Sexually Transmitted Disease Surveillance 2018:

Gonococcal Isolate Surveillance Project (GISP) Supplement & Profiles

Division of STD Prevention
April 2020

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
CENTERS FOR DISEASE CONTROL AND PREVENTION
NATIONAL CENTER FOR HIV/AIDS, VIRAL HEPATITIS, STD, AND TB PREVENTION
DIVISION OF STD PREVENTION
ATLANTA, GEORGIA 30329-4027

Acknowledgments

Publication of this report would not have been possible without the contributions of all participating state and local health departments, sexually transmitted disease clinics, public health laboratories, and regional laboratories. Contributions from eight locations were received through the Strengthening the US Response to Resistant Gonorrhea (SURRG) project led by Karen Schlanger, Epidemiology and Statistics Branch of the Division of STD Prevention, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, Centers for Disease Control and Prevention.

This report was prepared by:

Alesia Harvey, Viani Picchetti, Tremeka Sanders, and Sancta St. Cyr, Surveillance and Data Management Branch of the Division of STD Prevention, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, Centers for Disease Control and Prevention.

Additional contributions by Cau Pham, Laboratory Reference and Research Branch of the Division of STD Prevention, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, Centers for Disease Control and Prevention.

Suggested Citation

Centers for Disease Control and Prevention. *Sexually Transmitted Disease Surveillance 2018: Gonococcal Isolate Surveillance Project (GISP) Supplement and Profiles*. Atlanta: U.S. Department of Health and Human Services; 2020.

Web Site

The online version of this report is available at https://www.cdc.gov/std/gisp/default.htm.

Gonococcal Isolate Surveillance Project (GISP) Supplement and Profiles, 2018

Introduction

Although gonorrhea is an ancient disease that has affected humans for centuries and effective therapy has been available since the early twentieth century, this sexually transmitted disease (STD) remains prevalent: gonorrhea is the second most commonly reported notifiable disease in the United States and 583,405 cases were reported in 2018.[1] As with other STDs, the reporting of gonorrhea is incomplete and the Centers for Disease Control and Prevention (CDC) estimates that approximately 1,140,000 infections of gonorrhea occur annually in the United States.[2] Infections due to *Neisseria gonorrhoeae* are a major cause of pelvic inflammatory disease (PID) in the United States. PID can lead to serious reproductive outcomes in women, such as tubal factor infertility, ectopic pregnancy, and chronic pelvic pain.

The cornerstone of public health gonorrhea control is detection and treatment of gonorrhea, so as to prevent sequelae and limit disease transmission. For decades, gonorrhea has been easily treated with a single dose of a single antimicrobial agent. However, *N. gonorrhoeae* has progressively developed resistance to each antimicrobial used for treatment of gonorrhea. In the last decade, development of fluoroquinolone resistance resulted in the availability of only a single class of antimicrobials that met CDC's efficacy standards – the cephalosporins. As a method to improve treatment efficacy and to slow the emergence and spread of resistance to cephalosporins, dual therapy containing cephalosporins with doxycycline or azithromycin was recommended in 2010.[3] Declining susceptibility to cefixime resulted in a change to the 2015 CDC STD Treatment Guidelines. Now, therapy with ceftriaxone, combined with azithromycin is the only CDC-recommended treatment regimen for uncomplicated gonorrhea.[4] Therefore, continued surveillance of *N. gonorrhoeae* antimicrobial susceptibility is critical.

Gonococcal Isolate Surveillance Project (GISP) Overview

The Gonococcal Isolate Surveillance Project (GISP) was established in 1986 to monitor trends in antimicrobial susceptibilities of *N. gonorrhoeae* strains in the United States in order to establish an evidence-based rationale for selection of gonococcal therapies. GISP is a sentinel surveillance system and collaboration between participating STD clinics and their state or local public health authorities, regional laboratories, and CDC.

N. gonorrhoeae isolates are collected monthly from up to the first 25 men with gonococcal urethritis seeking care at participating STD clinics. Clinical and demographic data are abstracted from medical records. Isolates are shipped from participating clinics to the regional laboratories for agar dilution antimicrobial susceptibility testing. In 2018, isolates were tested to determine minimum inhibitory concentrations (MICs) of penicillin, tetracycline, ceftriaxone, cefixime, ciprofloxacin, azithromycin, and gentamicin. Cefixime susceptibility testing was discontinued in 2007 and re-started in 2009. Gentamicin susceptibility testing was first started in 2015.

