Antimicrobial Drug Prescription and *Neisseria gonorrhoeae* Susceptibility, United States, 2005–2013

Robert D. Kirkcaldy, Monina G. Bartoces, Olusegun O. Soge, Stefan Riedel, Grace Kubin, Carlos Del Rio, John R. Papp, Edward W. Hook III, Lauri A. Hicks

We investigated whether outpatient antimicrobial drug prescribing is associated with *Neisseria gonorrhoeae* antimicrobial drug susceptibility in the United States. Using susceptibility data from the Gonococcal Isolate Surveillance Project during 2005–2013 and QuintilesIMS data on outpatient cephalosporin, macrolide, and fluoroquinolone prescribing, we constructed multivariable linear mixed models for each antimicrobial agent with 1-year lagged annual prescribing per 1,000 persons as the exposure and geometric mean MIC as the outcome of interest. Multivariable models did not demonstrate associations between antimicrobial drug prescribing and *N. gonorrhoeae* susceptibility for any of the studied antimicrobial drugs during 2005–2013. Elucidation of epidemiologic factors contributing to resistance, including further investigation of the potential role of antimicrobial drug use, is needed.

Neisseria gonorrhoeae, the causative pathogen of gonorrhea, has been designated an urgent antimicrobial drug resistance threat by the Centers for Disease Control and Prevention (CDC) (*1*). Since the introduction of antimicrobial drugs in the first half of the 20th century, *N. gonorrhoeae* has successively developed resistance to each antimicrobial agent recommended for gonorrhea treatment (*2*). In the United States, the prevalence of resistance in *N. gonorrhoeae* often varies by sex of partner and by geographic region (*3*,*4*). Prevalence is often greater in isolates from gay, bisexual, and other men who have sex with men (MSM) than those from men who have sex only with women (MSW), and prevalence is often highest in the West and lowest in the South (*4*). Resistant strains, in particular penicillinase-producing *N. gonorrhoeae*, fluoroquinolone-resistant *N. gonorrhoeae* (PPNG), and gonococcal strains with reduced cephalosporin susceptibility, seemed to emerge initially in the West (Hawaii and the West Coast) before spreading eastward across the country (*5–9*). These geographic patterns seem to support the idea that importation of resistant strains from other regions of the world, such as eastern Asia, is a primary factor of the emergence of resistant gonococci in the United States (*5–9*). Whereas antimicrobial drug prescribing patterns have been clearly associated with the emergence of resistance in other bacterial pathogens, the degree to which domestic antimicrobial use and subsequent selection pressure contributes to the emergence of gonococcal antimicrobial resistance in the United States is unclear (*10–13*). Using an ecologic approach, we sought to investigate the potential geographic and temporal association between antimicrobial drug susceptibility among US *N. gonorrhoeae* isolates and domestic outpatient antimicrobial drug prescribing rates in the United States during 2005–2013.

Author affiliations: Centers for Disease Control and Prevention, Atlanta, Georgia, USA (R.D. Kirkcaldy, M.G. Bartoces, J.R. Papp, L.A. Hicks); University of Washington, Seattle, Washington, USA (O.O. Soge); Beth Israel Deaconess Medical Center, Boston, Massachusetts, USA (S. Riedel); Texas Department of State Health Services, Austin, Texas, USA (G. Kubin); Emory University, Atlanta (C. Del Rio); University of Alabama at Birmingham, Birmingham, Alabama, USA (E.W. Hook III)

DOI: https://doi.org/10.3201/eid2310.170488

Methods

Data Sources

We used data from 3 sources: *N. gonorrhoeae* antimicrobial drug susceptibility data from the Gonococcal Isolate Surveillance Project (GISP), antimicrobial drug consumption data from IMS Health, and US Census data for population denominators. GISP is a CDC-supported sentinel surveillance system that has monitored gonococcal antimicrobial susceptibility in the United States since 1987 (*4*). GISP includes selected publicly funded sexually transmitted infection (STI) clinics in 25–30 cities and 4–5 regional laboratories each year. Each month, up to 25 *N. gonorrhoeae* urethral samples are collected consecutively from men with gonococcal urethritis attending participating STI clinics; these samples are submitted to regional laboratories for antimicrobial drug susceptibility testing

according to a common protocol (*4*). Sampling men with gonococcal urethritis is an efficient means to detect gonococcal infections: urethral infections in men are likely to be symptomatic (prompting patients to seek healthcare), and gonococcal urethritis can be rapidly diagnosed by Gram stain (*4*). In addition, sampling of men allows for monitoring of susceptibility among infections in MSM and heterosexual sexual networks (*4*).

We abstracted deidentified epidemiologic data from medical records. When analyzing data, we limited the number of isolates to ≤300/city/year to minimize overrepresentation of individual cities; we chose isolates at random for removal from the analytic dataset when >300 isolates were submitted from a site in a year. Gonococcal isolates collected at each clinic are subcultured at the clinic's local public health laboratory on supplemented chocolate medium and frozen in trypticase soy broth containing 20% glycerol. Isolates are shipped monthly to 1 of the regional laboratories for β-lactamase production testing and agar dilution antimicrobial drug susceptibility testing. From 2005 through 2013, the testing panel consistently included azithromycin, ceftriaxone, ciprofloxacin, penicillin, spectinomycin, and tetracycline. Cefixime susceptibility testing was conducted from 2005 through 2006, temporarily halted in 2007 due to lack of availability of cefixime in the United States, and resumed in 2009. Cefpodoxime susceptibility testing was conducted from 2009 through 2012. Standardized bacterial suspensions are inoculated on Difco GC Medium Base supplemented with 1% IsoVitaleX Enrichment (Becton, Dickinson and Company Diagnostic Systems, Sparks, MD, USA).

For antimicrobial drug prescribing data, we extracted QuintilesIMS (Danbury, CT, USA) data on systemic oral antimicrobial drug prescriptions dispensed in the United States during 2005–2013. During the study period, QuintilesIMS captured >70% of all outpatient prescriptions in the United States, reconciled them to wholesale deliveries, and projected to 100% coverage of all prescription activity using a patented projection method based on a comprehensive sample of patient-deidentified prescription transactions (collected from pharmacies that report their entire pharmacy business to the company each week) (*14*). These data represent outpatient prescriptions across all payers and include county of prescriber (used in this analysis); data are from community pharmacies and federal government and nongovernmental mail service pharmacies. The IMS projection method standardizes these data into estimated prescription counts and uses geospatial methods to align the estimated prescriptions for the non-sample pharmacies to prescribers with observed prescribing behaviors for the same product in nearby sample pharmacies. The method is routinely validated at various levels of granularity by IMS Health statistical and analytic teams (*15*). We obtained population data on age, sex, and county from US Census bridged-race population estimates published by the CDC.

Data Analysis

We restricted the analysis to GISP sites that participated continuously from 2005 through 2013. We focused on azithromycin, cefixime, ceftriaxone, and ciprofloxacin because these agents are currently recommended for gonorrhea treatment (azithromycin and ceftriaxone), are in the same antimicrobial class as a recommended antimicrobial drug (cefixime), or are widely used for outpatient treatment of non-STD infections or are of renewed interest because of potential novel diagnostics for detection of resistance determinants (ciprofloxacin) (*16*,*17*). We calculated geometric mean MICs and the percentage of isolates with resistance or reduced susceptibility for each antimicrobial drug by GISP site and year. Per Clinical and Laboratory Standards Institute criteria, we categorized ciprofloxacin resistance as MIC ≥1 μg/mL (*18*). In the absence of established resistance breakpoints for other antimicrobial drugs of interest, we categorized reduced cefixime susceptibility as ≥0.25 μg/mL, reduced ceftriaxone susceptibility as ≥0.125 μg/mL, and reduced azithromycin susceptibility as ≥2.0 μg/mL.

