

Four Decades of Epidemiologic Science on HIV Infection and Disease, and Its Impact on Public Health Practice and Policy for Sexual and Gender Minority Persons

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Abstract

Even at the cusp of the second decade of the new millennia, HIV continues to be a significant public health challenge for sexual and gender minorities (SGM). Men who have sex with men and transgender women, in particular, continue to report higher rates of HIV incidence compared to their heterosexual counterparts, while facing significant barriers to comprehensive sexual healthcare. In Delaware, HIV infection impacts a substantial number of individuals with approximately 14.5 incident cases per 100,000. This ranks Delaware as the 14th highest for HIV incidence among U.S. states. However, the largest healthcare provider in Delaware, Christiana Care Health System, has created many health initiatives to support the health needs of SGM and those living with HIV. The current sustained rate of HIV infection indicates the need for enhanced epidemiologic work to identify HIV cases in subgroups of diverse sexuality and gender identity, collaboration within and across research institution and community organizations, as well as engagement in creative solutions that target the multiple levels of factors contributing to HIV incidence. In addition, it is imperative that local agencies and health organizations continue to support these communities of SGM individuals during the current sociopolitical climate of the national U.S. government.

Introduction

Disparities of HIV infection within and across populations in the United States have been evident since the earliest days of the HIV epidemic. Sociodemographic determinants of infection, including age, gender, race, ethnicity, and exposure to poverty, as well as sexuality, injection drug use and commercial sex work and other proxies for individual risk factors have modulated the risk of HIV infection, morbidity, and mortality.¹⁻⁵ Additionally, disclosure of HIV risk, and willingness to access HIV testing and counseling, and treatment and/or clinical care have been impacted by sociopolitical conservative ideologies that have stigmatized and marginalized sexual and gender minorities (SGM) and other high-risk populations, including persons who inject drugs (PWID). These high-risk populations continue to be at greatest risk for infection due to individual-level (e.g., condomless anal intercourse or sharing of syringes and other injecting paraphernalia) and population-level (e.g., limited access to prevention services and structural stigma related to same-sex orientation or injection drug use) risks.¹⁻⁴

Since the early 1980s, epidemiologic research has informed our understanding of HIV prevention strategies and treatment. Epidemiologists have been pivotal in the development of surveillance systems that have tracked HIV infection in high-risk subpopulations,⁶ established national standards for HIV diagnosis, treatment, and prevention,⁷ visualized geographic distributions of infection using various mapping techniques,⁸ and employed molecular epidemiologic techniques to elucidate HIV transmission in sexual networks.⁹ All of these

approaches strategically inform the use of limited HIV prevention resources. Finally, demonstration of the efficacy of antiretroviral treatment as prevention, and more recently, pre-exposure antiretroviral prophylaxis has emerged a critical tool for HIV prevention.^{10,11}

In the present commentary, not only do we discuss how epidemiology as a scientific discipline has informed public health practices and policies targeting SGM, but we suggest potential epidemiologic approaches to address unmet prevention challenges that could reduce the HIV infection disparities among highly stigmatized and marginalized communities.

Epidemiology of HIV in the United States with a focus on Delaware

Initial Description of First Case Series of Community-Acquired Immune Suppression

HIV was first recognized in the United States during the early 1980s when five cases of *Pneumocystis carinii* pneumonia¹² were reported to the Center for Disease Control and Prevention (CDC). The initial report raised concerns because all five cases were previously healthy, gay men in Los Angeles that developed a rare opportunistic infection. Shortly after the initial report, additional cases of an unknown disease occurring in gay men from New York described the development of Kaposi sarcoma as well as *Pneumocystis pneumonia*.¹³ Researchers had posited the potential pathology and one of the earliest case series documented reductions of T-4 cells and suggested potential cell mediated immune dysfunction as a mechanism.¹⁴ In addition to early recognition the pathogenesis, investigators hypothesized that HIV transmission may have been related to the “homosexual lifestyle.”¹³ This potentially stigmatizing inference that these opportunistic infections were due to “homosexual lifestyle”, leading to the initial labeling of Gay-Related Immune Deficiency (GRID) to designate HIV-associated immune dysfunction, has remained prevalent in social discourse—even as we are on the cusp of the second decade of the new millennium. Not surprisingly, researchers have reported many adverse consequences due to HIV-related stigma, including lower access to and engagement in antiretroviral therapy.^{15,16}

