HHS Public Access

Author manuscript

Sex Transm Dis. Author manuscript; available in PMC 2021 December 27.

Published in final edited form as:

Sex Transm Dis. 2021 December 01; 48(12): S118–S123. doi:10.1097/OLQ.0000000000001541.

Demographic and epidemiological characteristics associated with reduced antimicrobial susceptibility to *Neisseria gonorrhoeae* in the United States, Strengthening the U.S. Response to Resistant Gonorrhea (SURRG), 2018–2019

Karen Gieseker, PhD[1,*], **Emily R. Learner, PhD**[2,*], **Kerry Mauk, MSPH**[2], **Lindley A. Barbee, MD**[3], **Candice J. McNeil, MD**[4], **Gerald L. Hasty, PhD**[5], **Jamie M. Black, MPH**[6], **Kimberly Johnson, MPH**[7], **Trang Quyen Nguyen, PhD**[8], **Dhana Shrestha, MPH**[9], **Cau D. Pham, PhD**[2], **Sancta St. Cyr, MD**[2], **Karen Schlanger, PhD**[2], **Robert D. Kirkcaldy, MD**[2], **SURRG Working Group**

[1]Colorado Department of Public Health and Environment, Denver, CO

[2]Centers for Disease Control and Prevention, Atlanta, GA

[3]Department of Medicine, Infectious Diseases, University of Washington, Seattle, WA

[4]Wake Forest University School of Medicine/Guilford County Department of Health, NC

[5]Hawaii Department of Health, Honolulu, HI

[6]Indiana Department of Health, Indianapolis, IN

[7]New York City Department of Health and Mental Hygiene, New York, NY

[8]San Francisco Department of Public Health, San Francisco, CA

[9]Milwaukee Health Department, Milwaukee, WI

Abstract

Background: Jurisdictions participating in Strengthening the United States Response to Resistant Gonorrhea (SURRG) implemented specimen collection for culture and antimicrobial susceptibility testing (AST) from a sample of persons of all genders (at multiple anatomic sites) attending STD clinics and community clinics. We describe the percentage and characteristics of patients whose isolates demonstrated reduced susceptibility (RS) to azithromycin, ceftriaxone, or cefixime.

Methods: We included patients from clinics that participated in SURRG whose isolates underwent AST by Etest. We defined RS as azithromycin minimum inhibitory concentrations

Corresponding Author: Emily Learner, PhD, kvd7@cdc.gov, Centers for Disease Control and Prevention, 1600 Clifton Road NE, Atlanta, GA 30329.

*These co-authors contributed equally

Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the CDC.

Conflict of Interest Statement:
The authors have no conflicts of interest to disclose.

(MICs) ≥2 μg/ml (AZM-RS), ceftriaxone MICs ≥0.125 μg/ml (CRO-RS), or cefixime MICs ≥0.25 μg/ml (CFX-RS). Patients with repeated infections appeared >1 time in the data. We calculated the frequency and percentage of patients with an isolate demonstrating RS by epidemiological characteristics.

Results: During 2018–2019, 10,013 patients from eight jurisdictions provided 10,735 isolates. Among 10,013 patients, 11.0% (n=1,099) had ≥1 isolate with AZM-RS (range by jurisdiction 2.5%–18.0%). Approximately 11.3% of 8,771 of patients visiting STD clinics and approximately 8.8% of 1,242 patients visiting community clinics had an AZM-RS isolate. Nearly 6% of 1,013 females had an AZM-RS isolate; among males, the percent of patients with an AZM-RS isolate was 17.7% among 4,177 men who have sex only with men and 6.1% among 3,581 men who have sex only with women. Few (0.4%) patients had isolates with CFX-RS (n=40) or CRO-RS (n=43).

Conclusions: Although infections with reduced cephalosporin susceptibility were rare, AZM-RS infections were prevalent in this sample of patients in multiple jurisdictions and across gender and gender of sex partner categories.

Short Summary: Data from SURRG demonstrated that 11% of sampled patients attending STD clinics and community clinics had an isolate with reduced azithromycin susceptibility; <1% had reduced cephalosporin susceptibility.