Using IMS data for each county corresponding to each of the 23 included GISP sites, we summarized antimicrobial drug prescription counts by specific antimicrobial drug (azithromycin, cefixime, ceftriaxone, and ciprofloxacin) and aggregated antimicrobial category (macrolides, cephalosporins, and fluoroquinolones). To reflect the sex and age distribution of men with gonorrhea sampled in GISP, we limited the antimicrobial drug prescription counts to prescriptions to men 10–59 years of age. We calculated prescription rates for the aggregated antimicrobial drug categories (defined as the number of prescriptions per 1,000 men 10–59 years of age) by county and year using US Census data for denominators. Using the prescribing rate for each antimicrobial category by county and year, we calculated the median prescribing rate for each county across years. The degree of overlap between the county and catchment area of the corresponding STD clinic is expected to be somewhat imprecise and vary by geographic site: some clinic catchment areas may include a small section of a large county, whereas other catchment areas may extend beyond the borders of the corresponding county.

We performed linear regression analyses in which the dependent variable was antimicrobial susceptibility (geometric mean MIC) at each GISP site and the independent variable of interest was the prior year prescription rate (i.e., the prescribing rate during the year before the year corresponding to the antimicrobial drug susceptibility results) at each county and year. We considered 2 representations of the prescribing rate variable: the original lag variable and

the centered lag variable (*19*,*20*). We used the noncentered lag variable to calculate the results. We performed separate longitudinal models for each drug by geometric mean MIC and the rate of prescribing of the corresponding antimicrobial class (azithromycin susceptibility and macrolide prescribing; cefixime and ceftriaxone susceptibility and cephalosporin prescribing; and ciprofloxacin susceptibility and fluoroquinolone prescribing) (*19*,*20*). We performed exploratory analyses to determine if there was a linear relationship between the susceptibility outcome and time. The linear assumption was satisfied, so we did not perform any transformation. To examine the association between susceptibility outcomes and prescribing rate, we then constructed multivariable linear mixed models for repeated measures with intercept and time as random effects. The models included 3 potential confounders based on a priori decisions (as these variables have been found to be associated with antimicrobial drug prescribing and/or gonococcal susceptibility): geographic region; sex of sex partner (defined as the percentage of MSM at each GISP site per year, based on GISP data); and race (defined as the percentage of men with urethral gonorrhea who were black or African American at each GISP site per year, based on GISP data) (*3*,*4*,*15*,*21*). We conducted all analyses in SAS version 9.3 (SAS Institute, Inc., Cary, NC, USA), using Proc Mixed for restricted maximum-likelihood estimation for small size samples. We calculated CIs at $\alpha = 0.05$ to determine statistically significant associations.

Results

Antimicrobial Susceptibility

Of 33 GISP sites that participated at some point during 2005 through 2013, 23 participated continuously and were included. From these sites, 44,957 isolates were collected and submitted to GISP (range per site in a given year 49–393) and, after removal of observations if >300 isolates were submitted by a site in a year, we included data from 43,852 (97.5%) isolates in the analysis. The percentage of gonococcal isolates with reduced cefixime susceptibility increased from 0.1% in 2005 to 1.6% in 2011 and decreased to 0.5% by 2013 (Table 1). Overall, geometric mean cefixime MICs increased slightly from 2006 to 2009 and then remained stable. The percentage of isolates with reduced ceftriaxone susceptibility increased slightly from 2005 to 2011 and then decreased; the geometric mean increased slightly from 2006 to 2007 and then remained stable. The percentage of isolates with reduced

Table 1. Antimicrobial drug resistance and reduced susceptibility in gonococcal isolates by drug, Gonococcal Isolate Surveillance Project, United States, 2005–2013*

Results†	Cefixime	Ceftriaxone	Azithromycin	Ciprofloxacin
2005				
Geometric mean MIC	0.009	0.006	0.189	0.011
Reduced susceptibility, %	0.1	0.1	0.6	10.1
2006				
Geometric mean MIC	0.010	0.005	0.204	0.016
Reduced susceptibility, %	0.1	0.1	0.3	15.4
2007				
Geometric mean MIC	NT	0.010	0.240	0.027
Reduced susceptibility, %	–	0.1	0.5	16.0
2008				
Geometric mean MIC	NT	0.010	0.242	0.024
Reduced susceptibility, %	–	0.1	0.2	14.7
2009				
Geometric mean MIC	0.020	0.010	0.192	0.031
Reduced susceptibility, %	0.9	0.3	0.3	10.8
2010				
Geometric mean MIC	0.020	0.010	0.174	0.039
Reduced susceptibility, %	1.6	0.4	0.6	14.2
2011				
Geometric mean MIC	0.020	0.010	0.171	0.039
Reduced susceptibility, %	1.6	0.4	0.3	14.4
2012				
Geometric mean MIC	0.020	0.010	0.183	0.042
Reduced susceptibility, %	1.0	0.3	0.3	16.1
2013				
Geometric mean MIC	0.021	0.010	0.202	0.043
Reduced susceptibility, %	0.5	0.1	0.6	17.1

*Results are for 23 sites that participated in GISP for the entire study period. Cefixime MIC testing range was 0.001–0.5 μg/mL during 2005–2006 and 0.015–0.5 μg/mL during 2009–2013; ceftriaxone MIC testing range was 0.001–2.0 μg/mL during 2005–2006 and 0.008–2.0 μg/mL during 2007–2013; azithromycin MIC testing range was 0.008–16 μg/mL during 2005–2006 and 0.03–16 μg/mL during 2007–2013; ciprofloxacin MIC testing range was 0.001–16 μg/mL during 2005–2006 and 0.008–16 μg/mL during 2007–2013. NT, not tested.

†Reduced susceptibility indicates isolate's resistance or reduced susceptibility to the indicated drug. Reduced cefixime susceptibility was defined as MIC ≥0.25 μg/ml, reduced ceftriaxone susceptibility MIC ≥0.125 μg/mL, reduced azithromycin susceptibility MIC ≥2 μg/mL, and ciprofloxacin resistance defined as MIC ≥1 μg/mL.

azithromycin susceptibility varied between 0.2% and 0.6%; the geometric mean appeared to peak in 2008 and increased again during 2011–2013. The percentage of isolates with ciprofloxacin resistance increased during 2005–2007 and increased again during 2009–2013; the geometric mean MIC increased during 2005–2013. For each antimicrobial drug, geometric mean MICs varied by site and year (online Technical Appendix Tables 1–4, 8, https://wwwnc.cdc.gov/EID/article/23/10/17-0488-Techapp1.pdf). Sites with the highest median cefixime and ciprofloxacin geometric mean MICs were in the West; those with the lowest were in the South and Midwest (online Technical Appendix Tables 1, 4). Sites with highest median azithromycin geometric means were in the Midwest and West, and those with the lowest were in the South (online Technical Appendix Table 3). We found little variation in median ceftriaxone geometric mean MICs across sites (online Technical Appendix Table 2).

Antimicrobial Drug Use

Counties with the highest cephalosporin, macrolide, and fluoroquinolone prescribing rates, such as Jefferson County, Alabama, and Oklahoma County, Oklahoma, were located in the South (online Technical Appendix Tables 5–7). Counties with the lowest prescribing rates, such as Multnomah County, Oregon, and San Diego and San Francisco, California, were located in the West. Cephalosporin prescribing rates increased in many counties but decreased in sites such as those in Honolulu, Hawaii, and Los Angeles, California (online Technical Appendix Table 5). During 2005–2013, macrolide prescribing increased in all counties (online Technical Appendix Table 6). Fluoroquinolone prescribing increased in most counties, with the largest absolute increases occurring in counties in the South (online Technical Appendix Table 7). The multivariable models did not demonstrate associations between *N. gonorrhoeae* susceptibility and antimicrobial drug prescribing for any of the studied antimicrobial drugs (Table 2).

Discussion

Using an ecologic approach, we did not find an association between population-level outpatient prescribing rates of clinically relevant antimicrobial drugs and *N. gonorrhoeae* antimicrobial drug susceptibility among urethral isolates from men in the United States. Prescribing rates were lowest in sites both where ciprofloxacin resistance and reduced cefixime susceptibility initially emerged and where the prevalence of resistance or reduced susceptibility has been highest, such as Honolulu, Hawaii, and West Coast sites (*4*,*22*,*23*). Conversely, prescribing rates are highest in the southern United States, the region where the prevalence of gonococcal resistance has tended to be the lowest (*4*).