Findings from GISP have directly contributed to the CDC's STD Treatment Guidelines released in 1993, 1998, 2002, 2006, 2010, and 2015 and the updates released in 2000, 2004, 2007, and

2012. Data from GISP have also been presented in multiple scientific papers and conference presentations. Additional information on GISP and links to recent publications can be found on the GISP website: https://www.cdc.gov/std/gisp/default.htm.

2018 GISP Sites and Regional Laboratories

STD clinics affiliated with 33 state or city health departments contributed 5,160 gonococcal isolates to GISP in 2018. Of these sites, 11 current sites have participated continuously since 1987: Albuquerque, New Mexico; Atlanta, Georgia; Birmingham, Alabama; Honolulu, Hawaii; New Orleans, Louisiana; Philadelphia, Pennsylvania; Phoenix, Arizona; Portland, Oregon; San Diego, California; San Francisco, California; and Seattle, Washington. The other current sites are Anchorage, Alaska (1987-2003, 2018); Boston, Massachusetts (1987–1992, 2014–2018); Buffalo, New York (2014–2018); Chicago, Illinois (1996–2018); Cleveland, Ohio (1991–2018); Columbus, Ohio (2012–2018); Dallas, Texas (1999–2018); Denver, Colorado (1987-2013, 2018); Greensboro, North Carolina (2002–2018); Indianapolis, Indiana (2013–2018); Kansas City, Missouri (1992–2001, 2007–2018); Jackson, Mississippi (2018); Los Angeles, California (2003–2018); Las Vegas, Nevada (2002–2018); Miami, Florida (1998-2013, 2018); Milwaukee, Wisconsin (2018); Minneapolis, Minnesota (1992–2018); New York, New York (2006–2018); Orange County, California (1991–2018); Pontiac, Michigan (2012–2018); Tripler Army Medical Center, Hawaii (2001–2018); and Washington, District of Columbia (2018).

Starting in 2017, four of the seven Antibiotic Resistance Laboratory Network state public health laboratories began functioning as GISP Regional Laboratories. In 2018, antimicrobial susceptibility testing of all isolates was conducted by these same four laboratories: Maryland Department of Health and Mental Hygiene (Baltimore, Maryland), Tennessee Department of Health (Nashville, Tennessee), Texas Department of State Health Services (Austin, Texas), and Washington State Department of Health (Seattle, Washington).

Susceptibility to Antimicrobial Agents

Susceptibility to cefixime

Susceptibility testing for cefixime began in 1992, was discontinued in GISP in 2007, and was re-started in 2009. The distribution of cefixime MICs each year from 2014–2018 is displayed in Figure 1 and Table 1. Each year, approximately 90% of isolates exhibited cefixime MICs ≤0.03 µg/ml. The percentage of isolates with elevated cefixime MICs (≥0.25 µg/ml) fluctuated around 0.4% between 2014 and 2018. Site-specific data are presented in the Site Profiles section of this report (Figure H).

Additional data on susceptibility to cefixime can be found in *Sexually Transmitted Disease Surveillance 2018*.[1]

Susceptibility to ceftriaxone

Susceptibility testing for ceftriaxone began in 1987. The distribution of ceftriaxone MICs each year from 2014–2018 is displayed in Figure 2 and Table 2. Each year, approximately 90% of isolates exhibited ceftriaxone MICs ≤0.015 µg/ml. The percentage of GISP isolates that exhibited

elevated ceftriaxone MICs, defined as ≥0.125 µg/ml, has fluctuated around 0.2% between 2014 and 2018. Site-specific data are presented in the Site Profiles section of this report (Figure G).

Additional data on susceptibility to ceftriaxone can be found in *Sexually Transmitted Disease Surveillance 2018*.[1]

Susceptibility to azithromycin

Susceptibility testing for azithromycin began in 1992. The distribution of azithromycin MICs each year from 2014–2018 is displayed in Table 3 and Figure 3. Most isolates had azithromycin MICs of 0.125–0.500 µg/ml. The proportion of GISP isolates with azithromycin MICs of ≥2.0 µg/ml increased from 2.4% in 2014 to 4.6% in 2018. Site-specific data are presented in the Site Profiles section of this report (Figure J).