Background

Neisseria gonorrhoeae, the causative organism of gonorrhea, is an important sexually transmitted pathogen of the urethra, cervix, pharynx, and rectum. In 2019, 616,392 gonorrhea cases were reported to the Centers for Disease Control and Prevention (CDC); CDC estimated that more than half of all infections were resistant to at least one antimicrobial.[1] *N. gonorrhoeae* has demonstrated a remarkable ability to develop antimicrobial resistance, and gonococcal resistance has been designated by CDC as an urgent antimicrobial resistance public health threat in the United States.[2]

Over the past thirty years, CDC has monitored gonococcal susceptibility through the Gonococcal Isolate Surveillance Project (GISP).[3] As part of GISP, participating sexually transmitted disease (STD) clinics in over 30 jurisdictions collect up to 25 *N. gonorrhoeae* isolates from men with gonococcal urethritis each month for antimicrobial susceptibility testing (AST) by agar dilution at regional laboratories. Selected demographic and clinical data are abstracted from medical records. GISP surveillance data have repeatedly prompted proactive changes to gonorrhea treatment guidelines prior to widespread resistance and failure of treatment.[3,4] Additionally, data from GISP have also provided important insights into the epidemiology of gonococcal resistance: GISP has previously demonstrated that isolates from the western United States have higher prevalences of fluoroquinolone, penicillin, and tetracycline resistance than other regions of the United States.[3] Isolates from gay, bisexual, and other men who have sex with men (MSM) were also demonstrated to have higher prevalences of reduced cephalosporin susceptibility than isolates from men who report sex only with women (MSW).[3,5] In 2014, initial declines in azithromycin susceptibility were observed primarily among isolates from the Midwest and MSM, but were observed in all US regions and among MSW.[3]

A robust understanding of the epidemiology of gonococcal antimicrobial resistance, which can inform prevention and control efforts, may be enriched by expanding the scope of specimen collection. Such an expansion was conducted by the CDC-supported Strengthening the United States Response to Resistant Gonorrhea (SURRG) project. To enhance local capacity for rapid detection of gonococcal resistance, jurisdictions participating in SURRG implemented specimen collection for culture and AST from select persons of all genders, at multiple anatomic sites, and for persons attending STD clinics and other (non-STD clinic) community clinics. To deepen the understanding of recent epidemiology of gonococcal antimicrobial susceptibility and inform prevention and control efforts, we used demographic and behavioral data from SURRG to describe the characteristics of patients whose *N. gonorrhoeae* isolates demonstrated reduced susceptibility (RS-GC) to azithromycin, ceftriaxone, and cefixime.

Methods

We used data from SURRG collected during 2018–2019. SURRG is a CDC-supported multisite project designed to enhance local capacity to rapidly detect and respond to antimicrobial-resistant gonorrhea. SURRG was implemented in eight jurisdictions across the United States: California (City and County of San Francisco); Colorado (Denver County/ Denver); Indiana (Marion County/Indianapolis); Hawaii (Honolulu County/Honolulu); New York (New York City); North Carolina (Guilford County/Greensboro); Washington (King County/Seattle); and Wisconsin (City of Milwaukee). Comprehensive details about SURRG are described elsewhere.[6]

Participating jurisdictions identified STD clinics and community clinics in which to implement specimen collection for *N. gonorrhoeae* culture. To allow jurisdictions to bolster local detection and response capacity in ways that aligned strategically with local epidemiology and resources, SURRG allowed each jurisdiction and clinic to define their own criteria to identify patients and anatomic sites from which to collect culture specimens; however, specimens for culture were generally collected from all exposed anatomic sites of symptomatic patients, patients returning to the clinic for treatment after NAAT-diagnosed gonorrhea, or sexual partners of infected persons over the last two to three months. Most STD clinics conducted specimen collection for *N. gonorrhoeae* culture over the entire study period, but some community clinics began specimen collection part way through the study period. Thus, there was not a wholly standardized and consistent sampling frame. Clinical and demographic data, including race/ethnicity, gender, sex of sex partner, HIV status, HIV pre-exposure prophylaxis (PrEP) use, and history of gonorrhea were collected at clinic visits through routine registration and clinical protocols or patient interview. Specimens were collected from patients at one or more anatomic sites (urethral, endocervical, rectal, or pharyngeal) for gonorrhea nucleic acid amplification testing (NAAT) and *N. gonorrhoeae* culture, according to local protocols. Local public health laboratories performed AST with Etest® gradient strips (bioMérieux, France) for azithromycin, cefixime, and ceftriaxone susceptibility on all gonococcal isolates. Laboratories were trained on Etest® and participated in ongoing quality assurance protocols to ensure standardization across sites.