Bacterial antimicrobial drug resistance is clearly broadly linked to antimicrobial drug use, but the association is probably complex, interacting through several possible mechanisms and varying by bacteria, mode of transmission, antimicrobial drug, prevalence of resistance, and geographic location (*24*). For some bacterial pathogens, such as *Streptococcus pneumoniae* and *Escherchia coli,* associations between population-level antimicrobial drug prescribing and resistance in the United States and Europe have been described (*10–13*). We did not find such an association for *N. gonorrhoeae*.

There are at least 2 possible explanations for the apparent lack of county-level association between domestic antimicrobial drug prescribing and *N. gonorrhoeae* susceptibility. First, factors other than population-level prescribing rates, such as importation of resistant strains from other countries, might contribute to emergence of gonococcal resistance in the United States. Previously

Table 2. Adjusted linear regression coefficients for change in antimicrobial geometric mean MIC associated with 10% increase in corresponding antimicrobial prescribing rate for 23 sites, Gonococcal Isolate Surveillance Project, United States, 2005–2013*

Effect	β coefficient	SE	d.f.	95% CI of β coefficient
Azithromycin				
Time	–0.0087	0.003	155	–0.0146, –0.0029
Macrolide prescribing†	–0.0155	0.002	155	–0.0502, 0.0191
Cefixime				
Time	0.0011	0.0001	109	0.0008, 0.0014
Cephalosporin prescribing‡	0.0016	0.0013	109	–0.0010, 0.0041
Ceftriaxone				
Time	0.0004	0.0001	155	0.0002, 0.0005
Cephalosporin prescribing‡	0.0002	0.0006	155	–0.0009, 0.0013
Ciprofloxacin				
Time	0.0004	0.0021	155	–0.0038, 0.0045
Fluoroquinolone prescribing§	0.0004	0.0230	155	–0.0451, 0.0458

*All models were adjusted for percent of MSM at each site (using GISP data), race (percentage of men coded as black versus non-black in GISP data), percentage, and geographic region. Time was based on 1-year intervals. Estimate is statistically significant if the 95% CI of β coefficient does not cross 0.
†Per 10% increase in macrolide prescribing during the previous year; includes azithromycin, clarithromycin, and erythromycin.
‡Per 10% increase in cephalosporin prescribing during the previous year; includes cefaclor, cefadroxil, cefdinir, cefditoren pivoxil, cefixime, cefpodoxime proxetil, cefprozil, ceftibuten, cefuroxime axetil, cephalexin, cephradine, and loracarbef.
§Per 10% increase in fluoroquinolone prescribing during the previous year; includes ciprofloxacin, gemifloxacin, levofloxacin, moxifloxacin, norfloxacin, ofloxacin, and trovafloxacin.

published epidemiologic data have strongly suggested that resistant strains, such as PPNG and fluoroquinolone-resistant *N. gonorrhoeae*, and strains with reduced cefixime susceptibility (also investigated with genomic data), emerged initially in other parts of the world, particularly eastern Asia, and subsequently spread to the United States through Hawaii and the West Coast (*5*–*9*).

Second, it is possible that our data sources, methodology, or both lacked sufficient sensitivity to detect an association. The time period analyzed might have played a role: antimicrobial drug prescribing could conceivably be of greater or lesser importance during different phases of the emergence or persistence of resistance. As an inherent limitation of an ecologic approach, it is also possible that the prescribing rates we used in our analysis do not necessarily reflect antimicrobial drug use patterns among persons at risk for gonorrhea. For example, men seeking care in publicly funded STI clinics may be underinsured and thus lack access to routine medical care and be less likely to receive antimicrobial drug prescriptions. On the other hand, men diagnosed with gonorrhea in STI clinics may have been exposed to repeated antimicrobial drug courses for repeated STIs. Antimicrobial drug use might differ between MSM and MSW, so the availability of population-level drug prescribing data that include the sex of sex partners would be helpful.

Future investigations of associations between antimicrobial drug use and gonococcal susceptibility may also be strengthened by the availability of the indication for treatment (not available in the QuintilesIMS data), allowing for analyses linking susceptibility to antimicrobial drug use specifically for gonorrhea treatment. Investigators have previously identified links between individual-level antimicrobial drug use and gonococcal resistance in the United States (*25*,*26*). Nearly 30 years ago, Zenilman et al. found that persons with gonorrhea in Dade County, Florida, who had medicated themselves with illicit antibacterial drugs were more likely to be infected with PPNG than penicillin-sensitive strains (odds ratio 3.6; 95% CI 1.9–6.8) (*25*). Of note, our dataset does not include illicit or nonprescribed antimicrobial drugs. Among persons with gonorrhea in California during 2000–2003, antimicrobial drug use in the 3 months before diagnosis with gonorrhea was independently associated with infection with a fluoroquinolone-resistant strain (*26*). Using multisite GISP data for 2005–2010, we previously found that recent antimicrobial drug use was independently associated with *N. gonorrhoeae* ciprofloxacin, penicillin, and tetracycline resistance among men with gonococcal urethritis (*3*). However, the magnitude of the association between resistance and antimicrobial drug use was dwarfed by the magnitude of the association between resistance and geographic region and sex of sex partner, and use of an antimicrobial drug was not associated with reduced susceptibility to azithromycin, cefixime, and ceftriaxone.

The antimicrobial drugs that clinicians choose to treat gonorrhea may influence the susceptibility of *N. gonorrhoeae* populations. In the early 1970s, an increase in the recommended dosage of penicillin in response to increased resistance was followed by a plateau in penicillin resistance; experts speculated that the updated and highly effective treatment schedule retarded the selection of resistant mutants (*27*). Recently, cephalosporin susceptibility in the United States appeared to improve following updates in CDC treatment guidelines that recommended routine dual therapy, a preference for injectable ceftriaxone over oral cefixime, and a higher ceftriaxone dose (*28*). In contrast, some gonorrhea treatment approaches might promote resistance. Treatment with azithromycin alone is not recommended because of concerns about the ease with which *N. gonorrhoeae* can develop macrolide drug resistance; previously published cases seem to illustrate selection of higher azithromycin MICs following gonorrhea treatment with azithromycin monotherapy (*29*–*31*). Spectinomycin resistance was observed to emerge rapidly among US service members stationed in South Korea after spectinomycin was adopted as the primary gonorrhea treatment by the US military (following the emergence of PPNG) (*32*).

Emergence and persistence of gonococcal-resistant phenotypes is probably influenced by a complex (and not yet fully understood) interplay of bacterial and host factors, such as the ease with which the gonococcal strain can acquire necessary mutation(s); the effect of the mutation(s) on bacterial fitness; the anatomic site of infection (which can influence symptomatology, likelihood of treatment success, and coexistence of *N. gonorrhoeae* with other bacteria with which DNA may be shared); host mobility (including international travel); host sexual behavior; the nature of the sexual network within which the resistant strain emerges; prevalence of resistance; provider screening practices; and antimicrobial drug exposure (*32*–*37*). Furthermore, the relative importance of each factor may differ by resistance phenotype. The framework posited by Lipsitch and Samore may prove useful for considering mechanisms by which antimicrobial drugs might contribute to *N. gonorrhoeae* resistance, such as emergence of resistance during treatment or clearance of a susceptible majority bacterial population and subsequent transmission of a resistant minority population (*24*,*29*). However, much work remains to be done to understand these complex relationships.