Additional data on susceptibility to azithromycin can be found in *Sexually Transmitted Disease Surveillance 2018*.[1]

Susceptibility to ciprofloxacin

Susceptibility testing for ciprofloxacin began in 1990. The proportion of GISP isolates with ciprofloxacin resistance (MIC ≥1 µg/ml) initially peaked in 2007 at 14.8%. Following a decline in 2008 and 2009, the proportion increased to 31.2% by 2018. The prevalence of resistance increased sharply among isolates from gay, bisexual and other men who have sex with men (MSM) during the 2000s and peaked at 39.0% in 2006 before decreasing to 20.1% in 2009 (Figure 4). In 2018, 40.8% of isolates from MSM exhibited ciprofloxacin resistance. The prevalence of ciprofloxacin resistance increased during 2000–2007 among isolates from men who report sex exclusively with women (MSW), decreased during 2008 and 2009, and increased during 2010–2018. In 2018, 25.2% of isolates from MSW exhibited ciprofloxacin resistance. Site-specific data on intermediate resistance and resistance to ciprofloxacin are presented in the Site Profiles section of this report (Figure I).

Site Profiles

The Site Profiles consist of figures depicting the demographic and clinical data of the men who submitted specimens for GISP and the antimicrobial susceptibility results of the *N. gonorrhoeae* isolates submitted. Each figure is labeled with the participating site and the number of isolates on which the site's data are based. The maximum number of isolates submitted by each site annually is 300. The number of isolates submitted is fewer for some sites located in areas with lower gonorrhea morbidity.

Definitions of terms, abbreviations and notes used in the site-specific figures

Figure A: Cases with unknown age were excluded.

Figure B: Cases are reported using Office of Management and Budget (OMB) compliant race and ethnicity categories. The "Other" category includes participants who selected more than one race category and participants with unknown race.

Figure C: Men who self-identified as gay or bisexual or reported recent male sex partners were categorized as men who have sex with men.

Figure D: Other = other less frequently used drugs, including azithromycin.

Figure E: Azi/Ery = azithromycin/erythromycin; Doxy/Tet = doxycycline/tetracycline.

Figure F: 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*.

GISP Antimicrobial Susceptibility Criteria

Antimicrobial susceptibility criteria used in GISP in 2018 are as follows:

- Ceftriaxone, minimum inhibitory concentration (MIC) ≥0.5 µg/ml (decreased susceptibility)*
- Ceftriaxone, MIC ≥0.125 µg/ml (elevated MIC)*
- Cefixime, MIC ≥0.5 µg/ml (decreased susceptibility)*
- Cefixime, MIC ≥0.25 µg/ml (elevated MIC)*
- Azithromycin, MIC ≥2.0 µg/ml (elevated MIC)*
- Ciprofloxacin, MIC 0.125–0.5 µg/ml (intermediate resistance)
- Ciprofloxacin, MIC ≥1.0 µg/ml (resistance)
- Penicillin, MIC ≥2.0 µg/ml or Beta lactamase positive (resistance)
- Tetracycline, MIC ≥2.0 µg/ml (resistance)
- Gentamicin (MIC values correlated with susceptibility and resistance have not been established)*

The majority of these criteria are also recommended by the Clinical and Laboratory Standards Institute (CLSI).[5]

* As of December 2018, the CLSI criteria for resistance to ceftriaxone, cefixime, gentamicin, and azithromycin and for susceptibility to azithromycin and gentamicin have not been established for *N. gonorrhoeae*.

Additional resources

Additional information on GISP, as well as useful resources and links, can be found on the CDC Division of STD Prevention (DSTDP) Antimicrobial Resistant Gonorrhea website: **https://www.cdc.gov/std/Gonorrhea/arg/default.htm**

Other United States surveillance data on *N. gonorrhoeae* and other STDs and additional data from GISP may be found on the CDC DSTDP Surveillance and Statistics website: **https://www.cdc.gov/std/stats/**

Data on antimicrobial resistance in *N. gonorrhoeae* and other bacterial pathogens may be found in CDC's report, Antibiotic Resistance Threats in the United States, 2019: **https://www.cdc.gov/drugresistance/biggest-threats.html**

References

1. CDC. *Sexually Transmitted Diseases Surveillance 2018*. Atlanta: US Department of Health and Human Services; 2019.
2. CDC. Antibiotic Resistance Threats in the United States, 2019. Atlanta, GA: U.S. Department of Health and Human Services, CDC; 2019.
3. CDC. Sexually transmitted diseases treatment guidelines, 2010. *MMWR* Recomm Rep 2015; 59(12):1–110.
4. CDC. Sexually transmitted diseases treatment guidelines, 2015. *MMWR* Recomm Rep 2015; 64(3):1–137.
5. Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing. 28th ed. CLSI Supplement, M100. Wayne, PA: Clinical and Laboratory Standards Institute, 2018.

