MINI-REVIEW

Laboratory Perspective on Racial Disparities in Sexually Transmitted Infections

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Background: Rates of sexually transmitted infections (STI) have risen steadily in recent years, and racial and ethnic minorities have borne the disproportionate burden of STI increases in the United States. Historical inequities and social determinants of health are significant contributors to observed disparities and affect access to diagnostic testing for STI.

Content: Public health systems rely heavily on laboratory medicine professionals for diagnosis and reporting of STI. Therefore, it is imperative that clinicians and laboratory professionals be familiar with issues underlying disparities in STI incidence and barriers to reliable diagnostic testing. In this mini-review, we will summarize contributors to racial/ethnic disparity in STI, highlight current epidemiologic trends for gonorrhea, chlamydia, and syphilis, discuss policy issues that affect laboratory and public health funding, and identify specific analytic challenges for diagnostic laboratories.

Summary: Racial and ethnic disparities in STI in the US are striking and are due to complex interactions of myriad social determinants of health. Budgetary cuts for laboratory and public health services and competition for resources during the COVID-19 pandemic are major challenges. Laboratory professionals must be aware of these underlying issues and work to maximize efforts to ensure equitable access to diagnostic STI testing for all persons, particularly those most disproportionately burdened by STI.

INTRODUCTION

Health disparities in the United States (US) population have existed for decades. Of the nearly 500 objectives in the national Healthy People 2010 initiative, sexually transmitted infections (STI) were consistently among the top health disparities identified for non-Hispanic Blacks or African Americans, Hispanics, American Indian/Alaska Natives (Al/AN), and Asian Americans (1). These disparities persist today, particularly for Black and Hispanic Americans (2), and reflect the intersectionality of multiple systemic factors including social determinants of health and historical racial inequality in the US. Clinical laboratories play a critical role in public health efforts to curb rising trends in STI, and it is imperative that laboratory professionals be cognizant of current epidemiology in STI and the disparate impact of limited healthcare access on all groups. This mini-review summarizes the current state of racial/ethnic health disparities in STI in the US from the

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IMPACT STATEMENT

Diagnosis and reporting are necessary for the quantification and control of the burden of sexually transmitted infections (STI). Laboratory and public health professionals are indispensable to this effort and should be aware of contributors to disparities in STI quantitative measures. In this review, we discuss the major racial/ethnic disparities in STI within the United States and outline issues that undercut national laboratory funding and threaten operating capacity.

Laboratory Medicine perspective and focuses on the history and factors underlying disparities, epidemiology, issues with healthcare access and diagnostics, and policies affecting public health and laboratory capacity. For the purposes of this review, STIs are limited to the 3 most common bacterial infections: chlamydia, gonorrhea, and syphilis. The significant disparities for human immunodeficiency virus (HIV) infection are well-documented (3) and beyond the scope of this review.

BACKGROUND

For years, researchers have sought to understand the contributing factors to long-standing racial/ethnic disparities in many health outcomes, particularly STI (4). Medical anthropologists first described the idea of syndemics (synergistic epidemics) as a theory to conceptualize the observed relationship of violence, substance use, and HIV infection in urban Hispanic communities in the 1990s (5). Over time, this model has been adapted broadly across multiple disciplines and coalesces with our contemporary understanding of the complex interactions of many social determinants of health, which are in turn strongly associated with STI prevalence through specific epidemiologic contexts. Factors at both the community and individual level contribute to ongoing STI transmission and drive observed racial/ethnic disparities in STI in the US.

Social scientists note that the key motif underlying these factors is the history and persistence of segregation as the primary manifestation of structural racism and racial inequality in the US (6), a phenomenon with far-reaching implications within medicine and research. Perhaps the most appalling examples from the last century are the unethical syphilis natural history studies conducted by the US Public Health Service on Guatemalans during World War II (7) and on Black men in the South from 1932–1972 (8). These historical blemishes, in addition to experienced discrimination and differential delivery of care due to race/ethnicity or socioeconomic status, provider bias, and cultural insensitivity, are thought to contribute collectively to mistrust in the medical system that limits public health efforts to reduce STI (9–11).

Several social determinants of health are strongly associated with STI acquisition. Poverty rates, often considered a surrogate measure for socioeconomic health, are most pronounced in Black, Hispanic, and AI/AN subgroups in the US (12), and evidence suggests that areas with greater racial/ethnic disparity in income are also areas with higher STI rates (13). In a national survey of young adults, coexistent depression for Hispanic women and low educational attainment by heads of household for Black women were positively associated with STI (14). Additionally, access to healthcare systems has been decreased by programmatic budget cuts (2, 15) and is further limited by poor health insurance coverage within reproductive age populations (16).