Recent Estimates of HIV Infection Prevalence

Since the initial case findings, there are approximately 1.1 million people (ages 13 or older) living with HIV in the United States, including an estimated amount of 162,549 (14%) people that were unaware of their infection in 2015.^{17,18} The prevalence of those living with HIV has substantially increased due to increased surveillance of new infections, as well as the development of highly active antiretroviral therapy (HAART). Although the magnitude of the United States epidemic is less severe than other regions of the world such as Sub-Saharan Africa, there remains subpopulations of individuals that are disproportionately affected by HIV infection. These critical health disparities have been well documented in previous studies: Black and Latino individuals comprise only 13% and 17% of the United States population,¹⁹ yet account for 44% and 26% of persons living with HIV, respectively.¹⁷ Similarly, gay, bisexual, and men who have sex with men (MSM) represent a very small percentage of the population (~2%), yet continue to be the most affected group, representing approximately 56% of prevalent HIV cases.^{17,20} In 2016, the CDC estimated that one in two black MSM and one in four Latino MSM will be diagnosed with HIV over their lifetime.²¹

In Delaware, surveillance data demonstrates a similar trend to the United States. The estimated number of people living with HIV in 2015 was 3,449 (365 per 100,000 population), with black

individuals accounting for 60% (n = 2,075) of those with HIV.²² Racial disparities in HIV infection also persist in Delaware as the prevalence of black men and women living with HIV are approximately 1.5 times and 3 times the rates observed for white men and women in 2015, respectively.²² As is observed nationally, MSM remain one of the groups most impacted by HIV: of total HIV infections, 33% were as attributed to MSM high-risk behavior despite comprising about 1% (n = 13,049) of the population in Delaware (prevalence: 14.7%).^{20,22} Moreover, black MSM accounted for the largest proportion of those with HIV infection from 2011 to 2014. Since 2015, surveillance data suggest among HIV infections attributable to MSM, 46% were among white and 42% were among black men.²²

New Infections: Incidence

HIV incidence estimates are critical as they provide insights concerning HIV transmission trends from which public health professionals can appropriately target prevention efforts and resources. Through the CDC's HIV Surveillance system, 2016 HIV incidence was estimated to be as approximately 40,000 new infections annually in the United States.^{17,18} Populations with the highest proportion of incident cases included adolescents 13–24 (n = 8,593; 22%) and young adults 25–35 (n = 13,592; 34%) years of age, black adults or adolescents (n = 17,269; 43%), and MSM (n = 26,844; 67%). The highest number of new infections among MSM was observed among young Black MSM 13–24 years old (n = 3,994; 15%).¹⁷ Among states, Delaware was ranked 14th highest for HIV incidence with a rate of 14.5 per 100,000.¹⁷ Accordingly, the lifetime risk for HIV diagnosis among an individual living in Delaware was estimated to be 1 in 96.²¹ Epidemiologic data also suggest that female sex workers and incarcerated individuals have a heightened risk for HIV; factors associated with increased infection among these risk groups may include alcohol and drug use, lower healthcare access, stigma, and poverty.^{23,24} One of the most critical challenges in providing resources for these groups is the denigration of sex work and incarceration, which potentially limits population-based studies to estimate counts of HIV among sex workers and those in the criminal justice system.^{23,24} Without sufficient data, it is difficult to ascertain the burden of HIV and factors associated with infection as well as develop tailored programs for HIV prevention.

While HIV incidence continues to increase in virtually all of these high-risk populations, new infections among persons who inject drugs have declined in recent years, most likely due to the implementation of harm reduction and syringe exchange programs.¹⁷ Despite this, high numbers of new HIV infections have unfortunately remained stable without evidence of decrease, highlighting the need for enhanced epidemiologic works to understand potential causes of sustained infection (including the characteristics and impact of HIV transmission networks)—all of which can guide the development of strategies to interrupt potential new infections.