Our analytic dataset included all patients whose *N. gonorrhoeae* isolates underwent AST. We defined reduced susceptibility as azithromycin minimum inhibitory concentrations (MICs) ≥2 μg/ml (AZM-RS), ceftriaxone MICs ≥0.125 μg/ml (CRO-RS), or cefixime MICs ≥0.25 μg/ml (CFX-RS).[6] The MIC breakpoints for SURRG were based on Clinical and Laboratory Standards Institute (CLSI) criteria, however breakpoints for ceftriaxone and cefixime are lower than the CLSI breakpoints and were selected to allow for detection of emerging resistance.[7] We calculated the frequency and percentage of isolates demonstrating AZM-RS, CRO-RS, and CFX-RS by anatomic site, as well as the frequency and percentage of patients with at least one isolate demonstrating AZM-RS, CRO-RS, and CFX-RS by clinical and demographic characteristics.. Patients who provided specimens for culture at clinic visits that occurred over 30 days apart and who were not returning for a test of cure were generally classified as separate patient observations with separate gonococcal infections, per jurisdictions' discretion. We included these patients (i.e., patients with multiple, separate gonococcal infections during the study) as separate patient observations in our analysis. For this analysis, MSM were defined as individuals who self-identified as male (cis or transgender male) and reported only male sex partners in the past two or three months (the duration varied by jurisdiction). Men who have sex with women (MSW) were self-identified males who reported only female partners in the past two or three months. Men who have sex with men and women (MSMW) were defined as males who reported both female and male partners in the past two or three months. Males who reported unknown, non-binary, or other gender sex partners were classified as unknown.

CDC's Institutional Review Board reviewed the SURRG protocol and determined the project to be a public health activity and not human subject research.

Results

During 2018–2019, 10,013 patients from eight jurisdictions provided 10,735 gonococcal isolates that underwent AST. Of the 10,013 patients, most patients (93.5%) provided one isolate for AST for a single gonococcal infection; few provided two isolates (6.2%) or three isolates (0.3%) for AST from different anatomic sites at the same diagnostic event. Over 90% (n=9,072) of patients contributed *N. gonorrhoeae* isolate(s) for AST once; the remainder (n=941, 9.4%) contributed isolates for AST at two or more separate diagnostic events. Among the 10,735 isolates provided by 10,013 patients, most isolates were from urethral/urine specimens (62.5%), followed by rectal (15.3%), pharyngeal (14.2%) and endocervical/vaginal (7.9%) (Table 1).

Among the 10,013 patients, nearly 30% were from New York City and only 3.4% were from Honolulu, Hawaii; other patients were relatively evenly distributed across the other six jurisdictions (Table 2). Most (87.6%) patients were diagnosed at an STD clinic; just over 12% were diagnosed at a community clinic. Nearly 90% self-identified as male (cis or transgender male), 10.4% as female (cis or transgender female), and fewer than 1% as another gender. Among males (inclusive of transgender males), 46.8% were MSM, 40.1% were MSW, and 4.0% were MSMW. Nearly half of patients were non-Hispanic Black (46.2%), one quarter were non-Hispanic White (25.0%), and 17.2% were Hispanic/Latino. Approximately 5% of patients were known to be HIV positive, 35.9% were known to be

HIV negative, and 60% had unknown HIV status. Nearly 7% were taking HIV pre-exposure prophylaxis (PrEP). Nearly 40% were known to have a previous gonococcal infection.

Among the 10,013 patients, 1,099 (11.0%) had at least one isolate (during a specific gonococcal infection) that demonstrated AZM-RS (Table 2). The percentage ranged by jurisdiction from 2.5% in Guilford County, North Carolina to 18.0% in San Francisco County, California. Approximately 11% of patients in our dataset who visited STD clinics had an isolate demonstrating AZM-RS, and approximately 9% in our dataset who visited community clinics had an isolate that demonstrated AZM-RS. The percentage of patients who had an AZM-RS isolate was higher among males (11.6%) and transgender males (20.0%) than females (5.8%) and transgender females (4.0%), though the sample sizes of transgender males (N=10) and transgender females (N=25) were small. Among males (including transgender males), the percent of patients with an isolate that demonstrated AZM-RS was higher among MSM (17.7%) and MSMW (13.0%) compared to MSW (6.1%). We also observed a relatively high percentage of patients with AZM-RS among non-Hispanic White (14.4%), American Indian/Alaska Native (13.8%), and Asian (16.2%) individuals. Over 90% of Asian patients with an isolate with AZM-RS were in Honolulu County, Hawaii, New York City, New York, King County/Seattle, Washington, and San Francisco County, California, counties in which most Asian patients in our study resided. The percentage was lower among Hispanic/Latino (12.4%) and non-Hispanic Black patients (8.3%). Approximately 14.0% of patients who were noted to be HIV positive had an isolate that demonstrated AZM-RS, and 19.7% of patients known to be taking PrEP had an isolate that demonstrated AZM-RS.