Beyond these social factors, one's individual risk for STI acquisition is determined by the type of sex one has (anatomic sites exposed, condom use or not), the composition of one's sexual network, and the burden of STI in that network or community. For instance, the incidence of STI in Blacks has been consistently high over the last several years (2), resulting in a larger pool of prevalent STI in this subpopulation. Research suggests many Black men who have sex with men (MSM) and women exhibit racial homophily with partners (choosing sex partners of the same race/ethnicity) (17) and, compared to whites, are more likely to have sexual partners who themselves have 4 or more partners (18). Therefore, it is possible that a person's otherwise low individual risk for STI can be magnified by his or her interaction with potentially larger sexual networks of partners with higher risk—a pattern that has been observed directly in studies of Black individuals in the Southern US (19) and among mothers of infants with congenital syphilis (CS) (20).

EPIDEMIOLOGY OF RACIAL/ETHNIC DISPARITIES IN STIS

STI incidence has steadily increased in the US for 5 consecutive years (2). Disparities by race/ethnicity vary in magnitude but are apparent and marked for each STI. We review notable statistics below by condition.

Pelvic Inflammatory Disease

Surveillance data show that from 2014 to 2018 (2) office visits sharply increased for pelvic inflammatory disease (PID), a condition resulting from spread of STI to the upper female genital tract that has potential implications on fertility. National survey data from 2013 to 2014 indicate the estimated lifetime prevalence of PID for women with

a prior STI diagnosis was nearly equal. However, among women without a prior self-reported history of STI, PID lifetime prevalence varied by race/ ethnicity (Black: white ratio, \sim 2:1) (2), suggesting both a lack of early STI detection and treatment in Black women.

Chlamydia

With 1.8 million reported cases in 2018, chlamydia is the most prevalent notifiable STI with considerable disparities across racial/ethnic groups (Fig. 1). Reported cases of chlamydia per 100 000 among non-Hispanic Blacks are 5.6x the rate for whites (2), while rates for multiracial persons and Asians are less than the rate for whites (Fig. 1A). Between these extremes, rate ratios range from 1.9 (Hispanics) to 3.3 for Native Hawaiians/Other Pacific Islanders (NHOPI) and 3.7 for AI/AN. Sex-specific rate ratios were noticeably higher for women from AI/AN and NHOPI populations and Black men, but virtually identical for Hispanic and multiracial populations (Fig. 1). For women across racial groups, the incidence of chlamydia is higher than in men (Table 1) by nearly 2fold, likely reflecting differential screening of women, particularly those 24 years old and younger in accordance with the U.S. Preventive Services Task Force recommendations (2).

Gonorrhea

Gonorrhea is the second most common STI with over 580 000 cases reported in 2018. Race/ ethnicity disparities for gonorrhea (Fig. 1B) are similar to those for chlamydia, although of greater magnitude for Blacks (7.7 overall rate ratio) and Al/AN (4.6 overall rate ratio) (Table 1). Gonorrhea rates among NHOPI, particularly women in this group, are 2.6-fold higher than in whites (Table 1). In most racial groups, there is a modest predominance of male gonorrhea cases. Al/AN women are one notable exception, with a higher proportion of gonorrhea (Table 1). For Asians, rates of



States for 2018. Gray solid bars represent overall reported cases per 100 000, which includes cases where sex was not reported. Green solid bars represent cases in female patients, and blue checkered bars represent cases in males. Separate panels for chlamydia (A), gonorrhea (B), and primary and secondary syphilis (C). Data from Centers for Disease Control and Prevention, Sexually Transmitted Disease Surveillance Report, 2018.

gonorrhea are about half that of whites (Table 1) and there is a strong bias towards male cases (Table 1).

Syphilis

Syphilis is less common than gonorrhea and chlamydia with just over 35 000 cases in 2018, but cases continue to rise across demographics groups. The consequences of undiagnosed and untreated syphilis infections are significant-potential permanent sensory losses or stroke with neurosyphilis, and significant morbidity with congenital infection. Unlike either gonorrhea or chlamydia, the rate of syphilis in males is approximately 6-fold higher than in females overall and within race/ethnicity groups rates are 2x-10x higher in males compared to within-group women. Compared to whites (Fig. 1C), disparities are most pronounced in rate ratios for Blacks (5 for men and women), and AI/AN women (5.4), followed by NHOPI (approximately 2 for men and women), Hispanics (2.2 for men, 1.7 for women), and AI/AN males (2.1). Rates of syphilis in Asians overall and Asian males are similar to those for whites (rate ratios 0.8 and 0.9, respectively), and markedly lower for Asian women (Fig. 1C).