Figure 1. Distribution of Cefixime Minimum Inhibitory Concentrations (MICs) Among *Neisseria gonorrhoeae* Isolates, Gonococcal Isolate Surveillance Project (GISP), 2014-2018

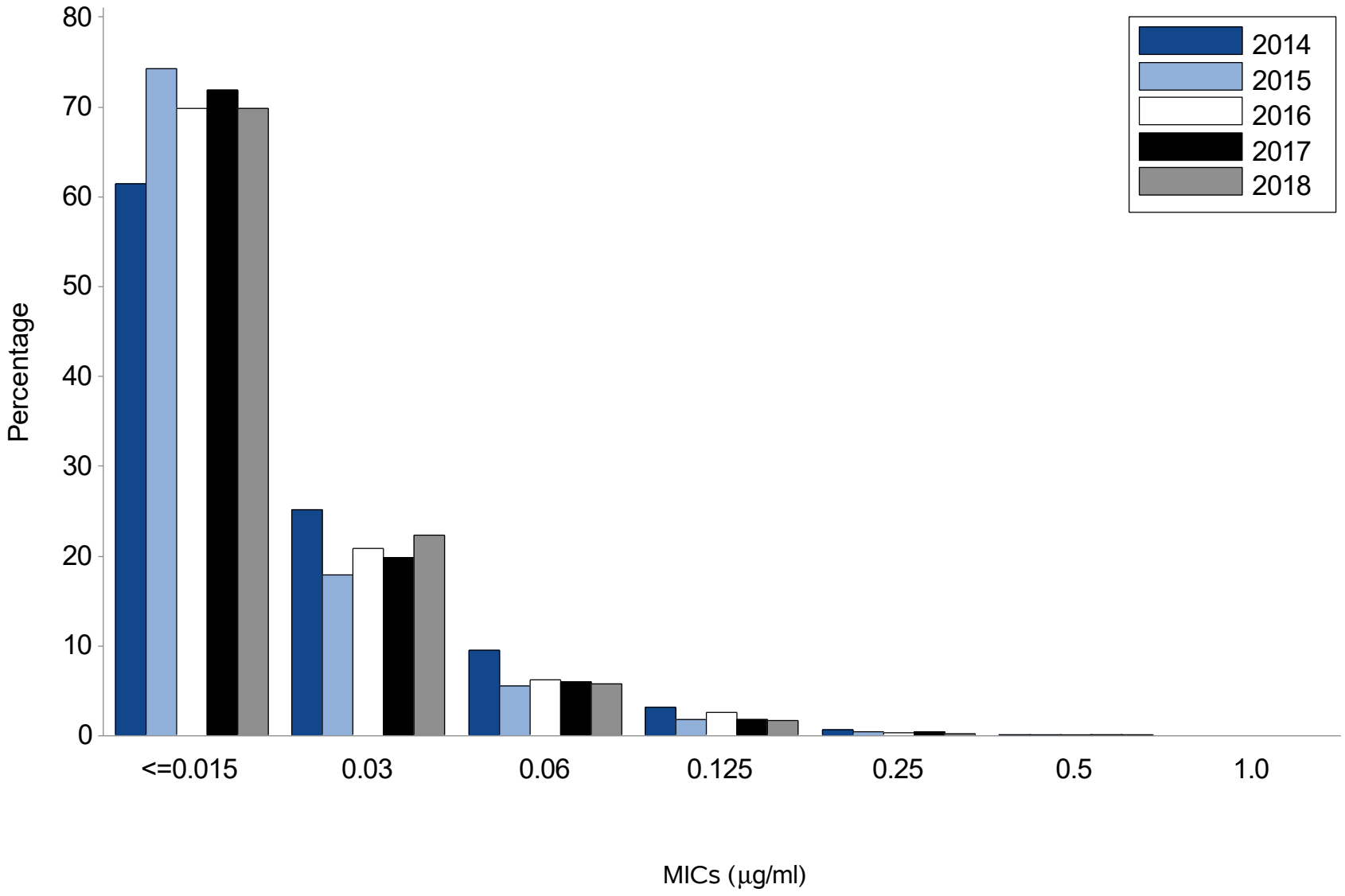


Figure 2. Distribution of Ceftriaxone Minimum Inhibitory Concentrations (MICs) Among *Neisseria gonorrhoeae* Isolates, Gonococcal Isolate Surveillance Project (GISP), 2014-2018