Our analysis has other limitations. Ecologic analyses are limited by the potential for unmeasured and uncontrolled confounding. Conclusions of this ecologic analysis are based on counties or geographic site, rather than individual patients. Prescribing data were derived from counties that in some instances do not fully overlap with the STD

clinic catchment areas from which the susceptibility data were derived. Our analyses were limited to data from men. However, the inclusion of data from women is unlikely to have influenced the results: women may consume more antimicrobial drugs than men, and gonococcal isolates from women tend to be more susceptible to antimicrobial drugs than those from men (similar to isolates from MSW and substantially more susceptible than isolates from MSM) (*38*,*39*). An important caveat is that our findings are only applicable to the United States: they should not be extrapolated to other countries and regions. It is possible that rates of population-level antimicrobial drug prescribing or use in other countries may select for resistant gonococcal strains, which in turn may spread across international borders. Further investigation to understand region- or county-specific factors contributing to resistance is urgently needed.

The findings of our analysis suggest that population-wide domestic antimicrobial drug prescribing rates might not play a prominent role in the emergence of gonococcal resistance in the United States. Other means, such as importation from other countries, might play larger roles. Through this lens, enhanced surveillance for and public health capacity to respond to imported resistant strains are important strategies. However, it is possible that the choice of antimicrobial drugs that clinicians prescribe for gonorrhea therapy might influence the persistence or spread of resistant gonococcal strains that emerge in the United States. US-based healthcare providers should treat gonorrhea according to CDC STI treatment guidelines with dual therapy of 250 mg ceftriaxone as a single intramuscular dose plus 1 g azithromycin orally (*16*). The remarkable ability of *N. gonorrhoeae* to develop resistance to each antimicrobial drug used for treatment (*2*), combined with the declining number of new drugs (*40*), highlight the need to develop and apply interventions to slow the emergence and spread of gonococcal resistance.

Dr. Kirkcaldy is the team lead of the Epidemiology Research Team in the Division of STD Prevention, National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention, Centers for Disease Control and Prevention, Atlanta, GA. His research interests include STI epidemiology, antimicrobial drug resistance in bacterial STIs, and gonorrhea treatment.

References

1. Centers for Disease Control and Prevention. Antibiotic resistance threats in the United States, 2013 [cited 2017 May 2]. http://www.cdc.gov/drugresistance/pdf/ar-threats-2013-508.pdf
2. Unemo M, Nicholas RA. Emergence of multidrug-resistant, extensively drug-resistant and untreatable gonorrhea. Future Microbiol. 2012;7:1401–22. http://dx.doi.org/10.2217/fmb.12.117
3. Kirkcaldy RD, Zaidi A, Hook EW III, Holmes KK, 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;158:321–8. http://dx.doi.org/10.7326/0003-4819-158-5-201303050-00004
4. 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(No. SS-7):1–19. http://dx.doi.org/10.15585/mmwr.ss6507a1
5. Jaffe HW, Biddle JW, Johnson SR, Wiesner PJ. Infections due to penicillinase-producing *Neisseria gonorrhoeae* in the United States: 1976-1980. J Infect Dis. 1981;144:191–7. http://dx.doi.org/10.1093/infdis/144.2.191
6. Trees DL, Sandul AL, Neal SW, Higa H, Knapp JS. Molecular epidemiology of *Neisseria gonorrhoeae* exhibiting decreased susceptibility and resistance to ciprofloxacin in Hawaii, 1991–1999. Sex Transm Dis. 2001;28:309–14. http://dx.doi.org/10.1097/00007435-200106000-00001
7. Iverson CJ, Wang SA, Lee MV, Ohye RG, Trees DL, Knapp JS, et al. Fluoroquinolone resistance among *Neisseria gonorrhoeae* isolates in Hawaii, 1990–2000: role of foreign importation and increasing endemic spread. Sex Transm Dis. 2004;31:702–8. http://dx.doi.org/10.1097/01.olq.0000145846.45781.a4
8. Wang SA, Lee MV, O'Connor N, Iverson CJ, Ohye RG, Whiticar PM, et al. Multidrug-resistant *Neisseria gonorrhoeae* with decreased susceptibility to cefixime—Hawaii, 2001. Clin Infect Dis. 2003;37:849–52. http://dx.doi.org/10.1086/377500
9. Grad YH, Kirkcaldy RD, Trees D, Dordel J, Harris SR, Goldstein E, et al. Genomic epidemiology of *Neisseria gonorrhoeae* with reduced susceptibility to cefixime in the USA: a retrospective observational study. Lancet Infect Dis. 2014;14:220–6. http://dx.doi.org/10.1016/S1473-3099(13)70693-5
10. Hicks LA, Chien YW, Taylor TH Jr, Haber M, Klugman KP; Active Bacterial Core Surveillance (ABCs) Team. Outpatient antibiotic prescribing and nonsusceptible *Streptococcus pneumoniae* in the United States, 1996-2003. Clin Infect Dis. 2011; 53:631–9. http://dx.doi.org/10.1093/cid/cir443
11. Bronzwaer SL, Cars O, Buchholz U, Mölstad S, Goettsch W, Veldhuijzen IK, et al.; European Antimicrobial Resistance Surveillance System. A European study on the relationship between antimicrobial use and antimicrobial resistance. Emerg Infect Dis. 2002;8:278–82. https://wwwnc.cdc.gov/eid/article/8/3/01-0192_article
12. van de Sande-Bruinsma N, Grundmann H, Verloo D, Tiemersma E, Monen J, Goossens H, et al.; European Antimicrobial Resistance Surveillance System Group; European Surveillance of Antimicrobial Consumption Project Group. Antimicrobial drug use and resistance in Europe. Emerg Infect Dis. 2008;14:1722–30. http://dx.doi.org/10.3201/eid1411.070467
13. Riedel S, Beekmann SE, Heilmann KP, Richter SS, Garcia-de-Lomas J, Ferech M, et al. Antimicrobial use in Europe and antimicrobial resistance in *Streptococcus pneumoniae*. Eur J Clin Microbiol Infect Dis. 2007;26:485–90. http://dx.doi.org/10.1007/s10096-007-0321-5
14. Boardman C. inventor; IMS Health Incorporated, assignee. System and method for estimating product distribution using a product specific universe. United States patent US 7174304. 2007 Feb 6.
15. Hicks LA, Bartoces MG, Roberts RM, Suda KJ, Hunkler RJ, Taylor TH Jr, et al. US outpatient antibiotic prescribing variation according to geography, patient population, and provider specialty in 2011. Clin Infect Dis. 2015;60:1308–16.
16. Workowski KA, Bolan GA; Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. MMWR Recomm Rep. 2015;64(RR-03):1–137.
17. Hemarajata P, Yang S, Soge OO, Humphries RM, Klausner JD. Performance and verification of a real-time PCR assay targeting the *gyrA* gene for prediction of ciprofloxacin resistance in *Neisseria gonorrhoeae.* J Clin Microbiol. 2016;54:805–8. http://dx.doi.org/10.1128/JCM.03032-15

18. Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing; twenty-sixth informational supplement (M100–S26). Wayne (PA): The Institute; 2016.
19. Raudenbush SW, Bryk AS. Hierarchical linear models: applications and data analysis methods. 2nd ed. Thousand Oaks (CA): Sage Publications; 2002.
20. Singer JD, Willett JB. Applied longitudinal data analysis: modeling change and event occurrence. Oxford/New York: Oxford University Press; 2003.
21. Fleming-Dutra KE, Shapiro DJ, Hicks LA, Gerber JS, Hersh AL. Race, otitis media, and antibiotic selection. Pediatrics. 2014;134:1059–66. http://dx.doi.org/10.1542/peds.2014-1781
22. Centers for Disease Control and Prevention. Increases in fluoroquinolone-resistant Neisseria gonorrhoeae—Hawaii and California, 2001. MMWR Morb Mortal Wkly Rep. 2002;51:1041–4.
23. Centers for Disease Control and Prevention. Sexually transmitted disease surveillance 2013: Gonococcal Isolate Surveillance Project (GISP) supplement and profiles cited [cited 2017 May 2]. http://www.cdc.gov/std/gisp2013/gisp-2013-all-profiles.pdf
24. Lipsitch M, Samore MH. Antimicrobial use and antimicrobial resistance: a population perspective. Emerg Infect Dis. 2002;8:347–54. https://wwwnc.cdc.gov/eid/article/8/4/01-0312_article
25. Zenilman JM, Bonner M, Sharp KL, Rabb JA, Alexander ER. Penicillinase-producing *Neisseria gonorrhoeae* in Dade County, Florida: evidence of core-group transmitters and the impact of illicit antibiotics. Sex Transm Dis. 1988;15:45–50. http://dx.doi.org/10.1097/00007435-198801000-00011
26. Bauer HM, Mark KE, Samuel M, Wang SA, Weismuller P, Moore D, et al. Prevalence of and associated risk factors for fluoroquinolone-resistant *Neisseria gonorrhoeae* in California, 2000–2003. Clin Infect Dis. 2005;41:795–803. http://dx.doi.org/10.1086/432801
27. McCormack WM. Treatment of gonorrhea—is penicillin passé? N Engl J Med. 1977;296:934–6. http://dx.doi.org/10.1056/NEJM197704212961610
28. Kirkcaldy RD, Hook EW III, Soge OO, del Rio C, Kubin G, Zenilman JM, et al. Trends in *Neisseria gonorrhoeae* susceptibility to cephalosporins in the United States, 2006–2014. JAMA. 2015;314:1869–71. http://dx.doi.org/10.1001/jama.2015.10347
29. Soge OO, Harger D, Schafer S, Toevs K, Raisler KA, Venator K, et al. Emergence of increased azithromycin resistance during unsuccessful treatment of *Neisseria gonorrhoeae* infection with azithromycin (Portland, OR, 2011). Sex Transm Dis. 2012;39:877–9. http://dx.doi.org/10.1097/OLQ.0b013e3182685d2b
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. http://dx.doi.org/10.1258/0956462971920127
31. Ison CA, Hussey J, Sankar KN, Evans J, Alexander S. Gonorrhoea treatment failures to cefixime and azithromycin in England, 2010. Euro Surveill. 2011;16:19833.
32. Boslego JW, Tramont EC, Takafuji ET, Diniega BM, Mitchell BS, Small JW, et al. Effect of spectinomycin use on the prevalence of spectinomycin-resistant and of penicillinase-producing *Neisseria gonorrhoeae.* N Engl J Med. 1987;317:272–8. http://dx.doi.org/10.1056/NEJM198707303170504
33. Holmes AH, Moore LSP, Sundsfjord A, Steinbakk M, Regmi S, Karkey A, et al. Understanding the mechanisms and drivers of antimicrobial resistance. Lancet. 2016;387:176–87. http://dx.doi.org/10.1016/S0140-6736(15)00473-0
34. Kunz AN, Begum AA, Wu H, D'Ambrozio JA, Robinson JM, Shafer WM, et al. Impact of fluoroquinolone resistance mutations on gonococcal fitness and in vivo selection for compensatory mutations. J Infect Dis. 2012;205:1821–9. http://dx.doi.org/10.1093/infdis/jis277
35. Weinstock H, Workowski KA. Pharyngeal gonorrhea: an important reservoir of infection? Clin Infect Dis. 2009;49:1798–800. http://dx.doi.org/10.1086/648428
36. Ameyama S, Onodera S, Takahata M, Minami S, Maki N, Endo K, et al. Mosaic-like structure of penicillin-binding protein 2 gene (*penA*) in clinical isolates of *Neisseria gonorrhoeae* with reduced susceptibility to cefixime. Antimicrob Agents Chemother. 2002;46:3744–9. http://dx.doi.org/10.1128/AAC.46.12.3744-3749.2002
37. Moran JS. Treating uncomplicated *Neisseria gonorrhoeae* infections: is the anatomic site of infection important? Sex Transm Dis. 1995;22:39–47. http://dx.doi.org/10.1097/00007435-199501000-00007
38. Frenk SM, Kit BK, Lukacs SL, Hicks LA, Gu Q. Trends in the use of prescription antibiotics: NHANES 1999–2012. J Antimicrob Chemother. 2016;71:251–6. http://dx.doi.org/10.1093/jac/dkv319
39. Kidd S, Moore PC, Kirkcaldy RD, Philip SS, Wiesenfeld HC, Papp JR, et al. Comparison of antimicrobial susceptibility of urogenital *Neisseria gonorrhoeae* isolates obtained from women and men. Sex Transm Dis. 2015;42:434–9. http://dx.doi.org/10.1097/OLQ.0000000000000312
40. Shlaes DM, Sahm D, Opiela C, Spellberg B. The FDA reboot of antibiotic development. Antimicrob Agents Chemother. 2013;57:4605–7. http://dx.doi.org/10.1128/AAC.01277-13

Address for correspondence: Robert D. Kirkcaldy, Centers for Disease Control and Prevention, 1600 Clifton Road, Mailstop E02, Atlanta, GA 30329-4027, USA; email: rkirkcaldy@cdc.gov

Article DOI: https://doi.org/10.3201/eid2310.170488

Antimicrobial Drug Prescription and *Neisseria gonorrhoeae* Susceptibility, United States, 2005–2013

Technical Appendix

Technical Appendix Table 1. Geometric mean of cefixime MICs by site and year, Gonococcal Isolate Surveillance Project (GISP), 2005–2013*

GISP site	Corresponding county in analysis	2005	2006	2007, 2008	2009	2010	2011	2012	2013
Northeast									
Philadelphia, Pennsylvania	Philadelphia	0.016	0.009	–	0.020	0.019	0.021	0.021	0.020
Midwest									
Chicago, Illinois	Cook County	0.007	0.007	–	0.021	0.019	0.02	0.019	0.019
Cleveland, Ohio	Cuyahoga County	0.007	0.008	–	0.017	0.017	0.017	0.018	0.017
Minneapolis, Minnesota	Hennepin County	0.007	0.009	–	0.024	0.023	0.019	0.022	0.022
South									
Baltimore, Maryland	Baltimore County	0.014	0.008	–	0.019	0.022	0.023	0.023	0.019
Dallas, Texas	Dallas County	0.005	0.007	–	0.018	0.019	0.019	0.019	0.019
Atlanta, Georgia	Fulton County	0.011	0.011	–	0.016	0.016	0.018	0.017	0.016
Greensboro, North Carolina	Guilford County	0.009	0.007	–	0.016	0.017	0.018	0.019	0.016
Birmingham, Alabama	Jefferson County	0.013	0.007	–	0.019	0.018	0.019	0.019	0.019
Miami, Florida	Miami-Dade County	0.014	0.011	–	0.017	0.018	0.019	0.019	0.018
Oklahoma City, Oklahoma	Oklahoma County	0.013	0.008	–	0.017	0.018	0.019	0.020	0.017
New Orleans, Louisiana	Orleans Parish	0.012	0.011	–	0.017	0.018	0.018	0.017	0.017
West									
Albuquerque, New Mexico	Bernalillo County	0.012	0.013	–	0.018	0.018	0.02	0.019	0.018
Las Vegas, Nevada	Clark County	0.006	0.008	–	0.021	0.020	0.018	0.020	0.019
Denver, Colorado	Denver County	0.010	0.009	–	0.020	0.019	0.020	0.021	0.020
Honolulu, Hawaii	Honolulu County	0.005	0.010	–	0.026	0.028	0.020	0.018	0.020
Seattle, Washington	King County	0.006	0.010	–	0.030	0.030	0.030	0.030	0.030
Los Angeles, California	Los Angeles County	0.011	0.014	–	0.026	0.025	0.023	0.022	0.022
Phoenix, Arizona	Maricopa County	0.012	0.014	–	0.022	0.020	0.018	0.019	0.019
Portland, Oregon	Multnomah County	0.009	0.011	–	0.024	0.023	0.022	0.022	0.022
Orange County, California	Orange County	0.014	0.015	–	0.023	0.026	0.024	0.030	0.024
San Diego, California	San Diego County	0.015	0.017	–	0.028	0.030	0.029	0.028	0.028
San Francisco, California	San Francisco County	0.007	0.012	–	0.023	0.023	0.023	0.023	0.023

*Cefixime susceptibility not tested in 2007 and 2008. MIC range was 0.001–0.5 µg/mL in 2005–2006; range was 0.015–0.5 µg/mL during 2009–2013.