Transmission Routes

Routes of HIV transmission include condomless intercourse, injection drug use, blood transfusion, and mother-to-child transmission during pregnancy, birth, or post-partum breastfeeding. In the United States, HIV transmission due to condomless anal intercourse is the primary mode of infection,²⁵ with risk of HIV infection highest for those engaging in receptive anal intercourse due to microtears in rectal epithelium that can facilitate transmission.²⁶ Compared to earlier stages of the epidemic, blood transfusion is longer a substantial risk factor for HIV due to rigorous testing of the blood supply in the United States.²⁵ In addition,

surveillance data indicate that perinatal acquired infections have decreased annually in the United States, with approximately 100 new HIV infections in 2016¹⁷ despite challenges in data collection for vertical transmission.^{27,28} However, evidence suggests that avoidance of breastfeeding and elective cesarean section among HIV positive women may be effective in reducing the risk of vertical transmission, with recommendations suggesting complete avoidance of breastfeeding even if the HIV infected mother is adherent to antiretrovirals.^{29,30}

HIV-Related Morbidity and Mortality

The advent of HAART has greatly improved the survival among persons living with HIV. Current estimates suggest that expected life expectancy for a 20-year-old HIV-infected individual receiving antiretrovirals is approximately 70 years.³¹ With current guidelines recommending antiretrovirals for all HIV-infected persons regardless of CD4 count,³² chronic diseases will most likely become a growing concern as more patients are engaged in care and consequently living longer. In addition, other bio-medical innovations such as treatment as prevention (TasP: taking antiretrovirals to reduce HIV viral load to an undetectable level) and pre-exposure prophylaxis (PrEP, i.e., taking antiretrovirals to prevent HIV infection) will likely beneficially impact HIV transmission. However, prevention of infection by PrEP use may be reduced by increased rates of high-risk behaviors (risk-compensatory behaviors) resulting from perceived lower risk for infection due to pre-exposure prophylaxis.³³ Additionally, questions remain concerning the long-term side effects of pre-exposure prophylaxis, including bone fragility, kidney disease, and gastrointestinal disorders.³⁴

HIV Infection Among Sexual and Gender Minorities

Defining Sexual and Gender Minority Populations

It is important to understand that sexual orientation and gender identity are distinctive entities: sexual orientation denotes to whom a person feels romantic or sexual attraction towards^{35,36} whereas gender identity is a person's innermost sense of self, which may not correspond to that their assigned sex at birth.³⁷ The term "sexual minorities" typically refers to individuals who identify as gay, lesbian, bisexual, or any other non-heterosexual orientation, whereas the term "gender minorities" refers to individuals who have gender identities that are not associated with their birth sex. Increasingly, there is recognition that self-identification of gender can be non-binary, with some individuals experiencing a gender identity that is outside the categories of man or woman.³⁸ Taken together, sexual and gender minorities may include lesbian, gay, bisexual, queer, transgender, gender non-binary or non-conforming, gender fluid, intersex, and asexual individuals. However, HIV transmission does not occur as a result of one's sexual orientation; rather, risk is conferred by sexual behaviors that facilitates infection. For the purpose of our commentary, we will focus on homosexually-active men and male-to-female transgender persons, since these individuals are more likely to engage in higher-risk sexual behaviors.

Men Who Have Sex with Men and Transgender Women Face Unique Challenges and Barriers to Medical/HIV treatment

MSM and transgender women (TGW) traditionally have faced significant barriers to health care, resulting in decreased access and utilization of services, and particularly preventative care services that may have downstream effects on HIV infection.^{39,40} One method of conceptualizing this cascade is through the HIV care continuum—a model for measuring HIV care engagement,

including screening and diagnosis, linkage to care, retention in care, prescription of antiretrovirals, and viral suppression (Figure 1).⁴¹ Overall, estimates suggest a high proportion of those HIV infected are diagnosed, however, only 50% of those diagnosed are retained in care.⁴¹ Of those initially diagnosed, younger individuals, women, as well as racial/ethnic minorities tend to have lower HIV care engagement.⁴² In addition, HIV infected individuals that are unaware of their infection status represent a great challenge to slowing the epidemic as the risk of transmission is greatest among untreated individuals who may have higher viral loads. Since MSM and TGW have the highest prevalence and risk for HIV among all risk groups, identifying gaps in their HIV care continuum is vital for resource allocation and targeted intervention strategies.