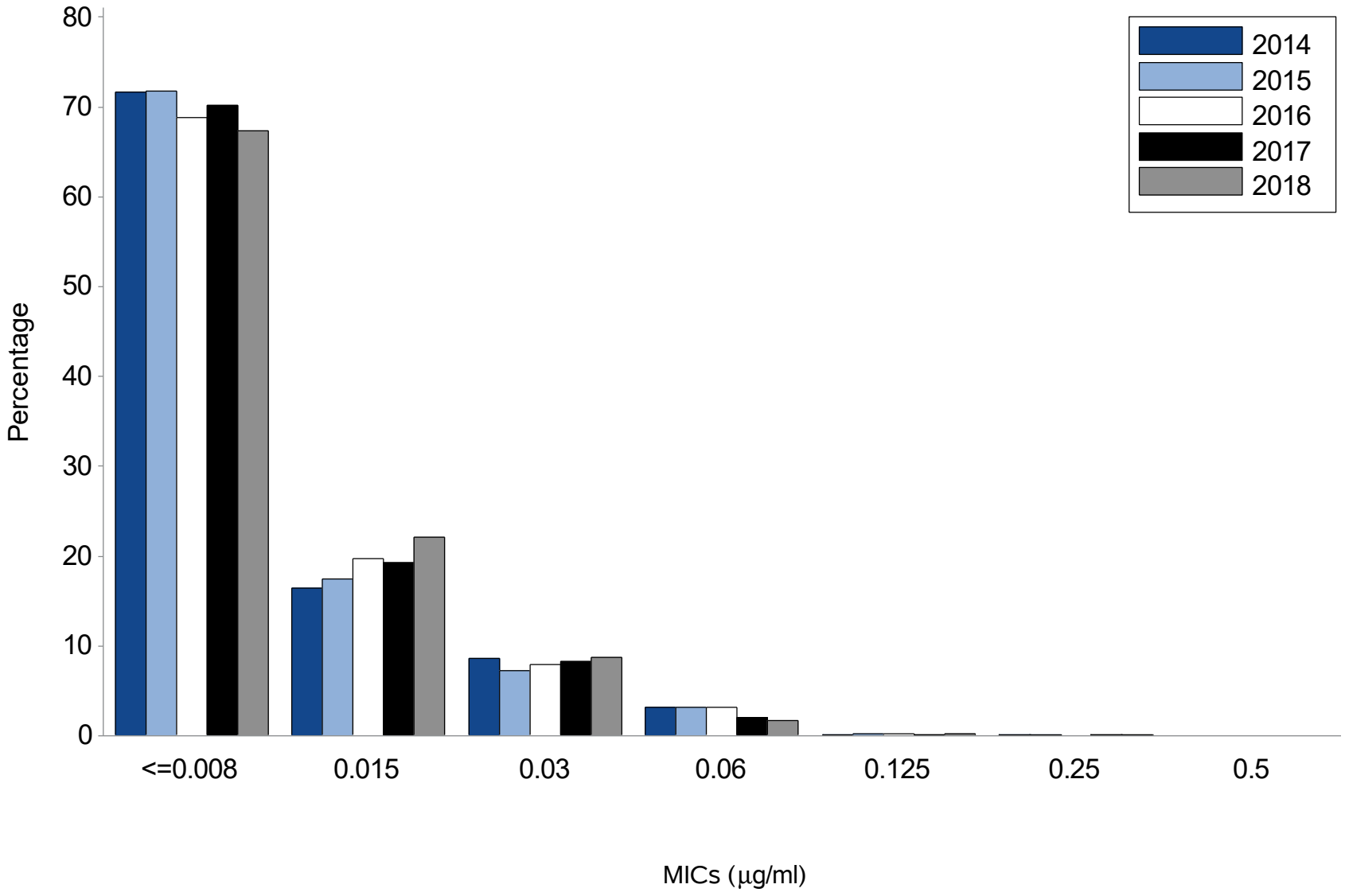


Figure 3. Distribution of Azithromycin Minimum Inhibitory Concentrations (MICs) Among *Neisseria gonorrhoeae* Isolates, Gonococcal Isolate Surveillance Project (GISP), 2014-2018