Forty (0.4%) patients had an isolate that demonstrated CFX-RS; by jurisdiction, patients from Honolulu County, Hawaii had the highest percentage (n=4; 1.2%) and New York City, New York had the highest frequency (n=20; 0.7%) (Table 2). The frequency and percentage of patients who had an isolate that demonstrated CFX-RS was slightly higher among males (n=37; 0.4%) than females (n=3, 0.3%). Among males, the percentage was slightly higher among MSM (n=26; 0.6%) compared to MSW (n=11; 0.3%). When stratified by race/ethnicity, Asian patients had the highest percentage of patients who had an isolate that demonstrated CFX-RS (1.9%).

Forty-three (0.4%) patients had an isolate that demonstrated CRO-RS. The percentage ranged from 0.1% in Marion County, Indiana (n=1) and Guilford County, North Carolina (n=1), to 1.0% in San Francisco County, California (n=9). The frequency and percentage of patients who had an isolate that demonstrated CRO-RS was slightly higher among males (n=41; 0.5%) than females (n=2, 0.2%), and for males, slightly higher among MSM (n=29; 0.7%) compared to MSW (n=7; 0.2%). Asian patients had the highest percentage of patients who had an isolate that demonstrated CRO-RS (n=8; 1.9%), but the frequency was highest among non-Hispanic Black individuals (n=13, 0.3%).

Of the 10,735 isolates, the percentage demonstrating AZM-RS was highest among rectal (14.8%) and pharyngeal isolates (14.6%), and lower among urethral (10.0%) and endocervical (5.5%) isolates (Table 1). CFX-RS was slightly higher among rectal (0.6%) and pharyngeal isolates (0.5%) than among urethral (0.3%) and endocervical/vaginal (0.2%)

isolates. CRO-RS was highest among pharyngeal isolates (0.9%), followed by urethral (0.4%), rectal (0.2%) and endocervical/vaginal (0.1%)

Discussion

Among this sample of patients with gonorrhea in eight jurisdictions, a large percentage had *N. gonorrhoeae* isolates with AZM-RS. Geographic differences were observed. Whereas gonococcal resistance in the United States has historically started highest on the West Coast, we also observed high percentages of AZM-RS in Milwaukee, Wisconsin and Denver, Colorado.[3] A high percentage was observed among MSM, and percentages were lower but still notable among women and MSW. AZM-RS was observed across multiple racial/ethnic categories. CFX-RS and CRO-RS was rare overall, but some populations, such as those in Honolulu, Hawaii and non-Hispanic Asians, demonstrated higher percentages of isolates with these phenotypes than other populations.

While SURRG is not a sentinel surveillance program, these azithromycin susceptibility data from jurisdictions participating in SURRG complement susceptibility data observed in GISP. Azithromycin susceptibility observed in GISP has declined over time, and the percentage of isolates with AZM-RS increased from 0.6% in 2013 to 5.1% in 2019.[1,4] These GISP data helped to spur the recent change in CDC's gonorrhea treatment guidelines, which no longer recommend azithromycin for treatment of gonorrhea and instead recommend a single dose of intramuscular ceftriaxone as monotherapy for uncomplicated urogenital, rectal, and pharyngeal infections.[4] As context, the World Health Organization has traditionally used a criterion of ≥95% effectiveness (and thus <5% resistance) for recommended treatment regimens.[8,9] Increasing antimicrobial reduced susceptibility can predict the emergence of resistance, and because evidence for a ≥5% resistance threshold is limited, other considerations, such as declining cefixime susceptibility, maintenance of ceftriaxone effectiveness, and antimicrobial stewardship, have been applied in recent years.[4,10]

The relatively high percentages of AZM-RS in the City and County of San Francisco, California (on the West Coast of the United States) and among MSM are consistent with epidemiological patterns of gonococcal resistance – particularly emerging ciprofloxacin resistance and declining cephalosporin susceptibility — described previously (and suggested by the cephalosporin susceptibility data in this report).[3] However, the epidemiology of AZM-RS in this sample does differ in some ways from previously-described resistance patterns of other antimicrobials. High percentages of AZM-RS were observed on the West Coast, but also in the Northeast (New York City), and Midwest (Milwaukee). Our finding of a high AZM-RS percentage among patients in the Midwest is not entirely surprising, however: GISP isolates from the Midwest demonstrated a sharp increase in AZM-RS in 2014, and a cluster of *N. gonorrhoeae* isolates with high-level azithromycin resistance was identified in Indiana during 2017–2018, and Ohio during 2017.[3,11,12] This widespread geographic pattern of emerging AZM-RS might be due, at least in part, to the emergence of mutations conferring reduced azithromycin susceptibility (such as mutations in the mtrR promoter, mosaic mtrR, and 23s rRNA mutations) in multiple genetic lineages, rather than clonal emergence and spread.[13,14]