Figure 1. HIV care continuum in the United States. Abbreviation: ART, antiretroviral therapy



Lack of health insurance has been a major barrier for HIV care engagement among MSM and TGW, particularly those infected with HIV. One major resource for providing HIV care among low-income or uninsured persons living with HIV is the Ryan White HIV/AIDS program, which allocates funding to state and local governments, as well as community-based organizations to deliver essential primary care and HIV treatment. Moreover, the enactment of the Affordable Care Act and expansion of marriage rights have served to expand health care insurance coverage; many MSM and TGW now qualify for coverage through employers or spousal insurance policies, Medicaid, Medicare, or the Office of Veterans Affairs.⁴³ Despite these recent healthcare access advances, MSM and TGW continue to report more cost-related barriers to care and unmet needs than heterosexual peers^{40,44} in particular, transgender individuals have specific challenges in accessing appropriate healthcare for sexual health and gender reassignment. In 2016, attempts to expand Medicare and Medicaid coverage to include gender transition-related costs were met with opposition, and current regulations concerning transition-related care and issues are deferred to states' discretion.⁴⁵ In Delaware, costs related to gender transition are not covered under Medicare or Medicaid; however, private insurance are prohibited from discriminating against transgender individuals.⁴⁵

Beyond insurance obstacles, MSM and TGW often struggle with finding medical providers who have training and experience working with SGM populations and often face discrimination from health care providers.^{40,46,47} In Delaware, numerous healthcare and community-based organizations have made concerted efforts to provide culturally competent healthcare for MSM and TGW. For example, the largest healthcare provider in Delaware, Christiana Care Health System, has established comprehensive health initiatives specifically for MSM and TGW as well as those living with HIV.⁴⁸ As gender identity is increasingly understood to exist along a spectrum, with some individuals not identifying exclusively as man or women—the lack of data about non-binary gender minorities presents another obstacle to evidence-based care.⁴⁹ Creating an inclusive, culturally responsive, and welcoming clinical environment is an important first step in providing optimal clinical care services for MSM and TGW and for reducing HIV acquisition and transmission risk within these communities. This process can involve training in cultural

awareness and diversity, along with educating clinical staff about the unique health needs of SGM populations. A prime example of culturally responsive care is Christiana Care’s provider referral listing for MSM and TGW, which includes both primary care providers and specialists that are trained to handle healthcare issues related to same-sex and transgender health.⁴⁸

How Does Epidemiology Address the HIV Epidemic among MSM and TGW

The epidemiology of HIV among MSM and TGW in the United States has evolved over the past four decades. Assessments of infection patterns traditionally relied on HIV surveillance data to document the burden of the epidemic. The United States National HIV Surveillance system has characterized the epidemic since the initial cases in 1981.^{12,13} Initially used to count and describe cases of HIV/AIDS, the surveillance system has grown as the evidence and our understanding of the disease unfolded. In addition, syndromic surveillance (i.e., methods that rely on patterns of behavior and symptoms to detect HIV infection prior to a confirmed diagnosis) played a critical role in capturing information about “hidden populations” such as MSM and TGW who are at a greater risk for infection. For example, the National HIV Behavioral Surveillance system collects data of individuals who were marginalized and had the highest HIV incidence (e.g., MSM and PWID).⁵⁰ These surveillance systems allowed for the identification of high-risk groups, which can inform targeted interventions and resource allocation. As persons infected with HIV began to live longer due to earlier diagnoses and linkage to antiretroviral therapy, these national surveillance programs have evolved to capture a more complete spectrum of HIV-related exposures and outcomes; including behavioral, molecular (e.g., genetic data that is used to monitor HIV trends and drug resistance), and HIV-related morbidity data.⁵¹

Other traditional epidemiologic methods such as case-control and longitudinal cohort studies have been useful in understanding the underlying behavioral mechanism of HIV transmission among MSM and TGW. Thus, our understanding of HIV infection traditionally revolves around behavioral risk factors such as condomless anal intercourse.^{52,53} However, there is a growing body of evidence examining how sexual networks and the social determinants of health impact HIV infection among MSM and TGW.⁵⁴⁻⁵⁷ For example, TGW face higher levels of social marginalization, resulting from the underlying transphobia, which contribute to their vulnerability for infection. Stigma related to sexuality has also been reported to lower healthcare access, increased levels physical and sexual trauma, as well as higher rates of other sexually transmitted infections (i.e., chlamydia, gonorrhea, and syphilis).^{15,39,58,59} Therefore, engaging in rigorous epidemiologic methods allows a thorough assessment of the potential gaps in healthcare and HIV prevention services for MSM and TGW and determine appropriate points in the HIV continuum to intervene.