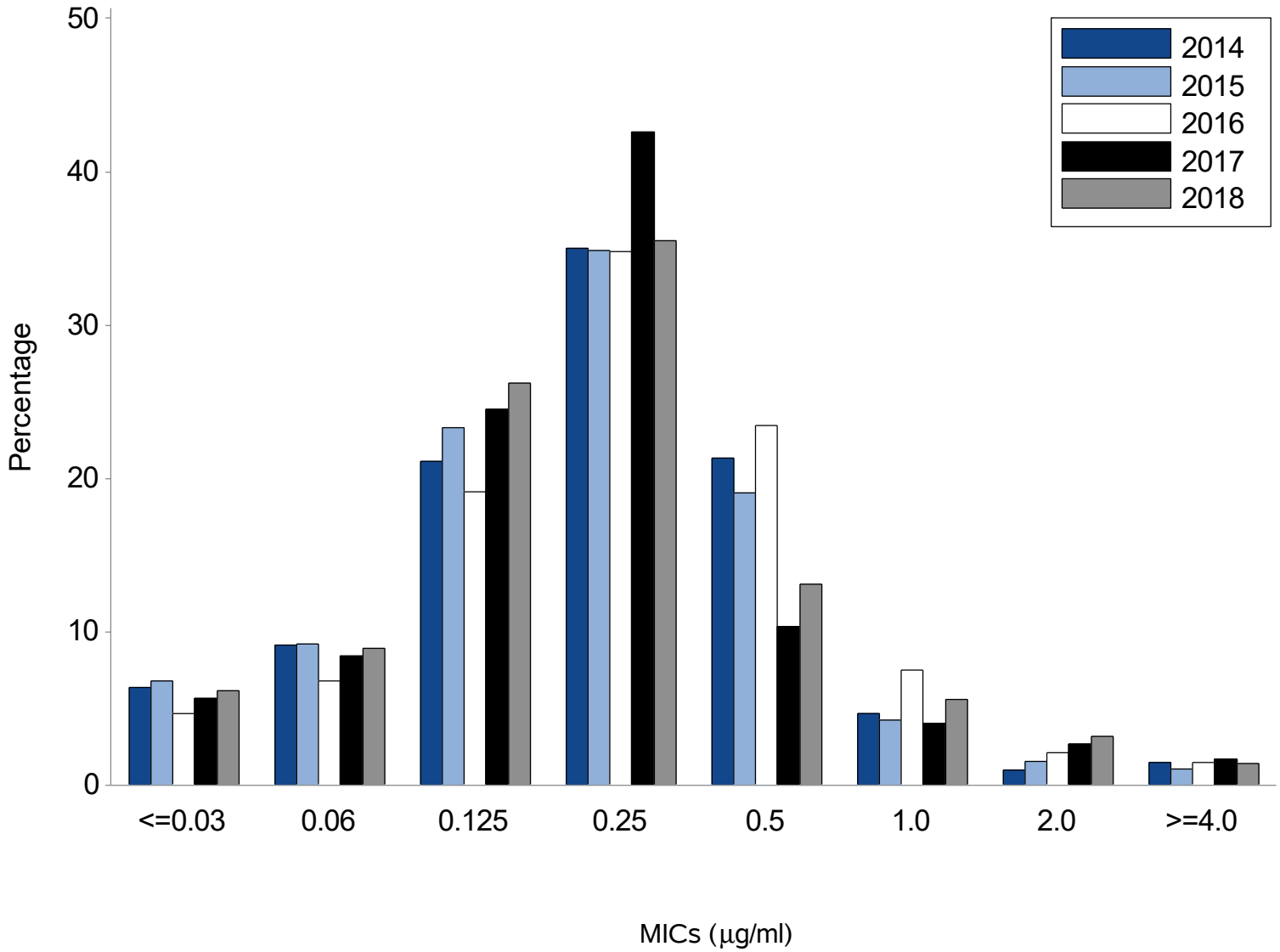