Notably, approximately 6% of women and MSW – populations that historically had very low prevalence of gonococcal resistance – had isolates with AZM-RS. Although detection of *N. gonorrhoeae* with reduced azithromycin susceptibility among heterosexuals might represent lagged transmission from sexual networks of MSM to those of women and MSW, heterosexuals seem to have been at the forefront of recently declining azithromycin susceptibility. From 2013 to 2014 (when azithromycin susceptibility began a sustained decline in the United States), the percentage of GISP isolates from MSW with AZM-RS increased from 0.4% to 1.4%.[3] During 2014–2015, a cluster of high-level azithromycin (≥256 μg/ml) resistant gonococcal infections among heterosexuals was identified in Leeds, North England.[15]

In our data, the percentages of reduced azithromycin and cephalosporin susceptibility were notable among non-Hispanic Asians. Few antimicrobial susceptibility data by race/ethnicity from the United States have been published recently. We cannot conclude whether the high percentages we observed among Asians may reflect true, high prevalences among this group or whether the high percentages we observed reflect the influence of geography, as the majority of Asian patients in our study resided in areas with a high population proportion of Asians. Further monitoring is warranted for greater understanding of resistance emergence in these areas and populations.

We observed high percentages of AZM-RS among individuals who were diagnosed with gonorrhea at community clinics (nearly 9%). These data serve as reminders that patients with RS-GC seek care in settings other than STD clinics. To identify and care for patients seeking care outside of STD clinics, healthcare providers are thus encouraged to routinely take sexual histories from their patients and screen patients who meet gonorrhea screening criteria (e.g., women <25 years and older women at increased risk and sexually-active MSM). Policy and financial barriers can pose challenges to gonorrhea screening (especially extragenital screening); resources to address financial challenges, such as from the National Coalition of STD Directors, are available.[16,17] Once a patient is diagnosed, healthcare providers should adhere to current CDC treatment recommendations and remain vigilant for possible unsuccessful treatment due to resistance.[4,18] For patients with suspected treatment failures, healthcare providers are encouraged to collect specimens for culture and phenotypic AST.[19] To facilitate this, healthcare providers are encouraged to maintain the ability and supplies to collect specimens for culture and be knowledgeable of laboratories to which they can send specimens for culture. Local or state health departments may be useful resources to assist with facilitating access to culture specimen collection supplies, transport of specimens to laboratories for culture and AST, and conducting partner services if needed. We also observed a high proportion of patients with unknown HIV status in our data, suggesting that there may have been missed opportunities for HIV screening at STD or community clinics. However, the high proportion of missing data likely also reflects data collection and transmission challenges, and we expect that the true proportion of patients with unknown HIV status is smaller.

It is important to note that our results represent the percentages of patients with an RS isolate among patients who met specific criteria for culture specimen collection per the locally-developed SURRG protocol of each participating jurisdiction. Jurisdictions generally

followed a standardized culture collection protocol, but jurisdictions were also encouraged to tailor collection criteria to optimize resources and maximize culture yield, resulting in some sampling variability across jurisdictions with respect to which patients and anatomic sites had a specimen collected for culture.[6] Additionally, the patient populations attending participating clinics and within participating jurisdictions do not necessarily accurately represent the overall population of persons with gonococcal infections with reduced azithromycin or cephalosporin susceptibility in the United States. Jurisdictions were selected for participation in SURRG in part because their geographic location or patient populations are associated with disproportionately higher risk of emerging gonococcal resistance. For these reasons, our results should not be interpreted as valid estimates of prevalence or generalized to the broader population. Percentages in this report should only be interpreted as percentages of patients with individual infections with RS-GC within SURRG.[20]

This analysis has several limitations. Our analysis included a small proportion of patients who had multiple gonococcal infections during the study period. Patients with multiple infections might be part of sexual networks with a higher prevalence of gonorrhea and RS-GC, and might be more likely to acquire gonorrhea or RS-GC. Thus our results, especially overall RS-GC percentages, may be slightly elevated and are not expected to be nationally representative. The low percentage of isolates with CRO-RS or CFX-RS limited our ability to discern differences by population. Higher percentages of reduced azithromycin and cephalosporin susceptibility among extragenital isolates may reflect high prevalence of reduced susceptibility among MSM or in jurisdictions that contributed greater numbers of extragenital isolates. The MIC thresholds for reduced susceptibility do not necessarily equate to resistance and as noted above, the susceptibility thresholds used in this analysis differ from those of CLSI.[7] Additionally, susceptibility thresholds established by different organizations, such as CLSI and the European committee on antimicrobial susceptibility testing (EUCAST), differ.[21]

Surveillance for gonococcal resistance serves as a foundation for detection of emerging resistance trends and understanding the epidemiology of gonococcal resistance. Data from SURRG complement those from GISP and have provided insight into the antimicrobial susceptibility of gonococcal infections among persons of all genders and of those diagnosed outside of STD clinics. Continuing efforts to not only strengthen surveillance, but also to ensure optimal treatment of patients with gonorrhea, develop new antimicrobials and prevention approaches, and respond to the emerging threat of gonococcal resistance, are urgently needed.