Unmet Needs and Challenges Related to the Current Epidemic

Recent work has pointed the major gaps in the response to the epidemic in relation to sexual diversity⁶⁰; however, translation of such work into programming have been slow. In addition, various key methodological issues remain a major concern for association studies.^{60,61} We, therefore, highlight current challenges in studies assessing HIV risk among SGM and future directions in which epidemiologic methods can be used to address these issues.

One of the major methodological challenges relates to the changing context and needs of SGM individuals such as accurately capturing the diversity of gender identity and sexual orientation among SGM across cultures and lifespan.⁶⁰ Current studies rely on data collection instruments

that may have inappropriate use of language or reporting intervals for capturing low- and high-risk behaviors. In various subpopulations of racial, ethnic, and religious SGM, sexual activity among men is not commonly discussed and referred to indirectly.⁶⁰ The term “sex” may be reserved to describe activities that potentially lead to reproduction, and “sex with other men” may not elicit responses that include sex with transgender individuals.⁶⁰ This could lead to misclassification of the exposure and potentially bias HIV risk estimates. Current analytical techniques such as sensitivity analysis or Bayesian analysis are quite robust in assessing and adjusting for such biases; however, such methods remain underutilized in studies estimating HIV risk among MSM and other SGM populations.⁶¹ In addition, bias in sampling is often a problem because samples are often small and derived using non-probability sampling methods.⁶² SGM samples are rarely ever representative of the population and more prone to selection bias.^{62–64} Incorporating various advancements in epidemiologic techniques for sampling hard-to-reach populations will be vital to produce accurate HIV risk estimates and determine mechanisms in which prevention strategies can intervene.^{65,66}

There are also several limitations with the use of surveillance data when assessing the magnitude of the HIV epidemic, particularly for SGM who are racial/ethnic minorities. Individuals captured through surveillance only include those that have been diagnosed and reported to a surveillance system. For example, CDC estimates that NHSS data are representative of 80% of all HIV cases in the United States.⁶⁷ Establishing cohorts that follow high risk groups such as young, Black MSM may allow researchers to better characterize risk behaviors, social and sexual networks, as well as allow for more rapid diagnosis of incident infections and thus preventing ongoing transmission.⁶⁸

Overall, there is a need to develop data collection instruments with increased sensitivity and specificity. One potential avenue is for national surveys to use language that can accurately assess sexual orientation and behaviors, as well as be familiar and inclusive of transgender individuals. In addition, better strategies to engage hard-to-reach SGM such as those geographically isolated, non-gay identified men, and racial/ethnic minorities are needed to enumerate HIV cases as well as provide targeted and appropriate interventions. Part of this work will require the development of methods in the context of the prison system as well as clients and sex partners of sex workers. Therefore, epidemiologic methods are crucial in accurately informing responses to the HIV epidemic.

Conclusion

In conclusion, an epidemiologic perspective on public health practice and policy can be effective for identifying gaps in HIV medical care and social services among SGM. In addition to determining prevalence and factors associated to disease end-points, epidemiologic methods can be used to determine components associated with intermediate outcomes, for example medical care retention in the HIV care continuum. Results from these assessments can be used to direct future directions for research and inform intervention strategies and policies. However, entities engaging in HIV research and practice often take place in their respective silos. Without collaboration across disciplines, HIV control and prevention for SGM will not be feasible. From an epidemiologic viewpoint, there is a need for providers and policy makers to: 1) improve their understanding of the factors that contribute to HIV infection among sexually and racially diverse communities, 2) recognize the existence of non-binary individuals and provide culturally sensitive and tailored healthcare, 3) collaborate across disciplines and organizations to improve

delivery of medical services, and 4) engage in creative solutions that tackles the multiple levels of factors (individual, interpersonal, and structural) that influence HIV transmission and retention in HIV care. In Delaware, various healthcare and community-based organization have begun their efforts to improve medical and prevention services for SGM, such as Christiana Care's SGM health initiatives. Maintenance of prevention strategies will require capable leadership and long-term investment from key stakeholders throughout Delaware to ensure the health equity of individuals that long been marginalized.

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