Congenital syphilis (CS) warrants special consideration given its potential for significant yet preventable maternal-fetal consequences. With 1306 CS cases reported in 2018, rates have risen 261% from 2013 to 2018 (2, 21), largely due to lack of prenatal care and inadequate maternal treatment despite a timely syphilis diagnosis (21). Rates of stillbirth ranged from 3.9%-7.5% and sequelae of CS were observed in 24.4%–44.7% of infants born to infected mothers (21). Conversely, firsttrimester laboratory screening and prompt treatment of maternal syphilis infection lead to much improved outcomes: in mothers who were treated, clinical signs of CS were observed in < 5%of neonates (21). CDC data from 2017 to 2018 demonstrate uneven rate increases and disease burden across racial/ethnic groups. There was a 500% increase among AI/AN, 275% increase among whites, 263% increase among Hispanics, and 127% increase among Blacks (2). Examining only the growth rates masks important differences

Table 1. Female-to-male rate ratio of chlamydia, gonorrhea, and syphilis by race/ethnicity in the United States, 2018.*							
	American Indians / Alaska Natives	Asian	Black	Hispanic	Native Hawaiian / Other Pacific Islander	White	Multi racial
Chlamydia	2.8	1.5	1.5	2.2	2.8	2	1.8
Gonorrhea	1.5	0.3	0.6	0.8	0.8	0.7	0.7
Syphilis Primary & Secondary	0.5	0.1	0.2	0.1	0.1	0.2	0.1
* Data from Centers for Disease Control and Prevention, Sexually Transmitted Disease Surveillance Report, 2018.							

in disease prevalence. For AI/AN, rates of infection per 100 000 are 5x-10x that of white controls, and for Blacks the estimated ratio is 6.4x-24x that for Whites. Thus, Black and AI/AN Americans bear the brunt of this disparity.

Geographic Differences

Racial, ethnic, and other population disparities in STI infection rates are not homogenous and the 2018 Sexually Transmitted Disease Surveillance Report from the CDC identified important differences across the US. For chlamydia, disparities in incidence compared to whites for NHOPI and Blacks are relatively similar across regions, while for Hispanics the difference is most pronounced in the Northeastern US at 2:1 and approaches 1:1 in the West. For AI/AN, differences are most pronounced in the Midwest and Western US. Similar trends were observed for gonorrhea and syphilis. The reasons for these geographic differences are likely multifactorial and may include regional differences in access to care or medical outreach. Wide variation in demographics of patients seen for STI testing across a national network of safety net clinics (22) suggests underlying differences in population structure may also contribute to geographic differences in racial disparities.

PRE-ANALYTICAL CHALLENGES

An essential component to eliminating disparities in STI is equitable access to sexual health services. STIs are diagnosed in a variety of healthcare settings. In the US, a significant proportion of all STI testing is performed at safety-net clinics, including public health, family planning, and STI specialty clinics that offer confidential, same-day services from expert providers at reduced or no cost, reaching many who otherwise would not have access to care for STI (22-24). Safety-net clinics primarily serve marginalized populations including racial/ethnic minority groups and the uninsured/underinsured (22). In a recent study of a CDC-supported collaborative network of safetynet STI clinics, 58.1% of patients who received care across the clinic network (range, 18.1%-89.6%) were non-Hispanic Black and 17.8% were Hispanic (range, 2.4%-36.1%) (22), similar to findings from other studies (24).

Given the importance of safety-net clinics for uninsured patients, expanded insurance coverage under the Affordable Care Act (ACA) raised important questions about the future of these clinics. Implementation of the ACA in 2010 decreased the uninsured rate from a baseline of 16% to 9.1% in 2015 through the expansion of the Medicaid program in many states and increased access to private insurance (25). Despite the ACA, studies have shown safety-net STI clinics continue to play a vital role, particularly for providing STI care and prevention services to marginalized populations (24, 26). Even in a state with a high proportion of residents with insurance (>95%) due to the ACA and Medicaid expansion, 40% of patients who sought care at a state STI clinic were uninsured and were more likely to be non-white compared to insured patients (26).

