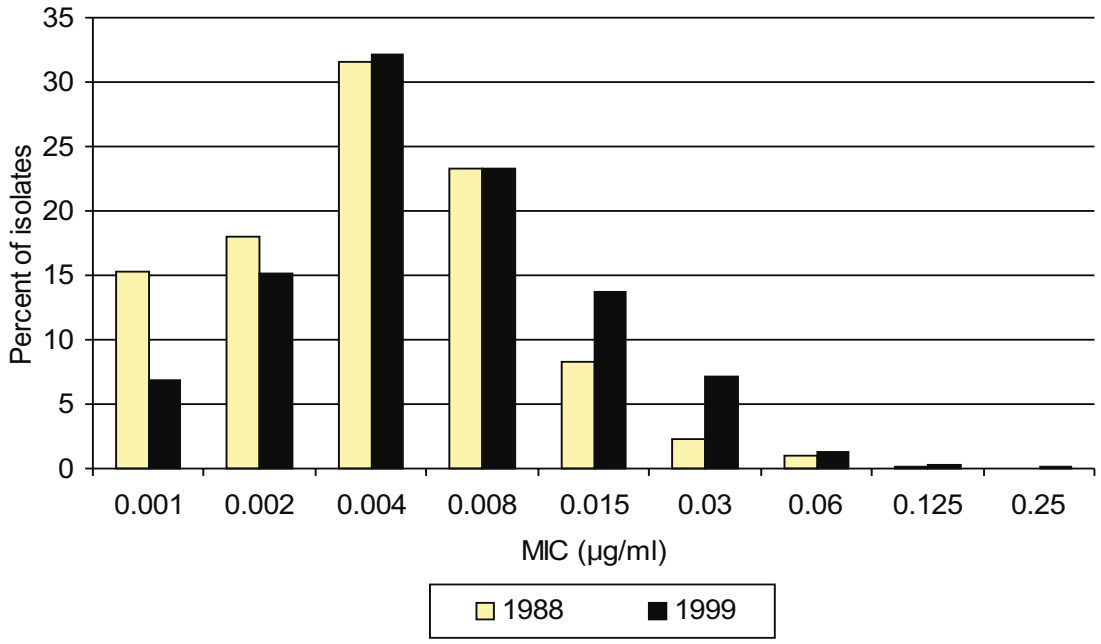
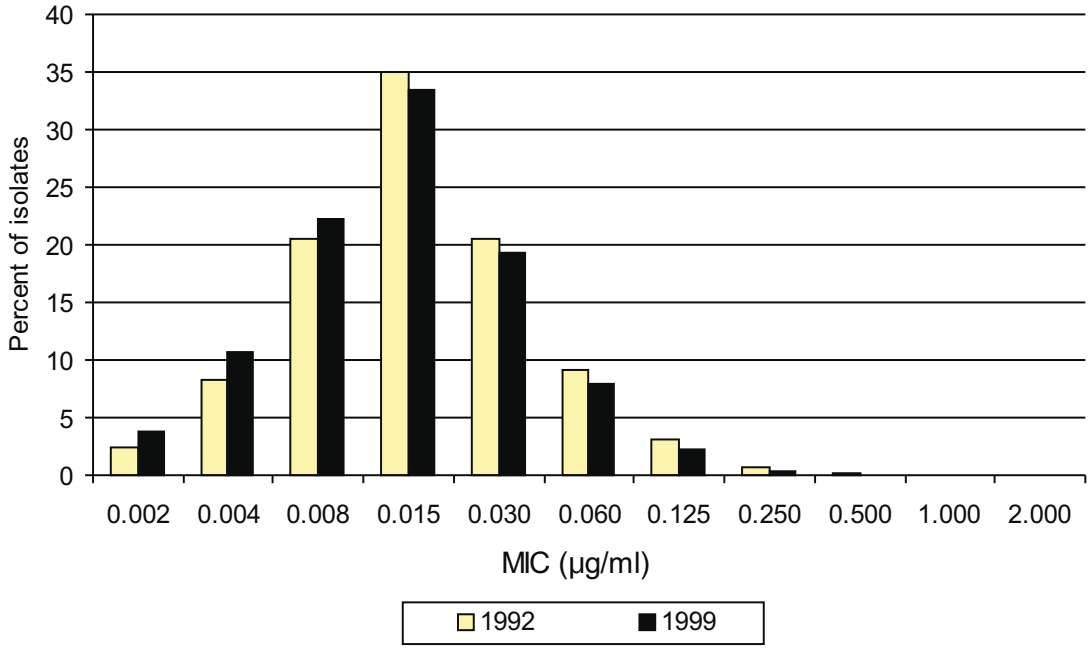
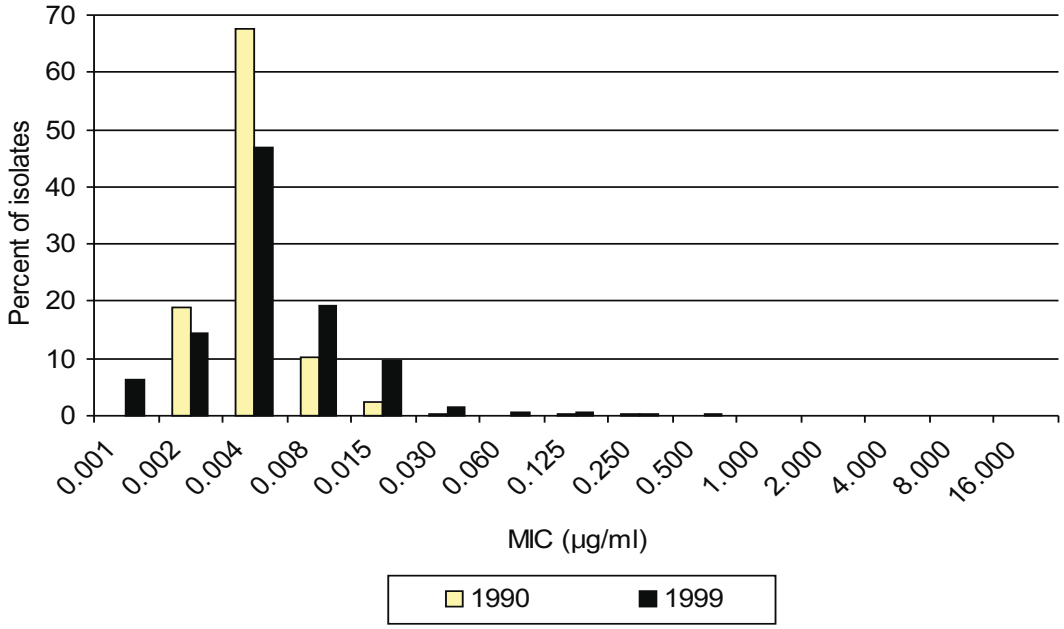