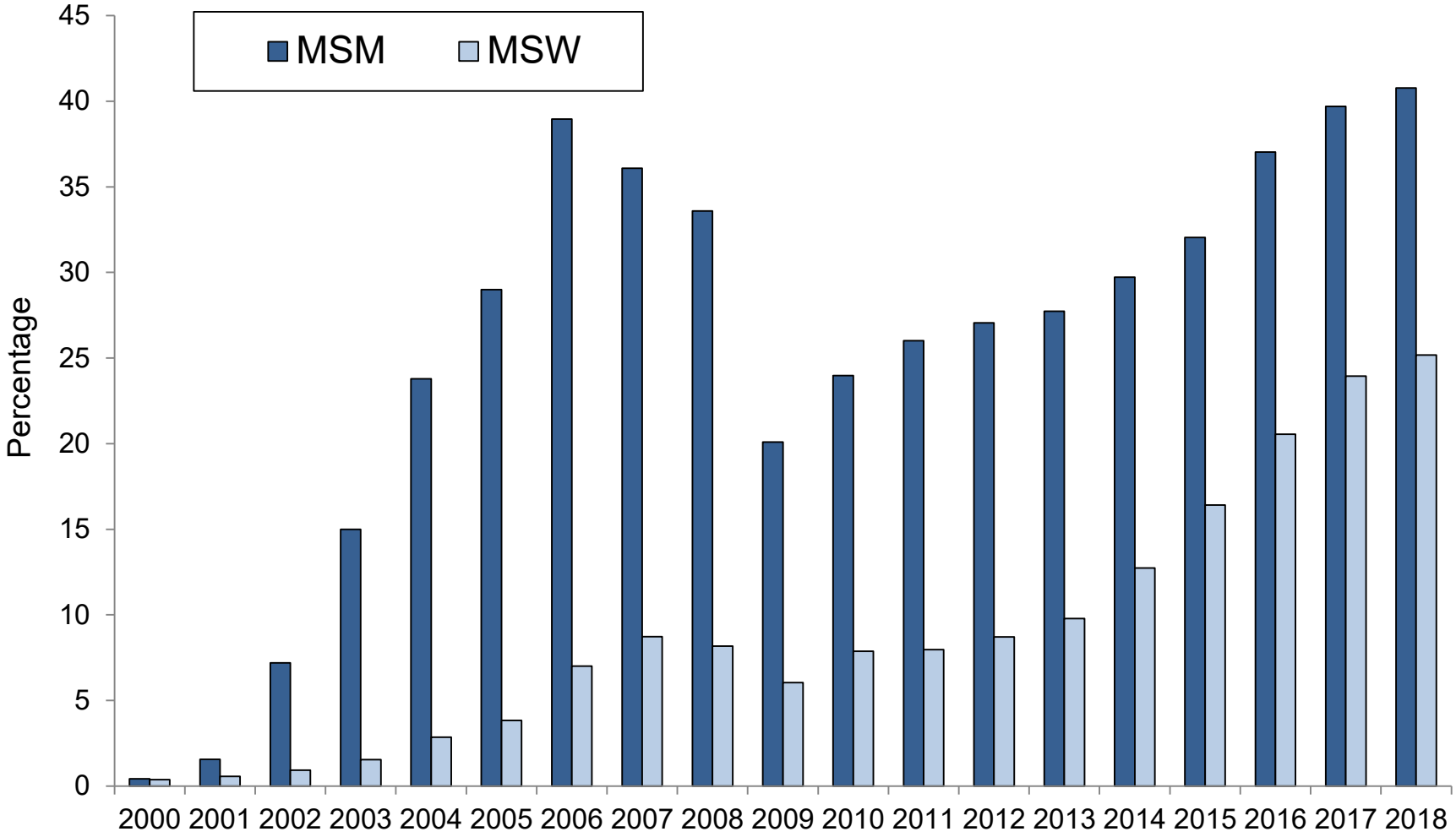