Technical Appendix Table 2. Geometric mean ceftriaxone MICs by GISP site and year, Gonococcal Isolate Surveillance Project (GISP), 2005–2013*

GISP site	Corresponding county in analysis	2005	2006	2007	2008	2009	2010	2011	2012	2013
Northeast										
Philadelphia, Pennsylvania	Philadelphia	0.008	0.006	0.011	0.010	0.011	0.011	0.009	0.010	0.009
Midwest										
Chicago, Illinois	Cook County	0.004	0.004	0.010	0.010	0.011	0.011	0.010	0.010	0.009
Cleveland, Ohio	Cuyahoga County	0.003	0.004	0.009	0.009	0.009	0.009	0.009	0.009	0.009
Minneapolis, Minnesota	Hennepin County	0.004	0.005	0.011	0.012	0.014	0.012	0.012	0.010	0.012
South										
Baltimore, Maryland	Baltimore County	0.006	0.004	0.009	0.009	0.009	0.010	0.009	0.010	0.009
Dallas, Texas	Dallas County	0.005	0.004	0.009	0.009	0.009	0.009	0.009	0.010	0.0100
Atlanta, Georgia	Fulton County	0.005	0.005	0.010	0.010	0.009	0.009	0.009	0.010	0.010
Greensboro, North Carolina	Guilford County	0.004	0.004	0.009	0.009	0.010	0.009	0.009	0.010	0.008
Birmingham, Alabama	Jefferson County	0.005	0.003	0.009	0.009	0.009	0.009	0.009	0.009	0.008
Miami, Florida	Miami-Dade County	0.006	0.006	0.010	0.009	0.010	0.10	0.010	0.011	0.012
Oklahoma City, Oklahoma	Oklahoma County	0.005	0.004	0.009	0.009	0.009	0.008	0.009	0.010	0.010
New Orleans, Louisiana	Orleans Parish	0.006	0.006	0.010	0.009	0.010	0.009	0.010	0.009	0.009
West										
Albuquerque, New Mexico	Bernalillo County	0.006	0.005	0.011	0.009	0.011	0.010	0.011	0.011	0.010
Las Vegas, Nevada	Clark County	0.004	0.005	0.012	0.011	0.010	0.010	0.010	0.009	0.010
Denver, Colorado	Denver County	0.005	0.004	0.010	0.009	0.009	0.010	0.010	0.011	0.011
Honolulu, Hawaii	Honolulu County	0.005	0.005	0.010	0.010	0.011	0.011	0.013	0.011	0.010
Seattle, Washington	King County	0.006	0.006	0.011	0.010	0.011	0.013	0.013	0.014	0.016
Los Angeles, California	Los Angeles County	0.006	0.007	0.010	0.009	0.010	0.011	0.012	0.013	0.013
Phoenix, Arizona	Maricopa County	0.006	0.006	0.010	0.011	0.011	0.011	0.010	0.009	0.009
Portland, Oregon	Multnomah County	0.008	0.005	0.010	0.012	0.010	0.013	0.015	0.013	0.013
Orange County, California	Orange County	0.008	0.008	0.011	0.012	0.012	0.012	0.011	0.011	0.012
San Diego, California	San Diego County	0.008	0.009	0.013	0.012	0.011	0.012	0.013	0.012	0.011
San Francisco, California	San Francisco County	0.008	0.007	0.010	0.010	0.009	0.010	0.012	0.012	0.013

* MIC range was 0.001–2.0 µg/mL in 2005–2006; range was 0.008–2.0 µg/mL during 2007–2013.

Technical Appendix Table 3. Geometric mean azithromycin MICs by GISP site and year, Gonococcal Isolate Surveillance Project (GISP), 2005–2013*

GISP site	Corresponding county in analysis	2005	2006	2007	2008	2009	2010	2011	2012	2013
Northeast										
Philadelphia, Pennsylvania	Philadelphia	0.31	0.273	0.369	0.343	0.328	0.298	0.228	0.226	0.24
Midwest										
Chicago, Illinois	Cook County	0.226	0.231	0.291	0.267	0.244	0.324	0.269	0.276	0.285
Cleveland, Ohio	Cuyahoga County	0.197	0.258	0.278	0.265	0.212	0.294	0.303	0.213	0.229
Minneapolis, Minnesota	Hennepin County	0.242	0.28	0.292	0.361	0.314	0.347	0.361	0.284	0.385
South										
Baltimore, Maryland	Baltimore County	0.264	0.261	0.316	0.251	0.219	0.234	0.191	0.211	0.211
Dallas, Texas	Dallas County	0.1	0.081	0.096	0.102	0.106	0.068	0.084	0.137	0.162
Atlanta, Georgia	Fulton County	0.181	0.188	0.167	0.297	0.079	0.097	0.029	0.099	0.118
Greensboro, North Carolina	Guilford County	0.128	0.194	0.194	0.256	0.15	0.119	0.1	0.115	0.175
Birmingham, Alabama	Jefferson County	0.248	0.289	0.324	0.325	0.207	0.228	0.157	0.171	0.166
Miami, Florida	Miami-Dade County	0.166	0.178	0.192	0.245	0.199	0.109	0.104	0.1000	0.153
Oklahoma City, Oklahoma	Oklahoma County	0.222	0.257	0.271	0.242	0.229	0.183	0.153	0.143	0.219
New Orleans, Louisiana	Orleans Parish	0.162	0.239	0.184	0.234	0.103	0.125	0.096	0.112	0.139
West										
Albuquerque, New Mexico	Bernalillo County	0.182	0.182	0.258	0.239	0.114	0.123	0.09	0.136	0.113
Las Vegas, Nevada	Clark County	0.216	0.259	0.294	0.276	0.243	0.317	0.299	0.192	0.23
Denver, Colorado	Denver County	0.18	0.161	0.223	0.128	0.101	0.065	0.13	0.183	0.161
Honolulu, Hawaii	Honolulu County	0.100	0.134	0.168	0.206	0.187	0.148	0.152	0.21	0.133
Seattle, Washington	King County	0.142	0.156	0.191	0.154	0.162	0.158	0.147	0.213	0.234
Los Angeles, California	Los Angeles County	0.195	0.204	0.247	0.189	0.181	0.127	0.145	0.213	0.22
Phoenix, Arizona	Maricopa County	0.193	0.182	0.256	0.295	0.316	0.383	0.353	0.232	0.300
Portland, Oregon	Multnomah County	0.149	0.155	0.200	0.235	0.259	0.157	0.219	0.238	0.217
Orange County, California	Orange County	0.253	0.280	0.273	0.406	0.508	0.496	0.287	0.218	0.279
San Diego, California	San Diego County	0.210	0.233	0.315	0.424	0.438	0.460	0.292	0.271	0.236
San Francisco, California	San Francisco County	0.137	0.188	0.210	0.216	0.204	0.126	0.150	0.244	0.238

* MIC testing range was 0.008–16 µg/mL in 2005–2006; range was 0.03–16 µg/mL during 2007–2013.