Figure 18. Distribution of MICs to cefixime among GISP isolates, 1992 and 1999



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.

Figure 19. Distribution of MICs to ciprofloxacin among GISP isolates, 1990 and 1999



In 1999, there were six isolates with MIC 1.0 µg/ml, four isolates with MIC 2.0 µg/ml, five isolates with MIC 4.0 µg/ml, two isolates with MIC 8.0 µg/ml, and two isolates with MIC 16.0 µg/ml.

Figure 20. Percentage of GISP isolates with intermediate resistance or resistance to ciprofloxacin, 1990-1999

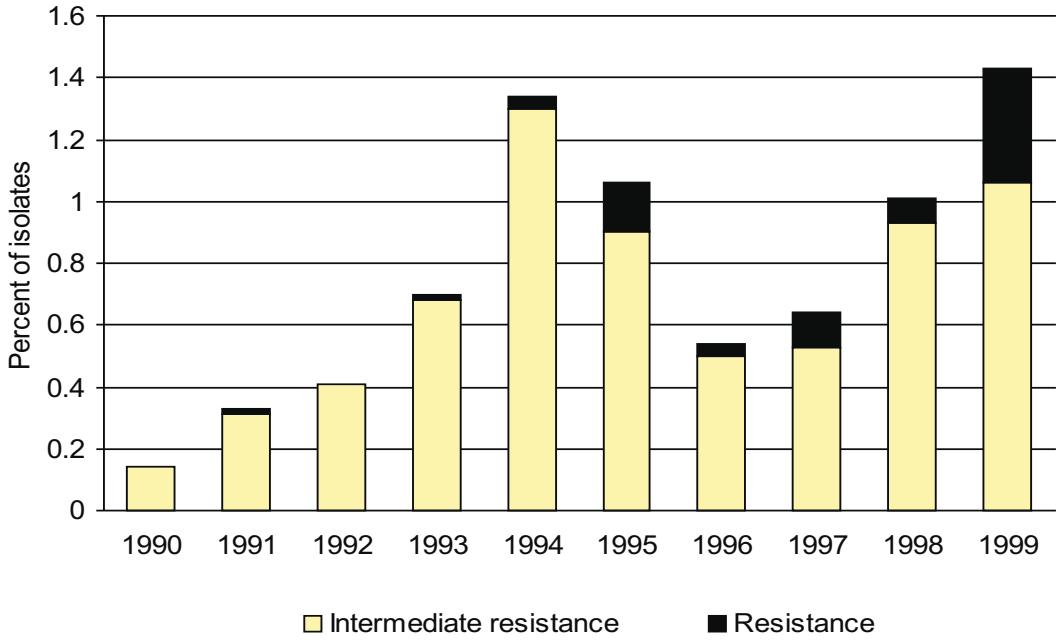
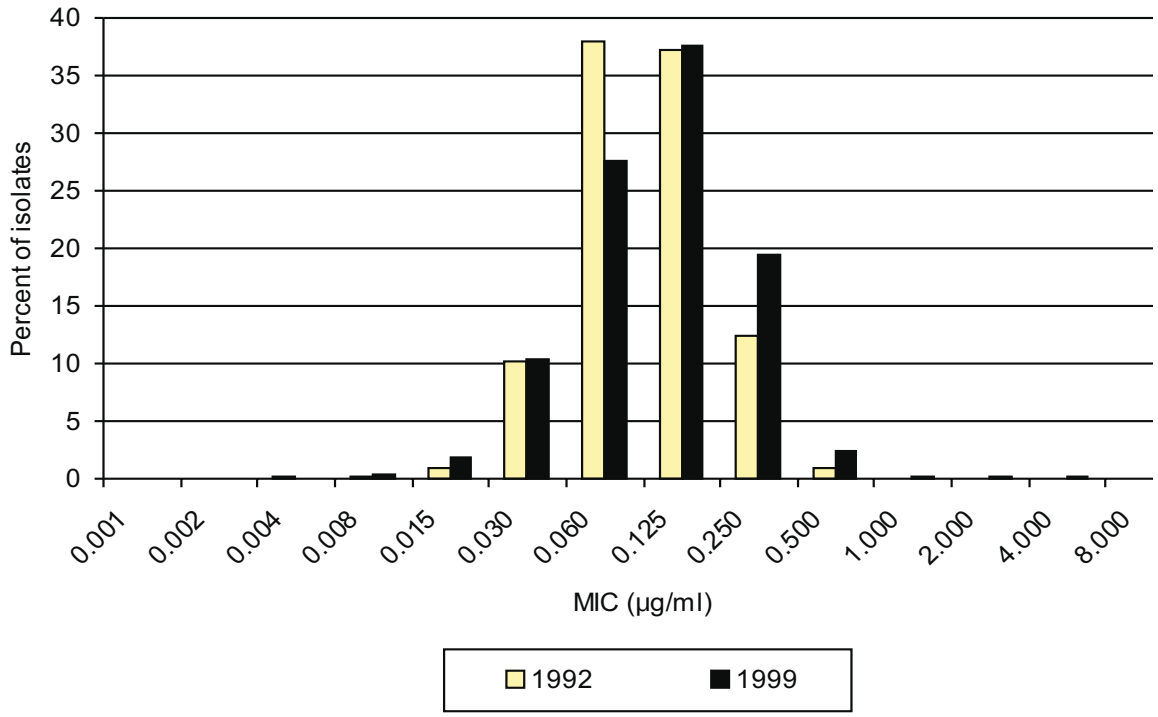


Figure 21. Distribution of MICs to azithromycin among GISP isolates, 1992 and 1999



In 1999, there was one isolate with MIC 8.0 µg/ml.

CLINIC-SPECIFIC DEMOGRAPHIC, CLINICAL, AND LABORATORY DATA

The remainder of this report provides clinic-specific figures for each of the 26 currently participating clinics. Individual figures for each clinic show demographic and clinical characteristics of the men with gonorrhea enrolled in GISP, as well as antimicrobial susceptibilities for the *N. gonorrhoeae* isolates. The number of isolates submitted by each clinic is 300 when the full sample of 25 isolates per month is obtained. However, the number of isolates submitted is lower for many clinics located in areas with low gonorrhea rates. Each page of figures is labeled with the city of the participating clinic and the actual number of isolates on which the clinic's 1999 data are based.

Definitions of terms and abbreviations used in the clinic-specific figures are given below.

Figure D: contact=has sexual partner with gonorrhea

Figure F: ceftriaxone 250=ceftriaxone 250 mg
ceftriaxone 125=ceftriaxone 125 mg
other cephalo=other cephalosporins

Figure G: azi/ery=azithromycin/erythromycin
doxy/tet=doxycycline/tetracycline

Figure H: PPNG=penicillinase-producing *N. gonorrhoeae*
TRNG=plasmid-mediated tetracycline resistant *N. gonorrhoeae*
PPNG-TRNG=plasmid-mediated penicillin and tetracycline resistant *N. gonorrhoeae*
PenR=chromosomally mediated penicillin resistant *N. gonorrhoeae*
TetR=chromosomally mediated tetracycline resistant *N. gonorrhoeae*
CMRNG=chromosomally mediated penicillin and tetracycline resistant *N. gonorrhoeae*

Figure K: intermediate res=intermediate resistance