Acknowledgements

SURRG Working Group: Rebecca Abelman, Lizzette Alvarado, Janet Arno, Tamara Baldwin, Lindley Barbee, Kyle Bernstein, Ruthie Burich-Weatherly, Lance Chinna, Alberto Clemente, Stephanie Cohen, Michael M. Denny, Joey Dewater, Rose Finney, Kim M. Gernert, Alesia Harvey, Christine Heumann, Sopheay Hun, Roxanne Kerani, Ellen Kersh, Robert Kohn, Noah Leigh, Jennifer Ludovic, Christie Mettenbrink, Evelyn Nash, Elizabeth Palavecino, Ruchi Pandey, Rushlenne Pascual, Preeti Pathela, Zachary Perry, Elisabeth Phillips, Brian Raphael, Jennifer Reimche, Brad Roland, Madeline Sankaran, Julia Schillinger, Kevin Sellers, Brandy Sessoms, Samera Sharpe, Olusegun O. Soge, Erica Terrell, Christina Thibault, Cindy Toler, Lizzi Torrone, Katy Town, Chun Wang, Karen Wendel, Wendy Wittman

Source of Support:

Funding for the Strengthening the U.S. Response to Resistant Gonorrhea activities described in this paper were supported with federal Antibiotic Resistance Initiative funding and administered through the U.S. Centers for Disease Control and Prevention's (CDC) Epidemiology and Laboratory Capacity for the Prevention and Control of Infectious Diseases (ELC) Cooperative Agreement [CK19-1904].

References

1. Centers for Disease Control and Prevention. 2019 STD Surveillance Report [Internet]. 2019 [cited 2020 Apr 16]. Available from: https://www.cdc.gov/std/statistics/2019/default.htm
2. Prevention, Centers for Disease Control and Prevention. Antibiotic Resistance Threats in the United States, 2019. Atlanta, GA: U.S. Department of Health and Human Services, CDC; 2019.
3. Kirkcaldy RD, Harvey A, Papp JR, del Rio C, Soge OO, Holmes KK, et al. Neisseria gonorrhoeae antimicrobial susceptibility surveillance - The Gonococcal Isolate Surveillance Project, 27 sites, United States, 2014. MMWR Surveill Summ. 2016;65(7):1–19.
4. St. Cyr S, Barbee L, Workowski KA, Bachmann LH, Pham C, Schlanger K, et al. Update to CDC's Treatment Guidelines for Gonococcal Infection, 2020. MMWR Morb Mortal Wkly Rep. 2020;69(50):1911–6. [PubMed: 33332296]
5. Kirkcaldy RD, Zaidi A, Hook EW, Holmes KH, Soge O, Del Rio C, et al. Neisseria gonorrhoeae antimicrobial resistance among men who have sex with men and men who have sex exclusively with women: The gonococcal isolate surveillance project, 2005–2010. Ann Intern Med. 2013;158(5):321–8. [PubMed: 23460055]
6. Schlanger K, Learner ER, Pham C. Strengthening the US Response to Resistant Gonorrhea (SURRG): an overview of a multi-site program to enhance local response capacity for antibiotic-resistant Neisseria gonorrhoeae. Sex Transm Dis. (submitted as part of the supplement).
7. Clinical and Laboratory Standards Institute. Clinical and Laboratory Standards Institute (CLSI). Performance Standards for Antimicrobial Susceptibility Testing. 30th ed. CLSI Suppl M100. 2020;
8. Moran JS, Levine WC. Drugs of choice for the treatment of uncomplicated gonococcal infections. Clin Infect Dis. 1995;20(Suppl 1):S47–65. [PubMed: 7795109]
9. Unemo M, Lahra M, Cole M. World Health Organization global gonococcal antimicrobial surveillance project (WHO GASP): review of new data and evidence to inform international collaborative actions and research efforts. Sex Heal. 2019;16(5):412–425.
10. del Rio C, Hall G, Holmes KK. Update to the CDC's sexually transmitted diseases treatment guidelines, 2010: Oral cephalosporins no longer a recommended treatment for gonococcal infections. MMWR. 2012;61(31):590–4. [PubMed: 22874837]
11. Holderman J, Thomas JC, Schlanger K, Black JM, Town K, St. Cyr SB, et al. Sustained Transmission of Neisseria gonorrhoeae with High-Level Resistance to Azithromycin, in Indianapolis, Indiana, 2017–2018. Clin Infect Dis. 2021;PAP.
12. Bazan JA, Roberts MW, Soge OO, Torrone EA, Dennison A, Ervin M, et al. Rapid Increase in Gonorrhea Cases with Reduced Susceptibility to Azithromycin in Columbus, Ohio. Sex Transm Dis. 2018;45(2):e5–6. [PubMed: 29329182]
13. Thomas JC, Seby S, Abrams AJ, Cartee J, Lucking S, Vidyaprakash E, et al. Evidence of recent genomic evolution in gonococcal strains with decreased susceptibility to cephalosporins or azithromycin in the United States. J Infect Dis. 2019;220:294–305. [PubMed: 30788502]
14. Grad YH, Harris SR, Kirkcaldy RD, Green AG, Marks DS, Bentley SD, et al. Genomic epidemiology of gonococcal resistance to extended-spectrum cephalosporins, macrolides, and fluoroquinolones in the United States, 2000–2013. J Infect Dis. 2016;214:1579–87. [PubMed: 27638945]
15. Chisholm SA, Wilson J, Alexander S, Tripodo F, Al-Shahib A, Schaefer U, et al. An outbreak of high-level azithromycin resistant Neisseria gonorrhoeae in England. Sex Transm Infect. 2016;92(5):365–7. [PubMed: 26601852]
16. Landovitz RJ, Gildner JL, Leibowitz AA. Sexually Transmitted Infection Testing of HIV-Positive Medicare and Medicaid Enrollees Falls Short of Guidelines. Sex Transm Dis. 2018;45(1):8–13. [PubMed: 29240633]
17. STD-Related Reproductive Health Training and Technical Assistance Center (STD TAC) and National Coalition of STD Directors. Coding Guide for nucleic acid amplification testing to