Despite the ACA's success increasing the number of Americans with health insurance, parallel cuts to public health funding threaten to disrupt the provision of essential STI services. Federal STI funding has not been increased since 2003, and in 2017 Congress cut STI funding by \$5 million (15). In 2012, the ACA's Prevention and Public Health Fund was cut by \$6.25 billion and per-capita public health funding fell by 9.3% between 2005 and 2015 and is expected to decline through 2023 (27, 28). In a survey of local health departments in the US, over 60% reported funding cuts for fiscal years 2011-2012. Budget cuts at local health departments had negative impacts on numerous services provided, including reductions in routine screening for STIs, staffing, clinic hours, and specialty STI clinic closures. Public health partner services, which are crucial for STI contact tracing, diagnostic testing, and treatment to disrupt transmission networks, were reduced (28-30). The CDC reported budget cuts in more than 50% of local and state health departments as one factor contributing to the increase in STIs (2, 31). Such cuts undermine efforts to achieve equitable access to STI services, as many clinics are forced to close or reduce testing and staffing, which in turn may lead to reductions in treatment and partner services.

In response to budget cuts, some clinics have implemented payment structures, including billing insurance for services provided or initiated, or increased fees or copays (28, 32, 33). Such fees reduce STI clinic utilization, either because patients with concerns about confidentiality may wish to avoid using their private health insurance and/or because lower income patients cannot afford the expense (26, 32–34). Although decreased utilization was similar across racial/ethnic groups within the patient population of one STI clinics' experience (32) the societal impact may nonetheless exacerbate such disparities, given that non-white groups constitute a higher proportion of uninsured patients in the post-ACA landscape (35). Interestingly, the ACA appears to have expanded insurance coverage for Asians such that uninsured rates are similar to Whites and lower than most other non-white groups (36). Higher rates of health insurance coverage could contribute to lower rates of STIs observed for Asians.

Changes to Title X, the only federal grant program that provides comprehensive family planning and preventative health care, further reduced equitable access to STI services. Title X grants support over 4000 clinics and include state and local health departments as well as nonprofit family planning and community health centers. In 2017, over 6 million STI screening services were provided by Title X programs (37). Title X programs prioritize care for low income individuals and serve a large proportion of racial/ethnic minorities. Nearly a third of patients who receive services at from Title X providers identified as Hispanic or Latinx, and nearly a quarter as Black or African American (38). In 2019, the White House finalized new rules that prevent Title X awardees from providing abortion services. This rule resulted in 25% of Title X sites withdrawing (39), reducing availability of STI care services to many low income and racial/ethnic minorities.

UNIQUE IMPACT OF COVID-19

While racial/ethnic health disparities in STIs have existed for years, the emergence of the SARS-CoV-2 pandemic has once again highlighted the significance of these disparities. COVID-19 has disproportionately affected non-white, historically marginalized communities in the US, ranging from African Americans (40) to Native Americans (41). Moreover, the COVID-19 pandemic continues to threaten access to sexual health services, including follow-up care such as expedited partner tracing (42, 43), and thus may further exacerbate existing racial/ethnic health disparities. A recent

survey of sexual health providers indicated that only 18% of respondents could offer STI testing to asymptomatic patients, 80% were treating patients without diagnostic testing, and only 25% of respondents could maintain HIV testing (42). Recommendations for providing STI clinical care during the COVID-19 pandemic include deferring asymptomatic patient screening visits, resorting to syndromic management using phone-based interviews, and treating with oral instead of intramuscular antibiotics (43).

COVID-19 continues to place extraordinary stress on clinical and public health laboratories that still contend with significant supply chain limitations. Many of the high-throughput instruments used routinely to diagnose STIs are also in demand for detection of SARS-CoV-2 (44). Such competition for different assays run on the same platform could also contribute to disparities in testing availability for certain race/ethnicity groups. Additionally, increased workloads and staff furloughs contribute to burnout and are likely to further strain laboratory capacity.

ANALYTICAL CONSIDERATIONS

Fortunately, analytical platforms used in STI diagnostic testing are agnostic to specimen metadata, including race/ethnicity, country of origin, sexual orientation, and gender identity. Therefore, disparities at the analytical stage primarily reflect specimen throughput, turnaround time, and cost per reaction. Most diagnostic testing for gonococcus and chlamydia are FDA-cleared nucleic acid amplification tests (NAAT) that have high sensitivity and specificity (45). These assays can be performed with high throughput on platforms by Abbott, Hologic, Cepheid, and Roche (45). Many NAAT platforms currently in use have received FDA approval for patient-collected specimens: urine in asymptomatic men, and vulvovaginal swabs for both asymptomatic and symptomatic