Technical Appendix Table 4. Geometric mean ciprofloxacin MICs by GISP site and year, Gonococcal Isolate Surveillance Project (GISP), 2005–2013*

GISP site	Corresponding county in analysis	2005	2006	2007	2008	2009	2010	2011	2012	2013
Northeast										
Philadelphia, Pennsylvania	Philadelphia	0.015	0.036	0.063	0.033	0.042	0.038	0.025	0.053	0.035
Midwest										
Chicago, Illinois	Cook County	0.009	0.007	0.016	0.013	0.029	0.051	0.029	0.026	0.021
Cleveland, Ohio	Cuyahoga County	0.008	0.007	0.010	0.011	0.016	0.016	0.016	0.016	0.017
Minneapolis, Minnesota	Hennepin County	0.009	0.008	0.017	0.014	0.076	0.059	0.063	0.03	0.042
South										
Baltimore, Maryland	Baltimore County	0.005	0.004	0.009	0.012	0.02	0.028	0.016	0.021	0.05
Dallas, Texas	Dallas County	0.006	0.006	0.014	0.013	0.024	0.028	0.022	0.032	0.029
Atlanta, Georgia	Fulton County	0.007	0.008	0.01	0.018	0.021	0.02	0.024	0.024	0.031
Greensboro, North Carolina	Guilford County	0.007	0.005	0.012	0.011	0.017	0.017	0.02	0.023	0.017
Birmingham, Alabama	Jefferson County	0.005	0.004	0.015	0.014	0.029	0.032	0.056	0.036	0.029
Miami, Florida	Miami-Dade County	0.011	0.024	0.035	0.025	0.033	0.041	0.064	0.062	0.062
Oklahoma City, Oklahoma	Oklahoma County	0.005	0.005	0.012	0.011	0.018	0.015	0.017	0.019	0.022
New Orleans, Louisiana	Orleans Parish	0.010	0.011	0.029	0.023	0.025	0.034	0.033	0.029	0.036
West										
Albuquerque, New Mexico	Bernalillo County	0.009	0.011	0.026	0.014	0.024	0.066	0.064	0.048	0.042
Las Vegas, Nevada	Clark County	0.009	0.009	0.032	0.029	0.032	0.024	0.026	0.052	0.074
Denver, Colorado	Denver County	0.013	0.017	0.025	0.018	0.033	0.042	0.049	0.044	0.047
Honolulu, Hawaii	Honolulu County	0.020	0.076	0.075	0.137	0.271	0.128	0.096	0.042	0.034
Seattle, Washington	King County	0.012	0.099	0.129	0.123	0.073	0.500	0.214	0.119	0.262
Los Angeles, California	Los Angeles County	0.018	0.032	0.041	0.027	0.036	0.048	0.084	0.122	0.12
Phoenix, Arizona	Maricopa County	0.010	0.016	0.015	0.026	0.039	0.039	0.028	0.029	0.030
Portland, Oregon	Multnomah County	0.029	0.046	0.070	0.429	0.059	0.093	0.075	0.06	0.039
Orange County, California	Orange County	0.045	0.073	0.129	0.081	0.048	0.061	0.076	0.111	0.214
San Diego, California	San Diego County	0.038	0.074	0.110	0.063	0.054	0.058	0.138	0.215	0.109
San Francisco, California	San Francisco County	0.069	0.179	0.081	0.057	0.031	0.050	0.110	0.122	0.130

*MIC testing range was 0.001–16 µg/mL in 2005–2006; range was 0.008–16 µg/mL during 2007–2013.

Technical Appendix Table 5. Outpatient oral cephalosporin* prescriptions per 1,000 men 10–59 y by county, Gonococcal Isolate Surveillance Project (GISP), 2005–2013

County (and associated GISP site)	2005	2006	2007	2008	2009	2010	2011	2012	2013
Northeast									
Philadelphia, Pennsylvania	70	62	61	59	57	54	76	75	78
Midwest									
Cook County, Illinois (Chicago)	18	20	33	57	56	53	67	67	67
Cuyahoga County, Ohio (Cleveland)	56	75	80	91	81	66	88	86	102
Hennepin County, Minnesota (Minnesota)	21	31	41	64	65	66	76	74	76
South									
Baltimore County, Maryland (Baltimore)	71	64	60	61	60	57	67	68	65
Dallas County, Texas (Dallas)	50	56	67	85	86	86	90	96	91
Fulton County, Georgia (Atlanta)	62	97	93	91	96	96	92	92	93
Guilford County, North Carolina (Greensboro)	78	80	75	75	72	69	75	77	75
Jefferson County, Alabama (Birmingham)	116	137	138	149	140	133	164	162	160
Miami-Dade County, Florida (Miami)	25	27	32	45	44	41	45	45	44
Oklahoma County, Oklahoma (Oklahoma City)	50	60	83	134	127	126	140	144	148
Orleans Parish, Louisiana (New Orleans)	13	39	48	69	66	59	91	84	80
West									
Bernalillo County, New Mexico (Albuquerque)	13	19	36	75	71	73	80	76	74
Clark County, Nevada (Las Vegas)	48	45	52	71	66	64	63	61	62
Denver County, Colorado (Denver)	16	27	32	45	44	42	57	57	55
Honolulu County, Hawaii (Honolulu)	65	64	63	59	55	48	56	56	52
King County, Washington (Seattle)	45	48	50	60	58	53	65	62	59
Los Angeles County, California (Los Angeles)	61	56	54	55	54	50	56	54	54
Maricopa County, Arizona (Phoenix)	33	33	44	74	75	76	81	79	77
Multnomah County, Oregon (Portland)	21	30	32	41	39	38	52	47	47
Orange County, California	62	64	64	67	64	60	65	61	63
San Diego County, California (San Diego)	44	43	40	40	38	38	42	43	43
San Francisco County, California (San Francisco)	7	17	26	42	40	41	58	54	54

*Includes cefaclor, cefadroxil, cefdinir, cefditoren pivoxil, cefixime, cefpodoxime proxetil, cefprozil, ceftibuten, cefuroxime axetil, cephalexin, cephradine, and loracarbef

Technical Appendix Table 6. Outpatient oral macrolide* prescriptions per 1,000 men 10–59 y by county, Gonococcal Isolate Surveillance Project (GISP), 2005–2013

County (and associated GISP site)	2005	2006	2007	2008	2009	2010	2011	2012	2013
Northeast									
Philadelphia, Pennsylvania	103	91	101	112	117	103	139	135	126
Midwest									
Cook County, Illinois (Chicago)	31	32	62	120	130	116	150	145	127
Cuyahoga County, Ohio (Cleveland)	92	108	122	155	155	141	187	169	144
Hennepin County, Minnesota (Minnesota)	34	44	64	113	112	115	132	124	108
South									
Baltimore County, Maryland (Baltimore)	96	88	97	121	125	113	135	133	115
Dallas County, Texas (Dallas)	61	66	98	135	137	131	141	151	142
Fulton County, Georgia (Atlanta)	98	124	134	165	172	155	143	148	133
Guilford County, North Carolina (Greensboro)	109	108	121	140	135	120	132	144	124
Jefferson County, Alabama (Birmingham)	136	159	186	244	261	240	260	280	260
Miami-Dade County, Florida (Miami)	41	45	61	98	112	98	106	110	100
Oklahoma County, Oklahoma (Oklahoma City)	57	62	118	216	204	193	213	217	188
Orleans Parish, Louisiana (New Orleans)	17	62	80	136	135	125	176	165	147
West									
Bernalillo County, New Mexico (Albuquerque)	19	27	53	121	118	120	133	122	111
Clark County, Nevada (Las Vegas)	61	52	65	113	117	107	118	111	105
Denver County, Colorado (Denver)	26	39	49	75	72	66	91	87	81
Honolulu County, Hawaii (Honolulu)	17	26	45	85	88	90	105	92	90
King County, Washington (Seattle)	68	66	77	98	94	81	114	105	88
Los Angeles County, California (Los Angeles)	74	65	70	84	91	85	102	89	89
Maricopa County, Arizona (Phoenix)	49	44	66	123	129	126	144	134	120
Multnomah County, Oregon (Portland)	28	36	45	64	61	60	86	74	65
Orange County, California	107	100	106	125	128	120	136	115	115
San Diego County, California (San Diego)	61	57	57	63	64	67	77	67	66
San Francisco County, California (San Francisco)	17	26	45	85	88	90	105	92	90

*Includes azithromycin, clarithromycin, and erythromycin

Technical Appendix Table 7. Outpatient oral fluoroquinolone* prescriptions per 1,000 men 10–59 y by county, Gonococcal Isolate Surveillance Project (GISP), 2005–2013