diagnose nongenital infections with gonorrhea and chlamydia [Internet]. 2016 [cited 2021 Apr 20]. Available from: https://www.ncsddc/org/wp-content/uploads/2019/05/NAAT_CodeGuide_FINAL-for-STD-TAC-website-posting-11.1.16.pdf

18. Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. MMWR Recomm Reports. 2015;64(No. RR-3):10–5.
19. Papp J, Schachter J, Gaydos C, Van Der Pol B. Recommendations for the laboratory-based detection of Chlamydia trachomatis and Neisseria gonorrhoeae−−2014. Vol. 63, MMWR. 2014.
20. Kirkcaldy RD, Schlanger K, Papp JR, Torrone EA. Considerations for Strengthening Surveillance of Neisseria gonorrhoeae Antimicrobial Resistance and Interpreting Surveillance Data. Sexually Transmitted Diseases. 2017.
21. EUCAST Development Laboratory for Antimicrobial Susceptibility Testing. Breakpoint tables for interpretation of MICs and zone diameters, version 10.0, 2020 [Internet]. 2020. Available from: https://www.eucast.org/clinical_breakpoints/.

Table 1.

Reduced antimicrobial susceptibility among *Neisseria gonorrhoeae* isolates by anatomic site of specimen source, Strengthening the U.S. Response to Resistant Gonorrhea (SURRG), 2018–2019.

	Isolates that underwent AST		Isolates with Azithromycin MIC ≥2.0μg/mL		Isolates with Cefixime MIC ≥0.25μg/mL		Isolates with Ceftriaxone MIC ≥0.125μg/mL	
Anatomic specimen source	**n**	**Col %**	**n**	**Row %**	**n**	**Row %**	**n**	**Row %**
Total *	10,735	100.0	1,185	11.0	41	0.4	44	0.4
Urethral/Urine	6,712	62.5	671	10.0	22	0.3	26	0.4
Endocervical/ Vaginal	849	7.9	47	5.5	2	0.2	1	0.1
Rectal	1,646	15.3	244	14.8	10	0.6	4	0.2
Pharyngeal	1,528	14.2	223	14.6	7	0.5	13	0.9

Note: AST=antimicrobial susceptibility testing, MIC=minimum inhibitory concentration

* n=10 isolates had ceftriaxone MIC ≥0.125μg/mL and cefixime MIC ≥0.25μg/mL; n=2 isolates had azithromycin MIC ≥2.0μg/mL and cefixime MIC ≥0.25μg/mL; n=2 isolates had azithromycin MIC ≥2.0μg/mL, ceftriaxone MIC ≥0.125μg/mL, and cefixime MIC ≥0.25μg/mL

Table 2.