women (46). Patient-collected specimens are at least as sensitive and specific as providercollected specimens and may increase casefinding for gonorrhea and chlamydia (47, 48) Self-collection may also increase uptake of STI testing (47, 48). In May 2019, the FDA cleared two assays, the Hologic, Inc. Aptima Combo 2 assay, and Cepheid Xpert CT/NG, for diagnostic testing of throat and rectal samples for gonococcus and chlamydia. As the availability of testing of extragenital samples may further increase uptake of STI testing, clinical laboratories should validate these new specimen types for diagnostic testing (49). While the performance of multiplex STI PCR panels have been evaluated, to our knowledge, none of these panels are currently FDA-cleared (50 - 52).

Syphilis is primarily diagnosed through serologic assays, either using a traditional or reverse sequence algorithm (53). While the CDC offers an organism-specific PCR for *Treponema pallidum*, the etiologic agent of syphilis, we are not aware of T. pallidum-specific NAATs performed in Clinical Laboratory Improvement Amendments-approved laboratories. Although systematic data describing direct detection of T. pallidum from patient specimens is sparse, this approach may be useful as an adjunct for neurosyphilis diagnosis (54). Several target loci may prove viable for clinical assays with reported sensitivities of 70%-75% and specificities of 87%-above 90% (54). We are not aware of systematic data describing the utility or performance of broad-range 16S rDNA PCR for detection of T. pallidum, only scant case reports and anecdotes.

POST-ANALYTICAL CHALLENGES

Timely reporting of laboratory results and timely treatment are important drivers in reducing sequelae and disrupting transmission. The CDC recommends treatment not be delayed while

waiting for diagnostic test results. Empiric, same day treatment may decrease complications (e.g., pelvic inflammatory disease) due to delayed care or loss to follow-up and reduce transmission (23).

Public health partner services are crucial for identifying and treating undiagnosed infections, preventing reinfection, and for STI prevention through the disruption of transmission networks. Partners might be notified by their sex partners and/or through public health disease intervention specialists. Patients may receive treatment for their partner at the same visit through expedited partner therapy (EPT) programs. EPT is not legal in all states, and many states do not allow billing of the patient's insurance for their partner's treatment, creating a financial barrier to care than may adversely affect marginalized groups (39). In addition, budget cuts or reassignment of public health staff for other public health responses, such as the ongoing SARS-CoV-2 pandemic, can negatively impact patient follow-up and partner services (28-30, 42, 43).

CONCLUDING REMARKS

This review has summarized key disparities in the burden of STIs among racial and ethnic groups in the US. In addition to rising incidence of chlamydia, gonorrhea, and syphilis, particularly congenital syphilis across all demographic groups, a notable trend is higher incidence of these diseases in marginalized groups, particularly Blacks, AI/AN, and NHOPI (Table 1). These STI disparities are but one example of pervasive, unequal burden of disease in the US.

The alarming trends of rising STI incidence and persistent health disparities, coupled with limited funding for public health and safety-net clinics, cannot be solved by laboratories alone but require data-driven public policy solutions. Laboratory testing data are therefore critical to inform and monitor the success of public health responses to STIs. Public policy in turn influences the availability of STI epidemiologic data, particularly through policies that support access to health care and robustly fund public health laboratories. Clinical and public health laboratories can thus play a role in reducing these important disparities. For this to occur, public health systems for STI detection and treatment require robust, stable funding, continued collaboration with clinical laboratories, and must remain key stakeholders in developing creative solutions that expand access to care.

No matter the efforts or good intentions of laboratorians, STI disparities cannot be reduced without addressing root causes, including racism and discrimination, distrust of healthcare systems, and socioeconomic factors. Laboratory professionals might partner with clinicians and policy experts to ensure innovative solutions fit into or enhance existing STI testing infrastructure as part of these efforts. Since lowering barriers to both clinical care and high-quality diagnostic testing may help reduce disparities, validating self-collected samples is one concrete step that laboratories can take in partnership with clinicians and STI clinics. Lasting solutions will require painstaking longitudinal work that could be durable and beneficial for health systems at large.

Nonstandard Abbreviations: STI, sexually transmitted infections; US, United States; AI/AN, American Indian/Alaska Natives; HIV, human immunodeficiency virus (HIV); MSM, men who have sex with men; PID, pelvic inflammatory disease; CS, congenital syphilis; NHOPI, Native Hawaiians/Other Pacific Islanders; ACA, Affordable Care Act; NAAT, nucleic acid amplification test; AST, antibiotic susceptibility testing.

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