Figure 4. Percentage of *Neisseria gonorrhoeae* Isolates that are Ciprofloxacin-Resistant by Reported Sex of Sex Partners, Gonococcal Isolate Surveillance Project (GISP), 2000-2018



MSM=Gay, bisexual, and other men who have sex with men; MSW=men who have sex with women only.

Table 1. Distribution of Cefixime Minimum Inhibitory Concentrations (MICs) Among *Neisseria gonorrhoeae* Isolates, Gonococcal Isolate Surveillance Project (GISP), 2014–2018

	Minimum Inhibitory Concentrations (µg/ml)							
Year	**≤0.015** n (%)	**0.030** n (%)	**0.060** n (%)	**0.125** n (%)	**0.250** n (%)	**0.500** n (%)	**1.000** n (%)	**Total** N
2014	3132 (61.5)	1282 (25.2)	482 (9.5)	159 (3.1)	36 (0.7)	2 (0.0)	0 (0.0)	5093
2015	3821 (74.2)	923 (17.9)	286 (5.6)	92 (1.8)	20 (0.4)	5 (0.1)	0 (0.0)	5147
2016	3673 (69.9)	1099 (20.9)	330 (6.3)	137 (2.6)	16 (0.3)	1 (0.0)	0 (0.0)	5256
2017	3637 (71.9)	1005 (19.9)	305 (6.0)	92 (1.8)	21 (0.4)	1 (0.0)	0 (0.0)	5061
2018	3605 (69.9)	1155 (22.4)	297 (5.8)	88 (1.7)	13 (0.3)	2 (0.0)	0 (0.0)	5160

Note: Percentages represent row percentages.

Table 2. Distribution of Ceftriaxone Minimum Inhibitory Concentrations (MICs) Among *Neisseria gonorrhoeae* Isolates, Gonococcal Isolate Surveillance Project (GISP), 2014–2018

	Minimum Inhibitory Concentrations (µg/ml)							
Year	**≤0.008** n (%)	**0.015** n (%)	**0.030** n (%)	**0.060** n (%)	**0.125** n (%)	**0.250** n (%)	**0.500** n (%)	**Total** n
2014	3650 (71.7)	839 (16.5)	437 (8.6)	160 (3.1)	5 (0.1)	2 (0.0)	0 (0.0)	5093
2015	3694 (71.8)	901 (17.5)	373 (7.2)	165 (3.2)	13 (0.3)	1 (0.0)	0 (0.0)	5147
2016	3619 (68.9)	1036 (19.7)	419 (8.0)	168 (3.2)	14 (0.3)	0 (0.0)	0 (0.0)	5256
2017	3553 (70.2)	976 (19.3)	417 (8.2)	105 (2.1)	7 (0.1)	3 (0.1)	0 (0.0)	5061
2018	3477 (67.4)	1141 (22.1)	447 (8.7)	86 (1.7)	8 (0.2)	1 (0.0)	0 (0.0)	5160

Note: Percentages represent row percentages.

Table 3. Distribution of Azithromycin Minimum Inhibitory Concentrations (MICs) Among *Neisseria gonorrhoeae* Isolates, Gonococcal Isolate Surveillance Project (GISP), 2014–2018

	Minimum Inhibitory Concentrations (µg/ml))										
Year	**≤0.030 n (%)**	**0.060 n (%)**	**0.125 n (%)**	**0.250 n (%)**	**0.500 n (%)**	**1.000 n (%)**	**2.000 n (%)**	**4.000 n (%)**	**8.000 n (%)**	**≥16.00 n (%)**	**Total n**
2014	323 (6.3)	464 (9.1)	1077 (21.1)	1782 (35.0)	1086 (21.3)	236 (4.6)	50 (1.0)	37 (0.7)	28 (0.5)	10 (0.2)	5093
2015	349 (6.8)	475 (9.2)	1198 (23.3)	1793 (34.8)	980 (19.0)	219 (4.3)	80 (1.6)	32 (0.6)	9 (0.2)	12 (0.2)	5147
2016	247 (4.7)	357 (6.8)	1006 (19.1)	1827 (34.8)	1234 (23.5)	395 (7.5)	111 (2.1)	42 (0.8)	14 (0.3)	23 (0.4)	5256
2017	286 (5.7)	427 (8.4)	1241 (24.5)	2157 (42.6)	525 (10.4)	204 (4.0)	137 (2.7)	36 (0.7)	26 (0.5)	22 (0.4)	5061
2018	318 (6.2)	459 (8.9)	1354 (26.2)	1832 (35.5)	675 (13.1)	287 (5.6)	163 (3.2)	16 (0.3)	25 (0.5)	31 (0.6)	5160

Note: Percentages represent row percentages.