Percentages of patients with *Neisseria gonorrhoeae* isolates demonstrating reduced susceptibility to azithromycin, cefixime, or ceftriaxone by epidemiological characteristics, Strengthening the U.S. Response to Resistant Gonorrhea (SURRG), 2018–2019

	Patients with ≥1 isolates with AST		Patients with ≥1 isolates with Azithromycin MIC ≥2.0μg/mL		Patients with ≥1 isolates with Cefixime MIC ≥0.25μg/mL		Patients with ≥1 isolates with Ceftriaxone MIC ≥0.125 μg/mL	
Characteristics	**n**	**Col %**	**n**	**Row %**	**n**	**Row %**	**n**	**Row %**
Total	10,013	100.0	1,099	11.0	40	0.4	43	0.4
Jurisdiction								
Denver, County, CO	1258	12.6	122	9.7	0	0.0	4	0.3
Guilford County, NC	1021	10.2	26	2.5	2	0.2	1	0.1
Honolulu County, HI	340	3.4	23	6.8	4	1.2	3	0.9
Marion County, IN	1266	12.6	82	6.5	1	0.1	1	0.1
Milwaukee, WI	1095	10.9	146	13.3	2	0.2	2	0.2
New York City, NY	2941	29.4	431	14.7	20	0.7	17	0.6
Seattle-King County, WA	1155	11.5	100	8.7	8	0.7	6	0.5
San Francisco County, CA	937	9.4	169	18.0	3	0.3	9	1.0
Clinic Type								
STD Clinic	8771	87.6	990	11.3	37	0.4	38	0.4
Community Clinic	1242	12.4	109	8.8	3	0.2	5	0.4
Gender								
Male	8919	89.1	1033	11.6	37	0.4	41	0.5
Female	1013	10.1	59	5.8	3	0.3	2	0.2
Transgender Male	10	0.1	2	20.0	0	0.0	0	0.0
Transgender Female	25	0.2	1	4.0	0	0.0	0	0.0
Another Gender Identity	46	0.5	4	8.7	0	0.0	0	0.0
Sexual Partners among Males and Transgender Males								
MSM	4177	46.8	739	17.7	26	0.6	29	0.7
MSW	3581	40.1	218	6.1	11	0.3	7	0.2
MSMW	355	4.0	46	13.0	0	0.0	4	1.1
Unknown	816	9.1	32	3.9	0	0.0	1	0.1
Race/Hispanic Ethnicity								
AIAN, NH	29	0.3	4	13.8	0	0.0	0	0.0
Asian,NH	419	4.2	68	16.2	8	1.9	8	1.9
Black/African American, NH	4625	46.2	386	8.3	9	0.2	13	0.3
Native Hawaiian, NH	52	0.5	3	5.8	0	0.0	0	0.0
White, NH	2505	25.0	360	14.4	14	0.6	10	0.4
Other, NH	171	1.7	21	12.3	2	1.2	0	0.0
Hispanic/Latino	1723	17.2	214	12.4	6	0.3	11	0.6
Multirace, NH	224	2.2	28	12.5	1	0.4	1	0.4

Characteristics	Patients with ≥1 isolates with AST		Patients with ≥1 isolates with Azithromycin MIC ≥2.0μg/mL		Patients with ≥1 isolates with Cefixime MIC ≥0.25μg/mL		Patients with ≥1 isolates with Ceftriaxone MIC ≥0.125 μg/mL	
	n	Col %	n	Row %	n	Row %	n	Row %
Unknown	265	2.6	15	5.7	0	0.0	0	0.0
HIV Status								
HIV-positive	514	5.1	74	14.4	1	0.2	4	0.8
HIV-negative	3593	35.9	453	12.6	25	0.7	20	0.6
Not tested/Unknown/Missing	5906	59.0	572	9.7	14	0.2	19	0.3
History of Gonorrhea								
Yes	3844	38.4	497	12.9	15	0.4	17	0.4
No	2689	26.9	269	10.0	18	0.7	14	0.5
Unknown/Missing	3480	34.8	333	9.6	7	0.2	12	0.3
Current PrEP Use								
Yes	692	6.9	136	19.7	11	1.6	6	0.9
No	3337	33.3	361	10.8	15	0.4	14	0.4
Not applicable	884	8.8	106	12.0	2	0.2	9	1.0
Unknown/Missing	5100	50.9	496	9.7	12	0.2	14	0.3

Note: AIAN=American Indian/Alaska Native, AST=antimicrobial susceptibility testing, CA=California, CO=Colorado, HI=Hawaii, IN=Indiana, MIC=minimum inhibitory concentration, MSM=men report sex only with men, MSMW=men who report sex with men and women, MSW=men who report sex only with women, NC=North Carolina, NH=non-Hispanic/Latino, NY=New York, PrEP=HIV pre-exposure prophylaxis, WA=Washington, WI=Wisconsin