County (and associated GISP site)	2005	2006	2007	2008	2009	2010	2011	2012	2013
Northeast									
Philadelphia, Pennsylvania	68	72	75	77	70	62	88	88	89
Midwest									
Cook County, Illinois (Chicago)	19	22	39	70	62	55	71	71	70
Cuyahoga County, Ohio (Cleveland)	47	66	75	87	78	62	86	82	92
Hennepin County, Minnesota (Minneapolis)	17	27	39	65	59	55	64	61	58
South									
Baltimore County, Maryland (Baltimore)	78	71	72	76	65	58	71	70	66
Dallas County, Texas (Dallas)	41	50	68	91	82	74	80	88	87
Fulton County, Georgia (Atlanta)	74	115	119	131	117	108	109	107	104
Guilford County, North Carolina (Greensboro)	70	78	79	84	75	69	77	80	77
Jefferson County, Alabama (Birmingham)	75	103	119	141	130	120	153	180	179
Miami-Dade County, Florida (Miami)	29	33	45	65	61	56	63	63	62
Oklahoma County, Oklahoma (Oklahoma City)	34	46	74	124	108	103	115	120	117
Orleans Parish, Louisiana (New Orleans)	11	45	61	83	72	64	104	107	105
West									
Bernalillo County, New Mexico (Albuquerque)	8	13	23	47	43	43	52	50	46
Clark County, Nevada (Las Vegas)	37	38	48	71	61	54	54	55	57
Denver County, Colorado (Denver)	15	28	35	49	44	39	54	50	47
Honolulu County, Hawaii (Honolulu)	41	47	52	52	48	42	53	53	50
King County, Washington (Seattle)	36	38	44	51	45	39	48	46	41
Los Angeles County, California (Los Angeles)	38	39	42	46	41	37	45	44	44
Maricopa County, Arizona (Phoenix)	22	25	36	63	58	56	59	57	53
Multnomah County, Oregon (Portland)	17	29	33	43	37	37	50	46	44
Orange County, California	49	53	58	62	56	50	53	52	52
San Diego County, California (San Diego)	32	33	33	33	30	29	33	33	33
San Francisco County, California (San Francisco)	7	18	34	60	53	55	74	68	67

*Includes ciprofloxacin, gemifloxacin, levofloxacin,moxifloxacin, norfloxacin, ofloxacin, and trovafloxacin

Technical Appendix Table 8. *Neisseria gonorrhoeae* antimicrobial drug susceptibility (median annual geometric mean MICs and median annual prescribing rates of counties corresponding to the 23 sites continuously participating in the Gonococcal Isolate Surveillance Project (GISP) by site, 2005–2013*

					Antimicrobial drug susceptibility (Median and interdecile range of annual geometric mean MIC values)								Outpatient prescriptions per 1,000 men 10–59 (Median and interdecile range of annual values)					
					Azithromycin		Ciprofloxacin		Cefixime		Ceftriaxone		Macrolide		Fluoroquinolone		Cephalosporin	
County (associated GISP site)	Total no. isolates	Mean age of men who submitted isolates (SD)	% of isolates from MSM	% of isolates from black men	Median	Inter-decile range	Median	Inter-decile range	Median	Inter-decile range	Median	Inter-decile range	Median	Inter-decile range	Median	Inter-decile range	Median	Inter-decile range
Northeast																		
Philadelphia, Pennsylvania	2486	31 (10)	21	88	0.298	0.143	0.038	0.048	0.02	0.012	0.01	0.005	112	48	75	27	62	24
Midwest																		
Cook County (Chicago), Illinois	2290	28 (9)	26	82	0.269	0.098	0.021	0.044	0.019	0.014	0.01	0.007	120	119	62	52	56	49
Cuyahoga County (Cleveland), Ohio	2081	28 (9)	8	94	0.258	0.106	0.016	0.01	0.017	0.011	0.009	0.006	144	95	78	45	81	46
Hennepin County (Minneapolis), Minnesota	1305	30 (9)	31	70	0.314	0.143	0.03	0.068	0.022	0.017	0.012	0.01	112	98	58	48	65	55
South																		
Baltimore County (Baltimore), Maryland	2552	28 (9)	11	97	0.234	0.125	0.016	0.046	0.019	0.015	0.009	0.006	115	47	71	20	64	14
Dallas County (Dallas), Texas	2576	26 (8)	16	100	0.1	0.094	0.022	0.026	0.019	0.014	0.009	0.006	135	90	80	50	86	46
Fulton County (Atlanta), Georgia	2068	28 (9)	19	99	0.118	0.268	0.02	0.024	0.016	0.007	0.009	0.005	143	74	109	57	93	35
Guilford County (Greensboro), North Carolina	1497	27 (9)	9	94	0.15	0.156	0.017	0.018	0.016	0.012	0.009	0.006	124	36	77	15	75	11
Jefferson County (Birmingham), Alabama	2004	27 (9)	4	97	0.228	0.168	0.029	0.052	0.019	0.012	0.009	0.006	244	144	130	105	140	48
Miami-Dade County (Miami), Florida	1916	28 (10)	22	88	0.166	0.145	0.035	0.053	0.018	0.008	0.01	0.094	98	71	61	36	44	20
Oklahoma County (Oklahoma City), Oklahoma	2181	27 (9)	6	82	0.222	0.128	0.015	0.017	0.017	0.012	0.009	0.006	193	160	108	90	127	98
Orleans Parish (New Orleans), Louisiana	1703	27 (9)	11	95	0.139	0.143	0.029	0.026	0.017	0.007	0.009	0.004	135	159	72	96	66	78
West																		
Bernalillo County (Albuquerque), New Mexico	1112	28 (9)	24	19	0.136	0.168	0.026	0.057	0.018	0.008	0.01	0.006	118	114	43	44	73	67
Clark County (Las Vegas), Nevada	2617	28 (9)	21	63	0.259	0.125	0.029	0.065	0.019	0.015	0.01	0.008	107	66	54	34	62	26
Denver County (Denver), Colorado	2069	29 (9)	32	50	0.161	0.158	0.033	0.036	0.02	0.012	0.01	0.007	72	65	44	39	44	41
Honolulu County (Honolulu), Hawaii	705	31 (9)	47	41	0.152	0.11	0.076	0.251	0.02	0.023	0.01	0.008	88	88	50	12	56	17

County (associated GISP site)	Total no. isolates	Mean age of men who submitted isolates (SD)	% of isolates from MSM	% of isolates from black men	Antimicrobial drug susceptibility (Median and interdecile range of annual geometric mean MIC values)								Outpatient prescriptions per 1,000 men 10–59 (Median and interdecile range of annual values)					
					Azithromycin		Ciprofloxacin		Cefixime		Ceftriaxone		Macrolide		Fluoroquinolone		Cephalosporin	
					Median	Inter-decile range	Median	Inter-decile range	Median	Inter-decile range	Median	Inter-decile range	Median	Inter-decile range	Median	Inter-decile range	Median	Inter-decile range
King County (Seattle), Washington	1682	34 (10)	62	34	0.158	0.092	0.123	0.488	0.03	0.024	0.011	0.01	88	48	44	15	58	20
Los Angeles County (Los Angeles), California	1384	29 (9)	53	52	0.195	0.12	0.041	0.104	0.022	0.015	0.01	0.007	85	37	42	9	54	11
Maricopa County (Phoenix), Arizona	2382	29 (9)	29	36	0.295	0.201	0.028	0.029	0.019	0.01	0.01	0.005	123	100	56	41	75	48
Multnomah County (Portland), Oregon	1318	31 (10)	56	30	0.217	0.11	0.06	0.4	0.022	0.015	0.012	0.01	61	58	37	33	39	31
Orange County, California	984	31 (10)	58	100	0.28	0.29	0.076	0.169	0.024	0.016	0.011	0.004	115	36	53	13	64	7
San Diego County (San Diego), California	1869	34 (10)	74	22	0.292	0.25	0.074	0.177	0.028	0.015	0.012	0.005	64	20	33	4	42	6
San Francisco County (San Francisco), California	2294	35 (10)	71	29	0.204	0.118	0.081	0.148	0.023	0.016	0.01	0.006	88	88	55	67	41	51

*MSM, men who have sex with men.